# Estimates of On-Farm Antimicrobial Usage in Broiler Chicken and Turkey Production in the United States, 2013 – 2017

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# Summary

Antimicrobial use in any setting is a key selective force behind the emergence of resistant bacteria. Therefore, optimizing strategies for more efficacious and targeted antimicrobial use ('stewardship') is an essential component of efforts to combat antimicrobial resistance. To bolster stewardship programs in animal agriculture, processes are needed for the systematic collection of on-farm antimicrobial use data to advance knowledge of the principal indications for use and methods of administration (dose, route, duration) of specific antimicrobial compounds. Ideally these systems would also collect information on therapeutic outcomes. This report demonstrates the development of a systematic data collection approach and presents a longitudinal analysis of data on antimicrobial use in the U.S. broiler chicken and turkey industries. Participation was completely voluntary, and all companies were guaranteed anonymity and data confidentiality.

The scope of the data collection was antimicrobial use in broiler chickens and turkeys from the hatchery until the day of slaughter. The data were collected for the period of 2013-2017 to straddle the changes to the Veterinary Feed Directive (VFD) Rule that went into effect on October 1, 2015 and full implementation of FDA Guidance for Industry (GFI) #213 on January 1, 2017.

To estimate the representativeness of the collected industry data to the total annual volume of U.S. broiler and turkey production, a list provided annually by WATT Poultry USA regarding the amount of production in the major U.S. broiler chicken and turkey companies was used. This list includes all of the major broiler and turkey companies of the U.S. and includes the vast majority of total U.S. production. The total production on this list (total pounds liveweight produced) was summed for the companies that participated in the project for each year of data collection. This annual total served as the numerator. All of the production (total pounds liveweight produced) reported in each annual WATT list was totaled and used as the annual denominator. For 2017, the broiler data represent up to 93% of the broiler chicken produced by the companies on the WATT list, and the turkey data represent up to 82% of the turkey produced by the companies on the WATT list. The actual data that were submitted for 2017 are based on more than 7,500,000,000 broiler chickens and 164,000,000 turkeys slaughtered. The representativeness of the collected data to U.S. broiler and turkey production increased from 2013 to 2017 and will likely continue to increase for the next report that will include 2018 data. No attempts were made to extrapolate the data collected in this project to the entire U.S. poultry industry; the results reported herein are specifically from the data submitted by the companies that participated.

Data regarding antimicrobial use were submitted in a variety of formats, and these are described in the report. The availability of data and the granularity of the data increased from 2013 to 2017, in large part due to the changes made by FDA in GFI #213 and the VFD, in particular bringing the feed and water administration of antimicrobials under veterinary supervision. Once aggregated, the data and analyses were audited by USDA:APHIS:VS:CEAH collaborators. Data are expressed as total kilograms of each antimicrobial used for each specific route of administration and as total grams of antimicrobial per 100,000 birds placed (for hatchery antimicrobial administration) and per 1,000,000 pounds liveweight produced (for feed and water-soluble administration). As granularity of the data improves, such as detailed flock-level records

of antimicrobial administration, additional metrics for analyzing antimicrobial usage data will be incorporated. Data are not adjusted with denominators such as population correction units (PCU) for reasons that are discussed in the report. No comparison of these data is made to the sales data presented in the FDA Sales and Distribution Report from 2017.

For both the broiler chicken and turkey industries, reductions were observed in antimicrobial use over the 5-year period. Key findings are listed below, and details are provided in the report. While a reduction in antimicrobial use may be an important indicator of improved stewardship, reducing the need for antimicrobials through improved disease prevention should be considered a more holistic indicator of overall flock health and optimal antimicrobial use.

The current effort lacks data on exposure to poultry pathogens and the overall disease burden in broiler chicken and turkey production. Without this information, it is difficult to evaluate the amount of antimicrobial use that would be expected to manage the annual risk of disease experienced in the poultry industry. It is conceivable that antimicrobial use could increase in a given year, even though all of the use is consistent with good stewardship, simply due to an increase during that year in the disease burden that necessitates antimicrobial therapy. Conversely, antimicrobial use could decline if therapeutic thresholds (e.g. percentage of the flock exhibiting clinical signs of disease) were altered, potentially resulting in an increase in disease incidence, and potential decline in animal welfare, due to concomitant reduction in antimicrobial use. Future efforts will seek approaches to capture the underlying disease risk within the broiler chicken and turkey industries.

Overall, the full implementation of FDA GFI #213 and the changes to the VFD rule likely resulted in a couple of key improvements in antimicrobial stewardship. First, antimicrobials used in broiler chicken and turkey production shifted to veterinary supervision, thereby making medical decision-making the responsibility of the veterinarian. This shift likely improved overall antimicrobial stewardship within the participating companies. Second, noticeable improvements in data management with respect to antimicrobial administration occurred over the five-year time span of this report. Data from these two industries will continue to be collected, and because of greatly improved record-keeping initiated by the industries, we expect that the data in future reports will have greater granularity at the flock level, thereby enabling the application of more precise antimicrobial use metrics.

The total amount of medically important antimicrobial usage by antimicrobial class with the percentage change over the time period 2013 to 2017 and 2016 to 2017 are shown below (taken from Tables 32 and 33 of the report). These date ranges are presented in the tables because the 2013-2017 period spans the entire period of this data collection effort, and the 2016-2017 period straddles the full implementation of FDA Guidance for Industry (GFI) #213 on January 1, 2017. These tables should be interpreted with caution for a couple of important reasons. First, specific antimicrobial active ingredients within an antimicrobial class have been aggregated, but as FDA acknowledges in the FDA Sales and Distribution Report from 2017, “Antimicrobial class includes drugs of different molecular weights.” Consequently, different antimicrobials will contribute disproportionately to the total amount of drug in each class. Second, the totals within each antimicrobial class are summed across routes of administration; combining injectable and orally administered antimicrobial use data into a single total precludes the differentiation of potency by route. This full report presents the data by route of administration and by individual active ingredient, when feasible.

It is important to note that overall representation of the collected data to the U.S. poultry industry increased from 2013 to 2017, and therefore, more birds are represented in the 2016 and 2017 data than in the 2013 data. Consequently, data are also presented as grams of drug per 1,000,000 pounds liveweight produced to standardize the data over time.

Table 32 of report. Medically important antimicrobial drugs used in broiler chickens for 2013, 2016 and 2017. Data are shown as total amount of each antimicrobial class in kilograms and as total grams of each antimicrobial class per 1,000,000 pounds of liveweight produced. Percentage differences in both metrics are shown for the 2013 to 2017 and 2016 to 2017 periods.

| | **Antimicrobial Usage in Broilers (kg of antimicrobial)** | | | **% Change** | |
|---|---|---|---|---|---|
| Antimicrobial Class | 2013 | 2016 | 2017 | 2013-2017 | 2016-2017 |
| Aminoglycosides | 1,651 | 837 | 508 | -69% | -39% |
| Lincosamides | 3,584 | 4,360 | 2,604 | -27% | -40% |
| Macrolides | 8,048 | 10,591 | 900 | -89% | -92% |
| Penicillins | 17,309 | 27,955 | 17,398 | 1% | -38% |
| Sulfonamides | 5,221 | 1,915 | 1,892 | -64% | -1% |
| Tetracyclines | 107,633 | 22,103 | 15,366 | -86% | -30% |

| | **Antimicrobial Usage in Broilers (g of antimicrobial per million lbs liveweight)** | | | **% Change** | |
|---|---|---|---|---|---|
| Antimicrobial Class | 2013 | 2016 | 2017 | 2013-2017 | 2016-2017 |
| Aminoglycosides | 42.5 | 17.7 | 10.6 | -75% | -40% |
| Lincosamides | 96.0 | 93.1 | 54.9 | -43% | -41% |
| Macrolides | 201.0 | 223.3 | 19.0 | -91% | -92% |
| Penicillins | 474.4 | 596.8 | 366.6 | -23% | -39% |
| Sulfonamides | 143.3 | 40.8 | 39.8 | -72% | -2% |
| Tetracyclines | 2,662.9 | 470.7 | 322.0 | -88% | -32% |

Table 33 of report. Medically important antimicrobial drugs used in turkeys for 2013, 2016 and 2017. Data are shown as total amount of each antimicrobial class in kilograms and as total grams of each antimicrobial class per 1,000,000 pounds of liveweight produced. Percentage differences in both metrics are shown for the 2013 to 2017 and 2016 to 2017 periods.

| | **Antimicrobial Usage in Turkeys (kg of antimicrobial)** | | | **% Change** | |
|---|---|---|---|---|---|
| Antimicrobial Class | 2013 | 2016 | 2017 | 2013-2017 | 2016-2017 |
| Aminoglycosides | 11,382 | 9,278 | 6,579 | -42% | -29% |
| Amphenicols | 27 | 87 | 153 | 461% | 76% |
| Cephalosporins | 19 | 8 | 0 | -100% | -100% |
| Lincosamides | 4,364 | 5,424 | 2,847 | -35% | -48% |
| Macrolides | 246 | 320 | 693 | 182% | 117% |
| Penicillins | 399,003 | 384,933 | 280,901 | -30% | -27% |
| Sulfonamides | 21,782 | 15,888 | 20,851 | -4% | 31% |
| Tetracyclines | 186,624 | 164,662 | 111,836 | -40% | -32% |

| | **Antimicrobial Usage in Turkeys (g of antimicrobial per million lbs liveweight)** | | | **% Change** | |
|---|---|---|---|---|---|
| Antimicrobial Class | 2013 | 2016 | 2017 | 2013-2017 | 2016-2017 |
| Aminoglycosides | 2,643.2 | 1,767.1 | 1,270.5 | -52% | -28% |
| Amphenicols | 6.4 | 16.6 | 29.6 | 366% | 79% |
| Cephalosporins | 4.0 | 1.6 | 0.0 | -100% | -100% |
| Lincosamides | 1,014.7 | 1,033.0 | 549.8 | -46% | -47% |
| Macrolides | 57.2 | 60.9 | 133.8 | 134% | 120% |
| Penicillins | 92,774.9 | 73,312.7 | 54,244.5 | -42% | -26% |
| Sulfonamides | 5,065.1 | 3,026.0 | 4,026.5 | -21% | 33% |
| Tetracyclines | 40,841.5 | 31,360.8 | 21,596.5 | -47% | -31% |

Broiler Chicken Summary

- Broiler companies participated voluntarily and represented a large percentage of the overall U.S. broiler chicken production
  - The antimicrobial use datasets represent 72% to 93% of broiler chicken produced annually based on the companies included in the published WATT Poultry USA list
  - The antimicrobial use data that were submitted for 2017 include information on approximately 7,900,000,000 chicks placed, 7,500,000,000 chickens slaughtered, and 48,000,000,000 pounds liveweight produced
- Several key diseases were targeted by antimicrobial administration
  - Necrotic enteritis, a clostridial disease of chickens, remains one of the most important diseases of chickens that requires antimicrobial therapy
  - Colibacillosis, a broad category of *E. coli* diseases that affect chickens, results in much of the antimicrobial use in feed and water
  - Gangrenous dermatitis, another clostridial disease, necessitates a considerable fraction of the overall antimicrobial use in chicken production
- Hatchery antimicrobial use decreased substantially between 2013 and 2017
  - The approximate percentage of broiler chicks placed that received hatchery antimicrobials decreased from 93% in 2013 to 17% in 2017
  - Hatchery gentamicin use in broiler chicks decreased approximately 74% between 2013 and 2017
- Medically important in-feed antimicrobial drug use decreased substantially
  - In-feed virginiamycin use decreased approximately 60% between 2013 and 2017
  - In-feed tetracycline use decreased approximately 95% between 2013 and 2017
  - Some approved uses of in-feed antimicrobial drugs were discontinued with implementation of GFI #213
    - There are no remaining approved uses of in-feed tylosin in broiler chickens, and thus in-feed tylosin use went to zero in 2017
- There was a shift to antimicrobial drugs that are not considered medically important
  - In-feed bacitracin remained a commonly-used antimicrobial drug for the prevention of necrotic enteritis
  - In-feed avilamycin use increased in 2017; it is a not medically important antimicrobial drug for the prevention of necrotic enteritis
- Medically important water-soluble antimicrobial use decreased substantially
  - Water-soluble penicillin use decreased approximately 21% between 2013 and 2017 and approximately 42% since the peak in 2015
  - Water-soluble tetracycline use decreased approximately 47% between 2013 and 2017
  - Water-soluble lincomycin use decreased approximately 28% between 2013 and 2017 and approximately 58% since the peak in 2015
  - Water-soluble sulfonamide use decreased approximately 72% between 2013 and 2017
  - Water-soluble tylosin use decreased approximately 46% between 2013 and 2017
- This report documents substantial reductions in the use of most medically important antimicrobials in broiler production, regardless of route of administration

Turkey Summary

- Turkey companies participated voluntarily and represented a large percentage of the overall U.S. turkey production
  - The antimicrobial use datasets represent 77% to 82% of turkey produced annually based on the companies included in the published WATT Poultry USA list.
  - The antimicrobial use data that were submitted for 2017 include information on approximately 187,000,000 poults placed, 164,000,000 turkeys slaughtered, and 5,000,000,000 pounds liveweight produced
- Several key diseases were targeted by antimicrobial administration
  - Gangrenous dermatitis, a clostridial disease of turkeys, remains one of the most important diseases of turkeys that requires antimicrobial therapy
  - Bacterial enteritis also comprised a considerable fraction of the overall antimicrobial use in turkey production
  - Colibacillosis, a broad category of *E. coli* diseases that affect turkeys, results in much of the antimicrobial use in feed and water
- Hatchery antimicrobial use decreased substantially between 2013 and 2017
  - The approximate percentage of turkey poults placed that received hatchery antimicrobials decreased from 96% in 2013 to 41% in 2017
  - Hatchery gentamicin use in turkey poults decreased approximately 42% between 2013 and 2017
  - Hatchery ceftiofur use in turkey poults went to zero between 2013 and 2017 for the birds represented in this dataset
- Medically important in-feed antimicrobial drug use decreased substantially
  - In-feed tetracycline use decreased approximately 67% between 2013 and 2017
  - Some approved uses of in-feed antimicrobial drugs were discontinued with implementation of GFI #213
    - There are no remaining approved uses of virginiamycin or in-feed tylosin in turkeys, and thus use of both of these antimicrobial drugs in-feed went to zero in 2017
- Medically important water-soluble antimicrobial use decreased substantially for most antimicrobials
  - Water-soluble penicillin use decreased approximately 42% between 2013 and 2017 and approximately 26% between 2016 and 2017
  - Water-soluble tetracycline use decreased approximately 28% between 2013 and 2017 and approximately 15% between 2016 and 2017
  - Water-soluble lincomycin use decreased approximately 46% between 2013 and 2017
  - Water-soluble neomycin use decreased approximately 49% between 2013 and 2017
  - Water-soluble erythromycin use decreased approximately 65% between 2013 and 2017
  - Water-soluble tylosin use increased approximately 275% between 2013 and 2017
  - Florfenicol use increased more than fivefold between 2013 and 2017
- There are very few not medically important antimicrobial options approved for use in turkey production
- This report documents substantial reductions in the use of most medically important antimicrobials in turkey production, regardless of route of administration

# Contents

# Introduction

Antimicrobial use in any setting is a key selective force behind the emergence of resistant bacteria. Therefore, optimizing strategies for more efficacious and targeted antimicrobial use ('stewardship') is an essential component of efforts to combat antimicrobial resistance. To bolster stewardship programs in animal agriculture, processes are needed for the systematic collection of on-farm antimicrobial use data to advance knowledge of the principal indications for use and methods of administration (dose, route, duration) of specific antimicrobial compounds. Ideally these systems would also collect information on therapeutic outcomes. This report demonstrates the development of a systematic data collection approach and presents a longitudinal analysis of data on antimicrobial use in the U.S. broiler chicken and turkey industries. Participation was completely voluntary, and all companies were guaranteed anonymity and data confidentiality.

In an effort to improve antimicrobial stewardship and overall judicious use of antimicrobials in animal agriculture, the U.S. Food and Drug Administration (FDA) has made substantive changes to antimicrobial policy in recent years. In 2012, FDA published Guidance for Industry (GFI) #209 (1) describing their overall policy direction regarding antimicrobial drugs. As stated by FDA, "The principles of FDA's judicious use policy include 1) limiting medically important antimicrobial drugs to uses in food-producing animals that are considered necessary for assuring animal health; and 2) limiting medically important antimicrobial drugs to uses in food-producing animals to those that include veterinary oversight or consultation" (https://www.fda.gov/animal-veterinary/safety-health/antimicrobial-resistance). These therapeutic uses that could be necessary for assuring animal health included disease prevention, disease treatment and disease control; production uses of medically important antimicrobials, which would include the use of antimicrobials for increased rate of weight gain and improved feed efficiency, would no longer be allowed. FDA's GFI #152 (3) defined "medically important" antimicrobials and listed them in Appendix A of the document.

In 2013, GFI #213 was published, providing more detail on implementing the key principles in GFI #209 (2). This document provided guidance to sponsors on how to remove label claims relating to production uses (growth promotion/feed efficiency) of the medically important antimicrobials. Although some have misinterpreted this change as a voluntary decision to be made by the veterinarian, in actuality it was made by the drug manufacturers who removed the increased weight gain/improved feed efficiency label claim from the medically important antimicrobial drugs. Because neither the Animal Medicinal Drug Use Clarification Act nor the Veterinary Feed Directive (VFD) Rule allows the extra-label use of animal drugs in or on feed of broilers or turkeys (see FDA's Compliance Policy Guide 615.115 for details), this voluntary removal of the label claims eliminated the use of the medically important antimicrobials for production uses in the U.S. Finally, GFI #213 brought the remaining therapeutic antimicrobial uses under veterinary oversight by changing the marketing status of medically important antimicrobials administered in feed or water from over-the-counter (OTC) to veterinary feed directive (VFD) or prescription (Rx). These changes were fully implemented by January 2017.

The regulatory changes did not include a system to measure on-farm antimicrobial use. FDA thus issued a Request for Applications to address this gap and stated that a system for collecting on-farm antimicrobial use data should: 1) Provide detailed antimicrobial drug use data that accurately reflects actual on-farm use, 2) Provide "baseline" data on antimicrobial use (i.e., data prior to the implementation of Guidance For Industry (GFI) #213), 3) Pilot methodologies for collecting, summarizing, and reporting antimicrobial use data, 4) Foster public-private partnerships/collaboration, 5) Leverage existing data systems and minimize burden and disruption to animal producers, and 6) Incorporate strategies for protecting farm/producer identity and other confidential information (https://grants.nih.gov/grants/guide/rfa-files/RFA-FD-16-046.html). This project is an initial attempt to fill these data and knowledge gaps for broiler chickens and turkeys.

This report details the data collection effort for the broiler chicken and turkey industries of the U.S. The data presented in this report cover a large percentage of annual U.S. poultry production. Data were collected for the years 2013 through 2017, thus straddling the full implementation of GFI #213 and the changes to the VFD rule. Data that were collected from participating companies include total amount of each antimicrobial drug class used per year by route of administration, age of onset for some of the key poultry diseases that necessitate antimicrobial therapy, estimates of the percentage of each antimicrobial drug use that was used to target some of the major poultry diseases, and typical durations of water soluble drug administration for different antimicrobial diseases. This is the first report for this on-farm antimicrobial use in poultry production data collection effort; data continue to be collected. Future reports will present data with greater granularity, as will be explained later in this document.

# General Approach

## Industry Participation

The goal of this effort was to develop and demonstrate an approach for collecting quantitative on-farm antimicrobial use data from the poultry industry. To accurately establish temporal trends in antimicrobial use practices within the industry, data were collected for the period of 2013 through 2017 for this initial effort. By collecting data from 2013 through 2017, this effort includes "baseline" data on antimicrobial use prior to full implementation of GFI #213 that took effect January 1, 2017. Many companies and producers started changing antimicrobial use practices long before 2017, in part due to the anticipation of the regulatory changes, in part due to improvements in antimicrobial stewardship, and in part due to changing demands of customers and consumers.

The poultry industry data collection effort targeted all of the major companies that raise broilers and turkeys commercially in the U.S. As will be discussed below, the WATT Poultry USA annual list was used to determine the representativeness of the data actually collected to annual U.S. broiler and turkey production. Companies that agreed to participate were informed that they would need to track data on production parameters, antimicrobial use data from the hatchery and antimicrobial use in feed and water. This tracking would include all antimicrobial administrations for production purposes and for disease prevention, treatment and control. Companies would need to track the indication for use, and ideally capture this information retrospective to 2013. This was not easy for most companies, as prior to January 1, 2017, antimicrobials were not necessarily under veterinary supervision, especially for the antimicrobials administered in feed. While the use of antimicrobials would have been supervised by someone within the company, the record-keeping was not typically centralized, and therefore, many companies did not have an easy-to-access record keeping system for retrieving all antimicrobial administration data.

## Evolution of Data Collection Instruments

In 2014, a pilot program was initiated by Dr. Randall Singer with the goal of collecting antimicrobial use data from the U.S. poultry production system. The project was started with the support of the U.S. Poultry & Egg Association (USPOULTRY) and additional assistance from the National Chicken Council (NCC), the National Turkey Federation (NTF), and the American Association of Avian Pathologists (AAAP). One aim of this program was to develop a survey capable of capturing quantitative on-farm antimicrobial use estimates. Because of their expertise in survey design and implementation, experts within USDA:APHIS:VS:CEAH (CEAH) were included in the program design from the outset.

Different surveys were required for broiler chickens and turkeys due to differences in production, record keeping, and available antimicrobial options. However, both surveys required the same basic components: antimicrobial compound, indication, route, dose, duration, age at administration, and number of animals receiving the drug. Furthermore, population estimates were needed for each survey response to estimate the denominator of animals that could have received antimicrobial during the time period.

In 2016, this project was expanded to include the entire U.S. broiler chicken and turkey industries. This project aimed to enroll a large fraction of annual U.S. poultry production and to have a mechanism to quantify the representativeness of participation when compared to total annual production in the U.S. The initial survey design was developed using the web-based Qualtrics platform. The information from this survey was also developed in an Excel spreadsheet. The survey was designed to collect antimicrobial use data from the hatchery through the end of the growout period (growout being defined as the period when the meat birds are being raised, the end of which is marked by transport to the processing plant). The survey included sections on company production parameters and antimicrobial use information including injectable, water-soluble and in-feed weights for both medically and not medically important antimicrobials.

After a series of conversations with industry representatives and individuals within participating companies, it became apparent that the data collection approach would have to be customized for every company due to differences in data format and availability. Furthermore, data were often challenging to access for earlier years of the data collection interval (2013-2017). While some companies were able to use the online or spreadsheet version of the survey, for many of the companies it was necessary to consider a variety of data recovery options; a single, standardized approach to data collection was practically impossible for this first data collection effort. Details of the various formats in which data were submitted are provided in the Data Collection sections of this report.

## Medically Important and Not Medically Important Antimicrobials

The antimicrobials that are used in poultry production can be classified as Medically Important (MI) or Not Medically Important (NMI), based on their importance in human medicine. FDA's GFI #152 (3) lists antimicrobial classes and active ingredients within each class that are considered MI. Further, Appendix A in GFI #152 differentiates these MI drugs as Critically Important, Highly Important or Important. In the 4 tables that follow, the antimicrobials that were used in broiler and turkey production in 2017 that are included in this report are presented by their medical importance. The tables include the route of administration, the antimicrobial class, the classification of the MI antimicrobial class, and the active ingredients that were used within each class.

Table 1. Medically Important (MI) antimicrobials used in broiler chicken production in the U.S. in 2017 that are included in this report, categorized by route of administration. Antimicrobial drugs that were used within each class are shown as well as classification of importance per Appendix A of FDA's GFI #152 (3).

| Route of Administration | Drug Class | Classification | Active Ingredient |
|---|---|---|---|
| **Injectable** | | | |
| | Aminoglycosides | Highly Important | Gentamicin |
| **Feed** | | | |
| | Diaminopyrimidines | Critically Important | Ormetoprim |
| | Streptogramins | Highly Important | Virginiamycin |
| | Sulfonamides | Critically Important | Sulfadimethoxine |
| | Tetracyclines | Highly Important | Chlortetracycline<br>Oxytetracycline |
| **Water** | | | |
| | Aminoglycosides | Highly Important | Neomycin<br>Spectinomycin |
| | Lincosamides | Highly Important | Lincomycin |
| | Macrolides | Critically Important | Tylosin |
| | Natural penicillins | Highly Important | Penicillin G |
| | Sulfonamides | Critically Important | Sulfadimethoxine<br>Sulfamerazine<br>Sulfamethazine<br>Sulfaquinoxaline |
| | Tetracyclines | Highly Important | Chlortetracycline<br>Oxytetracycline<br>Tetracycline |

Table 2. Antimicrobials that are Not Medically Important (NMI) and that were used in broiler chicken production in the U.S. in 2017, categorized by route of administration. Antimicrobial drugs that were used within each class are shown.

| Route of Administration | Drug Class | Active Ingredient |
|---|---|---|
| **Feed** | | |
| | Glycolipids | Bambermycins |
| | Ionophores | Lasalocid |
| | | Monensin |
| | | Narasin |
| | | Salinomycin |
| | Orthosomycins | Avilamycin |
| | Polypeptides | Bacitracin |
| **Water** | | |
| | Polypeptides | Bacitracin |

Table 3. Medically Important (MI) antimicrobials used in turkey production in the U.S. in 2017 that are included in this report, categorized by route of administration. Antimicrobial drugs that were used within each class are shown as well as classification of importance per Appendix A of FDA's GFI #152 (3).

| Route of Administration | Drug Class | Classification | Active Ingredient |
|---|---|---|---|
| **Injectable** | | | |
| | Aminoglycosides | Highly Important | Gentamicin |
| | 3rd Generation Cephalosporins | Critically Important | Ceftiofur |
| | Natural penicillins | Highly Important | Penicillin G |
| **Feed** | | | |
| | Tetracyclines | Highly Important | Chlortetracycline<br>Oxytetracycline |
| **Water** | | | |
| | Aminoglycosides | Highly Important | Gentamicin<br>Neomycin<br>Spectinomycin |
| | Amphenicols | Highly Important | Florfenicol |
| | Lincosamides | Highly Important | Lincomycin |
| | Diaminopyrimidines | Critically Important | Trimethoprim |
| | Macrolides | Critically Important | Erythromycin<br>Tylosin |
| | Natural penicillins | Highly Important | Penicillin G |
| | Sulfonamides | Critically Important | Sulfadimethoxine<br>Sulfamerazine<br>Sulfamethazine<br>Sulfaquinoxaline<br>Sulfadiazine |
| | Tetracyclines | Highly Important | Chlortetracycline<br>Oxytetracycline<br>Tetracycline |

Table 4. Antimicrobials that are Not Medically Important (NMI) and that were used in turkey production in the U.S. in 2017, categorized by route of administration. Antimicrobial drugs that were used within each class are shown.

| Route of Administration | Drug Class | Active Ingredient |
|---|---|---|
| **Feed** | | |
| | Glycolipids | Bambermycins |
| | Ionophores | Lasalocid |
| | | Monensin |
| | Polypeptides | Bacitracin |
| **Water** | | |
| | Polypeptides | Bacitracin |
| | Pleuromutilins | Tiamulin |

## Data Aggregation, Auditing and Reporting

Data from each company were first validated and aggregated in Microsoft Excel spreadsheets. Errors were often identified during this process, and any data that appeared to be erroneous were discussed in conversations with the submitting company. A relational database was created using Microsoft Access, and records were then imported into this database. Customized Visual Basic scripts further assisted with error checking and data validation. Once in the same format, data from all companies were then aggregated, for example to estimate the total amount of a specific antimicrobial used in feed during a given year.

Collaborators at the Center for Epidemiology and Animal Health within USDA:APHIS (USDA:APHIS:VS:CEAH, referred to as CEAH for the remainder of the report) played the primary role of auditing the data collection, aggregation and analysis processes in this project. Over a period of two years, collaborators at CEAH reviewed all stages of this effort, including survey design, estimating representativeness of data to the industry as a whole, data validation protocols, data aggregation and metrics for data reporting. During in-person visits with CEAH collaborators, randomly selected de-identified raw data files were reviewed and data validation methods applied. Steps to aggregate the individual company records into an industrywide database were reviewed during these meetings.

Data in this document are reported in several ways. For the hatchery antimicrobials, the data are reported as total kilograms of each antimicrobial used per year as well as total grams of each antimicrobial class used per year per 100,000 birds placed during that year. For antimicrobials used in feed or water, data are reported as total kilograms of each antimicrobial used per year as well as total grams of each antimicrobial used per year per 1,000,000 pounds liveweight slaughtered during that year. Within each section, antimicrobials are labeled as to whether they are considered medically important (MI) or not medically important (NMI) as per Appendix A of FDA GFI #152 (3), as shown in Tables 1-4 above.

The weights of antimicrobials that are presented in this report will not be summed across antimicrobial classes or across routes of administration. This is an inappropriate and inaccurate attempt to simplify data reporting. If antimicrobial use data are to be helpful for improving stewardship efforts, they need to be assessed by drug class for specific diseases and not assessed as an aggregate across all drug classes for all diseases. This data aggregation does not enhance the ability to compare usage estimates across countries or regions, although this has been performed in various reports that exist nationally and internationally (4, 5, 6). When weights of different antimicrobial classes and routes of administration are summed into a single number, an implicit assumption is made that these antimicrobials have identical molecular weights/potencies, pharmacokinetic/pharmacodynamics (PK/PD) properties, and are used for specific diseases at the same dosages.

No comparison of the data in this report will be made to the sales data presented in the FDA Sales and Distribution Report from 2017 (6). [1] On page 6 of the FDA report, it states specifically:

> Regarding the collection and reporting of species-specific data, the percentages provided by the sponsors are estimates of product sales and distribution. The data is not intended to be a substitute for actual usage data and should be used in conjunction with on-farm species-specific data on antimicrobial use. Also, there are a variety of factors that confound direct comparison of species-specific sales estimates, including differences in population size, weight, lifespan, and drug metabolism. (6, p. 6)

To purportedly enable comparability of datasets, some reports incorporate a species-specific population correction unit (PCU) as a denominator for the usage data. The PCU calculation that is commonly employed is derived from European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) reports (4, 5). The PCU is intended to normalize antimicrobial usage amounts across species by providing a standard weight at treatment for different species: 1kg for broiler chickens and 6.5 kg for turkeys (4, 5). If granular data were available that had specific age/weight information for every antimicrobial administration, this adjustment might not be necessary. As will be seen in this report, the diseases affecting broilers and turkeys rarely occur at the standard weight described by ESVAC, and furthermore, not all antimicrobials are used for all diseases, implying that certain antimicrobials will be used more frequently at certain ages and weights. Finally, different regions of the world experience different disease patterns in their animal populations, and thus it is unlikely that a single standard weight of when the antimicrobial therapy is likely to occur would allow comparability of antimicrobial data across countries and regions. This report will provide some preliminary distributions for age of disease onset for broilers and turkeys, and also show the drugs that are most commonly used for these diseases. To minimize bias, no PCU or other assumption about timing of treatment will be applied in this report. Future reports will be based on more granular antimicrobial use data that will enable more precise estimations of antimicrobial therapy metrics.

Below are two turkey disease examples that help demonstrate the potential biases of aggregating all antimicrobial weights into a single total and of using a denominator such as a PCU. Further, the examples demonstrate the problems associated with setting antimicrobial reduction targets as an indicator of good antimicrobial stewardship.

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[1] On 18 December 2018, CVM posted its 2017 Summary Report On Antimicrobials Sold or Distributed for Use in Food-Producing Animals. https://www.fda.gov/media/119332/download
This document is referred to as CVM’s 2017 Sales and Distribution Report in this document.

Example 1: Gangrenous Dermatitis

Gangrenous dermatitis is a clostridial disease of broiler chickens and turkeys and typically occurs later in the production lifespan of the bird (see Primary Disease Challenge sections for broilers and turkeys). In this example, it is assumed that the affected turkey flock consists of 17-week-old hens with an average weight of 20 pounds (9.09 kg). The hypothetical affected flock has 12,500 birds and will receive a water-soluble antimicrobial over a 7-day course of therapy. The two most commonly used antimicrobials for this disease are penicillin and lincomycin.

| | Penicillin | Lincomycin |
|---|---|---|
| **Number of packs of drug** | 60 packs | 25 packs |
| **Active drug per pack** | 1 billion IU / pack | 192 g / pack |
| **Total IU** | 60,000,000,000 IU | N/A |
| **Total active drug (g)** | ~ 37,616 g * | 4,800 g |
| | | |
| **Active drug per bird** | 3,010 mg / bird | 384 mg / bird |
| **Active drug per kg body weight (BW)** | 331.1 mg / kg BW | 42.2 mg / kg BW |
| **Active drug per kg per day** | 47.3 mg / kg BW / day | 6.03 mg / kg BW / day |
| **Animal-Days of therapy** | 87,500 | 87,500 |
| **Therapeutic regimens** | 12,500 | 12,500 |

*1,595,066 IU / g

As can be seen in this example, the same number of birds (12,500) are receiving the same regimens with either antimicrobial, and each drug has the same total number of animal-days of therapy (87,500). However, due to regimen differences based on drug molecular weight/potency and PK/PD properties, the amount of each drug used is vastly different. The amount of penicillin used, on a total gram of active drug administered, is almost 8 times higher than for lincomycin.

Example 2: Colibacillosis

Colibacillosis is comprised of many different diseases caused by *E. coli*. These diseases can occur in all phases of the production lifespan, but often occur in younger birds (see Primary Disease Challenge sections). In this example, it is assumed that the affected turkey flock consists of 8-week-old toms with an average weight of 7 pounds (3.18 kg). The affected flock has 25,000 birds and will receive a water-soluble antimicrobial over a 5-day course of therapy. Two of the most commonly used antimicrobials for this disease are sulfadimethoxine and tetracycline.

| | Sulfadimethoxine | Tetracycline |
|---|---|---|
| **Number of packs of drug** | 25 packs | 31 packs |
| **Active drug per pack** | 480 g / pack (gallon) | 1,400 g / pack |
| **Total active drug (g)** | 12,000 g | 43,400 g |
| | | |
| **Active drug per bird** | 480 mg / bird | 1,736 mg / bird |
| **Active drug per kg body weight (BW)** | 150.9 mg / kg BW | 545.9 mg / kg BW |
| **Active drug per kg per day** | 30.2 mg / kg BW / day | 109.2 mg / kg BW / day |
| **Animal-Days of therapy** | 125,000 | 125,000 |
| **Therapeutic regimens** | 25,000 | 25,000 |

As can be seen in this example, the same number of birds (25,000) are receiving the same regimens with either antimicrobial, and each drug has the same total number of animal-days of therapy (125,000). However, due to regimen differences based on drug molecular weight/potency and PK/PD properties, the amount of each drug used is vastly different. The amount of tetracycline used, on a total gram of active drug administered, is almost 4 times higher than for sulfadimethoxine.

Summary

It should be clear from these examples that there are multiple antimicrobials that can be used for the same disease indication within a flock, but these antimicrobials have very different properties resulting in vastly different amounts of active ingredient being used for therapy of the exact same condition. The ages at which these diseases manifest are vastly different, demonstrating the bias of incorporating a standard PCU. Finally, if reduction targets were set, the veterinarian could switch to the antimicrobial that has fewer total grams of active ingredient, which is not consistent with the practice of good antimicrobial stewardship, as the relationship between weight of different antimicrobials and resistance selection is unknown. Data in this report will not be aggregated across antimicrobial classes or across routes of administration; instead data will be reported separately for each antimicrobial class by route of administration.

## Data Collection

The data collected from the broiler and turkey industries were aggregated into calendar year totals. Some companies had fiscal year rather than calendar year data. In those instances, calendar year totals were estimated from multiple fiscal year reports. Also, antimicrobial use data were based on the calendar year during which the antimicrobials were used. However, some flocks that were placed at the end of a calendar year might not have been slaughtered (settled) until the following calendar year; consequently, the production data for these flocks would not necessarily be tallied in the same calendar year as their antimicrobial use data. Over time, all production data and antimicrobial use data are accounted for, but there can be some year-to-year mismatch. This is an issue that continues to be addressed.

The data were provided by the participating companies in a variety of formats, thereby making a single, standardized approach to data collection practically impossible.

Some of the data were submitted as detailed flock-level records. The frequency of these flock-level record submissions increased greatly in 2017, likely due to the veterinary supervision associated with implementation of GFI #213. For each antimicrobial administered to a flock, the record typically included: number of animals, disease indication, age, estimated weight, antimicrobial, total amount of antimicrobial administered, and duration of administration. These flock-level records, if available, were mainly for the water-soluble antimicrobials.

Another data type that was submitted, especially for the earlier years of the data collection interval, was the total amount of each antimicrobial drug that was used during the calendar year. These data were sometimes stratified by disease indication for each antimicrobial, but there were times when the antimicrobial administrations had to be partitioned into the diseases for which antimicrobials would have been administered during the year. This step was normally performed by a practicing veterinarian within the company. When this approach was needed, the veterinarian could usually describe the most common dose and duration of therapy as well as the typical age when this therapy would have been administered. Because the veterinarian was estimating the percentage of the total antimicrobial administration that would have been used for specific diseases, these estimates are subject to recall bias. In other words, the total amount of each antimicrobial class used during a given year would not be biased, but the partitioning of this total into specific indications for use will likely have error. This is a challenge with the retrospective data that were targeted in the first phase of this data collection effort. Because of the better record-keeping within the companies over time, especially beginning in 2017 with implementation of GFI #213, improved granularity of the data and accuracy of the usage estimates is expected in subsequent reports, the next which will focus on 2017 and 2018 annual antimicrobial usage.

For the antimicrobials administered in feed, some companies produced data from the feed mills regarding the total amount of feed produced during each year, including amount of feed for each ration formulation (starter, grower, finisher and withdrawal). The veterinarian would reference the antimicrobial program used by the company to estimate the total amounts of each antimicrobial administered in the feed during each time period.

Companies were asked to query their past accounting/purchase records for all antimicrobial purchases during each calendar year. In theory this database query represented the maximum amount of antimicrobial that the company could have used during the year. Most companies that submitted these types of data were also able to submit detailed flock therapy records for a short period of time. These flock-level datasets could then be used to validate the purchase records and also to partition the antimicrobial amounts to specific diseases, doses, and number of birds receiving therapy. For companies lacking other data types, the data from the purchase records were used as the antimicrobial estimates for that company, again being partitioned into the diseases for which the antimicrobial would have been used.

Finally, for the injectable (hatchery) and water-soluble antimicrobial data, some companies submitted the number of birds receiving therapy with each antimicrobial for different diseases; amount of antimicrobial administered was not provided. Occasionally the age of the flock at the time of administration was also unavailable. In these instances, a water consumption table (for example, Table 5 below for broilers) was used to determine the amount of antimicrobial that would have been administered, using the age of bird, antimicrobial dose administered, and duration of administration.

