U.S. FOOD & DRUG ADMINISTRATION

Combating AMR through Antimicrobial Stewardship

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Antimicrobial Stewardship in Veterinary Settings

- Antimicrobial resistance (AMR) is a complex, multifactorial issue; to preserve the availability and effectiveness of antimicrobials for both human and animal health, a multisectoral, One Health, approach is needed to combat AMR
- The U.S. Food and Drug Administration (FDA) is responsible for ensuring the safety of animal drugs. This includes assessing AMR risks and implementing actions to mitigate those risks, as appropriate.
- In 2018, FDA published a 5-year plan for supporting antimicrobial stewardship in veterinary settings.
  - we believe that fostering good antimicrobial stewardship practices in veterinary settings and optimizing use can help slow the development of antimicrobial-resistant bacteria

Antimicrobial Stewardship in Veterinary Settings

Key Areas of Focus (Goals of FDA 5-year AMR plan)

- Evaluating use conditions of animal antimicrobial drug products
- Promoting/supporting antimicrobial stewardship at the user level
- Collecting data to monitor animal antimicrobial use and antimicrobial resistance

FDA Approach for Implementing Change in Veterinary Sector

- Focusing actions or mitigations on drugs of greatest concern: drugs that are important human therapies ("medically important antimicrobials")
- Emphasizing collaboration and seeking cooperation from industry to take action voluntarily **

**Note: Once drug company voluntarily takes action to change approved use condition of a drug product, the end user is required to follow new conditions of use

Evaluating drug products: Important Actions

Year	Action	Purpose
2003	**Guidance #152**, implemented new guidance for evaluating AMR risks as part of drug approval process	Outlines recommended risk assessment process for use by drug sponsors seeking approval of new proposed uses of medically important antimicrobials in food-producing animals
2013	**Guidance #213**, implemented guidance recommending certain changes be made to already approved feed and water uses of medically important antimicrobials	Outlined a 3-year plan for drug sponsors to voluntarily eliminate growth promotion uses and transition products from over-the-counter (OTC) availability to use under oversight of licensed veterinarians
2021	**Guidance #263**, implemented guidance to compete process of bringing medically important antimicrobials under vet oversight	Outlines 2-year plan for drug sponsors to voluntarily transition to veterinary oversight all medically important antimicrobials that are still available OTC

Changes completed in 2017 (Guidance #213)

All affected drug sponsors worked voluntarily with FDA

Of the **292** approved animal drug applications affected by **Guidance for Industry #213**:

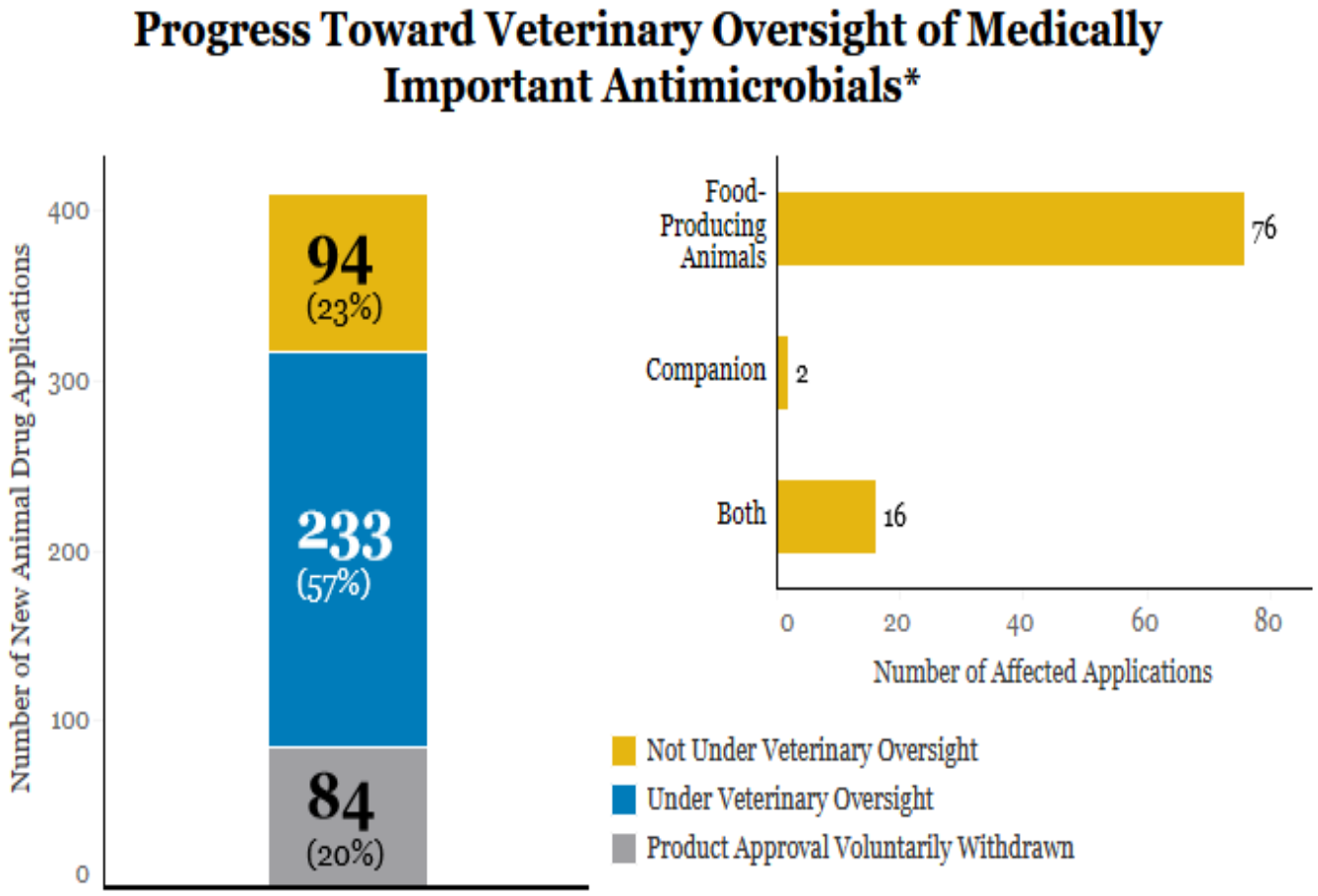
- **84** were completely withdrawn

Of the remaining **208** applications,

- **93** (water products) – converted OTC to Rx
- **115** (feed products) – converted OTC to veterinary feed directive (VFD)

All production (e.g., growth promotion) indications were withdrawn (**31** applications)

Veterinary Oversight of Medically Important Antimicrobials



* Performance measures: Percent and number of medically important antimicrobial animal drug applications approved for use in food-producing and companion animals by marketing status.

- With implementation of Guidance #213 in 2017, all feed and water uses were transitioned to veterinary oversight (blue) or were withdrawn (gray)
- With full implementation of Guidance #263 (June 2023), all remaining OTC products** will be transitioned to prescription

**Includes products that are approved for routes of administration other than feed or drinking water (e.g., injectables, intramammary).

Antimicrobial Stewardship in Veterinary Settings

Collecting data to monitor animal antimicrobial use and antimicrobial resistance

- Scientifically-sound data are needed to guide actions taken to address AMR and to assess their effectiveness
- Three important data streams include:
  - Antimicrobial resistance data
  - Antimicrobial sales/distribution data
  - Antimicrobial use data

Collecting Data to Monitor Antimicrobial Resistance in Animals

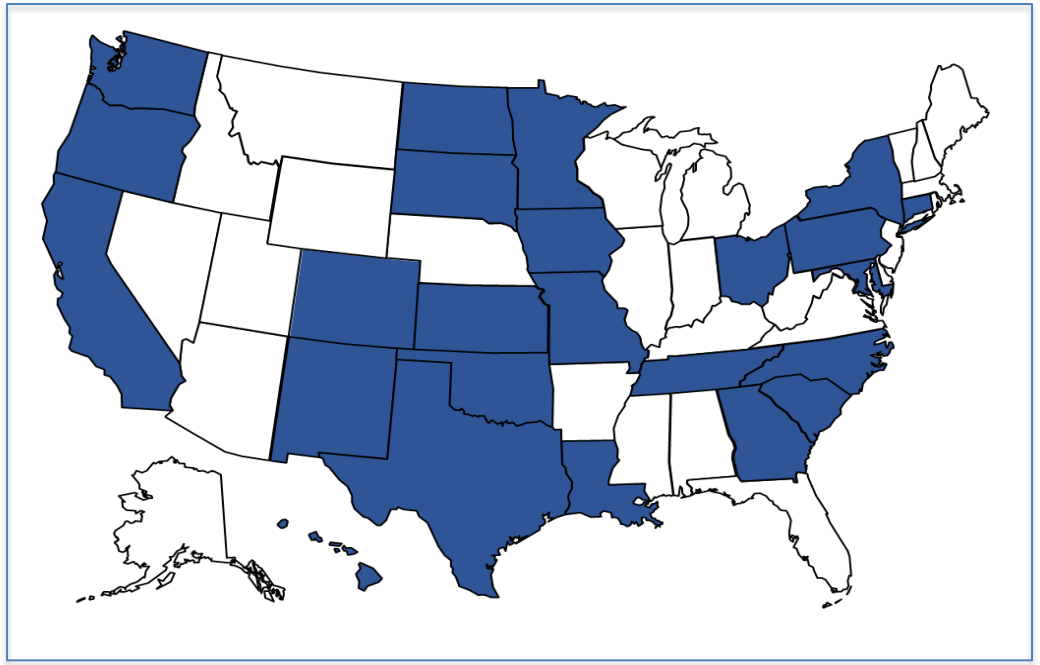
NARMS
National Antimicrobial Resistance Monitoring System

FDA → **Random stratified sampling of retail meat; seafood testing being developed**

