

CHAPTER 71: POST APPROVAL MONITORING OF ANIMAL DRUGS, FEEDS, AND DEVICES

SUBJECT: ILLEGAL DRUG RESIDUES IN MEAT, POULTRY, SEAFOOD, AND OTHER ANIMAL DERIVED FOODS		IMPLEMENTATION DATE: 04/07/2023
DATA REPORTING		
PRODUCT CODES	PRODUCT/ASSIGNMENT CODES	
Industry codes: 15, 16, 17, 21, 56, 60, 61, 62, 67-69	71006, 71S006, 71023, 71S023	

FIELD REPORTING REQUIREMENTS:

Report completed operations in eNSpect/FACTS per [Investigations Operations Manual \(IOM\)](#) Subchapter 5.11.1 – *Establishment Inspection Report (EIR)* under Program Assignment Code (PAC) 71006 or 71S006 (State Contract). Investigational reports must be prepared per [IOM](#) Subchapter 8.1.9 – General Investigation Reporting.

After inspections of all sources of a violative drug residue sample reported by USDA (United States Department of Agriculture), Food Safety and Inspection Service (FSIS), Supervisory Investigators and/or Drug Residue Program Monitors must:

- Complete the [Post Inspection Report](#) (fillable Excel template found at [CVM Drug Residue Program Resources](#)), identifying the responsibility of each source for a violative sample and any source changes/updates.
- E-mail completed Post Inspection Reports to Center for Veterinary Medicine’s (CVM) Division of Food Compliance at [CVM’s Regulator Technical Assistance Network \(rTAN\)](#).
 - Post Inspection Reports are due by COB on the first Friday of each month. See [Part III – 2. Reporting](#) for additional information.

For violative inspection reporting, see Part [V – 5. Enforcement Actions](#).

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GLOSSARY

Comprehensive drug residue inspection – is conducted at sources that typically medicate and market food-producing animals (e.g., producers) and serve as broad-based evaluations. These inspections determine responsibility for and cause of the drug residue in the violative animal and identify systemic failures related to drug use, drug management, and medicated animal management. A comprehensive inspection also provides FDA the opportunity to educate producers and related establishments about avoidance measures to reduce the likelihood of future violative drug residues. The inspectional approach must adhere to the information outlined in the ‘Producer Inspection’ resource. See [CVM Drug Residue Program Resources – Producer Inspection](#).

Directed inspection – is conducted to collect evidence to document violations and/or to support regulatory action at either (1) sources that do not typically medicate food producing animals or (2) veterinary firms of patients with violative drug residue. A directed inspection of the veterinary firm is required when the drug associated with a violative residue was prescribed or administered by a veterinarian.

Drug residue avoidance measures – are actions used to avoid violative drug residues in food-producing animals. These measures can include proper use (dosage, route of administration, etc.) of approved animal drugs as directed; management of drugs (treatment records, drug inventory, etc.); and management of medicated animals (segregation, identification, etc.).

Edible tissue – for the purposes of this document, edible tissue includes liver, muscle, kidney, fat, honey, and whole eggs from food-producing animals.

Extralabel Drug Use (ELDU) – ELDU refers to the use of an approved drug in a manner that is not in accordance with the approved label directions. Licensed veterinarians are permitted to prescribe extralabel uses of certain approved animal drugs and approved human drugs for animals under certain conditions under the Animal Medicinal Drug Use Clarification Act of 1994 (AMDUCA). Under AMDUCA and its implementing regulations published at [Title 21, Code of Federal Regulations, Part 530 \(21 CFR Part 530\)](#), any extralabel use of an approved animal or approved human drug must be by or on the lawful order of a veterinarian within the context of a veterinarian-client-patient relationship (VCPR). ELDU must also comply with other provisions of 21 CFR Part 530. Deviations from FDA-approved labeled directions include use in another species, use for a different indication, use at a different dose, duration, or frequency, and use via a different route of administration. A list of drugs specifically prohibited from extralabel use appears in 21 CFR 530.41.

Firm – for purposes of this document, the term ‘firm’ is implicitly used to refer to entities (e.g., farms, haulers, dealers, veterinary firms) that are exempt from [21 CFR Part 1, Subpart H, Registration of Food Facilities](#).

Inspections – FDA conducts inspections to determine a firm's compliance with applicable laws and regulations, such as the Federal Food, Drug, and Cosmetic Act. Inspections require a notice

of inspection (Form FDA 482). During an inspection, ORA investigators may observe conditions or practices they deem to be objectionable. These observations are listed on an FDA Form 483 when, in an investigator's judgement, the observed conditions or practices indicate that an FDA-regulated product may be in violation of FDA's regulations.

Inspection Prioritization Score (IPS) – a score that CVM assigns to each sample and source combination to ensure consistent assessment of inspectional priorities. The IPS, which ranges from 0.53 to 3.0 (3.0 being the higher priority), is based on three elements: the residue toxicity of the drug, likelihood of exposure from the source, and exposure level of the drug (See [CVM Drug Residue Program Resources](#) – [Calculation of Inspection Priority Score](#)). While all violative drug residues are viable for inspection (i.e., all are violations warranting inspectional follow-up), these scores are intended to help ORA Divisions compare and prioritize the violative samples within their geographical boundaries. This does not mean that a Division is obligated to inspect only samples with the highest priority scores. There are many factors to consider when assigning a violative sample for follow-up (e.g., geographical location, available resources, cost, etc.), so the IPS should be used in addition to these other considerations. For example, if a Division had two violative samples in the same general area, one with a score of 1.33 and the other 2.00, and only had resources to investigate one sample, the Division would select the sample with the higher IPS. If, however, the violative sample with the lower score was a short distance from a Resident Post and the sample with the higher score would require travel, the Division would justifiably choose the sample with the lower score.

Investigations – The purpose of an investigation is to determine and document facts concerning an issue. Information obtained during an investigation may lead to other operations such as sample collections or inspections. An information gathering investigation is generally received by the ORA Division from an outside source (e.g., Center, ORA headquarters, or another Division) and will generally be a request to obtain specific information from a firm or other source. For example, an assignment to collect interstate documentation from a shipper of a product located in one Division to support regulatory action against a manufacturer in another Division.

National Residue Program (NRP) – The U.S. National Residue Program for Meat, Poultry, and Egg Products is an interagency program that is designed to identify, prioritize, and analyze chemical residues and contaminants in meat, poultry, and egg products. The U.S. Department of Agriculture's (USDA) Food Safety and Inspection Service (FSIS) administers the NRP. Other agencies that participate in the NRP include USDA Animal Plant Health and Inspection Service (APHIS), USDA Agricultural Marketing Service Packers and Stockyards (AMSPS), the U.S. Environmental Protection Agency (EPA), and FDA.

Producer – for the purposes of this document, a producer refers to a source that typically medicates and markets food-producing animals.

Source – FSIS provides FDA with information about samples with violative drug residues and the individual or company, referred to as a 'source', which is suspected of causing the violation

(commonly a producer). Identification of a source by FSIS is what initiates FDA's inspectional response to a drug residue violation.

Sources that typically do not medicate food-producing animals - for the purposes of this document, these sources refer to sale barns, haulers, and dealers of food-producing animals.

USDA establishment – is an official establishment involved in slaughtering, cutting, boning, meat canning, curing, smoking, salting, packing, rendering or similar of meat and poultry subject to inspection by USDA under [9 CFR Chapter III – Food Safety and Inspection Service, Department of Agriculture](#).

Veterinary-Client-Patient Relationship (VCPR) – This the basis for interaction among veterinarians, their clients, and their patients and is critical to the health of animals. A VCPR is present when all the following requirements of [21 CFR 530.3\(i\)](#) are met:

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.

Violative Sample/Animal – tissue samples from animals at slaughter or from animal-derived food with drug residues at or above the set tolerance.

PART I – BACKGROUND

The purpose of this compliance program is to provide Food and Drug Administration (FDA) Office of Regulatory Affairs (ORA) and commissioned State agency personnel with instructions, priorities, and resources to facilitate investigative and compliance activities that protect consumers from violative drug residues in animal-derived foods.

The U.S. National Residue Program (NRP) for Meat, Poultry, and Egg Products is an interagency program that is designed to identify, prioritize, and analyze chemical residues and contaminants in meat, poultry, and egg products. The U.S. Department of Agriculture's (USDA) Food Safety and Inspection Service (FSIS) administers the NRP. Other agencies that participate in the NRP include USDA Animal Plant Health and Inspection Service (APHIS), USDA Agricultural Marketing Service Packers and Stockyards (AMSPS), the U.S. Environmental Protection Agency (EPA), and FDA.

FSIS collects, analyzes, and reports violative drug residue samples to FDA under a Memorandum of Understanding ([MOU 225-85-8400](#)). Under the MOU, FSIS provides FDA with information about samples with violative drug residues and the individual or company, referred to as a 'source', who is suspected of causing the violation (commonly a producer). FDA's inspectional response to a drug residue violation is initiated once FSIS has identified the source and provided FDA with the sample and source information. When FDA conducts the inspection at the source, inspectional findings may dictate the need for investigation (or inspection) of other entities (e.g., veterinarians, sale barns, dealers, haulers, etc.) to support and/or determine responsibility for the violative drug residue.

In addition to reports from FSIS, FDA also responds to violative drug residues in edible tissue (e.g., whole eggs, honey, seafood, etc.) reported by FDA's Center for Food Safety and Applied Nutrition (CFSAN) under this compliance program.