To illustrate this calculation, consider an example of 100,000 broilers that will receive therapy with lincomycin for necrotic enteritis. This is a commonly used antimicrobial for necrotic enteritis, as will be seen later in this report. In this example, the birds are 26 days of age and will receive therapy for 5 days. Lincomycin comes in 80g packs which contain 32g of active ingredient. When mixed according to label, the final concentration will be 64 mg/gallon. Based on the water table, the birds will drink an estimated 299.2 gallons of water per 1,000 birds over the 5 days. The total amount of lincomycin estimated to be administered in the water over the 5-day course of therapy is:

100,000 birds x 299.2 gallons/1,000 birds x 0.64 g lincomycin/gallon = 1,914.8 grams.

Table 5. Estimated water consumption table for broiler chickens. Table supplied by one of the participating companies.

| Bird Age (days) | Gallons per 1,000 Birds | Liters per 1,000 Birds | Bird Age (days) | Gallons per 1,000 Birds | Liters per 1,000 Birds |
|---|---|---|---|---|---|
| 1 | 3.0 | 11.4 | 31 | 66.1 | 250.2 |
| 2 | 5.6 | 21.2 | 32 | 67.9 | 257.0 |
| 3 | 7.9 | 29.9 | 33 | 69.7 | 263.8 |
| 4 | 11.3 | 42.8 | 34 | 71.4 | 270.2 |
| 5 | 12.9 | 48.8 | 35 | 73.0 | 276.3 |
| 6 | 14.2 | 53.7 | 36 | 74.6 | 282.4 |
| 7 | 15.3 | 57.9 | 37 | 76.1 | 288.0 |
| 8 | 16.8 | 63.6 | 38 | 77.6 | 293.7 |
| 9 | 18.4 | 69.6 | 39 | 79.0 | 299.0 |
| 10 | 19.8 | 74.9 | 40 | 80.4 | 304.3 |
| 11 | 21.2 | 80.2 | 41 | 81.7 | 309.2 |
| 12 | 22.9 | 86.7 | 42 | 83.0 | 314.2 |
| 13 | 24.8 | 93.9 | 43 | 84.4 | 319.5 |
| 14 | 26.9 | 101.8 | 44 | 85.9 | 325.1 |
| 15 | 28.9 | 109.4 | 45 | 87.4 | 330.8 |
| 16 | 30.9 | 117.0 | 46 | 88.8 | 336.1 |
| 17 | 33.1 | 125.3 | 47 | 90.2 | 341.4 |
| 18 | 35.4 | 134.0 | 48 | 91.5 | 346.3 |
| 19 | 38.0 | 143.8 | 49 | 92.8 | 351.2 |
| 20 | 40.4 | 152.9 | 50 | 94.0 | 355.8 |
| 21 | 42.8 | 162.0 | 51 | 95.2 | 360.3 |
| 22 | 45.3 | 171.5 | 52 | 96.3 | 364.5 |
| 23 | 47.9 | 181.3 | 53 | 97.3 | 368.3 |
| 24 | 50.4 | 190.8 | 54 | 98.2 | 371.7 |
| 25 | 52.6 | 199.1 | 55 | 99.0 | 374.7 |
| 26 | 55.0 | 208.2 | 56 | 99.7 | 377.4 |
| 27 | 57.5 | 217.6 | 57 | 100.9 | 381.9 |
| 28 | 60.2 | 227.9 | 58 | 102.1 | 386.4 |
| 29 | 62.3 | 235.8 | 59 | 103.3 | 390.8 |
| 30 | 64.2 | 243.0 | 60 | 104.4 | 395.2 |

# Broiler Industry

## Representativeness

The goal of the broiler chicken aspect of this project was to collect on-farm antimicrobial use data from the companies that produce the majority of the domestic supply of chicken meat in the U.S. To estimate the industry representativeness of the data that are being collected in this effort, a list published by WATT Poultry USA that contains the major broiler chicken companies in the U.S. and their annual production data (http://www.wattpoultryusa-digital.com/201811/) was used. This WATT list includes the size of each company based on the total number of birds slaughtered and the total pounds liveweight produced per week for each company. These annual totals for each year of the data collection period (2013-2017) were used as the denominator for the calculation of national representativeness of the data; the sum of the production totals for the companies that were enrolled in the project and that submitted data served as the numerator for the industry representativeness calculation.

Not all companies were able to submit data for each year of the 5-year data collection period. In addition, not all companies were able to submit all data types for each year. Consequently, industry representativeness for each data type (hatchery, ionophore, in-feed, and water-soluble) was estimated for each year of the data collection interval. These estimates of industry representativeness are presented in tables at the beginning of each section.

Table 6 below shows the WATT list for broiler chicken production in 2016. Similar data exist for each year of the data collection effort (2013-2017). The industry representativeness of the dataset was calculated for each year of the collection period using the corresponding WATT list for each year. The representativeness estimates in this report are presented as a range. This range helps mask the exact companies that participated in this data collection effort. The width of the industry representativeness interval was set at 5% around the actual estimate, with the range not necessarily being centered around the actual estimate; a random interval of 5% width was generated for each section of this report. If two years had the same estimated representativeness, an identical range was used for each of these years.

It is important to note that this calculation is only used to estimate representativeness; the actual number of birds placed, birds slaughtered and pounds liveweight produced that are included in the report results are based on data submitted by the participating companies.

Table 6. Weekly production numbers for the major U.S. broiler companies for 2016, published by WATT Poultry USA (http://www.wattpoultryusa-digital.com/201703/index.php#/18).

| Rank | Company | 2016 | |
|---|---|---|---|
| | | **Million head/week** | **Million lbs liveweight/week** |
| **1** | **Tyson Foods** | 35.0 | 202.3 |
| **2** | **Pilgrim's** | 28.6 | 165.1 |
| **3** | **Sanderson Farms Inc.** | 9.8 | 79.2 |
| **4** | **Perdue Foods** | 13.0 | 78.0 |
| **5** | **Koch Foods Inc.** | 12.0 | 63.6 |
| **6** | **Wayne Farms LLC** | 6.8 | 52.1 |
| **7** | **Mountaire Farms LLC** | 6.5 | 52.7 |
| **8** | **House of Raeford Farms Inc.** | 3.5 | 31.5 |
| **9** | **Peco Foods** | 4.3 | 37.2 |
| **10** | **Keystone Foods LLC** | 3.6 | 27.0 |
| **11** | **Foster Farms** | 5.6 | 33.5 |
| **12** | **George's Inc.** | 5.3 | 25.3 |
| **13** | **Amick Farms Inc.** | 2.7 | 24.6 |
| **14** | **Case Foods Inc.** | 2.9 | 22.0 |
| **15** | **Fieldale Farms** | 3.1 | 20.0 |
| **16** | **MarJac Holdings** | 4.6 | 19.4 |
| **17** | **O.K. Industries** | 3.0 | 17.0 |
| **18** | **Simmons Foods Inc.** | 3.9 | 18.9 |
| **19** | **GNP Company** | 1.9 | 9.9 |
| **20** | **Claxton Poultry Farms** | 2.2 | 10.5 |
| **21** | **Allen Harim Foods** | 1.7 | 10.5 |
| **22** | **Harrison Poultry Inc.** | 0.9 | 6.0 |
| **23** | **Golden-Rod Broilers Inc.** | 1.1 | 4.5 |
| **24** | **Farmers Pride Inc.** | 1.0 | 5.5 |
| **25** | **OMP Foods/Ozark Mountain Poultry** | 1.3 | 7.8 |
| **26** | **MBA Poultry LLC (Tecumseh Poultry)** | 0.6 | 3.4 |
| **27** | **Holmes Foods** | 0.8 | 3.1 |
| **28** | **Gerber's Poultry** | 0.5 | 2.2 |
| **29** | **Gentry Poultry Co. Inc.** | 0.3 | 1.1 |
| **30** | **Hain Pure Protein Corp.** | 0.4 | 2.3 |
| **31** | **Miller Poultry** | 0.3 | 1.7 |
| **32** | **Empire Kosher Poultry Inc.** | 0.3 | 1.6 |
| **33** | **Murray's Chickens** | 0.3 | 1.3 |
| **34** | **Agri Star Meat & Poultry LLC** | 0.1 | 0.4 |
| | | | |
| | TOTAL | **167.6**[A] | **1,041.2** [B] |

[A] The companies in this list represent 167.6 million birds slaughtered per week * 52 weeks ≈ 8,715,200,000 birds slaughtered annually in the U.S.

[B] The companies in this list represent 1,041.2 million pounds liveweight per week * 52 weeks ≈ 54,142,400,000 pounds liveweight annually in the U.S.

## Primary Disease Challenges – Broiler

This section details some of the main diseases of broiler chickens that result in therapeutic antimicrobial drug use (prevention, control or treatment of disease).

### Necrotic Enteritis

According to Diseases of Poultry:

> Clinical Necrotic Enteritis (NE) can be defined as a disease of primarily young chickens, caused by infection with, and toxin production by, *Clostridium perfringens* type A and type C. The clinical infection is characterized by sudden onset, high mortality, and necrosis of the mucous membrane of the small intestine. The disease is also known as clostridial enteritis, enterotoxemia, and rot gut. … The source of NE-producing strains of *C. perfringens* is, ultimately, the chickens themselves. Small numbers of NE strains may be resident, permanently or transiently, in the gut of normal chickens. Chicks may acquire these strains from hatching and growing environments. Additional birds may then become colonized, with contamination of the litter increasing exponentially. Given proper conditions in the intestines of other birds, outbreaks of NE could occur, further increasing the availability of NE strains. NE is sometimes exacerbated by co-infection with coccidia. *Clostridium perfringens* numbers are several logs higher in birds with acute coccidiosis than in normal birds (7).

According to reports of the broiler industry presented at the annual meetings of the United States Animal Health Association, necrotic enteritis ranked second of the disease-related issues that broiler production veterinarians faced in 2016 and 2017 (8, 9). Antimicrobials are used therapeutically for necrotic enteritis.

### Colibacillosis

According to Diseases of Poultry:

> Colibacillosis refers to any localized or systemic infection caused entirely or partly by avian pathogenic *Escherichia coli* (APEC), including colisepticemia, hemorrhagic septicemia, coligranuloma (Hjarre's disease), air sac disease (chronic respiratory disease, CRD), swollen-head syndrome, venereal colibacillosis, coliform cellulitis (inflammatory or infectious process, IP), peritonitis, salpingitis, orchitis, osteomyelitis/ synovitis (including turkey osteomyelitis complex), panophthalmitis, omphalitis/yolk sac infection, and enteritis. Colibacillosis in mammals is most often a primary enteric or urinary tract disease, whereas colibacillosis in poultry is typically a localized or systemic disease occurring secondarily when host defenses have been impaired or overwhelmed by virulent *E. coli* strains (10).

Antimicrobials are used in the hatchery to prevent disease associated with *E. coli*, such as omphalitis (yolk sac infection) and to decrease mortality in the first week of life. Antimicrobials are used therapeutically for diseases associated with *E. coli*.

### Gangrenous Dermatitis

According to Diseases of Poultry:

> Gangrenous dermatitis (GD) is a disease of chickens and turkeys caused by *Clostridium septicum*, *C. perfringens* type A, and *Staphylococcus aureus*. Characterized by a sudden onset of acute mortality, the primary lesion in affected birds is necrosis of the skin and subcutaneous tissue, usually involving the breast, abdomen, wing, or thigh. Because the mortality associated with the disease occurs quickly and the disease generally appears in close-to-market-age broilers and turkeys, economic losses are associated with any lost investment in production costs (chick/poult cost and feed consumed) and the loss of income related to the reduction in marketable pounds. … Clostridia are ubiquitous in the poultry house environment and can be isolated from soil, feces, dust, contaminated litter or feed, and intestinal contents. Staphylococci are also ubiquitous and common inhabitants of skin and mucous membranes of poultry and areas where poultry are hatched, reared, and processed. Despite the ubiquitous nature of Clostridia and Staphylococci, the presence of these organisms does not necessarily indicate a disease challenge. Other contributing factors … are thought to play a major role in the development of clinical disease within a flock (11).

Although GD is not listed in the top disease-related issues that broiler production veterinarians faced in 2016 and 2017 (8, 9), antimicrobials are used therapeutically in clinically-affected flocks.

### Kinky Back (Enterococcal Spondylitis)

Kinky back, more correctly termed enterococcal spondylitis, is an important cause of lameness and mortality in some broiler companies. The condition has also been referred to as vertebral osteoarthritis (VOA). The condition is caused by localized infection of the vertebrae by *Enterococcus cecorum* and subsequent partial paralysis of the posterior extremities of affected birds. It can be seen in both broilers and broiler breeders. The pathogenesis and epidemiology of this disease are poorly understood. It appears only rarely in some companies but causes significant problems in other companies, requiring antimicrobial therapy for the disease and to relieve suffering.

### Coccidiosis

According to Diseases of Poultry:

> Coccidiosis is a disease of universal importance in poultry production. The protozoan parasites of the genus *Eimeria* multiply in the intestinal tract and cause tissue damage, with resulting interruption of feeding and digestive processes or nutrient absorption, dehydration, blood loss, loss of skin pigmentation and increased susceptibility to other disease agents. … Like many parasitic diseases, coccidiosis is largely a disease of young animals because immunity quickly develops after exposure and gives protection against later disease outbreaks. Unfortunately, no cross immunity exists between species of *Eimeria* in birds, and later outbreaks may be the result of different species. … The tissue damage and

> changes in intestinal tract function may allow colonization by various harmful bacteria, such as *Clostridium perfringens*, leading to Necrotic Enteritis or *Salmonella typhimurium*. Cecal coccidiosis (*E. tenella*) may contribute to increased severity of the blackhead organism (*Histomonas meleagridis*) in chickens (12).

According to reports of the broiler industry presented at the annual meetings of the United States Animal Health Association, coccidiosis (specifically *E. maxima*) ranked first of the disease-related issues that broiler production veterinarians faced in 2016 and 2017 (8, 9). FDA categorizes ionophores as not medically important antimicrobials. They are considered coccidiostats and are used to reduce the infectious burden and subsequent morbidity and mortality linked to coccidiosis and secondary bacterial infections. Other non-antimicrobial therapeutic options include chemical coccidiostats, which are not included in this report.

## Hatchery Antimicrobials – Broiler

Hatchery antimicrobials are presented in their own section because they are the only injectable antimicrobials used in substantial amounts in broiler production.

The data presented in this Hatchery section represent 80-93% of annual U.S. broiler production by companies on the WATT Poultry USA list; representativeness ranges from 80-85% in 2013 to 88-93% in 2017. This estimate of representativeness is based on total pounds liveweight produced annually by companies that submitted hatchery data. The numbers are derived from the annual WATT Poultry USA lists, as described in the Broiler Representativeness section.

Table 7. Broiler hatchery antimicrobial data representativeness, shown as a range for each year of data in the report.

| | 2013 | 2014 | 2015 | 2016 | 2017 |
|---|---|---|---|---|---|
| **Based on Pounds Liveweight** | | | | | |
| Range of Representativeness | | | | | |
| Lower | 80% | 80% | 85% | 88% | 88% |
| Upper | 85% | 85% | 90% | 93% | 93% |

The data collected for this project begin in 2013, one year after the extra-label prohibition on the use of cephalosporins was implemented (13). In the broiler chicken industry, hatchery antimicrobials are generally given *in ovo* rather than subcutaneously to the day-old chick because of the number of birds hatching on a daily basis. The label for ceftiofur sodium states that it is indicated for the control of early mortality associated with *E. coli* organisms susceptible to ceftiofur in day-old chicks. Administration is via subcutaneous injection in the neck region of day-old chicks at the dosage of 0.08 to 0.20 mg ceftiofur/chick. During the 2013-2017 interval, no ceftiofur use was reported.

The main antimicrobial used in the hatchery was gentamicin given *in ovo*, which is also an extra-label administration. The label of gentamicin sulfate for use in broiler chickens states that it is recommended for the prevention of early mortality in day-old chickens associated with *Escherichia coli*, *Salmonella* Typhimurium and *Pseudomonas aeruginosa* susceptible to gentamicin sulfate. The dose that was given to the broilers ranged from 0.1 to 0.2 mg per egg.

Finally, there was some use of penicillin between 2013 and 2016. There was no reported use of penicillin in the hatchery in 2017. The dose that was given to broilers was typically 2,500 IU per egg.

Summary: Data are based on the annual placement of between 6,900,000,000 and 7,900,000,000 birds, depending on the year. There was no reported ceftiofur use during the 2013-2017 period. When using the metric of total grams of drug per 100,000 birds placed, hatchery use of gentamicin decreased approximately 74% between 2013 and 2017. Hatchery use of penicillin dropped to 0 in 2017. The percentage of broiler chicks placed that received hatchery antimicrobials decreased from approximately 93% in 2013 to 17% in 2017.

**Medically Important Antimicrobials**

Figure 1. Gentamicin use in broiler hatcheries, 2013-2017. Total kilograms of gentamicin are shown by the bars (left Y-axis) and total grams/100,000 birds placed are shown by the line (right Y-axis).

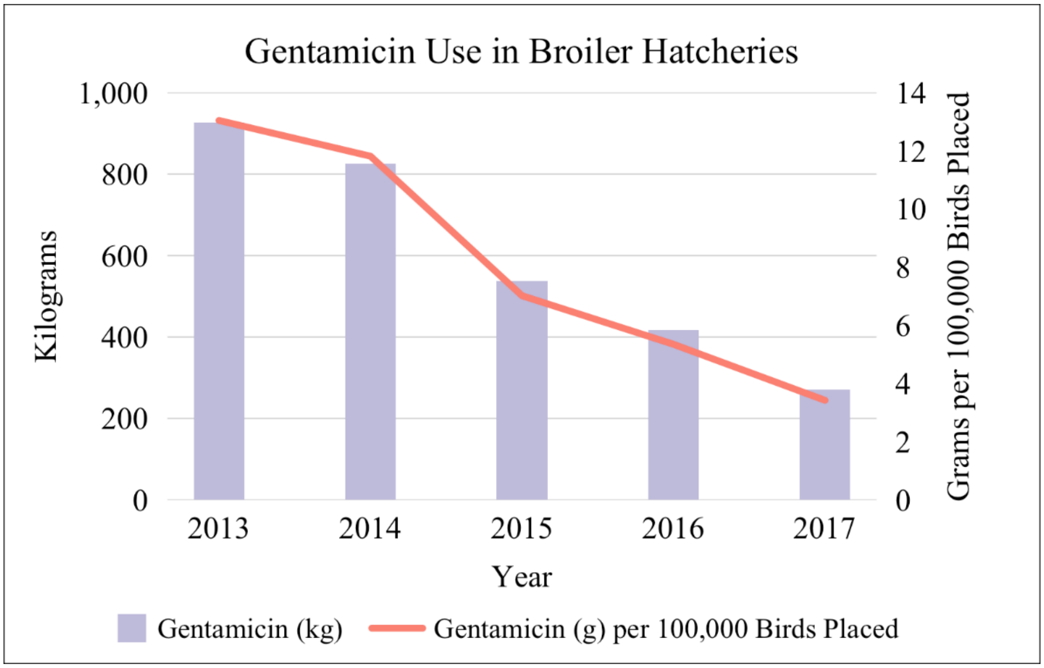



Figure 2. Penicillin use in broiler hatcheries, 2013-2017. Total kilograms of penicillin are shown by the bars (left Y-axis) and total grams/100,000 birds placed are shown by the line (right Y-axis).

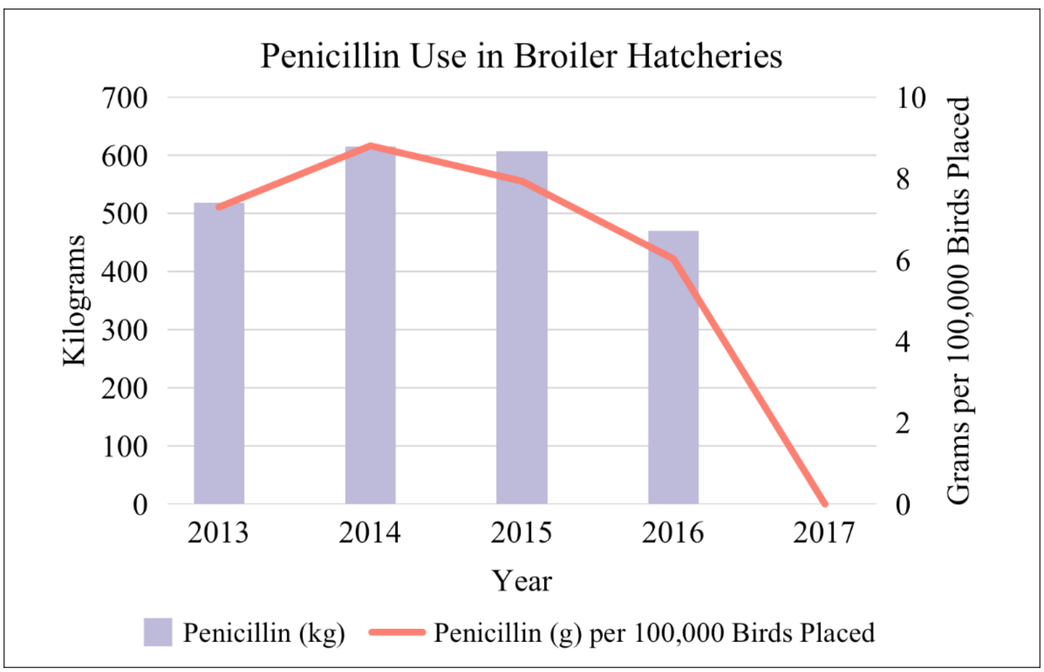
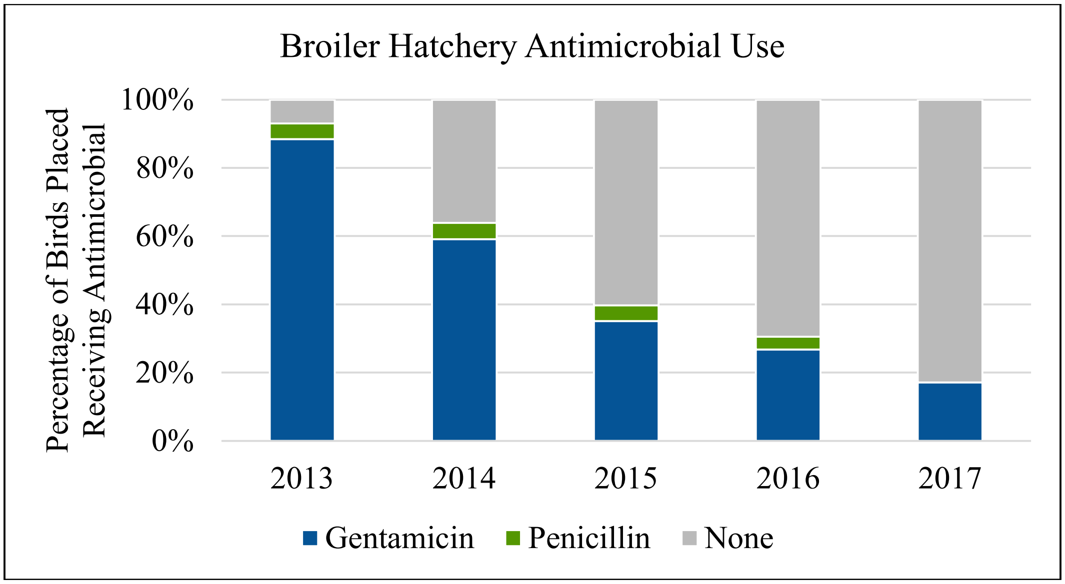


Figure 3. Broiler hatchery antimicrobial use during the years 2013-2017, as a percentage of total birds placed. The graphs show the percentage of birds placed that received gentamicin, penicillin or no antimicrobial.



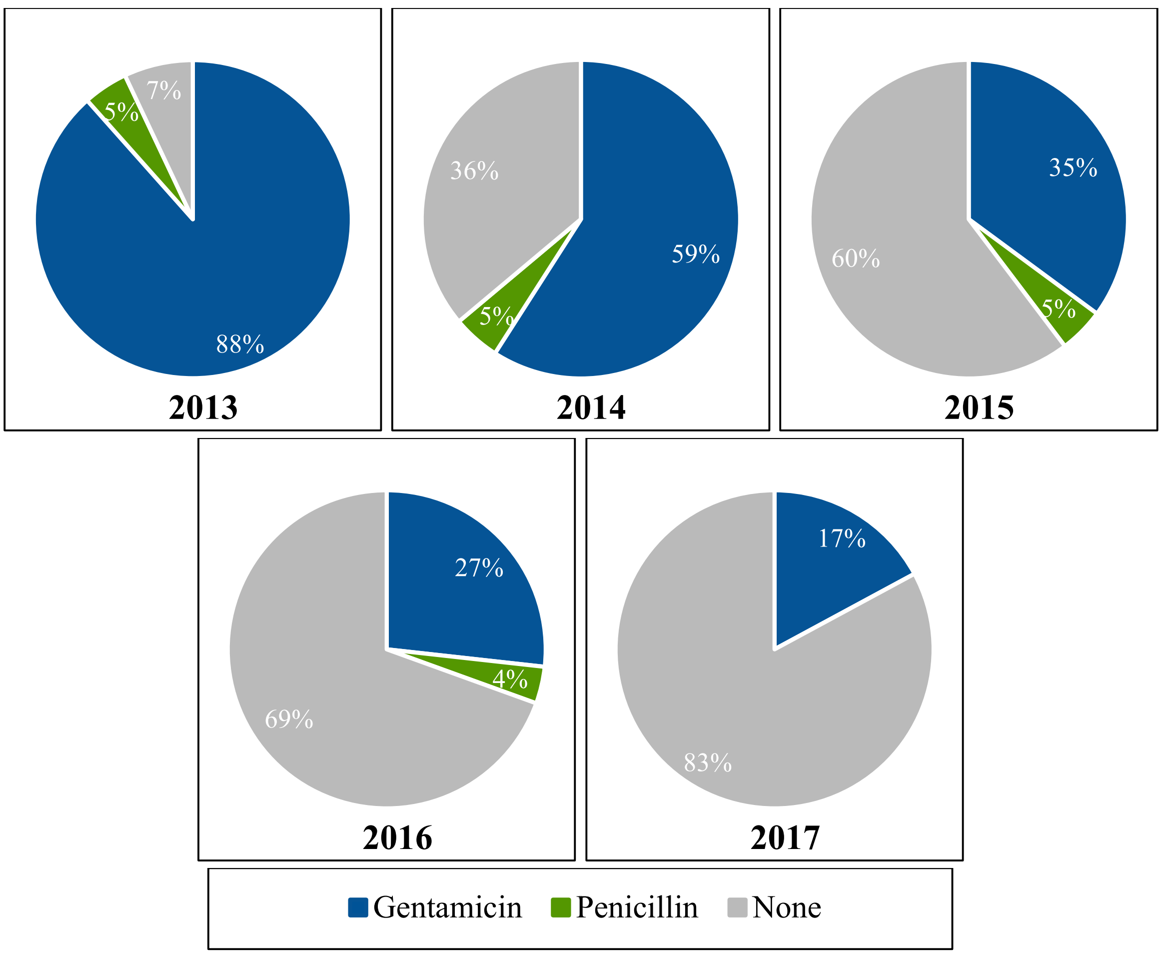



Table 8. Amount of injectable antimicrobial drug use in broiler hatcheries, 2013-2017. Data are reported by active ingredients within drug classes; all hatchery antimicrobials are medically important. Weights are reported as total kg of antimicrobial.

| | | Antimicrobial Usage in Broiler Hatcheries (kg of antimicrobial) | | | | |
|---|---|---|---|---|---|---|
| **Drug Class** | **Active Ingredient** | **2013** | **2014** | **2015** | **2016** | **2017** |
| **Medically Important** | | | | | | |
| Aminoglycosides | Gentamicin | 926.0 | 825.8 | 537.2 | 417.3 | 270.5 |
| Natural Penicillins | Penicillin G | 518.0 | 615.3 | 607.0 | 469.8 | - |

Table 9. Amount of injectable antimicrobial drug use in broiler hatcheries, 2013-2017. Data are reported by active ingredients within drug classes; all hatchery antimicrobials are medically important. Weights are reported as total g of antimicrobial per 100,000 birds placed.

| | | Antimicrobial Usage in Broiler Hatcheries (g of antimicrobial per 100,000 birds placed) | | | | |
|---|---|---|---|---|---|---|
| **Drug Class** | **Active Ingredient** | **2013** | **2014** | **2015** | **2016** | **2017** |
| **Medically Important** | | | | | | |
| Aminoglycosides | Gentamicin | 13.0 | 11.8 | 7.0 | 5.4 | 3.4 |
| Natural Penicillins | Penicillin G | 7.3 | 8.8 | 7.9 | 6.0 | - |

## Ionophores – Broilers

**Ionophores are Not Medically Important Antimicrobials.** Ionophores are in-feed antimicrobials but are presented in their own section because their principal use is to prevent disease associated with coccidial parasites.

The data presented in this Ionophore section represent 80-93% of annual U.S. broiler production by companies on the WATT Poultry USA list; representativeness ranges from 80-85% in 2013 to 88-93% in 2017. This estimate of representativeness is based on total pounds liveweight produced annually by companies that submitted ionophore data. The numbers are derived from the annual WATT Poultry USA lists, as described in the Broiler Representativeness section.

Table 10. Broiler ionophore data representativeness, shown as a range for each year of data in the report.

| | 2013 | 2014 | 2015 | 2016 | 2017 |
|---|---|---|---|---|---|
| **Based on Pounds Liveweight** | | | | | |
| Range of Representativeness | | | | | |
| Lower | 80% | 80% | 85% | 88% | 88% |
| Upper | 85% | 85% | 90% | 93% | 93% |

The data in this Ionophore section include the four ionophores currently being used in the broiler industry: lasalocid, narasin, monensin, and salinomycin. As described in the Primary Disease Challenges section, coccidiosis is an important disease in broiler chicken production. It can cause clinical illness in the birds and can also predispose the birds for other disease conditions that necessitate antimicrobial therapy. Ionophores are considered antimicrobial drugs by the U.S. FDA (although are not considered antimicrobials in most other countries).

The FDA Annual Sales Report of 2017 states: "Ionophores … lack utility in human medicine and their use in animals, primarily as coccidiostats, does not pose cross resistance concerns; thus, they do not have the same public health risks as medically important antimicrobials." (6).

Summary: Data are based on the annual slaughter of between 6,700,000,000 and 7,500,000,000 birds, depending on the year. When using the metric of total grams of drug per 1,000,000 pounds liveweight produced, there was an approximate 42% reduction of lasalocid use, 7% reduction of monensin use, 46% reduction of narasin use, and 31% reduction of salinomycin use between 2013 and 2017. These reductions were not consistent among the ionophores. Monensin use increased approximately 11% between 2015 and 2017.

Figure 4. Lasalocid use in broiler feed, 2013-2017. Total kilograms of lasalocid are shown by the bars (left Y-axis) and total grams/1,000,000 pounds liveweight are shown by the line (right Y-axis).

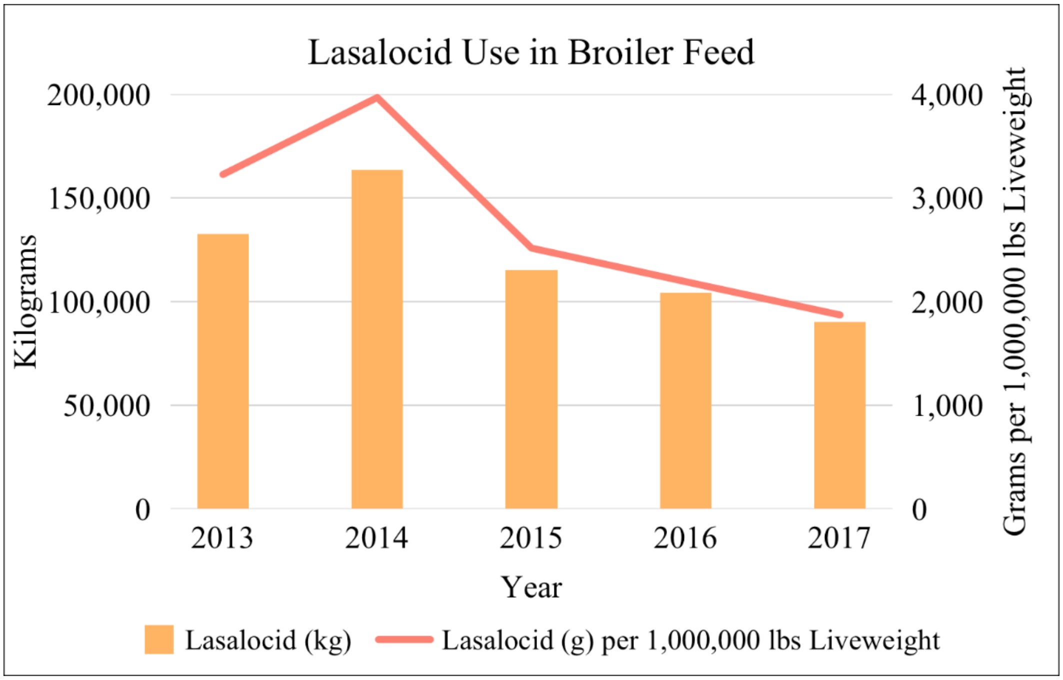



Figure 5. Monensin use in broiler feed, 2013-2017. Total kilograms of monensin are shown by the bars (left Y-axis) and total grams/1,000,000 pounds liveweight are shown by the line (right Y-axis).

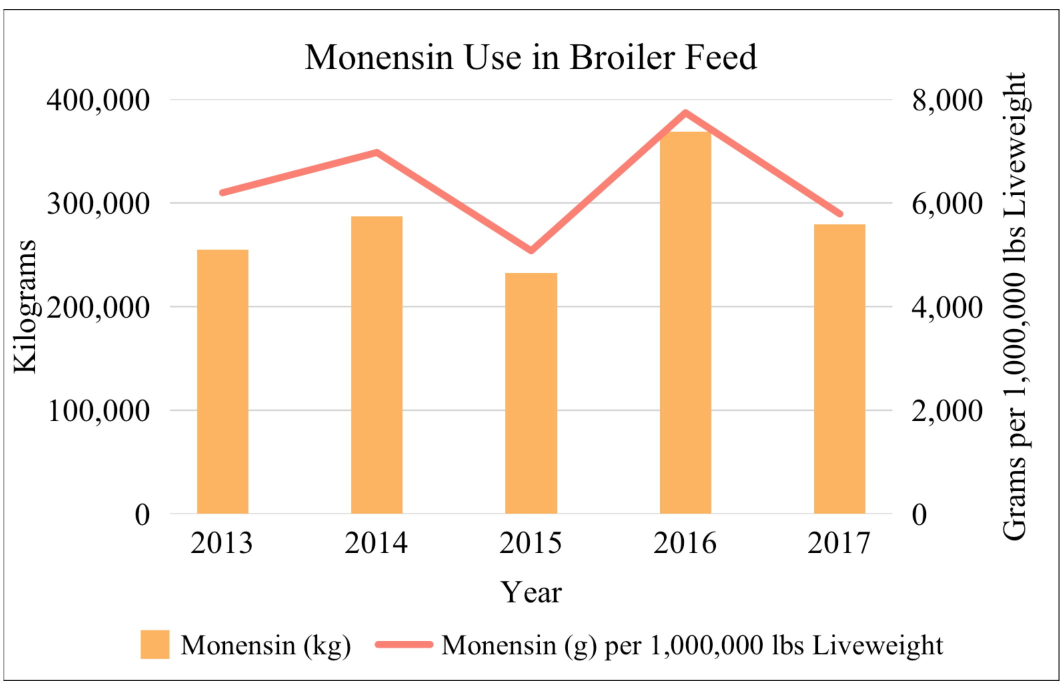


Figure 6. Narasin use in broiler feed, 2013-2017. Total kilograms of narasin are shown by the bars (left Y-axis) and total grams/1,000,000 pounds liveweight are shown by the line (right Y-axis).

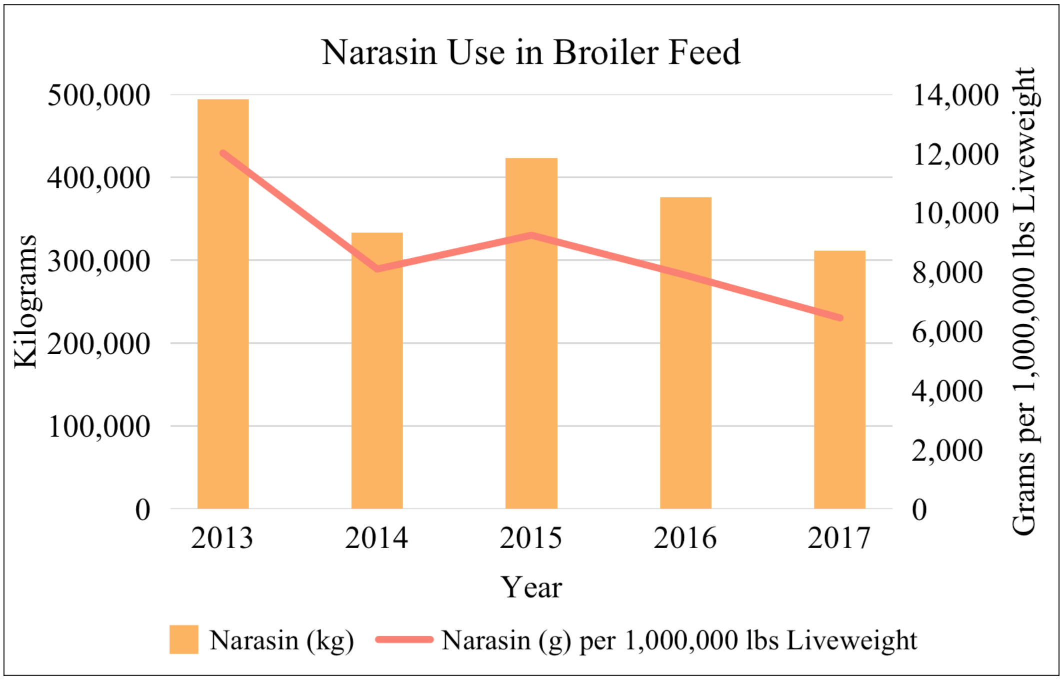



Figure 7. Salinomycin use in broiler feed, 2013-2017. Total kilograms of salinomycin are shown by the bars (left Y-axis) and total grams/1,000,000 pounds liveweight are shown by the line (right Y-axis).

