Antimicrobial Use and Resistance in ANIMAL AGRICULTURE in the United States

2016-2019

EXECUTIVE SUMMARY

Center for Veterinary Medicine

JUNE 2022

U.S. FOOD & DRUG
ADMINISTRATION

Background

Antimicrobial drugs have been successfully and widely used in human and veterinary medicine for decades to fight bacterial infections. Their use and misuse, however, can promote the development of antimicrobial-resistant bacteria. Loss of antimicrobial drug effectiveness through the emergence, distribution, and persistence of antimicrobial resistance in bacteria is a serious threat to the continued successful therapy of infectious diseases. Any use of antimicrobials, whether in humans, animals, or the environment (crops and plants), can contribute to the creation of selective pressure and the emergence of resistant bacteria. As a global problem with complex epidemiology, addressing antimicrobial resistance requires a broad and integrated One Health approach including research, surveillance, and interventions across human, animal, and environmental sectors. One Health is a collaborative, multisectoral, and transdisciplinary approach – working at the local, regional, national, and global levels – with the goal of achieving optimal health outcomes recognizing the interconnection between people, animals, plants, and their shared environment (CDC, 2020).

The science underlying the selection, transmission, and persistence of antimicrobial-resistant bacteria is complex. More research is needed to improve our understanding of many aspects of resistance, including what actions will best contribute to mitigating the risk. Since antimicrobial use is one driver in the development of antimicrobial resistance, implementation of good antimicrobial stewardship practices among the human, animal, and environment sectors is essential to help slow the emergence of resistance and preserve the effectiveness of antimicrobials.

Ongoing surveillance and monitoring of both antimicrobial resistance and antimicrobial use across all sectors will inform efforts to preserve the effectiveness of potentially life-saving antimicrobial drugs. It is important to note that the availability of effective antimicrobial therapies for food-producing animals is vital for maintaining animal health and welfare. Antimicrobial stewardship describes measures that can be taken to help mitigate the risks associated with antimicrobial use, including the risk of antimicrobial resistance. Many activities are ongoing across the One Health spectrum aimed at slowing the development of antimicrobial resistance and promoting antimicrobial stewardship. In animal agriculture, cooperation and collaboration between government agencies across the United States (U.S.) at the local, state, and federal levels, multinational organizations, animal drug manufacturers, animal industry organizations, veterinary and public health organizations, academia and researchers, non-governmental consumer and advocacy groups, veterinarians, and producers are essential to continue building upon important progress made in this sector to date.

Purpose and Scope of the Report

Antimicrobial Use and Resistance in Animal Agriculture in the United States is the first report prepared by the U.S. Food and Drug Administration's (FDA) Center for Veterinary Medicine (CVM) intended to provide a variety of data elements to help describe antimicrobial use and resistance in animal agriculture in the U.S., especially as it relates to certain foodborne pathogens. As part of its regulatory mission, CVM is responsible for monitoring the safety and effectiveness of animal drugs. The efforts described in this report highlight just some of the ongoing endeavors by CVM and across multiple government agencies and stakeholders to promote antimicrobial stewardship in the animal agriculture sector and to enhance monitoring efforts for antimicrobial use and resistance. As part of activities related to assessing antimicrobial stewardship, it is important to develop appropriate metrics for antimicrobial use that can help evaluate progress. While integrating antimicrobial use and resistance data is desired, at this time we primarily describe the separate inputs (sales, use, and resistance) that have been monitored. In addition to monitoring antimicrobial use and resistance, it is also important for veterinarians and animal producers to evaluate animal health outcomes in order to help inform the development and uptake of alternative management practices that may help reduce the need for antimicrobial use in food-producing animals. The report is not intended to be an exhaustive review of all antimicrobial resistance-related activities in which the U.S. government is involved, but rather focuses on activities in which CVM plays a role.

The report is organized into several chapters and appendices, including introductory chapters about the threat of antimicrobial resistance and activities in which CVM has been involved to help mitigate the threat. A number of data sources are described, and data are presented on antimicrobial sales, use, and resistance in separate species chapters for the four major food-producing species (cattle, swine, chickens, and turkeys). As of January 1, 2017, medically important antimicrobials administered in the feed or water of food-producing animals are only available through a Veterinary Feed Directive (VFD) order or prescription from a licensed veterinarian. Therefore, the data summarized in the report are focused on 2016 through 2019, in order to highlight some of the initial impacts of this change. Future reports will provide updates and highlight continued progress.

The objectives of the report are to describe:

Current U.S. government monitoring and surveillance systems for antimicrobial sales, use, and resistance in animal agriculture and the related food chain

Publicly available data regarding antimicrobial sales, use, and resistance in animal agriculture and select foodborne pathogens, focusing on 2016 - 2019

Recent progress made and continued plans for promoting and supporting antimicrobial stewardship in animal agriculture

General Approach for Data Included in the Report

The report is not an in-depth review of all U.S. government programs and projects involved with surveillance and monitoring of antimicrobial use and resistance. Rather, the focus is on the following sources of data:

Medically important antimicrobial sales and distribution data collected and reported by CVM on an annual basis, including species-specific estimates for the four major food-producing species (cattle, swine, chickens, turkeys)

Antimicrobial sales and distribution data are one component that CVM utilizes to assess broad shifts in the amounts of antimicrobial drugs introduced into the marketplace and intended for use in food-producing animals. Since 2009, every sponsor (i.e., manufacturer) of an approved animal drug containing an antimicrobial active ingredient must report to CVM the amount of each such ingredient in these drug products sold or distributed for use in food-producing animals. CVM summarizes this information and makes it available to the public in annual summary reports. Medically important antimicrobial sales data for 2016 through 2019 are highlighted in the report, including species-specific sales estimates. Medically important antimicrobials are those antimicrobials that are important for therapeutic use in humans. At this time, FDA considers all antimicrobial drugs listed in Appendix A to Guidance for Industry (GFI) #152 to be medically important (FDA, 2003). As described in the report, FDA is in the process of reassessing this list and issued a concept paper on October 9, 2020, describing a potential approach for an updated ranking of antimicrobial drugs according to their importance in human medicine.

Animal biomass-adjusted medically important antimicrobial sales and distribution data for the four major food-producing species

Animal biomass is the total mass of an animal species, determined by multiplying that species' population by their average weights in a given year. In the context of antimicrobial sales and distribution data, biomass may be considered a denominator – it represents the population of animals that could potentially be exposed to antimicrobial drugs. The goal of applying an animal biomass denominator to antimicrobial sales and distribution data is to provide estimates that represent trends in annual antimicrobial sales and distribution relative to the U.S. livestock population in which the antimicrobials may be used. CVM's proposed biomass denominator method is described and applied to estimated species-specific antimicrobial sales data for 2016 through 2019.

Summaries of available antimicrobial use information

Antimicrobial sales data are not indicative of how antimicrobials were actually used in animals (e.g., for what indications, doses, or durations); therefore, CVM and others, such as the U.S. Department of Agriculture Animal and Plant Health Inspection Service (USDA APHIS) National Animal Health Monitoring System (NAHMS), have been active in exploring strategies for collecting on-farm antimicrobial use data. Knowledge about antimicrobial selection pressures is important to understand potential risk factors for development of antimicrobial resistance. Since antimicrobial use in food-producing animals is one contributing factor towards these selection pressures, information about antimicrobial use in animals is needed to further understand its role in the development of resistance. Antimicrobial use information is also needed to assist in the development of strategies to promote antimicrobial stewardship.

These two sources of antimicrobial use information were summarized for the report:

- Surveys completed in 2017 by USDA APHIS NAHMS, for antimicrobial use and stewardship practices on U.S. beef feedlots and U.S. swine operations in 2016

- FDA cooperative agreements awarded to researchers in 2016 and designed to pilot methodologies for on-farm antimicrobial use data collection for cattle, swine, chickens, and turkeys

Summaries of antimicrobial resistance data for animal pathogens from two sources

As part of a USDA-funded collaboration with the American Association of Veterinary Laboratory Diagnosticians (AAVLD), the USDA APHIS National Animal Health Laboratory Network (NAHLN) began a pilot project in 2018 to develop a sampling stream to monitor antimicrobial resistance profiles in animal pathogens routinely isolated by veterinary clinics and diagnostic laboratories across the U.S. Using this and other information from the survey and based upon the recommendations of an AAVLD working group, CVM developed a pilot program to assess the feasibility of using veterinary diagnostic laboratories in the FDA Veterinary Laboratory Investigation Response Network (Vet-LIRN) to monitor the antimicrobial susceptibility of select veterinary pathogens. Data on antimicrobial resistance in animal pathogens are important to collect and report on an ongoing basis since therapy of animal diseases caused by animal pathogens is the main driver for antimicrobial use in animals. Data from the first 2 years of the NAHLN pilot project (2018-2019) and first year (2017) of the Vet-LIRN pilot project are summarized in the report.

