EXHIBIT 19

CHAPTER: Post-Approval Monitoring of Animal Drugs, Feeds and Devices

SUBJECT: **Illegal Residues In Meat, Poultry, Seafood, and Other Animal Derived Foods**	IMPLEMENTATION DATE 08/01/2005 COMPLETION DATE Continuous

DATA REPORTING	
PRODUCT CODES	PRODUCT/ASSIGNMENT CODES
Industry codes: 16, 17, 67-69	71006, 71S006 71004 71003A

FIELD REPORTING REQUIREMENTS

1. Hardcopy Reporting

For all Federal and State investigations/inspections submit, Field Accomplishments Compliance Tracking System (Facts) Coversheet with endorsement, completed Tissue Residue Evaluation Form(s) (Attachment C), Drug Inventory Survey Form (Attachment G), to the Compliance Information Management Team, HFV-235, Attention: Fran Pell.

2. FACTS Reporting

a. Report time for all Federal drug residue follow-ups against Program Assignment Code (PAC) 71006. For state inspections of residue violations conducted under contract report time against PAC 71S006. For state inspections of residue violations conducted under cooperative agreements report the time under PAC 71006 with a state position class to identify the work as state-performed. For all inspections include the FSIS sample number in the description field of FACTS.

b. Report time for follow-up at medicated feed mills against PAC 71004.

c. Report time for Contamination Response System (CRS) investigations of non-drug residues against PAC 71003A.

PART I – BACKGROUND

This Compliance Program was developed to provide a cohesive framework for the Field to use that would include inspectional priorities, helpful technical information, and resources to facilitate the investigation of residue violations routinely reported to the Food and Drug Administration (FDA) by the United States Department of Agriculture (USDA), Food Safety and Inspection Service (FSIS). To protect consumers from potentially harmful residues in the food that they eat it is important that inspections are conducted to determine the cause of the illegal drug residues and to develop data descriptive of on-farm practices of management and animal drug use for program decision support, identification of educational needs, and policy development. This program also provides guidance for enforcement measures.. The Federal Food, Drug, and Cosmetic Act (the 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 statute 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. Tuente Livestock, 888 F. Supp. 1416, 1423-26 (S.D. Ohio 1995) (live hogs are food). More generally, courts have long held that unprocessed or unfinished articles are or can be food. *See* Otis McAllister & Co. v. United States, 194 F.2d 386, 387 (5th Cir. 1952) and cases cited there (unroasted coffee beans are food). Thus, live animals raised for food are "food" under the Act.

Tissue residue investigations may reveal:

- the illegal sale of veterinary prescription drugs
- the illegal use of bulk drugs
- the extra-label use of drugs (which includes inadequate pre-slaughter withdrawal period)
- cross-contamination of animal feeds due to poor Good Manufacturing Practices (GMPs) (21 CFR Parts 225 or 226)
- failure to follow good animal husbandry practices
- the misuse of drugs in medicated animal feeds
- the marketing of treated/medicated animals intended for rendering purposes being diverted to slaughter for human consumption
- inadequate animal identification

Protection of the public by assuring a safe meat and poultry supply is a responsibility shared by the USDA Food Safety and Inspection Service (FSIS), the Grain Inspection, Packers and Stockyards Administration (GIPSA), the Animal and Plant Health Inspection Service (APHIS), the Food and Drug Administration (FDA) and the Environmental Protection Agency (EPA), The FSIS exercises supervision over the slaughter and processing of meat and poultry products in federally inspected

establishments and is responsible for the safety of these food products. FSIS reports violative residues of drugs, and both violative and non-violative reisidues of pesticides, and other contaminants in meat and poultry to FDA for follow-up.

The GIPSA works closely with FSIS in regulating animal marketing practices. GIPSA is an enforcement agency within USDA charged with enforcing the Packers and Stockyards Act of 1921 (7 U.S.C. §181) through economic regulation. GIPSA has also assisted FDA in securing producer identification when sales are through auction barns or dealers.

A final rule on swine identification became effective on November 14, 1988. All swine in interstate commerce must be identified and records concerning identification must be maintained. USDA (APHIS and FSIS) is responsible for enforcement. (53 FR 40378, October 14, 1988).

The EPA establishes the tolerances for pesticide residues in meat and poultry. FDA enforces these tolerances.

FDA is responsible for the approval of new animal drugs, including the establishment of tolerances for residues of those drugs in edible tissues. FDA conducts investigations of FSIS-reported residues to determine the party responsible for causing the tissue residue violation and the party responsible for introducing the adulterated food into interstate commerce. The results of FDA investigations have shown that, in most instances, the animal producer is primarily responsible for the illegal drug residues because of failure to comply with drug withdrawal times, other label warnings, use of contaminated animal feeds, use of drugs for unapproved purposes, and employing poor animal husbandry practices. Investigations may also lead to other individuals such as a hauler, buyer, dealer, auction barn, veterinarian, or slaughter house.

FDA has the responsibility to ensure the safety of the seafood supply. In 1995, FDA published the final HACCP (Hazard Analysis and Critical Control Points) regulations for seafood processors (53 FR 40378, December 18, 1995) (21 CFR Parts 123 and 124). The final rule became effective on December 18, 1997. Primary processors of aquaculture products are responsible for ensuring that their HACCP Plans address systems for drug residue control. The Center for Food Safety and Applied Nutrition (CFSAN) issued a Compliance Program Guidance Manual (7304.018), Chemotherapeutics in Seafood, in FY 2002 outlining procedures for sampling aquaculture products to be tested for drug residues. This compliance program addresses sampling of product from both domestic and imported sources.

In 1994, Congress passed legislation that would allow veterinarians to prescribe drugs in a manner inconsistent with the approved new animal or new human drug labeling. This act 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 Title 21 Code of Federal Regulations Part 530. These regulations describe the specific conditions under which extralabel use is permitted.

Expansion of the Tissue Residue program has paralleled the Agency's growing concern about consumer exposure to drug residues in the edible products of food animals. For example, in 2002, the Agency became aware of the use of drugs in the production of honey, to treat diseases of honey bees. This Compliance Program has been expanded to address this concern.

In an effort continually to improve the program, CVM develops new training courses for Federal and State investigators to address identified training needs. CVM also organizes national cooperative meetings with officials from FDA, FSIS, GIPSA, APHIS and individual states, writes educational articles, and conducts industry outreach programs in an effort to provide message-specific information to educate firms on sound drug use and residue prevention practices.

CVM encourages the District Offices to develop cooperative agreements (i.e., contracts, partnership agreements, memoranda of understanding, and informal arrangements) with their state agencies to conduct initial inspections. These inspections are predominantly educational in nature and are extremely important in the prevention of future residues.

For residues detected in seafood products the ultimate goal is to determine the cause of the residue and pursue regulatory action. The current CFSAN sampling program focuses on drugs that are not approved for use in aquaculture.

There are currently only two drugs approved for use in honey bees, oxytetracycline and fumagillin. If a residue is reported of a drug other than the two approved drugs, then the residue was caused by an extra-label use, and may be considered a violation of AMDUCA .

PART II – IMPLEMENTATION

A. INTRODUCTION

This program provides a framework from which each District can fashion its own drug residue control initiatives. CVM requests that Districts receiving reports of violative tissue residues from USDA/FSIS take steps to protect the consumer by either conducting Federal or assigning State onsite investigations at the farm level and other points of responsibility throughout the marketing chain, and to initiate actions commensurate with the findings.

CVM will issue FACTS assignments to request Federal investigation of repeat violators. CVM will also issue inspectional assignments via FACTS for violative residues detected in seafood and other animal derived human food. The Districts are encouraged to recommend enforcement action for such violations.

B. OBJECTIVES

- To conduct investigations/inspections to determine the cause of illegal drug residues and/or shipment of adulterated food.
- To develop data descriptive of on-farm practices of management and animal drug use for program decision support, identification of educational needs, and policy development.
- To obtain correction through voluntary and/or enforcement actions.

C. PROGRAM MANAGEMENT INSTRUCTIONS

1. Inspectional

FDA Districts conduct on-site inspections in the follow-up of violative tissue residue findings of public health concern reported to them by FSIS. In association with these assignments the Districts should investigate all those in the marketing chain who may have acted irresponsibly.

Districts are encouraged to watch for trends or patterns in types of residues or involved parties; for example, the same buyer/dealer involved in a number of residues or a sudden increase in residue reports involving the same drug. The Residue Violation Information System (RVIS) is an excellent source for this type of data on residues.

