U.S. FOOD & DRUG ADMINISTRATION

# Center for Veterinary Medicine (CVM)

**FDLI Annual Conference**
**May 3, 2018**

Steven M. Solomon, D.V.M., M.P.H.
Director

# CVM Vision and Mission





## Vision

*"Excellence, Innovation, Leadership"*

## Mission

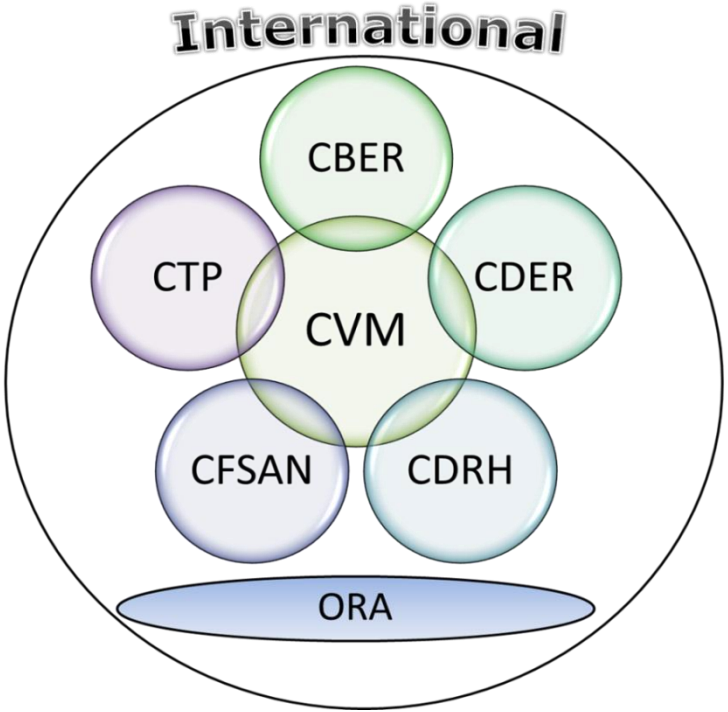
*"Protecting Human and Animal Health"*




# CVM Organizational Chart

# Microcosm of FDA

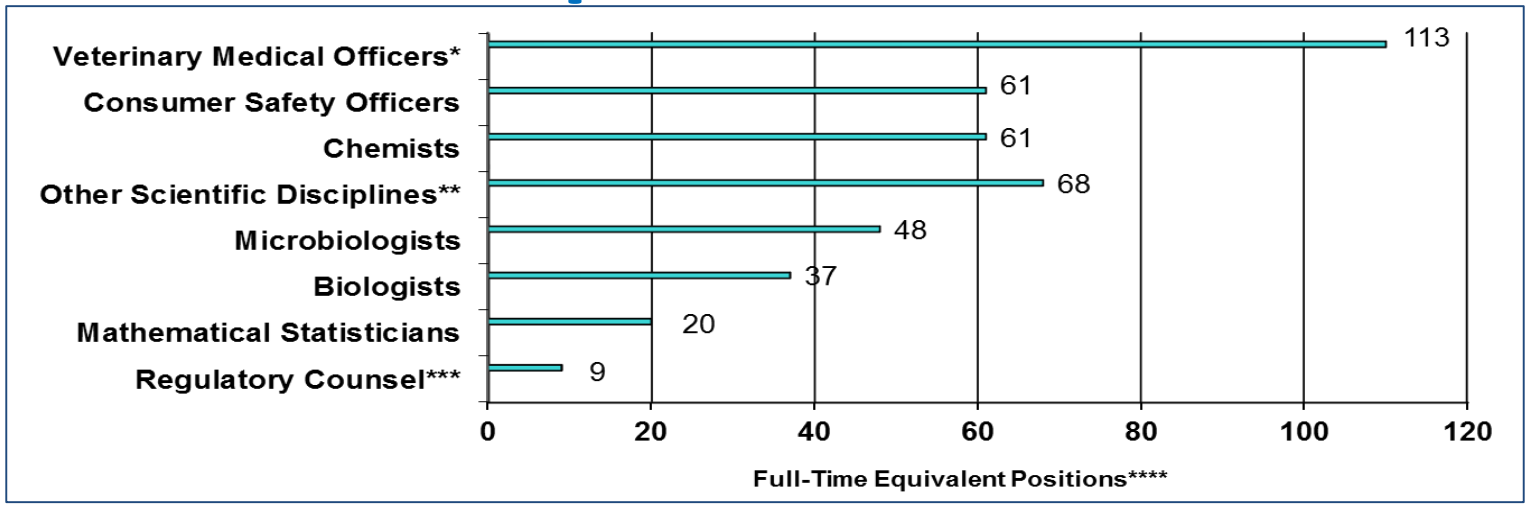
- ***Center for Biologics Evaluation and Research*** *(CBER):* Genetically Engineered Products
- ***Center for Drug Evaluation and Research*** *(CDER):* Animal Drugs
- ***Center for Devices and Radiological Health*** *(CDRH):* Animal Devices (post-market only)
- ***Center for Food Safety and Applied Nutrition*** *(CFSAN):* Food Safety and Feed Additive Petitions
- ***Center for Tobacco Products*** *(CTP):* Second-hand Smoke and Pet Health
- ***Office of Regulatory Affairs*** *(ORA):* Partner in Regulatory Oversight
- ***International Activities*** Strengthen animal drug and feed regulatory infrastructures in other countries and harmonize product standards



