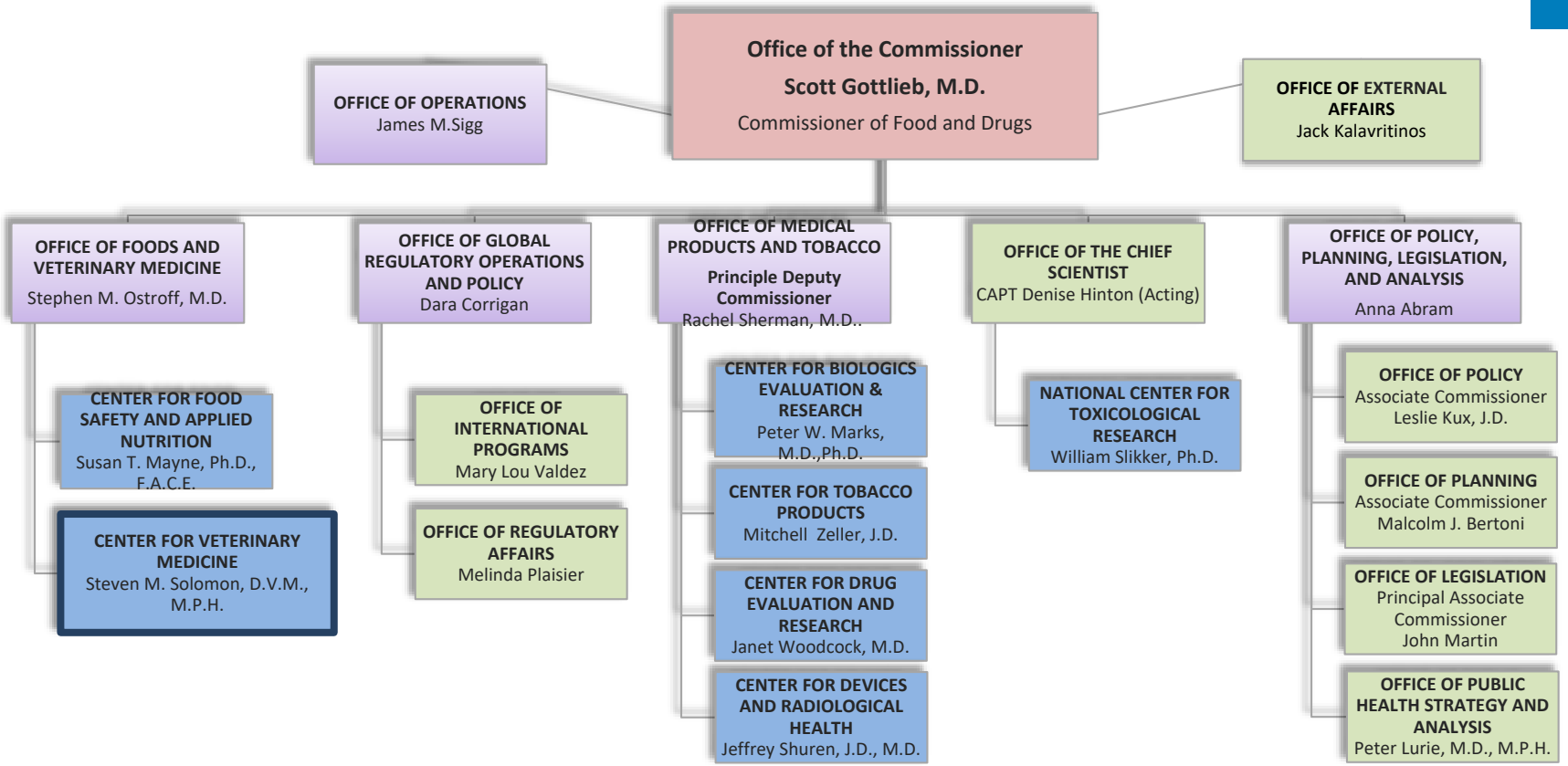
U.S. FOOD & DRUG ADMINISTRATION

