UNITED STATES
National Residue Program for Meat, Poultry, and Egg Products

2015 Residue Sampling Plans

United States Department of Agriculture
Food Safety and Inspection Service
Office of Public Health Science

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Preface

The *United States National Residue Program (NRP) for Meat, Poultry and Egg Products: Residue Sampling Plans* (traditionally known as the Blue Book) summarizes the process of sampling meat, poultry, and egg products for chemical contaminants of public health concern used by the Food Safety and Inspection Service (FSIS). This document details the principles and methods used to plan and design the following NRP sampling plans for: veterinary drugs, pesticides, and environmental contaminants. Explanations are provided with summary tables. The link on page 4 details the FSIS laboratory analytical methods, with species and tissue(s) validated for each method.

Contacts and Comments

Personnel from the Science Staff (SciS) and the Risk Assessment and Analytics Staff (RAAS), within the Office of Public Health Science (OPHS) at the United States Department of Agriculture's (USDA) Food Safety and Inspection Service (FSIS) coordinated this effort and are responsible for the publication of this material. Direct questions about the NRP to:

USDA/FSIS/OPHS
1400 Independence Avenue, SW
355 E Street - Patriot Plaza III
Washington, D.C. 20250-3700
Telephone: (202) 690-6409
Fax: (202) 690-6337
E-mail: ChemicalResidue@fsis.usda.gov

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Principal Authors (USDA/FSIS/OPHS)

Ms. Margaret O'Keefe
Dr. Jorge G. Muñiz Ortiz

Acronyms

AMDUCA – Animal Medicinal Drug Use Clarification Act
AMS – Agricultural Marketing Service
APHIS – Animal and Plant Health Inspection Service
ARS – Agricultural Research Service
CDC – Centers for Disease Control and Prevention
CHCs – Chlorinated Hydrocarbons
COPs – Chlorinated Organophosphates
FAST – Fast Antimicrobial Screening Test
FDA – Food and Drug Administration
FSIS – Food Safety and Inspection Service
EPA – Environmental Protection Agency
HACCP – Hazard Analysis and Critical Control Points
IPP – Inspection Program Personnel
IRSP – Import Reinspection Sampling Program
KIS™ test – Kidney Inhibition Swab Test
NASS – National Agricultural Statistics Service
NRP – U. S. National Residue Program (Domestic & Import)
NSAID – Non-Steroidal Anti-inflammatory Drug
OFO – Office of Field Operations
OPHS – Office of Public Health Science
PHIS – Public Health Information System
PHV – Public Health Veterinarian
SAT – Surveillance Advisory Team
TOI – Types of Inspection

Introduction

The U.S. National Residue Program (NRP) for Meat, Poultry, and Egg Products, administered by the U.S. Department of Agriculture's (USDA), Food Safety and Inspection Service (FSIS), is an interagency program designed to identify, rank, and test for chemical contaminants in meat, poultry, and egg products. FSIS publishes the NRP *Residue Sampling Plans* (traditionally known as the Blue Book) each year to provide information on the process of sampling meat, poultry, and egg products for chemical contaminants of public health concern.

FSIS administers this regulatory program under the Federal Meat Inspection Act (FMIA) (21 U.S.C. 601 et seq.), the Poultry Products Inspection Act (PPIA) (21 U.S.C. 453 et seq.), and the Egg Products Inspection Act (EPIA) (21 U.S.C. 1031 et seq.). The NRP's purpose is to protect the health and welfare of consumers by regulating the meat, poultry, and egg products produced in federally inspected establishments and to prevent the distribution in commerce of any such products that are adulterated or misbranded.

The NRP requires the cooperation and collaboration of several agencies for its successful design and implementation. FSIS, along with the Department of Health and Human Services' (HHS), Food and Drug Administration (FDA) and the Environmental Protection Agency (EPA) are the primary Federal agencies managing this program. The FDA, under the Federal Food, Drug, and Cosmetic Act, establishes tolerances for veterinary drugs and action levels for food additives and environmental contaminants. The EPA, under the Federal Insecticide, Fungicide, and Rodenticide Act (as modified by the Food Quality Protection Act), establishes tolerance levels for registered pesticides. Title 21 Code of Federal Regulations (CFR) includes tolerance levels established by FDA and Title 40 CFR includes tolerance levels established by EPA.

Representatives from FSIS, FDA, EPA, USDA's Agricultural Research Service (ARS), and the USDA's Agricultural Marketing Service (AMS), as well as HHS's Centers for Disease Control and Prevention (CDC), collaborate to develop the scheduled sampling program. These agencies work together to create the annual sampling plan, based on the following: prior NRP findings of chemical residues in meat, poultry, and egg products, FDA veterinary drug inventories completed during on-farm visits and, investigation information, and pesticides and environmental contaminants of current importance to EPA. The representatives convene to identify the residues of public health concern. Ultimately, FSIS publishes the completed sampling plan in the yearly Blue Book.

Chemical compounds tested in the program include approved and unapproved veterinary drugs, pesticides, and environmental compounds. The NRP is designed to: (1) provide a structured process for identifying and evaluating chemical compounds used in food animals; (2) analyze chemical compounds of concern; (3) collect, analyze, and report results; and, (4) identify the need for regulatory follow-up subsequent to the identification of violative levels of chemical residues.

FSIS has administered the NRP by collecting meat, poultry, and egg product samples and analyzing the samples for specific chemical compounds at FSIS laboratories since 1967 for meat and poultry, and beginning in 1995 for egg products. A violation occurs when an FSIS laboratory detects a chemical compound level in excess of an established tolerance or action level as well as if the residue detected has no approved tolerance. Once the laboratory analysis is complete, FSIS enters the detailed residue violation information into the FSIS Residue Violation Information System (RVIS), an FSIS/FDA interagency database. FSIS informs the establishment by providing them and the designated FSIS Inspection Program Personnel (IPP) with the analysis results and also notifies the producer via certified letter. Under best practices, the establishment should also notify the producer that an animal from that business has been identified as having a residue violation. In addition, FSIS shares the violation data with EPA and FDA, where the latter Agency has on-farm

jurisdiction. FDA and cooperating State agencies investigate producers linked to residue violations and, if conditions leading to residue violations are not corrected, can enforce legal action.

To notify the public and the industry of repeated residue violations by the same producer, FSIS posts a weekly Residue Repeat Violators List on its Web site that identifies producers with more than one violation on a rolling 12-month period. In addition, the list provides helpful information to the AMS-School Lunch Program purchase clearance processors and producers who are working to avoid illegal levels of residues, serves as a deterrent for violators, and enables FSIS and FDA to make better use of resources (list for processors and producers). Because FSIS updates are posted weekly, FDA may not have investigated each violation at the time of publication.

NRP Operating Structure

The NRP consists of three separate, but interrelated, chemical residue testing programs: scheduled sampling, inspector-generated sampling, and import sampling. This basic structure has been in existence since 1967. These testing programs provide data for FSIS to detect chemical residues of concern and have been modified over the years to respond to emerging and re-emerging chemical residue concerns and improved testing methodologies.