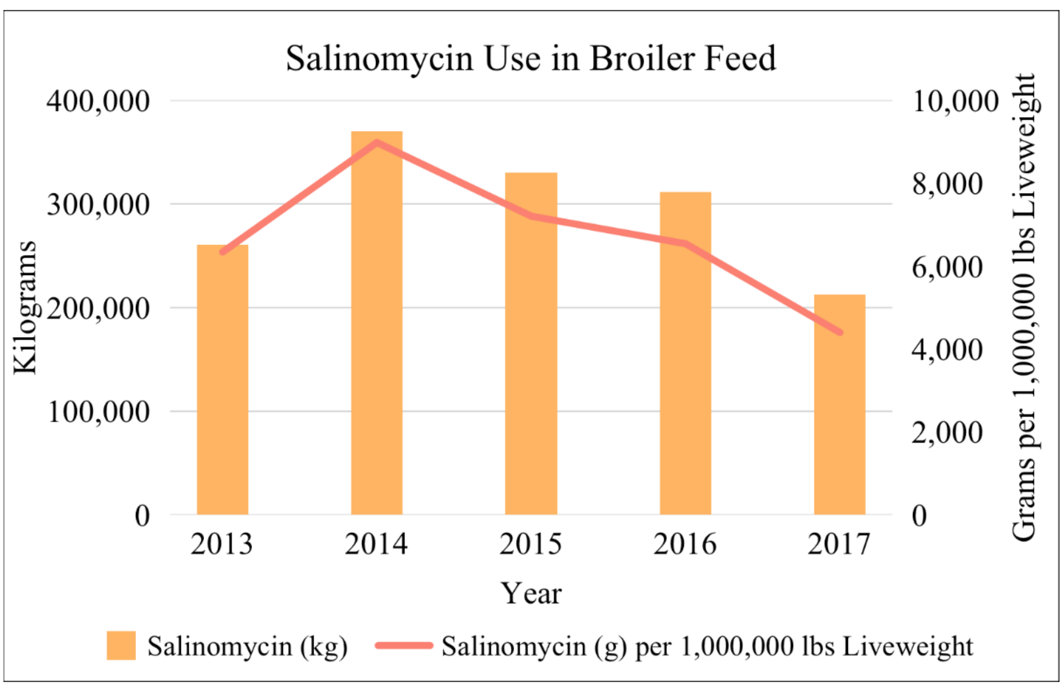


Table 11. Amount of ionophore use in broiler feed, 2013-2017. Data are reported by active ingredient; all ionophores are not medically important. Weights are reported as kg of antimicrobial.

| Drug Class | Active Ingredient | Antimicrobial Usage in Broiler Feed (kg of antimicrobial) 2013 | 2014 | 2015 | 2016 | 2017 |
|---|---|---|---|---|---|---|
| **Not Medically Important** | | | | | | |
| Ionophores | Lasalocid | 132,705.9 | 163,339.5 | 115,276.6 | 104,376.2 | 90,251.2 |
| | Monensin | 254,867.4 | 287,022.1 | 232,578.8 | 368,534.8 | 279,104.1 |
| | Narasin | 494,224.7 | 333,361.0 | 423,374.9 | 375,668.0 | 311,035.5 |
| | Salinomycin | 260,762.6 | 369,700.1 | 330,092.7 | 311,380.7 | 212,249.0 |

Table 12. Amount of ionophore use in broiler feed, 2013-2017. Data are reported by active ingredient; all ionophores are not medically important. Weights are reported as g of antimicrobial per 1,000,000 pounds liveweight produced.

| Drug Class | Active Ingredient | Antimicrobial Usage in Broiler Feed (g of antimicrobial per million lbs liveweight) 2013 | 2014 | 2015 | 2016 | 2017 |
|---|---|---|---|---|---|---|
| **Not Medically Important** | | | | | | |
| Ionophores | Lasalocid | 3,226.2 | 3,968.2 | 2,516.2 | 2,192.2 | 1,871.5 |
| | Monensin | 6,196.1 | 6,973.0 | 5,076.6 | 7,740.3 | 5,787.5 |
| | Narasin | 12,015.1 | 8,098.8 | 9,241.1 | 7,890.1 | 6,449.7 |
| | Salinomycin | 6,339.4 | 8,981.6 | 7,205.0 | 6,539.9 | 4,401.2 |

## In-Feed Antimicrobials – Broilers

The data presented in this In-Feed Antimicrobials section represent 80-93% of annual U.S. broiler production by companies on the WATT Poultry USA list; representativeness ranges from 80-85% in 2013 to 88-93% in 2017. This estimate of representativeness is based on total pounds liveweight produced annually by companies that submitted in-feed data. The numbers are derived from the annual WATT Poultry USA lists, as described in the Broiler Representativeness section.

Table 13. Broiler in-feed antimicrobial data representativeness, shown as a range for each year of data in the report.

| | 2013 | 2014 | 2015 | 2016 | 2017 |
|---|---|---|---|---|---|
| **Based on Pounds Liveweight** | | | | | |
| Range of Representativeness | | | | | |
| Lower | 80% | 80% | 85% | 88% | 88% |
| Upper | 85% | 85% | 90% | 93% | 93% |

### Changing Approved Labels

The data in this Feed Antimicrobials section include antimicrobials administered in the feed for any purpose, including both production (increased weight gain/improved feed efficiency) and therapeutic (prevention, control or treatment of disease) uses. Generally, antimicrobials administered in the feed are not used as often as water-soluble antimicrobials for disease therapy because sick birds may stop eating but often continue to drink water (14). Regardless, many of the antimicrobials used in feed have drug label claims for disease treatment, control or both.

With the changes to the VFD rule followed by the implementation in January 2017 of the label changes for in-feed antimicrobials described in GFI #213, the antimicrobials that could be used in feed changed. Some of these changes are reflected in the data presented below. Specifically, the full implementation of GFI #213 was developed by FDA to "eliminate production uses of medically important antimicrobials (i.e., antimicrobials important for treating human disease) and to bring all remaining therapeutic uses of these drugs under the oversight of licensed veterinarians." The list of antimicrobials that are currently considered by the FDA to be medically important are located in Appendix A of GFI #152 (3).

Below are some specific examples of label changes to key antimicrobials used in broiler chicken production.

Chlortetracycline and oxytetracycline both have labels for feed use in broiler chickens. Prior to January 1, 2017, the labeled indications for these antimicrobial drugs included: 1) Increased rate of weight gain and improved feed efficiency at 10-50 grams/ton of feed, 2) Control of infectious synovitis caused by *Mycoplasma synoviae* susceptible to the drug at 100-200 grams/ton of feed, 3) Control of chronic respiratory disease (CRD) and air sac infection caused by *Mycoplasma gallisepticum* and *Escherichia coli* susceptible to the drug at 200-400 grams/ton of feed, and 4) Reduction of mortality due to *Escherichia coli* infections susceptible to the drug at 500 grams/ton of feed. As of January 1, 2017, the weight gain/feed efficiency label claim was withdrawn by the drug sponsor(s), so the only remaining indications for use on the label are the disease control claims.

Virginiamycin is a streptogramin antimicrobial used in the feed of broiler chickens. Prior to January 2017, the labeled indications included: 1) Increased rate of weight gain and improved feed efficiency at 5-15 grams/ton of feed, and 2) Prevention of necrotic enteritis caused by *Clostridium perfringens* susceptible to the drug at 20 grams/ton of feed. As of January 1, 2017, the weight gain/feed efficiency label claim was voluntarily withdrawn by the drug sponsor. The only remaining indication for use on the label is the necrotic enteritis disease prevention claim.

Tylosin is a macrolide antimicrobial drug that was used in the feed of broiler chickens. Prior to January 2017, the labeled indications included: 1) Increased rate of weight gain and improved feed efficiency at 4-50 grams/ton of feed, and 2) Control of chronic respiratory disease associated with *Mycoplasma* at 800-1,000 grams/ton of feed. As of January 1, 2017, all tylosin label claims for feed uses in chickens were voluntarily withdrawn by the drug sponsor.

RofenAid, which is a combination drug consisting of sulfadimethoxine and ormetoprim, is used in the feed of chickens for the prevention of coccidiosis caused by all *Eimeria*, and bacterial infections due to *Haemophilus gallinarum* (infectious coryza), *Escherichia coli* (colibacillosis) and *Pasteurella multocida* (fowl cholera). Each pound of premix contains 113.5 g of sulfadimethoxine and 68.1 g of ormetoprim and is mixed into one ton of feed. The use of this product was placed into its own group in the report because of the few combination products available for use in poultry. The sulfonamide and diaminopyrimidine components are graphed separately.

Avilamycin, which is an NMI antimicrobial of the orthosomycin family, is used in the feed of broiler chickens for the prevention of mortality caused by necrotic enteritis associated with *Clostridium perfringens* in broiler chickens. It is mixed at 13.6-40.9 g/ton.

### In-Feed Antimicrobial Use

Summary: Data are based on the annual slaughter of between 6,700,000,000 and 7,500,000,000 birds, depending on the year. Overall, there were substantial reductions in antimicrobials used in feed over time, especially in 2017. When using the metric of total grams of drug per 1,000,000 pounds liveweight produced, there was an approximate 95% reduction of tetracycline use and 60% reduction of virginiamycin use between 2013 and 2017. Tylosin use in feed went to 0 in 2017 due to the withdrawal of all poultry labels. There was no reported lincomycin use in 2014-2017. In-feed bacitracin remained a commonly-used antimicrobial for the prevention of necrotic enteritis. Avilamycin, which is a non-medically important antimicrobial for the prevention of necrotic enteritis, was approved for use in 2016 and had a large increase in use in 2017. Bambermycins, another NMI antimicrobial, increased in usage over time.

**Medically Important Antimicrobials**

Figure 8. Lincomycin (lincosamide class) use in broiler feed, 2013-2017. Total kilograms of lincomycin are shown by the bars (left Y-axis) and total grams/1,000,000 pounds liveweight are shown by the line (right Y-axis).

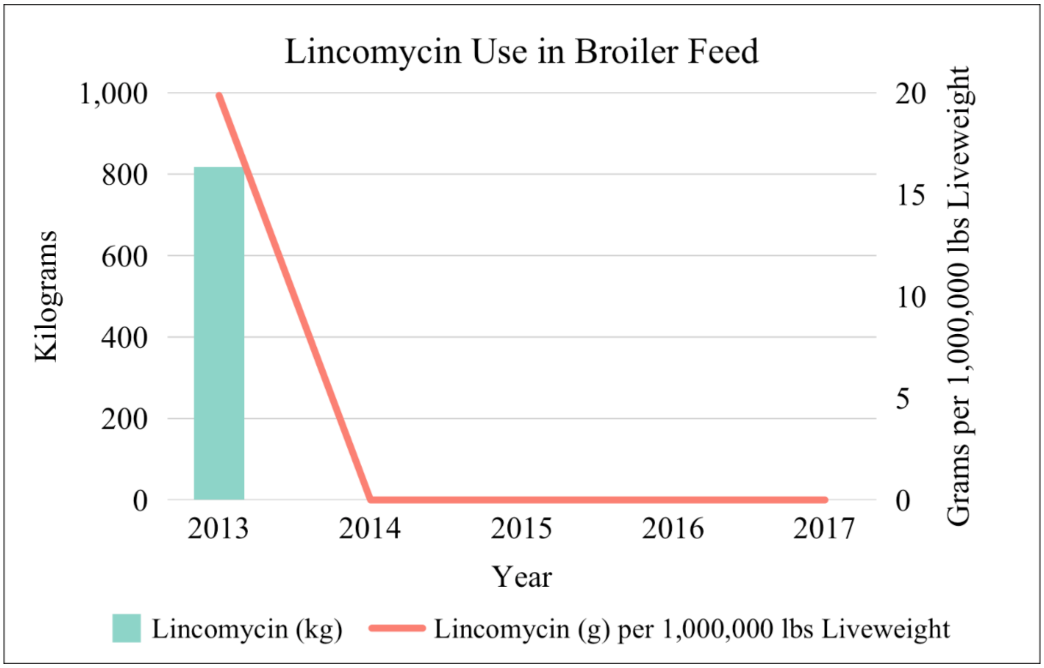



Figure 9. Tylosin (macrolide class) use in broiler feed, 2013-2017. Total grams of tylosin are shown by the bars (left Y-axis) and total grams/1,000,000 pounds liveweight are shown by the line (right Y-axis).

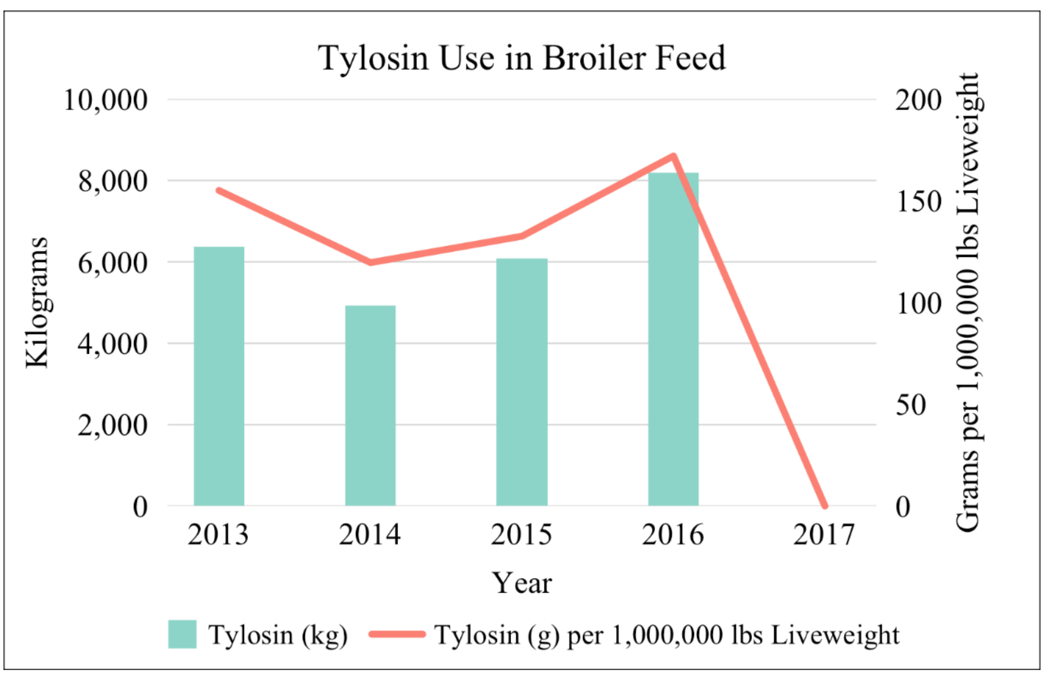
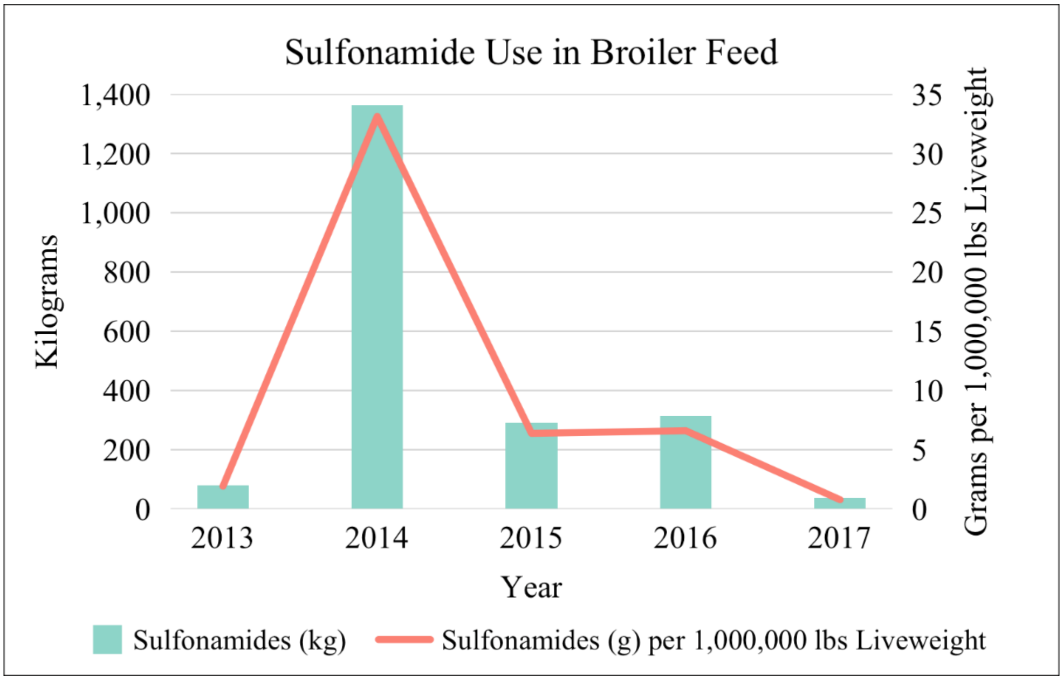


Figure 10. Potentiated sulfonamide use in broiler feed, 2013-2017. The only antimicrobial used was RofenAid, a combined drug comprised of sulfadimethoxine (sulfonamide class) and ormetoprim (diaminopyrmidine class). Amounts of each active ingredient are shown in separate graphs. Each pound of product contains 113.5g sulfadimethoxine and 68.1g ormetoprim. Total kilograms are shown by the bars (left Y-axis) and total grams/1,000,000 pounds liveweight are shown in the line (right Y-axis).



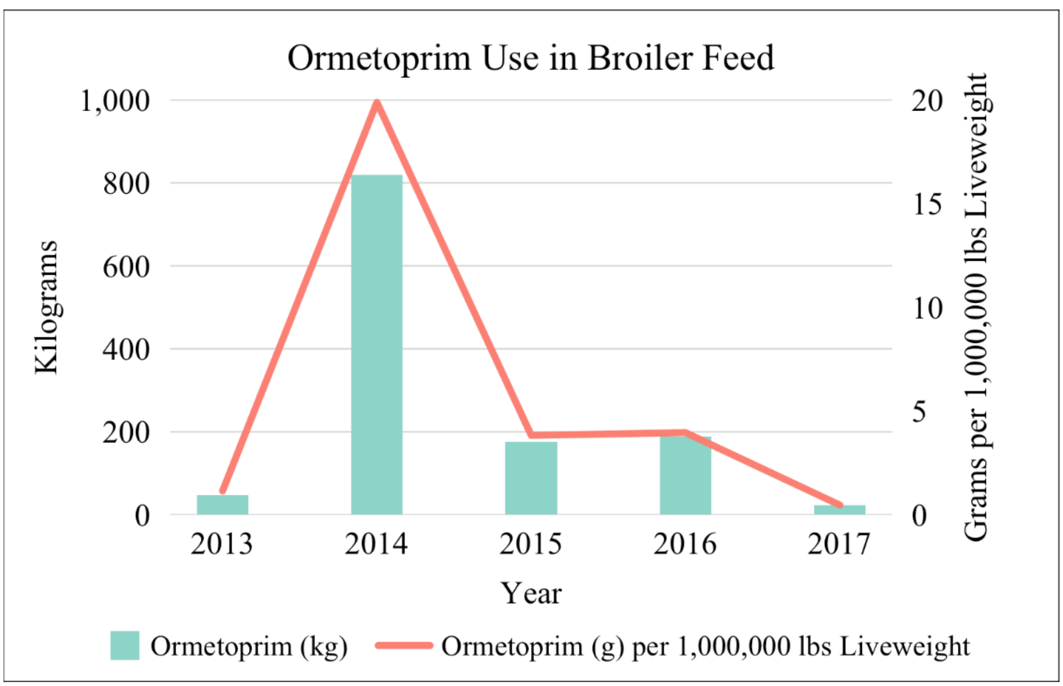



Figure 11. Virginiamycin (streptogramin class) use in broiler feed, 2013-2017. Total kilograms of virginiamycin are shown by the bars (left Y-axis) and total grams/1,000,000 pounds liveweight are shown by the line (right Y-axis).

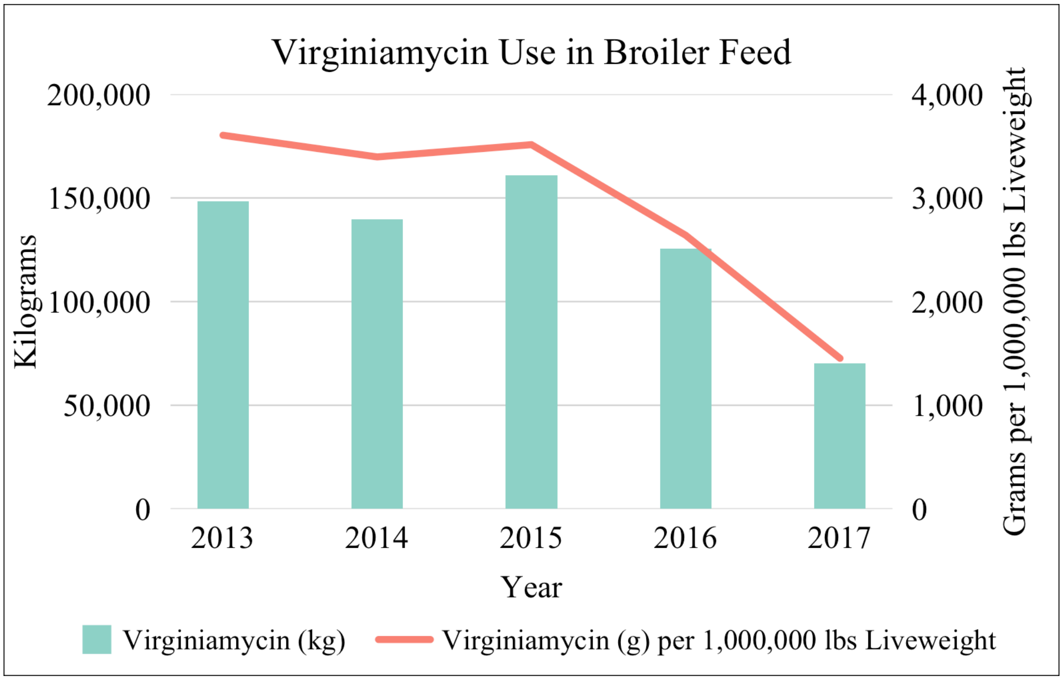
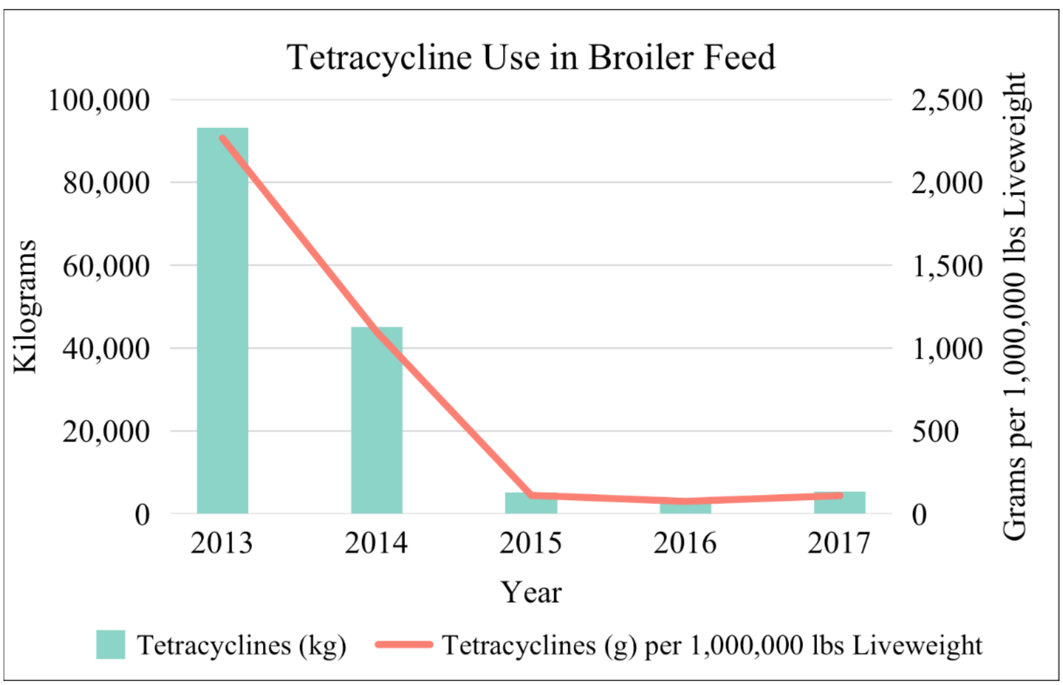



Figure 12. Tetracycline (tetracycline class) use in broiler feed, 2013-2017. Total kilograms of tetracycline are shown by the bars (left Y-axis) and total grams/1,000,000 pounds liveweight are shown by the line (right Y-axis). Specific active ingredients included in this total are chlortetracycline and oxytetracycline.



**Not Medically Important Antimicrobials**

Figure 13. Bambermycins (glycolipid class) use in broiler feed, 2013-2017. Total kilograms of bambermycins are shown by the bars (left Y-axis) and total grams/1,000,000 pounds liveweight are shown by the line (right Y-axis).

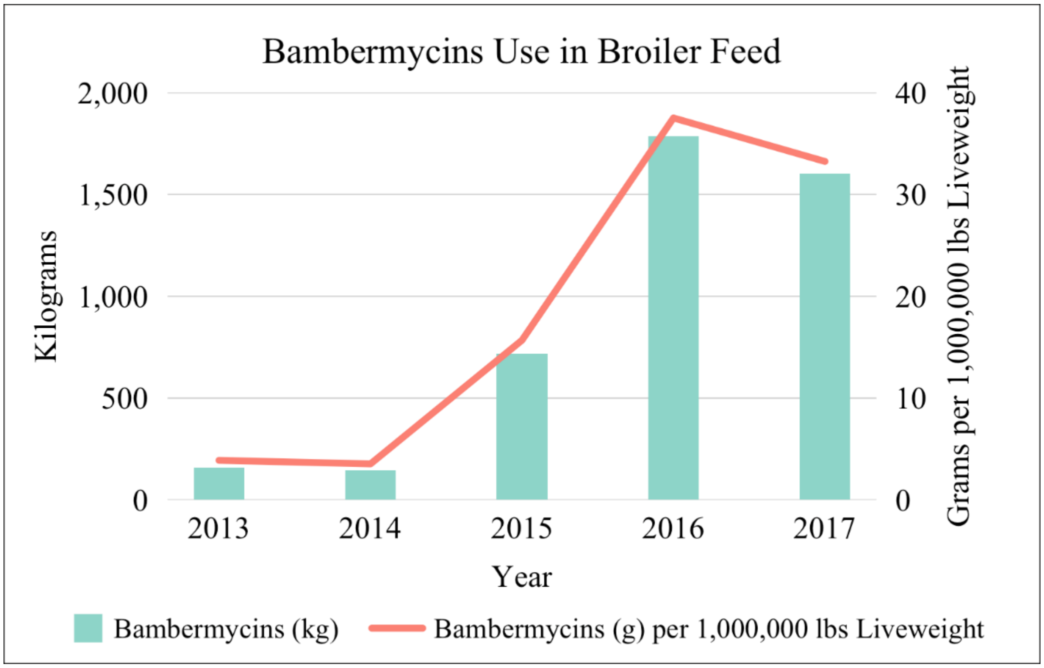



Figure 14. Avilamycin (orthosomycin class) use in broiler feed, 2013-2017. Total kilograms of avilamycin are shown by the bars (left Y-axis) and total grams/1,000,000 pounds liveweight are shown by the line (right Y-axis). Avilamycin was approved for use in broiler chickens in 2016.

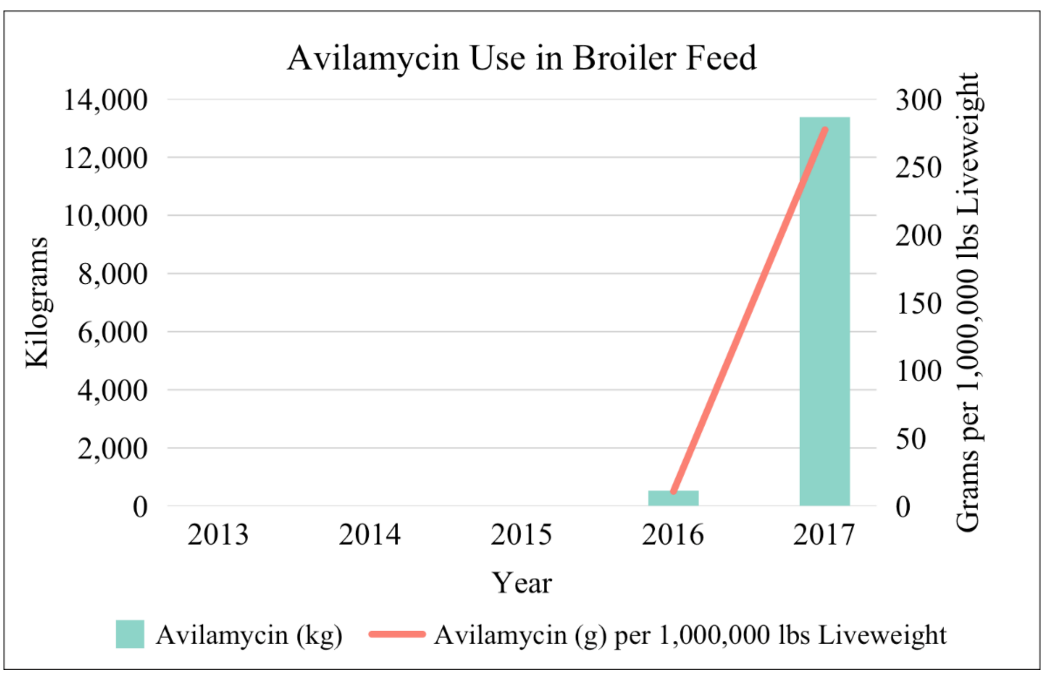


Figure 15. Bacitracin (polypeptide class) use in broiler feed, 2013-2017. Total kilograms of bacitracin are shown by the bars (left Y-axis) and total grams/1,000,000 pounds liveweight are shown by the line (right Y-axis).

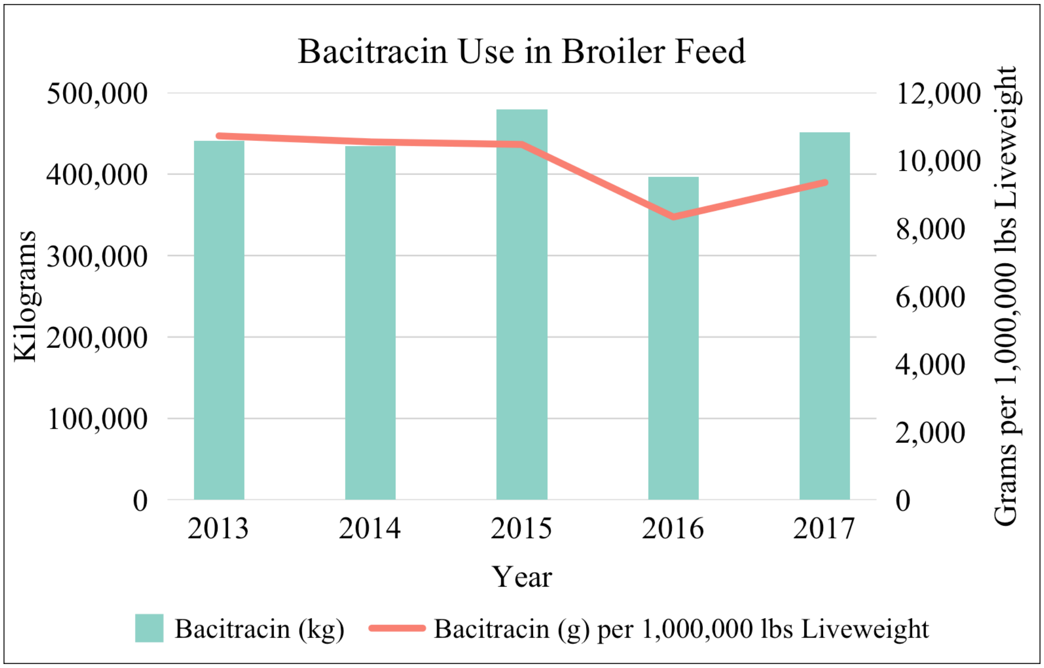


Table 14. Amount of antimicrobial drug use in broiler feed, 2013-2017. Data are reported by active ingredients within drug classes and are divided into medically important and not medically important. Weights are reported as total kg of antimicrobial.

| Drug Class | Active Ingredient | Antimicrobial Usage in Broiler Feed (kg of antimicrobial) | | | | |
|---|---|---|---|---|---|---|
| | | **2013** | **2014** | **2015** | **2016** | **2017** |
| **Medically Important** | | | | | | |
| Diaminopyrimidines | Ormetoprim | 47.5 | 818.1 | 175.4 | 188.6 | 22.6 |
| Lincosamides | Lincomycin | 816.8 | - | - | - | - |
| Macrolides | Tylosin | 6,378.7 | 4,923.7 | 6,075.6 | 8,190.7 | - |
| Streptogramins | Virginiamycin | 148,266.3 | 139,755.6 | 160,976.8 | 125,669.7 | 70,082.0 |
| Sulfonamides | Sulfadimethoxine | 79.1 | 1,363.6 | 292.4 | 314.4 | 37.7 |
| Tetracyclines | Tetracyclines[1] | 93,150.4 | 45,130.0 | 5,151.2 | 3,616.3 | 5,325.3 |
| **Not Medically Important** | | | | | | |
| Glycolipids | Bambermycins | 159.9 | 145.8 | 718.7 | 1,786.0 | 1,603.1 |
| Orthosomycins | Avilamycin | - | - | - | 519.8 | 13,372.4 |
| Polypeptides | Bacitracin | 441,210.7 | 434,205.3 | 479,788.3 | 396,882.2 | 451,077.3 |

[1]Includes chlortetracycline and oxytetracycline; as stated in the FDA Sales and Distribution Report from 2017 (6), “Antimicrobial class includes drugs of different molecular weights.”

Table 15. Amount of antimicrobial drug use in broiler feed, 2013-2017. Data are reported by active ingredients within drug classes and are divided into medically important and not medically important. Weights are reported as g of antimicrobial per 1,000,000 pounds liveweight produced.

| | | Antimicrobial Usage in Broiler Feed (g of antimicrobial per million lbs liveweight) | | | | |
|---|---|---|---|---|---|---|
| **Drug Class** | **Active Ingredient** | **2013** | **2014** | **2015** | **2016** | **2017** |
| **Medically Important** | | | | | | |
| Diaminopyrimidines | Ormetoprim | 1.2 | 19.9 | 3.8 | 4.0 | 0.5 |
| Lincosamides | Lincomycin | 19.9 | - | - | - | - |
| Macrolides | Tylosin | 155.1 | 119.6 | 132.6 | 172.0 | - |
| Streptogramins | Virginiamycin | 3,604.5 | 3,395.3 | 3,513.7 | 2,639.4 | 1,453.2 |
| Sulfonamides | Sulfadimethoxine | 1.9 | 33.1 | 6.4 | 6.6 | 0.8 |
| Tetracyclines | Tetracyclines[1] | 2,264.6 | 1,096.4 | 112.4 | 76.0 | 110.4 |
| **Not Medically Important** | | | | | | |
| Glycolipids | Bambermycins | 3.9 | 3.5 | 15.7 | 37.5 | 33.2 |
| Orthosomycins | Avilamycin | - | - | - | 10.9 | 277.3 |
| Polypeptides | Bacitracin | 10,726.3 | 10,548.7 | 10,472.5 | 8,335.6 | 9,353.6 |

[1]Includes chlortetracycline and oxytetracycline

## Water-Soluble Antimicrobials – Broilers

The data that are presented in this Water-Soluble Antimicrobials section represent 72-93% of annual U.S. broiler production by companies on the WATT Poultry USA list; representativeness ranges from 72-77% in 2013 to 88-93% in 2017. This estimate of representativeness is based on total pounds liveweight produced annually by companies that submitted water-soluble data. The numbers are derived from the annual WATT Poultry USA lists, as described in the Broiler Representativeness section.

Table 16. Broiler water-soluble antimicrobial data representativeness, shown as a range for each year of data in the report.

| | 2013 | 2014 | 2015 | 2016 | 2017 |
|---|---|---|---|---|---|
| **Based on Pounds Liveweight** | | | | | |
| Range of Representativeness | | | | | |
| Lower | 72% | 72% | 80% | 88% | 88% |
| Upper | 77% | 77% | 85% | 93% | 93% |

### Veterinary Oversight

As described previously, U.S. FDA GFI #209 and #213 brought therapeutic uses of medically important antimicrobials in water of food-producing animals under veterinary supervision by changing marketing status from over-the-counter (OTC) to prescription (Rx) (1, 2). Label claim changes for water-soluble antimicrobials described in GFI #213 took full effect in January 2017. As was stated previously, antimicrobials used in feed are not used as often as water-soluble antimicrobials for therapeutic purposes because sick birds may stop eating but often continue to drink water (14). Further, therapeutic intervention through the water can often be accomplished more quickly through the water than the feed.

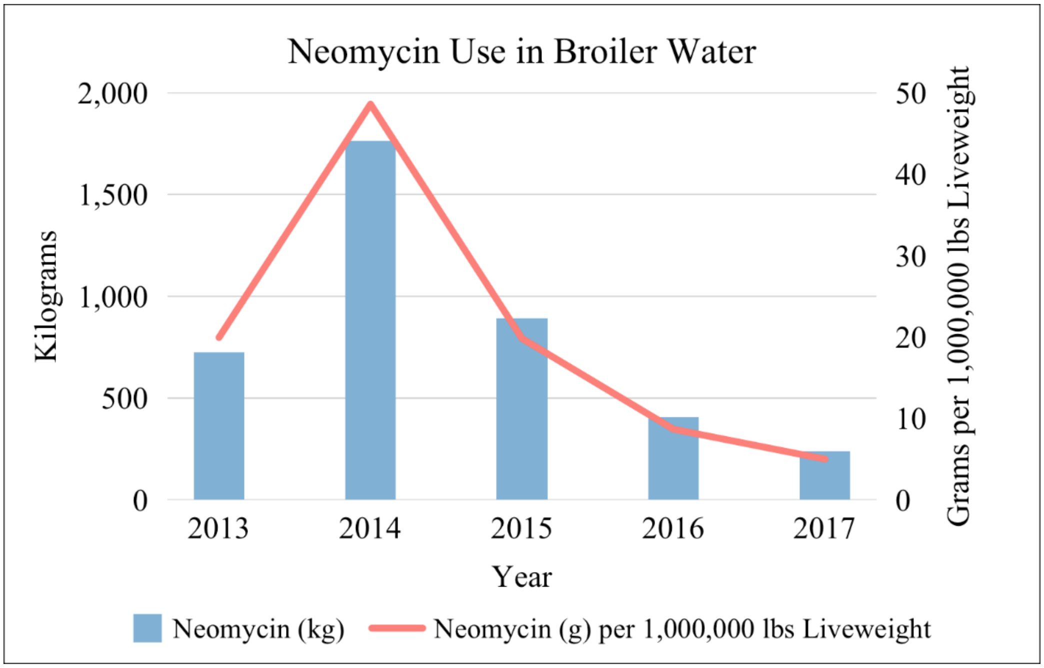
The data in this Water-Soluble section include antimicrobials that were administered therapeutically for disease. For many companies, some flock-level data were available to detail the ways in which these antimicrobials were administered, including the most common ages at therapy for specific diseases, the dose and the duration of therapy. Some companies only had information regarding number of birds receiving an antimicrobial for a specific disease, and in these instances, water consumption tables were used to estimate amount of drug administered.