The Agency's approach to focusing on individual firms for case development will be to use a coordinated team approach when determining which case(s) to pursue. If the District believes that it should develop a case on a specific producer or someone in the marketing chain please contact the Compliance Information Management

Team, HFV-235, Randy Arbaugh or Deborah Cera to discuss investigational approach/priority.

Districts should request intensified sampling of egregious firms in an effort to obtain timely residues to facilitate case development. Please submit such requests via email to the Compliance Information Management Team, HFV-235, Deborah Cera, who will handle coordination with the FSIS Technical Services Center. In order to facilitate successful sample collection please be sure to provide as much relevant information as possible regarding the firm's marketing practices, e.g., what slaughter plant(s) they use, are animals delivered directly to slaughter, or through a middleman (provide name), and on what day of the week do the animals generally go to slaughter.

NOTE:
The current CFSAN Compliance Program, 7304.018, Chemotherapeutics in Seafood, is a sample collection program designed to test for drugs that that are not approved for use in aquaculture. If a domestic sample is found to be positive, CVM will issue an assignment for follow-up to document the violation. Case development should be considered for such residues with all questions directed to the Compliance Information Management Team, HFV-235, Fran Pell.

To discuss case development for drug residues in meat and poultry contact the Enforcement and Regulatory Policy Team, HFV-232, Reginald Walker. For all other residues detected in animal derived foods, contact Compliance Information Management Team, HFV-235, Fran Pell, to discuss case development.

Pesticide and industrial chemical residues, mycotoxin contamination, microbiological residues, and heavy metals reported to the Districts by FSIS under its Contamination Response System (CRS) will be covered under the Feed Contaminants Program (7371.003). Under unique conditions, certain violative drug residues may be reported through the CRS. Follow-up investigational time for CRS drug residues should be charged to this program (7371.006). Contact the Enforcement and Regulatory Policy Team, HFV-232, Sandra Washington before initiating a follow-up to a CRS report.

a. On-Site Inspections by FDA of Meat and Poultry Violations

1) **Repeat Violators:** This is the **top priority** for FDA inspections/investigations. Firms or individuals who repeatedly present adulterated animals for slaughter may represent a significant public health risk. Therefore, CVM will issue an assignment to the District in FACTS requesting an FDA on-site investigation for each repeat violator. A repeat violator is an individual who sells a slaughter animal whose carcass is found to contain a violative concentration of a drug, pesticide, or environmental contaminant within a 12-month period after the first violation and after receiving the FSIS Notification Letter.

2) **First-time Violators:** As resource allow, conduct an on-site inspection/investigation for first-time violators when FSIS reports violative tissue residues for the following situations:

- Drugs prohibited from extra-label use in food-animal use - chloramphenicol, diethylstilbestrol (DES), nitrofurans (furazolidone, nitrofurazone), or nitroimidazoles (e.g., dimetridazole, ipronidazole), clenbuterol, sulfonamides in lactating dairy cattle (except approved use of sulfadimethoxine, sulfabromomethazine and sulfaethoxypyridazine), fluoroquinolines, glycopeptides, and phenylbutazone in female dairy cattle 20 months of age or older.

- Drugs not approved for food animal use: beta agonists (e.g., fenoterol, salbutamol), tranquilizers, etc.

- Very high level residues, indicating intentional misuse of the drug and/or a complete disregard for the withdrawal period.

- Drug tissue residues reported under the CRS. These assignments will be issued from CVM.

NOTE:
If none of the above criteria is met on an initial residue violation then resource constraints do not allow for an FDA investigation. Cooperating State agencies should be assigned inspections of all other first-time violators to determine the cause of the residue and to attempt to prevent a repeat violation through education and/or any regulatory action deemed appropriate by the State.

b. On-Site Inspections by FDA of Seafood.

The drugs that are being tested for in Seafood are for unapproved drugs. All violations require an FDA follow-up and a FACTS assignments will be issued by CVM.

c. Investigation of Food Animal Marketing Firms

Focusing on firms/people responsible for the delivery for introduction or the introduction into interstate commerce of adulterated products is an important concept under this program. Experience has shown that investigations can lead to producers, haulers, dealers, auction barns, and buyers, any one of which may be held responsible for the violation. Parties throughout the chain of distribution may act irresponsibly by not determining if animals they handle are medicated or not forwarding this information to the next person or firm in the marketing chain. For example, a dealer or auction barn can take precautions by determining if animals are medicated and selling them as such. Dealers have been found to purchase medicated animals supposedly for dog food and then offer them for sale at a slaughterhouse for human food. Please relay these incidences to the local Grain Inspection Packers and Stockyards Administration. Any animal offered for sale at a USDA licensed slaughter facility is for human food. Implementation of the marketing chain strategy should be coordinated at the local and national levels between FDA, FSIS, APHIS, and GIPSA and State agencies. For example, we can request that FSIS increase sampling of a producer or dealer's animals. The goal is to use the expertise and the legal tools possessed by each group. FDA is the lead agency in collecting evidence and initiating regulatory action.

Districts should work closely with the Enforcement and Regulatory Policy Team, HFV-232, Reginald Walker at the onset of selecting a firm or individual for possible regulatory action.

d. Inspections at Aquaculture Farms

There are six drugs approved for use in aquaculture. They are: oxytetracycline, sulfadimethoxine/ormetoprim, formalin, chorionic gonadotropin, tricaine methanesulfonate and sulfamerazine. Sulfamerazine is not currently marketed. The brand names, species approved for and conditions of use can be found at:

http://www.fda.gov/cvm/aqualibtoc.htm#ApprovedDrugs

All of the drugs in the current CFSAN testing program are not approved for aquaculture use in the United States. The drugs may be labeled for non-food fish and later diverted to food fish producers. It is important to determine if the drug manufacturer or distributor is marketing these drugs for this use. If an FDA approved drug was used in an extra label manner determine if a veterinarian was involved. If so, follow-up with the veterinarian as appropriate. Determine why the producer used the drug and, if not prescribed by a veterinarian, what information was used by the producer to determine how to use the drug.

e. Inspection of other Animal-Derived Products

During inspections of other animal-derived product producers, the drug identified by the residue may have been used in an extra-label manner, so determine if there was a veterinarian involved with the use, and whether all of the conditions of AMDUCA were met.

f. Extra-label Use

The Animal Medicinal Drug Use Clarification Act became law in 1994 and the regulations implementing this law can be found in Title 21 Code of Federal Regulations Part 530 (21CFR 530). The regulations describe the conditions under which FDA approved drugs can be used in a manner inconsistent with the approved labeling as long as such use is by or on the lawful written or oral order of a licensed veterinarian within the context of a Veterinary-Client-Patient Relationship (VCPR). This regulation only applies to FDA approved drugs and the use must be therapeutic in that the animal must be sick or might die if not treated, and there needs to be a valid veterinarian client patient relationship. For more details refer to the 21CFR 530.

While AMDUCA does not permit the extra-label use of an FDA approved drug in or on feed, CVM recognizes that for some species of animals this is not always practical. FDA published a Compliance Policy Guide (CPG Sec. 615.115), 'Extra-Label Use of Medicated Feeds for Minor Species', which permits the extra-label use of medicated feed for minor species under specific circumstances. Briefly, this extra-label use can only be done upon the order of a veterinarian, the feed must be manufactured according to the approval and there is no reformulating of the feed. For aquaculture species there are two approved medicated feeds for food fish. More details can be found at:

http://www.fda.gov/ora/compliance_ref/cpg/cpgvet/cpg615-115.html

g. FSIS Special Programs

(1) FAST

FAST (Fast Antimicrobial Screen Test) is a microbial inhibition screening test. It was designed to be used by an FSIS veterinarian or a designated food inspector in a slaughter plant, for the detection of antibiotic and sulfonamide residues in livestock kidney tissue. The FAST test reacts with at least 56 different antimicrobials.

The FAST test is based on the principle that if animal tissue contains a residue of previously administered antimicrobial, fluid from the tissue will inhibit the growth of a sensitive organism on a bacterial culture plate. The plates are examined for zones of inhibition around the sample, which constitutes a positive test. The significance of the FAST test is its high degree of sensitivity over the old CAST (Calf Antibiotic Sulfa Test) test and the fact that test results can be obtained after a minimum of **6 hours** incubation to a maximum of 24 hours from the time the plate is incubated.

If the result is negative the carcass is released. If the result is positive, tissue samples (muscle, kidney, and liver) are sent to the laboratory for bioassay testing and the carcass is retained pending laboratory results.