# Guiding Principles

- Public health
- Regulatory decisions are based off the best evidence and science
- Leverage and collaborate with domestic and international health and regulatory partners
- Operating openly and transparently is a core principle
- Continuous quality improvement
- Stakeholder engagement

# Scientific and Technical Disciplines at CVM




* In addition to the number of employees listed here as Veterinary Medical Officers, CVM employs approximately 20 additional employees with a D.V.M./V.M.D. degree who are in positions with titles other than Veterinary Medical Officer.

** Includes but is not limited to Animal Scientists, Toxicologists, Physical Scientists, Epidemiologists, Pharmacologists, and Physiologists.

*** CVM employs approximately 10 additional employees with a J.D. degree who are in positions with titles other than Regulatory Counsel to include Regulatory Policy Analyst and Government Information Specialist.

**** Total CVM FTEs are 578. Data as of September 30, 2017.

# CVM Budget

| | FY 2018 Enacted | FY 2019 President's Budget Request* |
|---|---|---|
| | Amount | Amount |
| FDA | $5,360,635,000 | $5,798,556,000 |
| CVM | $107,905,000 BA<br>$24,270,000 UF<br>$132,175,000 | $115,673,000 BA<br>$43,221,000 UF<br>$158,894,000 |
| CVM with Field | $198,171,000 | $225,065,000 |

* FY 2019 President's budget includes request for $9,700,000 that was previously appropriated in FY 2018.

# Additional Resources in FY 18

- FDA received additional resources in FY 18
- These funds will allow CVM to
  - ✓Make additional hires in ONADE to increase staff in our pre-approval program
  - ✓Fund additional research to support ONADE premarket review activities

# Requests for FY 19

- FDA requested additional resources in FY 19
- Looking forward (FYs 2019-2020), these funds will allow CVM to begin closing a long-standing budget gap
  - ✓ Expand the National Antimicrobial Resistance Monitoring System (NARMS)
  - ✓ Enhance our pharmacovigilance activities

# Key Initiatives

**Pre-market Animal Drug Review**

- Animal Drug User Fee Act (ADUFA)
- Animal Generic Drug User Fee Act (AGDUFA)
- Minor Use/Minor Species (MUMS)

**Food Safety Modernization Act (FSMA) Implementation**

**Antimicrobial Resistance Strategy**

- National Antimicrobial Resistance Monitoring System (NARMS)

**Emerging Technologies and Innovation**

- Genome Editing and Genetic Engineering
- Whole Genome Sequencing and Stem Cell Research

**Unapproved and Compounded Animal Drugs**

**Post-market Drug Safety, Effectiveness, and Quality**

- Adverse Drug Experiences (ADE)
- Veterinary Laboratory Investigation and Response Network (Vet-LIRN)

**Outreach to Consumers and Stakeholders**

# Significant Issues

- **Compounded Animal Drugs**
  - Withdrew **GFI #230**, "Compounding Animal Drugs from Bulk Substances," on November 7, 2017
  - New guidance forthcoming
  - New guidance will focus on veterinary medical needs of the multiple animal species within a veterinary-client-patient relationship
  - Clarifies that FDA is not applying the Drug Quality and Security Act to veterinary medical products

- **Unapproved Animal Drugs**
  - CVM looking at unapproved veterinary drugs
  - Prioritizing based on risk posed to human and animal health
  - FDA will develop strategies to address risk

# Innovation

**Significant new ways of reviewing products and getting products onto market**

- ADUFA
- AGDUFA
- MUMS

# ADUFA IV Performance Recommendations

## ADUFA proposals build on success of prior ADUFA achievements

- **Electronic Submission**
  - Require 100% electronic submission starting in FY 2019
- **Foreign Inspections**
  - CVM commits to working on implementation of the US-EU GMP Inspection Mutual Recognition Agreement for animal drug facilities
- **Additional Changes**
  - Amend the definition of “animal drug application” in ADUFA to allow user fee funds to be used for review of applications for conditional approval
  - For biopharma animals, exempt all fees except application fee
  - Revise the requirement that indexed products state their unapproved status on their labels
  - Require all approved drugs to include the NADA number on the labeling
  - Performance goal to schedule tissue residue method trial demonstrations
  - Performance goal for pre-submission conferences