In January 1997, FSIS implemented the Hazard Analysis and Critical Control Point (HACCP) inspection system in all federally inspected establishments. The HACCP regulation (HACCP GPO CFR) requires FSIS-inspected slaughter and processing establishments to identify all food safety hazards (including drug residues, chemical contaminants, and pesticides) that are reasonably likely to occur before, during, and after the food animal or product enters the slaughter establishment. The regulation also requires establishments to identify preventive measures to control these hazards. FSIS takes regulatory action against establishments that do not have an effective chemical residue control program in place. Minimizing food safety hazards from farm-to-fork protects consumers from the public health risks associated with chemical contaminants in food.

With greater public concern about the risks of chemical contaminants, focus has increased on strengthening the identification, prioritization, and testing for chemical hazards in meat, poultry, and egg products in the United States. The sampling plan for residues in FSIS-regulated products includes strengthening the focus of public health-based sampling. This approach includes broader screens for veterinary drugs, pesticides, and heavy metals, as well as conducting more analyses per sample.

The United States Government fiscal year (FY) runs from October 1 through September 30. To match this, FSIS has recently switched from implementing the NRP on a Calendar Year (CY) to a Fiscal Year (FY) basis. This change allows the program to run concurrently with the Federal budget cycle. For the FY 2015 NRP, FSIS will continue with the three-tiered approach initiated in 2012. The three-tiered system refers to scheduled sampling (Tier 1), targeted sampling at the production or compound class level (Tier 2), and targeted sampling at the herd/flock or compound class level (Tier 3). Tier 1 involves sampling the primary production classes (beef cows, bob veal, dairy cows, steers, heifers, market hogs, sows, young chickens, and young turkeys) for multiple residues, thus allowing FSIS to analyze more compounds per sample while taking fewer samples.

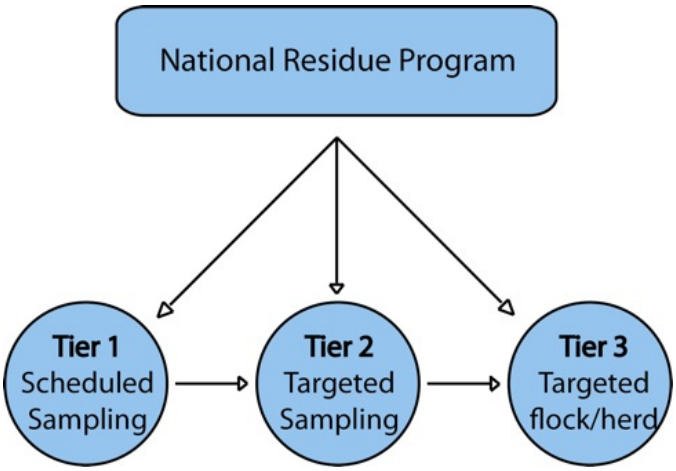
Tier 1 (scheduled sampling program) data collected serves as a baseline level for chemical residue exposure. Tier 1 consists of approximately 800 random samples for each of the production class tested (vs. 300 samples that were collected in previous years). By increasing the number of compounds tested with the multi-residue methodology, the probability of finding a violation, which was previously 95 percent increases to 99 percent, if the violation rate is equal to, or greater than 1 percent in the sample population.

For FY 2015, the Tier 1 sampling program will include analyses across the 9 production classes representing 95 percent of domestic meat and poultry consumption. This change will result in more analytical results for each production class. FSIS Eastern and Western Laboratories will conduct the multi-residue screening methods for Tier 1.

Tier 2 includes the traditional inspector-generated sampling program at the establishment level. When FSIS Public Health Veterinarians (PHVs) detect evidence of a disease that may have been treated or suspect the use of a drug, they retain the carcass and test samples from those carcasses to screen for the presence of chemical residues. In the FY 2015 NRP, inspection program personnel (IPP) continue to complete in-plant residue screens using the Kidney Inhibition Swab test (KIS™ test). The screen positive samples are submitted to the FSIS Midwestern Laboratory and analyzed by the lab to identify, quantify and confirm the contaminants. The lab uses a multi-residue screening method to test in-plant screen positives.

In addition, Tier 2 includes Agency-driven targeted testing at the production and compound class level as outlined in FSIS Directive 10,800.1 rev 1. FSIS can also adjust and implement targeted sampling plans (exploratory assessments) to respond to information about misuse of animal drugs and/or exposure to environmental chemicals provided by other agencies (such as FDA and EPA), as well as in response to Tier 1 analytical results.

The Tier 3 levels are similar in structure to the exploratory assessment program in Tier 2, with the exception that Tier 3 will encompass targeted testing at a herd or flock level. A targeted testing program designed for livestock or flocks originating from the same farm or geographic region may be necessary on occasion to determine the level of exposure to a chemical or chemicals. Tier 3 results may provide information that will support future policy development within the NRP. The NRP plan is outlined in the schematic below-.



The import reinspection sampling program will be structured using the Tier 1 and 2 frameworks. In FY 2014, FSIS intends to collect approximately 1,100 import samples (compared to 6,400 Tier I domestic samples)

New Policy and Procedures for Holding or Controlling Product

As of February 2013, the Agency requires producers to hold or maintain control of lots of product tested for adulterants until acceptable results become available. FSIS stated that the policy also would apply to livestock carcasses subject to FSIS testing for residues. FSIS explained that it will not hold poultry carcasses

pending test results for residues due to historically low residue problems and large lot size. This was outlined in a published Federal Register Notice 76 FRN 19955 (FRN on Applying Mark of Inspection).

Multi-Residue Methodologies

Based on interagency discussion and method improvements, FSIS began using a new screening method for animal drug residues in the second half of CY-2012. The multi-residue method (MRM) provides the following significant improvements: 1) screens and confirms for a variety of analytes, not just antibiotics; 2) target levels appropriate to each compound tolerance; 3) distinguishes individual analytes, even if multiple drugs are present in the same sample, by using mass spectrometry (MS); 4) mitigates unknown microbial inhibition responses; and 5) reduces the time and personnel needed to screen for multiple analytes.

The FSIS pesticide method has been in place since CY-2011. This method diversifies testing capability, improving on the previous pesticide method. The previous method could only test for halogenated compounds; the method now tests for 87 pesticides across multiple classes.

FSIS Laboratory Analytical Methods

FSIS uses analytical methods to detect, identify, and quantify residues that may be present in meat, poultry, and processed egg products. The Agency utilizes these methods for monitoring and for surveillance activities to determine product adulteration and for evaluations of human risk assessments. The Agency uses available methodologies to take appropriate regulatory action against adulterated products in a manner consistent with the reliability of the analytical data. The link below lists the analytical methods with access to each method.

View the FSIS Analytical Chemistry Laboratory Guidebook here.

Overview of the Sampling Plans

The FY 2015 NRP Residue Sampling Plans focus on chemical residues in domestic meat, poultry, and egg products and address import reinspection of meat and poultry products. The domestic sampling plan includes scheduled sampling and inspector-generated sampling. The import reinspection sampling plan encompasses normal sampling, increased sampling, and intensified sampling. Directive 10,800.1, Rev 1 provides further detail on the sampling procedures.

DOMESTIC SAMPLING PLAN

Scheduled Sampling (Tier 1)

Scheduled sampling plans involve taking tissue samples from randomly selected food animals that have passed ante-mortem inspection. The data collected serves as a baseline level for chemical residue exposure.