Antimicrobial resistance data reported through the National Antimicrobial Resistance Monitoring System (NARMS) program in 2019

Antimicrobial resistance monitoring and surveillance across the One Health spectrum are necessary to estimate the degree, patterns, and human and animal health risks of antimicrobial resistance at national, regional, and international levels. NARMS was originally established in 1996 as a collaborative effort of three federal agencies: the Centers for Disease Control and Prevention (CDC), the USDA, and the FDA, along with state and local health departments in all 50 states. This national surveillance system tracks changes in antimicrobial susceptibility of certain bacterial species from ill people (CDC), retail meats (FDA), and food animals (USDA). Since the comprehensive report focuses on animal agriculture, summaries of NARMS antimicrobial resistance trends for the four bacteria monitored from food-producing animals and retail meats are provided. NARMS also performs whole genome sequencing as part of routine processes in their analysis of *Salmonella* and *Campylobacter*, in addition to some sequencing of resistant strains of *E. coli* and *Enterococcus*. Resistance trends in this report are focused on antimicrobial susceptibility testing (i.e., phenotypic) results. The NARMS website can be explored for interactive data displays of resistance trends from all sources and bacteria monitored, including whole genome sequencing data.

Key Findings

In Chapters 4 through 7 of the report, information is presented for each of the four major food-producing species. In each species chapter, the following information is highlighted:

Animal Production and Disease

Antimicrobial Sales

Antimicrobial Use

Antimicrobial Resistance

Antimicrobial Stewardship

Highlights regarding medically important antimicrobial sales (including sales adjusted by a biomass denominator), use, and resistance tracked through the NARMS program are briefly summarized for each of the major food-producing species on the following pages of this Executive Summary and more detailed information is provided in the report.

CATTLE

General information about beef and dairy cattle production and examples of bacterial diseases of cattle are provided in Chapter 4 of the report. Antimicrobial sales estimates for cattle (including sales adjusted by a cattle biomass denominator), antimicrobial use information, and antimicrobial resistance data are also provided in Chapter 4. Highlights are provided below for antimicrobial sales, use, and resistance data collected through the NARMS program for retail ground beef. Table 1 at the end of this section provides a summary, and additional details are provided in the full report.

Sales of medically important antimicrobials estimated for cattle from 2016 through 2019:

As shown in **Figure 1**, for the 4 years combined (2016-2019), tetracyclines made up the majority (71.8%) of antimicrobials sold and estimated for use in cattle, while the critically important antimicrobial drug classes (fluoroquinolones, cephalosporins, macrolides) made up less than 11% of the overall total. For example, cephalosporins accounted for less than 1% of the total and macrolides made up about 9%. Sales for some medically important antimicrobial drug classes are not independently reportable (NIR) in order to protect confidential business information of animal drug manufacturers that report sales data. For cattle, these include amphenicols, diaminopyrimidines, fluoroquinolones, lincosamides, polymyxins, and streptogramins. Taken together, these NIR drug classes accounted for approximately 2% of overall sales estimated for cattle.

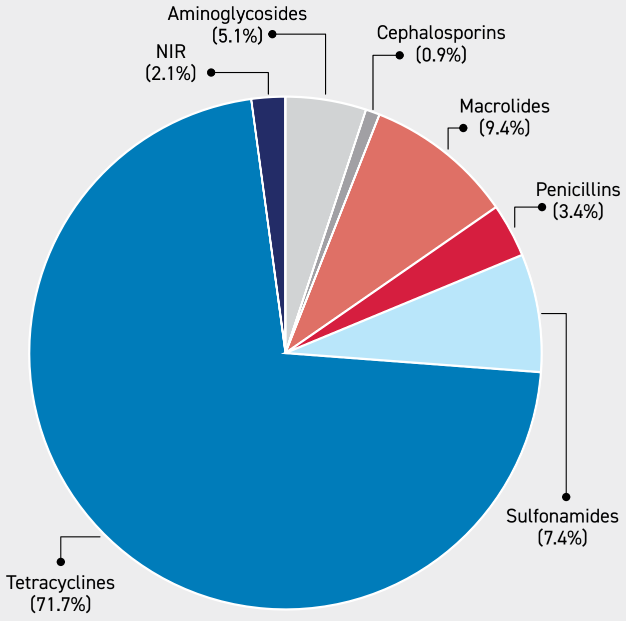
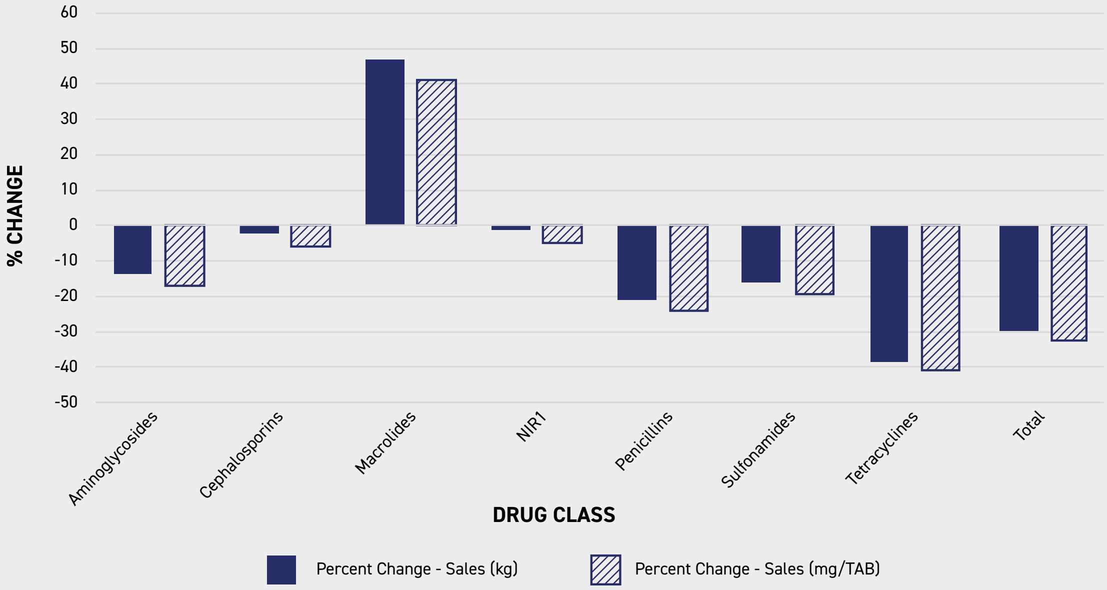


Figure 1: Medically important antimicrobial sales estimated for cattle, by drug class (for 2016-2019 combined)

NIR= Not independently reported drug classes for cattle (may include sales for the following antimicrobial drug classes: amphenicols, diaminopyrimidines, fluoroquinolones, lincosamides, polymyxins, and streptogramins). The value of NIR drug class sales is calculated as the overall sales total for cattle minus the sum of all reportable drug classes.

To allow for a more nuanced view of antimicrobial sales, sales in the context of animal populations can also be considered, in other words, the potential animal biomass that could receive antimicrobials each year. Using FDA's biomass denominator methodology for calculation, the estimated biomass of cattle increased from 40.5 to 42.2 billion kilograms between 2016 and 2019, which is an increase of about 4.1%. **Figure 2** shows the percentage change in unadjusted and biomass-adjusted sales estimated for cattle for each reportable medically important antimicrobial drug class, comparing 2016 to 2019.

Figure 2: Percent change in unadjusted sales (in kg) and biomass-adjusted sales (mg/TAB) estimated for cattle, comparing 2016 to 2019



NIR= Not independently reported drug classes for cattle (may include sales for the following antimicrobial drug classes: amphenicols, diaminopyrimidines, fluoroquinolones, lincosamides, polymyxins, and streptogramins). The value of NIR drug class sales is calculated as the overall sales total for cattle minus the sum of all reportable drug classes. The cattle biomass denominator is applied to the NIR category as a whole; therefore does not account for potential exclusions of cattle categories for the denominator that may otherwise apply to individual NIR classes.

Antimicrobial Use in Cattle

In 2017, the USDA APHIS NAHMS program conducted a survey about 2016 antimicrobial use and stewardship practices on U.S. beef feedlots from 22 top cattle-producing states. Overall, 55.6% of participating feedlots administered medically important antimicrobials in feed in 2016, with chlortetracycline the most frequently administered. Control and/or treatment of bovine respiratory disease was the most common reason for administration of medically important antimicrobials. More information about this study is provided in the full report.

