Summary Assessment of Veterinary Feed Directive Compliance Activities Conducted in Fiscal Years 2016 – 2018

Background

In January 2017, the U.S. Food and Drug Administration's (FDA) Center for Veterinary Medicine (CVM) and animal drug manufacturers completed the voluntary transition of all medically important antimicrobial drugs used in or on animal feed from over-the-counter (OTC) to Veterinary Feed Directive (VFD) marketing status, under the Guidance for Industry (GFI) #213 process.[1] All VFD drugs, including combination VFD drugs, require an authorization with a VFD from a licensed veterinarian prior to animals receiving the medicated VFD feed. These drugs include approved uses in all major food-producing animal species (e.g., cattle, swine), and a number of minor species (e.g., sheep, fish).

Education

FDA employed a phased-in compliance strategy for the VFD final rule and GFI #213 implementation efforts.[2,3] Under this strategy, FDA's initial focus has been to educate affected stakeholders (e.g., producers, veterinarians, feed mills, and retail establishments) on these new requirements before taking enforcement action. FDA has responded to various individual questions and challenges as they arose as part of this initial education phase.

In preparation for the VFD final rule, implementation of GFI #213, and throughout the phased-in compliance strategy executed in fiscal years 2016 – 2018, FDA collected stakeholder feedback from veterinarians and various segments of the animal agriculture industry. In that three-year period, CVM participated in more than 200 stakeholder meetings and webinars to provide education and training around its antimicrobial resistance strategy, including the VFD final rule. Several areas for additional stakeholder education emerged during those engagements. To address these, CVM prepared discrete stakeholder resources including the following:

- Draft Guidance for Industry (GFI) #120: Veterinary Feed Directive Regulation Questions and Answers, which contains comprehensive information about the VFD process, including information about the requirements for authorizing, manufacturing, distributing, and using VFD drugs in animal feed. In March 2019, CVM updated Draft GFI #120 to address a wider range of practical implementation issues. This includes revisions to 14 previous responses and the addition of 53 new questions and answers.

[1] FDA, Guidance for Industry #213: New Animal Drugs and New Animal Drug Combination Products Administered in or on Medicated Feed or Drinking Water of Food-Producing Animals: Recommendations for Drug Sponsors for Voluntarily Aligning Product Use Conditions with GFI #209, https://www.fda.gov/regulatory-information/search-fda-guidance-documents/cvm-gfi-213-new-animal-drugs-and-new-animal-drug-combination-products-administered-or-medicated-feed.

[2] FDA, Final Rule: Veterinary Feed Directive, https://www.federalregister.gov/documents/2015/06/03/2015-13393/veterinary-feed-directive.

[3] FDA's Strategy on Antimicrobial Resistance - Questions and Answers, https://www.fda.gov/regulatory-information/search-fda-guidance-documents/fdas-strategy-antimicrobial-resistance-questions-and-answers.

- GFI #233: Veterinary Feed Directive Common Format Questions and Answers, which provides examples illustrating how a common format for a VFD order might appear and how the animal drug sponsor may pre-populate certain information on the VFD. The issuing veterinarian can subsequently complete a pre-populated VFD with the additional relevant information for a particular client.

- Various other educational resources (e.g., VFD brochures in English and Spanish, videos, and presentations) regarding the requirements for affected stakeholders on the Veterinary Feed Directive website and two additional CVM Updates providing information for specific stakeholders in response to commonly asked questions:
    - FDA Clarifies Approved Free-Choice Feeding Options for Anaplasmosis Control in Cattle
    - FDA Provides Information on the Use of Medically Important Antimicrobials in Bees

Assessing Compliance with the VFD Final Rule

Along with publishing the VFD final rule in June 2015, CVM developed a framework for inspections of distributors, veterinarians, and producers involved in the VFD process. Inspection activities are carried out by FDA's Office of Regulatory Affairs (ORA) and under contract by participating state feed regulatory programs.

During fiscal years 2016 and 2017, inspections focused primarily on providing education to producers, veterinarians, and VFD medicated feed distributors (e.g., feed mills and retailers of VFD medicated feed) as part of the phased-in compliance strategy. In fiscal year 2018, FDA transitioned toward an inspectional approach focused on compliance with the VFD requirements and documenting violations when found.

These inspections and their findings have been valuable and have allowed FDA to respond to additional stakeholder questions about VFD implementation, gain understanding of industry practices related to the VFD final rule, and shape a broader inspection strategy to ensure ongoing compliance with the VFD regulation.

