



2015 INTEGRATED REPORT



To access the interactive version of the NARMS Integrated Report, see
<https://www.fda.gov/AnimalVeterinary/SafetyHealth/AntimicrobialResistance/NationalAntimicrobialResistanceMonitoringSystem/ucm059103.htm>.

A Message from the Director

Dr. Patrick McDermott, NARMS Director

Welcome to the NARMS 2015 Integrated Report. This report marks the 20th anniversary of the NARMS program. NARMS began in 1996 with the testing of human clinical strains of Salmonella in 14 sites. NARMS has grown over the years to include human data from all 50 states, as well as randomized, nationally-representative testing of food animals at slaughter. Retail meat surveillance began in 6 states in 2002. This report includes data from 14 states, and will soon have resistance information from 21 states.

Over the past two decades, the NARMS partners have worked to improve the program to better meet its public health mission. Whole genome sequencing has recently been incorporated into NARMS so that all the known resistance genes can now be tracked over time. All the genome sequences are deposited into GenBank at the National Center for Biotechnology Information (NCBI). In addition, NARMS has data on more than 185,000 isolates that can be downloaded in an accessible format. To help make these large data sets more accessible, the NARMS teams continue to develop new tools to enable users to explore them according to their own interests. As a public health surveillance system, the goal is continuous improvement and open, transparent data sharing. The NARMS partners believe this is the best way to foster a collaborative effort to combat antibiotic resistance.

Acknowledgements

NARMS is possible only because of the dedicated effort of many people across Federal, State, and academic institutions. A complete list of NARMS partners can be found in the supplemental material.

The NARMS Steering Committee consists of the following people:

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What's New?

New Interactive Data Displays:

Seven new interactive data displays have been added to this year's report. One display allows users to view multidrug resistance by the number of antibiotic classes. Another display shows the distribution of *Salmonella* antibiotic resistance genes by sample type over time. Several new displays enable users to explore the genetic data in more detail, with links to the whole genome sequence data deposited at NCBI, where NCBI online tools can be employed to do further analyses. The new interactive data displays can be found at <http://www.fda.gov/AnimalVeterinary/SafetyHealth/AntimicrobialResistance/NationalAntimicrobialResistanceMonitoringSystem/ucm570685.htm>.

Use of Decreased Susceptibility to Ciprofloxacin in the Definition of Multidrug Resistance:

In previous reports, we used resistance to nalidixic acid has been used as an indicator of emerging fluoroquinolone resistance. In 2013, the Clinical and Laboratory Standards Institute (CLSI) revised ciprofloxacin minimum inhibitory concentration (MIC) breakpoints for *Salmonella*, including those that define resistant and intermediate categories of susceptibility. Decreased susceptibility to ciprofloxacin (DSC, MIC $\geq$ 0.12 μ g/ml) is now used as a marker for emerging fluoroquinolone resistance (CLSI, 2017). *Salmonella* infections with DSC have been associated with treatment failure and delayed response (CLSI, 2017, Crump et al., 2003). Therefore, the DSC category (which includes resistant and intermediate susceptibility) is more clinically relevant than nalidixic acid resistance. For the 2015 report, a new definition of quinolone resistance as the presence of DSC and/or nalidixic acid resistance was used in the calculations of multidrug resistance (MDR). This new MDR definition was retrospectively applied to all historical NARMS *Salmonella* and *E. coli* data.

Background

NARMS generates a large dataset on bacteria from 14 distinct sources (see below). This report focuses on antimicrobial resistance to drug classes that are most important to human medicine (generally, first- or second-line treatments), multidrug resistance, and specific co-resistance profiles of epidemiological importance.

Salmonella* and *Campylobacter are the leading bacterial causes of foodborne illness in the United States. Nontyphoidal serotypes of *Salmonella enterica* can be present in intestinal tracts of a wide range of animals including wildlife, livestock, and domestic pets. The bacterium spreads through the fecal-oral route, mainly by contact with contaminated foods of animal origin, or less frequently by contact with animals or animal contaminated produce. Similarly, *Campylobacter* is commonly present in the gut flora of food-producing animals such as chickens, turkeys, swine, cattle, and sheep.