# AGDUFA III Performance Recommendations

**AGDUFA proposals reflect growth of generic animal drug industry**

- **Electronic Submission**
  - Require 100% electronic submission starting in FY 2019
- **Additional Changes**
  - Require all approved drugs to include the ANADA number on the labeling
- **Reduces Review Times**
  - Administrative ANADAs
  - ANADA originals/reactivations
  - Prior Approval Supplements (CMC)
  - Generic Investigational New Animal Drug (JINAD) data submissions
  - JINAD protocols

# ADUFA/AGDUFA Reauthorization


- Initial public meeting
- 30-day comment period

- Negotiations with regulated industry
- Publication of minutes
- Stakeholder meetings
- Industry clearance
- FDA, HHS, OMB clearance

- FR Notice: Recommendations
- 30-day comment period
- Public meeting
- Revised recommendations
- Final clearance

- ADUFA and AGDUFA packages submitted to Congress on 1/2/2018
- Senate HELP hearing on 2/13/2018
- House E&C hearing on 3/13/2018

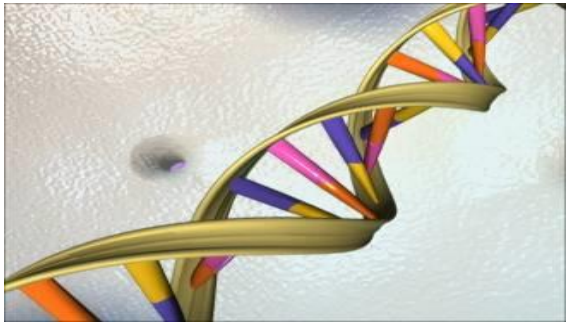
# Minor Use and Minor Species (MUMS) At a Glance

- **MUMS Programs from the Minor Use/Minor Species Animal Health Act of 2004**
  - **Designation** – Sponsor granted 7 years of exclusive marketing rights (similar to Orphan Drug Act) – **142** designations to date. Eligibility to apply for MUMS grants (initiated in FY 2009).
  - **Indexing** (for non-food minor species) – Sponsors allowed to legally market unapproved new animal drugs added to the index based partly on evaluation of an outside expert panel – **13** index listed products to date.
  - **Conditional Approval** – After completing all safety sections of a new animal drug application, a sponsor can market drug up to 5 years while collecting effectiveness data.
- Funding to develop MUMS-eligible drugs continues to be a challenge and the need continues to be great.

# Biotechnology

## Animal biotechnology

- Technology continues to advance (e.g., CRISPR)
- Flexible regulatory approach based on risk – genomic editing
- Great potential – especially biopharma



# Biotechnology

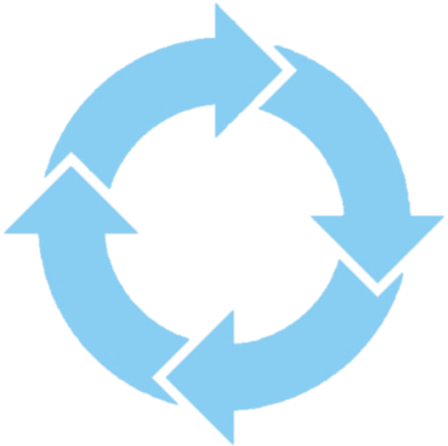
## Questions about regulatory oversight remain

- Focus on flexible, risk-based strategy
  - Enforcement discretion without FDA premarket review
  - Enforcement discretion following FDA review of sufficient information to determine that a product poses a low risk
  - Subject to full approval, but with varying data submission requirements based on the risk
- Increased interest in administrative record supporting our decisions




# Lifecycle Approach

- Looking more holistically at pre- and post-market drug review
- Similar to the approach taken by FDA's other medical product centers



- Allows CVM to leverage great expertise and anticipate and address post-market concerns to address **target animal safety** and **human user safety**

# Post-market Activities

- Renewing our commitment to work earlier with drug sponsors to address potential safety concerns
- Continuing to build our ability to collect and interpret signals through our ADE databases (both drugs and feed)

# Adverse Drug Experiences

**Monitors adverse events associated with approved animal drugs, unapproved animal drugs, and veterinary devices to identify safety signals and effectiveness issues of concern**

