NARMS Integrated Report: 2012-2013

The National Antimicrobial Resistance Monitoring System: Enteric Bacteria

Introduction

This report summarizes the major findings of the National Antimicrobial Resistance Monitoring System (NARMS) for calendar years 2012 and 2013. The most important resistance findings for *Salmonella, Campylobacter, Escherichia coli* and *Enterococcus* are highlighted.

Salmonella and *Campylobacter* are the leading bacterial causes of foodborne illness. Isolates from human laboratory-confirmed clinical cases are tested and compared with bacteria derived from various stages in the food production chain. Intestinal (cecal) samples are collected at slaughter from eight animal production classes (broiler chickens, turkeys, dairy cattle, beef cattle, steers, heifers, market hogs and sows) along with isolates from the processing line recovered from chicken rinses, turkey carcass swabs and ground product of chicken, turkey, and beef. This is coupled with *Salmonella* and *Campylobacter* from four retail meat products (chicken, ground turkey, ground beef and pork chops) purchased at retail outlets in 14 states on a monthly basis.

E. coli and *Enterococcus* from the animal and meat samples are also tested. These are used as indicator organisms for testing of resistance to antimicrobials that are active against Gram-negative and Gram-positive bacteria, respectively. Antimicrobial resistance data are generated using the same methods and analyzed in an integrated way to measure the dissemination of resistant bacteria and resistance genes through the food supply.

In this report we focus 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 patterns that have been linked to severe illness in humans.

Further details on resistance to antimicrobials not included in this summary can be found in the data tables and in the interactive graphs.

What is New in this Report?

Expanded Animal Testing: In 2013 NARMS implemented a new sampling scheme to culture the cecal (intestinal) contents of food-producing animals presented for slaughter. This represents a major change to NARMS and has resulted, for the first time, in a random and nationally representative sampling of all four major food animal species and antimicrobial susceptibility data on all four bacteria targeted in NARMS. Since NARMS began, the animal component tested antimicrobial susceptibility in *Salmonella* isolates that were collected as part of the United States Department of Agriculture (USDA) Pathogen Reduction Hazard Analysis and Critical Control Point program (PR/HACCP), which monitors the ability of processing plants to control microbiological hazards. Cecal specimens reflect the microbial status of individual animals that have not been exposed to in-plant processing, making them better indicators of the microbial status of animals on farm (WHO, 2013). In addition, the new in-plant sampling makes it possible to distinguish *market hogs* and *sows* among swine samples and *dairy* and *beef* among cattle samples. In this summary we distinguish cecal samples and PR/HACCP samples to indicate the point at which they were collected. Additional details on sample sources and sampling methodology can be found here.

Table 1. Isolate sources

Human	Chickens	Turkeys	Cattle	Swine
Clinical illness	Retail Chicken PR/HACCP Cecal	Retail Ground Turkey PR/HACCP Cecal	Retail Ground Beef PR/HACCP Cecal Beef Cecal Dairy	Retail Pork Chops PR/HACCP[†] Cecal Market Hogs Cecal Sows

[†]Swine PR/HACCP carcass sampling was discontinued in July 2011.

Interpreting *Campylobacter* Results: Unlike the other bacteria tested in NARMS, there are no formal clinical breakpoints established for *Campylobacter*. In this report, NARMS used a different approach to interpret antimicrobial susceptibility data for *Campylobacter* based on epidemiological cut-off values (ECOFFs). ECOFFs are used to distinguish isolates with any acquired resistance trait (non-wild type) from those without any acquired traits (wild type). In this report, non-wild-type *Campylobacter* isolates are termed *resistant*. It is important to emphasize that because ECOFFs are based only on features of the bacterium (*e.g.*, their MIC), they are distinct from clinical breakpoints. Clinical breakpoints define *resistance* using pharmacological parameters and data from clinical trial outcomes. This change facilitates detection of emerging resistance and is a step toward globally harmonized methods for *Campylobacter* surveillance. Please see the Guidance for Readers for a description of what ECOFFs are and how they differ from clinical breakpoints.

Cefepime breakpoints: In 2014, the Clinical and Laboratory Standards Institute (CLSI) revised the breakpoints for cefepime, an antimicrobial that is used to screen for extended-spectrum beta-lactamase (ESBL) production (CLSI M100-S24 document, 2014). The cefepime resistance breakpoint was lowered from ≥32 µg/mL to ≥ 16 µg/mL. Also included in the cefepime revision was the introduction of the *susceptible-dose dependent* (SDD)[1] category, which was created to address issues with different dosing regimens. The new breakpoints and SDD category have been applied in this report.