Extralabel use of drugs in food-producing animals by laypersons, outside the context of a lawful order under a valid veterinary-client-patient relationship (VCPR), is a key causative factor in violative drug residues in edible tissue. In 1994, Congress passed legislation that would allow veterinarians to prescribe approved animal drugs and approved human drugs for extralabel uses (i.e., in a manner that is not consistent with the approved animal or human drug labeling). This legislation is called the [Animal Medicinal Drug Use Clarification Act \(AMDUCA\)](#) (21 U.S.C. §360b(a)), and the regulations that implement AMDUCA are published in [21 Code of Federal Regulations \(CFR\) Part 530 – Extralabel Drug Use in Animals](#). These regulations describe the specific conditions under which extralabel drug use (ELDU) is permitted. [Compliance Policy Guide \(CPG\) Sec. 615.200 – Proper Drug Use and Residue Avoidance by Non-Veterinarians](#) provides guidance on measures that can be taken by non-veterinarians to ensure proper drug use and avoid violative drug residues.

For additional background information on Illegal Drug Residues, see [Attachment A – Program Framework](#).

There have been numerous modifications related to enforcement policy and operational procedures throughout this revised compliance program to include:

1. Changes to Regulatory Strategy
 - a. Direct Reference Authority has been discontinued and Center concurrence is required. See [Regulatory Procedures Manual \(RPM\)](#) Section 4-1-4 – Center Concurrence and Letters Issued by Center.
 - b. Inspectional follow-up to a Warning Letter, issued under this program, should follow the guidance in the [RPM](#) Section 4-1-8 – Warning Letter Follow-up.
 - c. Enforcement guidance was updated in [Part V– Regulatory/Administrative Strategy](#).
2. Changes to Inspections:
 - a. Bovine Spongiform Encephalopathy (BSE) inspections are no longer requested in conjunction with drug residue inspections.
 - b. Veterinary Feed Directive (VFD) inspections may be requested in conjunction with drug residue inspections, as applicable. See Appendix D – VFD Requirements (21 CFR §558.6) of [CPGM 7371.000 - Comprehensive Animal Food Inspection](#).
 - c. Residue Violation Information System (RVIS), hosted by USDA’s National Information Technology Center (NITC), was decommissioned.
 - d. Residue Violation Tracking (RVT), hosted by FSIS, has replaced RVIS.
 - e. Tissue Residue Information Management System (TRIMS) was decommissioned.
 - f. PART IV – ANALYTICAL page is now left blank.
 - g. Additional changes related to Inspections:
 - i. An Inspection Prioritization Score (IPS) is assigned to each sample and source combination to ensure consistent assessment of inspection priorities. See [CVM Drug Residue Program Resources – Calculation of Inspection Prioritization Score \(IPS\)](#).
 - ii. A comprehensive drug residue inspectional approach is to be employed to:
 1. evaluate sources that medicate and market food-producing animals;
 2. determine responsibility for and cause of the drug residue; and identify systemic failures related to drug use, drug management and medicated animal management.
 - iii. A directed inspection of the veterinary firm is required when the drug associated with a violative residue was prescribed or administered by a veterinarian.
3. Changes to Attachments:
 - a. Attachment A – *FSIS Reporting Codes* (a product of RVIS) was removed/withdrawn from use and has been replaced with Attachment A – *Program Framework*.
 - b. Attachment B3 – *Sample Warning Letter Illegal Drug Sale* was removed and withdrawn from use.

- c. Attachment C – *Tissue Residue Evaluation Form* (a product of TRIMS) was removed and withdrawn from use.
- d. Attachment D – *USDA Contacts* was removed and withdrawn from use (updated USDA info is in PART VI – *REFERENCES*).
- e. Attachment E – *GIPSA/Title 18 Memo* was removed and withdrawn from use.
- f. Attachment F1 – *Example of Slaughter Establishment Affidavit to Document Chain of Custody* was removed.
- g. Attachment F2 – *Example of Slaughter Plant Inspector Affidavit* was removed.
- h. Attachment G – *Drug Inventory Form* was removed and withdrawn from use.
- i. Attachment H – *Program Monitor Checklist* was removed and withdrawn from use.

PART II – IMPLEMENTATION

1. Objective

The objective of this Compliance Program is to reduce the likelihood of occurrence of violative drug residues in edible tissue and animal derived foods (e.g., liver, muscle, kidney, fat, honey, and whole eggs) through:

A. Inspections at the source of a violative drug residue(s) to:

- a. determine involvement in and responsibility for the residue(s);
- b. determine if drugs administered to food-producing animals were used according to label instructions and/or in compliance with extralabel drug use regulations (21 CFR Part 530); and
- c. determine if drug residue avoidance measures are established and utilized. See [Part III – INSPECTIONAL](#) and [CVM Drug Residue Program Resources](#) for additional information.

B. Inspections of veterinarian to:

- a. determine the veterinarian's involvement in treatment of the violative animal;
- b. determine compliance with the ELDU regulations (21 CFR Part 530); and
- c. determine if a valid veterinary-client-patient relationship (VCPR) existed and if the prescribed drug was used as directed by the veterinarian at the time of treatment of the violative animal.

C. Ancillary investigations to:

- a. meet evidentiary requirements;
- b. initiate compliance action, as warranted. See [Part V REGULATORY/ADMINISTRATIVE STRATEGY](#).

D. Educational materials, such as the [T.A.L.K Before You Treat](#) informational brochure (in English/Spanish).

E. Voluntary corrective action.

F. Compliance action, as warranted. See [Part V – REGULATORY/ADMINISTRATIVE STRATEGY](#).

2. Program Management Instructions

Investigative operations involving violative drug residues are unique in comparison to other FDA fieldwork. FDA-regulated products covered under this program include both food-producing animals and the drugs used to medicate them. Inspections and investigations are performed at a variety of entities (production farms, livestock dealers, sale barns, haulers, veterinarians, drug suppliers, slaughter establishments, etc.) to obtain evidence, establish animal traceback, and document both interstate commerce (IS) and responsibility for the violative drug residue.

Key investigative elements utilized in this program include:

- Inspectional approaches,

- Investigations,
- Pre-inspection notification procedures,
- Biosecurity measures, and
- Personal safety concerns.

In addition to these program elements, described in greater detail below, please also refer to the following resources:

- [IOM Subchapter 5.2 – Inspection Procedures](#),
- [IOM Subchapter 5.9 – Veterinary Medicine](#), and
- [CVM Drug Residue Program Resources](#).

A. Inspectional Approach Overview

A violative drug residue inspection by FDA is triggered by one of the following situations:

- Violative samples of edible tissues collected, analyzed, and provided by FSIS,
- Violative samples of animal derived foods collected, analyzed, and provided by CFSAN, or
- As follow-up to a previously violative drug residue inspection that resulted in enforcement action.

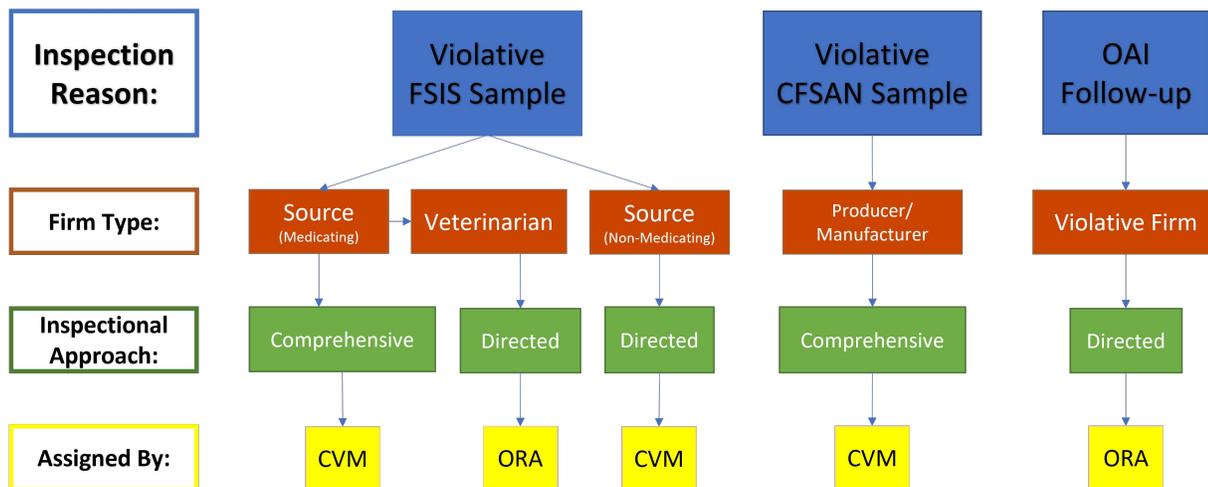
Regardless of what triggers a drug residue inspection, the inspectional approach will vary depending on the violation, the type of source and the other entities involved. Typically, one or more of the following inspectional approaches will be utilized during a drug residue follow-up:

- Comprehensive inspections at the source/producer,
- Directed inspections of:
 - Non-medicating sources
 - Veterinarians

Comprehensive inspections are conducted at sources that typically medicate and market food-producing animals (e.g., producers). These inspections are intended not only to determine responsibility for and cause of the drug residue in the violative animal, but to look at overall herd practices to identify systemic failures related to drug use, drug management, and medicated animal management. Comprehensive inspections also offer an opportunity to educate producers, who are not subject to routine FDA inspections, about avoidance measures to reduce the likelihood of future violative drug residues.