(2) STOP

STOP (Swab Test on Premises) is an in-plant test currently being used by FSIS plant inspectors on suspect animals to test for antibiotic microbial inhibitors. STOP-positive carcasses are retained pending the receipt of results of confirmatory tests, which are automatically conducted in FSIS laboratories.

h. FSIS Condemnation Practices

Where FDA has established a tolerance for a marker residue in a target tissue FSIS will condemn the entire carcass when a violative residue is confirmed in the target tissue. For other drugs, if the liver or kidney is found to contain violative residues, they alone are condemned. In all cases if the muscle contains a violative residue then the entire carcass is condemned.

An exception to the above is the routine condemnation of the entire carcass of any non-ruminating veal calf found to contain a hormonal implant.

2. District Monitor Responsibilities

Each District should assign an individual to serve as a monitor for this compliance program. The monitor's duties should include the following:

- Review Weekly Residue Report. CVM, in consultation with the District Program Monitor, will issue assignments to the District in FACTS for FDA Investigations and enter the appropriate assignment activity code in RVIS. The Monitor should enter all activity codes for assignments and follow-ups.

- Once an investigation is completed. The Program Monitor should, review the EIR for newly identified sources, name/address, firm-type corrections, and additional middleman information. This information should then be entered into RVIS.

- The Monitor should promptly enter appropriate activity codes covering Repeat Violator Status, Completed Investigations, Regulatory Reserve Samples, and Regulatory Actions taken. Every violation followed up by an FDA or State investigator should have the FDA Responsibility Flag entered into RVIS as responsible, not responsible, or involved. This information is needed before FSIS can post a firm to its Web Report of Repeat Violators.

- Periodically review RVIS for violator/violation trends, e.g., specific middleman involvement in a number of violations or an increase in the number of residues for a specific drug. Notify the Compliance Information Management Team, Deborah Cera, Fran Pell, or Randy Arbaugh if you believe that an investigation is warranted. Keep abreast of RVIS enhancements.

- Assign State investigations per guidance contained in Part II.C.1.a. of this program. Provide the state with computer-generated Attachment C forms for TRIMS data collection and remind them to complete the Drug Inventory Survey Form (Attachment G).

- Review completed EIRs/Attachment C forms and Drug Inventory Survey forms to determine if required fields have been completed. Discuss any incomplete reports with the appropriate parties to improve the quality of future data reported.

- For all Federal and State investigations/inspections submit a copy of the Field Accomplishments Compliance Tracking System (Facts) Coversheet with endorsement, completed Tissue Residue Evaluation Form(s) (Attachment C), Drug Inventory Survey Form (Attachment G), to the Compliance Information Management Team, HFV-235, Attention: Fran Pell

- Request that the inspectors/investigators contact the District Program Monitor before the start of an on-farm follow-up so that they can get an updated violator history to ensure that additional residues have not occurred since the assignment date.

- Request the Regulatory Reserve Portion of samples for all firms that might become the subject of an enforcement action. Requests should be timely to ease FSIS's burden of sample retention. All samples not requested will be destroyed after 12 months. All requests should be directed to Don Gordon, Donald.Gordon@FSIS.USDA.Gov, Tel. No. 314-263-2680 ext. 341.

- Monitors should maintain a list of samples that they have requested to be stored in an FDA laboratory. Periodically review this list and request a Sample Destruction Notices (SDNs) be prepared through the appropriate channels in your Districts once it becomes clear that the District will not be initiating enforcement action against a firm.

- Provide the District Director, and Directors of Compliance and Investigations, where appropriate, with a list of local Repeat Violators and associated District activities, at least twice annually.

- Serve as a clearinghouse for distribution of information to cooperating State officials.

- Inform District management of all CVM/ORA-sponsored training initiatives. Recommend training of all Federal/State personnel conducting residue investigations.

- Maintain routine communications with local representatives from FSIS, APHIS, GIPSA, and the States.

- Work with CVM to distribute Industry outreach materials appropriate to address local residue concerns.

3. Analytical

Ordinarily FSIS will analyze tissues and conduct confirmatory analyses. FDA confirmatory analyses of tissue samples collected, analyzed, and confirmed by FSIS are not necessary to support regulatory action. Other tissue samples **should not** routinely be sent to the Denver District Laboratory. FSIS has agreed to run confirmatory tests on those samples that the FDA District needs to support casework. For example, if during an investigation of a neomycin residue it is revealed that a sulfa was used in combination with neomycin, a portion of the reserve sample can be sent back to FSIS for analysis for sulfas.

One exception to the above would be when FSIS reports finding a hormone implant in a veal calf submitted by a "Repeat Violator". The District should request that the reserve sample of the actual implant be shipped to the Denver District Laboratory where hormones present in the implant will be identified.

Please contact the Compliance Information Management Team, HFV-235, Deborah Cera, to facilitate requests for additional analyzes.

4. Program Interaction

When the investigation implicates a medicated feed produced by either a commercial feed mill or an on-farm mixer/feeder, conduct a comprehensive GMP inspection. For example, carbadox residues in swine generally result from feed and not dosage form drugs. Charge all time expended for GMP inspections to the Feed Manufacturing Program PAC 71004, regardless of whether done at the feed mill or the mixer-feeder. Remember, the regulations in 21 CFR Part 225 sections 225.10 to 225.115 apply to facilities manufacturing one or more medicated feeds for which an approved medicated feed mill license is required. The regulations in 21 CFR Part 225 sections 225.120 to 225.202 apply to facilities solely manufacturing medicated feeds for which an approved medicated feed mill license is not required.

When the tissue residue results from a non-drug chemical contaminant, such as pesticides, metals, mycotoxins, or microbiological contaminants, charge the time expended for follow-up investigations to PAC 71003A - Feed Contaminants Program.

The success of the Agency's program to support the prevention of the introduction and amplification of BSE in the United States is dependent on the ability of investigators to identify violative firms and operations. While initial efforts by Federal and State investigators have identified and inspected most renderers and commercial feed mills, continued efforts are needed to identify and continue to inspect all firms subject to the regulation. Ruminant feeders are an important obligation that should receive additional attention. Unless another BSE inspection has recently been conducted, add-on BSE inspections should be conducted for each ruminant feeder visited during a tissue residue follow-up. Charge time expended for such inspections to PAC 71009 – BSE/Ruminant Feed Ban Inspections.

Tissue residue monitors should maintain close contact with their Regional Milk Specialists and State milk authorities. RVIS reports of dairy animal violations are supplied to these individuals on a quarterly basis. One long-term goal is for involved agencies to share all available information related to drug residues (milk and meat) in dairy animals. This effort can maximize resource utilization in targeting enforcement actions and promoting effective residue controls.

5. Inter-Agency Agreements

See MOU 225-85-8400 - MOU between FDA, FSIS, and EPA regarding regulatory activities concerning residues of drugs, pesticides and environmental contaminants in foods, which went into effect on February 1, 1985.

6. Federal/State Relations

States participate in this program under agreements (contract, MOU, partnership, and informal) to conduct inspections. The emphasis of the State programs is to determine the cause of the residue and to provide producer education in an effort to prevent future violations.

Regions/Districts are urged to develop cooperative work sharing agreements with **each of their** states. General guidance for the development of work-sharing agreements is found in RPM Chapter 3-20. Maintain a high level of communication with cooperating States and share with them the periodic RVIS reports of State findings and results of program evaluations.

For information on the formation of agreements with States, contact the Division of Federal-State Relations, HFC-150.

PART III - INSPECTIONAL

A. Inspectional Operations

The three elements of a case for which evidence should be collected by the investigator are: jurisdiction, violation(s), and responsibility. The order in which the evidence is gathered is at the District's discretion. Because of the public health significance, the District should be attentive to steps that can be taken to prevent adulterated animals from going to market. For example, if an on-farm investigation reveals that veal calves, due to go immediately to market, are still being fed a neomycin-containing milk replacer, steps should be taken to prevent their marketing by requesting State assistance (quarantine power or other enforcement tools) and by alerting the FSIS Regional Office of the potential offering of these animals at USDA licensed slaughter facilities.

1. Jurisdiction

Establish and document interstate (IS) commerce.

Obtain affidavits from the involved auction/sales barn or slaughter facility or processing plant attesting to the fact that it routinely deals in interstate commerce and include the approximate percentage of IS business. Examples of recent records of IS sales may also be appropriate as part of the documentation with slaughter facilities or the processing plant, a current affidavit (desirably no older than 6 months for injunction or prosecution cases) is acceptable for establishing IS commerce. Call the Enforcement and Regulatory Policy Team, HFV-232, Reginald Walker for assistance/advice.