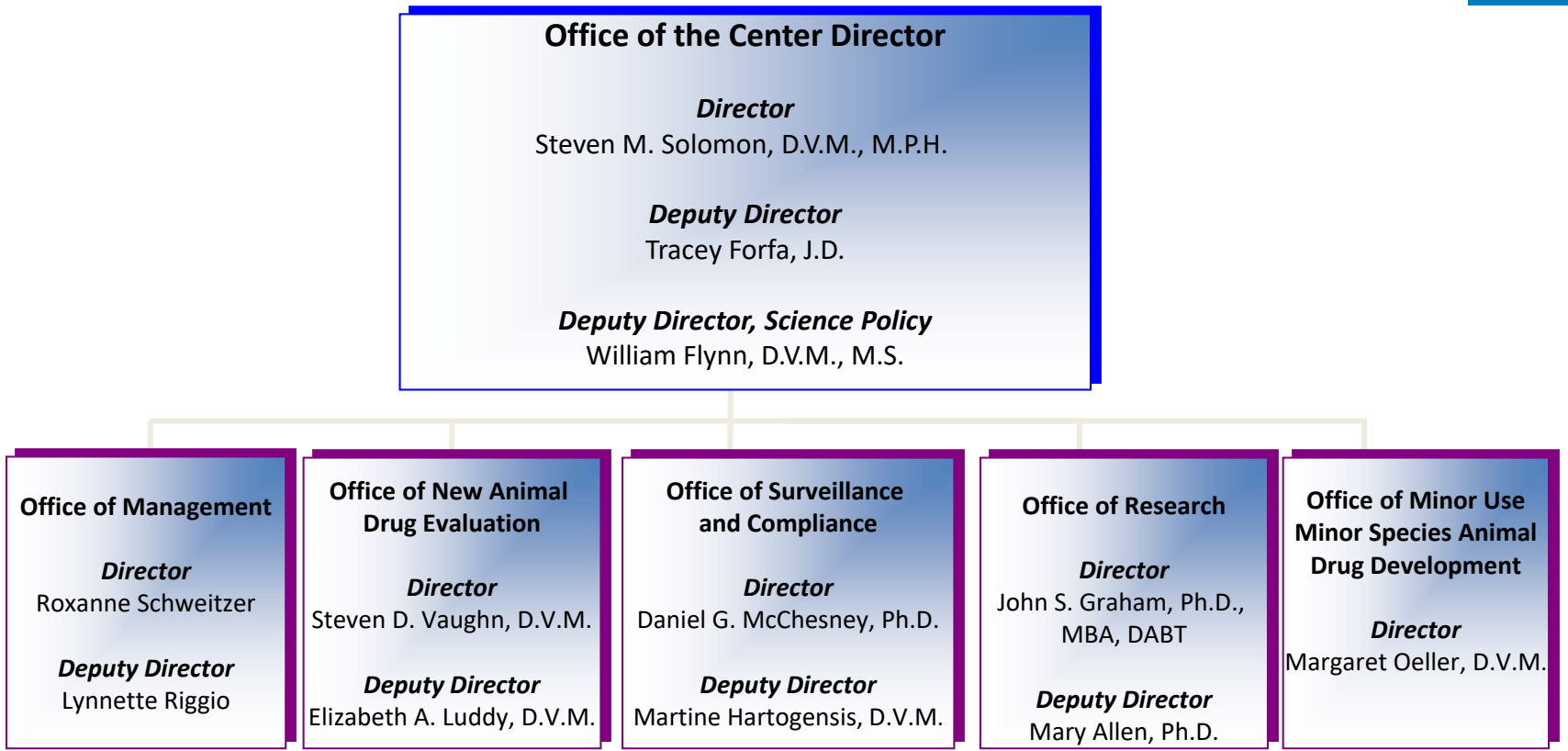
Center for Veterinary Medicine (CVM)