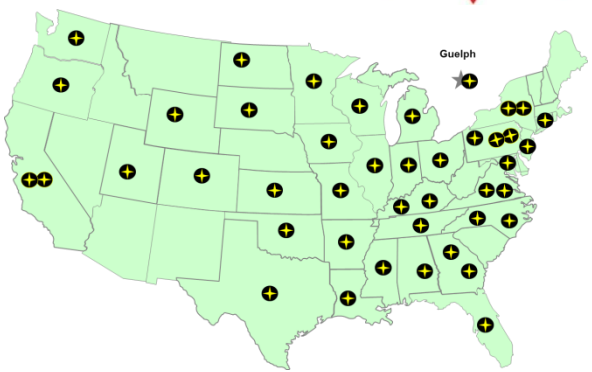
- For approved drug products, CVM scientists use the **adverse drug event database** to assist with decisions about product safety, which may include changes to the label or other regulatory action.
    - It is the largest animal drug adverse event regulatory agency database in the world, containing over 800,000 cases as of April 2018.
- CVM participates in outreach programs to encourage veterinarian participation in the pharmacovigilance program.
    - In FY 2017, approximately 101,000 Adverse Drug Experience (ADE) reports were received.

# Veterinary Laboratory Investigation and Response Network (Vet-LIRN)

**To promote human and animal health by collaborating with veterinary diagnostic laboratories to provide scientific information, build lab capacity, and investigate issues with CVM-regulated products**

This program coordinates facilities, equipment, and professional expertise of government and veterinary diagnostic laboratories across the country and Canada to respond to high priority chemical and microbial feed/drug contamination events.

- Network includes 43 laboratories
- Develop mechanisms for conducting investigations
  - Confidentiality agreements
  - Grants/contracts
  - Collaborate with other networks
- Activities
  - Proficiency and product testing
  - Fanconi testing
  - Necropsy examinations
  - Emergency response exercises
  - Investigate consumer complaint cases including jerky pet treats cases




ICLN USDA CDC

# Stakeholder Outreach

- **CVM Environmental Scan**
  - Consistent feedback both internal and external….
    We need to highlight who we are and what we do
    - ✓ Meetings
    - ✓ Congressional and Hill work
    - ✓ Renewed education and communication activities
    - ✓ One Health
- **Stakeholder Engagement**
  - More than 20 stakeholder meetings so far in FY 2018

# Animal Food Safety

- Both FSMA requirements and changes in the pet food industry present some new unique opportunities

- Safety for animals and people is everyone's highest priority

# FSMA

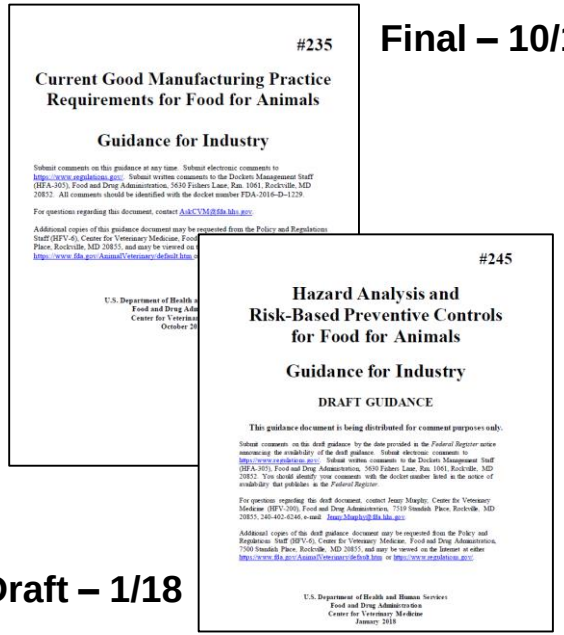
## Current Good Manufacturing Practice, Hazard Analysis, and Risk-Based Preventive Controls for Food for Animals (PCAF)

### Compliance Dates

- Large Business CGMPs: Sept 19, 2016
- Large Business Preventive Controls: Sept 18, 2017
- Small Business CGMPs: Sept 18, 2017
- Small Business Preventive Controls: Sept 17, 2018
- Very Small Business CGMPs: Sept 17, 2018
- Very Small Business Preventive Controls: Sept 17, 2019