### Water Soluble Antimicrobial Use

Summary: Data are based on the annual slaughter of between 6,300,000,000 and 7,500,000,000 birds, depending on the year. When using the metric of total grams of drug per 1,000,000 pounds liveweight produced, water-soluble penicillin use decreased approximately 21% between 2013 and 2017 and approximately 42% since the peak in 2015. Water-soluble lincomycin use decreased approximately 28% between 2013 and 2017 and approximately 58% since the peak in 2015. Water-soluble tetracycline use decreased approximately 47% between 2013 and 2017. Sulfonamide use decreased approximately 72% between 2013 and 2017. Water-soluble tylosin use decreased approximately 46% between 2013 and 2017. Overall, water-soluble bacitracin use was fairly steady from 2013 through 2016 but increased almost fourfold in 2017, in part due to its status as NMI.

## Medically Important Antimicrobials

<u>Figure 16</u>. Neomycin (aminoglycoside class) use in broiler water, 2013-2017. Total kilograms of neomycin are shown by the bars (left Y-axis) and total grams/1,000,000 pounds liveweight are shown by the line (right Y-axis).




<u>Figure 17</u>. Spectinomycin (aminoglycoside class) use in broiler water, 2013-2017. Total kilograms of spectinomycin are shown by the bars (left Y-axis) and total grams/1,000,000 pounds liveweight are shown by the line (right Y-axis).

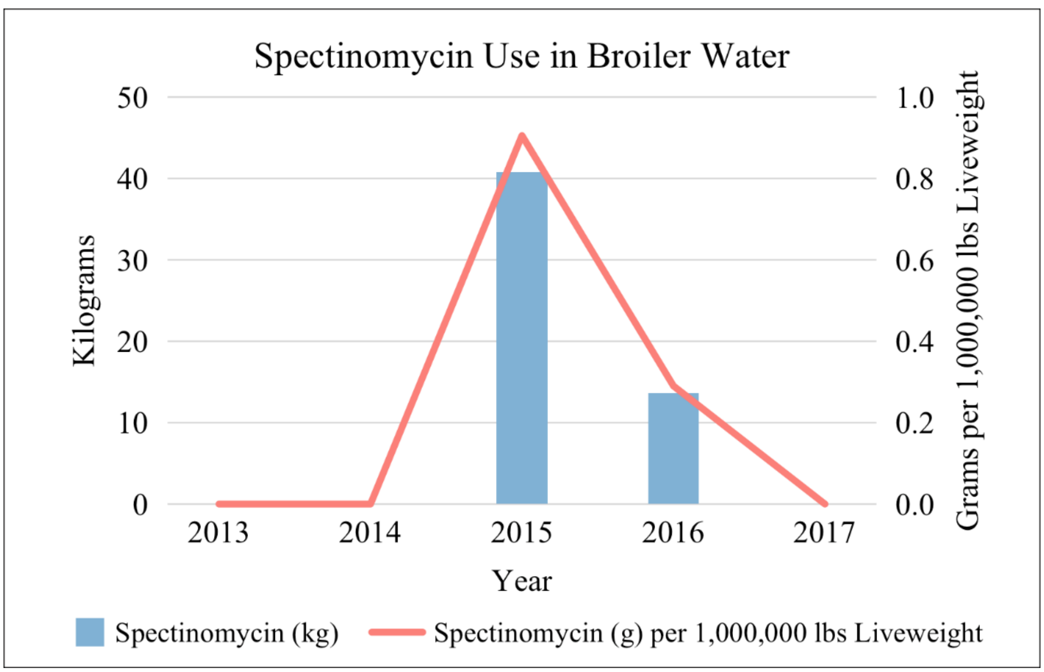


Figure 18. Lincomycin (lincosamide class) use in broiler water, 2013-2017. Total kilograms of lincomycin are shown by the bars (left Y-axis) and total grams/1,000,000 pounds liveweight are shown by the line (right Y-axis).

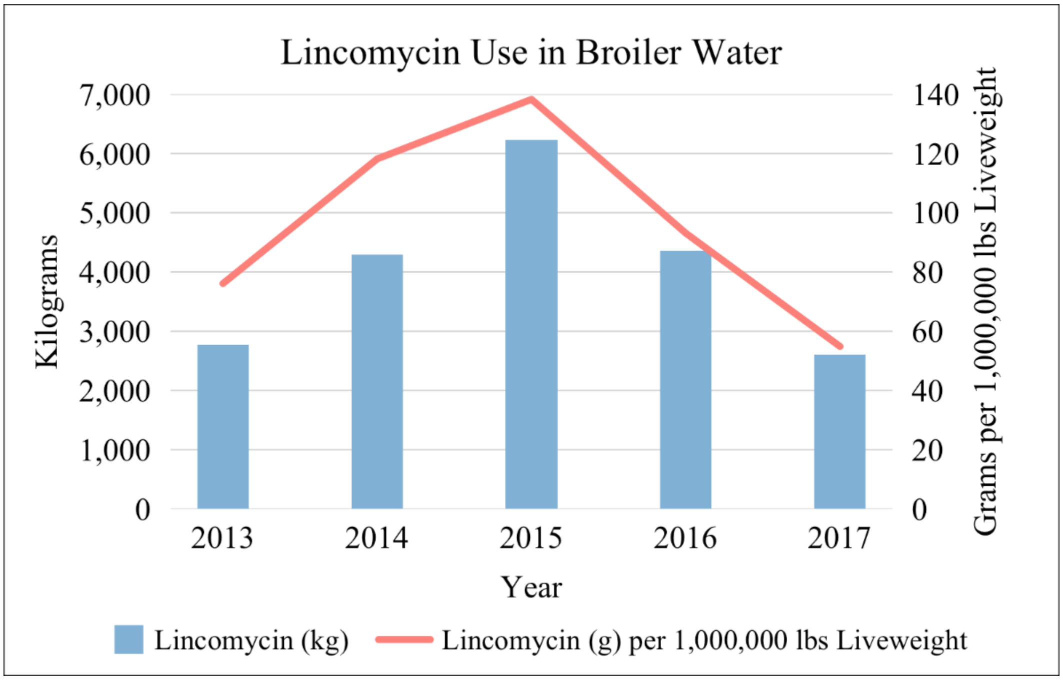



Figure 19. Erythromycin (macrolide class) use in broiler water, 2013-2017. Total kilograms of erythromycin are shown by the bars (left Y-axis) and total grams/1,000,000 pounds liveweight are shown by the line (right Y-axis).

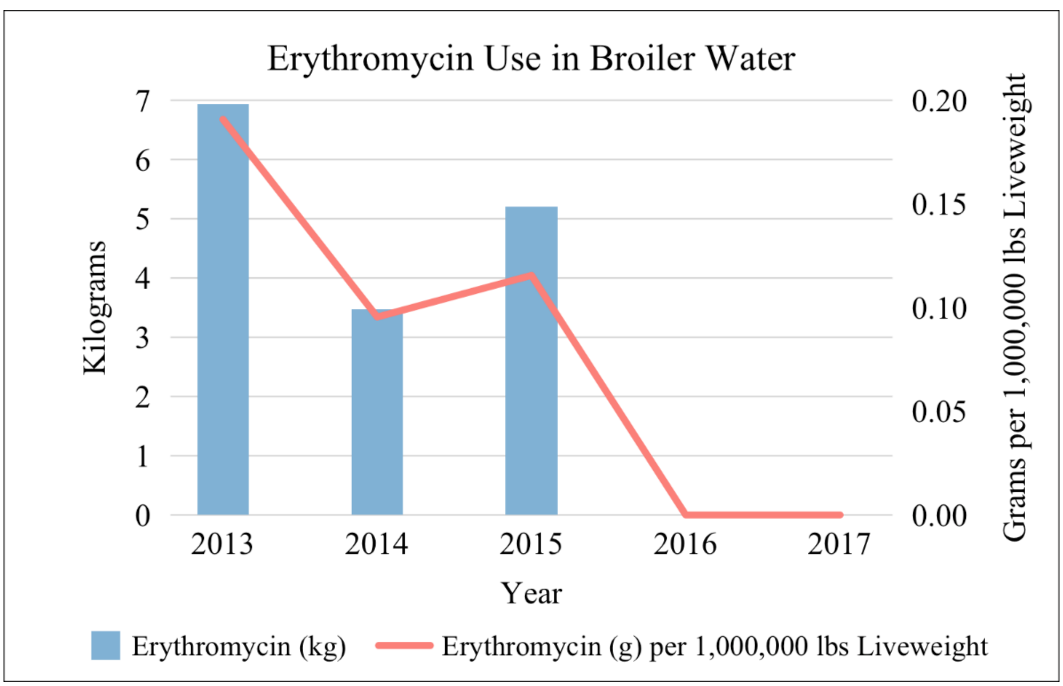


Figure 20. Tylosin (macrolide class) use in broiler water, 2013-2017. Total kilograms of tylosin are shown by the bars (left Y-axis) and total grams/1,000,000 pounds liveweight are shown by the line (right Y-axis).

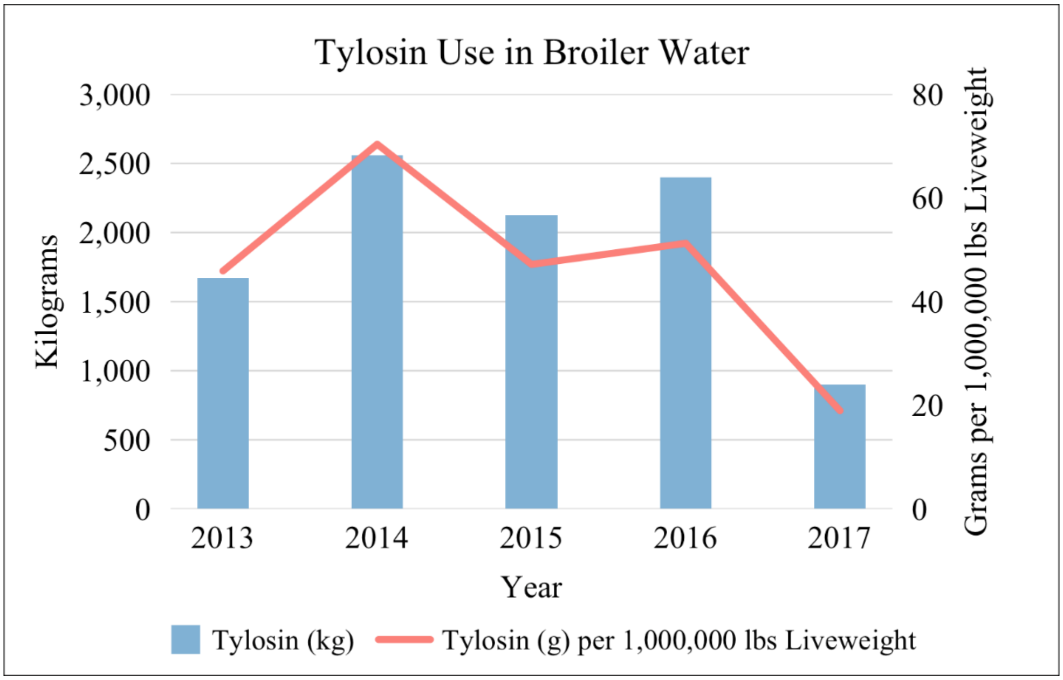



Figure 21. Penicillin (natural penicillin class) use in broiler water, 2013-2017. Total kilograms of penicillin are shown by the bars (left Y-axis) and total grams/1,000,000 pounds liveweight are shown by the line (right Y-axis).

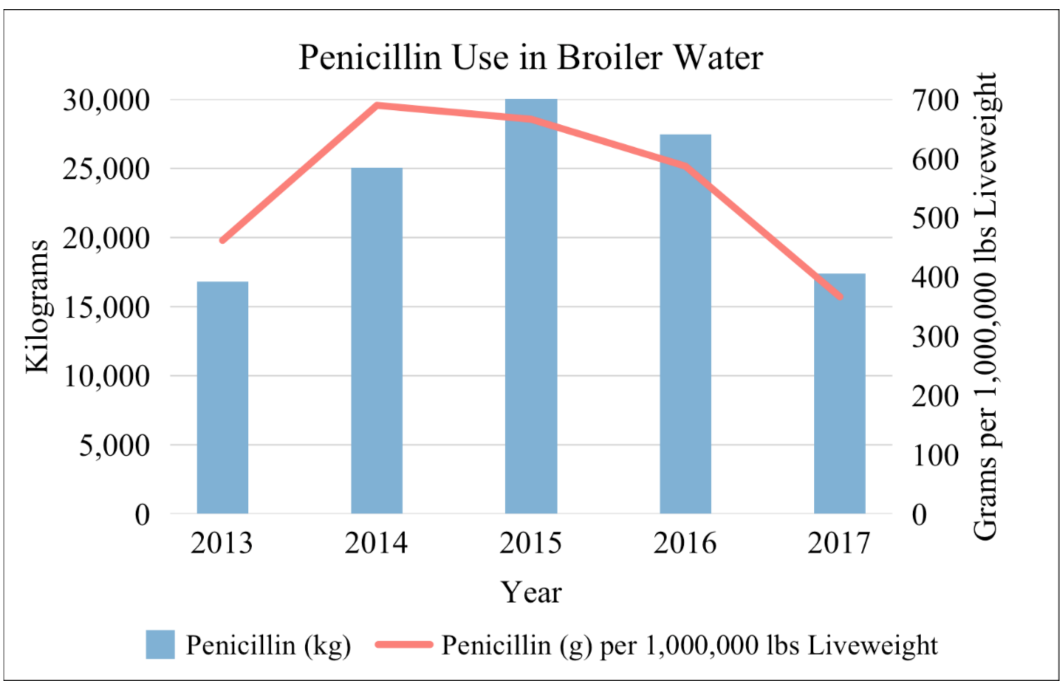


Figure 22. Sulfonamide (sulfonamide class) use in broiler water, 2013-2017. Total kilograms of sulfonamides are shown by the bars (left Y-axis) and total grams/1,000,000 pounds liveweight are shown by the line (right Y-axis). This total includes sulfadimethoxine, sulfamerazine, sulfamethazine, and sulfaquinoxaline.

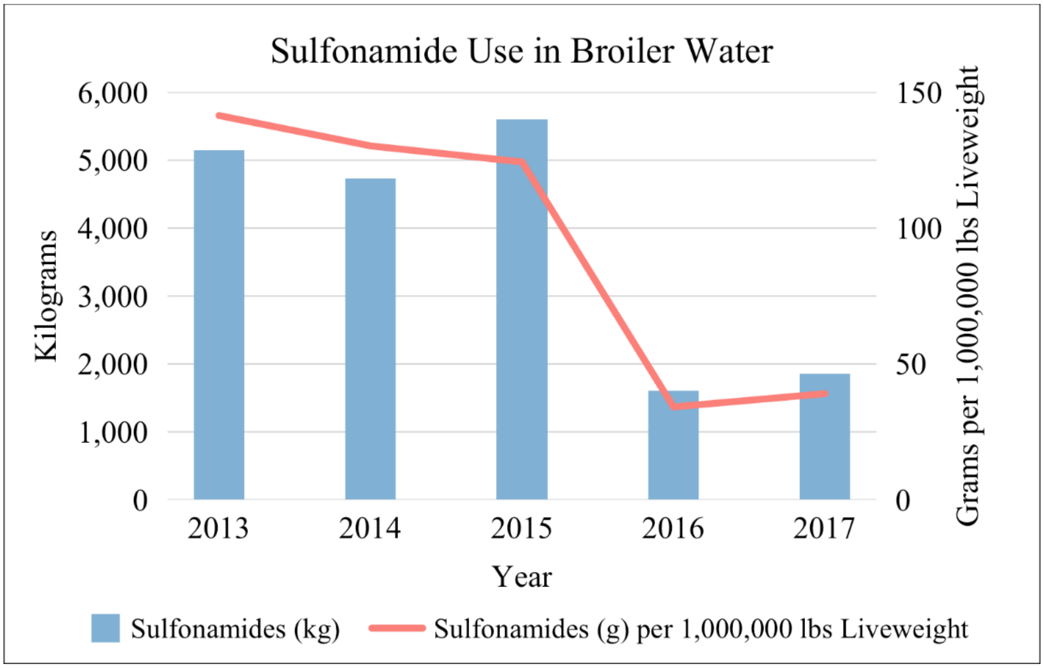
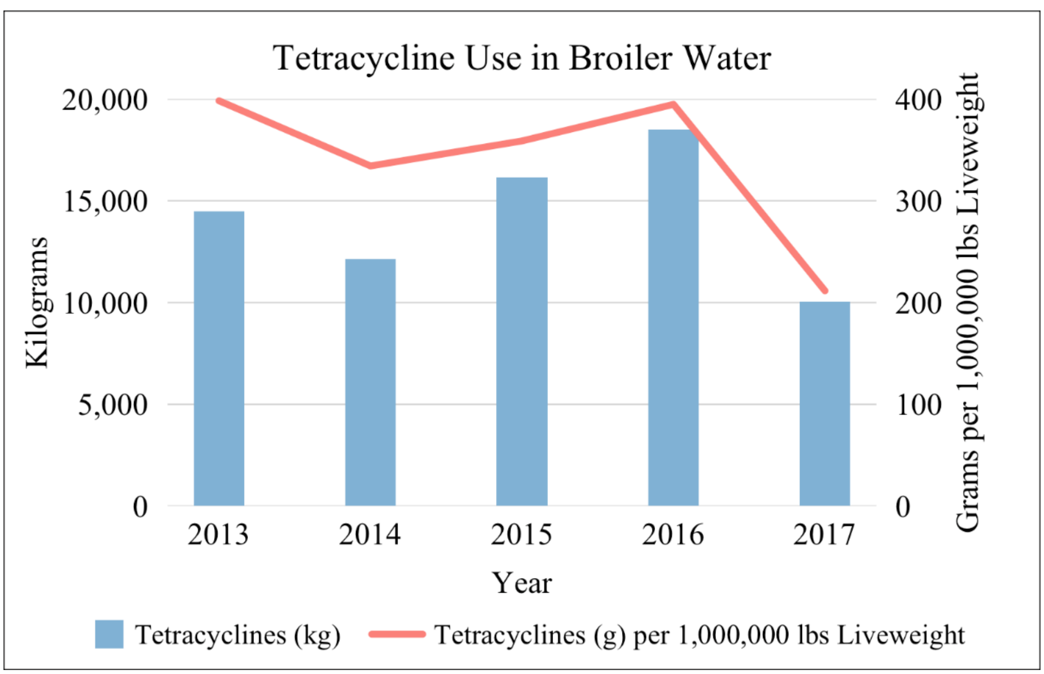



Figure 23. Tetracycline (tetracycline class) use in broiler water, 2013-2017. Total kilograms of tetracycline are shown by the bars (left Y-axis) and total grams/1,000,000 pounds liveweight are shown by the line (right Y-axis). Specific active ingredients included in this total are tetracycline, chlortetracycline and oxytetracycline.



**Not Medically Important Antimicrobials**

Figure 24. Bacitracin (polypeptide class) use in broiler water, 2013-2017. Total kilograms of bacitracin soluble are shown by the bars (left Y-axis) and total grams/1,000,000 pounds liveweight are shown by the line (right Y-axis).

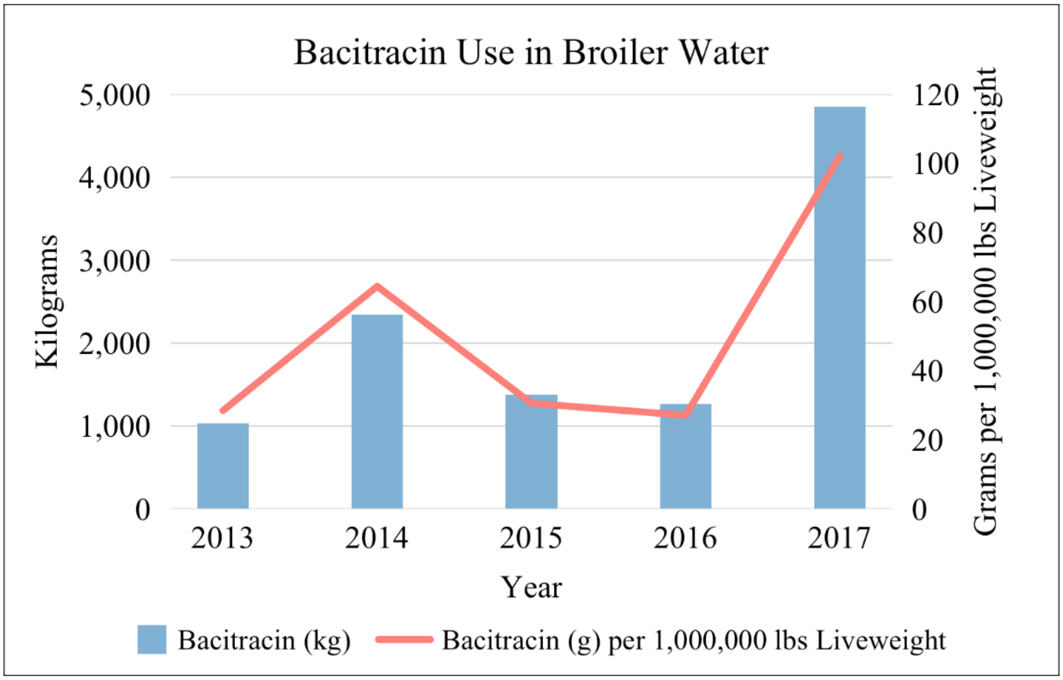


Table 17. Amount of antimicrobial drug use in broiler water, 2013-2017. Data are reported by active ingredients within drug classes and are divided into medically important and not medically important. Weights are reported as total kg of antimicrobial.

| Drug Class | Active Ingredient | Antimicrobial Usage in Broiler Water (kg of antimicrobial) | | | | |
|---|---|---|---|---|---|---|
| | | 2013 | 2014 | 2015 | 2016 | 2017 |
| **Medically Important** | | | | | | |
| Aminoglycosides | Neomycin | 725.2 | 1,764.8 | 892.3 | 406.4 | 237.8 |
| | Spectinomycin | - | - | 40.8 | 13.6 | - |
| Lincosamides | Lincomycin | 2,767.5 | 4,293.6 | 6,226.3 | 4,360.1 | 2,603.8 |
| Macrolides | Erythromycin | 6.9 | 3.5 | 5.2 | - | - |
| | Tylosin | 1,669.5 | 2,556.1 | 2,124.1 | 2,399.9 | 899.9 |
| Natural Penicillins | Penicillin G | 16,791.0 | 25,057.0 | 29,996.8 | 27,485.2 | 17,398.3 |
| Sulfonamides | Sulfonamides[1,3] | 5,142.0 | 4,731.5 | 5,598.1 | 1,601.1 | 1,854.0 |
| Tetracyclines | Tetracyclines[2,3] | 14,482.6 | 12,142.1 | 16,156.5 | 18,486.4 | 10,040.5 |
| **Not Medically Important** | | | | | | |
| Polypeptides | Bacitracin | 1,035.5 | 2,340.6 | 1,376.6 | 1,269.4 | 4,847.2 |

[1]Includes sulfadimethoxine, sulfamerazine, sulfamethazine, and sulfaquinoxaline
[2]Includes chlortetracycline, oxytetracycline and tetracycline
[3]As stated in the FDA Sales and Distribution Report (6), "Antimicrobial class includes drugs of different molecular weights."

Table 18. Amount of antimicrobial drug use in broiler water, 2013-2017. Data are reported by active ingredients within drug classes and are divided into medically important and not medically important. Weights are reported as g of antimicrobial per 1,000,000 pounds liveweight produced.

| | | Antimicrobial Usage in Broiler Water (g of antimicrobial per million lbs liveweight) | | | | |
|---|---|---|---|---|---|---|
| **Drug Class** | **Active Ingredient** | **2013** | **2014** | **2015** | **2016** | **2017** |
| **Medically Important** | | | | | | |
| Aminoglycosides | Neomycin | 19.9 | 48.6 | 19.8 | 8.7 | 5.0 |
| | Spectinomycin | - | - | 0.9 | 0.3 | - |
| Lincosamides | Lincomycin | 76.1 | 118.2 | 138.3 | 93.1 | 54.9 |
| Macrolides | Erythromycin | 0.2 | 0.1 | 0.1 | - | - |
| | Tylosin | 45.9 | 70.4 | 47.2 | 51.3 | 19.0 |
| Natural Penicillins | Penicillin G | 461.8 | 689.7 | 666.2 | 587.0 | 366.6 |
| Sulfonamides | Sulfonamides[1] | 141.4 | 130.2 | 124.3 | 34.2 | 39.1 |
| Tetracyclines | Tetracyclines[2] | 398.3 | 334.2 | 358.8 | 394.8 | 211.6 |
| **Not Medically Important** | | | | | | |
| Polypeptides | Bacitracin | 28.5 | 64.4 | 30.6 | 27.1 | 102.1 |

[1]Includes sulfadimethoxine, sulfamerazine, sulfamethazine, and sulfaquinoxaline
[2]Includes chlortetracycline, oxytetracycline and tetracycline

## Disease Indications – Broiler

This section of the report will describe two key aspects of the 2017 data that were collected. This analysis should be considered preliminary, as future reports will present these data in greater detail. The data in these sections represent approximately 60% of the annual broiler production that is within the full dataset for 2017. In other words, companies that supplied the data for this section represent approximately 60% of the broilers in the 2017 dataset. The specific aspects covered in this section are:

1. The distribution of age of onset for some of the important diseases for which water-soluble antimicrobials were administered. These data were generated from the flock-level therapy records, and therefore, if there were times when flocks were diseased but antimicrobials were not administered, these disease occurrences would not have been captured.
2. The percentage of each water-soluble antimicrobial that was administered for different disease indications. These estimates do not represent all of the submitted antimicrobial use data, as not every company had these data available.

At this point in time there is insufficient data to capture accurately the duration of administration of the water-soluble antimicrobials by disease. The next report will incorporate these data.

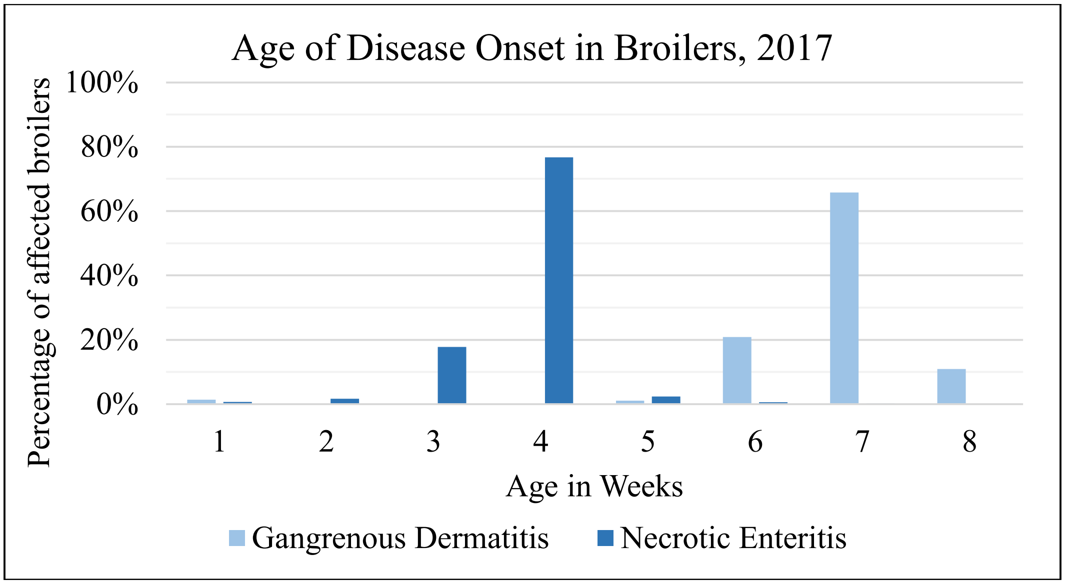
### Characteristics of Diseases Necessitating Antimicrobial Therapy

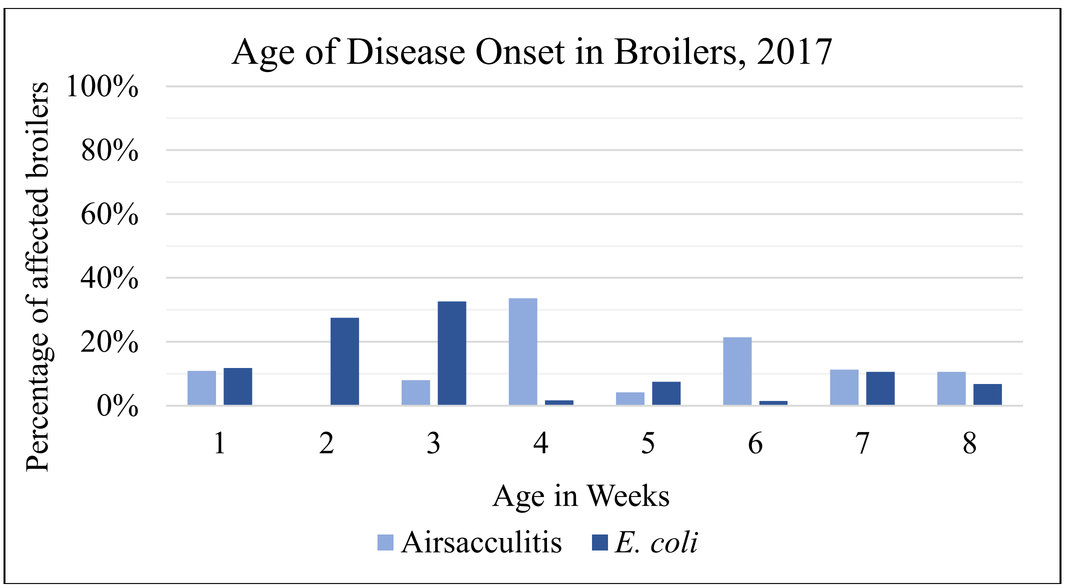
As described above in the Primary Disease Challenges section, the two clostridial diseases that affect broilers occur primarily in different stages of production. Necrotic enteritis is most often seen at 3-4 weeks of age while gangrenous dermatitis occurs most often later in the production cycle. Given the large difference in bird weights when these two clostridial diseases manifest, a much greater amount of antimicrobial would be used for gangrenous dermatitis compared to necrotic enteritis for the same number of birds receiving therapy.

Diseases associated with *E. coli* infection occur throughout the life of the chicken. There are certain conditions that are linked to specific ages, such as omphalitis (yolk sac infection occurring in the young chick), while others such as airsacculitis can occur throughout the bird's life.

These and other important diseases of broilers are shown in the figures below.

Figure 25. Distribution of age of disease onset for four of the major diseases affecting broilers in companies providing data for this analysis and for which antimicrobial drugs are often used in the water, 2017.



## Water-Soluble Antimicrobial Use by Disease

The graphs in this section depict the diseases that were targeted by water-soluble antimicrobials during 2017. These graphs depict how each water-soluble antimicrobial was used by stratifying the total amount of each antimicrobial used in 2017 into the disease indications for which it was administered. In other words, the total amount of each antimicrobial is separated into the disease indications for which it was used.

The data are presented in two ways. First, the percentage of broilers that received therapy with a given antimicrobial for each disease indication was calculated. Second, the percentage of the total amount of antimicrobial (in grams) that was administered for each disease indication was calculated.

As an example, in Figure 26 the use of lincomycin is shown, and this antimicrobial was primarily used for gangrenous dermatitis (GD) and necrotic enteritis (NE). In the figure, for the birds that received lincomycin, 57% were administered lincomycin for GD and 43% for NE. However, 67% of the total amount of lincomycin was administered for GD and 33% for NE.

It is important to note the difference between GD and NE. GD occurs later in life, and as shown in the data for 2017, it was the most common reason for use of lincomycin and penicillin in the water. Because the birds receiving therapy were older, they are heavier birds. In contrast, NE occurs earlier in life and requires less antimicrobial due to the lighter bird weight and consequent water consumption. The proportion of use by grams is greater when compared to proportion of use by number of birds for GD because the therapy is for heavier birds.

**Medically Important Antimicrobials**

Figure 26. Percentage of lincomycin use in the water of broilers by disease indication, 2017. For those birds that received lincomycin, the figure depicts the percentage of birds receiving therapy and the percentage of total grams of lincomycin by disease indication.

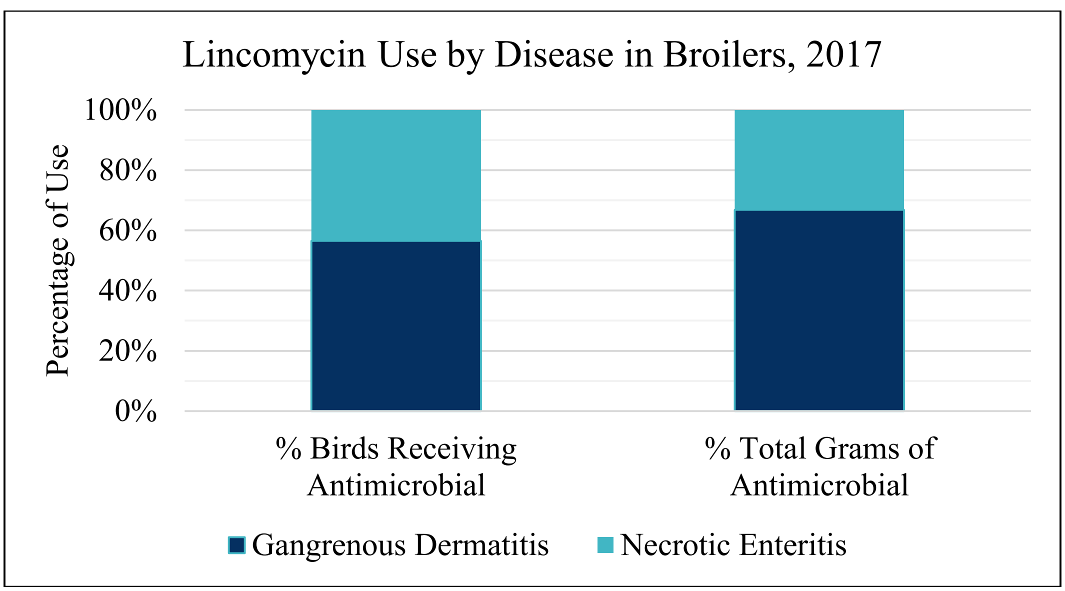


Figure 27. Percentage of neomycin use in the water of broilers by disease indication, 2017. For those birds that received neomycin, the figure depicts the percentage of birds receiving therapy and the percentage of total grams of neomycin by disease indication.

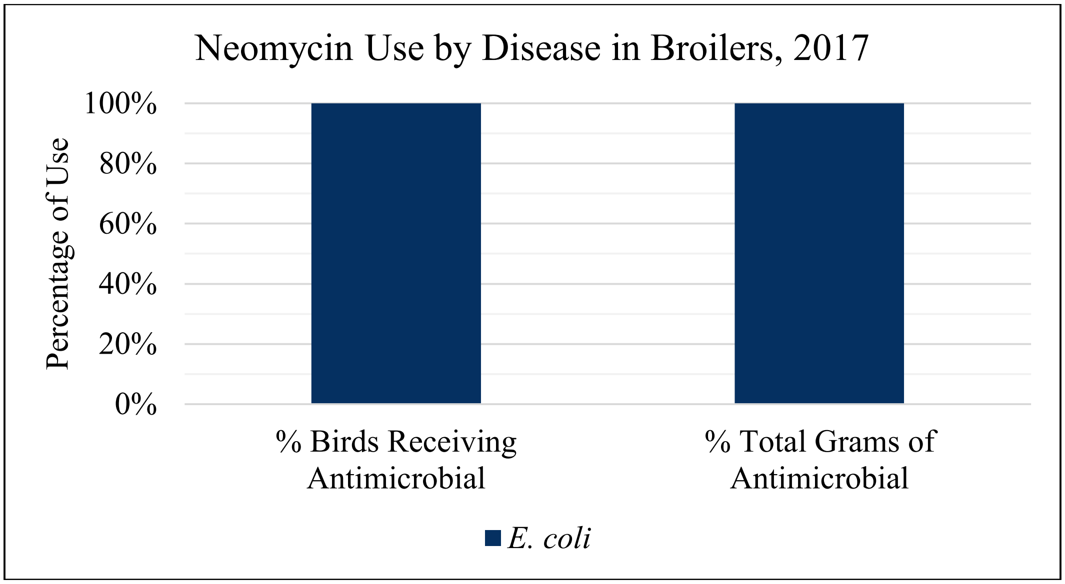



Figure 28. Percentage of penicillin use in the water of broilers by disease indication, 2017. For those birds that received penicillin, the figure depicts the percentage of birds receiving therapy and the percentage of total grams of penicillin by disease indication.