Figure 3 shows highlights of findings from the first 2 years of conduct (2016-2017) for an FDA cooperative agreement, ***Characterizing Antimicrobial Use in Feedlot and Dairy Cattle*** (5U01FD005868). This project was intended to pilot methodologies for collecting and reporting on-farm antimicrobial use data from beef feedlots and dairies.

The report provides additional information about these studies, including the challenges related to collecting and aggregating data from various production settings, as well as the study investigators' determination of the most appropriate antimicrobial use metrics for reporting the study data collected. Findings from these studies have been published recently.

Figure 3: Highlights of pilot studies conducted in FDA cooperative agreement for antimicrobial use on convenience samples of U.S. beef feedlots and dairies, for 2016-2017

PILOT STUDY:
22 U.S. Beef Feedlots

- 32% reduction in overall use (mg/kg liveweight basis) of medically important antimicrobials, comparing 2016 to 2017
- Nearly 60% reduction in tetracycline use (mg/kg liveweight basis) comparing 2016 to 2017
- Primary reason for medically important antimicrobial use: Bovine Respiratory Disease

PILOT STUDY:
29 U.S. Dairies

- Essentially no change in number of regimens used or overall amounts (grams) of medically important antimicrobials used, comparing 2016 to 2017
- Cephalosporin use was highest when measured by regimens, but penicillin use was highest when measured by overall amounts (grams)
- Primary reason for medically important antimicrobial use: Mastitis

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Antimicrobial Resistance in Retail Ground Beef

Information available for antimicrobial resistance trends in cattle pathogens and foodborne pathogens from cattle sources (retail ground beef, dairy cattle cecal samples, and beef cattle cecal samples) are presented in Chapter 4 of the report, and Appendix 5 of the report shows trends for 2015-2019 for each of the organisms monitored in the NARMS program. The report also describes some available resistance data for animal pathogen data (2017-2019). **Table 1** summarizes selected biomass-adjusted sales estimates, antimicrobial use information, and antimicrobial resistance information for retail ground beef. Unless otherwise noted, increases or decreases in resistance were not statistically significant.

Table 1: Summary of Selected Antimicrobial Sales, Use, and Resistance Data (Retail Meat) for Cattle

Medically Important Antimicrobial Sales Estimates for Cattle Adjusted by Cattle Biomass	Cattle Antimicrobial Use[1,2]	Antimicrobial Resistance – Retail Ground Beef[3]
From 2016 through 2019: • Considering all 4 years combined, tetracyclines accounted for over 70% of estimated sales of medically important antimicrobials for cattle. Macrolides (9.4%) and sulfonamides (7.4%) were the next highest volume of sales after tetracyclines. • Estimated cattle biomass increased by approximately 4.1%. • There was a 32.6% decrease in overall biomass-adjusted sales of medically important antimicrobials estimated for use in cattle. • Biomass-adjusted sales for 5 of the 6 reportable medically important antimicrobial classes for use in cattle decreased. • Macrolides were the only reportable class to show an increase in biomass-adjusted sales estimated for cattle, with an increase of 41.3%.	**In 2016[1]:** • About 56% of feedlots participating in a USDA NAHMS study administered medically important antimicrobials in feed. • Chlortetracycline was the most commonly used medically important antimicrobial for feedlot cattle. **From 2016 through 2017[2]:** • Overall mg/kg values for all uses of medically important antimicrobials decreased by about 32% in a pilot study of antimicrobial use on 22 feedlots. • Among medically important antimicrobials, use of tetracyclines decreased the most on participating feedlots. • There was essentially no change in antimicrobial use on 29 dairies participating in a pilot study, considering regimens and overall amounts. • Among participating dairies, cephalosporins or penicillins were the most used medically important antimicrobials, depending on the metric used (regimens vs grams).	**From 2018 through 2019**: • Tetracycline resistance was stable for *E. coli* and increased for *E. faecium,* but decreased for *E. faecalis* and *Salmonella.*[4] • No decreased susceptibility to azithromycin (a macrolide) in *E. coli* or *Salmonella* isolates was detected.[5] • Macrolide (erythromycin) resistance increased for *E. faecalis*[4] and significantly decreased for *E. faecium* isolates. • Sulfonamide (sulfisoxazole) resistance decreased for *E. coli* and *Salmonella.*[4] • Ampicillin resistance decreased for *E. coli* and *Salmonella* isolates.[4] • Penicillin resistance was not detected in *E. faecalis* isolates and decreased for *E. faecium* isolates.[4] • No ceftriaxone resistance in *E. coli* or *Salmonella* isolates was detected. • Decreased susceptibility to ciprofloxacin[6] was detected in only 2 of 286 *E. coli* isolates and in only 1 of 12 *Salmonella* isolates.[4] • Multidrug resistance remained stable in *E. coli* and *Enterococcus* spp. isolates and decreased for *Salmonella* isolates.[4]

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[1] USDA NAHMS report: *Antimicrobial Use and Stewardship on U.S. Feedlots, 2017*

[2] FDA Cooperative Agreement: *Characterizing Antimicrobial Use in Feedlot and Dairy Cattle*

[3] FDA NARMS: Based on antimicrobial susceptibility testing as reported by FDA NARMS program. See Appendix for AST trend data for retail ground beef, beef cecal samples and dairy cecal samples. All data is available on NARMS Now.

[4] Unless otherwise noted, increases or decreases in percentage resistance were not statistically significant (i.e., p-values were >0.05 using Fisher's exact test for comparing proportions).

[5] The azithromycin interpretive standards used for *Salmonella* serotypes other than serotype Typhi and for *E. coli* are NARMS-established breakpoints for monitoring and therefore referred to as decreased susceptibility (https://www.fda.gov/media/108180/download).

[6] NARMS uses decreased susceptibility to ciprofloxacin (MIC>=0.12µg/ml) as a marker for emerging fluoroquinolone resistance (https://www.fda.gov/media/108180/download).

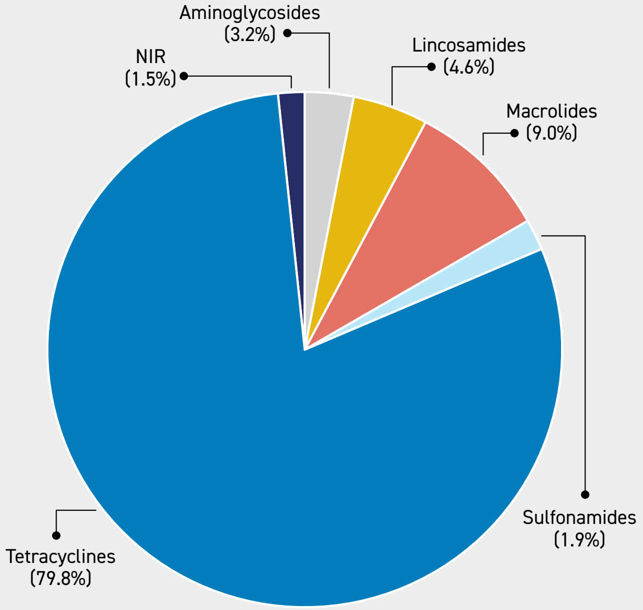
SWINE

General information about swine production and examples of bacterial diseases of swine are provided in Chapter 5 of the report. Antimicrobial sales estimates for swine (including sales adjusted by a swine biomass denominator), antimicrobial use information, and antimicrobial resistance data are also provided in Chapter 5. Highlights are provided below for antimicrobial sales, use, and resistance data collected through the NARMS program for retail pork. Table 2 at the end of this section provides a summary, and additional details are provided in the full report.

Sales of medically important antimicrobials estimated for swine from 2016 through 2019:

As shown in **Figure 4**, for the 4 years combined (2016-2019), tetracyclines made up the majority (79.8%) of antimicrobials sold and estimated for use in swine, while the critically important antimicrobial drug classes (fluoroquinolones, cephalosporins, macrolides) made up less than 10% of the overall total. For example, macrolides made up about 9% of total sales. Sales for some medically important antimicrobial drug classes are not independently reportable (NIR) in order to protect confidential business information of animal drug manufacturers that report sales data. For swine, these include amphenicols, cephalosporins, fluoroquinolones, and streptogramins. Taken together, these NIR drug classes accounted for only about 1.5% of overall sales estimated for swine.