September 21, 2017
Kansas State University
Olathe Center for Innovation

Where is CVM in FDA



CVM Organizational Chart



CVM's Vision and Mission

Vision

Excellence, Innovation, Leadership

Mission

Protecting Human and Animal Health

Guiding Principles

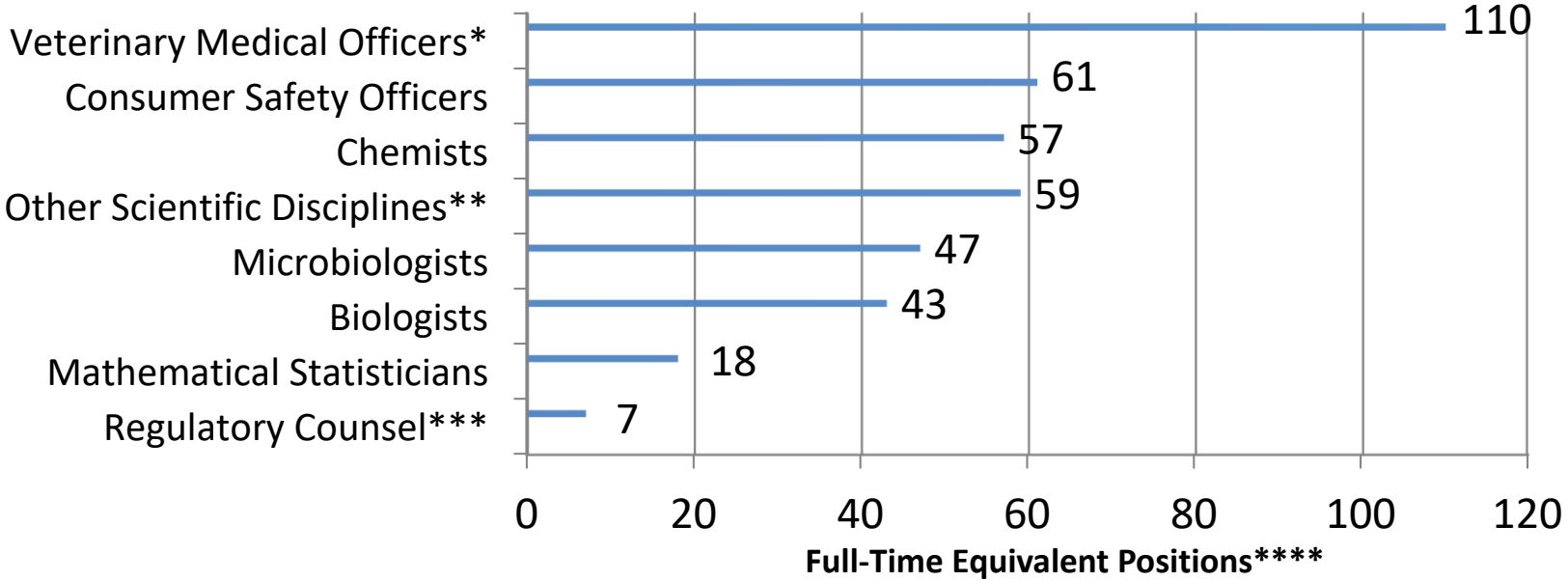
- Public health is the lens I look through
- Regulatory decisions are based off the best evidence and science
- Leverage and collaborate with domestic and international health and regulatory partnerships
- Operating openly and transparently is a core principle
- Continuous quality improvement
- Stakeholder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

CVM's Budget

	FY 2017 Enacted
CVM Program Level	$128,876,000
CVM Budget Authority	$98,205,000
ADUFA*	*$20,879,000*
AGDUFA*	*$9,792,000*

** Non-add, CVM portion only*

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.