Inspection activities carried out by ORA and participating state feed regulatory programs from fiscal years 2016 – 2018 included the following:

VFD Inspections

- In fiscal year 2016, FDA began a small "pilot" inspection program. This pilot consisted of three-part inspections conducted by FDA. For the first part, investigators started at the VFD distributor, discussed compliance with the regulations, then reviewed randomly selected VFDs for compliance with the requirements. To complete the other two parts of the inspection, the investigator selected one VFD at the distributor and then conducted further inspections of the veterinarian and producer (client) named on that VFD.

- In fiscal years 2017 and 2018, FDA continued to perform three-part inspections and expanded the inspection program to include state feed regulatory partners. In fiscal year 2017, state personnel inspected VFD distributors only and reviewed selected VFDs for compliance with the requirements. Beginning in fiscal year 2018, participating state feed regulatory programs began conducting three-part inspections, similar to those conducted by the FDA investigators as described above.

Other Medicated Feed Mill Inspections

FDA is expanding review of VFD medicated feed and VFD-related records in routine Current Good Manufacturing Practice (CGMP) inspections of medicated feed mills,[4] as appropriate and applicable.

Drug Residue Investigations

In calendar year 2018, FDA also began planning to incorporate VFD inspections into the Drug Residue Investigation Program. The goal of integrating these programs is to expand FDA's understanding of on-farm use of VFD medicated feeds and veterinarians' and clients' adherence to the VFD requirements. FDA investigators are conducting a small number of VFD inspections as part of drug residue inspections in fiscal year 2019.

Summary of VFD Inspections Conducted in Fiscal Years 2016 – 2018

VFD inspections are summarized in Table 1 based on final inspection classification codes. Inspections without significant deficiencies were classified as "NAI – no action indicated." Inspections with significant observations that may be deviations from the VFD requirements were classified as "VAI – voluntary action indicated," or "OAI – official action indicated," depending on the impact of the deviation on public health (human and animal health) and/or the facility's voluntary corrective action. Approximately 91% of the VFD final inspection classification codes for fiscal years 2016 – 2018 were classified as NAI.

Table 1: VFD Final Inspection Classification Summary

District Decision	Fiscal Year 2016	Fiscal Year 2017	Fiscal Year 2018	Total
No Action Indicated (NAI)	54	130	230	**414**
Voluntary Action Indicated (VAI)	3	0	38	**41**
Official Action Indicated (OAI)	0	0	1+	**1**
Total	57	130	269	**456**

\+ Refer to the *Enforcement Strategy* below for details on enforcement action taken

The detailed summary of VFD inspections provided in Table 2 through Table 10 is for a subset of VFD inspection summary findings.

[4] Additional information on medicated feed mill licensing is available at https://www.fda.gov/animal-veterinary/animal-food-feeds/medicated-feeds.

Table 2: VFD Inspections by FDA Investigators and State Feed Regulatory Programs[1]

Type of Firm[2]	Fiscal Year 2016 (Prior to GFI #213 Implementation)	Fiscal Year 2017	Fiscal Year 2018
VFD Distributor[3]	25	50	278
Producer (Client)	13	28	21
Veterinarian	19	33	14
Facility serving multiple roles[4]	2	4	5
Total Number of VFD Inspections	59	115	318

1. This summary table is based on VFD inspection findings available for review at the time of this report. As a subset of the overall VFD inspections for fiscal years 2016 – 2018, the inspection totals by firm type in Table 2 are not equivalent to the inspection classification totals in Table 1.
2. Some facilities were given a firm-type of "Other" by the FDA investigator or state inspector at the time of the inspection but were later reclassified by CVM during our detailed review to facilitate counting.
3. Includes distributors who manufacture VFD feed (e.g., feed mills) and those who do not manufacture VFD feed (e.g., retailers).
4. Some facilities fulfilled more than one role. For example, some veterinarians were also the VFD distributor. Therefore, the total number of inspections for a single stakeholder type may also include a facility that serves more than one VFD stakeholder role.

Summary of VFD Inspection Feedback and Findings

FDA investigators and state inspectors who conducted VFD inspections of producers, veterinarians, and VFD distributors were asked to provide details of their findings to CVM with respect to the requirements of the VFD final rule. Based on the initial VFD inspections conducted during fiscal years 2016 – 2018, feedback has shown that affected parties are generally aware of and in compliance with the VFD final rule. Additionally, early feedback from stakeholders highlighted areas where education was needed to comply with the VFD requirements, as detailed above.