Directed inspections are conducted at sources that do not typically medicate food producing animals. They are also conducted at the veterinarian, if the veterinarian was involved in prescribing the drug(s) that caused the violative drug residue. In either case, the directed inspections are focused on the animal with the violative drug residue, though the scope of the inspection may expand if the source or veterinarian is found to be responsible for causing the residue.

Overview of Inspectional Approaches



Note: all drug residue inspections are considered high priority

Figure 1. Visual Aid of Inspectional Approaches

Description of Inspectional Approaches

The following section describes the most common inspectional approaches employed during a drug residue inspection. All assignments under the drug residue CP are designated as high priority, except under rare circumstances when elevated to “top” priority (i.e., chloramphenicol residues).

(1) Violative FSIS Samples

This program is based on violative samples collected and analyzed by FSIS under the Meat, Poultry and Egg Products Inspection Acts. FDA operations typically begin with an inspection of the source of the violative animal after receipt of a “USDA Violation Notification Letter” from FSIS under the NRP.

While all violative drug residues are viable for inspection (i.e., all are violations warranting inspectional follow-up), CVM understands available resources are limited and do not allow for coverage of every violative residue that occurs. To aid in prioritizing inspectional coverage, CVM has developed a ranking system called the Inspection Priority Score (IPS). The IPS is a cumulative score assigned to each violative sample based on three elements: the residue toxicity of the drug, likelihood of exposure from the source, and exposure level of the drug. This score, which ranges from 0.53 to 3.0 (3.0 being the higher priority), should be used in conjunction with other considerations (e.g., geographic location of the source, available resources, cost, etc.) to determine which residue violators to inspect. See [CVM Drug Residue Program Resources – Calculation of Inspection Priority Score](#).

(a) Comprehensive Inspections

The purpose of a comprehensive inspection is to follow-up on the violative drug residue(s), to include a broad-based review of avoidance measures (drug use, drug management, and medicated animal management) to ensure that food-producing animals are not held in insanitary conditions due to:

- Improper drug use (not adhering to all components of legal use of the drug),
- Insufficient drug residue avoidance measures.

Comprehensive inspections at the source, which are assigned to the field by CVM, are fundamentally important to determine a source's overall compliance with the FD&C Act. The focus is not solely on the violative animal(s), but on overall herd practices that may cause future violations. Simultaneously, a comprehensive drug residue inspection provides an educational opportunity to discuss avoidance measures to reduce the likelihood of future violative drug residues. See [CVM Drug Residue Program Resources – Producer Inspection](#).

(b) Directed Inspections

Directed inspections fall into two categories; inspections of non-medicating sources (i.e., sources, such as dealers and sale barns that typically do not medicate food producing animals) and inspections at the veterinarian. Inspections at non-medicating sources are assigned by CVM. Inspections at the veterinarian are assigned by ORA after inspection at the source reveals the veterinarian was involved in prescribing or medicating the violative animal with the drug causing the residue. In either case, the directed inspection is a limited scope inspection focused on the violative animal(s) and the drug(s) used to medicate that/those animal(s).

Inspection of non-medicating source: Inspections of sources that typically do not medicate food-producing animals (e.g., dealers, sale barns) serve to evaluate the source's involvement in causing the drug residue violation and to identify other potential source(s) that may be responsible for the residue.

This directed inspection may expand in scope when conditions are uncovered that show:

- Traceability of the animal with a violative drug residue is not maintained or inaccurate (e.g., animal identification, shipping/purchase records),
- The inspected source is responsible for causing the violation.

Veterinarian: Inspections at the veterinarian are conducted when a comprehensive inspection at the source reveals the veterinarian prescribed the medication that caused the violative residue.

Inspection of a veterinarian is conducted to:

- Determine the veterinarian's involvement in treatment of the violative animal(s),
- Determine compliance with the ELDU regulations ([21 CFR Part 530](#)),
- Verify that a VCPR exists, and
- Determine if the prescribed drug was used as directed by the veterinarian.

These inspections may expand in scope when conditions show:

- The prescription drugs used in the treatment of the violative animal may have contributed or caused violative drug residues (e.g., examination of the prescription revealed inaccuracies or incomplete directions for use),
- The veterinarian's administration of a drug may have caused the violative drug residue,
- FDA-approved prescription drugs are not prescribed/dispensed by a licensed veterinarian under a lawful order (VCPR), or
- Non-FDA approved drugs are dispensed for treatment of food-producing animals.

(2) Violative CFSAN Samples

This program is based on violative samples involving animal-derived foods (e.g., honey, seafood, shell eggs). CVM will evaluate and prioritize violative animal-derived food sample findings provided by CFSAN on an individual basis, considering a variety of factors such as FDA recall classification (residue toxicity), a producer's compliance history, and the industry and product type sampled. Inspection assignments under this program are issued by CVM.

Note: To determine the source of the animal-derived food that was violative, an inspection or investigation at an FDA-regulated food facility (i.e., honey manufacturer) may be required before an inspection under this compliance program can be initiated. Please see [Part II – 5. When to contact other Offices within FDA](#).

(a) Comprehensive Inspections

The purpose of this inspection is to follow-up on a violative drug residue(s), to include a broad-based review of drug use and drug residue avoidance measures related to medicated food-producing animals to ensure that food is not held in insanitary conditions due to:

- Improper drug use (not adhering to all components of its legal directed use) potentially making for an unreliable withdrawal period, and/or
- Insufficient drug residue avoidance measures to prevent introduction into IS of an animal-derived food with a violative residue(s).

Comprehensive inspections at the producer/source are fundamentally important to determine a source's overall compliance with the FD&C Act. The focus is not solely on the violative product, but on overall firm practices that may cause or contribute to future violations. The inspection also provides an educational opportunity to discuss avoidance measures to reduce the likelihood of future violative drug residues. See [CVM Drug Residue Program Resources – *Producer Inspection*](#).

(3) Follow-up to Violative FDA Inspection

Inspections conducted as follow-up to a violative drug residue inspection (e.g., follow-up to Regulatory Meeting, Untitled Letter, Warning Letter, etc.) are assigned by ORA (typically by a Division's Compliance Branch). ORA Divisions will evaluate and prioritize the need for a follow-up inspection on an individual basis. For additional information regarding compliance follow-up inspections, please refer to [Part V – REGULATORY/ADMINISTRATIVE STRATEGY, Regulatory Procedures Manual \(RPM\) Section 4-1-8 – *Warning Letter Follow-Up*](#), and Section 6.7 of [FMD-86 – *Establishment Inspection Report Conclusions and Decisions*](#) for ORA's guidance on OAI follow-up activities.

Follow-up to violative FDA inspections should be dependent on the significance of the previous observations and the firm's violative drug residue history. Firms that have additional violative drug residues and those firms that have not initiated or promised corrective action are good candidates for re-inspection.

(a) Directed Inspections

When conducting a compliance follow-up inspection related to a violative drug residue, the focus will be on the observations from the previous inspection and whatever corrective actions have been made to reduce the likelihood of future residues. The scope of the inspection may be expanded if additional residues have occurred, the firm has not taken corrective action or has taken inadequate corrective action.

B. Investigations

Investigations of haulers, dealers, and sale barns may be performed in conjunction with inspections of sources identified by FSIS to collect additional evidence (i.e., IS, animal

identification) and to determine if anyone else in the chain of custody shares responsibility for the drug residue violation.

Note: If investigational findings reveal the hauler, dealer or sale barn contributed to or caused the drug residue violation, investigations may be converted to inspections.

C. Pre-inspection Notification to the Firm

Pre-announcement of inspection may be warranted under this compliance program for a variety of reasons, to include: the firm is not subject to routine FDA surveillance, the firm is in a remote location requiring travel, limited availability of essential personnel at the firm, and when personal safety or a firm's biosecurity practices are in question.

Ultimately, the decision to pre-announce an inspection is left to the Division's discretion (refer to [IOM](#) Chapter 5.2.1.1 – *Pre-Announcements*). If the Division pre-announces the inspection, the discussion should include the scope of the inspection and the firm's biosecurity policies. If the Division has made attempts to pre-announce the inspection but encountered difficulties in doing so (e.g., the farm does not have a phone number, made attempts to contact and no return phone calls were received, etc.), please document this in the Establishment Inspection Report (EIR). Lack of pre-announcement does not preclude inspection.

D. Biosecurity

The purpose of biosecurity is to protect human and animal health and to protect agricultural products through the prevention, control, and management of biological risk factors.

When conducting inspections on farms, at sale barns and slaughter establishments, adhere to biosecurity procedures as detailed in the [IOM](#) Chapter 5.2.10 – *Routine Biosecurity Procedures For Visits to Facilities Housing or Transporting Domestic or Wild Animals*.

E. Personal Safety

Attention to personal safety concerns and use of personal protective equipment are crucial for the safety of inspection personnel during an inspection. Refer to [IOM](#) Chapter 5.2.1.2 – 5.2.1.4, *Personal Safety – Personal Safety Plan*. See also [IOM](#) Chapter S for more detailed information about potentially hazardous conditions and unsafe practices related to field investigations and inspections. See [Part VI – 1 References](#). Field inspection staff should be aware they may be exposed to hazardous drugs when handling drug vials and needles, touch surfaces that are contaminated with these drugs, or come into contact with waste of treated animals. Needlesticks, skin absorption, inhalation, and ingestion are ways they may be exposed.