The Surveillance Advisory Team (SAT), is an interagency committee comprised of representatives from FSIS, FDA, EPA, AMS, ARS, and CDC. It consists of experts in veterinary medicine, toxicology, chemistry, and public health who provide professional advice, as well as information on veterinary drug and pesticide use in animal husbandry. The purpose of the SAT is to enhance communication, which includes obtaining and evaluating relevant toxicity and exposure information for each compound that supports the NRP. These agencies conduct coordinated evaluations of chemical compounds for inclusion in the NRP scheduled sampling plans. These evaluations include veterinary drugs, pesticides, and environmental contaminants that may appear in FSIS-regulated products, including Xenobiotics and naturally occurring compounds that may pose a potential human health hazard. SAT discussions are used to decide which compounds represent a public health concern and warrant inclusion in the NRP scheduled sampling plans. In addition, the SAT may propose, based on professional judgment and reliable field information, the initiation of exploratory assessments for directed sampling on a production class or region of the country after a residue problem has been detected.

Inspector-Generated Sampling (Tier 2)

FSIS inspection program personnel (IPP) conduct inspector-generated sampling when they suspect that animals may have violative levels of chemical residues. Currently, inspector-generated sampling targets individual suspect animals and suspect populations of animals and animals condemned for specific pathologies listed in FSIS Directive 10,800.1, Rev 1. When an inspector-generated sample is collected and the carcass is not already condemned, the sampled carcass is retained while specific samples are sent to the FSL for analysis and confirmation. If the in-plant test is negative for antimicrobial residues, the carcass is released to the establishment. If positive, the carcass is held pending the results of laboratory testing. The PHV condemns carcasses of animals found to contain violative levels of residues in the muscle or if an unapproved drug is detected in any tissue.

Sampling for individual suspect animals

Under the direction of the PHV, IPP are to conduct a KIS™ test on any carcass that based on herd history or ante-mortem or post-mortem findings inspection findings may contain a violative drug residue. IPP are to

follow the instructions provided in Directive 10,800.1, Rev 1, Chapter Three for circumstances warranting a KIS ™ test and Chapter Four for performing KIS™ tests and documenting the task in PHIS. The PHV selects a carcass for sampling based on the criteria outlined in FSIS Directive 10,800.1, Rev 1 (i.e., animal with disease signs and symptoms, producer history, or as a follow-up to results from random scheduled sampling). Usually, the sample is screened in the plant by the IPP and the screen-result verified when necessary by a PHV. Other samples are sent directly to the laboratory for analysis. For example, if the IPP suspects the misuse of a veterinary drug in an animal, she/he can perform the relevant in-plant screening test. If the result of a screening test is positive, the carcass is held (if it is not already condemned for other pathology or conditions that would make it unfit for human consumption), and the liver, kidney, and muscle samples from the carcass are then sent to an FSIS laboratory for analysis and confirmation.

Sampling for suspect animal populations

Sampling for suspect animal populations is directed by an FSIS regulation (9 CFR 310.21) and Directive 10,800.1, Rev 1. This is outlined for healthy appearing bob veal calves and show animals.

Actions taken on violations

A violation occurs when an FSIS laboratory confirms a residue that exceeds an established tolerance or action level, as well as if the residue detected has no tolerance. Once the laboratory analysis is complete, FSIS enters the detailed residue violation information into the FSIS Residue Violation Information System (RVIS), an FSIS/FDA interagency database. FDA has on-farm jurisdiction and evaluates the appropriate action to take as a follow-up to the violation. These actions range in severity from providing education to taking legal action.

Every week, FSIS posts a Residue Repeat Violator List on the official Agency website. The list identifies producers with more than one violation on a rolling 12-month basis. In addition, the list provides helpful information to processors and producers who are working to avoid illegal levels of residues, serves as a deterrent for violators, and enables FSIS and FDA to make better use of resources (list for processors and producers). Because FSIS updates this list weekly, FDA may not have investigated each violation at the time of publication.

IMPORT REINSPECTION SAMPLING PLAN

Imported meat, poultry, and egg products are sampled through the port-of-entry Import Reinspection Sampling Plan, a chemical residue monitoring program conducted to verify the equivalence of inspection systems in exporting countries to the United States standards. All imported products are subject to reinspection, and one or more types of inspection (TOI) are conducted on every lot[1] of product before it enters the U. S. Chemical residue sampling is included in the reinspection of imported products. The following three levels of chemical residue reinspection include:

- normal sampling: random sampling from a lot;
- increased sampling: above-normal sampling resulting from an Agency management decision; and
- intensified sampling: additional samples taken when a previous sample for a TOI that failed to meet U. S. requirements.

[1] An import lot is a group of products defined statistically and/or scientifically by production segments and certified from one country, one establishment. A lot consists entirely of the same species, process category, and product standard of identity (sub-category). A single lot can contain shipping cartons with varying sizes of immediate containers.

The Hold and Test policy, 76 FRN 19955, (FRN on Applying Mark of Inspection) applies also to normal and increased reinspection sampling. Additionally, for intensified sampling, the lot must be retained pending laboratory results.

The data obtained from laboratory analyses are entered into PHIS, an FSIS database designed to generate reinspection assignments, receive and store results, and compile histories for the performance of foreign establishments certified by the inspection system in the exporting country.

ANIMAL PRODUCTION CLASSES

Production class nomenclature includes**:**

Bovine

- Beef cows are mature, female cattle bred for muscle development, ordinarily having given birth to one or more calves.
- Bulls are mature, uncastrated male cattle.
- Calves/veal: The agency is currently engaging in rulemaking to define "veal." For sampling purposes under the NRP, veal calves are defined as immature cattle (including dairy breeds) lacking a functional rumen and intended for meat production. They are recognized as a separate class from suckling calves because of their handling, housing, and proximity to slaughter.
- Dairy cows are mature, female cattle bred for milk production, ordinarily having given birth to one or more calves.
- Heifers are young, female cattle more than 1 year old that have not yet given birth to a calf.
- Steers are male cattle castrated before sexual maturity.

Porcine

- Boars are mature swine showing male sexual characteristics.
- Market hogs are swine, usually marketed near 6 months of age and 200 to 300 pounds live weight.
- Roaster pigs are animals of both sexes and any age that are marketed with the carcass unsplit and with the head on.
- Sows are mature, female swine, ordinarily having given birth to one or more litters.
- Stags are male swine castrated after they have reached sexual maturity.

Poultry

- Ducks are birds of both sexes and any age.
- Egg products include yolks, whites, or whole eggs after breaking; eggs are processed as dried, frozen, or liquid.
- Geese are birds of both sexes and any age.
- Mature chickens are adult female birds, usually more than 10 months of age.
- Old Breeder turkeys are birds of both sexes and usually more than 15 months of age.
- Young chickens include broilers/fryers birds of both sexes that are usually less than 10 weeks of age.
- Roasters are chickens of both sexes, usually less than 12 weeks of age.
- Capons are surgically castrated male chickens usually less than 8 months of age.
- Young turkeys include fryer/roaster birds that are of both sexes and usually less than 12 weeks of age.
- Other poultry include ratites (e.g., ostriches, emus, rheas), guineas, squabs (young, unfledged pigeons), adult pigeons, pheasants, grouse, partridge, quail, etc.

Other Livestock

- Goats are animals of both sexes and any age.