In the following sections, FDA has summarized some of the initial findings with respect to the VFD inspections referenced in Table 2. While FDA investigators and state inspectors reviewed VFDs for all information required for a lawful VFD, only select requirements are included in the summaries below. In the following tables:

- The findings are represented as a percent and number of facilities inspected or number of VFDs for which selected records were reviewed (e.g. VFD, VFD feed labels, drug inventory or production records).
- If the FDA investigator's or state inspector's inspectional findings were silent on a requirement or the investigator/inspector indicated that the requirement was not applicable, those inspection results were not included in the summary count.
- The number of facility inspections may include those facilities serving multiple roles identified in Table 2 and therefore may not equal the totals by firm-type in Table 2.
- Each inspection could include review of records for one or more selected VFDs and therefore the number of VFDs does not correspond to the number of inspections in Table 2.

VFD Feed Manufacturing and Distribution

- The majority of inspected VFD feed distributors notified FDA of their intent to distribute VFD feeds.
    - Facilities are required to notify FDA prior to the first time they distribute animal feed containing a VFD drug.[5]
    - As of August 2019, there are over 9,600 facilities in all 50 states, Puerto Rico, and Canada that have notified FDA of their intent to distribute VFD medicated feed.[6] This is a substantial increase over the approximately 1,400 facilities on the VFD Feed Distributor Notification List at the end of 2015.

Table 3: Inspectional Findings: Requirement for Distributors to Notify FDA of Their Intent to Distribute VFD Feed

Finding	Fiscal Year 2016	Fiscal Year 2017	Fiscal Year 2018
Distributor had notified FDA of their intent to distribute VFD feeds	100% (25)	96.2% (51)	94.8% (253)

- The majority of VFD feed distributors who manufacture feed that were inspected had followed labeling and recordkeeping requirements showing that VFD feeds were generally manufactured in compliance with the VFD final rule.

Table 4: Inspectional Findings: Requirement for Distributors to Manufacture VFD Feed that Complies with the Terms of the VFD

Finding	Fiscal Year 2016	Fiscal Year 2017	Fiscal Year 2018
Distributors who distributed a VFD feed that complied with the terms of the VFD*	N/A+	83.3% (30)	91.5% (43)

* Not all firms who have notified CVM of their intent to distribute VFD feeds had distributed VFD feeds at the time of an inspection. If the inspection found that a VFD feed had not been distributed, this field was not included in this summary item. Therefore, these percentages do not necessarily apply to all the VFD distributors included in the count from Table 2.

\+ This information was not explicitly captured in the VFD inspection summary findings reviewed for fiscal year 2016.

Table 5: Inspectional Findings: Labeling and Recordkeeping Requirements Specific to Distributors Who Manufacture VFD Feed

Finding	Fiscal Year 2016	Fiscal Year 2017	Fiscal Year 2018
Distributors who manufacture VFD feed: Drug inventory or production records showed the correct amount of drug was added to the feed for the VFD reviewed	90.3% (28)	94.9% (37)	96.7% (323)

[5] 21 CFR part 558.6(c)(5).

[6] Veterinary Feed Directive Distributor Notification Lists are available at https://animaldrugsatfda.fda.gov/adafda.

Finding	Fiscal Year 2016	Fiscal Year 2017	Fiscal Year 2018
Distributors who manufacture VFD feed: Labels and formulas matched the VFD reviewed	96.6% (28)	87.2% (34)	91.0% (304)

- FDA investigators and/or state inspectors reviewed a limited number of VFD feed labels when inspecting distributors who also manufacture VFD feed and found occurrences of VFD feed labels that were missing the VFD caution statement.
    - Labels of VFD feeds are required to contain the following statement: "Caution: Federal law restricts medicated feed containing this veterinary feed directive (VFD) drug to use by or on the order of a licensed veterinarian."[7] Since the implementation of GFI #213, significantly more drugs, and therefore medicated feed, came under VFD marketing status.
    - Following the implementation of GFI #213, all Blue Bird labels[8] for VFD drugs were updated to include the VFD caution statement. Feed manufacturers should reference a current Blue Bird label to ensure labeling is consistent with the approved representative label.

Table 6: Inspectional Findings: Caution Statement Requirement for VFD Feed Labels

Finding	Fiscal Year 2016	Fiscal Year 2017	Fiscal Year 2018
Distributor's VFD feed labels contained the VFD caution statement	89.3% (25)	74.4% (29)	77.2% (250)

Veterinary Involvement[9]

A limited number of trace-back inspections were conducted at the veterinarian's clinic during these initial VFD inspections.[10] As noted above, however, FDA investigators and state inspectors reviewed select VFDs at distributors for their compliance with the requirements.

- All inspected veterinarians were licensed in the state where the VFD feed authorized on the VFD order(s) was being fed or were operating through reciprocity or a similar type of program.