Public health significance: *Salmonella* is estimated to cause over 1.2 million illnesses and 120 deaths, and *Campylobacter* is estimated to cause over 1.3 million illnesses and 120 deaths each year (Scallan et al., 2011).

Generic *E. coli* and *Enterococcus* isolates also are tested for antimicrobial susceptibility. These are cultured from animal samples at slaughter and from retail meats. Testing these organisms indicates resistance to antimicrobials that are active against gram-negative and gram-positive bacteria. For more information about these four bacterial organisms, visit the NARMS Website at <https://www.fda.gov/AnimalVeterinary/SafetyHealth/AntimicrobialResistance/NationalAntimicrobialResistanceMonitoringSystem/ucm059089.htm>.

This report presents consolidated information from the four data sources that form the NARMS system. The sources are listed below:

1. Human clinical isolates
2. Food-producing animal isolates from cecal (intestinal) samples at slaughter
3. Samples collected at slaughter as part of Pathogen Reduction/Hazard Analysis Critical Control Point (PR/HACCP) testing
4. Raw retail meats (chicken, ground turkey, ground beef, and pork chops) collected at retail outlets in 14 states.

Note: In 2015, only *Salmonella* was cultivated in all sample types targeted in NARMS. Swine PR/HACCP carcass sampling was discontinued in July 2011.

Percent of Animal and Food Samples Positive for Bacteria

For retail chicken meat testing in 2015, *Salmonella* recovery continued to decline to the lowest levels in 14 years of NARMS retail meat testing, falling to 6.1% in 2015. A parallel decline occurred in retail ground turkey (see below). Similarly, the occurrence of *Campylobacter* in retail chicken samples has declined steadily, down from a peak of 60% in 2004 to 24% in 2015.

As with *Salmonella* and *Campylobacter*, *E. coli* recovery from retail meat has declined since 2007. *Enterococcus* recovery was high among all retail meat and cecal samples.

2015 marked the third year of cecal sample collection. *Salmonella* recovery was highest among market swine and sows.

Campylobacter recovery was highest among cattle and swine cecal samples, and lowest in poultry.

*Please note that isolate recovery rates generated from NARMS retail meat sampling should not be compared to results from FSIS baseline studies and HACCP testing (available at <https://www.fsis.usda.gov/wps/portal/fsis/topics/data-collection-and-reports/microbiology/baseline/baseline>), as there are a number of underlying differences related to sample design, and collection methodology.

Salmonella

Salmonella-Multidrug Resistance

Background

Nontyphoidal *Salmonella* is estimated to cause over 1.2 million illnesses and 120 deaths each year (Scallan et al., 2011). Most *Salmonella* infections present as diarrhea, with fever and abdominal cramps. Some infections may spread to the blood and become life threatening. An estimated 100,000 infections and 40 deaths occur annually in the United States from drug-resistant nontyphoidal *Salmonella* (CDC, 2013).

Multidrug Resistance

For *Salmonella*, 14 antimicrobials from 9 classes were tested. To look at MDR by the number of drug classes or to explore specific MDR patterns, visit the NARMS data page at <http://www.fda.gov/AnimalVeterinary/SafetyHealth/AntimicrobialResistance/NationalAntimicrobialResistanceMonitoringSystem/ucm570685.htm>.

In 2015, 76% of *Salmonella* isolated from humans had no resistance to any of the antimicrobial drugs tested. Historically, isolates from turkey sources have been most frequently resistant to at least one antimicrobial. However, from 2014 to 2015 there was a 22% decline (from 73% to 57%) in the proportion of retail ground turkey isolates in this category. As has been cited in the past, bovine sources continued to have the lowest proportion of isolates with resistance to at least one antimicrobial agent.