- Lambs are sheep younger than 14 months and having a break joint in at least one leg.
- Rabbits are any of several lagomorph mammals of both sexes and any age.
- Sheep are mature animals of both sexes.
- Other livestock include bison, deer, elk, etc.

Summary of the Domestic and Import Reinspection Sampling Plans

Summary Tables I and II (Tier 1)

Summary Tables I and II provide an overview of both domestic and import sampling organized by chemical compound class. Each table covers: Animal Medicinal Drug Use Clarification Act (AMDUCA)-prohibited drugs, veterinary drugs, pesticides, and environmental contaminants. The tables also identify the FSIS laboratory conducting the analyses.

Summary Tables III – IV (Tier 2)

Summary Tables III and IV provide an overview of both domestic and import sampling organized by animal production class. Each table includes the following: Animal Medicinal Drug Use Clarification Act (AMDUCA)-prohibited drugs, veterinary drugs, pesticides, and environmental contaminants. Table III shows domestic Tier 2 sampling (sheep, goats, and mature turkeys) and Table IV lists the sulfonamide sampling for imports.

Overview of the Program Design

The sampling plan design begins with a list of residues that may occur in meat, poultry, and egg products and are of concern to human health. FSIS coordinates an annual meeting of the SAT members to identify and prioritize chemical compounds of public health concern and assemble detailed information on each compound. FSIS combines this information with historical data on violation rates for each chemical compound to develop the domestic sampling and import reinspection plans. These sampling plans guide the allocation of FSIS laboratory, supply, and inspection resources.

Factors considered when developing the domestic and import scheduled sampling plans include:

- Qualitative public health risk associated with each chemical compound or compound class in meat, poultry, and egg products;
- The food animals affected by each chemical compound or compound class;
- The analytical methods that are available to identify the chemical compound or compound classes;
- FSIS laboratory capacity to analyze chemical compounds or compound classes; and
- The existence of a regulatory tolerance.

The import reinspection plan design is similar to the domestic plan, with two important exceptions. Raw product testing from samples collected at the U.S. port-of-entry is rare, because concerns about foreign animal diseases limit many countries to ship processed products only. When import of raw products is allowed, most shipped raw product consists of muscle tissue only. Exporting countries are required to identify the animal species in each product, but they are not required to identify the production class. Imported meat and poultry testing is categorized by species (e.g., poultry or porcine); egg products are distinguished as a separate category. There are different compound applications by importing countries: allowance in food animals that are not approved for such use in the United States and different use practices for compounds that are approved in the United States. For these reasons, the compounds selected for analysis in the import plan may not necessarily be the same as those in the U.S. domestic plan.

Summary Table I. No. of Samples per Production Class by Compound Class
FY 2015 Domestic Scheduled Sampling: Tier 1

Methods	No. of Samples per Production Class *								
	Beef cows	Dairy cows	Steers	Heifers	Bob veal	Market hogs	Sows	Young chickens	Young turkeys
Multi-class	800	800	400	400	800	800	800	800	800
Aminoglycoside (AMG)	800	800	400	400	800	800	800	800	800
Pesticides	275	275	110	110	275	275	275	275	275
Metals	100	100	50	50	100	100	100	100	100
Hormones	300	300	200	200	300	0	0	0	0
β-Agonists	400	400	200	200	400	400	0	0	0
Avermectins	400	400	200	200	400	400	400	0	0
Carbadox	0	0	0	0	0	400	0	0	0
Arsenic	400	400	200	200	400	400	400	400	400

EL= FSIS Eastern Laboratory (Athens, GA); ML = FSIS Midwestern Laboratory (St. Louis, MO); WL = FSIS Western Laboratory (Alameda, CA)

*Note: 800 total samples collected/submitted for each production class except heifers/steers 400 each

Summary Table II. No. of Samples per Production Class by Compound Class
FY 2015 Import Scheduled Sampling: Tier 1

Methods	No. of Samples per Production Class											
	Fresh beef	**Processed beef**	**Fresh pork**	**Processed pork**	**Fresh veal**	**Processed Veal**	**Fresh lamb/mutton**	**Fresh goat**	**Fresh chicken**	**Processed chicken**	**Fresh turkey**	**Processed turkey**
Multi-class	150	0	150	0	75	0	0	0	150	0	40	0
Aminoglycoside	150	0	150	0	75	0	0	0	150	0	40	0
Pesticides	100	0	100	0	50	0	25	25	75	0	25	0
Hormones	100	0	0	0	0	0	0	0	0	0	0	0
β-Agonists	75	0	75		50	0	0	0	0	0	0	0
Avermectins	75	150	75	25	25	25	20	15	0	0	0	0
Arsenic	75	150	75	25	25	25	20	15	75	50	15	50
Metals	35	12	35	12	25	12	0		35	12	12	12

Summary Table III. No. of Samples per Production Class by Compound Class
FY 2015 Domestic Scheduled Sampling: Tier 2

Methods	**No. of Samples per Production Class**		
	Old Breeder Turkeys	Sheep	Goats
Multi-class (MRM)	100	300	300
Aminoglycosides		150	150
Pesticides		150	150
Avermectins		150	150
Arsenic		150	150
Metals	100		

*Note: 300 total samples collected/submitted for each sheep and goats

Summary Table IV. No. of Samples of Imported Processed Products Tested for Sulfonamides
FY 2015 Import Scheduled Sampling: Tier 2

Compounds for Analysis	**Import Production Class**	**Import Sample Size**
Sulfonamides	Processed beef	25
	Processed pork	15
	Processed turkey	10

Design of the Domestic Scheduled and Import Reinspection Sampling Plans:
Veterinary Drugs, Pesticides, and Environmental Contaminants

I. Selecting Compounds for Testing

A. Veterinary Drugs

FSIS selects compound classes for sampling from the list of prioritized veterinary drugs based on the relative public health concern. After identifying high-priority compounds and compound classes, FSIS applies other practical considerations to determine the compounds for sampling. The principal considerations include the availability of laboratory resources, especially the availability of appropriate analytical methods within the FSIS laboratories. When laboratory resources are limited, FSIS focuses resource allocation to domestic products because imported products have been inspected previously in the country of origin. However, if FSIS believes that a compound is being misused in a foreign country, then the compound and country will be added to the Import Reinspection Sampling Program (IRSP). Based on these considerations, the following compounds were evaluated for inclusion in 2014 scheduled sampling for domestic and imported products:

1. Antibiotics:

Tetracyclines: tetracycline, oxytetracycline, chlortetracycline (High Performance Liquid Chromatography [HPLC] or mass spectrometry [MS] for identification, quantitation by bioassay).

Aminoglycosides: spectinomycin, hygromycin, streptomycin, dihydrostreptomycin, amikacin, kanamycin, apramycin, gentamycin, neomycin (Liquid Chromatography/Mass Spectrometry/Mass Spectrometry [LC/MS/MS] for confirmation, quantitation of streptomycin, dihydrostreptomycin, gentamycin, and neomycin by bioassay).

Macrolides: lincomycin, pirlymycin, clindamycin, tilmicosin, erythromycin, tulathromycin, and tylosin are confirmed by LC/MS/MS. Tilmicosin is quantitated also by HPLC. Erythromycin and tylosin are quantitated by the bioassay.