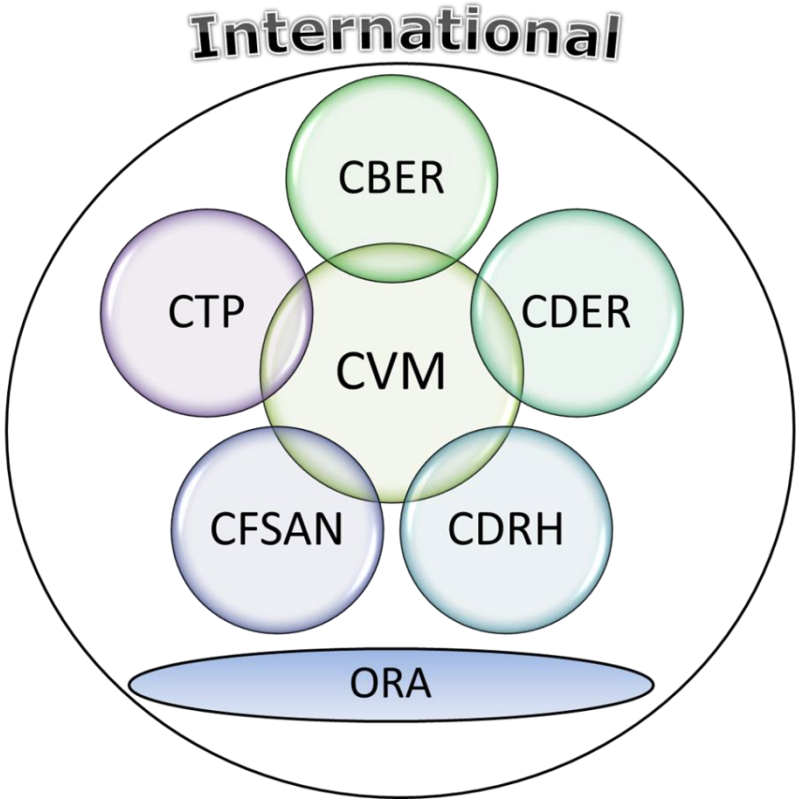
**Includes Animal Scientists, Health Scientists, Epidemiologists, Toxicologists, Pharmacologists, Physiologists, Physical Scientists, and Animal Caretakers.

***CVM employs approximately10 additional employees with a J.D. degree who are in positions with titles other than Regulatory Counsel to include Regulatory Policy Analysts and Government Information Specialists.

****Total CVM FTEs are 582. Data as of September 30, 2016.

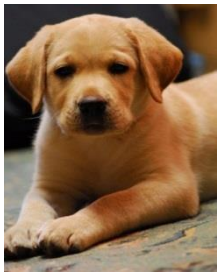
Microcosm of FDA

- *Center for Biologics Evaluation and Research (CBER):* Biologics produced by genetically engineered animals
- *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, Feed Additive Petitions and GRAS
- *Center for Tobacco Products* (CTP): Information on health effects of second hand smoke and pet health
- *Office of Regulatory Affairs (ORA):* Partner in Regulatory Oversight
- *International Activities*: Strengthen animal drug and feed regulatory infrastructures and harmonize product standards.



Companion Animal and Minor Species Medicine

CVM is responsible for regulating drugs, devices and food additives used in companion animals (dogs, cats and horses) and minor animal species



- Increase the availability and diversity of safe and effective products that relieve animal pain and suffering, sustain their health, and do not compromise human health.

- Minor Species include all animals other than the 7 Major Species: cattle, pigs, chickens, turkeys, horses, dogs and cats.

Animal Health and Animal Food Product Safety: Farm to Table

CVM is also responsible for regulating animal drugs, devices and food additives used in food producing animals

- ~2.1 billion chickens & turkeys
- ~162 million cattle & pigs
- ~7.9 million sheep & goats

- Animal Drug Manufacturers
- Domestic and Foreign Animal and Human Feed Manufacturers
- Livestock and Poultry Producers
- Specialized Industry/Firms

- Million of humans in the U.S. and other countries

CVM's Key Initiatives

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 Animal Drugs Strategy (including compounding)

Post-Market Safety and Quality

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

Outreach to Consumers and Stakeholders

Animal Drug Review

- CVM evaluates new animal drug applications for pioneer and generic drugs intended for animals that produce food, for companion animals, and for minor species.
- When the drug is for use in food-producing animals, not only must the safety to the animal be demonstrated, but also the safety of the food products derived from the treated animals that are intended for human consumption.
- CVM reviews safe, effective, quality manufactured, and properly labeled new animal drug products through a science-based approach in a regulatory environment.