Caution:

- Investigators may be exposed to the toxic hazards through needle-stick injuries, skin cuts, puncture wounds, and contact with skin and mucous membranes. Be

aware of the hazard of accidental injection of the antibiotic **tilmicosin (i.e., [Micotil 300®](#))**. The National Institute for Occupational Safety and Health (NIOSH) recommends that extreme care be given to following safe drug handling and injection since the cardiotoxic effects of Micotil 300® on the human heart can be **severe enough to cause death**.

- Investigative work under this program is usually conducted in a reasonable environment. Nonetheless, there may be times when you are confronted by unfriendly or hostile persons. See [IOM 5.2.5 – Inspection Refusal](#) for indicators, safety precautions and procedures on how to handle refusals and hostile and uncooperative individuals.
- In eNSpect, an “Active Personal Safety Alert (PSA)” may be added on the “Firm” page. The “Personal Safety Alert” tab on the “Firm Details” page in Management Services (FMS) should be checked for the existence of a PSA when assignments are designated and before inspections are conducted. This personal safety alert may be selected when there is a potential hazard identified:
 - Where a previous threat/assault or physical resistance occurred,
 - Where specific personal protective equipment is needed (respirators, etc.),
 - Where there are specific medical considerations for a population of investigators (e.g., the firm manufactures or administers a drug hazardous to women of child-bearing years or those with allergies to penicillin or other drug products).

3. Program Interactions

During a comprehensive inspection related to a violative drug residue, if it has been determined that the producer manufactured, received, and/or used a VFD feed, then a VFD inspection should be conducted even if use of the VFD feed did not result in the drug residue. The producer should be informed that in addition to determining the cause of the drug residue, the Agency is also conducting a broad-based review of all drugs that are used in the treatment of food-producing animals, including the use of VFD feeds. Refer to Appendix D – VFD Requirements (21 CFR §558.6) of [CPGM 7371.000 - Comprehensive Animal Food Inspection](#).

A comprehensive drug residue inspection, under CPGM 7371.006, does not involve inspectional coverage of CGMP medicated feed manufacturing. For CGMP medicated feed inspections, refer to Appendix C – Medicated CGMP Requirements (21 CFR part 225) of [CPGM 7371.000 - Comprehensive Animal Food Inspection](#).

4. Interactions with Other Federal Agencies, State, and Local Counterparts

This program is generally initiated through the sampling plan of FSIS. The FSIS NRP calls for sampling of animal tissues to verify that drug tolerances are not exceeded. The NRP domestic sampling plan includes scheduled sampling and inspector-generated sampling. Inspector-generated sampling is conducted by FSIS in-plant food inspectors and veterinarians when they suspect that an animal may have violative drug residues.

CVM, in cooperation with ORA's Office of Partnerships, can utilize contracts, grants, cooperative agreement programs and partnership agreements with state and local regulatory public health agencies. These agreements are designed to meet CVM's programmatic requirements and partnership programs.

5. When to Contact Other Offices Within FDA

When a violative drug residue is identified by FDA (rather than by FSIS) under a CFSAN sampling assignment, CFSAN may need to be contacted to determine if inspection of an FDA-regulated human food facility is required to:

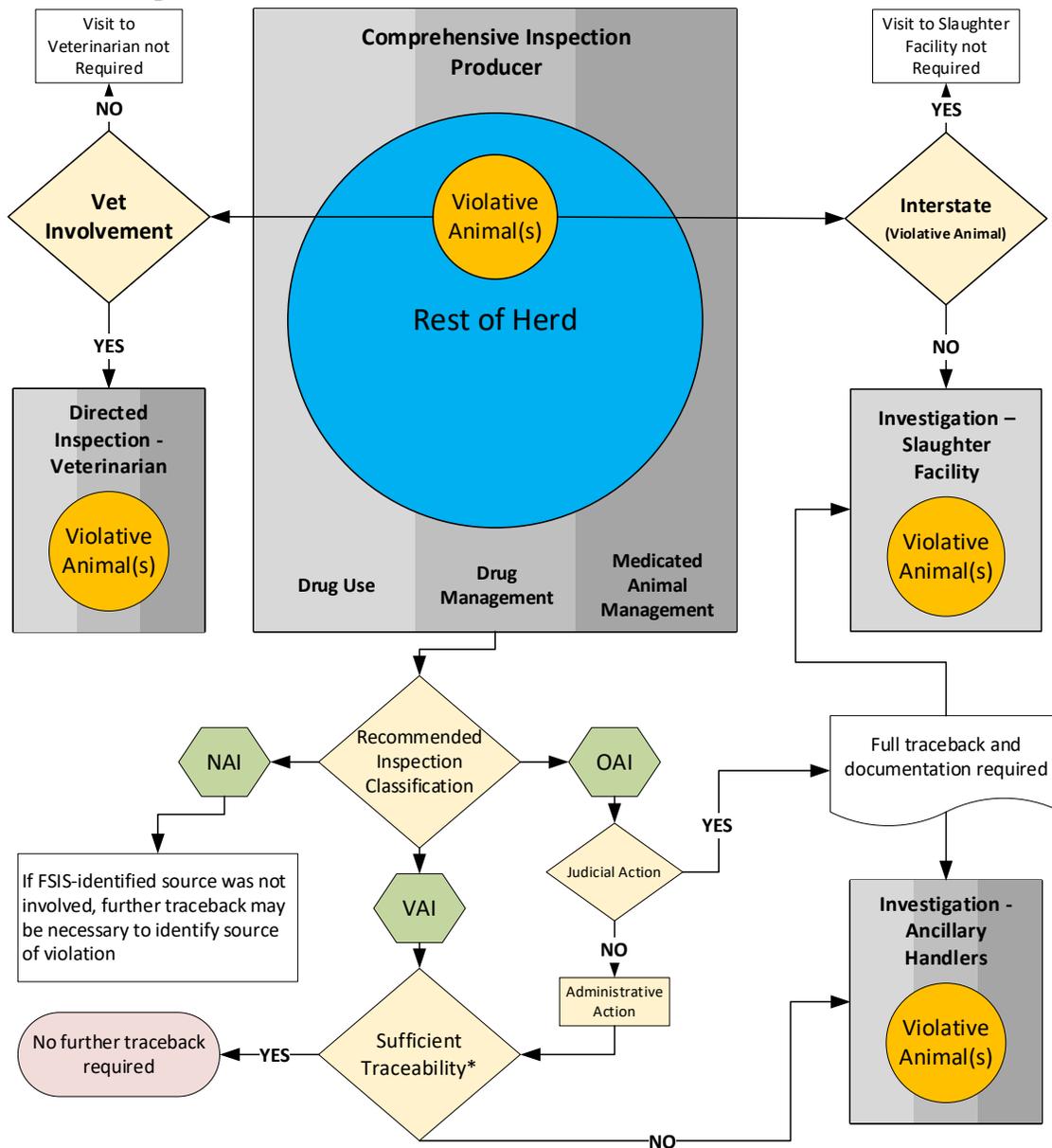
- Identify the source of the violative sample (animal-derived food that was violative with a drug residue), and
- Determine if CFSAN has additional requirements for follow-up to the violative sample (e.g., recalls, sampling, etc.).

Contact should be directed through CFSAN's rTAN (Regulatory Technical Assistance Network) at rTANWorkgroup@fda.hhs.gov.

PART III –INSPECTIONAL

This part provides an overview of inspectional programmatic requirements and expectations and is intended to be used in conjunction with the following inspectional resources located at CVM Drug Residue Program Resources – Producer Inspections, Veterinarian Inspections, and Ancillary Investigations.

1. Overview of Operations



*If case is recommended OAI for Administrative Action, in addition to traceability, there will also need to be sufficient evidence that the source is responsible for the violation and that no other IDs were placed on the animal (aside from those by FSIS and the slaughter facility).

Figure 2. Visual Aid of Comprehensive Inspection and Other Investigational Operations.

FDA operations involving violative drug residues are unique in comparison to other FDA fieldwork. Under this program, operations typically begin with a follow-up inspection of the source of the violative animal, as identified by FSIS under the FSIS NRP. Follow-up may also include additional inspections and/or investigations of other firms with some involvement with the violative animal (sale barns, dealers, haulers, veterinarians, drug suppliers, slaughter establishments, etc.) to obtain evidence, establish animal traceback, and document IS or responsibility for the violative drug residue.

The primary intent of this violative sample-based program is to focus compliance operations on the sources of violative samples. Figure 2 (above) outlines steps involving a comprehensive drug residue inspection at a producer. A comprehensive inspection involves a broad-based review of drug residue avoidance measures (drug use, drug management, and medicated animal management) to determine a source's overall compliance with the FD&C Act. A comprehensive inspection also provides FDA the opportunity to educate producers and related establishments about avoidance measures to reduce the likelihood of future violative drug residues. The inspectional approach must adhere to the information outlined in the 'Producer Inspection' resource. See [CVM Drug Residue Program Resources – *Producer Inspections*](#).

A directed inspection of the veterinary firm is required when the drug used to treat the violative animal was prescribed or administered by the veterinarian. See [CVM Drug Residue Program Resources – *Veterinarian Inspections*](#).