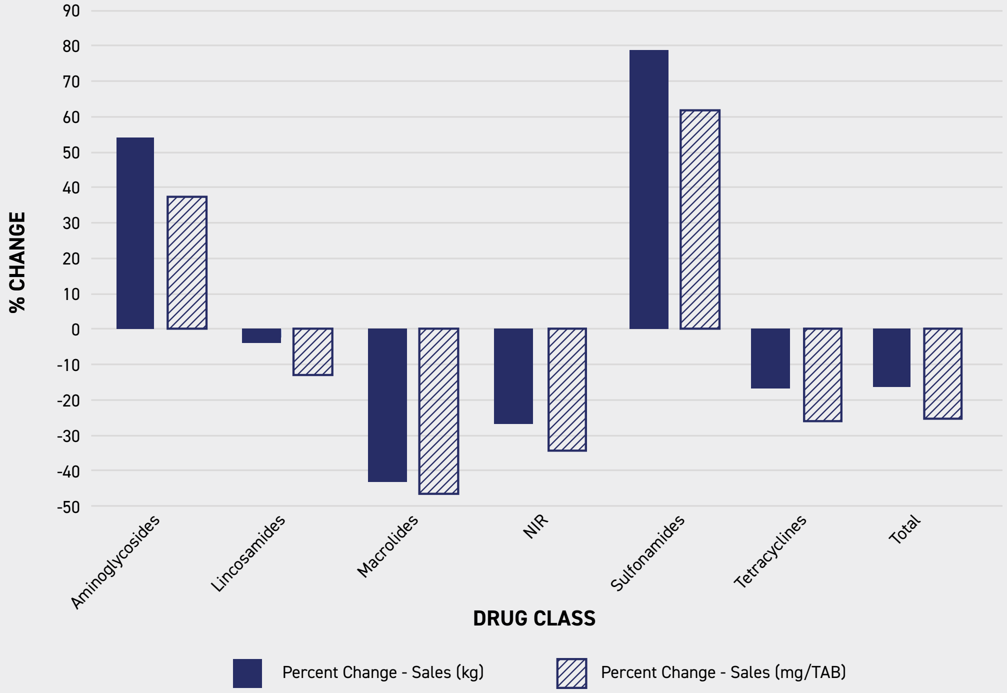
Figure 4: Medically important antimicrobial sales estimated for swine, by drug class (for 2016-2019 combined)



NIR= Not independently reported drug classes for swine (may include sales for the following antimicrobial drug classes: amphenicols, cephalosporins, fluoroquinolones, and streptogramins). The value of NIR drug class sales is calculated as the overall sales total for swine minus the sum of all reportable drug classes.

To allow for a more nuanced view of antimicrobial sales, sales in the context of animal populations can also be considered, in other words, the potential animal biomass that could receive antimicrobials each year. Using FDA's biomass denominator methodology for calculation, the estimated biomass of swine increased from 16.2 to 17.9 billion kilograms between 2016 and 2019, which is an increase of about 10.9%. **Figure 5** shows the percentage change in unadjusted and biomass-adjusted sales estimated for swine for each reportable medically important antimicrobial drug class, comparing 2016 to 2019.

Figure 5: Percent change in unadjusted sales (in kg) and biomass-adjusted sales (mg/TAB) estimated for swine, comparing 2016 to 2019



NIR= Not independently reported drug classes for swine (may include sales for the following antimicrobial drug classes: amphenicols, cephalosporins, fluoroquinolones, penicillins, and streptogramins). The value of NIR drug class sales is calculated as the overall sales total for swine minus the sum of all reportable drug classes. The swine biomass denominator is applied to the NIR category as a whole; therefore does not account for potential exclusions of swine categories for the denominator that may otherwise apply to individual NIR classes.

Antimicrobial Use in Swine

In 2017, the USDA APHIS NAHMS program conducted a survey about 2016 antimicrobial use and stewardship practices on U.S. swine operations from 13 top swine-producing states. Overall, 88.6% of participating sites administered medically important antimicrobials in feed in 2016, with chlortetracycline the most frequently administered. Control and/or treatment of swine respiratory disease/bacterial pneumonia was the most common reason for administration of medically important antimicrobials in the feed of grower-finisher pigs. More information about this study is provided in the full report.

Figure 6 shows highlights of findings from the swine portion of the first 2 years of conduct (2016-2017) for an FDA cooperative agreement, *Antibiotic Use Data Collection in U.S. Poultry and Swine Production* (5U01FD005878). This project was intended to pilot methodologies for collecting and reporting on-farm antimicrobial use data from poultry and swine operations.

Full report provides additional information about the study, including the challenges related to collecting and aggregating data from various types of production settings, as well as the study investigators' determination of the most appropriate antimicrobial use metrics for reporting. Findings from the study have recently been published.

Figure 6: Highlights of pilot study conducted in an FDA cooperative agreement for antimicrobial use data collection on nine participating swine sites, for 2016-2017

PILOT STUDY:
9 participating swine sites

- Tetracyclines represented the largest relative use for 2016-2017, between 55-62% of total use depending on the year
- Cephalosporins and fluoroquinolones accounted for less than 0.5% of relative use for both years
- Use of chlortetracycline fell by nearly 50% (mg/kg liveweight basis), comparing 2016 to 2017

Antimicrobial Resistance in Retail Pork

Information available for antimicrobial resistance trends in swine pathogens and foodborne pathogens from swine sources (retail pork, market swine cecal samples, and sow cecal samples) are presented in Chapter 5 of the report, and Appendix 6 of the report shows trends for 2015-2019 for each of the organisms monitored in the NARMS program. The report also describes some available resistance data for animal pathogen data (2017-2019). **Table 2** summarizes selected biomass-adjusted sales estimates, antimicrobial use information, and antimicrobial resistance information for retail pork. Unless otherwise noted, increases or decreases in resistance were not statistically significant.

Table 2: Summary of Selected Antimicrobial Sales, Use, and Resistance Data for Swine (Retail Meat)

Medically Important Antimicrobial Sales Estimates for Swine Adjusted by Swine Biomass	Swine Antimicrobial Use[1,2]	Antimicrobial Resistance – Retail Pork[3]
From 2016 through 2019: • Considering all 4 years combined, tetracyclines accounted for nearly 80% of estimated sales of medically important antimicrobials for swine. Macrolides (9%) and lincosamides (4.6%) were the next highest volume of sales after tetracyclines. • Estimated swine biomass increased by approximately 10.9%. • There was a 25.7% decrease in overall biomass-adjusted sales of medically important antimicrobial sales estimated for use in swine. • Biomass-adjusted sales for 3 of the 5 reportable medically important antimicrobial classes for use in swine decreased. • Aminoglycosides and sulfonamides were the two reportable classes that showed an increase in biomass-adjusted sales estimated for swine in 2019, although taken together these two classes represented only about 6% of total biomass-adjusted sales in 2019.	**In 2016[1]:** • About 88.6%% of swine operations participating in a USDA NAHMS study administered medically important antimicrobials to pigs in feed. • Chlortetracycline was the most commonly used medically important antimicrobial for grower-finisher pigs. **From 2016 through 2017[2]:** • Among medically important antimicrobial classes, tetracyclines represented the largest relative use in a pilot project of 9 participating swine systems. • On a mg/kg liveweight basis, chlortetracycline and lincomycin were the most used medically important antimicrobials on the 9 participating systems. Mg/kg liveweight values for use of chlortetracycline decreased by nearly 50% and for use of lincomycin decreased by about 76%.	**From 2018 through 2019**: • Tetracycline resistance significantly increased for *E. coli* and increased for *Salmonella* and *E. faecalis* isolates, but decreased for *E. faecium* isolates.[4] • Decreased susceptibility to azithromycin (a macrolide) in *E. coli* was detected in 2 of 229 isolates from retail pork and was not detected in *Salmonella* isolates.[4,5] • Macrolide (erythromycin) resistance increased for *E. faecalis* and decreased for *E. faecium* isolates.[4] • Sulfonamide (sulfisoxazole) resistance was stable for *E. coli* and decreased for *Salmonella* isolates.[4] • Gentamicin (an aminoglycoside) resistance remained stable for *E. coli* and *Salmonella*, and increased for *E. faecalis.*[4] • Ceftriaxone resistance increased for *E. coli* isolates and remained stable for *Salmonella* isolates.[4] • Decreased susceptibility to ciprofloxacin in *E. coli* isolates was decreased and for *Salmonella* isolates was increased.[4] • Multidrug resistance increased for *E. coli* and decreased for *Salmonella* isolates. For *E. faecalis* and *E. faecium* isolates, MDR increased.[4,6]

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1 USDA NAHMS report: *Antimicrobial Use and Stewardship on U.S. Feedlots, 2017*

2 FDA Cooperative Agreement: *Characterizing Antimicrobial Use in Feedlot and Dairy Cattle*

3 3FDA NARMS: Based on antimicrobial susceptibility testing as reported by FDA NARMS program. See Appendix for AST trend data for retail pork, market swine cecal samples and sow cecal samples. All data is available on NARMS Now.