A historically important MDR pattern in *Salmonella* is combined resistance to ampicillin, chloramphenicol, streptomycin, sulfonamides and tetracycline (ACSSuT). ACSSuT resistance has steadily declined among human isolates since 1996. This decline in ACSSuT resistance in Typhimurium has been the main driver behind an overall decline in MDR *Salmonella* in human isolates (Medalla et al., 2013). Overall, MDR among *Salmonella* isolated from humans declined from 17% in 1996 to 9.5% in 2008, remained near that level through 2014, and increased in 2015 to 12%. The slight increase in 2015 was largely driven by an increase in ASSuT resistance in a non-motile variant of serovar Typhimurium that is designated I 4,[5],12:i:-. ASSuT resistance rose from 43% in 2014 to nearly 60% in 2015 (CDC, 2017) among human I 4,[5],12:i:- isolates. In 2015, 65% of swine cecal I 4,[5],12:i:- isolates were resistant to ASSuT. A 2015 outbreak of ASSuT-resistant I 4,[5],12:i:- was linked to pork consumption (Kawakami et al., 2015).

Comparing PR/HACCP and cecal *Salmonella*, respectively, MDR was more common in isolates from turkey (48% vs. 40%) than those from chicken (9.5% vs. 15%) or cattle (21% HACCP vs. 5.6% [beef], 10% [dairy]) sources. MDR has increased from 27% to 48% in turkey PR/HACCP isolates over the past 11 years, which was largely driven by SSuT resistance.

In 2015, MDR in *Salmonella* serotype Dublin continued to increase, accounting for 11 out of 12 human isolates and 28 out of 31 cattle PR/HACCP isolates. The Dublin isolates tested annually have

high levels of MDR and ceftriaxone resistance, with some also exhibiting DSC. Dublin is a bovine-adapted serotype commonly present in cattle-HACCP and retail ground beef samples, but uncommon in human infections (CDC, 2017). When it does cause human disease, it tends to be more invasive and require antibiotic treatment, making it a rare but concerning serotype.

Salmonella – Decreased Susceptibility to Ciprofloxacin

Background

Fluoroquinolones (e.g., ciprofloxacin) are critically important for treating severe *Salmonella* infections in adults. Fluoroquinolones (e.g., enrofloxacin) also are approved for the treatment and control of certain respiratory infections in swine and cattle, and for the control of diarrhea associated with *E. coli* in weaned pigs. The extra-label use of fluoroquinolones in food-producing animals has been prohibited since 1997 (see

<https://www.fda.gov/animalveterinary/safetyhealth/antimicrobialresistance/ucm421527.htm>).

Since the 2005 FDA withdrawal of enrofloxacin use in poultry, fluoroquinolones are no longer approved for use in chickens and turkeys (see

<https://www.fda.gov/AnimalVeterinary/SafetyHealth/RecallsWithdrawals/ucm042004.htm>).

Decreased Susceptibility to Ciprofloxacin

Data in 2015 continued to indicate that ciprofloxacin resistance was uncommon in *Salmonella* isolates from all nonhuman sources monitored in NARMS. The percentage of *Salmonella* isolates with decreased susceptibility to ciprofloxacin (DSC) has remained below 10% since 1996 (when the NARMS program began). Since the FDA rescinded the poultry approvals for enrofloxacin in 2005, DSC in *Salmonella* has not exceeded 2.6% in isolates from turkey sources and 0.7% in isolates from chicken sources.

DSC has increased steadily among human *Salmonella* isolates, more than doubling from 2.7% in 2011 to nearly 6% in 2015, with nearly 14% of Enteritidis exhibiting DSC. In a similar manner, DSC has increased in cattle HACCP monitoring, reaching a high in 2015 of 4.8%. The three years of cecal sampling show DSC ranges from 1% to 5% in swine *Salmonella*.

Recent analyses have detected an increase in the number of isolates carrying qnr genes, a family of plasmid-mediated genes that confer DSC (see Plasmid-Mediated Quinolone Resistance in *Salmonella* from Swine section below). The presence of such plasmid-mediated quinolone resistance (PMQR) genes is of concern due to the potential transmission, either alone or together with other resistance genes, to susceptible strains of *Salmonella*.