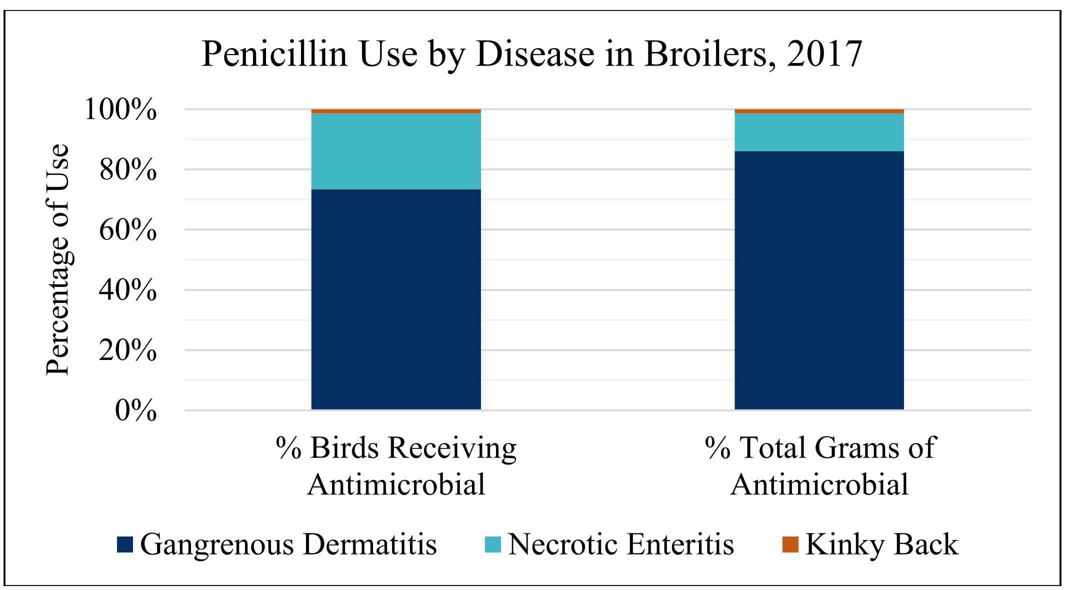


Figure 29. Percentage of sulfonamide use in the water of broilers by disease indication, 2017. Specific active ingredients included in this total are sulfadimethoxine, sulfamerazine, sulfamethazine, and sulfaquinoxaline. For those birds that received sulfonamides, the figure depicts the percentage of birds receiving therapy and the percentage of total grams of sulfonamides by disease indication.

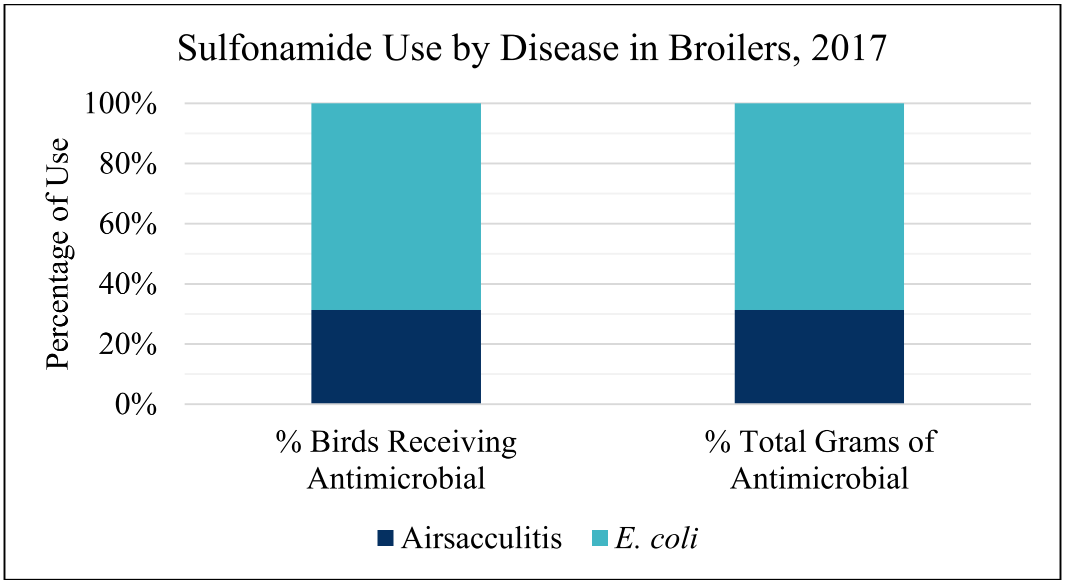



Figure 30. Percentage of tetracycline use in the water of broilers by disease indication, 2017. Specific active ingredients included in this total are tetracycline, chlortetracycline and oxytetracycline. For those birds that received tetracyclines, the figure depicts the percentage of birds receiving therapy and the percentage of total grams of tetracyclines by disease indication.

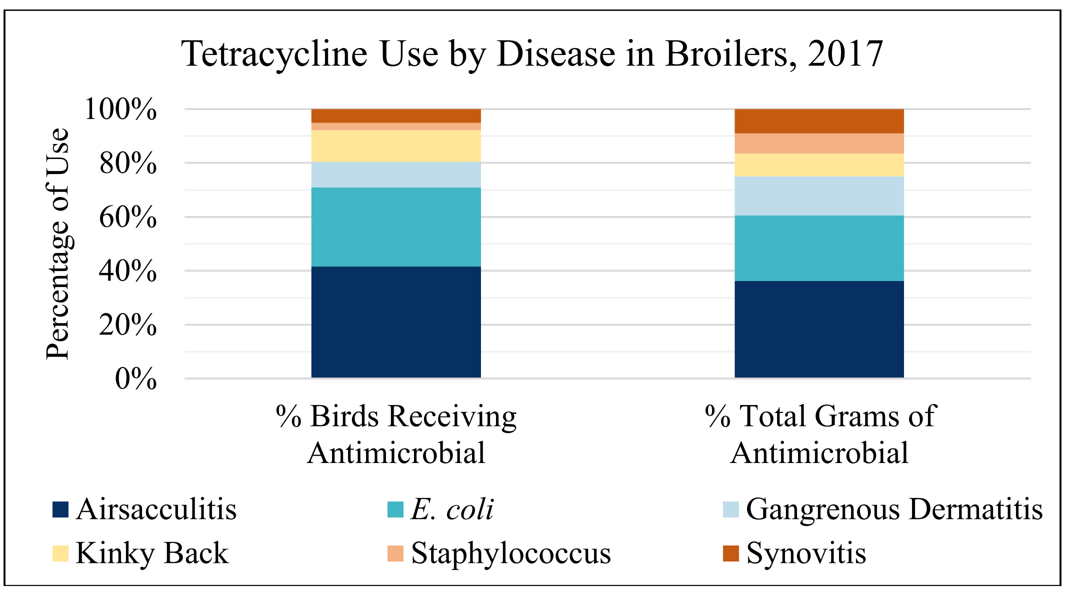
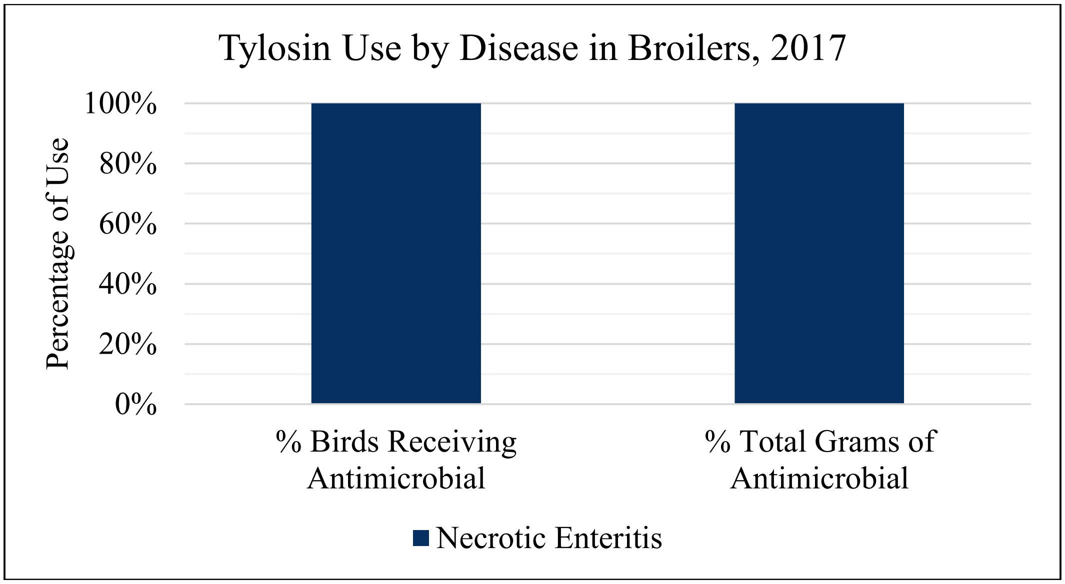
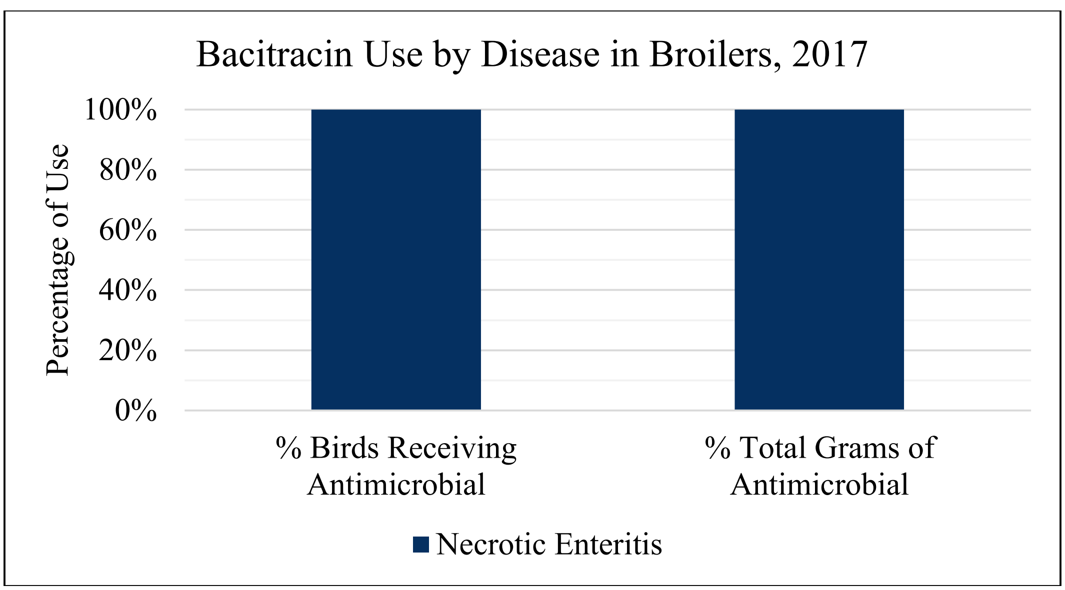


Figure 31. Percentage of tylosin use in the water of broilers by disease indication, 2017. For those birds that received tylosin, the figure depicts the percentage of birds receiving therapy and the percentage of total grams of tylosin by disease indication.




**Not Medically Important Antimicrobials**

Figure 32. Percentage of bacitracin use in the water of broilers by disease indication, 2017. For those birds that received bacitracin, the figure depicts the percentage of birds receiving therapy and the percentage of total grams of bacitracin by disease indication.



# Turkey Industry

## Representativeness

The goal of the turkey aspect of this project was to collect on-farm antimicrobial use data from the companies that produce the majority of the domestic supply of turkey meat in the U.S. To estimate the industry representativeness of the data that are being collected in this effort, a list published by WATT Poultry USA that contains the major turkey companies in the U.S. and their annual production data (http://www.wattpoultryusa-digital.com/201811/) was used. This WATT list includes the size of each company based on the total pounds liveweight produced annually for each company. These annual totals for each year of the data collection period (2013-2017) were used as the denominator for the calculation of national representativeness of the data; the sum of the production totals for the companies that were enrolled in the project and that submitted data served as the numerator for the industry representativeness calculation.

Not all companies were able to submit data for each year of the 5-year data collection period. In addition, not all companies were able to submit all data types for each year. Consequently, industry representativeness for each data type (hatchery, ionophore, in-feed, and water-soluble) was estimated for each year of the data collection interval. These estimates of industry representativeness are presented in tables at the beginning of each section.

Table 11 below shows the WATT list for turkey production in 2016. Similar data exist for each year of the data collection effort (2013-2017). The industry representativeness of our dataset was calculated for each year of the collection period using the corresponding WATT list for each year. The representativeness estimates in this report are presented as a range. This range helps mask the exact companies that participated in this data collection effort. The width of the industry representativeness interval was set at 5% around the actual estimate, with the range not necessarily being centered around the actual estimate; a random interval of 5% width was generated for each section of this report. If two years had the same estimated representativeness, an identical range was used for each of these years.

It is important to note that this calculation is only used to estimate representativeness; the actual number of birds placed, birds slaughtered and pounds liveweight produced that are included in the report results are based on data submitted by the participating companies.

Table 19. Annual production numbers for the major U.S. turkey companies for 2016, published by WATT Poultry USA (http://www.wattpoultryusa-digital.com/201703/index.php#/76).

| Rank | Company | 2016 |
|---|---|---|
| | | Million lbs liveweight |
| 1 | Butterball LLC | 1,380.0 |
| 2 | Jennie-O Turkey Store | 1,275.0 |
| 3 | Cargill Turkey & Cooked Meats | 1,000.0 |
| 4 | Farbest Foods | 559.0 |
| 5 | Tyson Foods | 334.0 |
| 6 | Perdue Foods | 283.0 |
| 7 | Virginia Poultry Growers Cooperative Inc. | 270.0 |
| 8 | Kraft Heinz Company | 267.0 |
| 9 | Michigan Turkey Producers | 225.0 |
| 10 | West Liberty Foods LLC | 222.8 |
| 11 | Hain Pure Protein Corp. | 221.0 |
| 12 | Foster Farms | 216.7 |
| 13 | Cooper Farms | 215.0 |
| 14 | Dakota Provisions | 190.0 |
| 15 | Turkey Valley Farms | 174.0 |
| 16 | Prestage Farms | 147.0 |
| 17 | Norbest Ind. (Moroni Feed Company) | 109.0 |
| 18 | Zacky Farms, LLC | 83.0 |
| 19 | Northern Pride Turkey | 45.0 |
| 20 | White Water Processing Co. | 30.0 |
| 21 | Empire Kosher Poultry Inc. | 25.2 |
| 22 | Koch's Turkey Farms | 19.4 |
| 23 | Jaindl Turkey Sales Inc. | 11.0 |
| | | |
| | TOTAL | **7,302.1** |

## Primary Disease Challenges – Turkeys

This section details some of the main diseases of turkeys that result in therapeutic antimicrobial drug use (prevention, control or treatment of disease).

### Gangrenous Dermatitis

Gangrenous dermatitis in turkeys is also known as Clostridial Dermatitis and Cellulitis. According to Diseases of Poultry:

> Gangrenous dermatitis (GD) is a disease of chickens and turkeys caused by *Clostridium septicum*, *C. perfringens* type A, and *Staphylococcus aureus*. Characterized by a sudden onset of acute mortality, the primary lesion in affected birds is necrosis of the skin and subcutaneous tissue, usually involving the breast, abdomen, wing, or thigh. Because the mortality associated with the disease occurs quickly and the disease generally appears in close-to-market-age broilers and turkeys, economic losses are associated with any lost investment in production costs (chick/poult cost and feed consumed) and the loss of income related to the reduction in marketable pounds. … Clostridia are ubiquitous in the poultry house environment and can be isolated from soil, feces, dust, contaminated litter or feed, and intestinal contents. Staphylococci are also ubiquitous and common inhabitants of skin and mucous membranes of poultry and areas where poultry are hatched, reared, and processed. Despite the ubiquitous nature of Clostridia and Staphylococci, the presence of these organisms does not necessarily indicate a disease challenge. Other contributing factors … are thought to play a major role in the development of clinical disease within a flock (11).

According to reports of the turkey industry presented at the annual meetings of the United States Animal Health Association, GD ranked third and fourth of the disease-related issues that turkey production veterinarians faced in 2016 and 2017, respectively (15, 16). Antimicrobials are used for therapy in affected flocks.

### Bacterial Enteritis

Bacterial enteritis, also referred to as dysbacteriosis, occurs predominately in young turkeys. It is often seen secondary to enteric pathogens including viral or protozoal diseases. Direct damage from these primary pathogens to the intestines or changes to feed consumption practices as a result of a primary disease can result in the overgrowth of certain enteric bacteria (dysbacteriosis). Antimicrobial therapy is used in affected flocks to allow them to restore normal intestinal flora.

## Colibacillosis

According to Diseases of Poultry:

> Colibacillosis refers to any localized or systemic infection caused entirely or partly by avian pathogenic *Escherichia coli* (APEC), including colisepticemia, hemorrhagic septicemia, coligranuloma (Hjarre's disease), air sac disease (chronic Respiratory disease, CRD), swollen-head syndrome, venereal colibacillosis, coliform cellulitis (inflammatory or infectious process, IP), peritonitis, salpingitis, orchitis, osteomyelitis/ synovitis (including turkey osteomyelitis complex), panophthalmitis, omphalitis/yolk sac infection, and enteritis. Colibacillosis in mammals is most often a primary enteric or urinary tract disease, whereas colibacillosis in poultry is typically a localized or systemic disease occurring secondarily when host defenses have been impaired or overwhelmed by virulent *E. coli* strains (10).

According to reports of the turkey industry presented at the annual meetings of the United States Animal Health Association, the withdrawal of the NADA (New Animal Drug Application) for enrofloxacin in 2005 for use in poultry left the industry with limited adequate therapeutic responses to colibacillosis, which ranked second of the disease-related issues that turkey production veterinarians faced in 2016 and 2017 (15, 16). When determined to be clinically effective, antimicrobials are used for therapy in affected flocks.

## ORT

ORT (*Ornithobacterium rhinotracheale*) is a highly contagious respiratory disease caused by a Gram-negative pleomorphic rod-shaped bacterium**.** ORT was first confirmed in the U.S. from turkeys in 1993. Horizontal transmission (such as, bird-to-bird, contaminated people and equipment) by direct and in-direct contact is the primary route of spread. No commercial vaccine is approved.

According to reports of the turkey industry presented at the annual meetings of the United States Animal Health Association, ORT ranked fourth and third of the disease-related issues that turkey production veterinarians faced in 2016 and 2017, respectively (15, 16). Antimicrobials are used for therapy in affected flocks.

## Coccidiosis

According to Diseases of Poultry, "Coccidiosis is a disease of universal importance in poultry production. The protozoan parasites of the genus *Eimeria* multiply in the intestinal tract and cause tissue damage, with resulting interruption of feeding and digestive processes or nutrient absorption, dehydration, blood loss, loss of skin pigmentation and increased susceptibility to other disease agents. … Like many parasitic diseases, coccidiosis is largely a disease of young animals because immunity quickly develops after exposure and gives protection against later disease outbreaks. Unfortunately, no cross immunity exists between species of *Eimeria* in birds, and later outbreaks may be the result of different species. … Coccidiosis in turkeys is common but is often unrecognized because the lesions in turkeys are less spectacular than those in chickens. Several species infect turkeys, but only about 4 are economically important. Typical signs of coccidiosis in turkeys are watery or mucoid diarrhea, blood-streaked feces, ruffled feathers, anorexia, and general signs of illness" (12)

According to reports of the turkey industry presented at the annual meetings of the United States Animal Health Association, coccidiosis has moved up in the ranking of importance (from #13 to #6), in part because programs that raise animals without antimicrobials do not permit the use of ionophores (8, 9). Ionophores are considered antimicrobial drugs by the FDA, although they are considered non-medically important. They are coccidiostats and are used to reduce the infectious burden and subsequent morbidity and mortality linked to coccidiosis. Antimicrobials are also used for therapy in affected flocks.

## Hatchery Antimicrobials – Turkeys

The data presented in this Hatchery section represent 77-82% of annual U.S. turkey production by companies on the WATT Poultry USA list. This estimate of representativeness is based on total pounds liveweight produced annually by companies that submitted hatchery data. The numbers are derived from the annual WATT Poultry USA lists, as described in the Turkey Representativeness section. The data include antimicrobial administered *in ovo* and via subcutaneous injection in the day-old poult.

Table 20. Turkey hatchery antimicrobial data representativeness, shown as a range for each year of data in the report.

| | 2013 | 2014 | 2015 | 2016 | 2017 |
|---|---|---|---|---|---|
| **Based on Pounds Liveweight** | | | | | |
| Range of Representativeness | | | | | |
| Lower | 77% | 77% | 77% | 77% | 77% |
| Upper | 82% | 82% | 82% | 82% | 82% |

In the turkey industry, hatchery antimicrobials are generally given as a subcutaneous injection in the day-old poult. The main antimicrobial used in the hatchery was gentamicin given as a subcutaneous injection in the day-old poult, although some of the administration was *in ovo*. The label of gentamicin sulfate for use in turkeys states that it is recommended as an aid in the prevention of early mortality of 1 to 3 day-old turkeys associated with *Arizona paracolon* infections susceptible to gentamicin sulfate. The labeled dose is 1 mg gentamicin/poult.

The data collected in this project begin in 2013, which is after the extra-label prohibition on the use of cephalosporins went into effect (13). The label for ceftiofur sodium states that it is indicated for the control of early mortality, associated with *E. coli* organisms susceptible to ceftiofur, in day-old turkey poults. Administration is via subcutaneous injection in the neck region of day-old poults at the dosage of 0.17 to 0.5 mg ceftiofur/poult.

Finally, there was some use of penicillin between 2013 and 2017. When used, penicillin was always used in combination with gentamicin. The dose of penicillin was 8 mg per poult. The penicillin drug amounts are reported separately from the gentamicin amounts, even if the two were used together.

Summary: Data are based on the annual placement of between 180,000,000 and 192,000,000 turkey poults, depending on the year. The data include antimicrobial administered *in ovo* and via subcutaneous injection in the day-old poult. When using the metric of total grams of drug per 100,000 birds placed, gentamicin use in the hatchery decreased approximately 42% between 2013 and 2017, while ceftiofur use in the hatchery went to zero during the same time period for the birds represented in this dataset. Hatchery penicillin use declined approximately 9% between 2013 and 2017. The percentage of poults placed that received hatchery antimicrobials decreased from approximately 96% in 2013 to 41% in 2017.

**Medically Important Antimicrobials**

Figure 33. Gentamicin (aminoglycoside class) use in turkey hatcheries, 2013-2017. Total kilograms of gentamicin are shown by the bars (left Y-axis) and total grams/100,000 birds placed are shown by the line (right Y-axis).

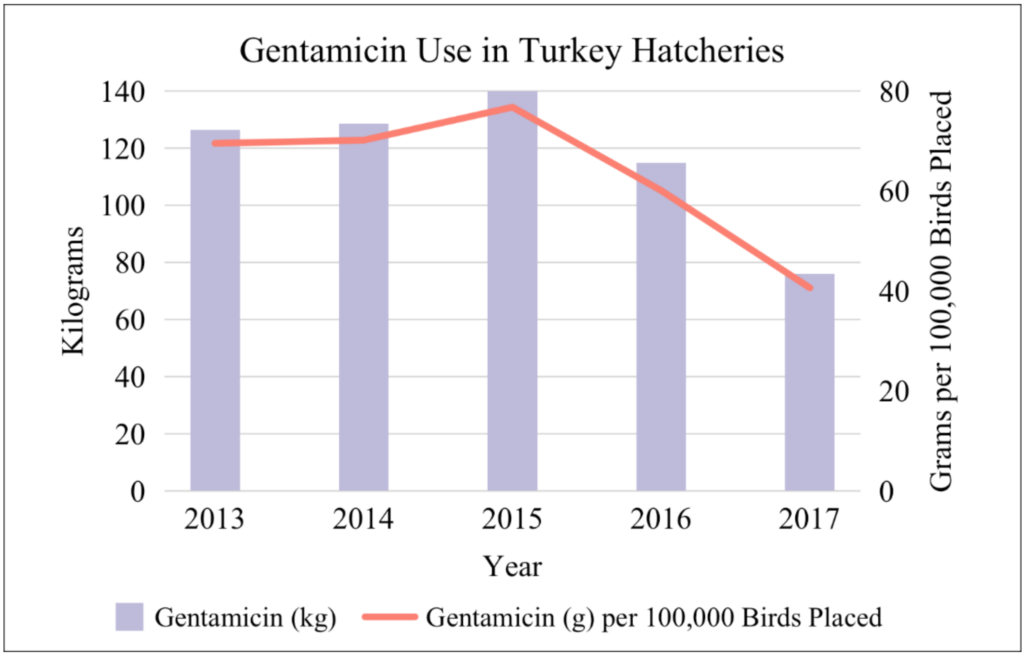



Figure 34. Ceftiofur (3rd generation cephalosporin class) use in turkey hatcheries, 2013-2017. Total kilograms of ceftiofur are shown by the bars (left Y-axis) and total grams/100,000 birds placed are shown by the line (right Y-axis).

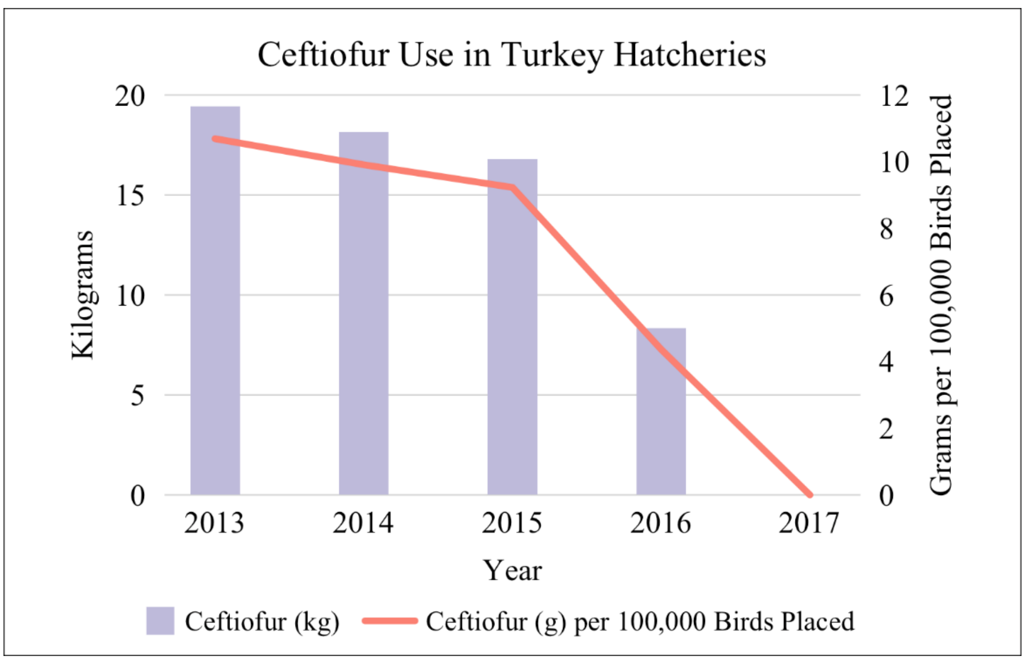


Figure 35. Penicillin (natural penicillin class) use in turkey hatcheries, 2013-2017. Total kilograms of penicillin are shown by the bars (left Y-axis) and total grams/100,000 birds placed are shown by the line (right Y-axis).

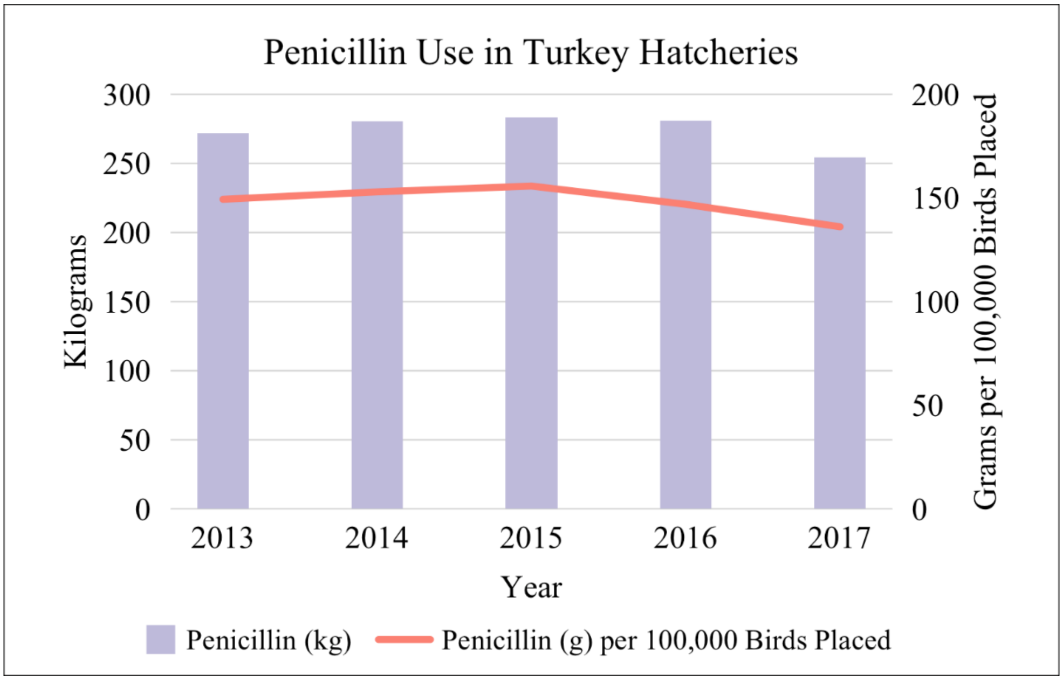


Figure 36. Turkey hatchery antimicrobial use during the years 2013-2017, as a percentage of total birds placed. The graphs show the percentage of birds placed that received gentamicin, ceftiofur, gentamicin and penicillin, or no antimicrobial.

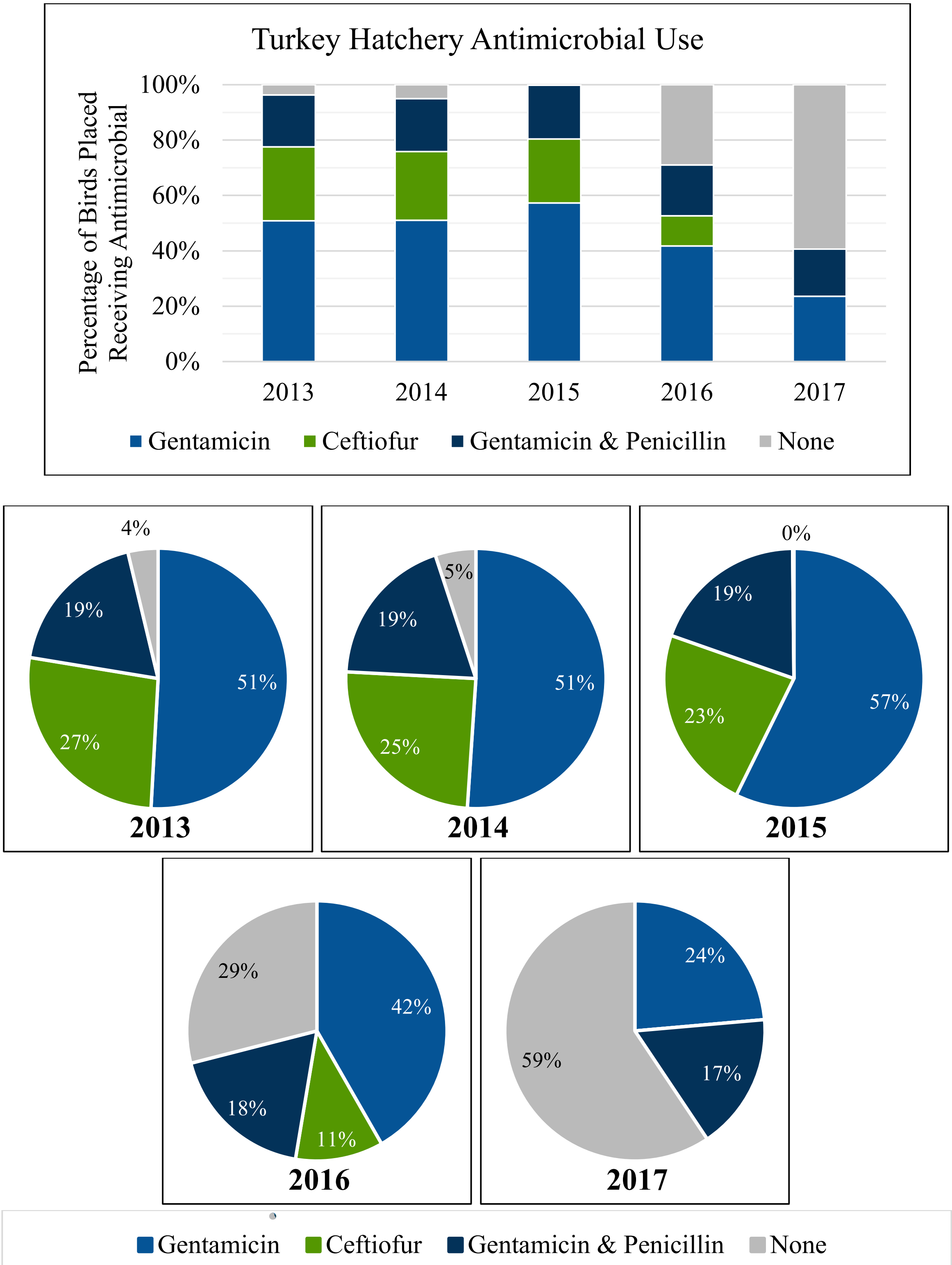


Table 21. Amount of injectable antimicrobial drug use in turkey hatcheries, 2013-2017. Data are reported by active ingredients within drug classes; all hatchery antimicrobials are medically important. Weights are reported as total kg of antimicrobial.

| Drug Class | Active Ingredient | Antimicrobial Usage in Turkey Hatcheries (kg of antimicrobial) | | | | |
|---|---|---|---|---|---|---|
| | | 2013 | 2014 | 2015 | 2016 | 2017 |
| **Medically Important** | | | | | | |
| Aminoglycosides | Gentamicin | 126.4 | 128.6 | 139.7 | 114.8 | 76.0 |
| 3rd Gen Cephalosporins | Ceftiofur | 19.4 | 18.2 | 16.8 | 8.3 | - |
| Natural Penicillins | Penicillin G | 271.5 | 280.3 | 283.5 | 280.7 | 254.5 |

Table 22. Amount of injectable antimicrobial drug use in turkey hatcheries, 2013-2017. Data are reported by active ingredients within drug classes; all hatchery antimicrobials are medically important. Weights are reported as total g of antimicrobial per 100,000 birds placed.

| Drug Class | Active Ingredient | Antimicrobial Usage in Turkey Hatcheries (g of antimicrobial per 100,000 birds placed) | | | | |
|---|---|---|---|---|---|---|
| | | 2013 | 2014 | 2015 | 2016 | 2017 |
| **Medically Important** | | | | | | |
| Aminoglycosides | Gentamicin | 69.5 | 70.2 | 76.8 | 60.1 | 40.6 |
| 3rd Gen Cephalosporins | Ceftiofur | 10.7 | 9.9 | 9.2 | 4.4 | - |
| Natural Penicillins | Penicillin G | 149.3 | 152.9 | 155.7 | 146.9 | 136.1 |

## Ionophores – Turkeys

**Ionophores are Not Medically Important Antimicrobials.** Ionophores are in-feed antimicrobials but are presented in their own section because their principal use is to prevent disease associated with coccidial parasites.

The data presented in this Ionophore section represent 77-82% of annual U.S. turkey production by companies on the WATT Poultry USA list. This estimate of representativeness is based on total pounds liveweight produced annually by companies that submitted ionophore data. The numbers are derived from the annual WATT Poultry USA lists, as described in the Turkey Representativeness section.

Table 23. Turkey ionophore data representativeness, shown as a range for each year of data in the report.

| | 2013 | 2014 | 2015 | 2016 | 2017 |
|---|---|---|---|---|---|
| **Based on Pounds Liveweight** | | | | | |
| Range of Representativeness | | | | | |
| Lower | 77% | 77% | 77% | 77% | 77% |
| Upper | 82% | 82% | 82% | 82% | 82% |

The data in this Ionophore section include the two ionophores currently approved for use in turkeys: lasalocid and monensin. As described in the Primary Disease Challenges section, coccidiosis is an important disease in turkey production. It can cause clinical illness in the birds and can also predispose the birds for other disease conditions that necessitate antimicrobial therapy. Ionophores are considered antimicrobial drugs by the U.S. FDA (although are not considered antimicrobials in most other countries).

The FDA Annual Sales Report of 2017 states: "Ionophores … lack utility in human medicine and their use in animals, primarily as coccidiostats, does not pose cross resistance concerns; thus, they do not have the same public health risks as medically important antimicrobials." (6).

Summary: Data are based on the annual slaughter of between 155,000,000 and 170,000,000 birds, depending on the year. When using the metric of total grams of drug per 1,000,000 pounds liveweight produced, there was an approximate 35% reduction of lasalocid use between 2013 and 2017; monensin use increased approximately 38% between 2013 and 2014 and then remained steady through 2017.

Figure 37. Lasalocid use in turkey feed, 2013-2017. Total kilograms of lasalocid are shown by the bars (left Y-axis) and total grams/1,000,000 pounds liveweight are shown by the line (right Y-axis).

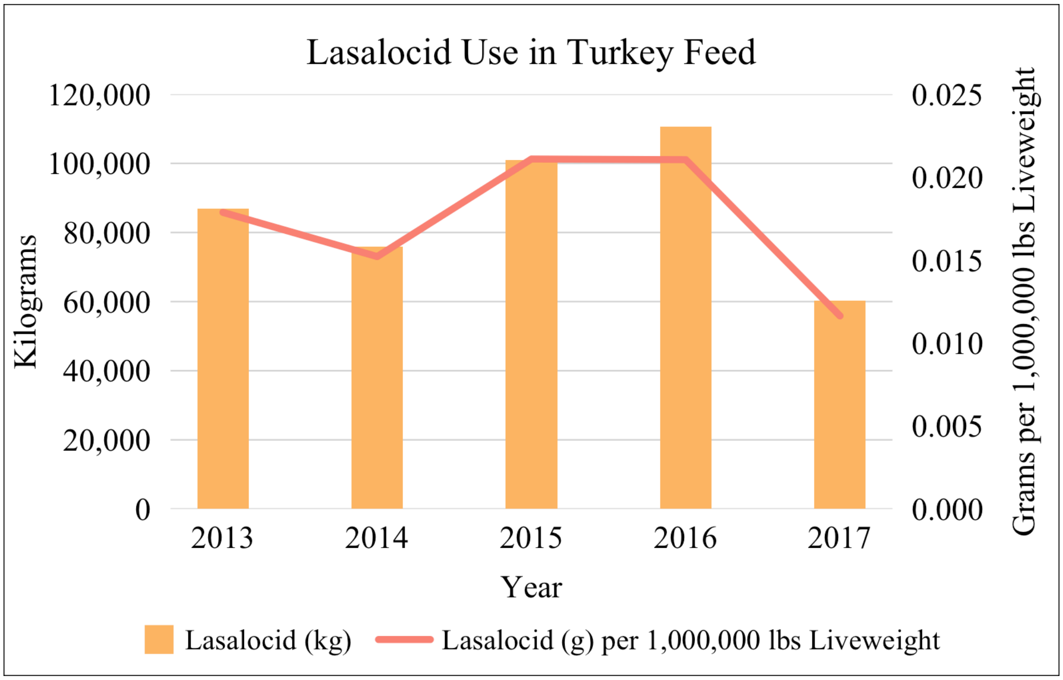



Figure 38. Monensin use in turkey feed, 2013-2017. Total kilograms of monensin are shown by the bars (left Y-axis) and total grams/1,000,000 pounds liveweight are shown in the line (right Y-axis).