β-Lactams: amoxicillin, ampicillin, cloxacillin, naficillin, cefazolin, DCCD, dicloxacillin, penicillin G, oxacillin, and desacetyl cephaprin (LC/MS/MS for confirmation, quantitation by bioassay for penicillin G and ampicillin).

Fluoroquinolones: ciprofloxacin, norfloxacin, danofloxacin, enrofloxacin, sarafloxacin, difloxacin, desethylene diprofloxacin, desmethyl danofloxacin (LC/MS/MS for confirmation).

2. Other Antibiotics:

- Avoparcin (classification: glycopeptide; AMDUCA prohibited)
- Chloramphenicol (classification: antibiotic; AMDUCA prohibited)

- Florfenicol (classification: antibiotic; chloramphenicol derivative)
- Fluoroquinolones (classification: antibiotic; AMDUCA prohibited; compounds: ciprofloxacin, desethyleneciprofloxacin, danofloxacin, difloxacin, enrofloxacin, marbofloxacin, orbifloxacin, and sarafloxacin)
- Thiamphenicol (classification: antibiotic; chloramphenicol derivative)
- Vancomycin (classification: glycopeptide; AMDUCA prohibited)

3. Other Veterinary Drugs:

- Amprolium (classification: coccidiostat)
- Arsenicals (detected as elemental arsenic)
- Avermectins (classification: anthelmintics; compounds: doramectin, ivermectin, and moxidectin)
- Benzimidazoles (classification: anthelmintics; compounds: thiabendazole and its 5-hydroxythiabendazole metabolite, albendazole 2-animosulfone metabolite, benomyl in the active hydrolyzed form carbendazim, oxfendazole, mebendazole, cambendazole, and fenbendazole)
- Carbadox (classification: antimicrobial)
- β-Agonists (ractopamine, clenbuterol, cimaterol, zilpaterol, and salbutamol; growth promotants)
- Clorsulon (classification: anthelmintic)
- Diethylstilbestrol (DES) (AMDUCA prohibited synthetic hormone)
- Dipyrone (classification: NSAID[2])
- Eprinomectin (classification: antiparasitic; avermectin)
- Etodolac (classification: NSAID)
- Flunixin (classification: NSAID)
- Halofuginone (classification: antiprotozoal, coccidiostat)
- Hormones, endogenous production (17-β estradiol, progesterone, testosterone)
- Hormones, xenobiotics (melengestrol acetate, trenbolone, zeranol)
- Lasalocid (classification: coccidiostat)
- Levamisole (classification: anthelmintic)
- Methyl prednisone (classification: glucocorticoid)
- Morantel and pyrantel (classification: anthelmintic)
- Nicarbazin (classification: coccidiostat)
- Nitrofurans (compounds: furazolidone, nitrofurazone; AMDUCA prohibited antimicrobials)
- Nitroimidazoles (classification: antiprotozoal compounds: dimetridazole, ipronidazole)
- Phenylbutazone (classification: NSAID)
- Prednisone (classification: glucocorticoid)
- Ronidazole (classification: antimicrobial; compound: nitroimidazole)
- Sulfonamides (classification: antimicrobials, and some are coccidiostats; compounds: sulfapyridine, sulfadiazine, sulfathiazole, sulfamerazine, sulfamethazine, sulfachlorpyridazine, sulfadoxine, sulfamethoxypyridazine, sulfaquinoxaline, sulfadimethoxine, sulfisoxazole, sulfacetamide, sulfamethoxazole, sulfamethizole, sulfanilamide, sulfaguanidine, sulfabromomethazine, sulfasalazine, sulfaethoxypyridazine, sulfaphenazole, and sulfatroxazole)
- Sulfanitran (classification: antibacterial, coccidiostat)[3]

[2] NSAID = non-s teroidal anti-inflammatory drug

- Thyreostats (compounds: 2-thiouracil, 6-methyl-2-thiouracil, 6-propyl-2-thiouracil, 2-mercapto-1-methylimidazole [tapazole], 6-phenyl-2-thiouracil, and 2-mercaptobenzimidazole)
- Veterinary tranquilizers (compounds: azaperone and its metabolite azaperol, xylazine, haloperidol, acetopromazine, propionylpromazine, and chlorpromazine)

In the 2015 NRP, FSIS will employ a number of analytical methodologies to identify and quantitate veterinary drug residues. These methodologies, listed in the link on page 4, analyze individual compounds and compound classes. The selection of the specific compounds and compound classes was justified by public health concerns.

4. Public Health Concern for Veterinary Drugs

i. Antibiotics

An antibiotic is a chemical substance with the capability in dilute solutions to destroy or inhibit the growth of microorganisms. The widespread use of antibiotics over time has allowed microorganisms to adapt and develop resistance to these drugs.[4,5] Hence, inappropriate use of and exposure to antibiotics can increase the risk of infections that resists antibiotic treatment.[6] In addition, allergies to antibiotics have been reported in children and adults[7] and use of antibiotics in infants has been associated with childhood asthma.[8] FSIS tests different classes of antibiotics: aminoglycosides, β-lactams, fluoroquinolones, macrolides, tetracyclines, and sulfonamides.

ii. Avermectins (Ivermectin and Doramectin) and Milbemycins (Moxidectin)

Avermectins (ivermectin and doramectin) and milbemycins (moxidectin) are macrocyclic lactones used in animal husbandry practices to prevent nematode and arthropod parasites. Ivermectin is an effective parasiticide. Doramectin is a potent endectocide that combines broad-spectrum activity with a prolonged duration of activity against the major internal and external parasites of cattle. Moxidectin is an antiparasitic drug that controls a range of internal and external parasites in sheep and cattle. Avermectins share their common antiparasitic activity via interaction at cell membrane receptors; mammals are less susceptible to the toxic effects because avermectins do not readily cross the blood-brain barrier. Nevertheless, adults and children are susceptible to effects on the nervous system ranging from nausea and vomiting, through dizziness, to coma and potentially death at high doses.[9]

iii. β-Agonists (Clenbuterol, Cimaterol, Ractopamine, Salbutamol, and Zilpaterol)

β-Agonists are used for growth promotion in food animals, increasing lean muscle mass. Clenbuterol, a growth promotant, is not currently registered for use in livestock in the United States and is listed in AMDUCA as prohibited from extra-label use in animals intended for food. Ractopamine is used for increased rate of weight gain, improved feed efficiency, increased carcass leanness, and prevention and/or control of porcine proliferative enteropathies (ileitis). Zilpaterol is used for increased rate of weight gain, improved feed efficiency, and increased carcass leanness in cattle fed in confinement for slaughter during the last 20 to 40 days on feed. While the other β-agonists are approved for use in the United States, cimaterol and salbutamol are not approved for use in food animals. In humans, clenbuterol and

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[3] FSIS, in consultation with FDA, rotated sulfanitran out of the NRP beginning in CY 2005.
[4] http://www.cdc.gov/drugresistance/about.html
[5] http://www.cdc.gov/drugresistance/pdf/public-health-action-plan-combat-antimicrobial-resistance.pdf
[6] http://www.cdc.gov/getsmart/antibiotic-use/know-and-do.html
[7] JM Langley and S Halperin (2002) *Can J Infect Dis*, **13(3)**:160-163 and http://www.allergy.org.au/health-professionals/hp-information/asthma-and-allergy/allergic-reactions-to-antibiotics
[8] Risnes *et al.* (2011) *Am J Epidemiol*, **173**:310–318
[9] http://www.asiatox.org/6th%20APAMT%20pdf/Mectins%20posioning%20vs%20Avermectin%20poisoning.pdf

salbutamol are used as bronchodilators by asthma sufferers and as performance-enhancing drugs by athletes. Human side effects include increased heart rate and blood pressure, anxiety, palpitation, and skeletal muscle tremors. The prolonged use of long-acting β-agonists can lead to the severe exacerbation of asthma symptoms[10].