Salmonella - Plasmid-Mediated Quinolone Resistance

Historically, quinolone resistance in *Salmonella* was mainly associated with specific mutations in the chromosomal genes, *gyrA* and *parC*. While these mutations can impede the ability to treat infections, they are not horizontally transmissible, thus limiting the spread of resistance to other

strains. In contrast, plasmid-mediated quinolone resistance (PMQR) genes may disseminate rapidly among diverse populations of bacteria, potentially resulting in a rapid rise in resistance in *Salmonella* in different geographical regions. PMQR genes are generally thought to be rare among *Salmonella* in the United States.

In 2015, several *Salmonella* isolates were identified from animal and retail meat sources that possessed PMQR genes. The most common PMQR gene in the US, *qnrB19*, was found in a retail pork isolate of *S. Derby*. Food animal testing identified *qnrB19* eight times: an isolate of Saintpaul from a turkey, a isolate of Muenster from a dairy cow, and six isolates of serotypes Anatum (3), Johannesburg(1), Typhimurium (1), and I 4,[5],12:i:- (1) from swine (both market hogs and sows); One instance of I 4,[5],12:i:- isolated from a market hog carried *qnrB2*.

Salmonella isolates from swine sources with *qnrB19*-containing plasmids were also identified in 2014, when one retail pork and 13 swine cecal isolates had this PMQR gene. Although the isolates are from diverse serotypes, it appears that two distinct ~3-kb clonal ColE-type plasmids are responsible for the wide dissemination of these resistance genes (Tyson et al., 2017).

Salmonella – Cephalosporin Resistance

Background

Extended-spectrum cephalosporins such as ceftriaxone are critically important drugs for treating severe *Salmonella* infections, especially in children. A related cephalosporin, ceftiofur, is approved for therapeutic use in food-producing animals (find more information at <https://animaldrugsfda.fda.gov/adafda/views/>). Resistance to ceftiofur may result in cross-resistance to other drugs of the same class.

Resistance

Ceftriaxone resistance increased between 2002 and 2010 in *Salmonella* recovered from retail turkey (2.6% in 2002 to 16% in 2010) and chicken (10% to 38%). Given the critical importance of this drug class, the FDA used these findings and other data to prohibit certain unapproved uses of cephalosporin drugs in cattle, swine, chickens, and turkeys. FDA announced the cephalosporin order of prohibition in 2008 (see <https://www.fda.gov/AnimalVeterinary/SafetyHealth/AntimicrobialResistance/ucm421538.htm>), and the order went into effect in April 2012.

Since 2012, ceftriaxone resistance has declined in NTS from all NARMS nonhuman sources except for turkey PR/HACCP isolates, where resistance remained at 16% in 2015. This decline in ceftriaxone resistance following FDA's targeted prohibition on extralabel cephalosporin use is similar to what others have observed following reductions in the use of ceftiofur in animal production (Agerso and Aarestrup, 2013; PHAC, 2014), indicating that the intervention may be having the intended effect on some bacteria.

Among human isolates, ceftriaxone resistance peaked at 4.4% in 2003, and was present in 3% of human isolates in 2015. Among specific serotypes, ceftriaxone increased in human isolates and some animal isolates of I 4,[5],12:i:- and Infantis since 2012 (see figure below).

Salmonella serotype Kentucky is a common poultry serotype that often exhibits ceftriaxone resistance (8.6% of PR/HACCP isolates in 2015). While ceftriaxone resistance declined among the predominantly poultry serotypes of Kentucky and Heidelberg, it remained high in Typhimurium, indicating that this serotype is a reservoir of resistance to extended-spectrum cephalosporins. Ceftriaxone resistance in *Salmonella* from cattle has long been most common in serotype Newport, with 5 out of 6 isolates resistant in 2015.

Historically, ceftriaxone resistance in *Salmonella* in the United States has been due to the *bla*_{CMY-2} gene. Recently, whole genome sequencing has shown *bla*_{CTX-M} genes among *Salmonella* strains in the United States, mainly among serotype Infantis (Tate et al., 2017). These genes are common in other parts of the world. NARMS continues to monitor this trend closely.