Pathogenic Bacteria

Non-Typhoidal *Salmonella*

Non-typhoidal *Salmonella* (*i.e*., serotypes other than Typhi, Paratyphi A, Paratyphi B, and Paratyphi C) usually cause diarrhea, fever and abdominal cramps. Some infections spread to the blood and can be life-threatening. Non-typhoidal *Salmonella* causes approximately 1.2 million illnesses, 23,000 hospitalizations, and 450 deaths each year in the United States (Scallan et al., 2011). Direct medical costs are estimated to be $3.6 billion annually (Economic Research Service, 2014).

Physicians rely on antimicrobials such as ceftriaxone and ciprofloxacin for treating patients with severe *Salmonella* infection. Therefore, preventing resistance to these classes of antimicrobials is important. It is estimated that approximately 100,000 drug-resistant non-typhoidal *Salmonella* infections and 40 deaths occur annually in the US (CDC, 2013).

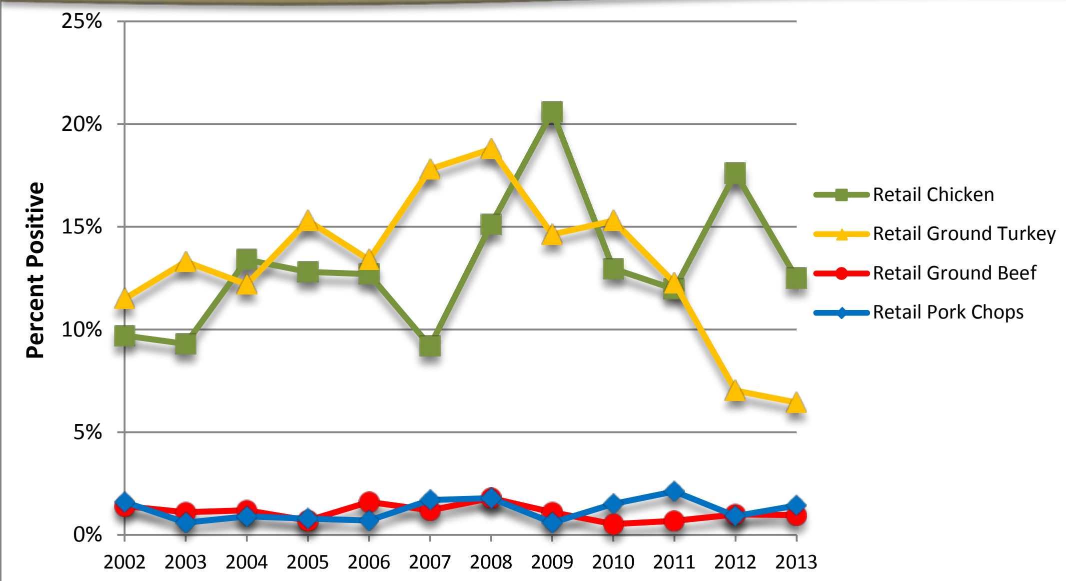
Prevalence of Non-Typhoidal *Salmonella*

In 2012, a total of 3,897 non-typhoidal *Salmonella* isolates were tested, 2,233 from humans, 345 from retail meats, and 1,319 from PR/HACCP samples.

For retail meat testing in 2012, *Salmonella* was isolated from 18% of chicken, 7% of ground turkey, 1% of ground beef, and 0.9% of pork chops (**Figure 1**).

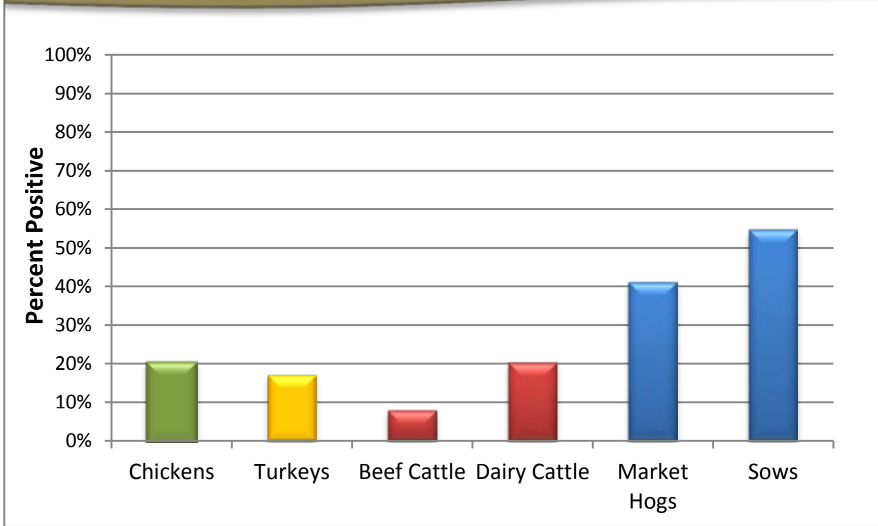
[1] Additional information on the definition and use of susceptible-dose dependent (SDD) category can be found at the following location http://community.clsi.org/micro/wp-content/uploads/sites/15/2013/07/Cefepime-BP-Change-for-Enterobacteriaceae_-Intro-of-SDD-For-Labs.pdf

Figure 1. Prevalence of *Salmonella* in Retail Meat Samples, 2002-2013



In 2013, a total of 4,514 non-typhoidal *Salmonella* isolates were tested, 2,178 from humans, 353 from retail meats, 917 from PR/HACCP testing, and 1,066 from food animal ceca (from March 2013).