Inspection Delay

### Guidance Documents



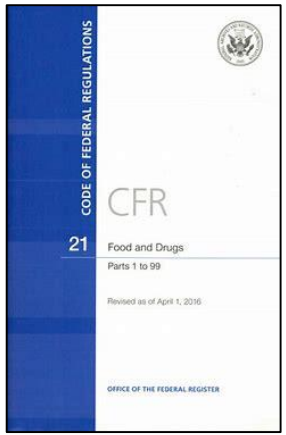

Final – 10/17

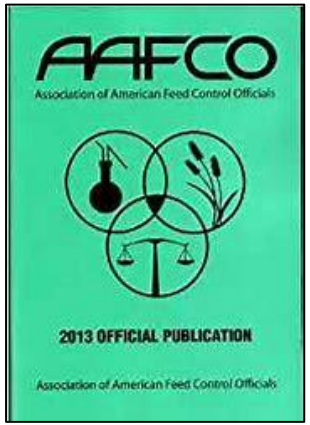
Draft – 1/18

# Animal Feed Ingredient Review

**New Ingredients – 3 pathways to market**

- Food Additive Petition to establish a regulation
- Conclusion that the intended use of the substance is GRAS
- New ingredient definition listed in the AAFCO Official Publication



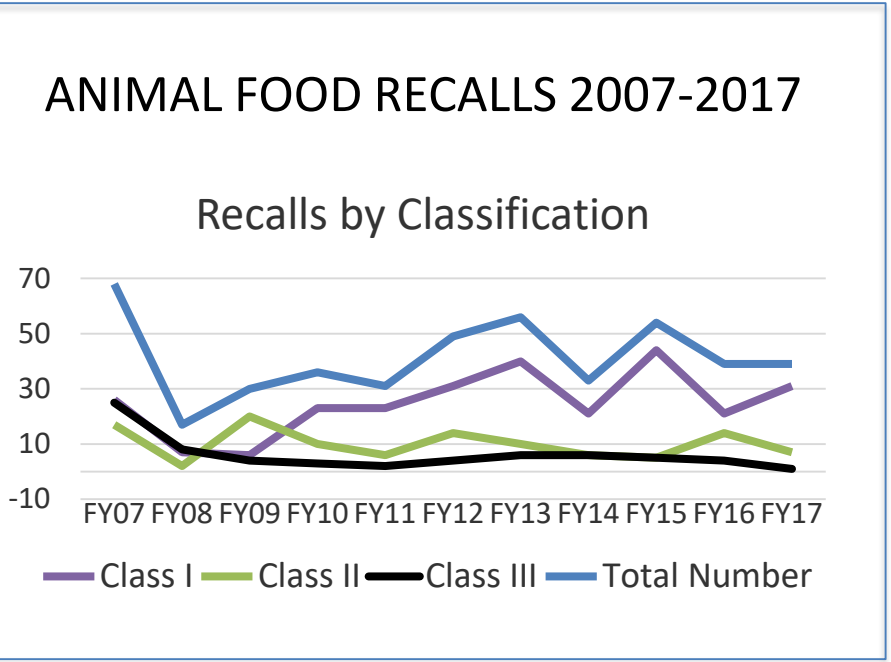



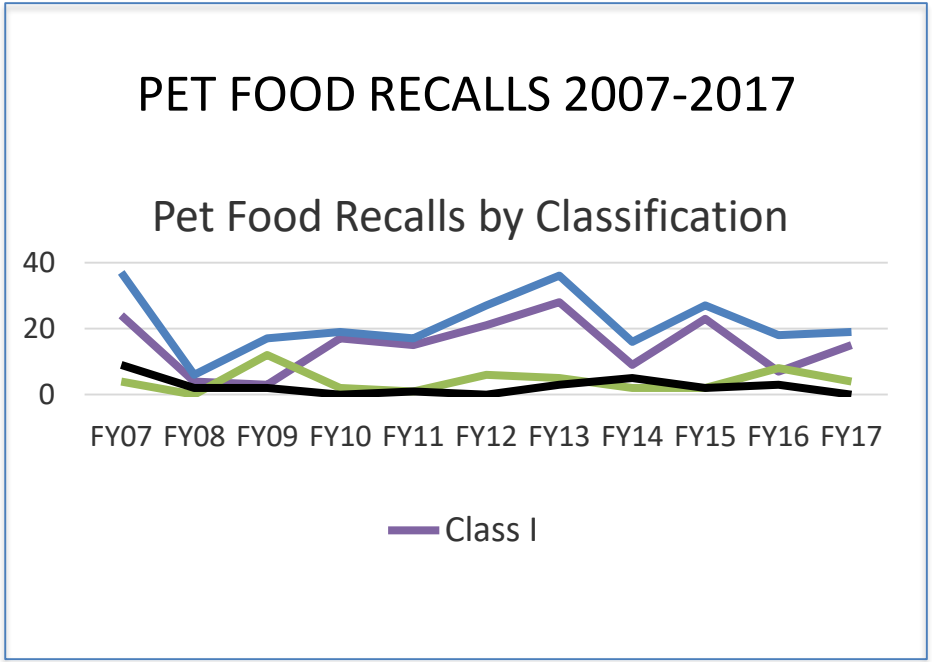
# Pet Food Safety

- A subset of animal feed is pet food. All pet food should be safe.
  - Free of unsafe hazards
    - Recent recalls for biological, chemical, and physical hazards in pet food
    - All pet food products should be free of pathogenic bacteria
  - Properly formulated
    - Nutrient imbalances continue to cause recalls