Animal Drug Review:
Animal Drug User Fee Act (ADUFA)

ADUFA provides CVM with resources to enhance the timeliness and predictability of new animal drug applications for pioneer drug products

- ADUFA is currently in the third authorization, which sunsets at the end of FY 2018
  - ADUFA I (FY2004-FY2008), ADUFA II (FY2009-FY2013), ADUFA III (FY2014-FY2018)
- ADUFA III includes a target revenue of $114 million over the 5 years
- ADUFA significantly reduced review times for a single cycle, from 500+ days prior to the authorization of ADUFA I to 180 days
- CVM has met and exceeded all performance goals since the start of the program in FY 2004
- CVM is working on reauthorization with the Animal Health Institute
  - Negotiations are set to finish in 2017, will move through clearance with FDA, HHS, and OMB, and must be submitted to Congress by January 15, 2018

Animal Drug Review:

Animal Generic Drug User Fee Act (AGDUFA)

AGDUFA provides CVM with resources to enhance the timeliness and predictability of generic new animal drug applications

- AGDUFA is currently in the second authorization, which sunsets at the end of FY 2018
  - AGDUFA I (FY2009-FY2013), AGDUFA II (FY2014-FY2018)
- AGDUFA II includes a target revenue of $38 million over the 5 years
- AGDUFA significantly reduced review times for a single cycle, from 700+ days prior to the authorization of AGDUFA I to 270 days
- CVM has met and exceeded all performance goals since the start of the program in FY 2009
- CVM is currently working on reauthorization of AGDUFA with the Generic Animal Drug Alliance
  - Negotiations are set to finish in 2017, will move through clearance with FDA, HHS, and OMB, and must be submitted to Congress by January 15, 2018

Animal Drug Review: Minor Use and Minor Species (MUMS)

Expand availability of drugs to treat minor animal species and uncommon diseases in the major animal species

- 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) – 137 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.
- Liaison to USDA's NRSP-7 program – research to support approval of new animal drugs for minor species of agricultural importance.

Food Safety Modernization Act (FSMA) Implementation

Protecting public health by preventing food safety problems

FSMA directs FDA to build a food and feed safety system based on the public health principles of comprehensive prevention, enhanced focus on risk-based resource allocation, and partnerships across the public and private sectors to minimize hazards from farm to table.

Enhanced Partnerships	Prevention	Inspection, Compliance and Response	Imports
- State/local and international capacity building - National agriculture and food defense strategy	- Mandatory preventive controls for facilities - Intentional contamination	- Administrative detention - Recalls (upon enactment) - Suspension of registration	- Foreign supplier verification program - Accredited third-party certification program - Voluntary Qualified Importer Program

Antimicrobial Resistance

The National Strategy outlines 5 goals and Objectives:

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 development and use of rapid diagnostic tests for identification and characterization of resistant bacteria.
4. Accelerate basic and applied research and development for new antibiotic, other therapeutics and vaccines.
5. Improve international collaboration and capacities for antibiotic resistance prevention, surveillance, control, and antibiotic research and development.

Antimicrobial Resistance Strategy

Provide safe use of antimicrobials in food animals while ensuring that significant human antimicrobial therapies are not compromised or lost

- Guidance for Industry #209 describes the overall policy direction regarding the judicious use of antimicrobial drugs.
  - Key principles are limiting use of medically important antimicrobial drugs in food-producing animals to those uses:
    - considered necessary for ensuring animal health (therapeutic uses)
    - that include veterinary oversight or consultation
- Limit the use of antimicrobial drugs in food-producing animals (eliminate growth promotion and feed efficiency claims on medically important antibiotics)
- Enhance the quality and accuracy of data on antimicrobial drug sales and distribution

Antimicrobial Resistance Strategy

- Guidance for Industry #213 provides more detail on implementing the judicious use principles outlined in Guidance #209:
  - Defines “medically important” (i.e., define what products are affected)
  - Establishes a 3-year implementation timeline to voluntarily remove claims relating to production uses, and bring remaining therapeutic uses under veterinary oversight by changing marketing status from over-the-counter (OTC) to veterinary feed directive (VFD) or prescription (Rx)
- As of January 3, 2017, all affected drug applications have either aligned with judicious use principles outlined , or their approvals have been voluntarily withdrawn.
- Of the 292 approved drug applications identified as being affected by Guidance for Industry #213 including pioneer, generic, and combination approvals:
  - 84 drug applications were withdrawn
  - 93 applications for oral dosage form products intended for use in water were converted from OTC to RX
  - 115 applications for products intended for use in feed were converted from OTC to VFD
- Production (e.g. growth promotion) indications were withdrawn from all affected applications