4 Unless otherwise noted, increases or decreases in percentage resistance were not statistically significant (i.e., p-values were >0.05 using Fisher's exact test for comparing proportions).

5 The azithromycin interpretive standards used for *Salmonella* serotypes other than serotype Typhi and for *E. coli* are NARMS-established breakpoints for monitoring and therefore referred to as decreased susceptibility (https://www.fda.gov/media/108180/download)

6 NARMS uses decreased susceptibility to ciprofloxacin (MIC>=0.12µg/ml) as a marker for emerging fluoroquinolone resistance (https://www.fda.gov/media/108180/download).

CHICKENS

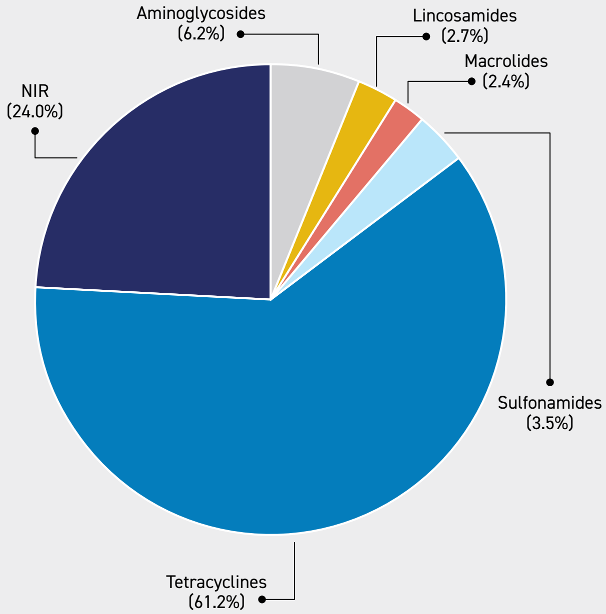
General information about chicken production and examples of bacterial diseases of chickens are provided in Chapter 6 of the report. Antimicrobial sales estimates for chickens (including sales adjusted by a chicken biomass denominator), antimicrobial use information, and antimicrobial resistance data are also provided in Chapter 6. Highlights are provided below for antimicrobial sales, use, and resistance data collected through the NARMS program for retail chicken. Table 3 at the end of this section provides a summary, and additional details are provided in the full report.

Sales of medically important antimicrobials estimated for chickens from 2016 through 2019:

As shown in **Figure 7**, for the 4 years combined (2016-2019), tetracyclines made up the majority (61%) of antimicrobials sold and estimated for use in chickens, while the more critically important antimicrobial drug classes made up less than 3% of the overall total. For example, macrolides made up about 2.4% of total sales. Sales for some medically important antimicrobial drug classes are not independently reportable (NIR) in order to protect confidential business information of animal drug manufacturers that report sales data. For chickens, these include cephalosporins, diaminopyrimidines, polymyxins, streptogramins, and sulfonamides (2018). Taken together, these NIR classes accounted for approximately 24% of overall sales estimated for chickens.

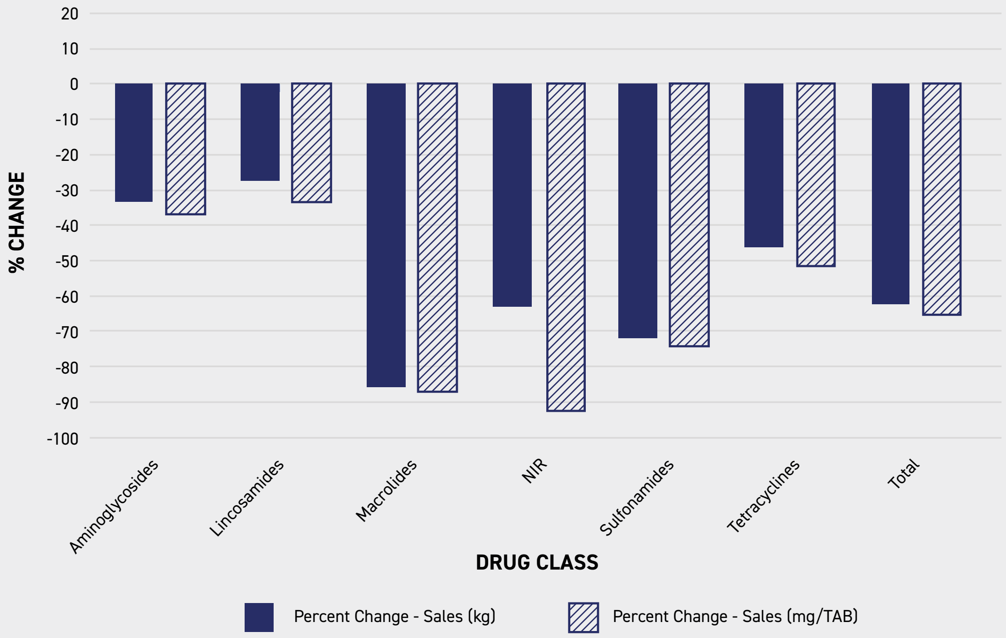
To allow for a more nuanced view of antimicrobial sales, sales in the context of animal populations can also be considered, in other words, the potential animal biomass that could receive antimicrobials each year. Using FDA's biomass denominator methodology for calculation, the estimated biomass of the chicken population increased from 24.9 to 26.8 billion kilograms between 2016 and 2019, which is an increase of about 7.5%. **Figure 8** shows the percentage change in unadjusted and biomass-adjusted sales estimated for chickens for each reportable medically important antimicrobial drug class, comparing 2016 to 2019. For the lincosamide drug class, a separate biomass denominator is applied (to include only young chickens) because the drug approvals for lincosamides in chickens are limited to this category (in addition to 0-7 day old chicks, which are considered to be included in the population of young chickens utilized for the chicken biomass denominator).

Figure 7: Medically important antimicrobial sales estimated for chickens, by drug class (for 2016-2019 combined)



NIR= Not independently reported drug classes for chickens (may include sales for the following antimicrobial drug classes: cephalosporins, diaminopyrimidines, polymyxins, and streptogramins). The value of NIR drug class sales is calculated as the overall sales total for chickens minus the sum of all reportable drug classes.

Figure 8: Percent change in unadjusted sales (in kg) and biomass-adjusted sales (mg/TAB) estimated for chickens, comparing 2016 to 2019



NIR= Not independently reported drug classes for chickens (may include sales for the following antimicrobial drug classes: cephalosporins, diaminopyrimidines, polymyxins, streptogramins, and sulfonamides for 2018). The value of NIR drug class sales is calculated as the overall sales total for chickens minus the sum of all reportable drug classes. The chicken biomass denominator is applied to the NIR category as a whole; therefore does not account for potential exclusions of chicken categories for the denominator that may otherwise apply to individual NIR classes. The biomass denominator for lincosamides only includes young chickens. The biomass denominator applied to the 'Total' excludes lincosamides, since it is calculated separately.

Antimicrobial Use in Chickens

Figure 9 shows highlights of findings from the chicken portion of the first 2 years of conduct (2016-2017) for an FDA cooperative agreement, *Antibiotic Use Data Collection in U.S. Poultry and Swine Production* (5U01FD005878). This project was intended to pilot methodologies for collecting and reporting on-farm antimicrobial use data from poultry and swine operations. For the poultry portion of the project, data were also collected for years prior to 2016, so trends for 2013-2017 were included.

The full report provides additional information about the study, including the challenges related to collecting and aggregating data from various types of production settings, as well as the study investigators' determination of the most appropriate antimicrobial use metrics for reporting. Findings from the study have recently been published.

Figure 9: Highlights of pilot study conducted in an FDA cooperative agreement for antimicrobial use data collection for participating broiler companies, for 2013-2017

PILOT STUDY:
Participating broiler companies

- In broiler hatcheries, the percentage of chicks receiving antimicrobials dropped from 93% to 17% between 2013-2017
- The primary medically important antimicrobial classes used in broiler feed were streptogramins and tetracyclines; in broiler water they were penicillins and tetracyclines
- Use of all medically important antimicrobial classes in broiler feed declined; for example, tetracycline use in feed decreased by 95%, comparing 2013 to 2017
- Use of most medically important antimicrobial classes in broiler water declined; for example, neomycin use in water decreased by 75%, comparing 2013 to 2017

Antimicrobial Resistance in Retail Chicken

Information available for antimicrobial resistance trends in chicken pathogens and foodborne pathogens from chicken sources (retail chicken and chicken cecal samples) are presented in Chapter 6 of the report, and Appendix 7 of the report shows trends for 2015-2019 for each of the organisms monitored in the NARMS program. The report also describes some available resistance data for animal pathogen data (2017-2019). **Table 3** summarizes selected biomass-adjusted sales estimates, antimicrobial use information, and antimicrobial resistance information for retail chicken. Unless otherwise noted, increases or decreases in resistance were not statistically significant.