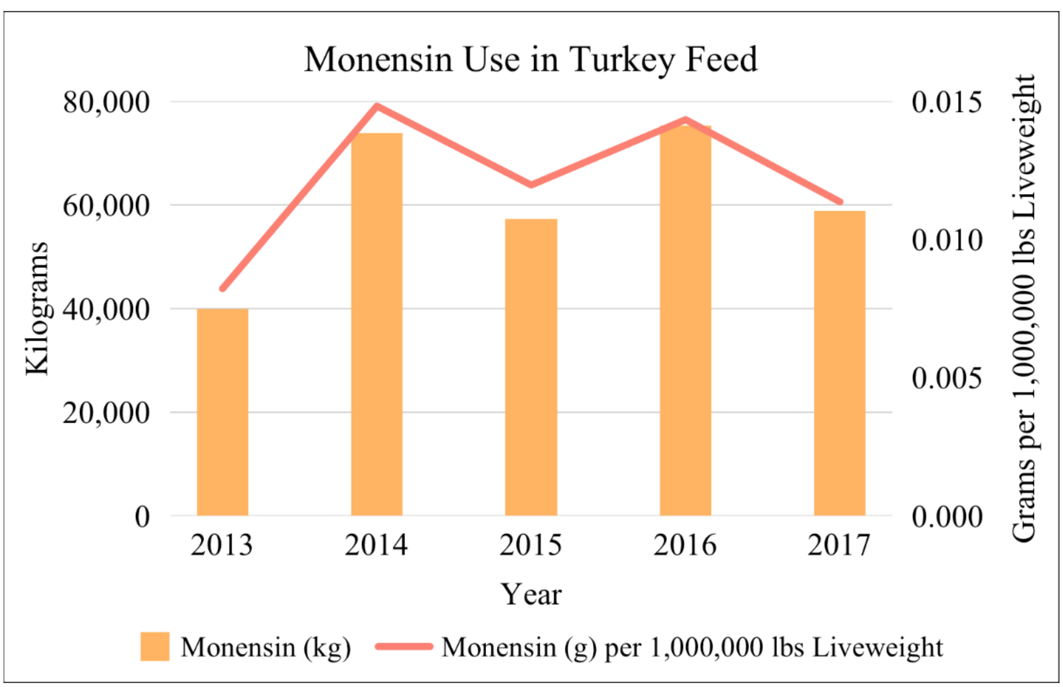


Table 24. Amount of ionophore use in turkey feed, 2013-2017. Data are reported by active ingredient; all ionophores are not medically important. Weights are reported as kg of antimicrobial.

| | | Antimicrobial Usage in Turkey Feed (kg of antimicrobial) | | | | |
|---|---|---|---|---|---|---|
| **Drug Class** | **Active Ingredient** | **2013** | **2014** | **2015** | **2016** | **2017** |
| **Not Medically Important** | | | | | | |
| Ionophores | Lasalocid | 86,846.4 | 75,876.4 | 100,913.9 | 110,550.3 | 60,268.6 |
| | Monensin | 39,933.3 | 73,930.4 | 57,248.0 | 75,271.0 | 58,837.8 |

Table 25. Amount of ionophore use in turkey feed, 2013-2017. Data are reported by active ingredient; all ionophores are not medically important. Weights are reported as g of antimicrobial per 1,000,000 pounds liveweight produced.

| | | Antimicrobial Usage in Turkey Feed (g of antimicrobial per million lbs liveweight) | | | | |
|---|---|---|---|---|---|---|
| **Drug Class** | **Active Ingredient** | **2013** | **2014** | **2015** | **2016** | **2017** |
| **Not Medically Important** | | | | | | |
| Ionophores | Lasalocid | 17,878.9 | 15,214.1 | 21,097.6 | 21,054.9 | 11,638.4 |
| | Monensin | 8,221.0 | 14,824.0 | 11,968.6 | 14,335.8 | 11,362.1 |

## In-Feed Antimicrobials – Turkeys

The data that are presented in this In-Feed Antimicrobials section represent 77-82% of annual U.S. turkey production by companies on the WATT Poultry USA list. This estimate of representativeness is based on total pounds liveweight produced annually by companies that submitted in-feed data. The numbers are derived from the annual WATT Poultry USA lists, as described in the Turkey Representativeness section.

Table 26. Turkey in-feed antimicrobial data representativeness, shown as a range for each year of data in the report.

| | 2013 | 2014 | 2015 | 2016 | 2017 |
|---|---|---|---|---|---|
| **Based on Pounds Liveweight** | | | | | |
| Range of Representativeness | | | | | |
| Lower | 77% | 77% | 77% | 77% | 77% |
| Upper | 82% | 82% | 82% | 82% | 82% |

### Changing Approved Labels

The data in this Feed Antimicrobials section include antimicrobials administered in the feed for any purpose, including both production (increased weight gain/improved feed efficiency) and therapeutic (prevention, control or treatment of disease) uses. Generally, antimicrobials administered in the feed are not used as often as water-soluble antimicrobials for disease therapy because sick birds may stop eating but often continue to drink water (14). Regardless, many of the antimicrobials used in feed have drug label claims for disease treatment, control or both.

With the changes to the VFD rule followed by the implementation in January 2017 of the label changes for in-feed antimicrobials described in GFI #213, the antimicrobials that could be used in feed changed. Some of these changes are reflected in the data presented below. Specifically, the full implementation of GFI #213 was developed by FDA to "eliminate production uses of medically important antimicrobials (i.e., antimicrobials important for treating human disease) and to bring all remaining therapeutic uses of these drugs under the oversight of licensed veterinarians." The list of antimicrobials that are currently considered by the FDA to be medically important are located in Appendix A of GFI #152 (3).

Below are some specific examples of label changes to key antimicrobials used in turkey production.

Chlortetracycline and oxytetracycline both have labels for feed use in turkeys. Prior to January 1, 2017, the labeled indications for these antimicrobial drugs included: 1) Increased rate of weight gain and improved feed efficiency at 10-50 grams/ton of feed, 2) Control of infectious synovitis caused by *Mycoplasma synoviae* susceptible to the drug at 200 grams/ton of feed, 3) Control of hexamitiasis caused by *Hexamita meleagridis* susceptible to the drug at 400 grams/ton of feed, 4) Control of chronic respiratory disease (CRD) and air sac infection caused by *Mycoplasma gallisepticum* and *Escherichia coli* susceptible to the drug at 200-400 grams/ton of feed and 5) Reduction of mortality due to paratyphoid caused by *Salmonella typhimurium* susceptible to the drug at 400 grams/ton of feed. As of January 1, 2017, the weight gain/feed efficiency label claim was withdrawn by the drug sponsor(s), so the only remaining indications for use on the label are the disease control claims.

Virginiamycin is a streptogramin antimicrobial that was used in the feed of turkeys. Prior to January 2017, the only labeled indication was for: 1) Increased rate of weight gain and improved feed efficiency at 10-20 grams/ton of feed. Unlike in broilers, there was no disease prevention claim. As of January 1, 2017, the weight gain/feed efficiency label claim was voluntarily withdrawn by the drug sponsor(s), and consequently there is no longer a label claim for virginiamycin use in turkey feed.

Tylosin is a macrolide antimicrobial drug that was used in the feed of turkeys. Prior to January 2017, the labeled indications included: 1) Increased rate of weight gain and improved feed efficiency at 4-50 grams/ton of feed, and 2) Control of chronic respiratory disease associated with *Mycoplasma* at 800-1,000 grams/ton of feed. As of January 1, 2017, all tylosin label claims for feed uses in turkeys were voluntarily withdrawn by the drug sponsor.

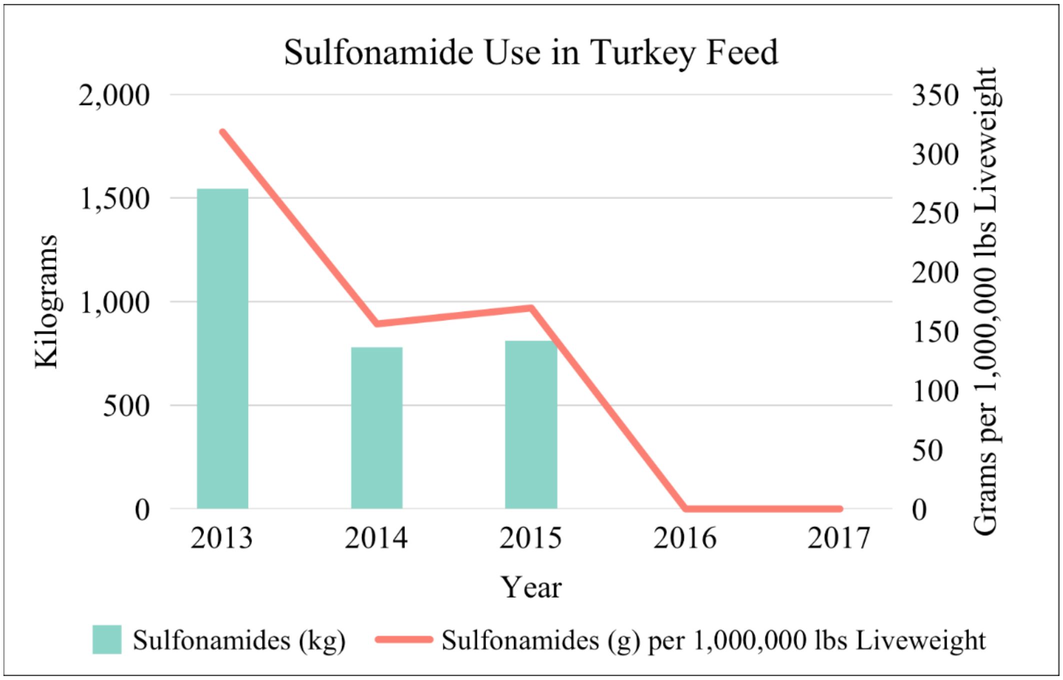
RofenAid, which is a combination drug consisting of sulfadimethoxine and ormetoprim, is used in the feed of turkeys for the prevention of coccidiosis caused by all *Eimeria*, and bacterial infections due to *Pasteurella multocida* (fowl cholera). Each pound of premix contains 113.5 g of sulfadimethoxine and 68.1 g of ormetoprim and is mixed into one ton of feed. The use of this product was placed into its own group in the report because of the few combination products available for use in poultry. The sulfonamide and diaminopyrimidine components are graphed separately.

### In-Feed Antimicrobial Use

Summary: Data are based on the annual slaughter of between 155,000,000 and 170,000,000 birds, depending on the year. When using the metric of total grams of drug per 1,000,000 pounds liveweight produced, there was an approximate 67% reduction of tetracycline use between 2013 and 2017. In-feed bacitracin decreased by approximately 22% between 2013 and 2016. Virginiamycin use went to 0 in 2017 due to the withdrawal of turkeys from all marketed drug product labels. No tylosin use in the feed of turkeys was reported for 2013 to 2016, and there are no longer any approved uses of in-feed tylosin in turkeys. Bambermycins, an NMI antimicrobial labeled for production purposes, increased in use between 2013 and 2017.

**Medically Important Antimicrobials**

Figure 39. Sulfadimethoxine (sulfonamide class) and ormetoprim (diaminopyrimidine class) use in turkey feed, 2013-2017. These two antimicrobials are sold as a combined drug, RofenAid. Amounts of each active ingredient are shown in separate graphs. Each pound of product (added to one ton of feed) contains 113.5g sulfadimethoxine and 68.1g ormetoprim. Total kilograms are shown by the bars (left Y-axis) and total grams/1,000,000 pounds liveweight are shown in the line (right Y-axis).



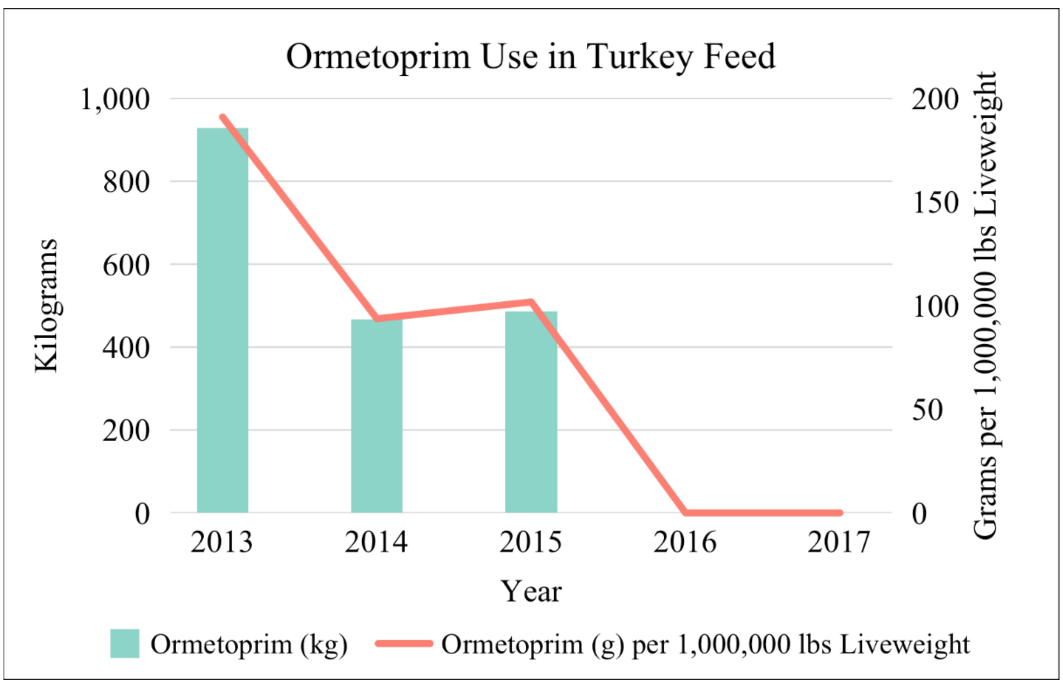



Figure 40. Virginiamycin (streptogramin class) use in turkey feed, 2013-2017. Total kilograms of virginiamycin are shown by the bars (left Y-axis) and total grams/1,000,000 pounds liveweight are shown by the line (right Y-axis).

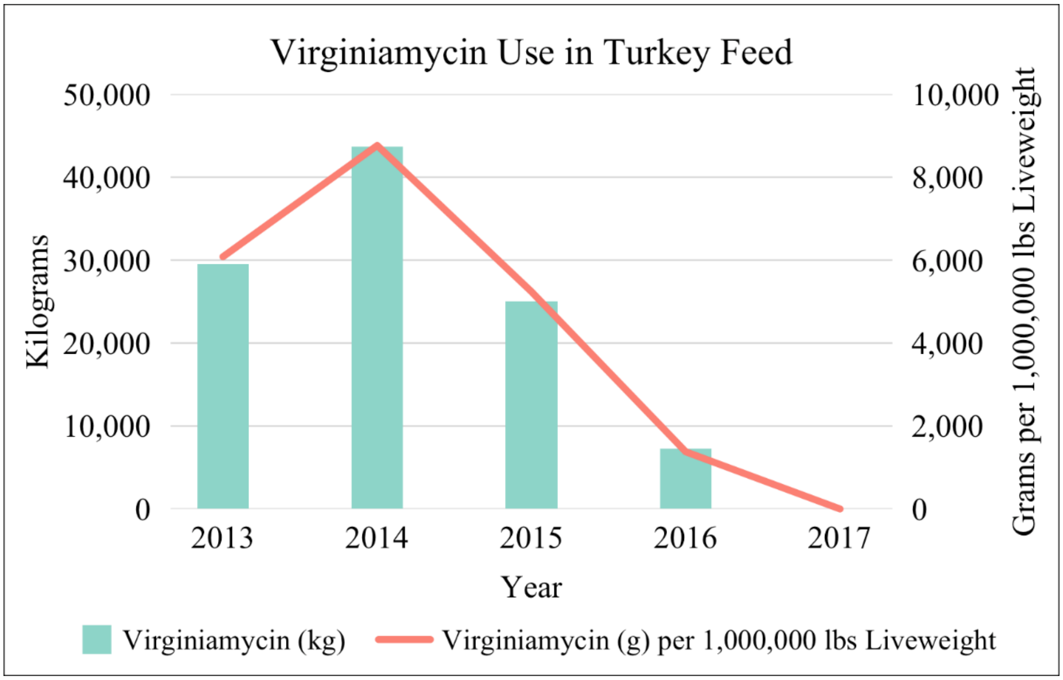
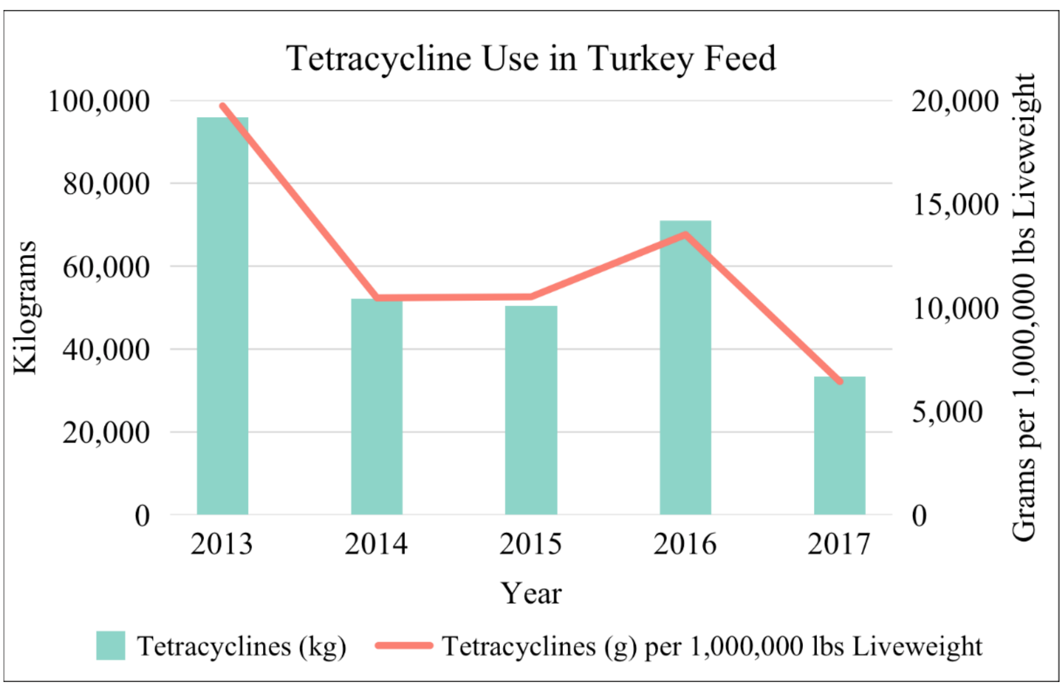



Figure 41. Tetracycline (tetracycline class) use in turkey feed, 2013-2017. Total kilograms of tetracycline are shown by the bars (left Y-axis) and total grams/1,000,000 pounds liveweight are shown by the line (right Y-axis). Specific active ingredients included in this total are chlortetracycline and oxytetracycline.



## Not Medically Important Antimicrobials

Figure 42. Bambermycins (glycolipids class) use in turkey feed, 2013-2017. Total kilograms of bambermycins are shown by the bars (left Y-axis) and total grams/1,000,000 pounds liveweight are shown by the line (right Y-axis).

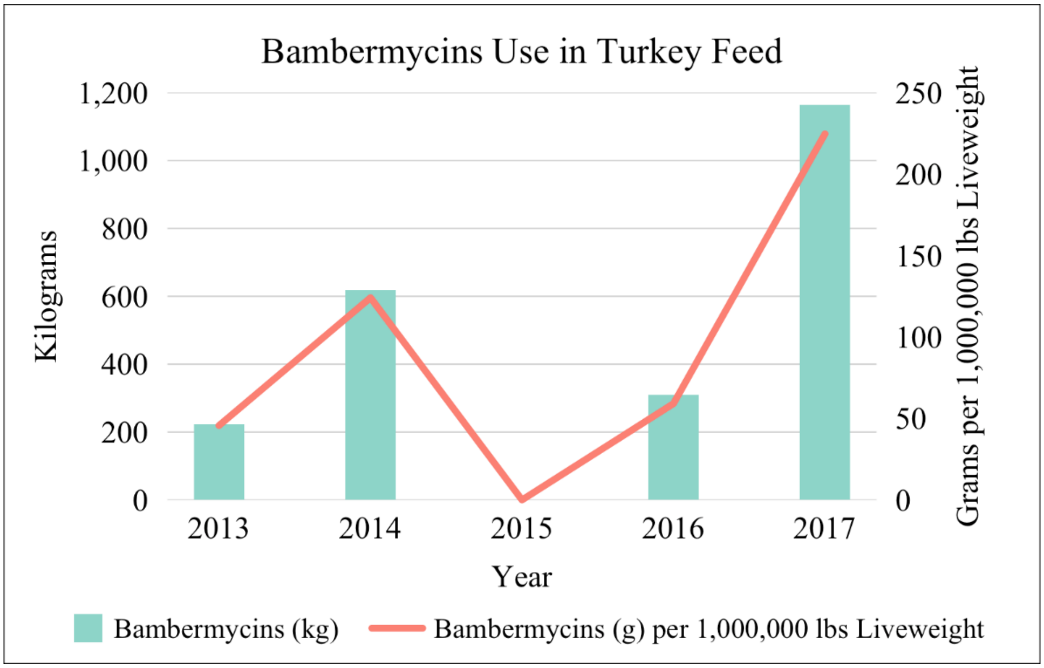



Figure 43. Bacitracin (polypeptide class) use in turkey feed, 2013-2017. Total kilograms of bacitracin are shown by the bars (left Y-axis) and total grams/1,000,000 pounds liveweight are shown by the line (right Y-axis).

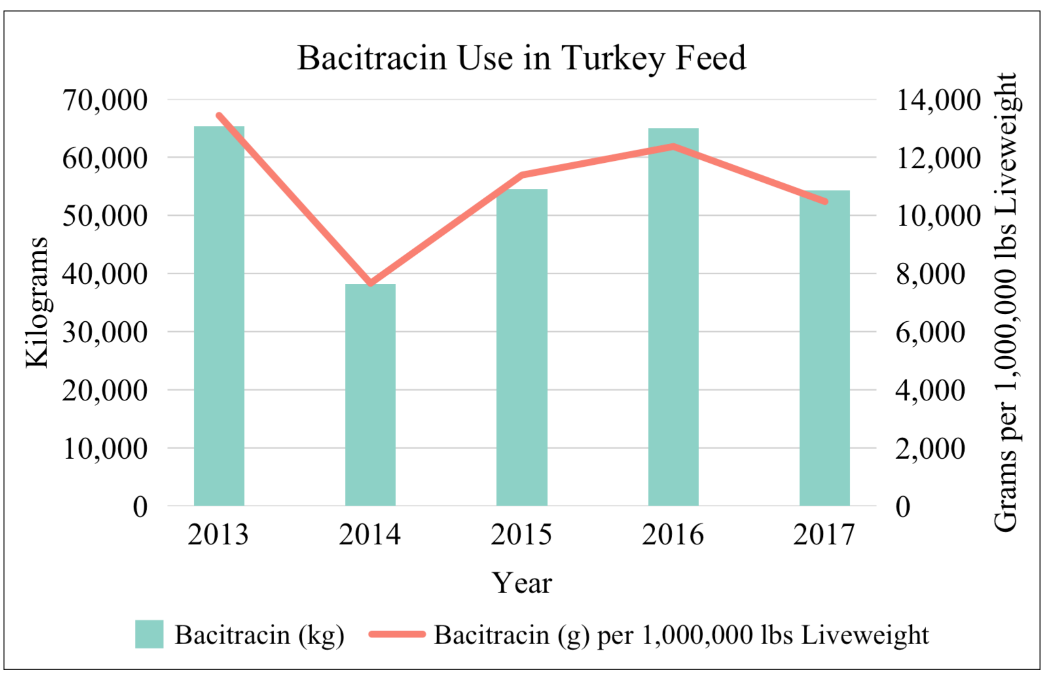


Table 27. Amount of antimicrobial drug use in turkey feed, 2013-2017. Data are reported by active ingredients within drug classes and are divided into medically important and not medically important. Weights are reported as total kg of antimicrobial.

| Drug Class | Active Ingredient | Antimicrobial Usage in Turkey Feed (kg of antimicrobial) | | | | |
|---|---|---|---|---|---|---|
| | | 2013 | 2014 | 2015 | 2016 | 2017 |
| **Medically Important** | | | | | | |
| Diaminopyrimidines | Ormetoprim | 927.5 | 467.2 | 486.8 | - | - |
| Streptogramins | Virginiamycin | 29,544.0 | 43,710.7 | 25,057.4 | 7,239.3 | - |
| Sulfonamides | Sulfadimethoxine | 1,545.9 | 778.7 | 811.3 | - | - |
| Tetracyclines | Tetracyclines[1] | 95,818.0 | 52,215.4 | 50,327.6 | 70,994.0 | 33,316.3 |
| **Not Medically Important** | | | | | | |
| Glycolipids | Bambermycins | 222.0 | 619.1 | - | 310.4 | 1,163.5 |
| Polypeptides | Bacitracin | 65,268.4 | 38,212.2 | 54,458.4 | 64,941.9 | 54,245.3 |

[1]Includes chlortetracycline and oxytetracycline; as stated in the FDA Sales and Distribution Report from 2017 (6), "Antimicrobial class includes drugs of different molecular weights."

Table 28. Amount of antimicrobial drug use in turkey feed, 2013-2017. Data are reported by active ingredients within drug classes and are divided into medically important and not medically important. Weights are reported as g of antimicrobial per 1,000,000 pounds liveweight produced.

| | | Antimicrobial Usage in Turkey Feed (g of antimicrobial per million lbs liveweight) | | | | |
|---|---|---|---|---|---|---|
| **Drug Class** | **Active Ingredient** | **2013** | **2014** | **2015** | **2016** | **2017** |
| **Medically Important** | | | | | | |
| Diaminopyrimidines | Ormetoprim | 190.9 | 93.7 | 101.8 | - | - |
| Streptogramins | Virginiamycin | 6,082.2 | 8,764.5 | 5,238.6 | 1,378.8 | - |
| Sulfonamides | Sulfadimethoxine | 318.2 | 156.1 | 169.6 | - | - |
| Tetracyclines | Tetracyclines[1] | 19,725.8 | 10,469.8 | 10,521.8 | 13,521.2 | 6,433.7 |
| **Not Medically Important** | | | | | | |
| Glycolipids | Bambermycins | 45.7 | 124.1 | - | 59.1 | 224.7 |
| Polypeptides | Bacitracin | 13,436.7 | 7,662.0 | 11,385.4 | 12,368.6 | 10,475.2 |

[1]Includes chlortetracycline and oxytetracycline

## Water-Soluble Antimicrobials – Turkeys

The data that are presented in this Water-Soluble Antimicrobials section represent 70-82% of annual U.S. turkey production by companies on the WATT Poultry USA list; representativeness ranges from 70-75% in 2013 to 77-82% in 2017. This estimate of representativeness is based on total pounds liveweight produced annually by companies that submitted water-soluble data. The numbers are derived from the annual WATT Poultry USA lists, as described in the Turkey Representativeness section.

Table 29. Turkey water-soluble antimicrobial data representativeness, shown as a range for each year of data in the report.

| | 2013 | 2014 | 2015 | 2016 | 2017 |
|---|---|---|---|---|---|
| **Based on Pounds Liveweight** | | | | | |
| Range of Representativeness | | | | | |
| Lower | 70% | 73% | 77% | 77% | 77% |
| Upper | 75% | 78% | 82% | 82% | 82% |

### Veterinary Oversight

As described previously, U.S. FDA GFI #209 and #213 brought therapeutic uses of medically important antimicrobials in water of food-producing animals under veterinary supervision by changing marketing status from over-the-counter (OTC) to prescription (Rx) (1, 2). Label claim changes for water-soluble antimicrobials described in GFI #213 took full effect in January 2017. As was stated previously, antimicrobials used in feed are not used as often as water-soluble antimicrobials for therapeutic purposes because sick birds may stop eating but often continue to drink water (14). Further, therapeutic intervention through the water can often be accomplished more quickly through the water than the feed.

The data in this Water-Soluble section include antimicrobials that were administered therapeutically for disease. For many companies, some flock-level data were available to detail the ways in which these antimicrobials were administered, including the most common ages at therapy for specific diseases, the dose and the duration of therapy.

### Water Soluble Antimicrobial Use

Summary: Data are based on the annual slaughter of between 140,000,000 and 170,000,000 birds, depending on the year. All of the water soluble medically important antimicrobials were reduced in their use over the 5-year data collection period. When using the metric of total grams of drug per 1,000,000 pounds liveweight produced, water-soluble penicillin use decreased approximately 42% between 2013 and 2017 and 26% between 2016 and 2017. Water-soluble tetracycline use decreased approximately 28% between 2013 and 2017 and 15% between 2016 and 2017. Water-soluble lincomycin use decreased approximately 46% between 2013 and 2017. Water-soluble neomycin use decreased approximately 49% between 2013 and 2017 and water-soluble erythromycin use decreased approximately 65% over the same period.

**Medically Important Antimicrobials**

Figure 44. Gentamicin (aminoglycoside class) use in turkey water, 2013-2017. Total kilograms of Gentamicin Soluble are shown by the bars (left Y-axis) and total grams/1,000,000 pounds liveweight are shown by the line (right Y-axis).

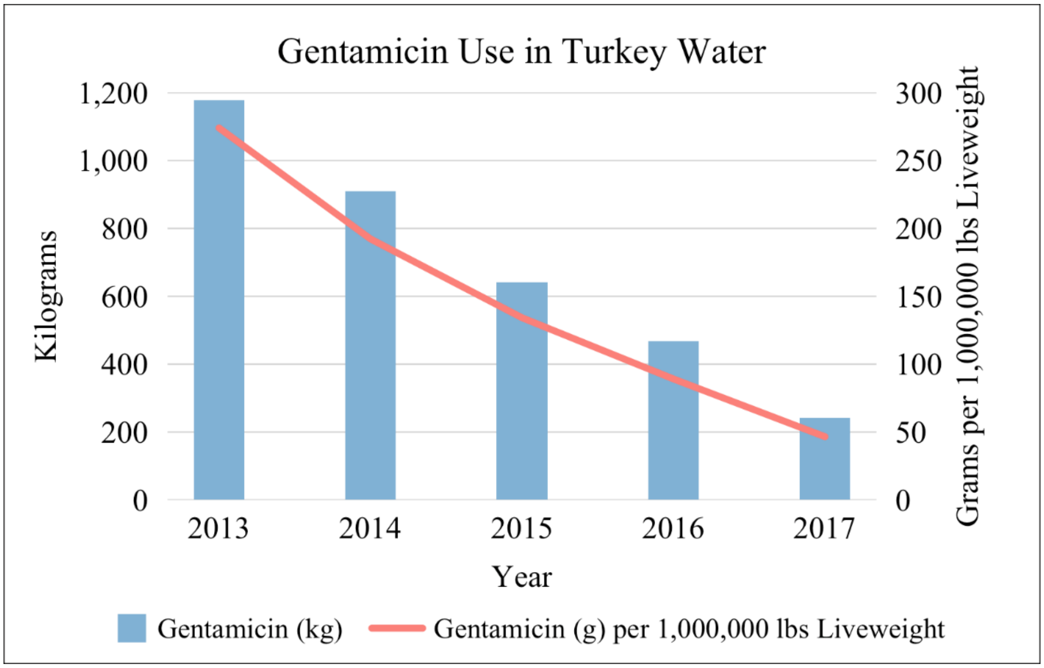



Figure 45. Neomycin (aminoglycoside class) use in turkey water, 2013-2017. Total kilograms of neomycin are shown by the bars (left Y-axis) and total grams/1,000,000 pounds liveweight are shown by the line (right Y-axis).

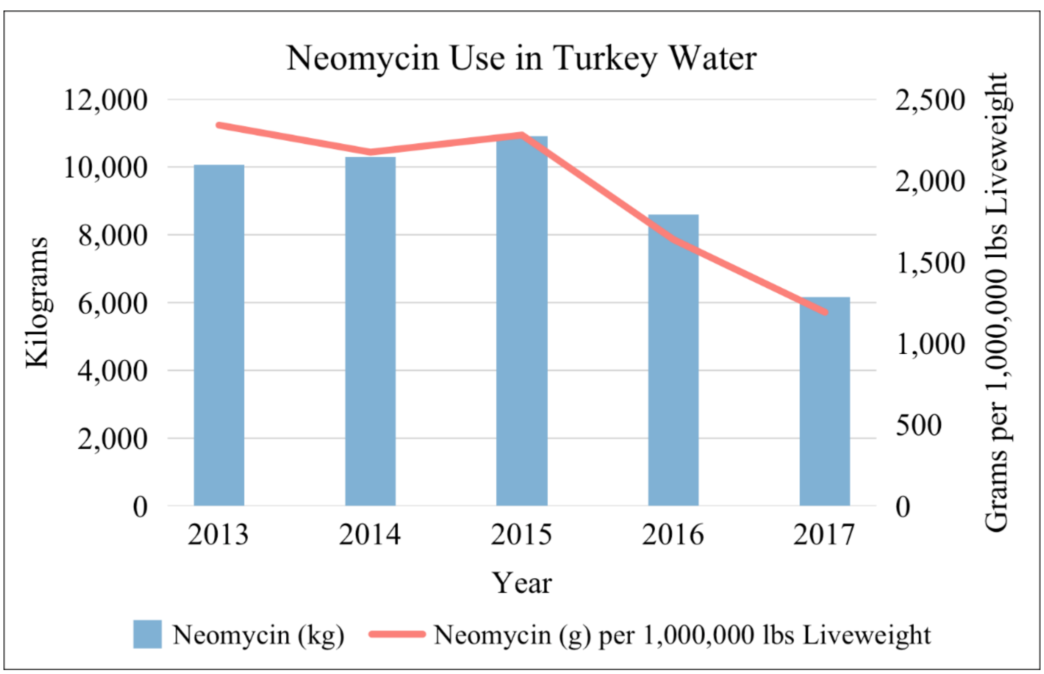


Figure 46. Spectinomycin (aminoglycoside class) use in turkey water, 2013-2017. Total kilograms of spectinomycin are shown by the bars (left Y-axis) and total grams/1,000,000 pounds liveweight are shown by the line (right Y-axis).

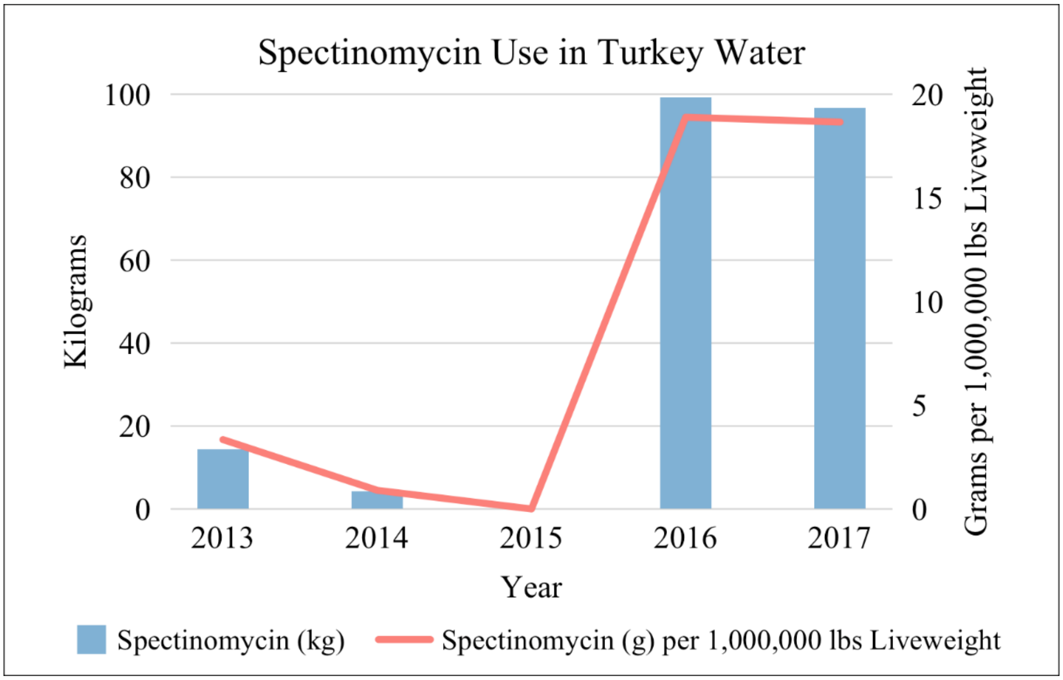



Figure 47. Florfenicol (amphenicol class) use in turkey water, 2013-2017. Total kilograms of florfenicol are shown by the bars (left Y-axis) and total grams/1,000,000 pounds liveweight are shown by the line (right Y-axis).

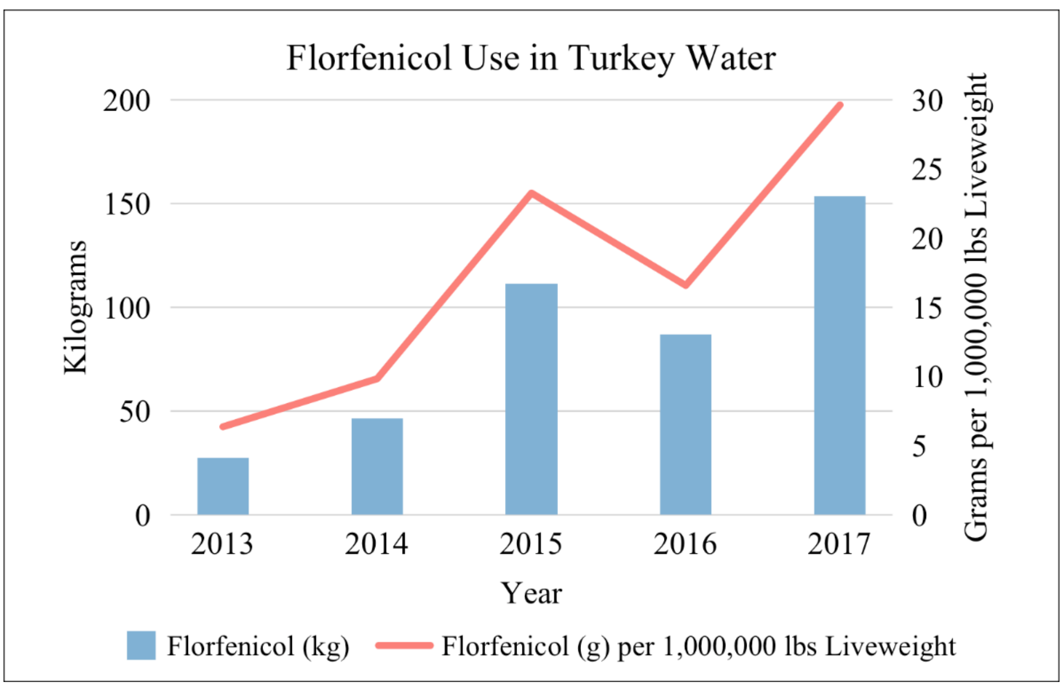


Figure 48. Lincomycin (lincosamide class) use in turkey water, 2013-2017. Total kilograms of lincomycin are shown by the bars (left Y-axis) and total grams/1,000,000 pounds liveweight are shown by the line (right Y-axis).