Notify the producer or other implicated person that animals or meat from animals he/she offers for sale may move in interstate commerce, even if the animals are not delivered directly into interstate commerce. In those cases in which extra-label use or other drug adulteration or misbranding charges may be appropriate, interstate jurisdiction over the drug(s) should be documented.

2. Violation

a. Meat and Poultry Residues

FSIS reports violative residues to FDA on a single-animal basis for FDA to follow-up. FSIS sample results show the amount and type of the drug detected. FSIS analysis may be limited to the identification of one drug. If investigational evidence supports the presence of another drug, call the Compliance Information Management Team (HFV-235), Deborah Cera or Fran Pell so that she can request analysis of the tissue sample for the additional compound. Animal identity problems should be worked out with the FSIS Technical Services Center, Dr. Julie Cornett, 402-221-7400, or local APHIS

Animal Identification Specialist. ID Specialists can be reached by contacting the local Veterinary Services Office. (See Attachment D) The identification of the responsible party given by FSIS **should** be positively confirmed by the FDA investigation. Use ear tag numbers, lot numbers, or other means to adequately link the animal to the producer/party responsible for the violation. FSIS, APHIS, and GIPSA can assist in responsible party identity.

NOTE: When doing a follow-up of a repeat violator that has received FDA prior warning, an affidavit should be obtained from all FSIS in-plant inspectors associated with each residue. Please notify the FSIS Technical Services Center, Dr. Julie Cornett, 402-221-7400 to arrange for and authorize a time for you to meet with the appropriate inspector(s) to obtain necessary documentation. (See Attachment F for an example of the kind of affidavit needed.)

Medication/treatment resulting in illegal residues may be performed by the grower/feedlot, veterinarian, or in rare cases, by the dealer, hauler, auction barn, buyer, or slaughterhouse. Because of the number of people involved in the marketing chain, it is essential that time factors and animal identity is well-documented. For example, if an animal is slaughtered within 24 hours of leaving the farm, it is unlikely that a middleman treated the animal. Collect affidavits from middlemen affirming that whether or not drugs were used on the animal.

Many residues are caused by conditions conducive to potential tissue residue violations at the farm, i.e., "poor husbandry practices." When doing an investigation at the producer, determine and describe the conditions you observe. That should include <u>at least</u> the following:

(1) Inventory all drugs on the premises (See Attachment G).

(2) Determine and list other drug-containing products, such as medicated feeds, or other drug sources, that could have been, or are being used in food-producing animals. Although most violative residues result from direct misuse of drugs in the animals, tissue residue investigations have revealed residues resulting from cross-contamination of withdrawal feeds with medicated feeds in feeding bins, or from feeding calves milk from treated cows. If possible, physical or documentary samples of drugs or feeds should be collected if implicated in the residue.

(3) Describe where the drugs are stored, how they are stored, and who has access to the drugs.

(4) Determine who administers medication and try to interview those individuals about their medication practices (who determines what animals are to be medicated, how are the medications selected, how are dosages determined, etc.).

(5) Determine identification systems and segregation/quarantine practices, if any, for medicated animals.

(6) Determine if medication records are maintained. Describe the record system. Do they include the date of medication, the drug used, the dosage administered, milk withholding and slaughter withdrawal times, etc.

(7) Determine how the producer has assured that **withdrawal times** are met prior to marketing.

Look for and document fraudulent buying or selling practices (violations of Packers and Stockyards Act and regulations) and the giving of false certificates or guarantees. GIPSA has been successful in levying substantial administrative fines for such violations. All swine in interstate commerce must be identified and records concerning identification must be maintained (9 CFR Part 71). This rule was published by USDA **(APHIS and FSIS) and they will** be responsible for its enforcement. If FDA Field offices encounter problems with identification of swine, these should be reported to, and worked out with your APHIS Animal ID Coordinator. We are also requesting that you alert CVM to these problems by reporting them to the Compliance Information Management Team, HFV-235, Deborah Cera.

We recommend objectionable conditions be listed on a FDA 483, and discussed with management at the conclusion of the inspection. Record the applicable information on Attachment C.

b. Seafood and Aquaculture Residues

All drugs that the Agency is currently testing for in seafood are not approved for use in aquaculture. The list of approved drugs can be found at:

http://www.fda.gov/cvm/aqualibtoc.htm#ApprovedDrugs

Some compounds are not traditional drugs but based on their intended use, 'to treat or mitigate a disease' they can be considered drugs. One example of a compound that falls into this category is malachite green. When doing an investigation at the producer, determine and describe the conditions that you observe. That should include at least the following:

(1) Inventory all drugs on the premises.

(2) Determine and list other drug-containing products, such as medicated feeds, or other drug sources, that could have been, or are being used in fish. Although most violative residues result from direct misuse of drugs in the fish, tissue residue investigations have revealed residues resulting from cross-contamination of withdrawal feeds with medicated feeds in feed storage bins. If possible, physical or documentary samples of drugs or feeds should be collected if implicated in the residue.

(3) Describe where the drugs are stored, how they are stored, and who has access to the drugs.

(4) Determine who administers medication and try to interview those individuals about their medication practices (who determines what fish are to be medicated, how are the medications selected, how are dosages determined, etc.).

(5) Determine identification systems and segregation/quarantine practices, if any, for medicated fish. Keep in mind fish are normally medicated in their pond/raceway/net pen. They would medicate all the fish in that group. Brood fish may be individually medicated.

(6) Determine if medication records are maintained. Describe the record system. Do they include the date of medication, the drug used, the dosage administered, and slaughter withdrawal times, etc.

(7) Determine how the producer has assured that **withdrawal times** have been met prior to marketing.

3. Responsibility

Determine and document who committed the violation, i.e., who did what, and when. This would include: misuse of approved drugs, use of illegal and unapproved drugs, GMP violations, and poor animal husbandry practices that could contribute to causing the violative drug residue, and the issuance of false certificates, guarantees, or any other statement on the medication status of the animal offered for sale. Keep in mind that more than one firm/individual in the marketing chain may be held responsible for tissue residue violations.

a. Dealer Involvement

Persons involved in handling, transporting, holding, and marketing food-producing animals should be encouraged to establish systems to ensure that if **they administer** drugs to animals in their control or care, those drugs are used properly, and to establish systems to prevent potentially hazardous drug residues in edible animal products.

Persons who do not administer medications but who acquire animals for sale for slaughter (such as livestock dealers) should also establish and implement a recordkeeping system. This system should include information on the source of the animal and whether the animal has been medicated (when, with what drug, and the withdrawal period) to preclude marketing of adulterated edible animal tissues.

Specifically, describe the system the dealer has for the following:

(1) Their system to identify the animals they purchase or acquire with records to establish traceability to the source of the animal;

(2) Their system to determine from the source of the animal whether the animal has been medicated and with what drug(s); and,

(3) If the animal has been medicated, their system to withhold the animal from slaughter for an appropriate period of time to deplete potentially hazardous residues of drugs from edible tissues. If they do not hold the medicated animal, then describe how they assure that the animal is clearly identified and sold as a medicated animal.

Such persons may be subject to regulatory action if they market animals containing illegal residues and have failed to take reasonable precautions to prevent the sale of adulterated food [21 U.S.C. 331(a)].

Seafood does not have dealers like the terrestrial animals. Fish haulers are sometimes either associated with the producer or the processor. Determine if any drugs or chemicals are put into the fish haul truck tanks to reduce stress to fish.

b. Veterinarian Involvement

If the investigation reveals that the drug involved in causing the residue was prescribed, administered, or dispensed by a veterinarian include the following:

(a) Describe the veterinarian/client/patient relationship that existed at the time the animals in question were treated. Refer to 21 CFR Part 530.

- Does the veterinarian regularly visit the farm premises and examine the animals?

- Is the veterinarian aware of the husbandry practices utilized by this firm?

- Did the veterinarian examine, prescribe, or administer the drug to the animal in question?

- If the veterinarian administered the drug, report the dosage and describe what kind of instructions he/she left for milk withholding and/or pre-slaughter withdrawal times. (Did the producer follow those instructions?)

- If the veterinarian did not administer the drug, with whom and what kind of instructions did he/she provide for drug administration and milk withholding and/or pre-slaughter withdrawal times? (Did the producer follow those instructions?)

(b) Describe how the veterinarian established the recommended withdrawal time and how he/she attempted to assure that the producer adhered to that time.

(c) Describe how the dispensed product was labeled.

(d) If the drug was one that the veterinarian prepared (by combining 2 or more products, or other manufacturing methods), list the products or ingredients, describe who prepares them, and how they are prepared. Use CPG Sec.608.400 - Compounding of Drugs for Use in Animals and 21 CFR Part 530.13 for additional guidance.

