



Supporting Antimicrobial Stewardship - FDA's 5-year Plan

123rd USAHA/ 62nd AAVLD Annual Meeting
Subcommittee – Pharmaceutical Issues
Providence, RI
October 29, 2019

Susan J. Bright, DVM, MPH, Dipl. ACVPM
Veterinary Medical Officer
Office of Surveillance & Compliance
Food & Drug Administration – Center for Veterinary Medicine



Topics

- Antimicrobial Resistance (AMR)
 - Changes implemented
 - Assessing impact
 - Next steps: 5-year AMR plan
 - Key Projects
- Other topics...

Guidance for Industry #209/213 Initiative



- Two key principles
 - Initially outlined in Guidance #209 (2012)
 - Implemented with Guidance #213 (2017)
- Limit use of medically important antimicrobial drugs in food-producing animals to those uses that:
 - Are considered necessary for assuring animal health **and**,
 - That include veterinary oversight or consultation

Guidance for Industry #209/213 Initiative



- Implementation plan initiated in 2013 to:
 - Eliminate production uses (e.g., growth promotion, increased feed efficiency)
 - Change marketing status from OTC to Rx (for water products) or VFD (for feed products)
- Plan issued in form of a Guidance for Industry (#213)
 - Voluntary changes by affected drug sponsors
 - New conditions mandatory once product labels updated



Implementation Timeline

- October 1, 2015
 - Updated VFD regulation went into effect
- January 1, 2017
 - As of this date, all medically important antimicrobials for use in or on feed require a VFD and those for use in drinking water require an Rx
 - And, it is no longer legal to use these drugs for production purposes

Note: “Medically important” antimicrobial drugs are those that are considered important for therapeutic use in humans



Summary of Changes

- All affected drug sponsors worked voluntarily with FDA
- Of the **292** new animal drug applications affected by Guidance for Industry #213:

- **84** were completely withdrawn

Of the remaining **208** applications,

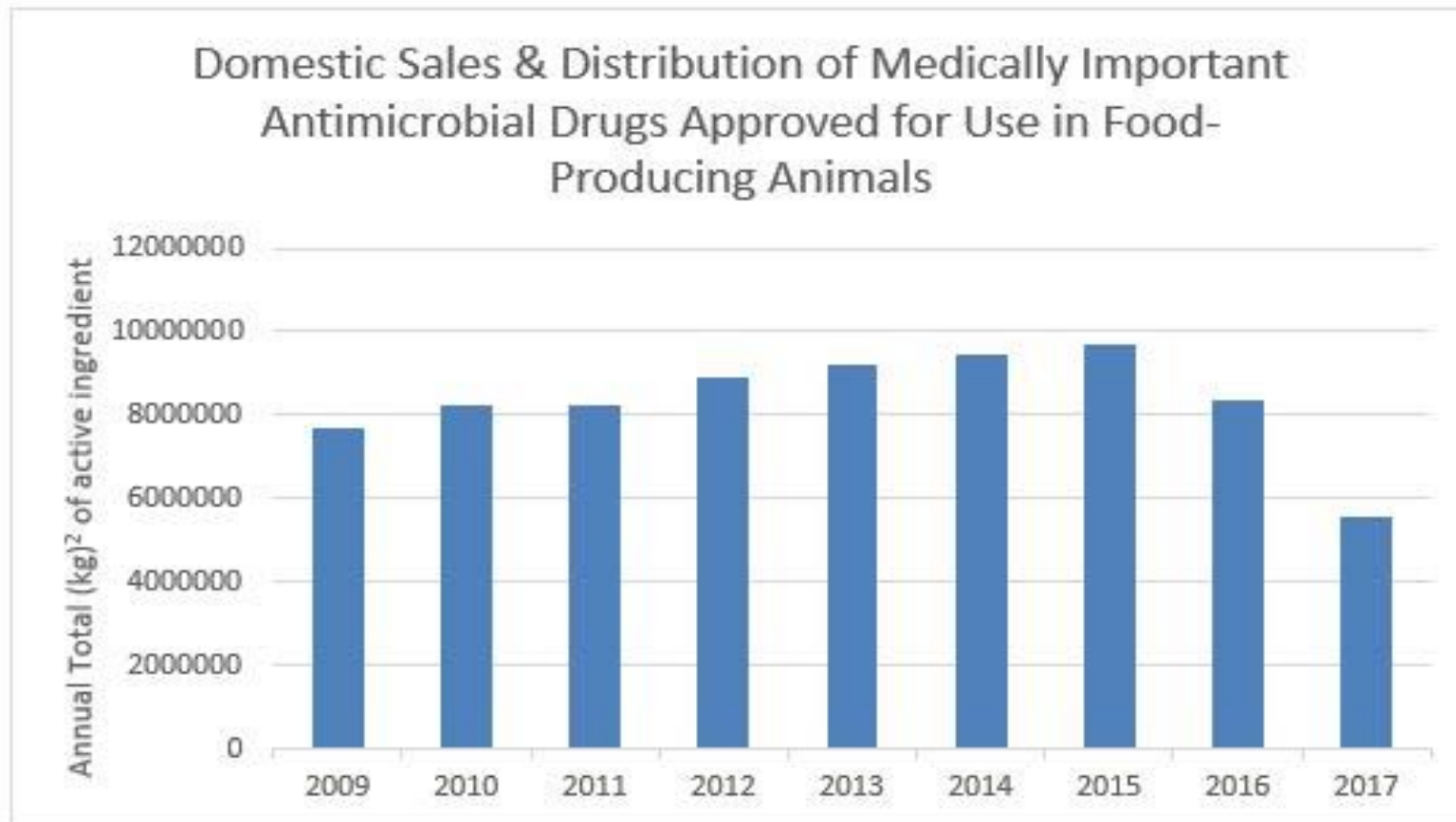
- **93** (water products) – converted OTC to Rx
- **115** (feed products) – converted OTC to VFD