Salmonella - Azithromycin Resistance

Azithromycin (AZM) is a clinically important macrolide often used for the treatment of nontyphoidal *Salmonella* (NTS) when treatment is indicated (DuPont, 2009). In recent years, azithromycin use for NTS has increased, likely due to concerns about resistance to fluoroquinolones (e.g., ciprofloxacin) (Sjölund-Karlsson et al., 2011) especially in returned travelers (Wen et al., 2017).

Since 2011, NARMS has tested *Salmonella* isolates from humans, retail meats, and food animals to determine susceptibilities to azithromycin using the CLSI investigational breakpoint of ≥ 32 $\mu\text{g}/\text{mL}$ developed for *Salmonella* Typhi. This correlates with NARMS genomic data that showed the presence of resistance mechanisms in NTS isolates with MICs ≥ 32 $\mu\text{g}/\text{mL}$.

Since azithromycin testing began in 2011, resistance from all NARMS sources doubled from 7 to 15 isolates. Eight azithromycin-resistant isolates were from humans and 7 were from poultry sources, including the first observed in retail meat (serotype Derby from ground turkey). Besides a human isolate of serotype Oranienburg, all azithromycin-resistant isolates exhibited resistance to additional antimicrobial agents. Five out of 8 azithromycin-resistant isolates from humans also displayed DSC. Azithromycin resistance was associated with the *mphA* gene in 5 (4 from humans and 1 from chicken ceca) of the 8 isolates sequenced. One isolate contained *mphE* and 2 isolates are being examined for a possible novel resistance mechanism.

Although azithromycin resistance in NTS is rare, the increased resistance along with co-resistance to other agents warrants close attention. NARMS is currently investigating the genetic mechanisms and epidemiology of both sporadic and outbreak-associated AZM-R *Salmonella* to determine the possible sources and outcomes of infection.

Campylobacter

Background

Campylobacter is estimated to cause over 1.3 million illnesses and 120 deaths in the United States each year (Scallan et al., 2011). Most people who become ill from *Campylobacter* develop diarrhea, abdominal pain and fever. Approximately 86% of human *Campylobacter* infections are caused by *Campylobacter jejuni* and 10% by *Campylobacter coli*. Case-control studies have shown poultry to be a major food source for these infections.

Macrolide Resistance

Macrolides are considered the first-line agents for the treatment of severe campylobacteriosis in humans (Allos and Blaser, 2010). Macrolides are also approved for use in all major classes of food-producing animals (for more information, see <https://animaldrugsatfda.fda.gov/adafda/views/#/search>).

C. jejuni from both humans and chicken sources have exhibited erythromycin resistance rates of less than 4% since NARMS testing began. In 2015, erythromycin resistance in *C. jejuni* was below 3% in isolates from all sources except for market hog cecal isolates, where resistance was present in 1 of 8 isolates (13%). Among *C. jejuni* cecal isolates from cattle, erythromycin resistance was absent in beef cows and very low in dairy cow (0.8%) isolates.

Historically, *C. coli* are more commonly resistant to erythromycin and other agents than *C. jejuni*. Erythromycin resistance in *C. coli* among human and chicken sources has increased 3- to 5-fold since 2011 (see figure below). So far, it does not appear that this rapid rise in resistance is due to a transmissible macrolide gene (FDA, 2016).

Fluoroquinolone Resistance

Fluoroquinolones are an alternative therapy for treating campylobacteriosis in adults (Allos and Blaser, 2010). Fluoroquinolones have not been used in chickens and turkeys since 2005. Currently, there are FDA approvals for fluoroquinolones in swine and some cattle, and FDA prohibits off-label uses (for more information, see <https://animaldrugsatfda.fda.gov/adafda/views/#/search>).

Ciprofloxacin resistance increased in *C. coli* from humans (from 34% in 2012 to 40% in 2015) and continued to increase or remained high in *C. jejuni* isolates from cattle (in beef ceca, it increased from 14% in 2013 to 20% in 2015) and chicken (HACCP) (ranging between 22% and 28% from 2012-2015).