B. GMP Inspections

Conduct GMP inspections at the feed mill or mixer/feeder when either is implicated as causing the residue violation. Use CP 7371.004 for guidance and be sure to use Form 2481 when conducting an inspection. See 21 CFR Part 225 sections 225.120 to 225.202 for GMP requirements for feed mills that do not require a license. The GMP regulations at 21 CFR Part 226 are for the manufacturers of Type A medicated articles.

C. Sampling

Collect samples (including both documentary samples and/or physical samples) to document violative conditions. See IOM Sampling Schedule Chart 16 for both potency and drug carryover in feeds.

If illegal or unapproved drugs, such as chloramphenicol or nitrofurans, are found on a food-producing animal farm, collect documentary samples of seizable-sized lots.

1. Sample Submission

Ship all medicated feed and animal drug samples for drug or microbiological analyses to the Denver Laboratory. Before shipping samples contact the Laboratory Director, Karen Kreuzer, HFR-SW260, at 303-236-3060, to discuss inspectional findings and required sample analyses.

2. Collection Report (CR)

Prepare a CR for the FSIS-collected sample only when regulatory action is being considered. CRs need to be prepared for each drug being used in an extra-label manner and for any other sample collected during the investigation

D. Reporting

Submit, Field Accomplishments Compliance Tracking System (Facts) Coversheet with endorsement, completed Tissue Residue Evaluation Form(s) (Attachment C), Drug Inventory Survey Form (Attachment G) to the Compliance Information Management Team, HFV-235, Attention: Fran Pell. Photocopy necessary forms for District use. The completion of Attachments C and G are essential for the success of the automated database, TRIMS (Tissue Residue Information Management System). Upon request CVM will provide information for comprehensive District reports. TRIMS is extremely useful in identifying trends in causes of tissue residues, e.g., illegal use of bulk drugs, extra-label use of dosage form drugs, medicated feeds, etc.

A copy of the fully completed FACTS coversheet, along with pertinent parts of the memo of investigation or EIR should be forwarded to the FSIS Technical Services Center. Please Fax or email any source information changes to FSIS immediately so they can issue a corrected notification letter to the appropriate individual and update RVIS. It is FDA's responsibility to provide FSIS with updated violator information for RVIS. Do not complete an Attachment C for violations in Seafood or Honey. Send the EIR with attachments to the Compliance Information Management Team, HFV-235, Attention: Fran Pell.

E. Criminal Activity Investigations

When illegal residue investigations uncover activities of a criminal nature, such as using false names, knowingly purchasing medicated animals for slaughter, purchasing animals with the understanding that they will be sold for rendering or other non-human food use and then offering the animals for slaughter for human food, you should consider referring the case to FDA's Office of Criminal Investigations (OCI). This Office has skills, contacts, and expertise that may be invaluable in conducting the investigation and pursuing the appropriate enforcement action. The formal procedure for referral is described in the Investigations Operations Manual (IOM) Chapter 9, Subchapter 980. **If OCI is unable to pursue a specific case, the District should still conduct follow-up inspections in accordance with this program.** OCI may be able to assist in certain areas or FDA investigators may work jointly with OCI agents in the investigation.

PART IV - ANALYTICAL

A. Responsibilities

1. Sample Preparation

Prepare feed samples for drug analysis as described in the AOAC 16th Ed.

2. Tissue Sample Storage

The analyzing FSIS laboratory will retain all FSIS-collected violative samples for up to 12 months. Once the FDA District Office decides that a firm may warrant regulatory action they should immediately request that the pertinent sample(s) be shipped to an FDA laboratory. Please note that unless a sample shipment request is received, all samples will be destroyed by FSIS after 12 months. Samples should be retained by FDA until a compliance action is completed or the firm sufficiently demonstrates its sustained ability to market animals free of violative residues.

Districts should devise a sample accountability system for the FSIS-collected tissue samples. A suggested system would be to prepare a sample accountability card for each sample received using the FSIS laboratory form number as the sample number. By using the form number, a CR would not be prepared, thereby eliminating the problem of how to report time for preparing the CR. A CR would, however, need to be prepared before a case is forwarded for regulatory consideration.

Tissue samples using this system are handled in the same manner as any FDA sample.

An FSIS Directive establishes a formal system to guarantee sample integrity. An intact FSIS official seal should be affixed to the sample container. Contact Compliance Information Management Team, Deborah Cera, if you find this not to be the case routinely. Although FDA would prefer all samples from FSIS to be sealed, the lack of a seal should not deter you from appropriate follow-up.

3. Problem Area Flags (PAF) for PACs

PAC 71003A - PAF (PES, NAR)
PAC 71004 - PAF (NAR, KIT, DRT, ANT, DRA)
PAC 71006 - PAF (NAR, DRT, ANT, DRA, KIT)

Note: This only applies to Meat and Poultry samples reported to FDA by USDA, FSIS. Follow C.P. 7304.018, Chemotherapeutics in Seafood, for information on seafood samples for drug residues.

PART V - REGULATORY/ADMINISTRATIVE

A. GENERAL

Enforcement follow-up activity is prioritized by the degree of human health risk potential involved in the residue violation(s). Additionally, enforcement action may be against individual(s) responsible for multiple residue violations involving drugs presenting a lesser human health risk. The following information covers most violative residue situations. Occasionally, however, unique situations are encountered which require new or special investigational or enforcement procedures. Discuss these new or special situations with CVM, Division of Compliance, Enforcement and Regulatory Policy Team, Reginald Walker as they occur so that an acceptable investigational or enforcement strategy can be developed. Also notify and discuss with the Compliance Information Management Team, Deborah Cera proposed joint interagency (FDA//FSIS/GIPSA) enforcement actions against individuals/firms (other than the producer) at the initial stage of development. CVM will contact FSIS, and GIPSA headquarters units and the District will contact FSIS, and GIPSA field units to implement interagency enforcement actions.

For aquaculture questions contact the Compliance Information Management Team, Fran Pell. For other animal derived human foods contact Deborah Cera, or Fran Pell.

Animals are considered food under the Act when offered or intended for slaughter for human food at slaughter facilities that ship their products into interstate commerce.

The Federal Food, Drug, and Cosmetic Act (the 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 statute 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. Tuente Livestock, 888 F. Supp. 1416, 1423-26 (S.D. Ohio 1995) (live hogs are food). More generally, courts have long held that unprocessed or unfinished articles are or can be food. *See* Otis McAllister & Co. v. United States, 194 F.2d 386, 387 (5th Cir. 1952) and cases cited there (unroasted coffee beans are food). Thus, live animals raised for food are "food" under the Act.

Regulatory action can be taken against a producer or other responsible persons when it has been documented that the animals offered for slaughter in interstate commerce resulted in illegal residue(s) in edible tissue. [21 U.S.C. 331(a)] For example, regulatory action can be taken against a producer who sells animals containing illegal drug residues to an intermediate party, which in turn sells them at

an auction, where they are purchased by a buyer who in turn sells them to a slaughter plant doing an interstate business. In such circumstances the producer can be charged with causing the delivery for introduction into interstate commerce of adulterated food, even if the producer has no specific knowledge of the ultimate destination of the animals.

The other parties involved in the scenario may also be charged with causing the delivery for introduction into interstate commerce of adulterated food, or they may be charged with offering for introduction into interstate commerce. Additionally, "caused to be introduced" charges may be brought against veterinarians, animal dealers, buyers, vendors, auction barns, or other persons who are responsible for having caused the residue or having introduced animals into interstate commerce without first assuring that the animals were free of illegal residues [21 U.S.C. 331(a)]

When treated animals remain on the premises, initiate action to prevent further processing of the animals, such as requesting that USDA/FSIS sample and hold future shipments made by the producer and/or requesting State detention/quarantine of the animals. Provide complete information (e.g., suspected shipment date, destination, drugs involved, etc.) to cooperating agencies and officials.

B. INITIAL VIOLATION

The FSIS Violation Notification Letter includes appropriate language to serve as FDA prior warning to the producer shipping animals with violative residues. Under the following circumstances it is appropriate to issue a Warning Letter to an initial violator (when the investigation confirms his culpability):

- Involvement of drugs considered of **high risk to human** health/safety whether approved or unapproved.
- Involvement of apparent extra-label use. Refer to 21 CFR Part 530.
- The occurrence of residue levels so high as to indicate intentional misuse of the drug
- Involvement of drugs where no tolerance has been established.