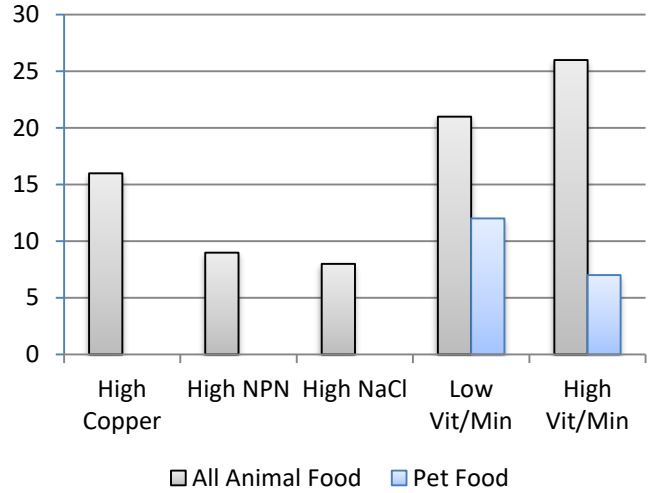
- FDA intends to apply requirements of the rule uniformly across the pet food industry

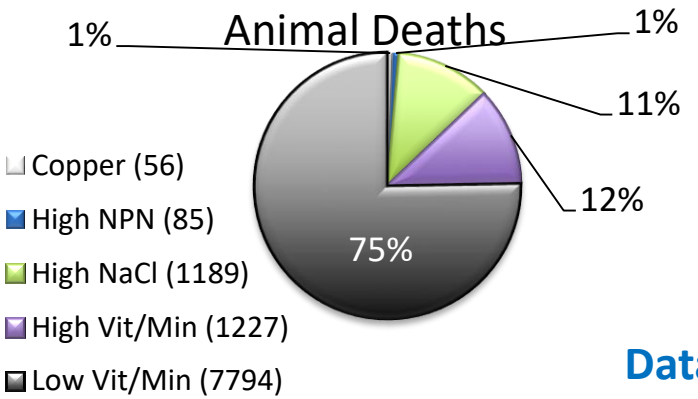
# Animal and Pet Food Recalls



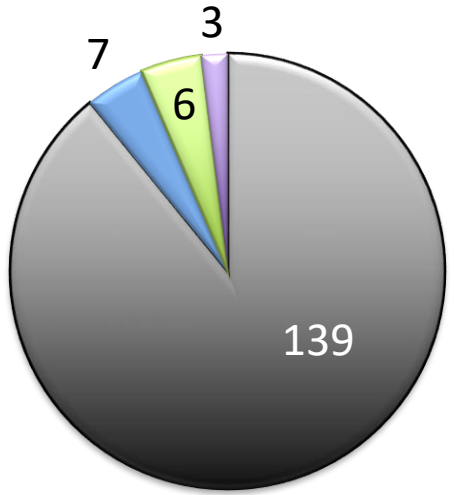



# Nutrient Associated Recalls




# Pathogen Associated Recalls




Salmonella
Listeria monocytogenes
Salmonella and L. mono
Clostrdium botulinum

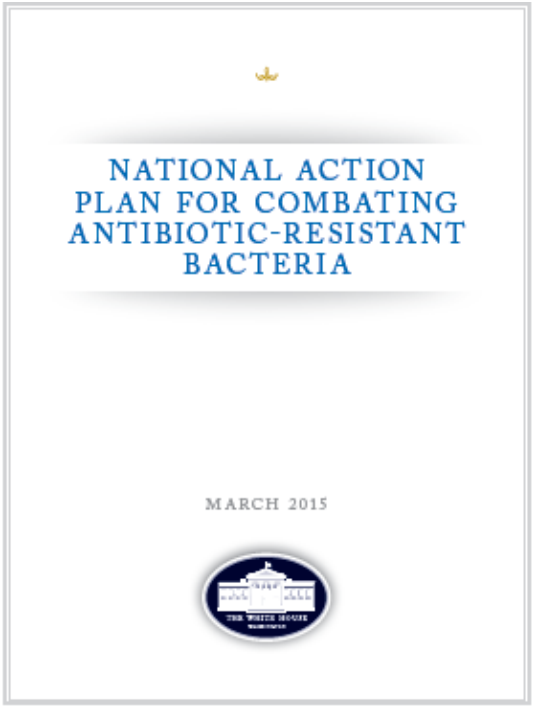
**Data for 2007–2017**

# Antibiotic Resistance

- **Human Health Impacts**
  - At least 2 million illnesses each year that are resistant to antibiotics
  - 23,000 deaths each year due to antibiotic-resistant bacteria
  - > 250,000 illness and ~ 15,000 deaths due to *clostridium difficile* infections each year
- **Health Costs**
  - Estimated at $20-35 billion annually
- **As bacteria develop new ways to resist antibiotics, we lose the ability to treat and prevent both common and serious infections**
  - In recent years, we have seen the emergence of a number of resistant organisms and a reduction in the utility of a number of antimicrobials

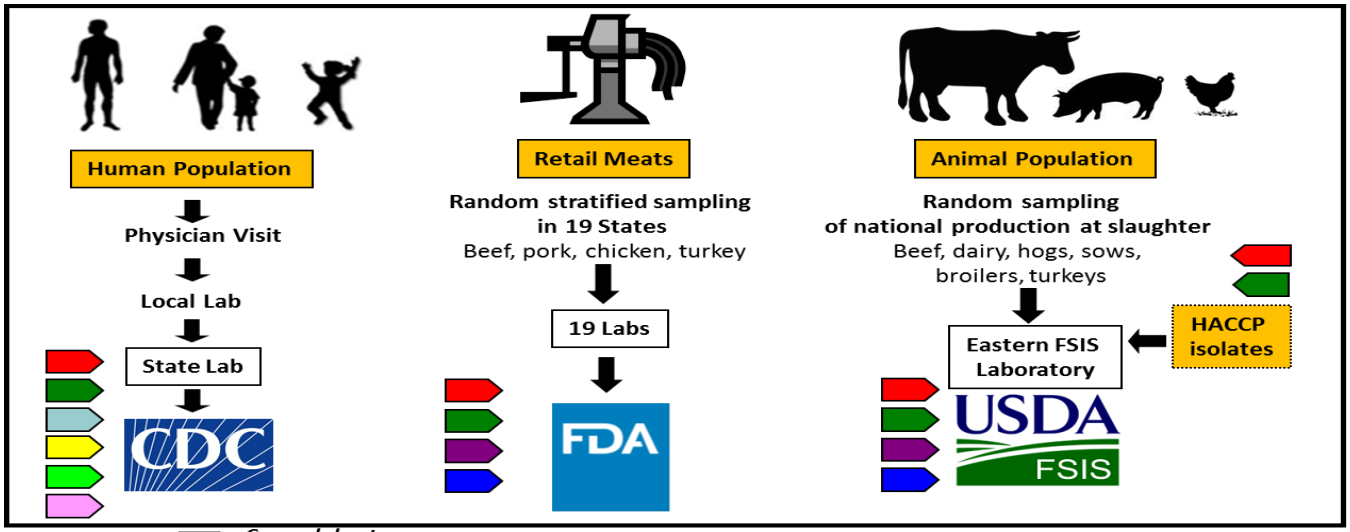
# Antimicrobial Resistance Strategy

1. Slow the emergence of resistant bacteria and prevent the spread of resistant infections