Generic Escherichia coli

Background

Escherichia coli are monitored as indicator organisms for antimicrobial resistance and for specific resistance genes that could be transferred to other pathogenic gram-negative bacteria (e.g.,

Salmonella). *E. coli* are tested for susceptibility to the same antimicrobials used in *Salmonella* testing. Antimicrobial resistance surveillance is not conducted for indicator organisms from healthy human populations.

Antibiotic Resistance in *E. coli*

As with *Salmonella*, in 2015, *E. coli* isolated from turkey sources were most frequently resistant to at least one antimicrobial (85% from ground turkey meat and 90% from turkey ceca), whereas cattle isolates were least frequently resistant (20% from retail ground samples, 41% from beef cow ceca and 24% from dairy cow ceca).

Cephalosporin Resistance

Ceftriaxone resistance in *E. coli* isolates from retail chicken meat decreased from a peak of 13% in 2011 to 6% in 2015. Among retail turkey isolates, ceftriaxone resistance declined from a peak of 10% in 2011 to 4% in 2014, then increased to 6% in 2015. This was the first increase in ceftriaxone resistance since its peak in 2011. Among *E. coli* isolated from cattle and swine cecal samples, ceftriaxone resistance remained below 1%. Isolates from turkey ceca had the highest resistance at 9%. Ceftriaxone resistance from *E. coli* isolated from chicken ceca increased from 2% in 2014 to 4% in 2015.

Multidrug Resistance

In 2015, retail ground turkey had the highest prevalence of resistance to three or more drug classes (57%), followed by isolates from retail chicken (31%), retail pork chops (12%), and retail ground beef (7%). Among cecal samples, turkey isolates had the highest prevalence of resistance to three or more drug classes (64%); dairy cow isolates had the lowest (11%).

Enterococcus

Background

Enterococcus species are a natural constituent of animal and human intestinal microflora and are a microbial indicator of fecal contamination of food. *Enterococcus* can be present in high numbers in food but is not considered a major foodborne pathogen. Antimicrobial resistance in *Enterococcus* species is monitored to understand resistance to antimicrobials active against gram-positive bacteria. As with *E. coli*, resistance in *Enterococcus* is not tracked in healthy human populations.

Antimicrobial Resistance

In samples collected in 2015, >98% of *E. faecalis* and >84% *E. faecium* isolates from retail meat were resistant to at least one antimicrobial class. Among cecal isolates, >78% of *E. faecalis* and >99% *E. faecium* were resistant to at least one antimicrobial class.

Ampicillin, alone or in combination with aminoglycoside, is the treatment of choice for susceptible *E. faecalis* infections. Penicillin resistance in *E. faecalis* has remained very low ($\leq 1\%$) across all NARMS

sources. In 2015, high-level gentamicin resistance to gentamicin was most common among retail poultry isolates (24% in chickens and 34% in turkeys) and least common in retail cattle and swine (0% and 1% respectively).

Other treatment options for enterococcal infections include vancomycin, daptomycin, and linezolid. Resistance to these three antibiotics is generally very low (<2%) in *E. faecalis* isolates from all NARMS retail and animal sources.

NARMS has not detected vancomycin or linezolid resistance in *Enterococcus* from retail meat. In 2015, none of the *E. faecalis* isolates from retail meat were resistant to daptomycin.

Multidrug Resistance

MDR has been consistently high among *E. faecium* and *E. faecalis* isolated from retail poultry. Cecal isolates of *E. faecium* and *E. faecalis* from swine tended to exhibit higher levels of MDR, when compared to retail pork.

Antimicrobial Use

The United States National Action Plan for Combating Antibiotic-Resistant Bacteria (available at https://www.cdc.gov/drugresistance/pdf/national_action_plan_for_combating_antibiotic-resistant_bacteria.pdf) emphasizes the importance of monitoring both antimicrobial resistance and antimicrobial use in humans and animals. Gathering information on the ways antibiotics are used is one essential component to ensuring judicious use of antimicrobials in all sectors (human, animal, and environment).