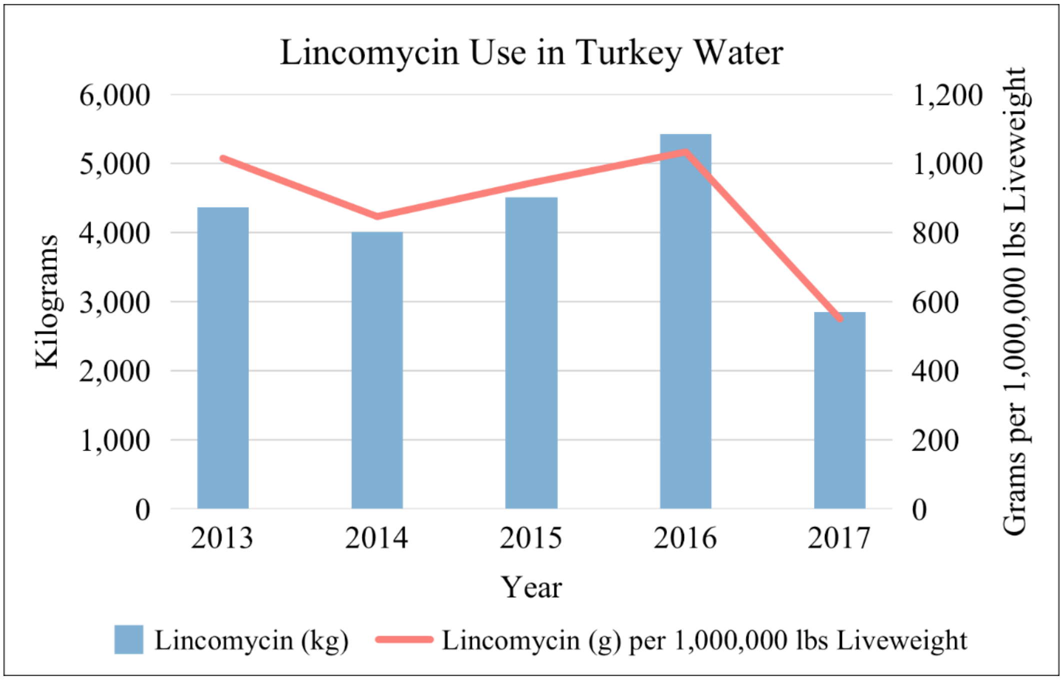



Figure 49. Erythromycin (macrolide class) use in turkey water, 2013-2017. Total kilograms of erythromycin are shown by the bars (left Y-axis) and total grams/1,000,000 pounds liveweight are shown by the line (right Y-axis).

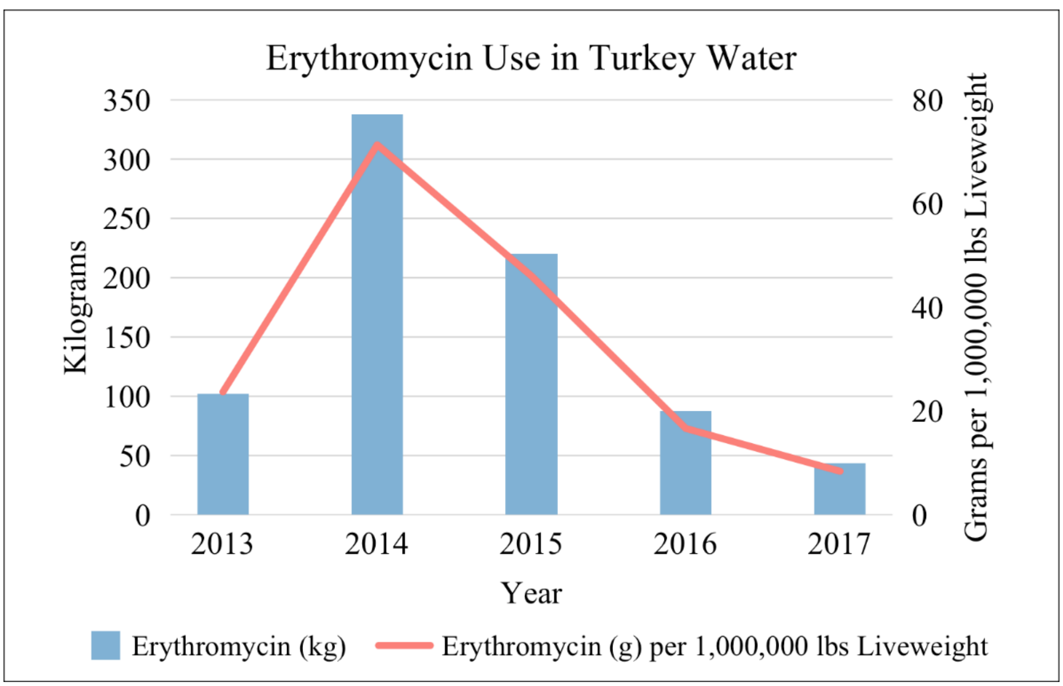


Figure 50. Tylosin (macrolide class) use in turkey water, 2013-2017. Total kilograms of tylosin are shown by the bars (left Y-axis) and total grams/1,000,000 pounds liveweight are shown by the line (right Y-axis).

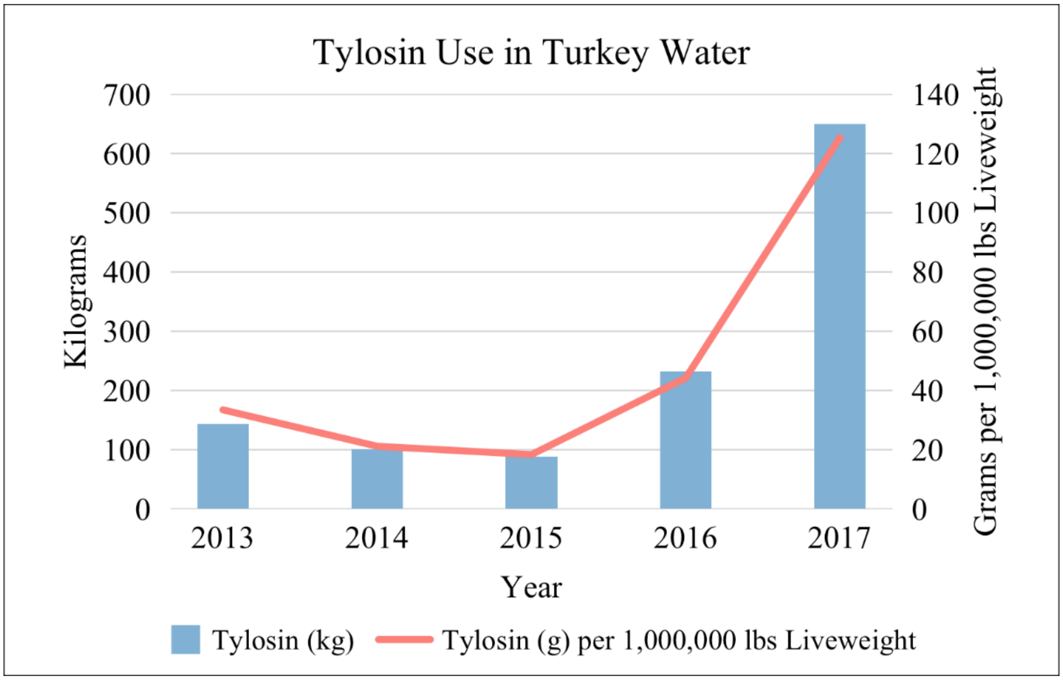



Figure 51. Penicillin (natural penicillin class) use in turkey water, 2013-2017. Total kilograms of penicillin are shown by the bars (left Y-axis) and total grams/1,000,000 pounds liveweight are shown by the line (right Y-axis).

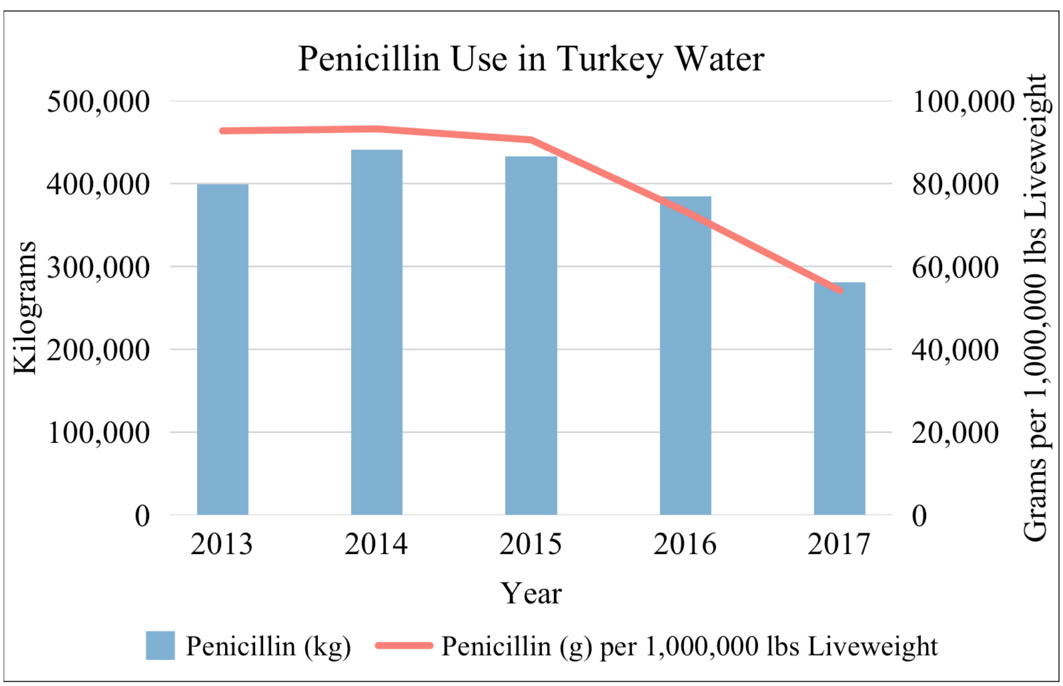
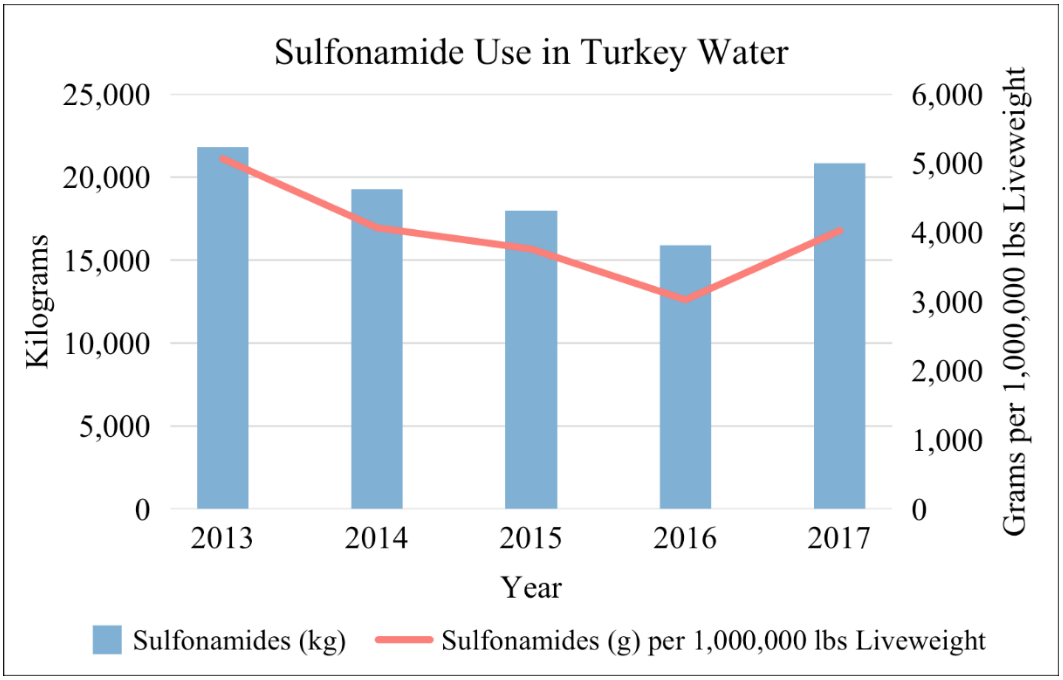
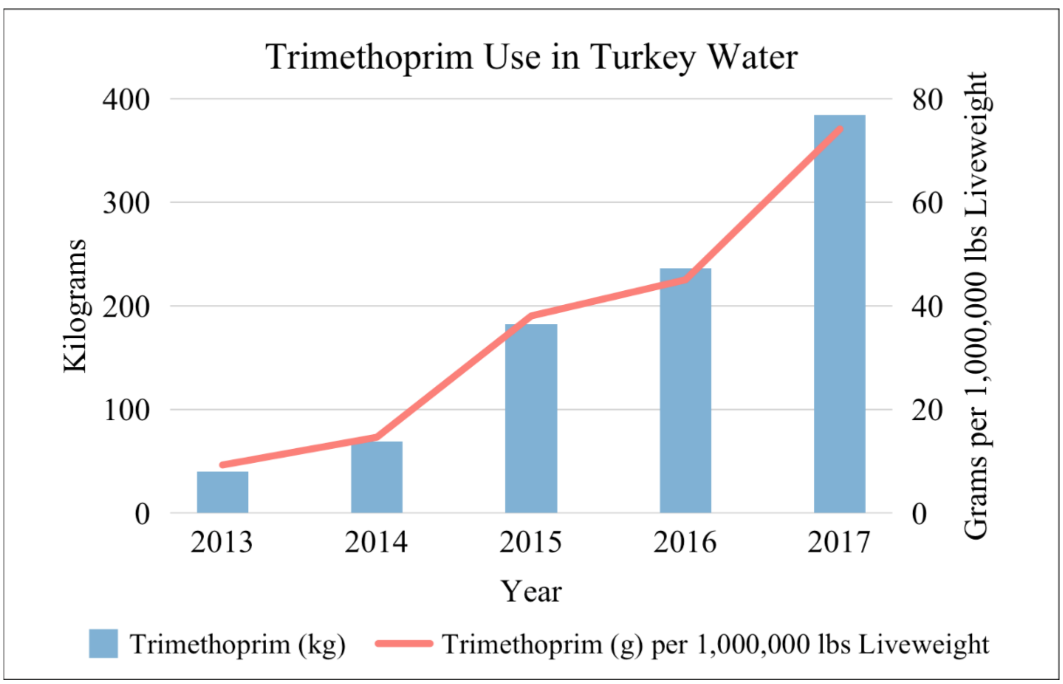
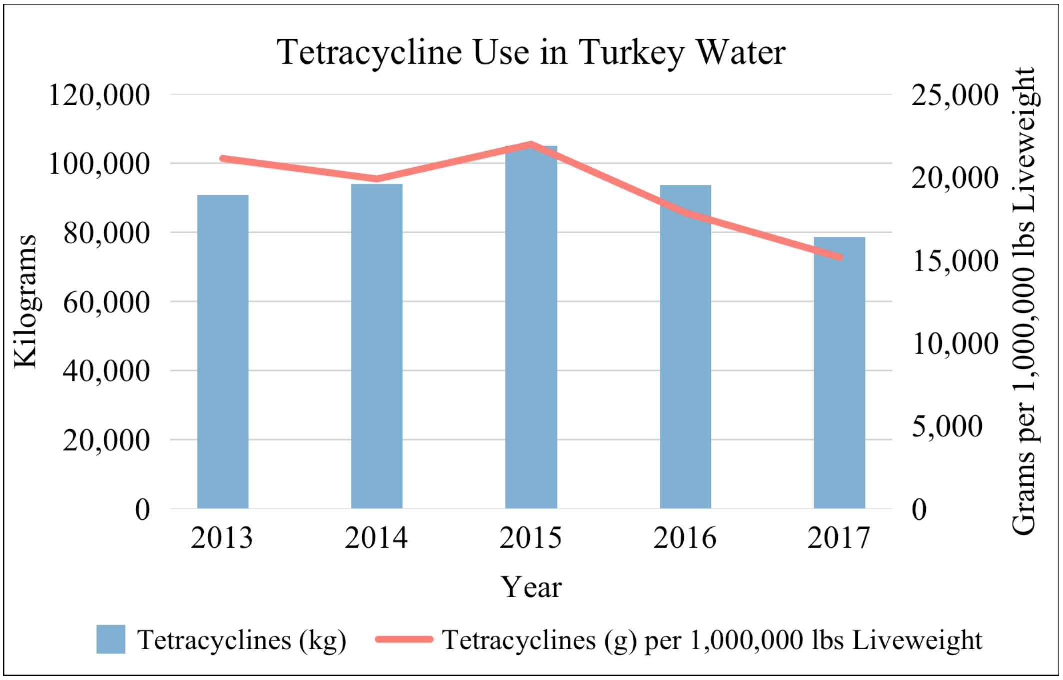


Figure 52. Sulfonamide use in turkey water, 2013-2017. Total kilograms of sulfonamide are shown by the bars (left Y-axis) and total grams/1,000,000 pounds liveweight are shown in the line (right Y-axis). This total includes potentiated sulfonamide use; the formulation for the potentiated sulfonamide is 333 mg sulfadiazine and 67 mg of trimethoprim (diaminopyrimidine class) per mL. Total kilograms of trimethoprim and total grams/1,000,000 pounds liveweight are also shown below. Other active ingredients included in the sulfonamide total include sulfadimethoxine, sulfamerazine, sulfamethazine, and sulfaquinoxaline.



<u>Figure 53</u>. Tetracycline (tetracycline class) use in turkey water, 2013-2017. Total kilograms of tetracycline are shown by the bars (left Y-axis) and total grams/1,000,000 pounds liveweight are shown by the line (right Y-axis). Specific active ingredients included in this total are tetracycline, chlortetracycline and oxytetracycline.



**Not Medically Important Antimicrobials**

Figure 54. Tiamulin (pleuromutilin class) use in turkey water, 2013-2017. Total kilograms of tiamulin are shown in the columns (left Y-axis) and total grams/1,000,000 pounds liveweight are shown in the line (right Y-axis).

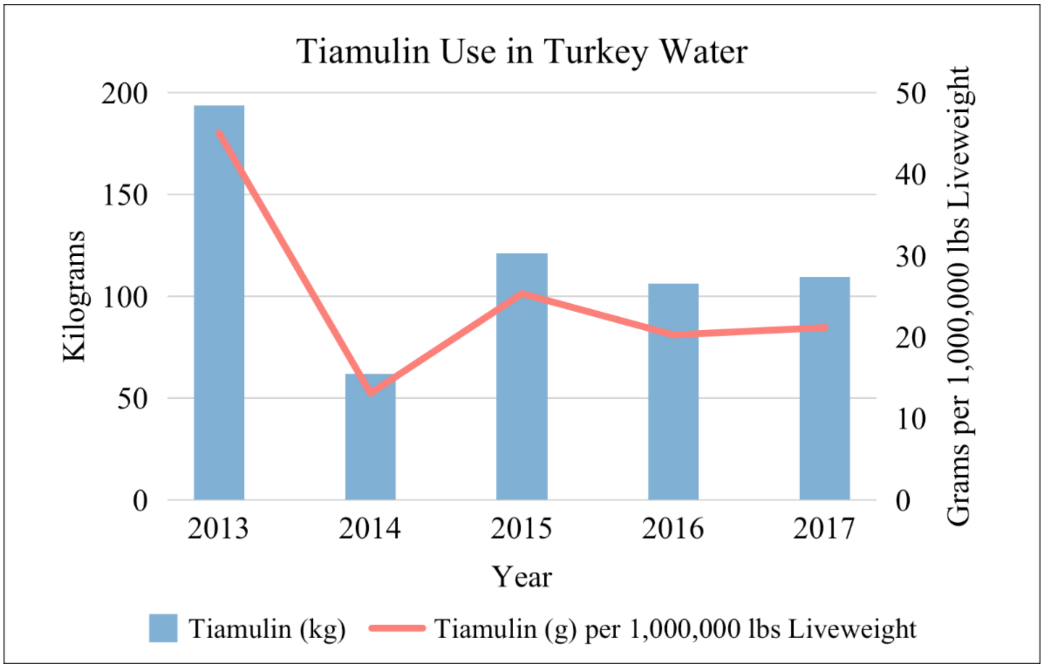



Figure 55. Bacitracin (polypeptide class) use in turkey water, 2013-2017. Total kilograms of bacitracin soluble are shown by the bars (left Y-axis) and total grams/1,000,000 pounds liveweight are shown by the line (right Y-axis).

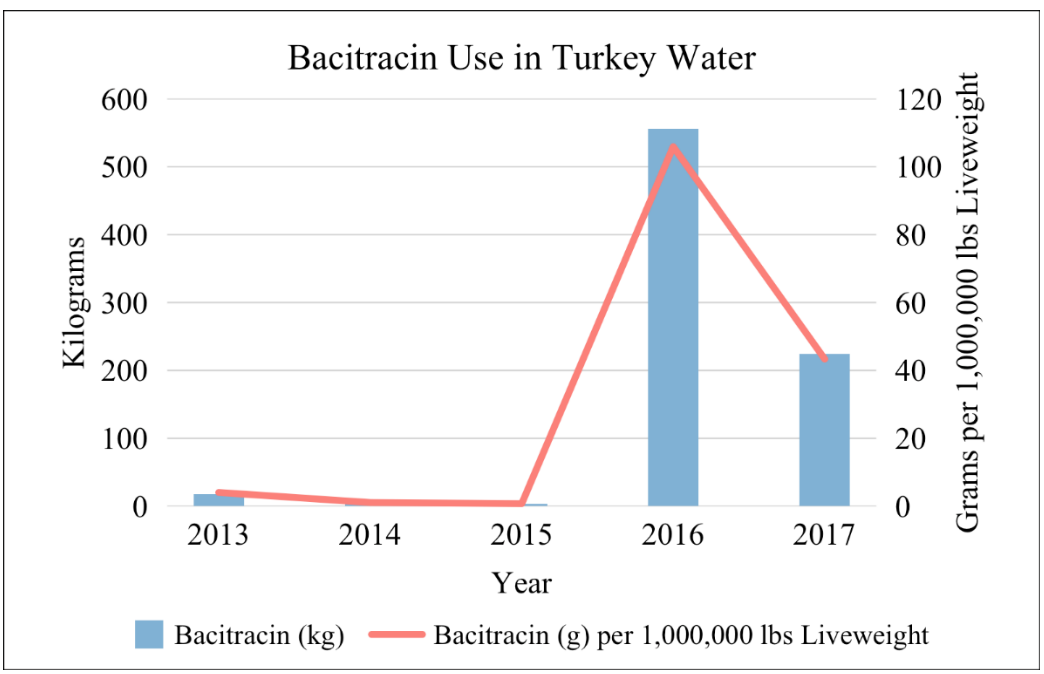


Table 30. Amount of antimicrobial drug use in turkey water, 2013-2017. Data are reported by active ingredients within drug classes and are divided into medically important and not medically important. Weights are reported as total kg of antimicrobial.

| Drug Class | Active Ingredient | Antimicrobial Usage in Turkey Water (kg of antimicrobial) 2013 | 2014 | 2015 | 2016 | 2017 |
|---|---|---|---|---|---|---|
| **Medically Important** | | | | | | |
| Aminoglycosides | Gentamicin | 1,178.2 | 909.9 | 641.9 | 467.9 | 241.2 |
| | Neomycin | 10,062.5 | 10,287.6 | 10,900.5 | 8,596.4 | 6,165.4 |
| | Spectinomycin | 14.4 | 4.3 | - | 99.2 | |
| Amphenicols | Florfenicol | 27.4 | 46.6 | 111.3 | 87.1 | 153.5 |
| Diaminopyrimidines | Trimethoprim | 39.9 | 69.4 | 182.1 | 236.5 | 383.9 |
| Lincosamides | Lincomycin | 4,363.5 | 4,004.2 | 4,512.8 | 5,424.0 | 2,847.2 |
| Macrolides | Erythromycin | 101.9 | 337.6 | 220.2 | 87.5 | 43.5 |
| | Tylosin | 143.9 | 100.2 | 87.9 | 232.3 | 649.5 |
| Natural Penicillins | Penicillin G | 398,731.3 | 441,101.9 | 433,039.8 | 384,652.2 | 280,647.0 |
| Sulfonamides | Sulfonamides[1,3] | 21,782.1 | 19,253.1 | 17,985.5 | 15,888.3 | 20,851.2 |
| Tetracyclines | Tetracyclines[2,3] | 90,806.3 | 94,081.0 | 105,098.4 | 93,667.9 | 78,519.7 |
| **Not Medically Important** | | | | | | |
| Pleuromutilins | Tiamulin | 193.7 | 62.0 | 121.2 | 106.4 | 109.6 |
| Polypeptides | Bacitracin | 17.4 | 5.1 | 3.6 | 556.0 | 224.5 |

[1]Includes sulfadiazine, sulfadimethoxine, sulfamerazine, sulfamethazine, and sulfaquinoxaline
[2]Includes chlortetracycline, oxytetracycline and tetracycline
[3]As stated in the FDA Sales and Distribution Report (6), "Antimicrobial class includes drugs of different molecular weights."

Table 31. Amount of antimicrobial drug use in turkey water, 2013-2017. Data are reported by active ingredients within drug classes and are divided into medically important and not medically important. Weights are reported as g of antimicrobial per 1,000,000 pounds liveweight produced.

| | | Antimicrobial Usage in Turkey Water (g of antimicrobial per million lbs liveweight) | | | | |
|---|---|---|---|---|---|---|
| **Drug Class** | **Active Ingredient** | **2013** | **2014** | **2015** | **2016** | **2017** |
| **Medically Important** | | | | | | |
| Aminoglycosides | Gentamicin | 274.0 | 192.2 | 134.2 | 89.1 | 46.6 |
| | Neomycin | 2,339.9 | 2,173.6 | 2,278.9 | 1,637.2 | 1,190.6 |
| | Spectinomycin | 3.3 | 0.9 | - | 18.9 | 18.7 |
| Amphenicols | Florfenicol | 6.4 | 9.8 | 23.3 | 16.6 | 29.6 |
| Diaminopyrimidines | Trimethoprim | 9.3 | 14.7 | 38.1 | 45.0 | 74.1 |
| Lincosamides | Lincomycin | 1,014.7 | 846.0 | 943.5 | 1,033.0 | 549.8 |
| Macrolides | Erythromycin | 23.7 | 71.3 | 46.0 | 16.7 | 8.4 |
| | Tylosin | 33.5 | 21.2 | 18.4 | 44.2 | 125.4 |
| Natural Penicillins | Penicillin G | 92,719.0 | 93,196.6 | 90,533.8 | 73,259.2 | 54,195.4 |
| Sulfonamides | Sulfonamides[1] | 5,065.1 | 4,067.8 | 3,760.2 | 3,026.0 | 4,026.5 |
| Tetracyclines | Tetracyclines[2] | 21,115.7 | 19,877.6 | 21,972.5 | 17,839.6 | 15,162.8 |
| **Not Medically Important** | | | | | | |
| Pleuromutilins | Tiamulin | 45.0 | 13.1 | 25.3 | 20.3 | 21.2 |
| Polypeptides | Bacitracin | 4.0 | 1.1 | 0.7 | 105.9 | 43.3 |

[1]Includes sulfadiazine, sulfadimethoxine, sulfamerazine, sulfamethazine, and sulfaquinoxaline
[2]Includes chlortetracycline, oxytetracycline and tetracycline

## Disease Indications – Turkeys

This section of the report will describe several key aspects of the 2017 data that were collected. This analysis should be considered preliminary, as future reports will present these data in greater detail. The data in these sections represent approximately 70% of the annual turkey production that is within the full dataset for 2017. In other words, companies that supplied the data for this section represent approximately 70% of the turkeys in the 2017 dataset. The specific aspects covered in this section are:

1. The distribution of age of onset for some of the important diseases for which water-soluble antimicrobials were administered. These data were generated from the flock-level therapy records, and therefore, if there were times when flocks were diseased but antimicrobials were not administered, these disease occurrences would not have been captured.
2. The percentage of each water-soluble antimicrobial that was administered for different disease indications. These estimates do not represent all of the submitted antimicrobial use data, as not every company had these data available.

At this point in time there is insufficient data to capture accurately the duration of administration of the water-soluble antimicrobials by disease. The next report will incorporate these data.

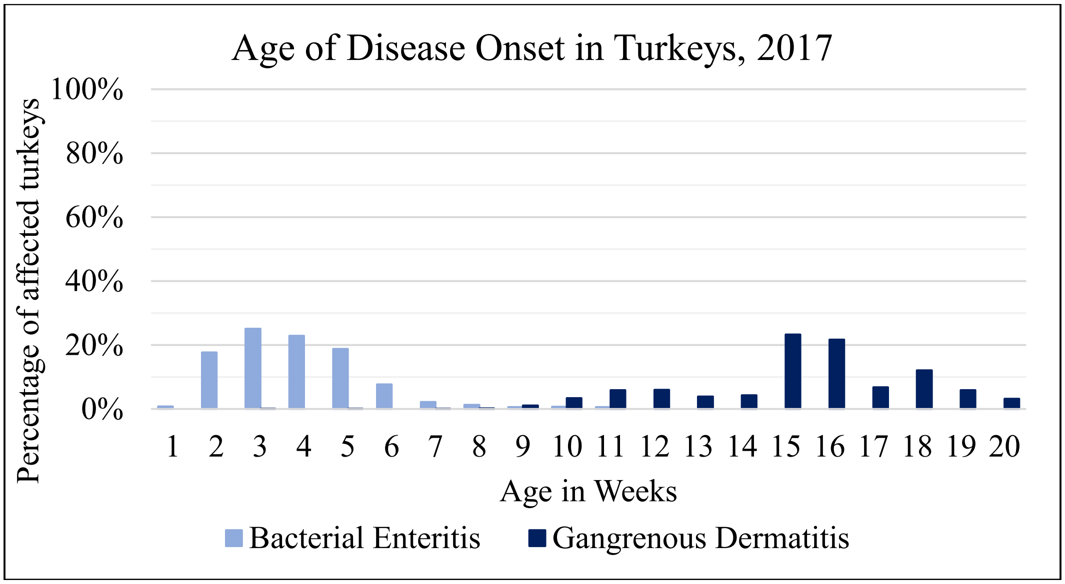
### Characteristics of Diseases Necessitating Antimicrobial Therapy

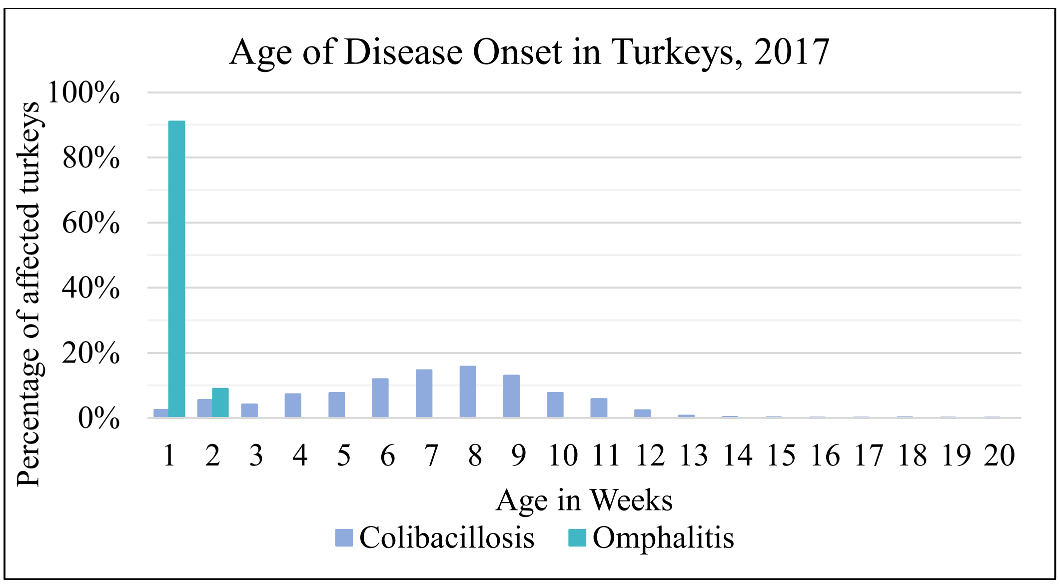
As described above in the Primary Disease Challenges – Turkeys section, the two most important diseases that affect turkeys occur primarily in different stages of production. Bacterial enteritis, sometimes referred to as dysbacteriosis, is most often seen at 2-5 weeks of age while gangrenous dermatitis occurs most often later in the production cycle, peaking around 15-16 weeks of age.

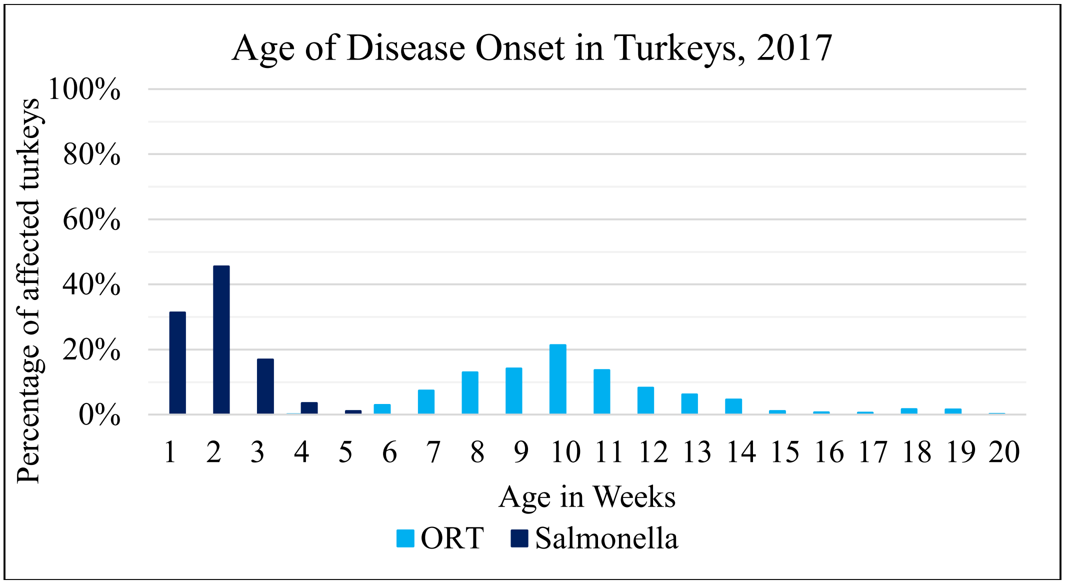
Diseases often associated with *E. coli* infection occur throughout the life of the turkey. There are certain conditions that are linked to specific ages, such as omphalitis, while others such as pneumonia can occur throughout the bird’s life. ORT tends to occur in the middle of the lifespan of the turkey, peaking around 9-11 weeks of age.

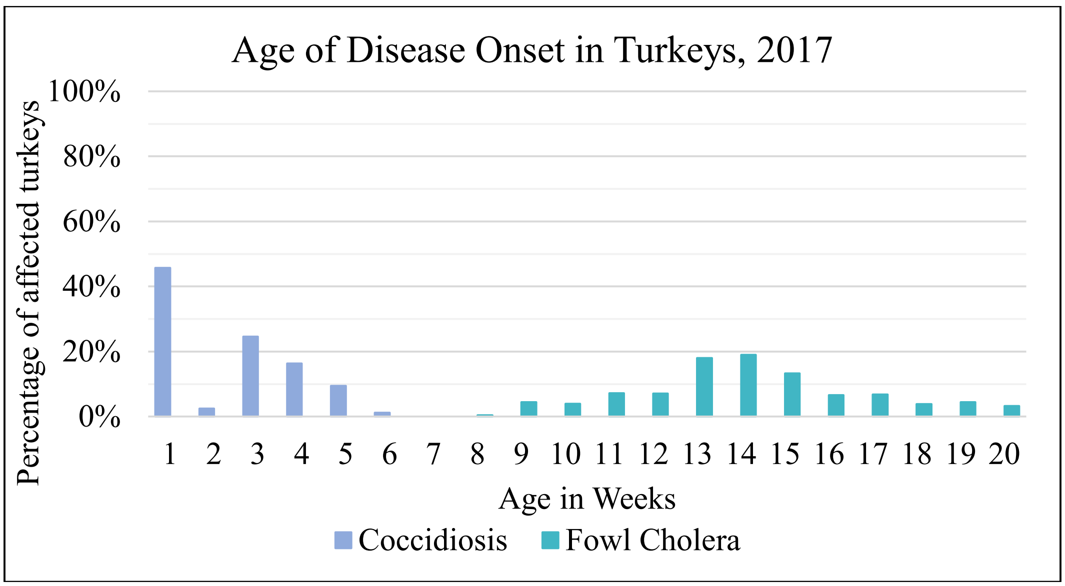
These and other important diseases of turkeys are shown in the figures below.

Figure 56. Distribution of age of disease onset for eight of the major diseases affecting turkeys in companies providing data for this analysis and for which antimicrobial drugs are often used in the water, 2017.




Age of Disease Onset in Turkeys, 2017
Percentage of affected turkeys
100%
80%
60%
40%
20%
0%
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20
Age in Weeks
ORT
Salmonella


Age of Disease Onset in Turkeys, 2017
Percentage of affected turkeys
100%
80%
60%
40%
20%
0%
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20
Age in Weeks
Coccidiosis
Fowl Cholera

## Water-Soluble Antimicrobial Use by Disease

The graphs in this section depict the diseases that were targeted by water-soluble antimicrobials during 2017. These graphs depict how each water-soluble antimicrobial was used by stratifying the total amount of each antimicrobial used in 2017 into the disease indications for which it was administered. In other words, the total amount of each antimicrobial is separated into the disease indications for which it was used.