Note: Inspectional findings at the producer may prompt the need for additional information regarding drugs that were prescribed to or used at the facility (e.g., extralabel drugs or drugs that are not FDA approved) but not used to medicate the violative animal. In this case, the Division may seek to obtain additional information regarding the prescribed drug or prescribing veterinarian (e.g., directions for use or verification of a valid VCPR).

After evaluation of inspectional findings, corrective actions, and compliance history, Divisions should recommend an inspectional classification. See [Part V – *REGULATORY/ADMINISTRATIVE STRATEGY*](#) for information on inspectional outcomes and compliance actions.

- Inspectional Classification and Investigative Follow-ups:
 - If Voluntary Action Indicated (VAI) is recommended **and** there is sufficient traceability of the violative animal(s) to the source, then additional investigative operations involving traceback should **not** be required.
 - If Official Action Indicated (OAI) and advisory action (e.g., regulatory meeting, Untitled Letter, Warning Letter) is recommended, additional investigative operations should **not** be required when the following conditions are met:
 - there is sufficient evidence showing traceability to the source,
 - there is sufficient evidence showing the source is responsible for causing the violative drug residue, **and**

- no further identification (e.g., backtag, sale tag) was applied to the violative animal by any subsequent handler (e.g., sale barn, dealer, etc.) excluding USDA or the slaughter establishment.
- If further identification was applied to the violative animal, excluding those added by USDA or the slaughter establishment, then investigative follow-up is requested at the firm/individual that applied the identification to document it and to determine if the handler (e.g., sale barn) obtained signed consignor/owner certificates stating that consigned livestock are not in violation of state or federal regulations (e.g., drug residues). See [Part V – REGULATORY/ADMINISTRATIVE STRATEGY](#) for more information on FD&C Act Citation Section 301(h) False Guaranty.
- A visit to the slaughter establishment should not be required provided there is sufficient evidence showing IS either through movement of the violative animal or through movement of food from the slaughter establishment. Note: When using evidence of IS from the slaughter establishment, IS must have been documented within six (6) months prior to collection of the violative sample.
Note: Evidence regarding admission of responsibility or chain of custody of the violative animal will be evaluated on a case-by-case basis. Traceability must be sufficient to show more likely than not the animal originated at the source; and documentation of ownership/treatment/violation must describe the likelihood of their responsibility.
- If OAI and judicial action (e.g., injunction) is recommended, investigative operations must be performed at all subsequent handlers, at the slaughter establishment and with FSIS in-plant inspection personnel.

A. Inspections

- (1) Program requirements for a comprehensive inspection of a producer as a source of a violative drug residue:
 - (a) Drug Use – Determine how drugs are used (violative animal and rest of herd)
 - Review all drugs on-site for application to animal type
 - Review use of all drugs used on the violative animal
 - Review use of at least three drugs (if available) that have a meat withdrawal period in its approved label or as prescribed by a licensed veterinarian (as directed), which can include those used on the violative animal.
 - Are drugs administered to treat species and class as directed?
 - Are drugs administered to treat conditions as directed?
 - Are drugs administered at the total dosage and site dosage level as directed?
 - Are drugs administered via route, site location, site rotation as directed?
 - Are drugs administered at the frequency and duration as directed?

- Are drug withdrawal periods observed?
 - Do prescribed drugs for extralabel use meet provisions of 21 CFR Part 530?
- (b) Drug Management – Determine drug residue avoidance measures related to drug use and drug storage practices (violative animal and rest of the herd)
- Does the producer maintain a system of treatment records?
 - Is drug inventory/accountability maintained?
 - Are veterinary prescription drugs only obtained through or on the lawful order of a licensed veterinarian based on a valid VCPR?
 - Are expired drugs discarded/segregated?
 - Is there a system in place to control the administration of drug treatments to food-producing animals?
 - Is cross-contamination of medicated and non-medicated feeds or liquids prevented?
- (c) Medicated Animal Management – Determine drug residue avoidance measures related to treated animals (violative animal and rest of herd)
- Is individual animal identity maintained?
 - Are treated animals identified or segregated from the herd?
 - Prior to marketing treated animals, is a pre-shipment review of approved directions and withdrawal periods conducted?
 - Is colostrum or milk from treated animals fed to veal calves?
 - Is animal medication status determined for new acquisitions?

Reminder: This part (Part III – Inspectional) must be used in conjunction with the following inspectional resources located at [CVM Drug Residue Program Resources – *Producer Inspections, Veterinarian Inspections, Ancillary Investigations, and Elements of Affidavits.*](#)

For situations where an inspection reveals the source identified by FSIS is not responsible for the violative drug residue, the Division should determine if follow-up is warranted to identify the true source of the animal and determine responsibility for the residue. Some things to consider include:

- information discovered during the inspection,
- the Division’s available resources to perform additional follow-up activities related to a new source, and
- priority scoring of the new source based on violative history.

The following are factors to consider when determining initial classification under PAC 71006. For Veterinary Feed Directive (PAC 71023), refer to [CPGM 7371.000 Comprehensive Animal Food Inspection.](#)

- Inspectional Findings:
 - Has ownership of the violative animal been established and documented?
 - Has responsibility for the violation been determined?
 - Were inspectional observations issued to and/or discussed with management?
- Corrective Actions:
 - Did the source take corrective action when notified by the slaughter establishment of the current violative drug residue(s)?
 - Was corrective action taken in response to the FSIS Violation Notification Letter?
 - Did the firm take corrective action after previous FDA inspection(s)?
 - Was corrective action initiated and verified during the current FDA inspection?
 - Was corrective action promised during/after the current FDA inspection?
- Compliance History:
 - Has the source caused or been involved in prior drug residue violations?
 - Has the source been inspected by FDA or state agencies in the past because of a drug residue(s)?
 - Has the source received an advisory (e.g., Untitled Letter [UL], Warning Letter [WL], Regulatory Meeting) or judicial action (e.g., Injunction, Seizure) because of a violative drug residue?

See [Part V – REGULATORY/ADMINISTRATIVE STRATEGY](#) for information on inspectional outcomes and compliance actions.

- (2) Directed inspection of other entities (e.g., haulers, dealers, sale barns), as a source of drug residue violation:

See [B. Investigations](#) below and [CVM Drug Residue Program Resources – Ancillary Investigations](#) and [Elements of Affidavits](#).

- (3) Directed inspection of a veterinary firm is required when the drug associated with a violative residue was prescribed or administered by the veterinarian to:
- determine the veterinarian’s involvement in treatment of the violative animal,
 - determine compliance with the ELDU regulations ([21 CFR Part 530](#)), and
 - determine if a valid VCPR exists and if the prescribed drug was used as directed by the veterinarian.

For additional inspection instructions, see [CVM Drug Residue Program Resources – Veterinarian Inspection, and Elements of Affidavits](#).

B. Investigations

Ancillary investigations of haulers, dealers, sale barns, or FSIS Establishments may be performed, in conjunction with inspections of sources identified by FSIS, to collect

additional evidence or determine if anyone else in the chain of custody shares responsibility for the drug residue violation(s). The need for investigations will be assessed on an individual basis, depending on inspectional findings at the source or if needed to support compliance actions.

Investigations should determine and document relevant information, including the following:

- animal identification and traceability,
- unusual time gaps in the movement of animal to market,
- interstate commerce,
- knowledge of the medication status of the violative animal(s), and
- medication treatment(s).

For additional inspection instructions, see [CVM Drug Residue Program Resources – Ancillary Investigations and Elements of Affidavits](#).

C. Sample Collections

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D. Import Activities

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2. Reporting

Investigators must follow reporting guidance identified in [IOM](#) Chapter 5.11 – Reporting.

Report completed operations in eNSpect/FACTS under Program Assignment Code (PAC) 71006 or 71S006 (State Contract).

After inspections of all sources of a violative drug residue sample reported by FSIS, Supervisory Investigators or Drug Residue Program Monitors must:

- Complete [CVM Drug Residue Program Resources – Post Inspection Report](#), (fillable Excel template), identifying the responsibility of each source for a violative sample and any source changes/updates.
- E-mail completed Post Inspection Reports to CVM, Division of Food Compliance (DFC), Regulatory Policy and Programs Team at CVMDrugResidueProgram@fda.hhs.gov.
 - Post inspection reports are due on the first Friday of each month.

For violative inspection reporting, see [Part V – 5. Enforcement Actions](#).

PART IV – ANALYTICAL

1. Analyzing Laboratories

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2. Analyses to be Conducted

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3. Methodology

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4. Reporting

Analytical Inquiries

ORA/ Office of Regulatory Science

oraorofflloiochem@fda.hhs.gov

PART V – REGULATORY/ADMINISTRATIVE STRATEGY

1. General Considerations

Voluntary correction is often the most effective and expedient means to protect public health and obtain compliance. ORA Divisions should take steps to encourage voluntary correction prior to considering enforcement action. When voluntary correction is not forthcoming or adequate, the Agency should pursue routine regulatory procedures to address significant observations. See [FMD-86 – Establishment Inspection Report Conclusions and Decisions](#) for further guidance.

For questions regarding advisory actions, inspectional findings, observations, or recommended actions, the Division should contact CVM prior to issuance of the Form FDA-483, Inspectional Observations. See CVM Program Contacts in [CVM Drug Residue Program Resources](#).