In 2012, FDA initiated strategy designed to promote judicious use of medically important antimicrobials in food-producing animals. As outlined in Guidance for Industry #209 (available at <https://www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/UCM216936.pdf>), this strategy has two main principles: 1) limit medically important antimicrobials to uses in food-producing animals that are necessary to assure animal health; and 2) new requirements for veterinary oversight of antibiotic use. This strategy was implemented in January 2017. Since then, the use of medically important antimicrobials for growth promotion and improved feed efficiency was no longer allowed, and veterinary oversight was required for their use in animal food and water.

Since 2009, FDA has collected and reported the annual sales and distribution of antimicrobials approved for use in food-producing animals. Along with new judicious use guidelines, the FDA enhanced drug sales data beginning in 2016, when drug sponsors were required to begin providing species-specific estimates of the sales and distribution data. While providing important information, a limitation of these sales and distribution data is that they reflect the total quantity of antimicrobial drug product that enters the market, but not how much or for what purpose these drugs are ultimately used in treated animals.

The 2015 Summary Report on Antimicrobials Sold or Distributed for Use in Food-Producing Animals (available at <https://www.fda.gov/downloads/ForIndustry/UserFees/AnimalDrugUserFeeActADUFA/UCM534243.pdf>) showed that for medically important agents, tetracyclines accounted for 71% of sales; penicillins for 10%; macrolides for 6%; sulfonamides for 4%; aminoglycosides for 4%; lincosamides for 2%; and phenicols, cephalosporins, and fluoroquinolones each for less than 1%. Domestic sales and distribution increased by 26% from 2009 through 2015, and increased by 2% from 2014 through 2015. Aminoglycoside data showed the greatest percentage increase in domestic sales (13%) from 2014 through 2015.

At the [USDA](#) and [FDA](#), efforts are ongoing to identify practicable long-term strategies for collecting and reporting actual drug use data that overcomes the limitation of summary sales and distribution data by drug class. For example, USDA has developed an action plan (available at <https://www.usda.gov/sites/default/files/documents/usda-antimicrobial-resistance-action-plan.pdf>), and FDA offers grants for data collection related to antimicrobial use and resistance (for more information, see <https://www.fda.gov/AnimalVeterinary/NewsEvents/CVMUpdates/ucm490556.htm>). This information will help FDA further target its efforts to ensure judicious use of these important drugs.

References

- Agerso Y, Aarestrup FM. Voluntary ban on cephalosporin use in Danish pig production has effectively reduced extended-spectrum cephalosporinase-producing *Escherichia coli* in slaughter pigs. *J Antimicrob Chemother* 2013; **68**:569-572.
- Allos BM, Blaser MJ. *Campylobacter jejuni* and related species. , p 2793-2802. In Mandell GL, Bennett, J.E., and Dolin, R. (ed), *Principles and Practice of Infectious Diseases*, 7 ed. 2010 Churchill Livingstone, Philadelphia, PA.
- Centers for Disease Control and Prevention (CDC). Antibiotic Resistance Threats in the United States, 2013. Atlanta, Georgia: U.S. Department of Health and Human Services, CDC, 2013
- Centers for Disease Control and Prevention (CDC). National Antimicrobial Resistance Monitoring System for Enteric Bacteria (NARMS): Human Isolates Surveillance Report for 2015 (Final Report). Atlanta, Georgia: U.S. Department of Health and Human Services, CDC, 2017
- Clinical and Laboratory Standards Institute (CLSI). Performance Standards for Antimicrobial Susceptibility Testing; Twenty-Seventh Informational Supplement. CLSI Document M100-S27. Wayne, PA: CLSI, 2017.
- Crump JA, Barrett TJ, Nelson JT, Angulo FJ. Reevaluating fluoroquinolone breakpoints for *Salmonella enterica* serotype Typhi and for non-Typhi salmonellae. *Clin Infect Dis* 2003; **37**:75-81.
- DuPont HL. Bacterial diarrhea. *N Engl J Med* 2009;**361**(16):1560–1569.
- Food and Drug Administration (FDA). National Antimicrobial Resistance Monitoring System-Enteric Bacteria (NARMS): 2014 Integrated Report. Rockville, MD: U.S. Department of Health and Human Service, FDA, 2016.
- Kawakami VM, Bottichio L, Angelo K, Linton N, Kissler B, Basler C, Lloyd J, Inouye W, Gonzales E, Rietberg K, Melius B, Oltean H, Wise M, Sinatra J, Marsland P, Li Z, Meek R, Kay M, Duchin J, Lindquist S. Notes from the Field: Outbreak of Multidrug-Resistant *Salmonella* Infections Linked to Pork--Washington, 2015. *MMWR Morb Mortal Wkly Rep* 2016; **65**(14):379-81.
- Medalla F, Hoekstra RM, Whichard JM, Barzilay EJ, Chiller TM, Joyce K, Rickert R, Krueger A, Stuart A, Griffin PM. Increase in resistance to ceftriaxone and nonsusceptibility to ciprofloxacin and decrease in multidrug resistance among *Salmonella* strains, United States, 1996-2009. *Foodborne Pathog Dis* 2013; **10**:302-309.
- Public Health Agency of Canada (PHAC). Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS), Surveillance Bulletin. Public Health Agency of Canada, 2014.
- Scallan E, Hoekstra RM, Angulo FJ, Tauxe RV, Widdowson MA, Roy SL, Jones JL, Griffin PM. Foodborne illness acquired in the United States--major pathogens. *Emerg Infect Dis* 2011;**17**:7-15.