Production indications were withdrawn from **31** applications

Impact of Changes

- To fully assess progress, FDA believes we need to consider broad set of data
 - Including data on antimicrobial resistance, antimicrobial use, animal demographics, and animal health
- FDA working on developing such an assessment
- Have reported sales/distribution data since 2009
 - Does not necessarily reflect actual antimicrobial use
 - But, observed reduction in sales volume is important indicator that ongoing efforts to support antimicrobial stewardship are having a significant impact

Antimicrobial Drug Sales



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

AMR – Next Steps

SUPPORTING ANTIMICROBIAL STEWARDSHIP IN VETERINARY SETTINGS

GOALS FOR FISCAL YEARS 2019 – 2023

FDA CENTER FOR VETERINARY MEDICINE

September 2018

INTRODUCTION

Antimicrobial resistance is a national and worldwide public health challenge. Antimicrobial drugs¹ have been successfully and widely used in human and veterinary medicine for more than 60 years. When used judiciously, antimicrobials can effectively fight bacterial infections. Their use and misuse, however, can promote the development of antimicrobial-resistant bacteria. When bacteria develop resistance to an antimicrobial drug, that drug may be less effective in fighting infection caused by that bacteria. It is critical that we apply a One Health approach to address this important public health concern, including implementing good antimicrobial stewardship practices in human healthcare and veterinary settings to slow the development of resistance and extend the useful life of antimicrobials. One Health is the integrative effort of multiple disciplines working locally, nationally, and globally to attain optimal health for people, animals, and the environment.² The focus of this plan is on actions being taken by the Food and Drug Administration's (FDA) Center for Veterinary Medicine (CVM) and other stakeholders to support antimicrobial stewardship in veterinary settings.

As part of its regulatory mission, CVM is responsible for ensuring the safety and effectiveness of animal drugs, including antimicrobials, and has taken important steps to update the approved use conditions of medically important antimicrobials (i.e., antimicrobials important for treating human disease) to support their judicious use in food-producing animals. While important progress has been made, additional work is needed to further address the challenge of antimicrobial resistance.