The graphs in this section depict the diseases that were targeted by each water soluble antimicrobial during 2017. The data are presented in two ways. First, the percentage of turkeys that received therapy with a given antimicrobial for each disease indication was calculated. Second, the percentage of the total amount of antimicrobial (in grams that was administered for each disease indication was calculated.

As an example, in Figure 57 the use of erythromycin is shown, and this antimicrobial was primarily used for *E. coli* and ORT. In the figure, for the birds that received erythromycin, 72% were administered erythromycin for *E. coli* and 28% for ORT. However, 62% of the total amount of erythromycin was administered for *E. coli* and 38% for ORT.

### Medically Important Antimicrobials

Figure 57. Percentage of gentamicin (aminoglycoside class) use in the water of turkeys by disease indication, 2017. For those birds that received gentamicin, the figure depicts the percentage of birds receiving therapy and the percentage of total grams of gentamicin by disease indication.

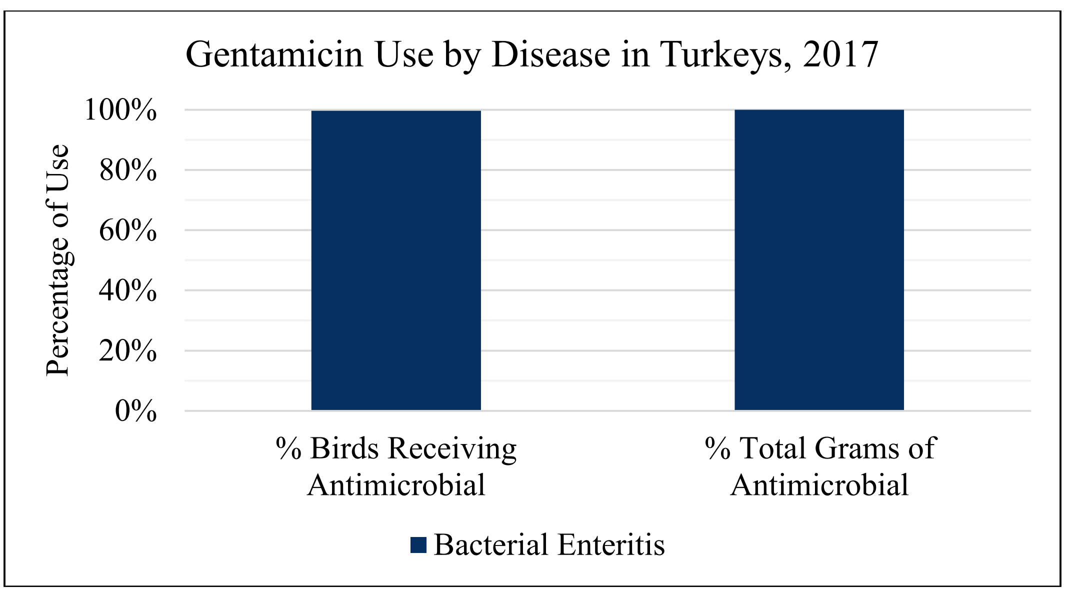


Figure 58. Percentage of neomycin (aminoglycoside class) use in the water of turkeys by disease indication, 2017. For those birds that received neomycin, the figure depicts the percentage of birds receiving therapy and the percentage of total grams of neomycin by disease indication.

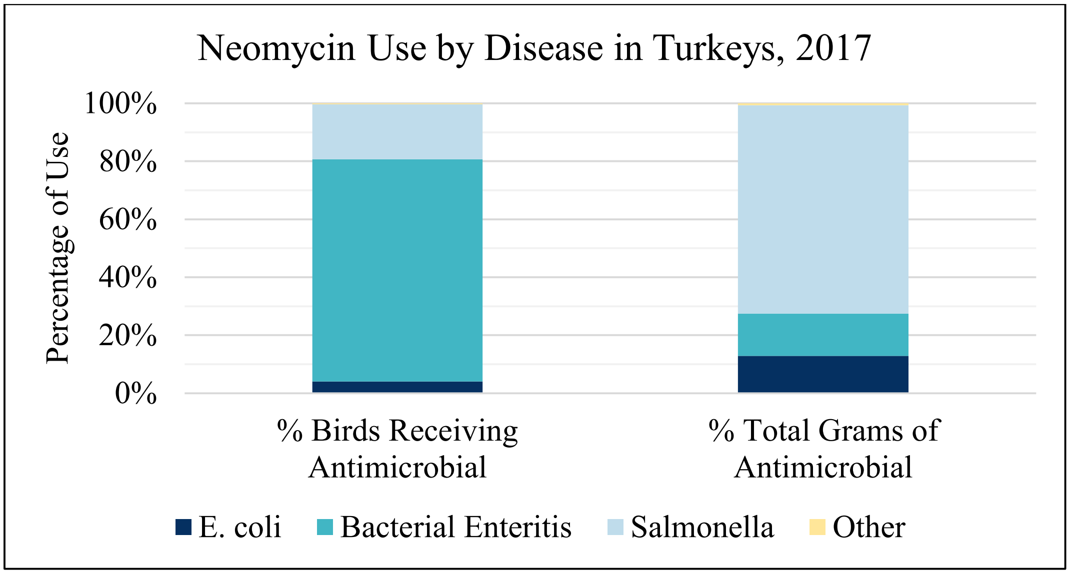



Figure 59. Percentage of florfenicol (amphenicol class) use in the water of turkeys by disease indication, 2017. For those birds that received florfenicol, the figure depicts the percentage of birds receiving therapy and the percentage of total grams of florfenicol by disease indication.

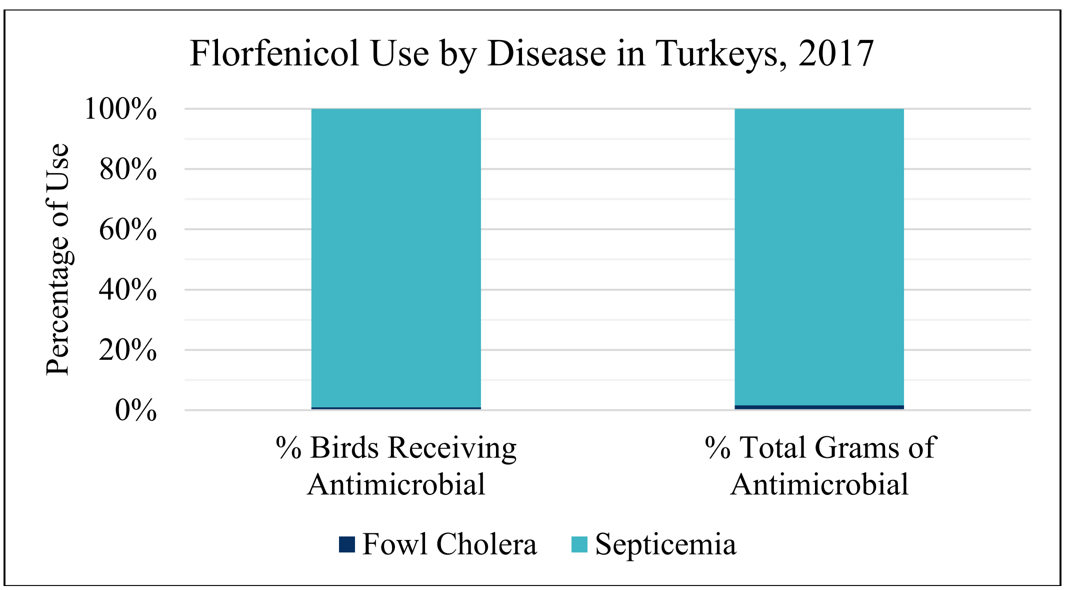


Figure 60. Percentage of lincomycin (lincosamide class) use in the water of turkeys by disease indication, 2017. For those birds that received lincomycin, the figure depicts the percentage of birds receiving therapy and the percentage of total grams of lincomycin by disease indication.

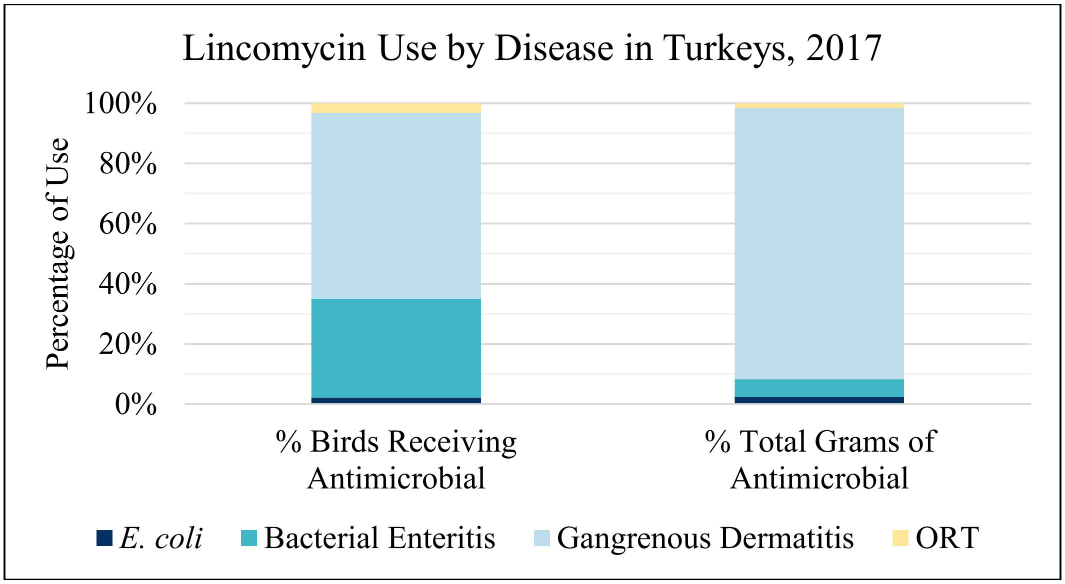



Figure 61. Percentage of erythromycin (macrolide class) use in the water of turkeys by disease indication, 2017. For those birds that received erythromycin, the figure depicts the percentage of birds receiving therapy and the percentage of total grams of lincomycin by disease indication.

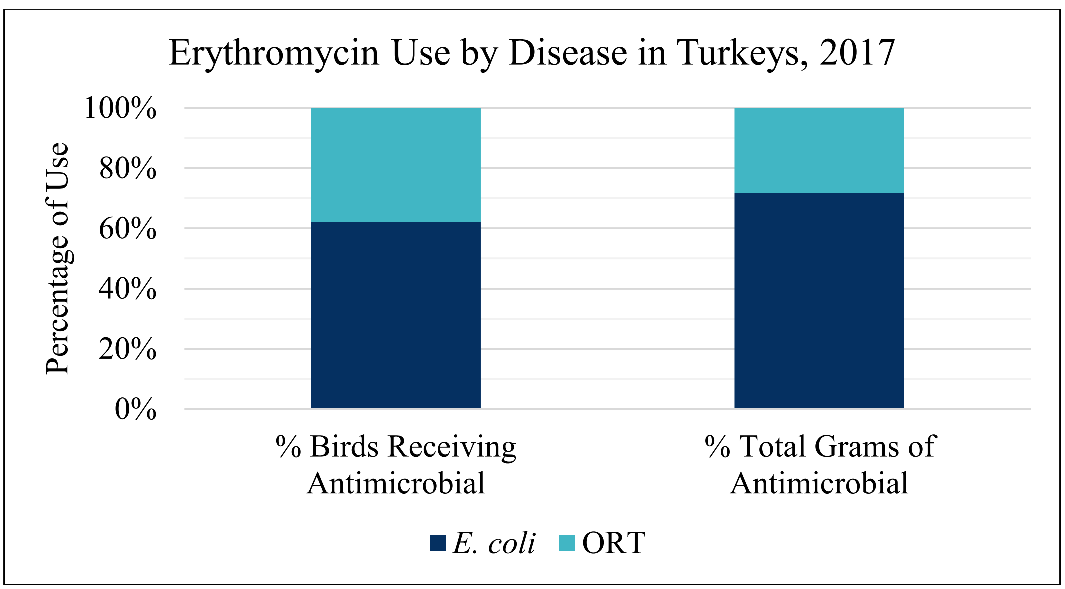


Figure 62. Percentage of tylosin (macrolide class) use in the water of turkeys by disease indication, 2017. For those birds that received tylosin, the figure depicts the percentage of birds receiving therapy and the percentage of total grams of tylosin by disease indication.

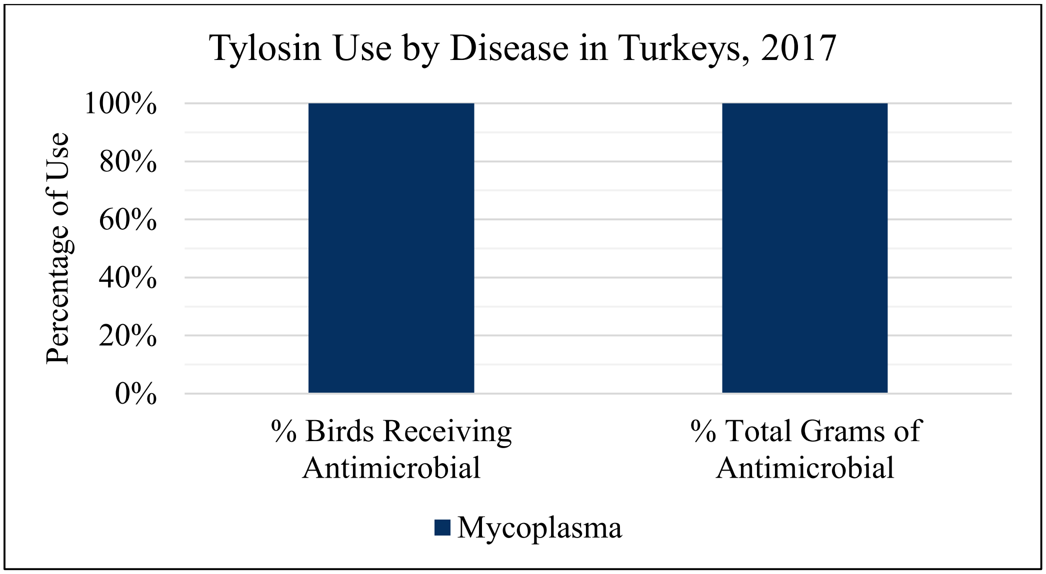
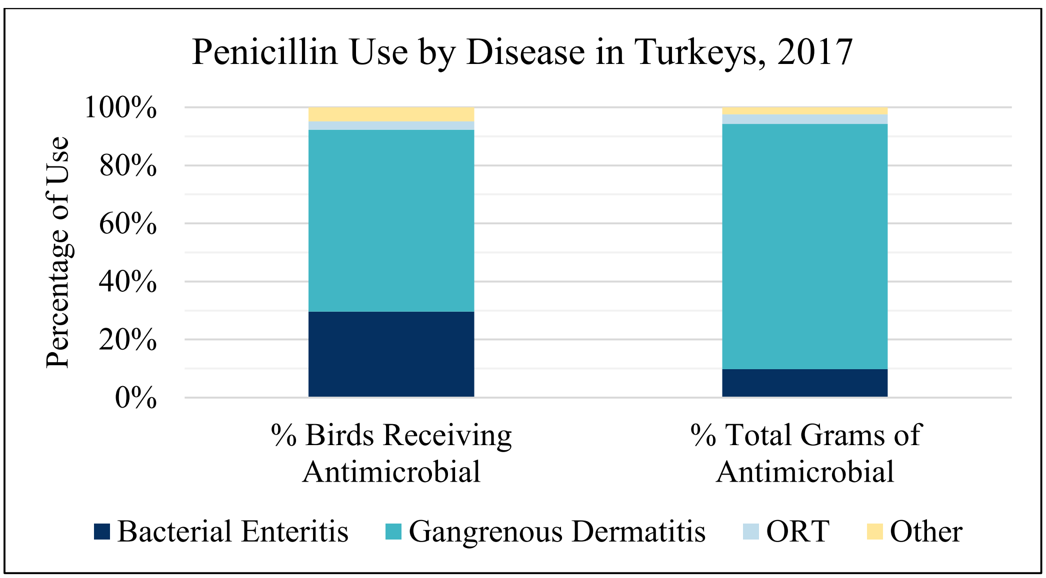



Figure 63. Percentage of penicillin use in the water of turkeys by disease indication, 2017. For those birds that received penicillin, the figure depicts the percentage of birds receiving therapy and the percentage of total grams of penicillin by disease indication.




It is important to note the difference between gangrenous dermatitis (GD) and bacterial enteritis. GD was the most common reason for use of penicillin in water and occurs later in life. Because the birds being treated were older, heavier birds are receiving therapy. In contrast, bacterial enteritis occurs earlier in life and requires less antimicrobial due to the lighter bird weight and consequent water consumption. The proportion of use by grams is greater when compared to proportion of use by number of birds for GD, due to the therapy for heavier birds.

Figure 64. Percentage of sulfonamide (sulfonamide class) use in the water of turkeys by disease indication, 2017. For those birds that received sulfonamides, the figure depicts the percentage of birds receiving therapy and the percentage of total grams of sulfonamides by disease indication. Specific active ingredients included in this total are sulfadimethoxine, sulfamerazine, sulfamethazine, sulfaquinoxaline and potentiated sulfonamides.

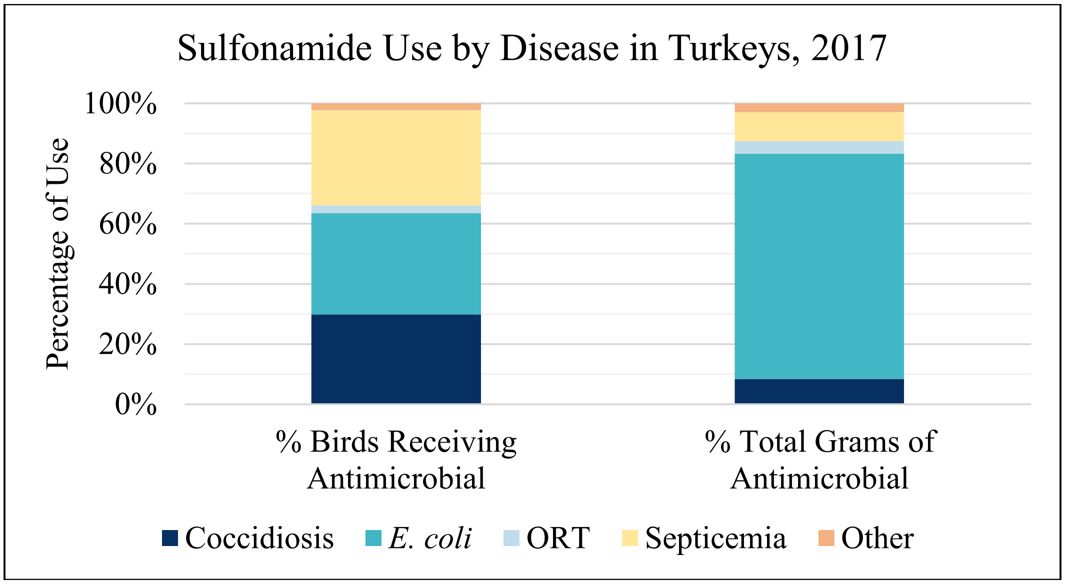
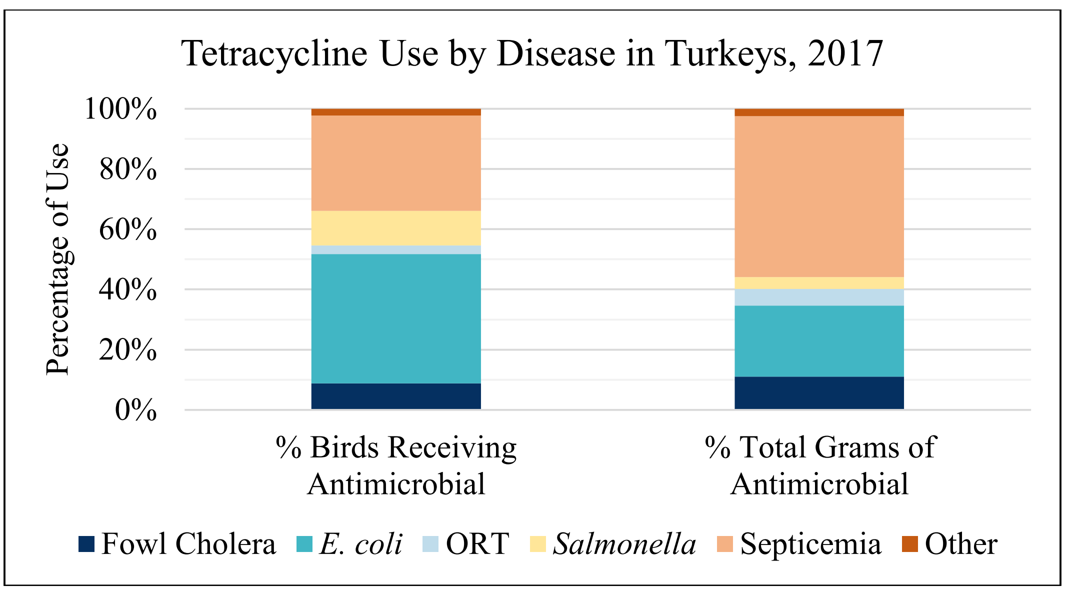



Figure 65. Percentage of tetracycline (tetracycline class) use in the water of turkeys by disease indication, 2017. For those birds that received tetracycline, the figure depicts the percentage of birds receiving therapy and the percentage of total grams of tetracycline by disease indication.



**Not Medically Important Antimicrobials**

Figure 66. Percentage of tiamulin (pleuromutilin class) use in the water of turkeys by disease indication, 2017. For those birds that received tiamulin, the figure depicts the percentage of birds receiving therapy and the percentage of total grams of tiamulin by disease indication.

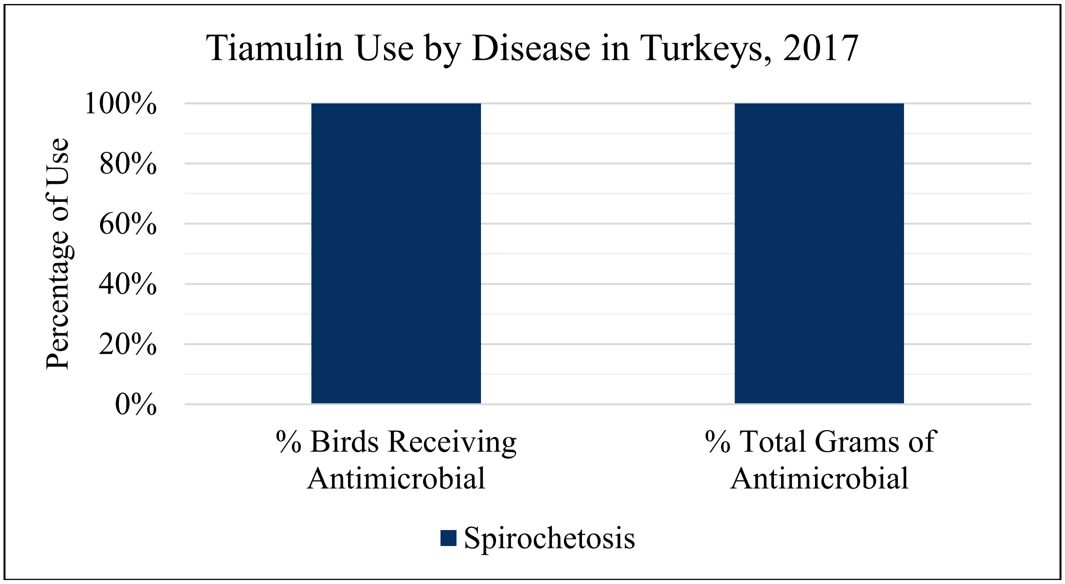
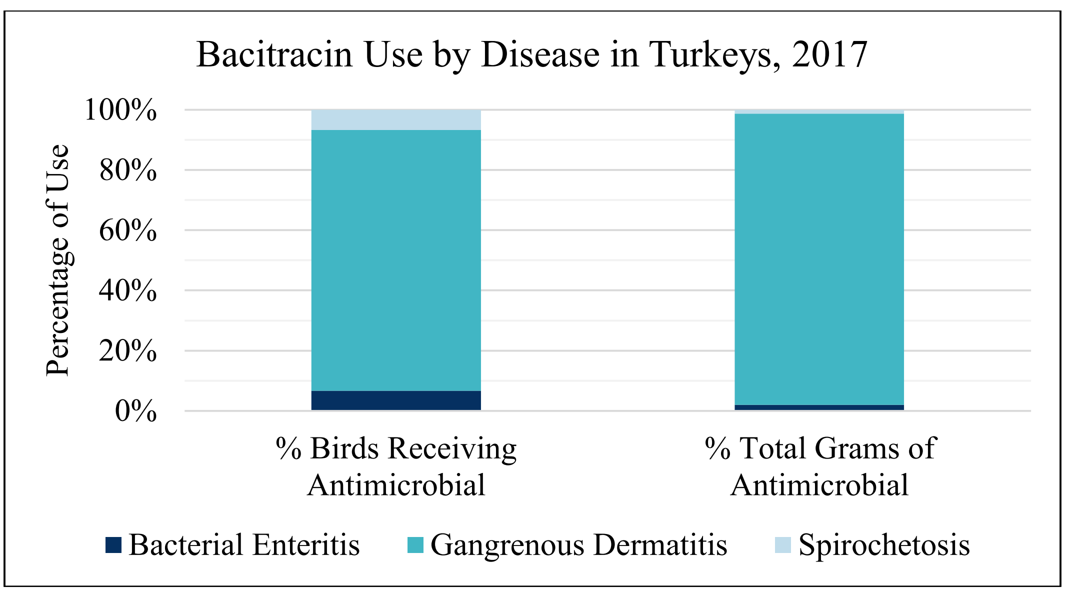



Figure 67. Percentage of bacitracin (polypeptide class) use in the water of turkeys by disease indication, 2017. For those birds that received bacitracin, the figure depicts the percentage of birds receiving therapy and the percentage of total grams of bacitracin by disease indication.



# Conclusions

This report describes the first phase of a large, industrywide effort to capture antimicrobial use data for a majority of the broiler chicken and turkey production in the U.S. between 2013 and 2017. Importantly, this interval would straddle the date of January 1, 2017, when FDA GFI #213 was fully implemented. Given that all medically important antimicrobial drug uses for production purposes were withdrawn in the U.S. and all medically important antimicrobials administered in the feed or water transitioned to veterinary supervision, it was expected that substantive changes in record keeping and indications for antimicrobial administration would be documented.

Thanks to the voluntary participation of the broiler chicken and turkey companies of the U.S., participation rates far exceeded our initial targets. Almost 90% of annual broiler chicken production and almost 80% of annual turkey production are represented in this report for the year 2017, based on the list published by WATT Poultry USA. The representativeness of the data varies by year, due in large part to challenges with data retrieval for the earlier years of the data collection interval. Going forward, the hope is to continue to increase the representativeness of the data in future reports and also to increase the granularity of the data, as many companies are now capturing detailed flock-level records of antimicrobial administration. In addition, collaboration with companies continues, regardless of their current data management system, to improve the types of data that are recorded regarding background levels of diseases and antimicrobials administered for these diseases.

Antimicrobial use in the broiler chicken and turkey industries of the U.S. decreased between 2013 and 2017. The following tables show the total amounts of medically important antimicrobial usage by antimicrobial class with the percentage change over the time periods 2013 to 2017 and 2016 to 2017. These date ranges are presented in the tables because the 2013-2017 period spans the entire period of this data collection effort, and the 2016-2017 period straddles the full implementation of FDA Guidance for Industry (GFI) #213 on January 1, 2017. These tables should be interpreted with caution for a couple of important reasons. First, specific antimicrobial active ingredients within an antimicrobial class have been aggregated, but as FDA acknowledges in the FDA Sales and Distribution Report from 2017, "Antimicrobial class includes drugs of different molecular weights." Consequently, different antimicrobials will contribute disproportionately to the total amount of drug in each class. Second, the totals within each antimicrobial class are summed across routes of administration; combining injectable and orally administered antimicrobial use data into a single total precludes the differentiation of potency by route. This full report presents the data by route of administration and by individual active ingredient, when feasible.

It is important to note that overall representation of the collected data to the U.S. poultry industry increased from 2013 to 2017, and therefore, more birds are represented in the 2016 and 2017 data than in the 2013 data. Consequently, data are also presented as grams of drug per 1,000,000 pounds liveweight produced to standardize the data over time.

Table 32. Medically important antimicrobial drugs used in broiler chickens for 2013, 2016 and 2017. Data are shown as total amount of each antimicrobial class in kilograms and as total grams of each antimicrobial class per 1,000,000 pounds of liveweight produced. Percentage differences in both metrics are shown for the 2013 to 2017 and 2016 to 2017 periods.

| | **Antimicrobial Usage in Broilers (kg of antimicrobial)** | | | **% Change** | |
|---|---|---|---|---|---|
| Antimicrobial Class | 2013 | 2016 | 2017 | 2013-2017 | 2016-2017 |
| Aminoglycosides | 1,651 | 837 | 508 | -69% | -39% |
| Lincosamides | 3,584 | 4,360 | 2,604 | -27% | -40% |
| Macrolides | 8,048 | 10,591 | 900 | -89% | -92% |
| Penicillins | 17,309 | 27,955 | 17,398 | 1% | -38% |
| Sulfonamides | 5,221 | 1,915 | 1,892 | -64% | -1% |
| Tetracyclines | 107,633 | 22,103 | 15,366 | -86% | -30% |

| | **Antimicrobial Usage in Broilers (g of antimicrobial per million lbs liveweight)** | | | **% Change** | |
|---|---|---|---|---|---|
| Antimicrobial Class | 2013 | 2016 | 2017 | 2013-2017 | 2016-2017 |
| Aminoglycosides | 42.5 | 17.7 | 10.6 | -75% | -40% |
| Lincosamides | 96.0 | 93.1 | 54.9 | -43% | -41% |
| Macrolides | 201.0 | 223.3 | 19.0 | -91% | -92% |
| Penicillins | 474.4 | 596.8 | 366.6 | -23% | -39% |
| Sulfonamides | 143.3 | 40.8 | 39.8 | -72% | -2% |
| Tetracyclines | 2,662.9 | 470.7 | 322.0 | -88% | -32% |

Table 33. Medically important antimicrobial drugs used in turkeys for 2013, 2016 and 2017. Data are shown as total amount of each antimicrobial class in kilograms and as total grams of each antimicrobial class per 1,000,000 pounds of liveweight produced. Percentage differences in both metrics are shown for the 2013 to 2017 and 2016 to 2017 periods.

| | **Antimicrobial Usage in Turkeys (kg of antimicrobial)** | | | **% Change** | |
|---|---|---|---|---|---|
| Antimicrobial Class | 2013 | 2016 | 2017 | 2013-2017 | 2016-2017 |
| Aminoglycosides | 11,382 | 9,278 | 6,579 | -42% | -29% |
| Amphenicols | 27 | 87 | 153 | 461% | 76% |
| Cephalosporins | 19 | 8 | 0 | -100% | -100% |
| Lincosamides | 4,364 | 5,424 | 2,847 | -35% | -48% |
| Macrolides | 246 | 320 | 693 | 182% | 117% |
| Penicillins | 399,003 | 384,933 | 280,901 | -30% | -27% |
| Sulfonamides | 21,782 | 15,888 | 20,851 | -4% | 31% |
| Tetracyclines | 186,624 | 164,662 | 111,836 | -40% | -32% |

| | **Antimicrobial Usage in Turkeys (g of antimicrobial per million lbs liveweight)** | | | **% Change** | |
|---|---|---|---|---|---|
| Antimicrobial Class | 2013 | 2016 | 2017 | 2013-2017 | 2016-2017 |
| Aminoglycosides | 2,643.2 | 1,767.1 | 1,270.5 | -52% | -28% |
| Amphenicols | 6.4 | 16.6 | 29.6 | 366% | 79% |
| Cephalosporins | 4.0 | 1.6 | 0.0 | -100% | -100% |
| Lincosamides | 1,014.7 | 1,033.0 | 549.8 | -46% | -47% |
| Macrolides | 57.2 | 60.9 | 133.8 | 134% | 120% |
| Penicillins | 92,774.9 | 73,312.7 | 54,244.5 | -42% | -26% |
| Sulfonamides | 5,065.1 | 3,026.0 | 4,026.5 | -21% | 33% |
| Tetracyclines | 40,841.5 | 31,360.8 | 21,596.5 | -47% | -31% |

There are likely several explanations for these reductions, including the full implementation of FDA GFI #213 and the changes to the VFD rule, veterinary supervision of all medically important antimicrobial administrations, overall improved antimicrobial stewardship, focus on improved preventative medicine and animal husbandry practices to reduce the need for antimicrobials, shifts to the use of non-medically important antimicrobials, increased production of animals raised without antimicrobials, and early diagnosis and intervention with non-antimicrobial therapies.

As described in this report, a simple reduction of total antimicrobial amount should not be the primary goal of changes to antimicrobial use programs. While reducing the amount of antimicrobials used is an important step in mitigating antimicrobial resistance, reducing the need for such use should be considered a more important objective. Enhancing antimicrobial stewardship should be considered a key goal. A major challenge that remains is the means by which antimicrobial stewardship in animal agriculture is measured and reported, and this challenge will be a continued focus of this project. Long-term, programs that monitor antimicrobial stewardship, animal health and welfare, and antimicrobial resistance that impacts human, animal and environmental health are needed.

Rather than focusing on whether overall antimicrobial use was reduced through accounting methods such as those used in this report, a better long-term goal should be how to determine and quantify antimicrobial stewardship as well as to quantify the outcomes of antimicrobial therapy. One aim should be to help veterinarians ensure that they are using good antimicrobial stewardship principles, that their antimicrobial choices are appropriate for the diagnosed disease, and that the chosen antimicrobial minimizes the likelihood of antimicrobial resistance development, spread and persistence. These are much more difficult goals to achieve, but hopefully the data collection program described in this report moves us closer to reaching these aims.

Many of the broiler and turkey companies use a service to assist with issuing VFDs and prescriptions. It should be noted that downloading the data from a prescription or VFD does not obviate the need for data validation and further communication with the veterinarians. For example, much of the VFD data that is being captured does not represent actual antimicrobial administration on the farm. This is due to the fact that poultry veterinarians will often write a VFD covering the total amount of production that might be placed during the temporal interval of the VFD. For actual antimicrobial amounts, it is still necessary to work with the veterinarian to determine the antimicrobials that were actually used. Furthermore, some of the antimicrobials used in feed do not require a VFD, and so it is necessary to get these data from the veterinarian directly. Finally, the prescription data that are retrievable from these services will contain instructions for antimicrobial administration (such as dose and duration of therapy) but do not always contain the disease indication or the number of birds receiving therapy. Future efforts in this program include working with these services to customize the records and to have the companies record all needed information into the online prescription for easier retrieval.

Some readers of this report will likely compare the results to the Antimicrobial Sales and Distribution Data released by FDA (6). Readers of this report will likely notice that no data aggregation across antimicrobial classes or routes of administration was performed, unlike results presented in Table 4b of the FDA Antimicrobial Sales and Distribution report (6, p. 20). Table 5b of this report presents the data by class, rather than as a single aggregate. Regardless, as stated previously, antimicrobial sales data are not meant to represent on-farm antimicrobial use data. As stated on page 6 of the FDA Antimicrobial Sales and Distribution report, “the data is not intended to be a substitute for actual usage data.” Programs are needed to acquire these more granular antimicrobial use data.

Combining drug totals can lead to misleading and misguided interpretations. For example, the turkey industry has been criticized because the CVM 2017 Report showed an estimated reduction of 11% between 2016 and 2017, and some wanted this percentage to be larger. This is an unfortunate conclusion to reach as it does not reflect the reductions that the turkey industry actually made nor does it capture the antimicrobials that were actually used and the reason for their use. The main medically important antimicrobial drug by weight used in the turkey industry is water-soluble penicillin. All of this therapeutic use is for serious diseases such as gangrenous dermatitis and bacterial enteritis. A 26% decrease in water soluble penicillin use was recorded between 2016 and 2017. For the turkey industry to reduce their total amount of antimicrobial administration by large percentages, they would either have to reduce the incidence of disease, which is problematic due to a lack of efficacious interventions for some of the more important turkey diseases, they would have to forego therapy for flocks that are experiencing illness (which is unethical), or they would need to switch to an antimicrobial that is more potent (fewer grams administered per regimen), as detailed in Example #2 in the Data Aggregation, Auditing and Reporting section. Of course, companies are always looking for interventions that reduce the incidence of key diseases such as gangrenous dermatitis and bacterial enteritis, but unfortunately, efficacious interventions for these diseases are limited.

Finally, the current effort lacks data on the background disease burden in broiler chicken and turkey production as well as outcome data following therapeutic administration of antimicrobials. Without the background disease information, it is difficult to evaluate the amount of antimicrobial use that would be expected to manage the annual disease burden. It is conceivable that antimicrobial use could increase in a given year, even though all of the use follows good stewardship principles, simply due to an increase in the disease burden that necessitates antimicrobial therapy in order to minimize the welfare impact on sick animals. Future efforts will seek approaches to capturing the underlying disease burden within the broiler chicken and turkey industries and to investigate metrics for evaluating the outcomes of therapeutic antimicrobial administration.

## Acknowledgments

This project is funded through a contract with the U.S. Food and Drug Administration (1U01FD005878-01) and support from the U.S. Poultry & Egg Association (USPOULTRY). Assistance on survey design, data collection methodology, data analysis and report review was provided by Dr. Michael Apley, Dr. Peter Davies, Dr. Nora Schrag, and Dr. Katie Hope. Collaboration on all aspects of this project and official auditing of the data were provided by Dr. Kathe Bjork and Dr. Lindsey Garber at USDA:APHIS:VS:CEAH. This project would not have been possible without the voluntary participation of most of the major companies in the broiler chicken and turkey industries of the U.S.

## Data Confidentiality

Eversheds Sutherland (US) LLP engaged Dr. Randall Singer as a technical consultant to assist in providing legal services in connection with USPOULTRY's assessment and development of a position on anticipated regulatory issues pertaining to the use of antibiotics in the production of poultry and poultry products. In this capacity, Dr. Singer implemented an antimicrobial usage survey designed to collect industry information relevant for these legal services. Industry-wide results and analysis of this survey are disclosed in this report. The underlying data is protected by the attorney-client privilege and will not be disclosed.

## Contact Information

Dr. Randall Singer is the founder of Mindwalk Consulting Group, LLC and can be reached at rsinger@mindwalkconsultinggroup.com regarding this report. Dr. Singer is also a Professor of Epidemiology at the University of Minnesota in the Department of Veterinary and Biomedical Sciences, College of Veterinary Medicine. His research and educational program has focused on predicting the emergence, spread and persistence of infectious diseases with an emphasis on food safety and antimicrobial resistance.

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