Sjölund-Karlsson M, Joyce K, Blickenstaff K, Ball T, Haro J, Medalla FM, Fedorka-Cray P, Zhao S, Crump JA, Whichard JM. Antimicrobial susceptibility to azithromycin among *Salmonella enterica* isolates from the United States. *Antimicrob Agents Chemother* 2011;55(9):3985–3989.

Tate H, Folster JP, Hsu CH, Chen J, Hoffmann M, Li C, Morales C, Tyson GH, Mukherjee S, Brown AC, Green A, Wilson W, Dessai U, Abbott J, Joseph L, Haro J, Ayers S, McDermott PF, Zhao S. Comparative Analysis of Extended-Spectrum- β -Lactamase CTX-M-65-Producing *Salmonella enterica* Serovar Infantis Isolates from Humans, Food Animals, and Retail Chickens in the United States 2017;61(7)

Tyson GH, Tate HP, Zhao S, Li C, Dessai U, Simmons M, McDermott PF. Identification of Plasmid-Mediated Quinolone Resistance in *Salmonella* Isolated from Swine Ceca and Retail Pork Chops in the United States. *Antimicrob Agents Chemother*. 2017.

Wen SC, Best E, Nourse C. Non-typhoidal *Salmonella* infections in children: Review of literature and recommendations for management. *Journal of Paediatrics and Child Health*. J Paediatr Child Health 2017; DOI:10.1111/jpc.13585.

Supplemental Materials

NARMS Interagency Laboratory Manual (see <https://www.fda.gov/downloads/AnimalVeterinary/SafetyHealth/AntimicrobialResistance/NationalAntimicrobialResistanceMonitoringSystem/UCM528831.pdf>)

NARMS Retail Meat Isolation Protocol (see <https://www.fda.gov/downloads/AnimalVeterinary/SafetyHealth/AntimicrobialResistance/NationalAntimicrobialResistanceMonitoringSystem/UCM456343.pdf>)

Methodology (see <https://www.fda.gov/downloads/AnimalVeterinary/SafetyHealth/AntimicrobialResistance/NationalAntimicrobialResistanceMonitoringSystem/UCM529808.pdf>)

Statistical Trend Analysis (see <https://www.fda.gov/AnimalVeterinary/SafetyHealth/AntimicrobialResistance/NationalAntimicrobialResistanceMonitoringSystem/ucm418884.htm>)

FDA Center for Veterinary Medicine Antimicrobial Resistance Page (see <https://www.fda.gov/AnimalVeterinary/SafetyHealth/AntimicrobialResistance/default.htm>)

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