Table 3: Summary of Selected Antimicrobial Sales, Use, and Resistance Data for Chickens (Retail Meat)

Medically Important Antimicrobial Sales Estimates for Chickens Adjusted by Chicken Biomass	Chicken Antimicrobial Use[1]	Antimicrobial Resistance – Retail Chicken[2]
From 2016 through 2019: • Considering all 4 years combined, tetracyclines accounted for about 61% of estimated sales of medically important antimicrobials for chickens. Aminoglycosides (6.2%) and sulfonamides (3.5%) were the next highest volume of sales after tetracyclines, except for the 'Not Independently Reported' classes, which together accounted for about 24% of estimated sales. • Estimated chicken biomass increased by approximately 7.5%. • There was a 65.3% decrease in overall biomass-adjusted sales of medically important antimicrobial sales estimated for use in chickens. • Biomass-adjusted sales for all of the reportable medically important antimicrobial classes for use in chickens decreased. The 'Not Independently Reported' classes also decreased.	**From 2013 through 2017:** • Among participating poultry companies, the percentage of broiler chicks receiving medically important antimicrobials in hatcheries decreased from 93% in 2013 to 17% in 2017. • The main antimicrobials used in broiler feed were streptogramins and tetracyclines. All of the medically important antimicrobial classes showed decreases in use from 2013 through 2017, with tetracyclines showing the largest decrease (95%). • The main antimicrobials used in broiler water were penicillins and tetracyclines. Most of the medically important antimicrobial classes showed decreases in use from 2013 through 2017, with aminoglycosides (neomycin) showing the largest decrease (75%).	**From 2018 through 2019**: • Tetracycline resistance was stable for *E. coli, Salmonella,* and *Enterococcus* spp., and significantly increased for *Campylobacter* spp. isolates.[3] • Aminoglycoside (gentamicin) resistance significantly decreased for *E. coli* and *Salmonella,* decreased for *Enterococcus* spp., and was stable for *Campylobacter* spp. isolates.[3] • Ceftriaxone resistance decreased in *E. coli* isolates, but significantly increased in *Salmonella* isolates in 2019.[3] • Sulfonamide (sulfisoxazole) resistance decreased for *E. coli* and significantly increased for *Salmonella* isolates.[3] • Decreased susceptibility to azithromycin was detected in 1 of 304 *E. coli* isolates and no *Salmonella* isolates in 2019.[3,4] • Decreased susceptibility to ciprofloxacin showed a significant increase in *Salmonella* isolates.[5] • Macrolide (erythromycin) resistance was detected in 1 of 428 *C. jejuni* isolates in 2019, and macrolide resistance increased for *C. coli.*[3] • Macrolide (erythromycin) resistance increased for *E. faecalis* and decreased for *E. faecium* isolates.[3] • Multidrug resistance in *E. coli* isolates decreased, but significantly increased for *Salmonella* isolates. For *C. coli,* MDR increased, and no MDR was detected in *C. jejuni* isolates in 2019. For *Enterococcus* spp. isolates, MDR decreased for *E. faecium* and increased for *E. faecalis.*[3]

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[1] FDA Cooperative Agreement: *Antibiotic Use Data Collection in U.S. Poultry and Swine Production*

[2] FDA NARMS: Based on antimicrobial susceptibility testing as reported by FDA NARMS program. See Appendix for AST trend data for retail chicken and chicken cecal samples. All data is available on NARMS Now.

[3] Unless otherwise noted, increases or decreases in percentage resistance were not statistically significant (i.e., p-values were >0.05 using Fisher's exact test for comparing proportions).

[4] The azithromycin interpretive standards used for *Salmonella* serotypes other than serotype Typhi and for *E. coli* are NARMS-established breakpoints for monitoring and therefore referred to as decreased susceptibility (https://www.fda.gov/media/108180/download).

[5] NARMS uses decreased susceptibility to ciprofloxacin (MIC>=0.12µg/ml) as a marker for emerging fluoroquinolone resistance (https://www.fda.gov/media/108180/download).

TURKEYS

General information about turkey production and examples of bacterial diseases of turkeys are provided in Chapter 7 of the report. Antimicrobial sales estimates for turkeys (including sales adjusted by a turkey biomass denominator), antimicrobial use information, and antimicrobial resistance data are also provided in Chapter 7. Highlights are provided below for antimicrobial sales, use, and resistance data collected through the NARMS program for retail ground turkey. Table 4 at the end of this section provides a summary, and additional details are provided in the full report.

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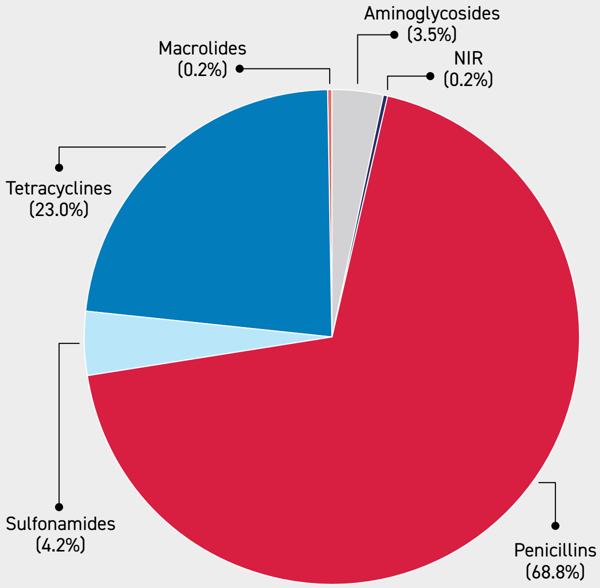
Sales of medically important antimicrobials estimated for turkeys from 2016 through 2019:

As shown in **Figure 10**, for the 4 years combined (2016-2019), penicillins made up the majority (68.8%) of antimicrobials sold and estimated for use in turkeys, while the more critically important macrolide class made up only about 0.2% of the overall total sales. Sales for some medically important antimicrobial drug classes are not independently reportable (NIR) in order to protect confidential business information of animal drug manufacturers that report sales data. For turkeys, these include cephalosporins, diaminopyrimidines, lincosamides, polymyxins, and streptogramins.

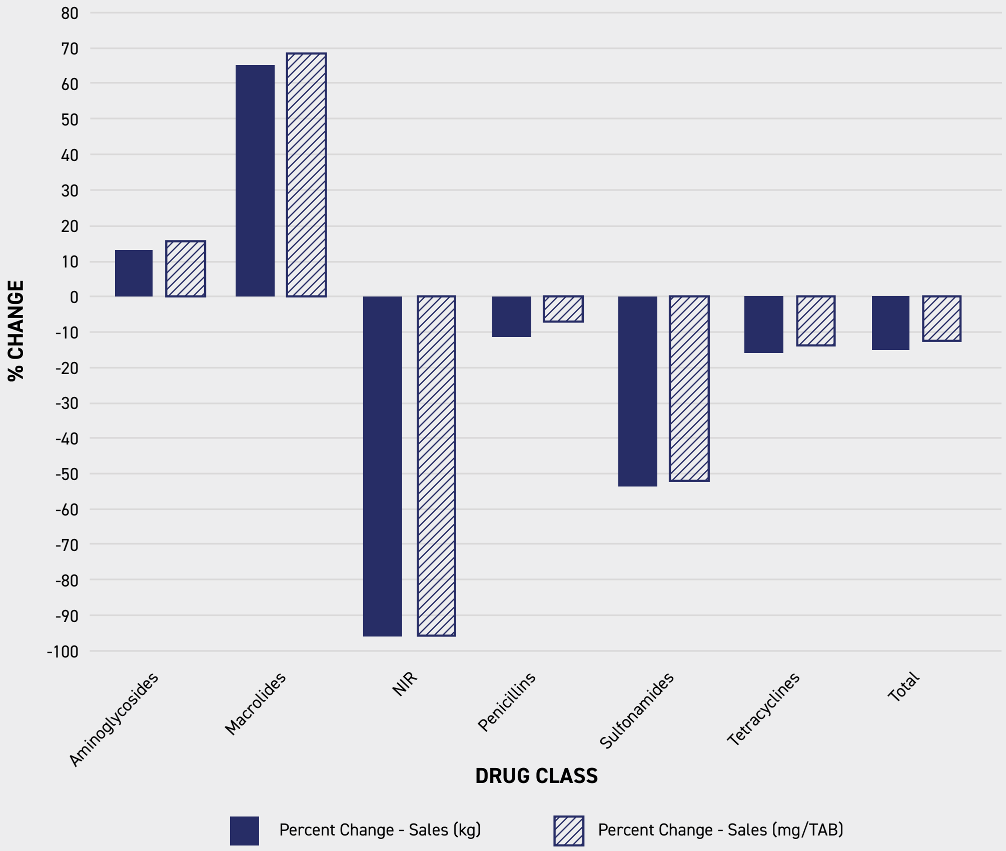
To allow for a more nuanced view of antimicrobial sales, sales in the context of animal populations can also be considered, in other words, the potential animal biomass that could receive antimicrobials each year. Using FDA's biomass denominator methodology for calculation, the estimated biomass of the turkey population decreased from 3.4 to 3.3 billion kilograms between 2016 and 2019, which is a decrease of approximately 1.4%. **Figure 11** shows the percentage change in unadjusted sales and biomass-adjusted sales estimated for turkeys for each reportable medically important antimicrobial drug class, comparing 2016 to 2019.