2. Strengthen national One Health surveillance efforts to combat resistance
3. Advance the development and use of rapid and innovative diagnostic tests for identifying and characterizing resistant bacteria
4. Accelerate basic and applied research and development of new antibiotics, other therapeutics, and vaccines
5. Improve international collaboration and capacities for antibiotic-resistance prevention, surveillance, control, and antibiotics research and development

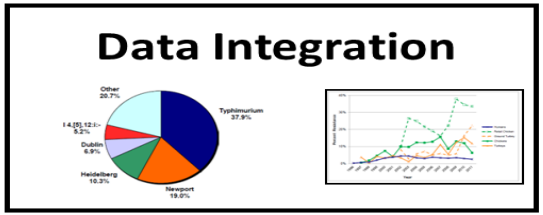


# Antimicrobial Resistance Strategy

## NARMS




- *Campylobacter*
- Non-typhoidal *Salmonella*
- *Enterococcus*
- Generic *E. coli*
- Typhoidal *Salmonella**
- *E. coli* O157*
- Non-cholera *Vibrio**
- *Shigella**




**NARMS Integrated Report: 2014**

The National Antimicrobial Resistance Monitoring System: Enteric Bacteria

*not included in the NARMS Integrated Report

# Recent CVM Actions

- Use of medically important antimicrobial drugs in food-producing animals limited to those uses:
  - Considered necessary for assuring animal health (i.e., eliminated production [growth promotion] uses)
  - That include veterinary oversight or consultation
- These concepts were first laid out in Guidance #209, and then implementation was addressed in more detail in Guidance #213