Seafood violations: All drugs for which seafood is currently tested are not approved for any food fish use in the United States. If the violation, jurisdiction, and responsibility can be documented, CVM would consider a Warning Letter for the initial violation.

C. REPEAT/MULTIPLE VIOLATIONS

Firms or individuals who repeatedly present adulterated animals for slaughter may represent a significant public health risk.

1. Warning Letter

A Warning Letter should be considered as a follow-up to a repeat violation. See Attachment B for model Warning Letters. Warning Letters for tissue residue violations may be issued directly by the District Director except those concerning tissue residue violations where no tolerance has been established, extra-label use is documented, and/or those which involve the use of compounded drugs or other drug adulteration. Warning Letters for aquaculture and other animal-derived products also require CVM concurrence prior to issuance. The exceptions listed above require CVM concurrence prior to issuance.

Warning Letters must be submitted to CVM no later than 8-10 weeks from the date of **last evidence collection** to meet Agency timeframes. In the past the regulatory time clock has routinely started on the date of investigation/inspection of the animal producer. However, since residue investigations frequently require additional time-consuming visits to fully document the violation, it is important to include dates of visits made to the veterinarian, auction barn, dealer, slaughter house, etc. in your recommendation to CVM. Include language in the Warning Letter that clearly specifies the beginning and end dates of the investigation.

Title 18 violations may also be included in the Warning Letter to inform the recipient that GIPSA or FSIS may take actions against these violations. (See Attachment E). These are circumstances where false certificates or guarantees are knowingly provided or when provided without any knowledge of the animal's medication status. Do not issue Warning Letters containing only Title 18 violations.

If the state inspection documents residue violation, responsibility, and jurisdiction, CVM will consider Warning Letter recommendations based on the state inspectional data.

2. Injunction

If a tissue residue violation(s) **occurs after the** issuance of a Warning Letter then injunction should be considered against a producer and/or other parties that are responsible for introducing animals into interstate commerce that result in illegal residues. As with most injunctive actions, we need a history of violations and a good description of scope and size of the violator's operation to help explain the need for court action to achieve compliance. Contact FSIS to initiate intensive sampling of the producer's animals. The injunction will be reviewed concurrently with the effort to obtain any additional documented violations. In order to proceed with a preliminary injunction a documented violative residue or, if it involves a

producer, an FDA inspection, no older than 60 days is required. If the 60-day time frame cannot be met, consider proceeding with a permanent injunction. If another residue violation occurs after a consent decree has been signed, and the inspection documents a violation, responsibility, and jurisdiction, the District should contact the Office of General Counsel (OGC) attorney who handled the original consent decree to discuss enforcement options. In the absence of the original attorney please contact Eric Blumberg, GCF-1 for further advice.

3. Prosecution

Prosecution may be considered when the residue violations involve one or more of the following elements and the individuals knowingly do or use:

- Drugs not permitted for extra-label use in food animals, banned or unapproved drugs that present significant human health safety concerns.
- Blatant misuse of toxicologically significant drugs resulting in residues substantially above tolerance.
- Issuing false guarantees that animals with violative residues were drug-free or had been properly withdrawn from the drug(s).
- Multiple misdemeanor counts and/or one or more felony counts.

The Office of Criminal Investigations (OCI) is responsible for reviewing all matters in FDA for which a criminal investigation is recommended, and is the focal point for all criminal matters.

FDA personnel must refer all criminal matters, regardless of their complexity or breadth, to OCI. This includes criminal search warrants, misdemeanor prosecutions, felony prosecutions, referrals for criminal investigation, and Section 305 meetings.

District management must communicate with its local OCI office before pursuing any criminal matter. This communication is absolutely essential to preclude potential interference with other on-going criminal investigations and to prevent confusion among the components of the Office of Chief Counsel and the Department of Justice that are responsible for handling FDA's criminal cases. During this communication, OCI is to be provided with all of the facts of the potential case and any additional information that is relevant to, or could impact, the case in any way. OCI will decide promptly whether or not it is interested in pursuing the case and will communicate its decision back to the District Office.

If OCI chooses not to pursue a criminal matter, the District Office is at liberty to proceed with the case in accordance with the procedures in Chapter 6 of the Regulatory Procedures Manual.

PART VI - CONTACTS, ATTACHMENTS, AND REFERENCES

A. PROGRAM CONTACTS

1. CVM

a. Program Inquiries

Deborah Cera, Program Manager
240-276-9209
Compliance Information Management Team, HFV-235
CVM/Division of Compliance
Deborah.cera@fda.hhs.gov

b. Technical Guidance

Frances Pell, 240-276-9211 or Deborah Cera, 240-276-9209
Compliance Information Management Team, HFV-235
CVM/Division of Compliance, HFV-235
Deborah.cera@fda.hhs.gov
Frances.pell@fda.hhs.gov

c. Regulatory Inquiries

Reginald Walker
240-276-9234
Enforcement and Regulatory Policy Team, HFV-232
CVM/Division of Compliance
Reginald.walker@fda.hhs.gov

d. Policy Questions

Gloria Dunnavan, Director
240-276-9200
CVM/Division of Compliance, HFV-230
Gloria.dunnavan@fda.hhs.gov

2. ORA

a. Inspectional Inquiries

Division of Field Investigations, HFC-132,
Telephone: Jim Dunnie, 301-827-5652

b. Analytical Inquiries

Division of Field Science, HFC-141,
Telephone: George Salem, 301-827-1031

c. Federal/State Relations Inquiries

Division of Federal-State Relations, HFC-152
Telephone: Glenn Johnson, 301-827-2907

B. LIST OF ATTACHMENTS

1. Attachment A - FSIS Laboratory Reporting Codes
2. Attachment B- Model Letters
3. Attachment C- Tissue Residue Evaluation Form
4. Attachment D - USDA Contacts
5. Attachment E - GIPSA/Title 18 Memo
6. Attachment F - Example of Slaughter Plant Affidavits
7. Attachment G - Drug Inventory Survey
8. Attachment H – Program Monitor Checklist

C. APPLICABLE REFERENCES OR AIDS

1. INVESTIGATIONS OPERATIONS MANUAL (IOM): Chapters 4 & 5 Sampling and Inspection.

2. 21 CFR Parts 500-599, Animal Drugs, Feeds, and Related Products.

3. Compliance Policy Guides:

   Sec. 608.400 - Compounding of Drugs for Use in Animals. (CPG 7125.40)

   Sec. 615.300 - Responsibility for Illegal Drug Residues in Meat, Milk and Eggs. (CPG 7125.05)

   Sec. 608.100 - Human-Labeled Drugs Distributed and Used in Animal Medicine. (CPG 7125.35)

   Sec. 615.200 - Proper Drug Use and Residue Avoidance by Non-Veterinarians. (CPG 7125.37)

   Sec. 615.115 - Extra-label Use of Medicated Feeds for Minor Species

4. Compliance Programs

   7303.039 National Drug Residue Milk Monitoring Program
   7371.002 Illegal Sales of Veterinary Prescription Drugs
   7371.003 Feed Contaminants
   7371.004 Feed Manufacturing
   7304.018 Chemotherapeutics in Seafood Compliance Program

5. Regulatory Procedures Manual.

6. AOAC Official Methods of Analysis, 16th Edition.

7. Memorandum of Understanding - MOU 225-85-8400 - Memorandum of Understanding between FDA, FSIS and EPA.

PART VII - CVM RESPONSIBILITIES

A. Program Evaluation

Information extracted from Attachment C Evaluation Forms will be entered into TRIMS (Tissue Residue Information Management System). This database will facilitate the management and analysis of information related to tissue residue violations.

The Compliance Information Management Team will periodically prepare reports of program findings.

B. Inter-Center Action

The Compliance Information Management Team will coordinate CVM efforts to exchange residue data with the Center for Food Safety and Applied Nutrition, especially when the data may indicate a potential for residues in seafood, milk, and/or eggs.

C. Compliance Information Management Team

The Compliance Information Management Team has the primary responsibility for managing/coordinating FDA-related tissue residue activities.

Significant functions include the following:

- To serve as the primary contact between the FDA District Tissue Residue Monitors and CVM; the objective is to exchange information and provide guidance on residue-related issues and to respond to any problems/needs the Field identifies.
- To identify, recommend, develop, and implement preventive measures to reduce the number violative residues.
- To prioritize work efforts for program-related resources.
- To identify specific residue/violator trends through the Residue Violation Information System (RVIS) and the Tissue Residue Information Management System (TRIMS).
- To provide CVM's Division of Compliance and the Field with relevant residue information to support enforcement actions.
- To coordinate all FDA efforts concerning the RVIS.
- To serve as the primary contact point between FDA and FSIS in an effort to provide meaningful input into the development and implementation of the National Residue Program for meat and poultry.