¹ The term "antimicrobial" refers broadly to drugs with activity against a variety of microorganisms including bacteria, viruses, fungi, and parasites. Antimicrobial drugs that have specific activity against bacteria are referred to as antibacterial or antibiotic drugs. The broader term "antimicrobial," however, commonly used in reference to drugs with activity against bacteria, is used in this document interchangeably with the terms antibacterial or antibiotic. Antimicrobial resistance is the ability of bacteria or other microbes to resist the effects of a drug. Antimicrobial resistance, as it relates to bacterial organisms, occurs when bacteria change in some way that reduces or eliminates the effectiveness of drugs, chemicals, or other agents designed to treat bacterial infections.

² American Veterinary Medical Association, "One Health – What is One Health?" <https://www.avma.org/KB/Resources/Reference/Pages/One-Health94.aspx>, accessed September 5, 2018.



AMR Next Steps

- On 9/14/2018, CVM published a 5-year plan for [Supporting Antimicrobial Stewardship in Veterinary Settings](#) that outlines the key goals and objectives that will be our focus during fiscal years 2019 – 2023
- We have divided our approach into two phases:
 - Phase 1 actions initiated between fiscal years 2019 – 2021
 - Phase 2 actions initiated between fiscal years 2022 – 2023
- Phases identified are meant to be target for initiating work and does not necessarily represent when the actions will be completed

AMR Next Steps



Goals of 5-Year Plan

1. Align antimicrobial **drug product** use with the principles of antimicrobial stewardship
2. Foster **stewardship** of antimicrobials in veterinary settings
3. Enhance **monitoring** of antimicrobial resistance and antimicrobial drug use in animals



5-Year AMR Plan: Objectives

Goal 1: Align antimicrobial drug products with the principles of antimicrobial stewardship

- Objective 1.1: Revise, as necessary, the use conditions for approved medically important antimicrobials in **food-producing animals**
- Objective 1.2: Develop and implement a strategy for promoting antimicrobial stewardship in **companion animals**
- Objective 1.3: Enhance processes to support new **product development**



5-Year AMR Plan: Objectives

Goal 2: Support efforts to foster stewardship of antimicrobials in veterinary settings

- Objective 2.1: Support **outreach and education** by providing information on antimicrobial stewardship
- Objective 2.2: Strengthen CVM **compliance** program activities to support antimicrobial stewardship
- Objective 2.3: Support **international outreach** and collaboration to foster antimicrobial stewardship in veterinary settings



5-Year AMR Plan: Objectives

Goal 3: Enhance monitoring of antimicrobial resistance and antimicrobial drug use in animals

- Objective 3.1: Collect and analyze data on antimicrobial **drug use** in animals
- Objective 3.2: Enhance the collection and analysis of antimicrobial **resistance data**
- Objective 3.3: Increase **data sharing and reporting** to aid in the monitoring of antimicrobial drug use practices and resistance

5-Year AMR Plan: Ongoing key projects

- Transition all OTC antimicrobial products to Rx
- Defining durations of use
- Updating list and ranking of medically important antimicrobials
- Antimicrobial use data collection pilot projects
- NARMS updates
- Assessment report



Ongoing AMR Activities

Key Project

Bring remaining dosage forms* of medically important antimicrobials under the oversight of licensed veterinarians

- **Target** - issue a draft strategy by end of September 2019
 - CVM Draft GFI #263 published in September 2019; open for comments through 12/24/2019
- Intent to follow similar model used in the implementation of GFI #213, including engaging affected stakeholders and updating the public of progress being made throughout the process

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



Ongoing AMR Activities

Key Project

Defining appropriate durations of use for medically important antimicrobial drugs used in the feed or drinking water of food-producing animals

- **Objective** - Update use conditions of affected products (to better define when and for how long to administer) so that effectiveness is maintained, but extent of exposure is minimized.
 - Take into consideration that products are now under veterinary oversight (VFD)



Ongoing AMR Activities

Key Project (continued)