As of January 1, 2017

# Outcomes

- Of the 292 new animal drug applications initially affected by Guidance for Industry #213:
  - 84 were completely withdrawn
- Of the remaining 208 applications:
  - 93 water-use NADAs – converted from OTC to Rx
  - 115 feed-use NADAs – converted from OTC to VFD
  - Production (e.g., growth promotion) indications were withdrawn from all 31 applications that included such indications for use

# Outcomes

- Unprecedented level of engagement and collaboration over 3-year implementation period
- Result: Fundamental change to how antimicrobials have been distributed and used in animal agriculture for decades
  - All feed/water uses of medically important antimicrobials now under veterinary oversight

# Next Steps

General areas of focus include:

- **Align products** – Align approved use conditions of medically important antimicrobial products with judicious use principles
- **Use practices** – Implement/reinforce antimicrobial stewardship in all veterinary settings
- **Monitor progress** – Enhance monitoring of antimicrobial resistance and antimicrobial drug use in animals

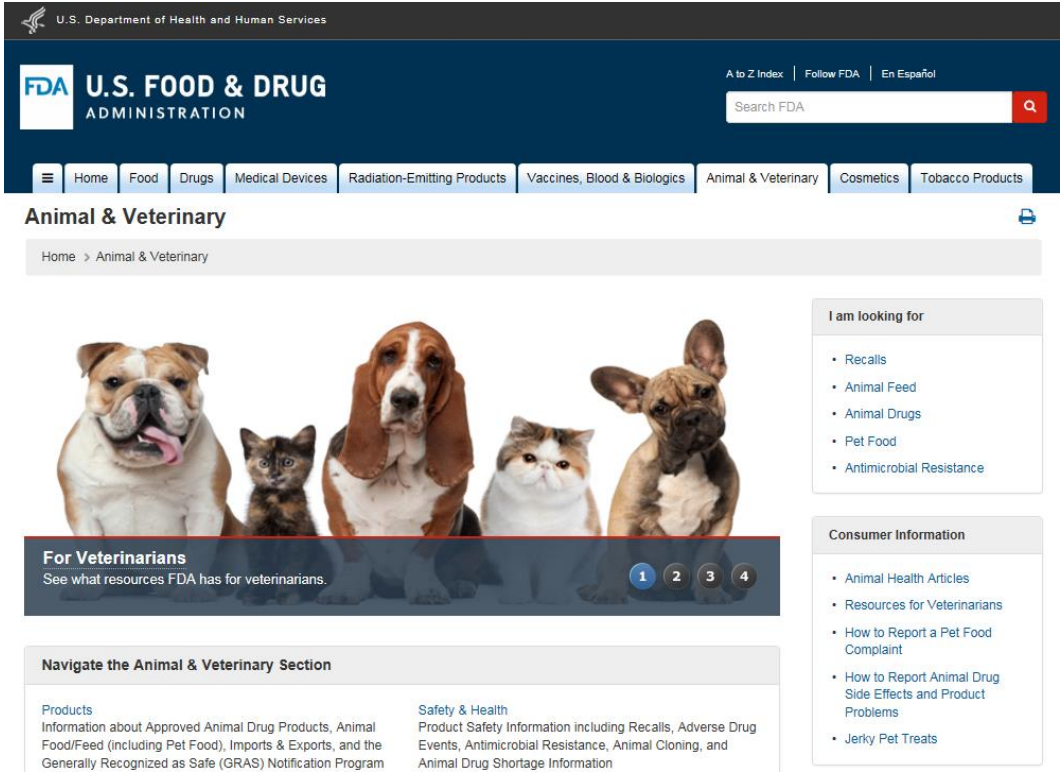
# International Activities

- **VICH** (International Cooperation on Harmonization of Technical Requirements for Registration of Veterinary Medical Produces) – Trilateral (EU-Japan-USA)
- **CODEX Alimentarius** (UN Food and Agriculture Organization / World Health Organization)
  - Codex Committee on Residues of Veterinary Drugs in Foods
  - Task Force on Antimicrobial Resistance
- **EMA** (European Medicines Agency)
- **EU-MRA** (Mutual Recognition Agreement) – Veterinary Drugs (EU)
- **VDD** (Veterinary Drugs Directorate – Canada
- **OIE** (World Organization for Animal Health)
- **Systems Recognition**

# Keep Up To Date

**http://www.fda.gov/AnimalVeterinary**

Reference the CVM Website for the most current information



Center for Veterinary Medicine
Protecting Human and Animal Health

# Thank you!