- To serve as the primary contact point between FDA's CVM and CFSAN to provide input into the development and implementation of drug residue testing programs.

D. Enforcement and Regulatory Policy Team

CVM's Enforcement and Regulatory Policy Team is responsible for the review of all CVM-related enforcement actions and can frequently help in determining the responsible parties. It can also provide guidance on the proper collection of the analytical, investigational, and other evidence needed to support a case. For questions involving case development, please contact the Enforcement and Regulatory Policy Team, HFV-232, Reginald Walker for assistance.

ATTACHMENT A – USDA REPORTING CODES
FSIS/USDA Laboratory Reporting Codes

USDA Residue	USDA Residue Name
0	CAST GENERAL
1	RESIDUE-ACTUAL SPIKED AMOUNT
30	AFLATOXIN
50	NITROSAMINES
51	N-NITROSADIMETHYLAMINE
52	N-NITROSADIETHYLAMINE
53	N-NITROSODIPROPYLAMINE
54	N-NITROSODIBUTYLAMINE
55	N-NITROSOPIPERDINE
56	N-NITROSOPYRROLIDINE
57	N-NITROSOMORPHOLINE
59	RECOVERY
60	CYANIDE
61	STYRENE
80	SYNTHETIC PYRETHRINS
81	CYPERMETHRIN
82	DELTAMETHRIN
83	FENVALERATE
84	FLUCYTHRINATE
85	PERMETHRIN
86	NATURAL PYRETHRINS
87	PYRETHRIN I
88	PYRETHRIN II
89	CINERIN I
90	CINERIN II
92	PIPERONYL BUTOXIDE
99	OTHER
100	HALOCARBON PESTICIDES
101	ALDRIN
102	BENZENE HEXACHLORIDE

USDA Residue	USDA Residue Name
103	CHLORDANE
104	DIELDRIN
105	DDT AND METABOLITES
106	ENDRIN
107	HEPTACHLOR AND METABOLITES
108	LINDANE
109	METHOXYCHLOR
110	TOXAPHENE
111	PCB'S
112	HEXACHLOROBENZENE
113	MIREX
114	STROBANE
115	NONACHLOR
116	OCTACHLORO DIBENZODIOXIN
117	HEPTACHLORO DIBENZODIOXIN
118	HEXACHLORO DIBENZODIOXON
119	TETRACHLORO DIBENZODIOXIN
120	DICHLOROPHENOL
121	TRICHLOROPHENOL
122	TETRACHLOROPHENOL
123	PENTACHLOROPHENOL
124	P,P-DDT
125	O,P-DDT
126	P,P-DDE
127	O,P-DDE
128	P,P-TDE
129	O,P-TDE
130	UNIDENTIFIED RET REL TO 101
131	UNIDENT PEAK 1 RETN REL TO 101
132	UNIDENT PEAK 2 RETN REL TO 101
133	UNIDENT PEAK 3 RETN REL TO 101
134	UNIDENT PEAK 4 RETN REL TO 101
135	UNIDENT PEAK 5 RETN REL TO 101
136	UNIDENT PEAK 6 RETN REL TO 101

USDA Residue	USDA Residue Name
137	UNIDENT PEAK 7 RETN REL TO 101
138	UNIDENT PEAK 8 RETN REL TO 101
139	UNIDENT PEAK 9 RETN REL TO 101
140	UNIDENTIFIED RET AMT TO 101
141	UNIDENT PEAK 1 AMT REL TO 101
142	UNIDENT PEAK 2 AMT REL TO 101
143	UNIDENT PEAK 3 AMT REL TO 101
144	UNIDENT PEAK 4 AMT REL TO 101
145	UNIDNET PEAK 5 AMT REL TO 101
146	UNIDENT PEAK 6 AMT REL TO 101
147	UNIDENT PEAK 7 AMT REL TO 101
148	UNIDENT PEAK 8 AMT REL TO 101
149	UNIDENT PEAK 9 AMT REL TO 101
150	KEPONE
161	PARA-DICHLORO-BENZENE
162	TETRACHLOROETHYLENE
163	HEPTACHLOR - CHECK SAMPLE REPORTING
164	HEPTACHLOR EPOXIDE - CHECK SAMPLE REP.
181	HALOWAX
191	PBB
192	ETHYLENEDIBROMIDE
193	METHYLBROMIDE
200	ANTIBIOTICS
201	PENICILLIN
202	STREPTOMYCIN

USDA Residue	USDA Residue Name
203	CHLORAMPHENICOL
204	TETRACYCLINE
205	TYLOSIN
206	ERYTHROMYCIN
207	NEOMYCIN
208	OXYTETRACYCLINE
209	CHLORTETRACYCLINE
210	UNIDENTIFIED MICROBIAL INHIBITOR
211	GENTAMICIN
212	LINCOMYCIN
213	CLOXACILLIN
214	APRAMYCIN
215	AMOXICILLIN
216	NOVOBIOCIN
217	SPECTINOMYCIN
218	VIRGINIAMYCIN
298	TETRACYCLINES (INJECTION SITE)
299	SWAB POSITIVE-BIOASSAY NEGATIVE
300	ORGANIC PHOSPHORUS PESTICIDES
301	COUMAPHOS AND OXYGEN ANALOG
302	DICHLORVOS
303	DIAZINON
304	ETHION AND OXYGEN ANALOG
305	MALATHION
306	PARATHION
307	RONNEL
308	CRUFOMATE
309	TRICHLORFON
310	METHYL PARATHION
311	DIOXATHION
312	DISULFOTON
313	FENETHROTHION
314	STIROFOS (OR TETRACHLORINPHOS)
315	CHLOPYRIFOS
316	FENTHION

USDA Residue	USDA Residue Name
318	CARBOPHENTHION (TRITHION R)
319	AZINPHOS-METHYL (GUTHION R)
320	CHLORFENVINPHOS
330	UNIDENTIFIED RET REL TO 306
331	UNIDENT PEAK 1 RETN REL TO 306
332	UNIDENT PEAK 2 RETN REL TO 306
333	UNIDENT PEAK 3 RETN REL TO 306
334	UNIDENT PEAK 4 RETN REL TO 306
335	UNIDENT PEAK 5 RETN REL TO 306
336	UNIDENT PEAK 6 RETN REL TO 306
337	UNIDENT PEAK RENT REL TO 306
340	UNIDENTIFIED RET AMT TO 306
341	UNIDENT PEAK 1 AMT REL TO 306
342	UNIDENT PEAK 2 AMT REL TO 306
343	UNIDENT PEAK 3 AMT REL TO 306
344	UNIDENT PEAK 4 AMT REL TO 306
345	UNIDENT PEAK 5 AMT REL TO 306
346	UNIDENT PEAK 6 AMT REL TO 306
347	UNDIENT PEAK 7 AMT REL TO 306
360	CHLORINATED ORGANIC PHOSPHORUS
361	ETHION METABOLITE
362	COUMAPHOS METABOLITE
363	CHLORPYRIFOS METABOLITE
370	ORGANIC PHOSPHORUS COMPOUNDS
371	2-ETHYLHEXYLDIPHENYL PHOSPHATE
400	ARSENIC
401	ARSENIC
402	MERCURY
403	COPPER
404	LEAD
405	ZINC
406	CADMIUM
407	ANTIMONY
408	SELENIUM
409	ALUMINUM

USDA Residue	USDA Residue Name
410	TITANIUM
411	IRON
412	NICKLE
413	COBALT
414	MANGANESE
415	CHROMIUM
416	TIN
417	SODIUM
418	PHOSPHORUS
419	CALCIUM
420	POTASSIUM
421	MAGNESIUM
500	HORMONES
501	DIETHYLSTILBESTROL
502	DIENESTROL DIACETATE
503	ESTRADIOL BENZOATE
504	MELENGESTROL ACETATE
505	PROGESTERONE
506	TESTOSTERONE
508	MEDROXYPROGESTERONE ACETATE
509	CHLOMADINONE ACETATE
510	ZEARALANOL (ZERANOL)
511	ESTRADIOL MONOPALMITATE
512	HEXESTROL
513	ZEARALENONE
514	TALERANOL
600	CARBAMATES
601	CARBARYL
602	ALDICARB & METABOLITES SULFOXIDE & SULFO
604	PROPOXUR
605	CARBOFURAN AND 3 HYDROXYCARBOFURAN
606	METHIOCARB AND ITS METABOLITE SULFOXIDE
607	BUFENCARB