Figure 10: Medically important antimicrobial sales estimated for turkeys, by drug class (for 2016-2019 combined)



NIR= Not independently reported drug classes for turkeys (may include sales for the following antimicrobial drug classes: cephalosporins, diaminopyrimidines, lincosamides, polymyxins, and streptogramins). The value of NIR drug class sales is calculated as the overall sales total for turkeys minus the sum of all reportable drug classes.

Figure 11: Percent change in unadjusted sales (in kg) and biomass-adjusted sales (mg/TAB) estimated for turkeys, comparing 2016 to 2019



NIR= Not independently reported drug classes for turkeys (may include sales for the following antimicrobial drug classes: cephalosporins, diaminopyrimidines, lincosamides, polymyxins, and streptogramins). The value of NIR drug class sales is calculated as the overall sales total for turkeys minus the sum of all reportable drug classes. The turkey biomass denominator is applied to the NIR category as a whole; therefore does not account for potential exclusions of turkey categories for the denominator that may otherwise apply to individual NIR classes.

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Antimicrobial Use in Turkeys

Figure 12 shows highlights of findings from the turkey portion of the first 2 years of conduct (2016-2017) for an FDA cooperative agreement, *Antibiotic Use Data Collection in U.S. Poultry and Swine Production* (5U01FD005878). This project was intended to pilot methodologies for collecting and reporting on-farm antimicrobial use data from poultry and swine operations. For the poultry portion of the project, data were also collected for years prior to 2016, so trends for 2013-2017 were included.

The full report provides additional information about the study, including the challenges related to collecting and aggregating data from various types of production settings, as well as the study investigators' determination of the most appropriate antimicrobial use metrics for reporting. Findings from the study have been recently published.

Figure 12: Highlights of pilot study conducted in an FDA cooperative agreement for antimicrobial use data collection for participating turkey companies, for 2013-2017

PILOT STUDY:
Participating turkey companies

- In turkey hatcheries, the percentage of poults receiving antimicrobials dropped from 96% to 41% between 2013-2017
- The primary medically important antimicrobial classes used in turkey feed were tetracyclines and streptogramins; in turkey water they were penicillins and tetracyclines
- Use of all medically important antimicrobial classes in turkey feed declined; for example, tetracycline use in feed decreased by 67%, comparing 2013 to 2017
- Use of most medically important antimicrobial classes in turkey water declined; for example, gentamicin use in water decreased by 83%, comparing 2013 to 2017

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Antimicrobial Resistance in Retail Ground Turkey

Information available for antimicrobial resistance trends in turkey pathogens and foodborne pathogens from turkey sources (retail ground turkey and turkey cecal samples) are presented in Chapter 7 of the report, and Appendix 8 of the report shows trends for 2015-2019 for each of the organisms monitored in the NARMS program. The report also describes some available resistance data for animal pathogen data (2017-2019). **Table 4** summarizes selected biomass-adjusted sales estimates, antimicrobial use information, and antimicrobial resistance information for retail ground turkey. Unless otherwise noted, increases or decreases in resistance were not statistically significant.

Table 4: Summary of Selected Antimicrobial Sales, Use, and Resistance Data for Turkeys (Retail Meat)

Medically Important Antimicrobial Sales Estimates for Turkeys Adjusted by Turkey Biomass	Turkey Antimicrobial Use[1]	Antimicrobial Resistance – Retail Ground Turkey[2]
From 2016 through 2019:	**From 2013 through 2017:**	**From 2018 through 2019**:
• Considering all 4 years combined, penicillins accounted for nearly 70% of estimated sales of medically important antimicrobials for turkeys. Tetracyclines (23%) and sulfonamides (4.2%) were the next highest volume of sales after penicillins. • Estimated turkey biomass decreased by approximately 1.4%. • There was a 12.7% decrease in overall biomass-adjusted sales of medically important antimicrobials estimated for use in turkeys. • Biomass-adjusted sales for 3 of the 5 reportable medically important antimicrobial classes for use in turkeys decreased. 'Not Independently Reported' classes also decreased. • Aminoglycosides and macrolides were the 2 reportable classes that showed an increase in biomass-adjusted sales estimated for turkeys (increases of 15.9% and 69.3%, respectively).	• Among participating turkey companies, the percentage of turkey poults receiving medically important antimicrobials in hatcheries decreased from 96% in 2013 to 41% in 2017. • The main antimicrobials used in turkey feed were streptogramins and tetracyclines. All of the medically important antimicrobial classes showed decreases in use between 2013 and 2017, with streptogramins decreasing to zero and tetracyclines decreasing by about 67%. • The main antimicrobials used in turkey water were penicillins and tetracyclines. Most of the medically important antimicrobial classes showed decreases in use between 2013 and 2017, with aminoglycosides (gentamicin) showing the largest decrease (83%).	• Tetracycline resistance increased for *Salmonella* and *C. coli* isolates, decreased for *E. coli*, *C. jejuni*, and *E. faecalis,* and remained the same for *E. faecium* isolates.[3] • Sulfonamide (sulfisoxazole) resistance decreased for *E. coli* and increased for *Salmonella* isolates.[3] • Ampicillin resistance significantly decreased for *Salmonella* isolates, and also decreased for *E. coli* and *E. faecium* isolates.[3] • Ceftriaxone resistance decreased for *E. coli* and *Salmonella* isolates.[3] • Aminoglycoside (gentamicin) resistance decreased for *Salmonella* and *E. coli* isolates, and also decreased for *Enterococcus* spp. isolates.[3] • Decreased susceptibility to azithromycin was detected in 1 of 496 *E. coli* isolates and not detected in *Salmonella* isolates in 2019.[4] • Decreased susceptibility to ciprofloxacin was stable for *E. coli* and decreased for *Salmonella.*[3,5] • No macrolide (erythromycin) resistance was detected for *C. jejuni,* and 3 of 7 *C. coli* isolates showed macrolide resistance in 2019.[3] • Macrolide (erythromycin) resistance decreased or remained stable for *Enterococcus* spp. isolates.[3] • Multidrug resistance in *E. coli* and *Salmonella* isolates decreased, remained stable for *E. faecalis,* and increased for *E. faecium.*[3]

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1 FDA Cooperative Agreement: *Antibiotic Use Data Collection in U.S. Poultry and Swine Production*

2 FDA NARMS: Based on antimicrobial susceptibility testing as reported by FDA NARMS program. See Appendix for AST trend data for retail chicken and chicken cecal samples. All data is available on NARMS Now.

3 Unless otherwise noted, increases or decreases in percentage resistance were not statistically significant (i.e., p-values were >0.05 using Fisher's exact test for comparing proportions).

4 The azithromycin interpretive standards used for *Salmonella* serotypes other than serotype Typhi and for *E. coli* are NARMS-established breakpoints for monitoring and therefore referred to as decreased susceptibility (https://www.fda.gov/media/108180/download).

5 NARMS uses decreased susceptibility to ciprofloxacin (MIC>=0.12µg/ml) as a marker for emerging fluoroquinolone resistance (https://www.fda.gov/media/108180/download).