For inspections likely to result in [judicial actions](#), Division management is required to schedule a pre-closeout meeting with CVM prior to issuance of the Form FDA-483, Inspectional Observations and closing the inspection. See CVM Program Contacts in [CVM Drug Residue Program Resources](#).

2. Inspection Classification

A comprehensive inspectional approach is utilized to evaluate sources that medicate and market food-producing animals, to determine responsibility for and cause of the drug residue of the violative animal, and to identify systemic deficiencies related to drug use, drug management and medicated animal management. Through this broad-based approach, we can best evaluate the factors leading to a violative drug residue and determine if they were isolated or systemic. See [Part III – INSPECTIONAL](#) and [CVM Drug Residue Program Resources](#).

Inspectional Observations which are listed on Form FDA-483, should be significant objectionable conditions and correlate to regulated products. See [IOM Chapter 5.2.3 – Reports of Observations](#). FDA-483 citations for use under this compliance program are categorized by the public health concern that noncompliance may pose. See [CVM Drug Residue Program Resources – CVM Drug Residue Cites](#). The citation categories are identified as minor, major, and critical in order of least to most significant. Citations categorized as major or critical are considered significant violations and should be listed on an FDA-483. Minor citations are not considered a significant public health concern and are generally considered to be discussion items that do not necessarily need to be listed on an FDA-483.

Determination of violative inspectional classification (VAI or OAI) and potential enforcement action should be based on current and historical regulatory noncompliance by a firm or individual(s). Current inspectional findings for consideration include evidence a firm, product, or individual is in violation of the law or regulations; violations

of regulatory significance; and reasonable expectation that the responsible firm or responsible individual(s) will take prompt corrective action. Regarding historical regulatory noncompliance, consider if there have been any significant violations attributed to the firm or individual(s), and when applicable, if any corrective actions have been implemented to prevent recurrence of those violations.

The potential for voluntary compliance should be assessed prior to final classification. See [RPM](#) Section 4-1-8.4 – *Inspection Classification* and Section 4-1-3 – *Issuing Warning Letters - Factors to Consider*.

The following are examples of inspectional classifications or situations warranting enforcement actions. This list is not intended to be all inclusive or eliminate evaluations on a case-by-case basis.

Note: All compliance actions require CVM review and concurrence (i.e., direct reference authority is not provided).

A. Voluntary Action Indicated (VAI)

When considering VAI, the situations referenced below generally apply to a source that does NOT have a history of violative drug residues or previous FDA regulatory action.

- Medicated food-producing animals held under conditions that lack sufficient measures to avoid violative drug residues (e.g., do not record drug treatments of drugs that require a withdrawal period, do not identify or segregate medicated animals, etc.).
- Drug use in food-producing animals that is contrary to approved use and not in conformance with ELDU regulations. *
- Responsibility for causing a violative drug residue in edible tissue. *
Note: The examples with an asterisk (*) may warrant OAI classification, regardless of violative drug residue history, under the following situations:
- A broad-based review of conditions could not be performed during an inspection due to a producer's lack of cooperation and an apparent lack of capability or willingness to voluntarily comply with FDA law or regulations, or
- an unapproved drug was used to treat food-producing animals.

Note: There may be situations in which the initial classification is OAI but changes to VAI. For instance, management provided an adequate response or corrective action within established timeframes (e.g., during the inspection or within fifteen (15) working days after the issuance of Inspectional Observations on Form FDA-483).

B. Official Action Indicated (OAI)

OAI classification may be warranted, regardless of violative drug residue history, under the following situations:

- A broad-based review of conditions could not be performed during an inspection due to a producer's lack of cooperation and an apparent lack of capability or willingness to voluntarily comply with FDA law or regulations, or
- an unapproved drug was used to treat food-producing animals.

Additionally, for sources with a history of violative drug residues or previous FDA regulatory action, OAI may be warranted if one or more of the following situations occurred:

- The violative drug residue was caused through use of a drug contrary to its approved labeling and not in conformance with ELDU regulations,
- source demonstrates a pattern of using a drug in food-producing animals contrary to approved labeling and not in conformance with ELDU regulations,
- source demonstrates a pattern of holding medicated food-producing animals under conditions that lack sufficient measures to avoid violative drug residues (e.g., do not record drug treatments for drugs requiring a withdrawal period, do not maintain a drug inventory, etc.), and
- significant adverse conditions are observed, and management does not provide an adequate response or corrective action plan that demonstrates effective and consistent implementation within established timeframes (e.g., no adequate corrective actions taken during inspection or reported after fifteen (15) working days).

3. Jurisdictional Considerations

A. What is Food

The Federal Food, Drug, and Cosmetic Act (the FD&C Act) (21 U.S.C. 321(f)) defines food as “(1) articles used for food or drink for man or other animals...and (3) articles used for components of any such article.” (Section 201(f)). Food-producing animals and fish, even though not in their final, edible form, have been held to be food under the FD&C Act (see *United States v. Tomahara Enterprises Ltd.*, Food Drug Cosm. L. Rep. (CCH) 38,217 (N.D.N.Y. 1983) (live calves intended as veal are food) and *United States v. Tunte Livestock*, 888 F. Supp. 1416, 1423-26 (S.D. Ohio 1995) (live hogs are food)). Thus, live animals raised for food are “food” under the FD&C Act.

B. Interstate Commerce (IS)

For FDA to take enforcement action, interstate commerce must be documented for each violation cited. For examples of documentation, see [IOM 4.4.7 – Documenting Interstate Shipments](#).

Interstate commerce for the drug may be established by:

- a bill of lading or other shipping records; or
- an approved drug label that states that the drug was manufactured in a different state or country; or
 - Note: Be sure this is where the drug was manufactured (e.g., manufactured at) and not the manufacturer’s headquarters location (e.g., manufactured by).
- a signed letter or affidavit from the drug manufacturer, dated within six months from when the animal was treated, stating where the drug is manufactured.
 - Note: See [CVM Drug Residue Program Resources – Drug Manufacturing Letters](#).

Interstate commerce for the food (either the living animal or edible tissues from the animal) may be supported by:

- documents showing the violative animal was acquired from an out-of-state vendor; or
- documents showing transport of the violative animal across state lines; or
- documents showing that the involved sale barn or slaughter/processing establishment ships food-producing animals or food in interstate commerce.
 - If documenting interstate commerce is dependent on the movement of food from the slaughter establishment and IS has been documented at that establishment within the six (6) months prior to collection of the violative sample, a visit to the slaughter establishment should not be required.

C. Responsibility

Persons directly or indirectly responsible for the introduction into interstate commerce of a violative animal may be charged with violations of the FD&C Act (see 21 USC sec. 331). For example, a buyer or seller may be held responsible if an animal was introduced into IS without assuring that the animal was free of violative residues.

4. Commonly used FD&C Act and Code of Federal Regulations (CFR) Citations

The citations used for illegal drug residue in edible tissue cases depend on the facts of each case. However, the most common citations are listed below:

- [21 CFR Part 530](#): Sets forth requirements for ELDU in animals. Specifically,

- 21 CFR 530.11: Identifies specific extralabel uses that are not permitted and result in the drug being deemed unsafe within the meanings of Section 512 of the FD&C Act.
- 21 CFR 530.41: Lists the approved animal drugs and approved human drugs, families of drugs, and substances that are prohibited from extralabel use in food-producing animals. Extralabel use of an approved drug that is prohibited from such use, results in the drug being deemed unsafe within the meaning of Section 512 of the FD&C Act.
- [Section 402\(a\)\(2\)\(C\)\(ii\)](#): Specifies that a food is adulterated if it contains a new animal drug(s), which is unsafe within the meanings of Section 512 of the FD&C Act. This citation may be used for analytical findings of illegal drug residue(s) in edible tissue(s) collected and reported by FSIS.
- [Section 402\(a\)\(4\)](#): Specifies that food is adulterated if it is held under insanitary conditions. This citation may be used when there is a systemic lack of drug residue avoidance measures such as: medicated food-producing animals that are not identified or segregated; treatment records of food-producing animals that are not maintained or complete; and feeding milk from medicated cows to calves intended for slaughter. See [CVM Drug Residue Program Resources – *Producer Inspection*](#) and [CPG 615.200 – *Proper Use and Residue Avoidance by Non-Veterinarian*](#) for additional considerations.
- [Section 501\(a\)\(5\)](#): Specifies that a drug is adulterated if it is a new animal drug which is unsafe within the meaning of Section 512 of the FD&C Act.
 - This citation may be used if the new animal drug is deemed unsafe because:
 - it is not approved, conditionally approved, or indexed; or
 - it is approved and not used in conformance with the approval, conditional approval, or index listing; or
 - it is not used in conformance with 21 CFR Part 530 – *Extralabel Drug Use in Animals*.
 - An example may be the use of an approved animal drug that is not in conformance with the approved directed use and without a valid VCPR and/or is not in conformance with 21 CFR Part 530.
- [Section 501\(a\)\(6\)](#): Specifies that a drug is adulterated if it is an animal feed bearing or containing a new animal drug, and such animal feed is unsafe within the meaning of Section 512 of the FD&C Act.
 - This citation may be used when an animal feed contains a new animal drug that is deemed unsafe because:
 - it is not approved, conditionally approved, or indexed; or
 - it is approved and not used in conformance with the approval, conditional approval, or index listing; or
 - it is used in an extralabel manner which is not permitted in 21 CFR Part 530 – *Extralabel Drug Use in Animals*.
 - An example may be medicated milk replacer fed to bob veal calves in an extralabel manner.