[7] 21 CFR 558.6(a)(6).
[8] Blue Bird labels are representative labels that function as a guide to manufacturers of medicated animal feeds in the preparation of final printed feed labels.
[9] While FDA encourages veterinarians to work together with the client, feed distributor, and/or other animal health professionals to gather the information necessary to write a complete and accurate VFD, it is ultimately the veterinarian's responsibility to issue the VFD and ensure that it is complete and in accordance with the VFD drug's approval, conditional approval, or index listing.
[10] See Table 2 for the number of inspections by firm type.

Table 7: Inspectional Findings: License Requirement for Veterinarians Issuing VFDs

Finding	Fiscal Year 2016	Fiscal Year 2017	Fiscal Year 2018
Veterinarians had an active license in the state where the VFD feed authorized on the VFD order(s) is being fed[11]	100% (18)	100% (35)	100% (16)

- Of the selected VFDs reviewed during the initial inspections, almost all VFDs included the veterinarians' electronic or written signature.
    - Investigators/inspectors found occurrences where the veterinarian's written or electronic signature appeared to be missing from the VFD due to technical issues. All parties are responsible for ensuring that the VFD is signed by the issuing veterinarian.[12]

Table 8: Inspectional Findings: Requirement for VFDs to be Signed by the Issuing Veterinarian

Finding	Fiscal Year 2016	Fiscal Year 2017	Fiscal Year 2018
VFDs included veterinarians' electronic or written signature	100% (75)	99.5% (185)	98.6% (681)

- A majority of VFDs contained caution and warning statements matching the indication for use. However, some VFDs were either missing withdrawal time, special instructions, and/or cautionary statements, or included caution or warning statements for combination VFD drugs when the combination was not ordered.
    - Information on the VFD should match the approved conditions of use for the VFD drug or combination VFD drugs being authorized.

Table 9: Inspectional Findings: Specific Information to be Included on the VFD

Finding	Fiscal Year 2016	Fiscal Year 2017	Fiscal Year 2018
VFDs included the withdrawal time, special instructions, and/or cautionary statements	100% (75)	97.9% (182)	95.3% (653)

Animal Producers' Use of VFD Feed

A limited number of trace-forward inspections were conducted at the producer during the fiscal year 2016 – 2018 VFD inspections.[13]

[11] Veterinarians are required to be licensed to practice veterinary medicine and 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).
[12] All parties are responsible for ensuring that the VFD is signed by the issuing veterinarian. If the VFD does not contain all the required information, including the issuing veterinarian's written or electronic signature, the distributor must not fill the VFD, and FDA recommends that the distributor notify the veterinarian that the order cannot be filled until all the necessary information is provided on the VFD (see 21 CFR 558.6(b)(3)(xv) and (c)(1)).
[13] See Table 2 for the number of inspections by firm type.

- Information obtained from inspections of producers have shown that VFD feed was fed according to the instructions on the feed label and the VFD in the majority of these inspections.
    - VFD feed is required to be labeled and fed according to the VFD drug approval, and the use must be consistent with the VFD authorizing the use, including any directions provided by the veterinarian.

Table 10: Inspectional Findings: VFD Requirements for Clients (Animal Producers)

Finding	Fiscal Year 2016	Fiscal Year 2017	Fiscal Year 2018
Client did not feed VFD feed beyond the expiration date on the VFD	91.7% (11)	75% (15)	100% (9)
Client fed VFD feed to the animals authorized on the VFD (number, species, and/or production class)	100% (12)	90.0% (27)	100% (19)
Client fed VFD feed for the duration identified on the VFD	100% (12)	89.3% (25)	100% (18)
Client complied with the special instructions on the VFD	100% (8)	91.3% (21)	100% (15)

Enforcement Strategy

During the initial educational phase, investigators were encouraged to discuss deficiencies that were not significant to public health (e.g., minor recordkeeping discrepancies) with the involved producer, veterinarian, or VFD distributor and obtain voluntary corrective action.

FDA issued one Warning Letter (WL) based on a fiscal year 2018 medicated feed CGMP and VFD inspection. The feed mill adulterated and misbranded VFD feed by distributing VFD feed to other distributors without first receiving an acknowledgment letter, in addition to adulterating and misbranding medicated and non-medicated feed for other reasons.

Conclusion

While a relatively small number of inspections were conducted initially in fiscal years 2016 – 2018, CVM will continue to expand the comprehensive VFD compliance strategy. FDA reminds stakeholders that VFD medicated feeds must be used in according to the approved conditions of use and must be under the oversight of a licensed veterinarian and consistent with a lawful VFD order.

The agency intends to continue monitoring compliance for all parties to ensure they are meeting their requirements under the VFD final rule. As VFD inspectional activities move forward, FDA will continue to provide education, but FDA will also use enforcement strategies when voluntary compliance with the VFD final rule requirements is not achieved.

Any questions about this document may be directed to AskCVM@fda.hhs.gov.