Antimicrobial Resistance Strategy

National Antimicrobial Resistance Monitoring System (NARMS)

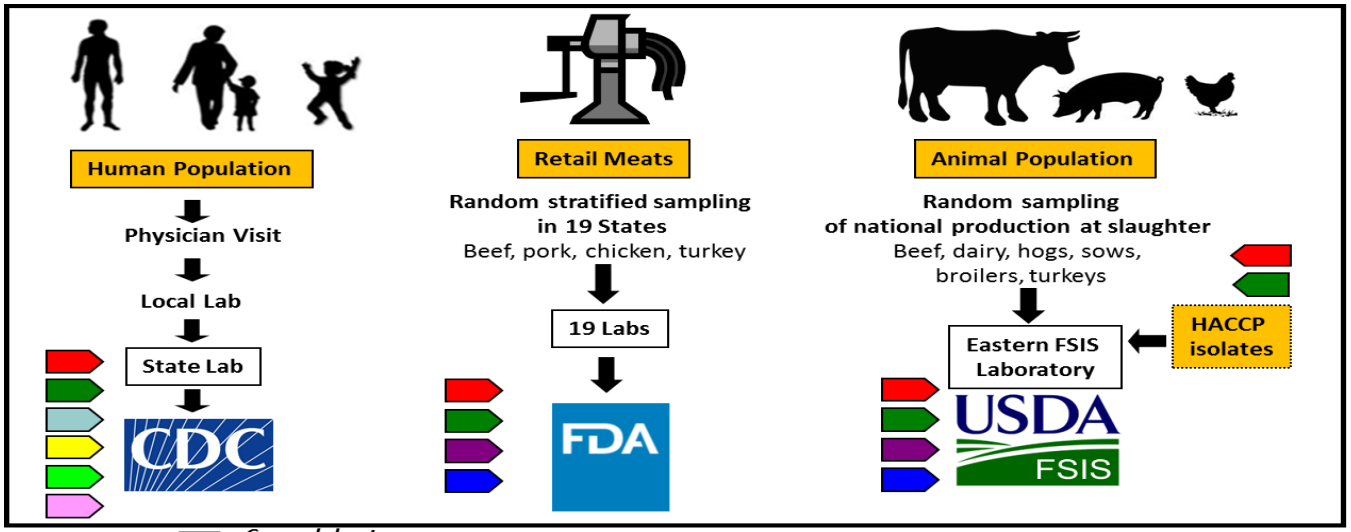
NARMS Mission

- Monitor trends in antimicrobial resistance among foodborne bacteria from humans, retail meats, and animals
- Disseminate timely information on antimicrobial resistance to promote interventions that reduce resistance among foodborne bacteria
- Conduct research to better understand the emergence, persistence, and spread of antimicrobial resistance
- Assist the FDA in making decisions related to the approval of safe and effective antimicrobial drugs for animals

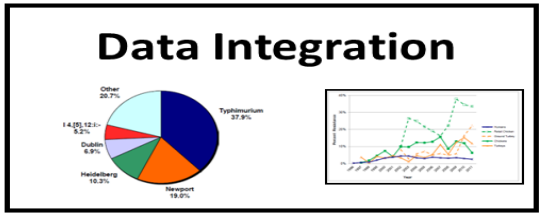
NARMS
National Antimicrobial Resistance Monitoring System

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

Emerging Technologies and Innovation

Genome Editing and Genetic Engineering

Revolutionary Crossroads in American Agriculture

- Genome Editing is the term used to describe a relatively new set of technologies that enable one to make *precise* changes in the DNA of a plant, animal or other living organism.
- Genetic Engineering is the process in which recombinant DNA (rDNA) technology is used to introduce desirable traits into organisms.
  - Current Guidance for Industry #187 *Regulation of Genetically Engineered Animals Containing Heritable Recombinant DNA Constructs*, published January 2009; revised draft GFI #187, *Regulation of intentionally Altered Genomic DNA in* Animals, issued January 19, 2017. Comment period closed June 19, 2017.
  - First food animal approval: Aqua Advantage Salmon
  - "Bio-pharm" animals are used to make human biologics or other therapeutics (e.g. ATryn – human anticoagulant – a therapeutic protein produced in milk of GE goats approved in February 2009).