CONCLUSIONS

Loss of antimicrobial effectiveness through the emergence, distribution, and persistence of antimicrobial resistant bacterial pathogens is a serious threat to the successful therapy of infectious diseases in both humans and animals, as well as control of diseases in plants or crops. Antimicrobial use in humans, animals, and plant cultivation all contribute to the development of antimicrobial resistance. According to the recent CDC report, *Antibiotic Resistance Threats in the United States, 2019*, more than 2.8 million antimicrobial resistant infections occur in the U.S each year, and more than 35,000 people die as a result (CDC, 2019). Antimicrobial resistance also results in adverse animal health outcomes, although there are limited data on the impact of antimicrobial resistance on animal populations. CVM believes that use of antimicrobials in a manner consistent with good stewardship principles in all settings can help to slow the rate at which antimicrobial resistance develops in clinically relevant pathogens.

The report provides a description of some of the data that FDA and partner organizations have been collecting and reporting regarding antimicrobial sales, use, and resistance in animal agriculture and the related food chain, with an initial focus on the 4-year period of 2016-2019. Continued and enhanced data collection on antimicrobial use and resistance are essential components to inform policies and strategies for the containment of antimicrobial resistance.

Some important highlights of data related to antimicrobial sales, use, and resistance are described below and in the full report:

ANTIMICROBIAL SALES

Trends in medically important antimicrobial sales for food-producing animals included:

- In 2019, tetracyclines and penicillins were the medically important antimicrobials with the highest volume of sales for food-producing animals, accounting for nearly 79% of all sales. From 2016 (prior to full implementation of GFI #213) through 2019, sales of tetracyclines and penicillins both showed substantial decreases.
- The critically important cephalosporin and fluoroquinolone antimicrobial classes together accounted for less than 1% of medically important antimicrobial sales for food-producing animals in 2019.
- Macrolides, also considered critically important, accounted for only 8% of total sales in 2019, and showed a decrease in sales of about 12% from 2016 through 2019.
- There were variable changes considering species-specific estimated sales of medically important antimicrobial sales comparing 2016 to 2019 and there were some increases in sales of certain antimicrobial classes from 2018 through 2019.
  - These increases could be the result of changes in animal population sizes, changes in the proportion of certain industry segments (e.g., proportion of nursery pigs vs. growing pigs, etc.), and/or changes in the incidence of diseases that require therapeutic antimicrobial use.
  - This demonstrates one reason why on-farm antimicrobial use data are important to collect – they can potentially provide for a better understanding of how and why broad shifts in antimicrobial sales occur from year to year.

ANTIMICROBIAL USE

Some notable differences in on-farm antimicrobial use between 2016 and 2017, from pilot data obtained in FDA cooperative agreements, included:

- On a sample of 22 U.S. beef feedlots, there were variable decreases in feedlot cattle uses of tetracyclines and macrolides, as well as decreases in fluoroquinolones and cephalosporin uses for control of bovine respiratory disease in groups of cattle.
- For nine large U.S. swine systems, there were substantial decreases in chlortetracycline and lincomycin use between 2016 and 2017.
- Feed and water uses of most medically important antimicrobial drug classes decreased for broiler chickens and turkeys between 2016 and 2017.
- Variable decreases in antimicrobial use in broiler and turkey hatcheries were also observed.

These pilot projects were essentially focused on developing methodologies for collection and evaluation of on-farm antimicrobial use data. They allowed for useful insights to be gained about the challenges associated with collecting and analyzing antimicrobial use data from multiple types of on-farm records, and in determining appropriate metrics for measuring and reporting antimicrobial use.

ANTIMICROBIAL RESISTANCE

Antimicrobial resistance trends in organisms monitored by the NARMS program and for some animal pathogens monitored by USDA NAHLN and FDA's Vet-LIRN program are summarized in the full report. Some highlights included:

- Trends in antimicrobial resistance for antimicrobials considered critical for treatment of human infections (e.g., ceftriaxone, ciprofloxacin, azithromycin) also showed important trends from 2018 through 2019. For example:
  - Ceftriaxone resistance in E. coli isolates decreased or remained stable with the exception of small increases in retail pork.
  - For *Campylobacter* and *Enterococcus* isolates from retail chicken and ground turkey, the percentage of isolates with ciprofloxacin resistance decreased or remained stable, with the exception of *C. coli* for retail ground turkey, which showed a small increase.
  - In 2019, there were very few retail meat *E. coli* isolates which showed decreased susceptibility to azithromycin (4 out of 1,215 isolates), and no Salmonella isolates (out of 1,992) showed decreased susceptibility to azithromycin.
  - For poultry sources, the percentage of *Campylobacter* and *Enterococcus* isolates with macrolide resistance decreased or remained stable, with the exception of *C. coli* in retail ground turkey, which increased.
  - Importantly, there continues to be no carbapenem, linezolid, or vancomycin resistance detected in any isolates from all retail meats sampled.

While it is desirable to monitor antimicrobial resistance trends in conjunction with changes in antimicrobial use patterns, more years of data are needed to better understand the relationships. For example, Zawack et al. modeled the relationship between changes in antimicrobial use policy (i.e., implementation of FDA's GFI #213) and changes in baseline resistance in bacteria monitored by the NARMS program, concluding that a 6% decrease in percent antimicrobial resistance could likely be detected in 6 years following establishment of a new resistance rate (Zawack, 2016). Rather than comparing trends in antimicrobial resistance to trends in antimicrobial sales (and use) within the same year, it may be more appropriate to evaluate antimicrobial resistance trends after allowing for some additional time lag to occur following changes in sales and/or use patterns.

Other countries have adopted a national policy, often through legislative actions, setting specific reduction targets for sales or use of medically important antimicrobials. The U.S. has not adopted a policy of setting specific reduction targets for sales or use of medically important antimicrobials. Rather, the focus has been on policies which promote and encourage the adoption of good antimicrobial stewardship practices which can help to reduce inappropriate antimicrobial use. As of January 1, 2017, use of medically important antimicrobials for production purposes (e.g., growth promotion) is no longer permitted, and veterinary oversight is now required for use of medically important antimicrobials in the feed and water of food-producing animals. In addition, in June 2021 FDA finalized GFI #263, which, when fully implemented, will bring all remaining dosage forms (e.g., oral, injectable, etc.) of approved medically important antimicrobials used in animals under veterinary oversight. FDA expects that full implementation of this guidance will be completed within a 2-year timeframe, by approximately June 2023. Veterinarians possess the necessary knowledge and expertise to provide oversight for antimicrobial use in food-producing animals, and work with animal producers to help design and institute disease prevention programs appropriate to the situation that can help reduce the need for antimicrobial use while protecting animal health. The American Veterinary Medical Association, as well as species-specific veterinary organizations and animal producer organizations, have developed antimicrobial stewardship principles which help support veterinarians and animal producers implement good stewardship (AVMA, 2020).

While progress has been made in animal agriculture to reduce the threat of antimicrobial resistance, there remain some important gaps in knowledge and data needed to inform risk assessments. While not a complete list, some of these knowledge or data gaps include the need for:

- Routine surveillance of animal health issues which typically necessitate antimicrobial use;
- Enhanced antimicrobial resistance data (e.g., additional sources and pathogens);
- Ongoing monitoring of on-farm antimicrobial use practices;
- Research on antimicrobial alternatives and other disease prevention strategies that could effectively reduce the need for antimicrobials; and
- More research to help better understand the determinants of resistance.

Filling these gaps will continue to require the combined and coordinated efforts of multiple government agencies, animal drug manufacturers, animal industry organizations, veterinary and public health organizations, academia and researchers, veterinarians, and producers.

It is important to try to measure the effects of changes in antimicrobial use policies to determine what impacts are made on antimicrobial stewardship, animal health, and public health. This report is an initial attempt to describe some of the data that should be considered. Additional data will need to be gathered and CVM intends to pursue additional opportunities to collect such information. Resistance data are now reported real-time with NARMS Now, allowing for important changes to be seen more swiftly, and also allowing for actions to be taken by industry stakeholders in a timely manner to address any potential problems.

The effects of antimicrobial use in food animal production on antimicrobial resistance in humans are challenging to quantify and the impacts of antimicrobial resistance on animal health and production are even less well-understood. Even in the absence of data, it is important to be good stewards of antimicrobials in order to maintain their effectiveness for therapy of bacterial infections in humans and animals, and also to manage important diseases of agricultural crops. In addition, stewardship of all antimicrobials is important, not just the antimicrobials of critical importance to human medicine. Veterinary professional and animal industry and producer organizations have been actively involved with antimicrobial stewardship initiatives. As more scientific research is conducted by the scientific community, CVM strives to consider this new evidence as it works with stakeholders to make science-based decisions to help address the threat of antimicrobial resistance.

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