- [Section 301\(h\)](#): The giving of a guaranty, which is a false guaranty. This citation may be used for a firm or producer signing a false statement that any animal(s) introduced or delivered for introduction into interstate commerce does not have illegal drug residues. Note that although Section 302 of the FD&C Act does not authorize injunctive relief for a Section 301(h) violation, you should include this citation in Warning and Untitled Letters. See [CVM Drug Residue Program Resources](#) – [Warning Letters](#) for specific placement of this citation within the letter.

5. Enforcement Actions

If it is determined that the firm's corrective action is inadequate to protect animal or human health, all available enforcement tools should be considered such as a regulatory meeting, untitled letter, warning letter, or injunction. For questions regarding advisory actions, inspectional findings, observations, or recommended actions, the ORA Division may contact CVM. For judicial actions (e.g., injunction), the ORA Division must contact CVM to discuss findings prior to inspectional close out.

Note: All regulatory actions taken due to violative drug residues in edible tissue require CVM concurrence (i.e., no direct reference authority).

A. Advisory Actions

Advisory Actions notify responsible parties about violations of the FD&C Act. These actions include Regulatory Meetings, Untitled Letters, and Warning Letters. See [IOM](#) Subchapter 4.4.3 – *Policy* and [RPM](#) Chapter 4 – *Advisory Actions*.

(1) Regulatory Meeting

A Regulatory Meeting is a meeting requested by FDA management, at its discretion, to inform responsible individuals or firms about how one or more products, practices, processes, or other activities are considered in violation of the law. Regulatory Meetings can be an effective tool to obtain prompt voluntary compliance and have been used successfully in a variety of different situations, including, but not limited to: (1) in conjunction with another advisory action (e.g., untitled or warning letter), (2) as a follow-up to other advisory actions, or (3) to communicate violations that would not warrant another type of advisory action. Regulatory meetings provide the benefit of a real time, two-way discussion about the violations and appropriate corrective actions. See [RPM](#) Section 10-3 – *Regulatory Meetings*.

(2) Untitled Letter

Untitled Letters (UL) are typically used in response to an inspection that has a final classification of OAI. See [Part V – 2 Inspectional Classification](#).

- Submit UL to CVM in accordance with timeframes identified in [RPM](#) Chapter 4 – *Advisory Actions*. Untitled Letters should be issued within six months of the date of last evidence collection and within twelve months of the date of the violative drug residue analysis.
- Include in the recommendation to CVM the last date evidence was collected. Also include dates of visits made to the veterinarian, sale barn, dealer, slaughter establishment, correspondence from the firm, etc.

See [6. Compliance Elements of a Case Package](#) below for additional guidelines on submitting a case for an UL to CVM.

(3) Warning Letter

A Warning Letter (WL) serves to establish notice of violations and provide an opportunity for the responsible party to take voluntary and prompt corrective action. Generally, a WL is in response to an inspection that has a final classification of OAI. See [CVM Drug Residue Program Resources – Warning Letters](#). Submit WL to CVM in accordance with timeframes identified in [RPM](#) Chapter 4 – *Advisory Actions*. WL should be issued within four months of the date of last evidence collection and within twelve months of the date of the violative drug residue analysis.

- Include in the recommendation to CVM the last date evidence was collected. Also include dates of visits made to the veterinarian, sale barn, dealer, slaughter establishments, correspondence from the firm, etc.

See [6. Compliance Elements of a Case Package](#) below for additional guidelines on submitting a case for a WL to CVM.

(4) Warning Letter Follow-Up Activities

Follow-up inspection to a WL is a valuable compliance activity to verify implementation of a firm's promised corrective actions. See [RPM](#) Section 4-1-8 – *Warning Letter Follow-Up*.

- High priority for follow-up inspection should be given to cases where a violative drug residue occurred after receipt of a prior WL and/or a pattern of widespread adverse conditions exists (as discussed in classification section above).
- Warning Letters based solely on 402 (a)(2)(C)(ii) citation may not lend themselves to WL follow-up inspection. This citation is based on violative sample findings as opposed to observations made during inspection. Therefore, unless there are subsequent violative drug residues, there may not be any corrective actions to verify.

- The Division should document the decision to perform a follow-up inspection as described in [RPM](#) Section 4-1-8 – *Warning Letter Follow-Up*.
- If the follow-up inspection reveals conditions that continue to be significantly adverse and/or widespread, the Division should document Inspectional Observations on an FDA Form-483. Depending on the egregiousness of the conditions found and the ineffectiveness of the implemented corrective actions, CVM may support additional actions such as holding a Regulatory Meeting to discuss these violations with the inspected firm. Contact CVM to discuss the follow-up inspection findings prior to classifying the inspection. See [FMD-86 – Establishment Inspection Report Conclusions and Decisions](#), 6.7 *Follow-up Inspections to Inspections Classified as OAI*.

B. Judicial Actions

CVM's general practice is to establish prior notice and attempt to obtain voluntary compliance using advisory actions prior to pursuing judicial action. When voluntary correction is not forthcoming or adequate, or violations present a significant risk to public health, the Agency may pursue judicial actions to obtain compliance. See [RPM](#) Chapter 6 – *Judicial Actions*.

(1) Injunction

Firms with a history of significant repetitive or ongoing violations that have not been corrected and are likely to recur are strong candidates for an injunction. To prevent the distribution of violative products in IS and to correct conditions that caused violations to occur, court action may be required.

When recommending injunction, include a description of the scope and size of the firm's operation and a summary of the firm's history of non-compliance, including jurisdiction, interstate commerce, violations, and responsibility.

Once a Court orders injunctive relief, it is essential that the Division conduct compliance follow-up inspections as described in the [RPM](#) Section 6-2-15 – *Compliance Follow-Up*. In addition, if another drug residue violation occurs after the Court orders injunctive relief or after the Court signs off on the Consent Decree, conduct a follow-up inspection.

Contact CVM to discuss findings of the follow-up inspection. CVM and the Division may then contact the Office of Chief Counsel (OCC) to discuss enforcement options.

(2) Seizure

Seizure should be considered in accordance with the guidelines and procedures in [RPM](#) Section 6-1-2 – *General Guidelines for Seizures* when unapproved animal

or human drugs that pose a reasonable likelihood of an immediate risk to human or animal health are found at the establishment. Live animals should not be considered for seizure.

(3) Prosecution

All criminal referrals, whether initiated by CVM or ORA, must be sent to the Office of Criminal Investigations. Refer to [RPM](#) Chapter 6-5 – *Prosecution*.

6. Compliance Elements of a Case Package

The ORA Division is responsible for submission of a complete package for violative drug residue cases. Every effort should be made to verify that all necessary documentation has been obtained, all relevant sample packages are included, and all evidence and supporting documentation are adequate. Evidence to demonstrate and document the elements of proof (Jurisdiction, Interstate Commerce, Violation, and Responsibility, or JIVR) is necessary for advisory and judicial action.

Upload the following, and any additional supporting documents, into CMS:

- Establishment Inspection Report(s) and Memorandum of Investigation(s),
- All related FSIS sample documents [FSIS's Sample package(s)],
- Notice of Inspection (Form FDA-482),
- Inspection Observations (Form FDA-483),
- Appropriate interstate documentation related to food or all drug(s) violations,
- Affidavits (Form FDA-463a) to support interstate commerce, practices, custody, and events related to the violative drug residue, drug misuse, and insufficient avoidance measures. See [CVM Drug Residue Program Resources – Elements of Affidavits](#),
- Exhibits of all applicable and/or violative drugs, and/or medicated feed labels and other pertinent labeling,
- Copies of certificate(s) of guarantee,
- Copies of food-producing animal treatment records that demonstrate treatment of the violative animal, improper drug use, or inadequate record keeping,
- Copies of any veterinary orders, instructions, or other documents with directions for medicating food-producing animals,
- Documentary samples:
 - For advisory action (e.g., untitled letters, warning letters, or regulatory meetings), JIVR should be collected and included as part of the EIR but does not need to be submitted as a documentary sample.
 - For judicial or administrative actions (e.g., injunction, seizure, warrant, prosecution, etc.), JIVR should be included with the EIR, and a documentary sample of interstate commerce records should be collected for each violative animal and for the drug(s) used to treat the animal(s).

- Division recommendation memorandum explaining the details of the case and noting any weaknesses,
- Draft Warning/Untitled Letter,
- Copies of firm's written response(s) and if applicable, examples of corrective actions to the current inspection.