Emerging Technologies and Innovation

Whole-Genome-Sequencing and Stem Cell Research

Whole-Genome-Sequencing (WGS)

- WGS reveals the complete DNA make-up of an organism, enabling FDA to better understand variations both within and between species.
- This technology is being used to perform basic foodborne pathogen identification, which has the potential to help reduce foodborne illnesses and deaths over the long term.

Mesenchymal stem cell (MSC)

- Expected to be the most common cell type for stem cell products.
- Dog and horse products are being developed.
- Draft Guidance for Industry #218 *Cell Based Products for Animal Use* published July 2014.
- Stem cell markers in canine MSC derived from various tissue sources have been identified
- Addresses data gap in cell identification.
- Assists with bioequivalence and safety requirements.

Unapproved Animal Drugs Strategy

(including compounding)

Bring marketed unapproved animal drugs into compliance with FDA laws and regulations

- These drugs are considered adulterated under the FD&C Act, and have the potential to compromise food safety, place animals or humans at undue risk from unsafe or ineffective treatment, and undermine the incentives to develop and submit new animal drug applications to FDA.
- Although Congress passed ***The Drug Quality & Security Act*** (11-2013) applicable to the compounding of human drugs, this legislation does not apply to the compounding of drugs intended for use in animals.
- CVM is developing enforcement strategies for unapproved drugs to further support the approval process and to protect human and animal health.
- CVM published draft Guidance for Industry #230, Compounding Animal Drugs from Bulk Drug Substances, in May 2015. We are currently revising and will issue a new draft guidance.

Post-Market Safety and Quality

Oversight and surveillance of post-market product use assures the safety of FDA-regulated products

Initial product safety and effectiveness data comes from small clinical trials, however once a product is approved and on the market for broader use we have to rely on post-market monitoring and surveillance to assure its safety and take action early on if needed.

Adverse Drug Experiences

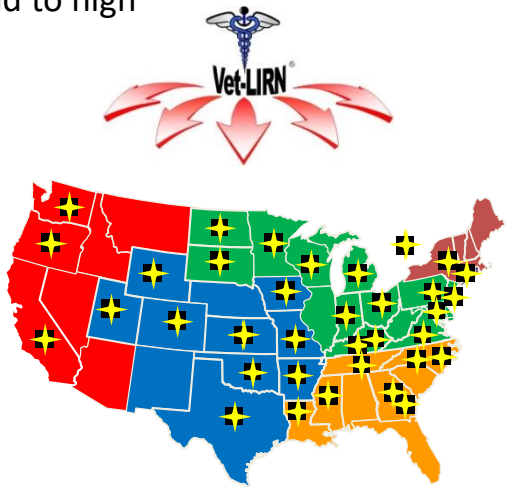
Monitors adverse events for approved animal drugs, unapproved animal drugs, and veterinary devices to identify safety signals and effectiveness issues of concern

- 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 719,000 cases as of April 2017.
- CVM participates in outreach programs to encourage veterinarian participation in the pharmacovigilance program.
  - In FY 2016, approximately 99,000 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 38 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

Outreach to Consumers and Stakeholders

Timely information for the benefit of all animals and humans

- With continuous communication and outreach, CVM *strives to* enhance public trust, promote safe and effective use of the animal health products we regulate, and share our scientific endeavors
- CVM provides reliable, science-based information to promote animal and human health
- Timely information provided to consumers, industry, trade, and government organizations via social media, consumer updates, email subscriptions, and Animal Health Literacy (AHL) articles written in plain language.