Defining appropriate durations of use

- **Target** – issue draft strategy by end of September 2020.
 - Expect to issue in form of draft guidance; will outline process, including timeline, for sponsors to revise the approved conditions of use accordingly
 - Further stakeholder input needed as strategy is developed
- **Funding opportunity** – announced April 2019; for studies that can help target and define durations of use for affected products; list of affected products was made available online.
 - Data needed to support science-based approach to addressing issue



Ongoing AMR Activities

Key Project

Update list of “medically important” antimicrobials

- **Target:** Initiate public comment process in 2020
- Originally published in 2003 as an Appendix to support the GFI #152 pre-approval assessment process
- Ranks antimicrobial drugs according to their importance in human medicine
- Defines which drugs are considered “medically important”

Ongoing AMR Activities



Key Project

Collecting Antimicrobial Use Data: ongoing pilot projects

- A funding opportunity was announced in March 2016 seeking proposals for collecting information on antimicrobial use practices in various animal production settings
 - Two projects were awarded in August 2016

- The awardees are developing and piloting methodologies to collect detailed information on antimicrobial drug use in cattle, swine, chickens, and turkeys

- Two ongoing projects:
 - Feedlot/dairy cattle
 - Broilers, turkeys, swine



Ongoing AMR Activities

Key Project

Update the NARMS Program

- Implement recommendations provided by FDA's Science Board including:
 - Expanding testing to other food commodities (e.g., farm-raised seafood products at retail),
 - Improving understanding of AMR using advanced genomic technologies and bioinformatics,
 - Expanding retail meat sampling to improve the representativeness of data



Ongoing AMR Activities

Key Project

Issue assessment report

- **Target** - Issue report in late 2020
- CVM intends to publish a comprehensive report that integrates and analyzes available information to antimicrobial use in veterinary settings
- Including:
 - Use data captured from the cooperative agreements
 - USDA survey data
 - NARMS resistance data
 - Sales and distribution data and an appropriate method for applying a denominator to available data
 - Animal demographic/health data



AMR Activities, cont.

Recent and Upcoming Publications

- VFD Compliance Assessment
 - Published August 26, 2019
- OTC-to-Rx Draft Guidance
 - Published September 23, 2019
- 2018 Sales and Distribution Report
 - Target: By end of December 2019
- 2016 – 2017 Summary NARMS Report
 - Target: By end of December 2019



AMR in Summary

- Significant progress has been made; changes implemented January 2017 were important milestone
- Antimicrobial stewardship requires the combined efforts of many stakeholders; more work is needed
- We are committed to working collaboratively with all key stakeholders; building on progress already made
- The 5-year plan is intended to guide CVM's activities moving forward; plan can be adjusted as needed in response to evolving science and available data

Draft Guidance for Industry #120



- Draft GFI #120 - *Veterinary Feed Directive Regulation Questions and Answers*, published March 2019
 - Expands on previous version (September 2015)
 - 53 new Q & As; 14 revised
 - Organized to address needs of veterinarians, VFD distributors, feed mills, producers
 - Comment period closed May 2019

Hemp and Cannabidiol (CBD)



- Animal food or feed uses
 - Animal feed ingredients must be the subject of an approved food additive petition or generally recognized as safe (GRAS) for their intended use in the intended species
 - CVM also recognizes ingredients listed in the AAFCO Official Publication
 - Currently no approved food additive petitions or AAFCO ingredient definitions for substances derived from hemp; no GRAS conclusions

Hemp and Cannabidiol (CBD)



- No approved animal food/feed or drug uses of hemp, cannabis, CBD
- Currently marketed products are illegally marketed
- FDA-CVM is exploring potential legal pathways
- Data gaps regarding safety exist
- FDA public meeting in May 2019
 - Over 4,000 comments received; under review



Compounding

- Unapproved animal drugs (including animal drugs compounded from bulk drug substances) are considered adulterated under the Federal Food, Drug, and Cosmetic Act
- FDA recognizes there are legitimate needs for animal drug compounding
- Previous compounding guidance (GFI #230) was withdrawn in November 2017
- A new draft guidance will be published soon with opportunity for public comment



Thank you!