USDA Residue	USDA Residue Name
608	METHOMYL
615	THIRAM
620	LARVICIDE
621	CYROMAZINE
622	MELAMINE
650	NITROGEN PESTICIDES
651	CARBOXIN
652	AMITRAZ
700	HERBICIDES
701	2,4,-D
702	2,4,5-T
703	METHNEARSONIC ACID
710	TRIAZINE
711	PROMETON
712	PROPAZINE
713	TERBUTYLAZINE
714	ATRAZINE
715	PROMETRYN
716	TERBUTRYN
717	SIMAZINE
718	AMETRYN
800	SULFAS
801	SULFAETHOXYPYRIDAZINE
802	SULFACHLORPYRIDAZINE
803	SULFADIMETHOXINE
804	SULFANITRAN
805	SULFAMETHAZINE
806	SULFACHLOROPYRAZINE
807	SULFAMETHOXYPYRIDAZINE
808	SULFAMERAZINE
809	SULFATHIAZOLE
810	SULFAQUINOXALINE
811	SULFABROMOMETHAZINE
812	SULFAMETHIZOLE
813	SULFANILAMIDE

USDA Residue	USDA Residue Name
814	SULFAPYRIDINE
815	SULFADIAZINE
816	SULFADOXENE
830	UNIDENTIFIED RET REL TO 814
831	UNIDENT PEAK 1 RETN REL TO 814
832	UNIDENT PEAK 2 RETN REL TO 814
840	UNIDENTIFIED RET AMT TO 814
841	UNIDENT PEAK 1 AMT REL TO 814
842	UNIDENT PEAK 2 AMT REL TO 814
900	DRUGS, GENERAL
901	CLOPIDOL
902	FURAZOLIDONE
903	NITROFURAZONE
904	DECOQUINATE
905	MONENSIN
906	IPRONIDAZOLE
907	CARBADOX
908	ROBENIDINE
910	LEVAMISOLE
911	DIMETRIDAZOLE
912	GENTIAN VIOLET
913	DIBUTYLTINDILAURATE
914	LYSERGIC ACID DIETHYLAMIDE
915	PHENCYCLIDINE
916	XYLAZINE
917	LASALOCID
918	NARASIN
921	MORANTEL TARTRATE
922	PYRANTEL TARTRATE
923	IVERMECTIN
924	ARSENIC (DRUGS)
926	HALOFUGINONE
927	CLORSULON
931	UNIDENT PEAK 1 RETN REL TO 2
932	UNIDENT PEAK 2 RETN REL TO 2

USDA Residue	USDA Residue Name
941	UNIDENT PEAK 1 AMT REL TO 29
942	UNIDENT PEAK 2 AMT REL TO 29
950	BENZIMIDAZOLES
951	ALBENDAZOLE
952	FENBENDAZOLE
953	THIABENDAZOLE & METABOLITE
954	MEBENDAZOLE
955	OXFENDAZOLE

USDA TISSUE LOOK-UP TABLE

Code	Name	Code	Name
01	Fat		
02	Liver		
03	Muscle	37	Cheeks
04	Kidney	38	Cloaca
06	Other	39	Colon
07	Lung	40	Comminuted Meat
08	Lymph Node	41	Corpus Luteum
09	Heart	42	Crop
10	Skin	43	Ductus Deferens
11	Spleen	44	Duodenum
12	Brain	45	Ears
13	Eye or Eye Lesion	46	Epididymis
14	Peritoneum	47	Esophagus
15	Nerve	48	Feather
16	Bursa Fabricius	49	Feather Follicle
17	Adrenal Gland	50	Fur
18	Abdomen	51	Gall Bladder
19	Abomasum	52	Ganglion
20	Air Sacs	53	Gizzard
21	Alveolar Duct	54	Gray Matter
22	Alveolar Sac	55	Hair
23	Alveoli	56	Hemal Node
24	Aorta	57	Hock
25	Artery	58	Hoof
26	Blood Vessel	59	Horn
27	Bone	60	Intestinal Glands
28	Bronchi	61	Joint
29	Bronchioles	62	Large Intestine
30	Cardiac Tissue	63	Larynx
31	Cartilage	64	Leg
32	Cecum	65	Lips
33	Cerebellum	66	Lymphatic
34	Cerebrum	67	Lymph Vessel
35	Ceruminous Glands	68	Mammary Gland
36	Cervix	69	Mesentery

USDA TISSUE LOOK-UP TABLE

Code	Name	Code	Name
70	Mouth	98	Thigh
71	Neck	99	Thorax
72	Nose	A1	Thymus
73	Omasum	A2	Thyroid Gland
74	Omentum	A3	Tongue
75	Ovary	A4	Tooth
76	Palate	A5	Trachea
77	Pancreas	A6	Tumor Mass
78	Parathyroid	A7	Ureter
79	Penis	A8	Urinary Bladder
80	Peripheral Nerve	A9	Uterine Horn
81	Phalanges	B1	Uterus
82	Pineal Gland	B2	Vagina
83	Pituitary Gland	B3	Vein
84	Placenta	B4	Ventriculus
85	Prostate Gland	B5	Villi
86	Proventriculus	B6	Vulva
87	Reticulum	B7	White Matter
88	Rectum	B8	Intestine
89	Rumen	B9	Blood Smears
90	Salivary Gland	C1	Oviduct
91	Sebaceous Gland	C2	Keel Bursa
92	Seminal Vesicle	C3	Blood
93	Small Intestine	C4	Serum
94	Spinal Cord	C5	Diaphragm
95	Stomach	C6	Parasite
96	Testis	C7	Multiple Specimens
97	Tissue Mass	C8	Plant Mat. - Soya

USDA TISSUE LOOK-UP TABLE

Code	Name	Code	Name
D1	Secretory Glands		
D2	Plant Fiber		
D3	Urine		
D4	Kidney B		
D5	Serum A		
D6	Serum B		
D7	Bile		
D8	Tailhead Fat		
D9	Brisket Fat		
E1	Hard Bone		
E2	Soft Bone		
E3	Eggs		
E4	Milk		
E5	Colostrum		
E6	Fatty Tissue		
E7	Saliva		
E8	Condensate		
E9	Feed		
F1	Edible Proc. Product		
U3	Urine		

MARCIS SPECIES CODES ON USDA RECORDS

Code	Name	Code	Name
00	Non-Species	51	Market Hog
01	Horse	52	Boar or Stag
10	Bovine	53	Sow
11	Bull	59	Other Red Meat
12	Steer	60	Chicken
13	Beef Cow	61	Young Chicken
14	Heifer	63	Mature Chicken
15	Dairy Cow	70	Turkey
20	Calf	71	Fry Roast Turkey
21	Bob Veal	72	Young Turkey
22	Formula Fed Veal	73	Mature Turkey
23	Non-formula Fed Veal	81	Duck
24	Heavy Calves >400 lbs.	82	Geese
30	Sheep	91	Rabbit
31	Mature Sheep	92	Deer
32	Lamb	97	Blank
40	Goat	98	Blank
50	Porcine	99	Other

SPECIES/ANIMAL LOOK-UP TABLE USED BY USDA

Species #	Species Name	Animal #	Animal Name
1	EQUINE	1	HORSE
10	CATTLE	10	COWS
		11	BULLS/STAGS
		12	STEERS
		13	COWS - BEEF
		14	HEIFERS
		15	COWS - DAIRY
20	CALVES	20	CALVES
		21	BOB - VEAL
		22	FORMULA FED VEAL
		23	NON FORMULA FED VEAL
		24	HEAVY CALVES
30	SHEEP	30	SHEEP
		31	MATURE SHEEP
		32	LAMBS & YEARLINGS
40	GOATS	40	GOATS
50	SWINE	50	SWINE
		51	BARROWS & GILTS / MARKET HOGS
		52	BOARS / STAGS
		53	SOWS
		54	ROASTER PIGS
59	OTHER	58	WATER BUFFALO
		59	OTHER (BUFFALO, ETC.)
		99	OTHER ANIMAL
60	CHICKENS	60	CHICKENS
		61	YOUNG CHICKENS
		63	MATURE CHICKENS
70	TURKEYS	70	TURKEYS
		71	FRYER ROASTER
		72	YOUNG TURKEY
		73	MATURE TURKEY
80	DUCKS	81	DUCKS
		82	GEESE
		84	QUAIL
90	RATITE	83	OSTRICH
		85	EMU
		86	RHEA
91	RABBITS	91	RABBITS
92	DEER	92	DEER