PART VI – REFERENCES, ATTACHMENTS, AND PROGRAM CONTACTS**1. References**

- A. Adequate Drug Treatment Records Help Ensure Food Safety**
- B. Animal Drugs @ FDA**
- C. Animal Medicinal Drug Use Clarification Act (AMDUCA)**
- D. Compliance Policy Guide (CPG) 615.200 – Proper Drug Use and Residue Avoidance by Non-Veterinarian**
- E. Classes of Major Food-Producing Animals**
- F. CPGM 7371.000 Comprehensive Animal Food Inspection – see VFD**
- G. eNSpect**
- H. FDA Label Search**
- I. FDA Regulation of Animal Drugs – Dispensing Veterinary Prescription Drugs**
- J. Field Management Directive (FMD) 86 – Establishment Inspection Report Conclusions and Decisions**
- K. Federal Food, Drug, and Cosmetic Act (FD&C Act)**
 - (1) Chapter 3 – Prohibited Acts and Penalties
 - a. Section 301 – Prohibited acts
 - (2) Chapter 4 – Food
 - a. Section 402 – Adulterated food
 - b. Section 403 – Misbranded food
 - (3) Chapter 5 – Drugs and Devices
 - a. Section 501 – Adulterated drugs and devices
 - b. Section 502 – Misbranded drugs and devices
 - c. Section 503 – Exemptions and consideration for certain drugs, devices, and biological products
 - d. Section 512 – New animal drugs
- L. Investigative Operations Manual (IOM)**
 - (1) Chapter S - Safety
 - (2) Chapter 4 – Sampling
 - a. IOM 4.4.7 – Documenting Interstate Shipments
 - b. IOM 4.4.8 – Affidavits
 - c. IOM 4.4.8.2 – Refusal to Sign the Affidavit
 - (3) Chapter 5 – Establishment Inspections
 - a. IOM 5.1.1.9 – Premises Used for Living Quarters
 - b. IOM 5.2 – Inspection Procedures
 - c. IOM 5.2.1.1 – Pre-Announcements
 - d. IOM 5.2.1.2 – Personal Safety
 - e. IOM 5.2.1.3 – eNSpect Personal Safety Alert
 - f. IOM 5.2.1.4 – Personal Safety Plan
 - g. IOM 5.2.3 – Reports of Observations

- h. IOM 5.2.10 – *Routine Biosecurity procedures for Visits to Facilities Housing or Transporting Domestic or Wild Animals*
 - i. IOM 5.9 – *Veterinary Medicine*
 - j. IOM 5.11 – *Reporting*
- M. MOU 225-85-8400 – *Memorandum of Understanding with USDA (FSIS and AMS) and EPA regarding regulatory activities concerning residues of drugs, pesticides, and environmental contaminants in foods***
- N. Regulatory Procedures Manual (RPM)**
- (1) Chapter 4 – *Advisory Actions*
 - a. RPM 4-1-4 – *Center Concurrence and Letters Issued by Center*
 - b. RPM 4-1-8 – *Warning Letter Follow-Up*
 - c. RPM 4-2 – *Untitled Letters*
 - (2) Chapter 6 – *Judicial Actions*
 - a. RPM 6-1-2 – *General Guidelines for Seizures*
 - b. RPM 6-2-16 – *Vacating Injunctions*
 - c. RPM 6-5 – *Prosecution*
 - (3) Chapter 10 – *Other Procedures*
 - a. RPM 10-3 – *Regulatory Meetings*
- O. T.A.L.K Before You Treat**
- (1) *In English*
 - (2) *In Spanish*
- P. Title 21 Code of Federal Regulations (CFR)**
- (1) Part 530 – *Extralabel Drug Use in Animals*
 - (2) Part 556 – *Tolerances for Residues of New Animal Drugs in Food*
- Q. United States Code**
- (1) 7 U.S.C. § 181 – *Short title*
 - (2) 15 U.S.C. § 50 – *Offenses and penalties*
 - (3) 18 U.S.C. § 1001 – *Statements or entries generally*
 - (4) 20 U.S.C. § 3508 – *Department of Health and Human Services*
 - (5) 21 U.S.C. § 331 – *Prohibited acts*
 - (6) 21 U.S.C. § 342 – *Adulterated food*
 - (7) 21 U.S.C. § 351 – *Adulterated drugs and devices*
 - (8) 21 U.S.C. § 360 – *Registration of producers of drugs or devices*
- R. United States Department of Agriculture (USDA)**
- (1) Agricultural Marketing Service
 - a. *Contact Packers and Stockyards*
 - (2) Animal and Plant Health Inspection Service
 - a. *Animal Disease Traceability*
 - (3) Food Safety Inspection Service (FSIS)
 - a. *Compliance Guide for Residue Prevention 2013*
 - b. *Egg, Poultry and Egg Product Establishment Directory*
 - c. *Office Locations and Phone Numbers*

d. Residue Repeat Violator List for Use by Livestock Markets and Establishments

2. Attachments

A. Attachment A – Program Framework

3. Program Contacts

Purpose	Name	E-mail Address
General Drug Residue Compliance Program Guidance and Submission of Post Inspection Report	Sean Cheney	CVMDrugResidueProgram@fda.hhs.gov or sean.cheney@fda.hhs.gov
CVM's Regulatory Technical Assistance Network	rTAN Coordinator	CVMAnimalFoodPrograms@fda.hhs.gov
CFSAN's Regulatory Technical Assistance Network	rTAN Coordinator	rTANWorkgroup@fda.hhs.gov

PART VII – CENTER RESPONSIBILITIES

CVM’s Division of Food Compliance (DFC) is responsible for management, evaluation, and coordination of the compliance program. DFC’s activities include but are not limited to the following:

- To serve as the liaison between FSIS and FDA’s ORA to provide input into the development and implementation of the NRP for meat and poultry.
- To provide programmatic information, education, and guidance to ORA. For instance,
 - providing ORA Division’s with their respective violative drug residue sample and source information and inspectional priority score,
 - coordinating programmatic priorities with Divisions to align resources with inspectional activities,
 - generating inspection assignments to Divisions under ORA work plans, and
 - providing subject matter resources for support of investigative, compliance and enforcement activities.
- Informing FSIS of ORA investigative outcomes using FSIS’ Residue Violator Tracking (RVT) system.
- To coordinate the exchange of violative drug residue data with CFSAN, especially when the data may indicate a potential for drug residues in seafood, milk, honey, or eggs.
- To identify specific residue and/or violator trends.
- To identify, recommend, develop, and implement policies, procedures, and guidance documents to reduce the number of violative drug-residues.

ATTACHMENT A – Program Framework

This compliance program addresses consumer exposure to violative drug residues in edible tissues of food-producing animals. As defined in 21 CFR 530.3, a residue is any compound present in edible tissues that results from the use of a drug, and includes the drug, its metabolites, and any other substance formed in or on food because of the drug's use. Exposure to drug residues in food can have an impact on human health.

Assuring a safe meat and poultry supply is a responsibility shared by FDA, USDA FSIS, USDA Animal Plant Health and Inspection Service (APHIS), USDA Agricultural Marketing Service Packers and Stockyards (AMSPS), and the Environmental Protection Agency (EPA).

FSIS regulates the slaughter and processing of meat, poultry, and liquid egg products in federally inspected establishments. As part of their oversight, FSIS collects samples of the edible tissues from slaughtered livestock and poultry to screen for drug residues. When a violative drug residue is detected, the sample is sent for confirmatory testing and identification of the drug(s). If the violative residue is confirmed, FSIS will condemn the meat product from which the sample originated and will identify the producer, or source, of the violation. Once identified, the source is sent an FSIS “Violation Notification Letter.” If a source has had more than one residue violation in the preceding 12 months, they are publicly named on FSIS’ [Residue Repeat Violator List](#). See FSIS’ establishment’s “[Compliance Guide for Residue Prevention \(2013\)](#).” FSIS reports violative drug residues, and both violative and non-violative pesticide residues and other contaminants in meat and poultry, to FDA for potential follow-up.

AMSPS works closely with FSIS in regulating animal marketing practices. AMSPS is a regulatory agency within USDA charged with enforcing the Packers and Stockyards Act of 1921 (7 U.S.C. §181) through economic regulation. AMSPS often assists FDA in securing source identification when sales are through licensed sale barns or dealers. APHIS also plays a role in traceability for livestock movement in interstate commerce ([9 CFR Part 86](#)).

EPA establishes the tolerances for pesticide residues in meat and poultry. FDA enforces these tolerances. FDA’s authority is derived from section 402(a)(2)(B) of the FD&C Act. FDA is also responsible for the approval of new animal drugs, including the establishment of tolerances for residues of those drugs in edible tissues. Tolerances are established based upon residues of drugs in edible products of food-producing animals that have been treated with drugs ([21 CFR Part 556](#)).

FDA protects public health by using a risk-based approach to inspections and enforcement. FDA’s inspections are performed in response to FSIS’ reports of violative residues in food-producing animals. FDA may also conduct inspections in response to violative samples of edible tissues (e.g., honey, seafood, etc.) provided by CFSAN or as follow-up to previously violative inspections that resulted in enforcement action. These inspections serve to evaluate

the causes of the drug residue violation, drug management practices, drug use and medicated animal management to obtain regulatory compliance.

Based on FDA inspectional findings, producers are responsible for most violative drug residues due to improper drug use or not instituting drug residue avoidance measures. Inspections at the producer may also lead to investigations of other individuals/facilities who interacted in some way with the violative animal, such as haulers, buyers, dealers, sale barns, veterinarians, or slaughter establishments. In some cases, these ancillary individuals or entities are found to share responsibility for the violative drug residue. FDA's mission to protect public health is accomplished through drug residue inspections that educate industry, promote voluntary compliance, and hold accountable those individuals and facilities responsible for causing drug residue violations.

To continually improve the program, CVM develops new training courses for Federal and State investigators and inspectors to address identified training needs. CVM also organizes national cooperative meetings with officials from FDA, USDA (FSIS, AMSPS, APHIS), EPA, and individual states to coordinate and assist in drug residue avoidance and compliance activities.