CVM's International Programs Harmonization Initiatives

- **VICH** = International Cooperation on Harmonization of **Technical Requirements** for Registration of Veterinary Medicinal Products
  - Encourages global product development approach
  - Provides a venue where highly experienced and qualified scientific experts exchange information
  - Encourages pooling of regulatory and industry resources
  - Provides more regulatory certainty
  - Reduces impediments to trade in VMPs and food
  - Supports animal welfare

- CODEX Committee on Residues of Veterinary Drugs in Foods
  - Recommends Maximum Residue Limits (MRLs) for veterinary drugs in foods

CVM's International Programs Harmonization Initiatives

- European Medicines Agency (EMA)
  - Quarterly bilateral meetings with the Veterinary Division of EMA These meetings promote a continuous exchange of scientific information including current products and innovative technologies.
  - Active exchange of cGMP reports
  - CVM has also hosted 4 extended visits by EMA Fellowship awardees.

- Health Canada Veterinary Drugs Directorate (VDD)
  - Regulatory Cooperation Council (RCC) established by President Obama and Prime Minister Harper
  - Ongoing exchange of regulatory Surveillance and Compliance information

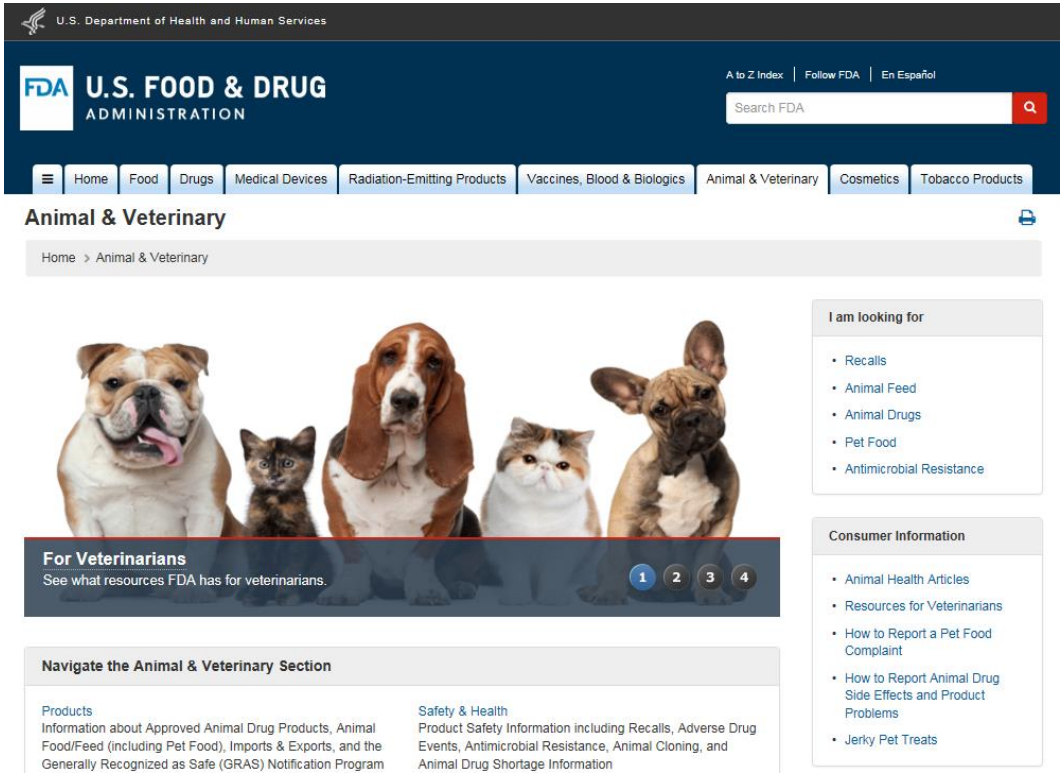
CVM's International Programs Outreach and Capacity Building

- OIE Collaborating Center for Veterinary Drug Regulatory Programs
  - strengthen veterinary medicine regulatory infrastructures worldwide, including the training of OIE's 180 Member Countries' National Focal Points for Veterinary Medicinal Products
- Global Animal Health Conference
  - improve market access for authorized veterinary medicines in developing and in-transition countries
- Health For Animals- Executive Secretariat

Keep Up To Date

http://www.fda.gov/AnimalVeterinary

Reference the CVM Website for the most current information



Thank you!

U.S. FOOD & DRUG ADMINISTRATION