iv. Carbadox

Carbadox is a growth-promoting and antibacterial drug[11] approved to prevent or treat gut inflammation (enteritis), as well as to improve feed efficiency and weight gain in swine. Carbadox and some of its metabolites (desoxycarbadox and hydrazine) are genotoxic and carcinogenic in rodents; however, the final metabolite, quinoxaline-2-carboxylic acid (QCA) is not mutagenic or carcinogenic in animals. Based on the genotoxicity data, an acceptable daily intake has not been established for carbadox.[12]

v. Chloramphenicol

Chloramphenicol is a potent, broad-spectrum antibiotic with severe toxic effects in humans including bone marrow suppression or aplastic anemia in susceptible individuals. While microorganisms have developed resistance to this drug, it is still used selectively in human and veterinary medicine to treat companion animal bacterial infections. This drug is AMDUCA-prohibited for extra label use in animals intended for food.

vi. Florfenicol

Florfenicol is a broad-spectrum bacteriostatic antibiotic. It is typically used to treat cattle (bovine respiratory disease and foot rot)[13], but it has recently been approved for freshwater fish.[14] Horses and other equine animals may experience diarrhea. Toxicity studies in dogs, rats, and mice have associated the use of florfenicol with testicular degeneration and atrophy.[15]

vii. Flunixin

Flunixin is a non-steroidal anti-inflammatory drug (NSAID) with approved use in swine and cattle to alleviate inflammation and pain associated with musculoskeletal disorders. In general, NSAIDs in animals and humans can produce gastrointestinal (GI) side effects if the drug is taken at high doses over a prolonged period. GI ulceration is the most common side effect; however, kidney damage and bleeding problems can also occur.[16]

viii. Nitrofurans

Nitrofurans are synthetic chemotherapeutic agents with a broad antimicrobial spectrum.[17] Furaltadone is a synthetic nitrofuran antibiotic used to prevent intestinal infections and mastitis. It is not approved for use in food-producing animals. Furazolidone, which has wide-ranging applicability, is used to treat intestinal infections and is AMDUCA-prohibited for extra-label use. In small calves, overuse can lead to neurotoxicity and result in head tremors, ataxia, visual impairment, and convulsions. Nitrofurans are potentially carcinogenic and are not generally recognized as safe under any conditions where animal product may become a component of food.[18]

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[10] http://www.fda.gov/Drugs/ResourcesForYou/HealthProfessionals/ucm219161.htm
[11] http://www.inchem.org/documents/jecfa/jecmono/v27je07.htm
And http://www.inchem.org/documents/jecfa/jecmono/v51je05.htm
[12] http://www.inchem.org/documents/jecfa/jeceval/jec_352.htm
[13] http://www.nuflor.com/
[14] http://www.merck-animal-health-usa.com/products/130_163256/productdetails_130_163418.aspx
[15] http://intervetus.naccvp.com/?m=product_view&u=intervetus&p=intervetus&id=1047137
[16] http://www.merckvetmanual.com/mvm/index.jsp?cfile=htm/bc/191606.htm&word=flunixin
[17] http://www.merckvetmanual.com/mvm/index.jsp?cfile=htm/bc/191283.htm
[18] http://www.accessdata.fda.gov/cms_ia/importalert_33.html

5. Veterinary Drugs Banned from Extra-Label Use under AMDUCA

Veterinary drugs banned from extra-label use under AMDUCA are of high public health concern. Therefore, these AMDUCA-prohibited veterinary drugs are not evaluated for inclusion using the ranking formula. Instead, all AMDUCA-prohibited veterinary drugs are assigned a high sampling priority and are included in the NRP, dependent on methodologies and resource availability.

For additional information on veterinary drugs, see the *Code of Federal Regulations, Title 21: Food and Drugs, Part 556: Tolerances for Residues of New Animal Drugs in Food* (21 CFR 556).

B. Pesticides

In the 2015 NRP, FSIS will employ a number of analytical methodologies to identify and quantitate pesticide residues. These methodologies, listed in the link on page 4, analyze individual compounds and compound classes. The selection of the specific compounds and compound classes was justified additionally by public health concerns.

1. Public Health Concern for Pesticides

Chlorinated hydrocarbons, chlorinated organophosphates, organophosphates, and pyrethroids are effective insecticides.[19] Some of these compounds, such as dichlorodiphenyltrichloroethane (DDT), are no longer marketed in the United States because of their extremely slow degradation in the environment (long half-life), but are still approved for use in other countries to fight malaria. Organophosphates and pyrethroids affect the nervous system, generally by disrupting the enzyme that regulates the neurotransmitter, acetylcholine. Typical symptoms of acute intoxication are headaches, dizziness, muscle twitching, weakness, tingling sensations, and nausea.[20] Children are at greater risk to some pesticides because their developing organs offer less protection than those of adults, they often eat different foods than adults, and they display different behaviors than adults.[21] Due to the exposures noted, chlorinated hydrocarbons can cause cancer.[22] Non-cancer effects in animals include effects on the immune system, the reproductive system, the nervous system, and the endocrine system.

For additional information on pesticides, see the *Code of Federal Regulations, Title 40: Protection of Environment, Part 180: Tolerances and Exemptions for Pesticide Chemical Residues in Food* (40 CFR 180).

C. Environmental Contaminants

SAT-selected environmental contaminants of concern currently include heavy metals. FSIS will conduct a targeted sampling assessment of heavy metals for the nine production classes for domestic sampling. This targeted sampling follows lead and cadmium sampling that began in 2003 for heifers and dairy cows. This study continued in 2004 for boars and stags, dairy cows, heifers, and mature chickens.

1. Public Health Concern for Metals

[19] http://www.epa.gov/pesticides/about/types.htm#chemical
[20] http://www.epa.gov/oppfead1/Publications/whatyouneed-hsstaff.pdf
[21] http://www.epa.gov/pesticides/food/pest.htm
[22] http://www.epa.gov/epawaste/hazard/tsd/pcbs/pubs/effects.htm

Heavy metals accumulate in animal organs, such as kidney and liver, which can then be ingested by humans. Cadmium, for example, can cause irritation of the stomach in the short-term, and accumulation over time can cause kidney damage and decreased bone strength in adults. Similar effects can be expected in children. Cadmium and cadmium compounds are known carcinogens. Lead affects the nervous system in children and adults, which can lead to decreased performance in adults and developmental and behavioral effects in children. Lead exposure can also cause anemia. At extremely high exposure concentrations, the brain and kidneys can be severely damaged in both adults and children, and can be fatal.

The predominant dietary source of arsenic is seafood, followed by rice/rice cereal, mushrooms, and poultry.[23] Ingestion of inorganic arsenic can cause gastrointestinal irritation and decreased red and white blood cell production, which can result in fatigue, abnormal heart rhythm, and nervous system effects; high oral doses can cause death. Similar effects are expected in children. Evidence suggests that following long-term exposure, children show lower IQ scores. Inorganic arsenic is a known human carcinogen.