USDA → **Random sampling of national food animal production at slaughter**

CDC → **Nationwide surveillance of foodborne bacteria from human isolates**

FDA Monitoring of AMR in Retail Meats: 24 States in 2021



Sampling: 49 packages per month

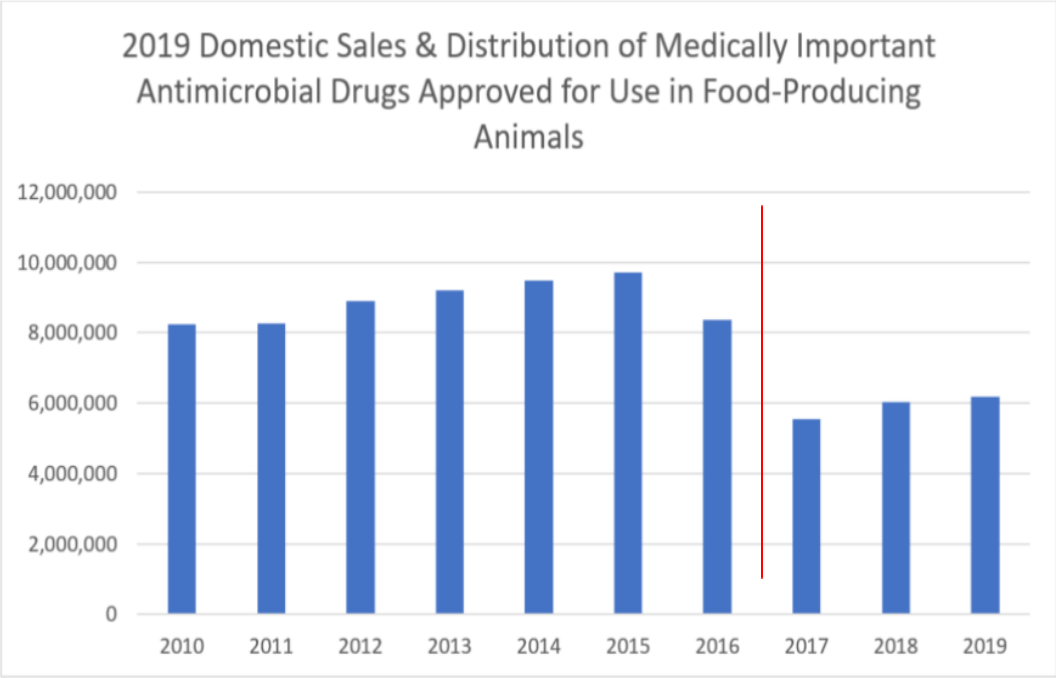
- ✓ 10 retail chicken
- ✓ 10 ground turkey
- ✓ 10 ground beef
- ✓ 10 pork chops
- ✓ 3 salmon
- ✓ 3 shrimp
- ✓ 3 tilapia

Microbiology

- ✓ Retail meat: *Salmonella, Campylobacter, E. coli, Enterococcus*
- ✓ Seafood: *Vibrio*, CRE, *Aeromonas*

Collecting Data on Antimicrobial Sales and Use

Sales Data



Domestic sales decreased
- 33% between years 2016 and 2017
- 43% since 2015 (peak year of sales/distribution)
- 28% since the first year of reported sales in 2009

Domestic sales increased 3% between 2018 and 2019

Source: 2019 Summary Report on Antimicrobials Sold or Distributed for Use in Food-Producing Animals

Use Data

- Sales collection requirement established by law in 2008; no requirement for use data
- Given the limitations of sales data, FDA has funded pilot projects to collect on-farm use data
  - Feedlot and dairy cattle (Kansas State University)
  - Broilers, turkeys, swine (University of Minnesota)
- In 2020, two pilot projects were funded to collect antimicrobial use information in the companion animal sector (dogs and cats)
- Planning for additional public/industry engagement to seek input on collaborative strategies for continued use data collection

Recent Publications/Ongoing Activities

	Action	Purpose
August 2020	Publication of NARMS Strategic Plan: 2021-2025	Outlines NARMS goals and objectives for 2021-2025. One Health theme including initiating work to expand testing to animal pathogens and environmental samples
October 2020	Published Concept Paper, "Potential Approach for Ranking of Antimicrobial Drugs According to Their Importance in Human Medicine: A Risk Management Tool for Antimicrobial New Animal Drugs," and Public meeting	Outlines potential approach for updating the current list of antimicrobial drugs ranked by their importance in human medicine (commonly referred to as "Appendix A" of FDA's Guidance for Industry (GFI) #152)
January 2021	Published Concept Paper, "Potential Approach for Defining Durations of Use for Medically Important Antimicrobial Drugs Intended for Use In or On Feed	Outlines potential framework for how animal drug sponsors could voluntarily make changes to the approved conditions of use for certain medically important antimicrobial drugs to establish a defined durations of use for those indications that currently lack a defined duration of use.

For more information on status of FDA's 5-year plan, please see: FDA-TRACK: Progress on FDA's Support of Antimicrobial Stewardship in Veterinary Settings

In Conclusion…

Key principles of U.S. approach include:

- Recognition of the need for One Health, multisectoral strategies
- Risk-based actions that are informed by sound science
- Focus on antimicrobial stewardship and optimizing the use of antimicrobials in veterinary sector
- Emphasis on stakeholder engagement in developing collaborative, voluntary strategies for implementing change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