2. Dioxin and Dioxin-Like-Compounds (DLCs)

Since the beginning of the NRP, FSIS has not tested routinely for dioxin. This is because there are no established tolerances for this compound in meat, poultry or egg products under FD&C Act or FQPA. However, every five years, starting in the mid-1990s, FSIS and the USDA Agricultural Research Service (ARS), conducts a periodic survey of dioxins and DLC in domestic meat and poultry.

The survey provides background levels of DLCs in FSIS-regulated meat and poultry products, and is compared to levels found in past survey results. Results are discussed in collaboration with other Agencies and samples with high levels are investigated to determine the cause of increased dioxin levels. FSIS has conducted surveys of the dioxin level in beef, pork, chicken and turkey fat samples. This is done to monitor the base levels of this compound, as the US has put into effect multiple measures to ensure that accidental environmental contamination from dioxin-like compounds are working.

The U. S. control measures to reduce dioxin have included the banning of Polychlorinated Biphenyl (PCB) in 1979, and the reduction of environmental releases of dioxins from all quantified sources have significantly decreased the dioxin levels in the U. S. This significant decrease in dioxin emissions can be attributed to successful U. S. government regulation as well as to the voluntary application of control technologies by industry.

In the 2012-13 dioxin survey, the same number of samples as in the previous survey was collected from beef and poultry and analyzed. The survey data was compared to past results to determine temporal trends. A comparison of the preliminary data shows an average finding of 0.10 TEQ/g lipid in poultry fat. This is a 33% decrease to the results reported in the FY-08 study.

For additional information on environmental contaminants, see the *Code of Federal Regulations, Title 21: Food and Drugs, Part 109: Unavoidable Contaminants in Food for Human Consumption and Food-Packaging Material* (21 CFR 109).

[23] http://www.atsdr.cdc.gov/ToxProfiles/tp2.pdf

II. Prioritizing Candidate Compounds for Testing *(it is important to note that FSIS has the flexibility to add/remove compounds during the fiscal year)*

A. Veterinary Drugs

After identification of AMDUCA drugs for high-priority compounds and compound classes, FSIS, to determine the compounds for sampling, applied the following practical considerations: availability of laboratory resources and appropriate analytical methods within the FSIS laboratories. For FY 2015 domestic sampling, FSIS has scheduled the following veterinary drugs:

- Veterinary Drugs in the Multi-Residue Method*
- Aminoglycosides
- Arsenicals
- Avermectins
- β-Agonists
- Carbadox
- Nitrofurans

***Veterinary Drugs in the Multi-Residue Method:**

- **Analgesic/Anti-inflammatory** - oxyphenylbutazone, flunixin, phenylbutazone
- **β-Agonist** - salbutamol, cimaterol, ractopamine
- **β -Lactam/Cephalosporin** - amoxicillin, cefazolin, desfuroylceftiofur (DCCD), ampicillin, penicillin G, oxacillin, cloxacillin, nafcillin, dicloxacillin
- **Fluoroquinolones** - desethylene ciprofloxacin, norfloxacin, ciprofloxacin, danofloxacin, enrofloxacin, sarafloxacin and difloxacin;
- **Hormones** - prednisone, melengestrol acetate, zeranol
- **Macrolide/Lincosamide** - lincomycin, pirlimycin, clindamycin, gamithromycin, tilmicosin, erythromycin, tylosin, tulathromycin
- **Phenicol** - florfenicol and chloramphenicol;
- **Sulfonamide** - sulfadiazine, sulfathiazole, sulfapyridine, sulfamerazine, sulfamethizole, sulfamethazine, sulfamethoxypyridazine, sulfachloropyridazine, sulfadoxine, sulfamethoxazole, sulfaethoxypyridazine, sulfadimethoxine, sulfaquinoxaline, sulfanitran;
- **Tetracycline** - oxytetracline, tetracycline, chlortetracycline
- **General Drugs** - 2-quinoxaline carboxylic acid (2-QCA;carbadox metabolite)

B. Pesticides

After identification of high-priority compounds and compound classes, FSIS applied practical considerations to determine the compounds for sampling. In addition, FSIS considered the availability of laboratory resources and appropriate analytical methods within the FSIS laboratories. FSIS has scheduled the following pesticides for 2015 domestic sampling and are now in the improved pesticide method. The FSIS pesticide method includes the following compounds:

Alachlor, Aldrin, Bifenthrin, Boscalid, Buprofezin, Carfentrazone ethyl, Chlordane *cis*, Chlordane, Chloroneb trans, Chlorpropham, Chlorpyrifos, Chlorpyrifos methyl, Cyhalothrin (Cyhalothrin-L), Cypermethrin, DDD, o,p'-, DDD, p,p'-, DDE, o,p'-, DDE, p,p'-, DDT, o,p'- + p,p'-, Deltamethrin, Dichlorvos (DDVP), Dieldrin, Difenoconazole, Endosulfan I, Endosulfan II, Endosulfan sulfate, Fenoxaprop-ethyl, Fenpropathrin, Fenvalerate, Fipronil, Fipronil desulfinyl, Fipronil sulfide, Fluridone,

Fluvalinate, Heptachlor, Hexazinone, Malathion, Metolachlor, Metribuzin, Mirex, Nonachlor, *trans*-, Oxychlordane, Permethrin (*cis & trans*), Piperonyl butoxide, Pronamide, Propachlor, Propanil, Propetamphos, Propiconazole, Pyriproxyfen, Resmethrin (*cis & trans*), Tefluthrin, 3-Hydroxycarbofuran , Acephate, Acetamiprid, Atrazine, Azoxystrobin, Carbaryl, Carbofuran, Carboxin, Clofentezine, Clothianidin, Coumaphos O, Coumaphos S, De-Ethyl Atrazine, Diflubenzuron, Diuron, Ethofumesate, Fluroxypyr-1-Methylhepyl-Ester, Imazalil, Imidacloprid, Indoxacarb, Linuron, Metalaxyl, Methomyl, Methoxyfenozide, Methoxyfenozide, Myclobutanil, Norflurazon, Profenofos, Pyraclostrobin, Pyridaben, Simazine, Tebufenozide, Thiabendazole, Thiamethoxam, Thiobencarb, Trifloxystrobin

The high-priority compounds chosen for the IRSP are the same as the domestic plan. After identifying high-priority compounds and compound classes, FSIS applies other considerations to determine which compounds to sample, specifically the availability of analytical methods within the FSIS laboratories.

III. Variables for Domestic Products

A. Veterinary Drugs

1. Regulatory Concern

Based on regulatory intelligence information (e.g., FDA on farm investigations) about possible misuse of veterinary drugs, FSIS makes professional judgments about the likelihood violations may occur. By conferring with subject matter experts, FSIS synthesizes information and recommends the level of regulatory concern.

2. Withdrawal Time

Producers using veterinary drugs approved for food animals are required to follow "conditions of use." Each veterinary drug in the approved production class specifies the dosing regimen and the withdrawal time. The withdrawal time, which is the number of days that must pass between completion of the dosing regimen and the time of slaughter, provides sufficient time for the concentration of the veterinary drug in the animal to decrease below the tolerance.

3. Impact on New and Existing Human Disease

The use or misuse of a veterinary drug in food animals may contribute to new and existing human disease by changing the patterns of antibiotic resistance in human pathogens.

4. Relative Number of Animals Treated

Animal treatment is considered based on economic data of doses sold, as well as surveys of treatment practices in animal populations that are representative of cattle feedlots, dairy, poultry, and swine production. Where data were unavailable, scores were estimated, based on comparison to related veterinary drugs with known usage levels.

5. Acute or Chronic Toxicity Concerns

Compound toxicity and the severity associated with the compound's toxic endpoint.

B. Pesticides

Regulatory Concern

EPA's professional assessment of the extent to which the acute or chronic dietary exposure to this compound may exceed the level of concern established by the EPA. For compounds other than carcinogens, this was determined by comparing either the compound's Acute or Chronic Population

Adjusted Dose (PAD) (whichever was lower) to the estimated level of exposure. The Acute and Chronic PADs are calculated as described below, and both carry uncertainty spanning an order of magnitude or greater.

The Acute Reference Dose (Acute RfD) estimates a single oral exposure level for the human population (including sensitive subpopulations) that is likely to be without an appreciable risk of deleterious effects.

The Chronic Reference Dose (Chronic RfD) estimates a daily oral exposure level for the human population (including sensitive subpopulations) that is likely to be without an appreciable risk of deleterious effects during a lifetime.

The Acute and Chronic RfDs are calculated by dividing the No Observed Adverse Effect Level[24] (NOAEL) or the Lowest Observed Adverse Effect Level[25] (LOAEL) by Uncertainty Factors. This calculation accounts for differences between individual humans (intraspecies variability) and for differences between the test animals and humans (interspecies extrapolation). If the LOAEL is used, an additional Uncertainty Factor is required.

RfD = (NOAEL or LOAEL)/Total UF

The Acute and Chronic Population Adjusted Dose (PAD) are the Acute and Chronic RfD, respectively, modified by the Food Quality Protection Act (FQPA) Safety Factor:

Acute or Chronic PAD = (Acute or Chronic RfD)/FQPA Safety Factor

The acute and chronic dietary risks are expressed as a percentage of the Acute or Chronic PAD. A dietary risk of 100% of the Acute or Chronic PAD (whichever is lower) is the target level of exposure that should not be exceeded. In the following, PAD is defined by the lower value, either the Acute or Chronic PADs.

Pre-Slaughter Interval

For pesticides that have been approved for direct dermal application, the pre-slaughter interval is the required time between the last dermal application and the time of slaughter.

Bioconcentration Factor

Bioconcentration is a measure of a compound's relative affinity for fat, as measured by the $K_{o/w}$. The $K_{o/w}$ is defined as the logarithm of the partition coefficient between octanol and water (log $P_{o/w}$). Compounds that have a high affinity for octanol (and thus a high $K_{o/w}$) tend to bioaccumulate in body fat. A bioconcentration value is determined according to the following criteria:

Endocrine Disruption

Endocrine disruption measures the extent that the compound changes endocrine function and causes adverse effects to individual organisms and/or their progeny, as well as to organism populations and subpopulations.

Toxicity

[24] The highest dose that gave no observable adverse effect.
[25] The lowest dose at which an adverse effect was seen.

The toxicity value represents EPA's professional judgment of the toxicity of the compound, including both the dose required to achieve a toxic effect and the severity of the toxic effect.

The categories of "Regulatory Concern," "Pre-slaughter Interval," and "Bioconcentration Factor" predict risk per unit of consumption from pesticides in animal products. The "Regulatory Concern" category reflects EPA's professional judgment of the likelihood that a compound or compound class will exceed EPA's level of concern in meat, poultry, or egg products. Thus, the category combines residue level and toxicity information.

FSIS expects that the "Withdrawal Time" category for veterinary drugs and the "Pre-slaughter Interval" category will correlate with residue level. The longer pre-slaughter intervals are less likely to be observed properly, and the carcass may contain violative levels of residues.

"Bioconcentration" measures the extent to which a pesticide concentrates within the fat deposits of animals. Pesticides that bioconcentrate are more likely to accumulate to higher levels within animal tissue, which is expected to increase the potential for human exposure. The "Toxicity" category reflects both the dose required to achieve a toxic effect and the severity of that effect.

IV. Allocation of Sampling Resources for Veterinary Drugs and Pesticides

Domestic:
As stated above, under the current system approximately 6,400 samples of two pounds of muscle and one pound each of kidney and liver will be collected. The muscle samples are larger and the total number of samples collected is smaller. The smaller number of samples required results in cost savings to FSIS that are realized through reductions in special delivery shipments and in IPP time spent collecting samples. Benefits to the public health occur because the Agency is able to test for more residues with the newer methods, but those benefits cannot be quantified at this time.

Import:
Similar to our domestic approach, the proposed plan remains statistically structured relative to sample collection of imported products. FSIS and other federal agencies will continue to select chemicals tested within the U.S. program using a risk-based approach. FSIS expects countries exporting meat, poultry, and egg products to the United States to control chemical residues in the products that they export. FSIS will continue to require foreign countries to maintain equivalent residue control programs (9 CFR 327.2(a)(2)(iv)(C)). Therefore, FSIS does not anticipate any trade concerns.

FSIS will not test (1) processed products from eligible foreign countries that also ship fresh products to the United States and (2) processed products from countries that source all their raw materials from other foreign countries that are eligible to ship fresh product and are actively exporting to the United States. This is due to the fact that the raw product is produced/originating from an eligible country. Processed products that are not tested due to this policy include:

(a) processed beef from Australia, Canada, Costa Rica, Mexico, New Zealand, and Uruguay;
(b) processed veal from Australia, Canada, and New Zealand;
(c) processed pork from Canada, Denmark, Mexico, the Netherlands, Poland, and Spain;
(d) processed mutton and lamb from Australia, Canada, and New Zealand;
(e) processed chicken from Canada and Mexico;
(f) processed turkey from Canada;
(g) other processed fowl from Canada and France; or
(h) processed varied combination products from Canada.

V. Next-Generation Selection and Ranking Process

Historically, FSIS methods tested for a single compound (analyte) and lacked the efficiency to meet current regulatory needs and deadlines. The recent advances and diversity in methodology have enabled FSIS to migrate to a new process for the identification and prioritization of hazards of public health concern. The proposed identification and prioritization approach is based, in part, on the EPA contaminant candidate list (CCL) process under the Safe Water Drinking Act.

To determine the "universe" of chemicals, FSIS will conduct searches and compile data, identifying hazards tested by U. S. federal agencies, international agencies, and specific countries. In addition, FSIS will take into account concerns of consumer groups and the public. To compile data on the universe of hazards, FSIS will search for databases containing toxicity and exposure data for veterinary drugs, pesticides, environmental contaminants, and human exposure.

To estimate risk, FSIS uses this basic equation: risk to public health = toxicity × occurrence.

Toxicity is how much of the hazard is too much (potency) and what kind of effect the hazard has *in vivo* (severity). Occurrence is exposure to the animal, in terms of how much is out there (magnitude) and how widespread it is (prevalence). Once the data have been gathered, FSIS will employ an appropriate model to prioritize the chemical hazards for consideration in the NRP.