Figure 2. Prevalence of *Salmonella* in Animal Cecal Samples, 2013



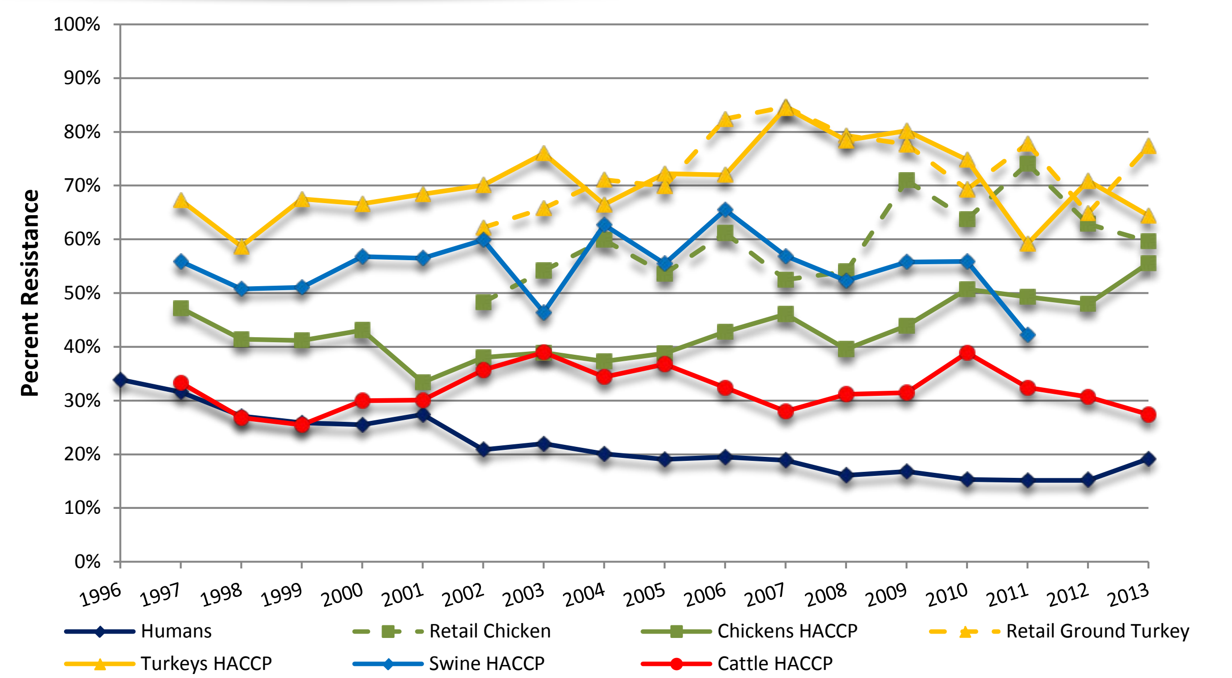
For retail meat testing in 2013, *Salmonella* was isolated from 13% of chicken meat, 6.4% of ground turkey, 0.9% of ground beef, and 1.4% of pork chops (**Figure 1**). Between 2008 and 2013 there has been a steady decline in the proportion of retail turkey samples that yielded *Salmonella* from 19% to 6.4% (**Figure 1**). The reason for this decline is not known.

For cecal samples, tested for the first time in 2013, *Salmonella* was isolated from 20% of chickens, 17% of turkeys, 7.9% of beef cattle, 21% of dairy cattle, 41% of market hogs and 55% of sows (**Figure 2**).

Antimicrobial Resistance in Non-Typhoidal *Salmonella*

In 2012, 85% of *Salmonella* isolated from humans had no resistance to any of the antimicrobials tested, and in 2013, 81% of *Salmonella* isolates from humans had no resistance to any of the antimicrobials tested. Among resistant bacteria from retail meats and PR/HACCP samples, isolates from turkey sources were more frequently resistant to at least one antimicrobial and those from bovine sources were least frequently resistant (**Figure 3**).

Figure 3. Non-typhoidal *Salmonella* from Foods, Animals and Humans Resistant to At Least 1 Antimicrobial, 1996-2013



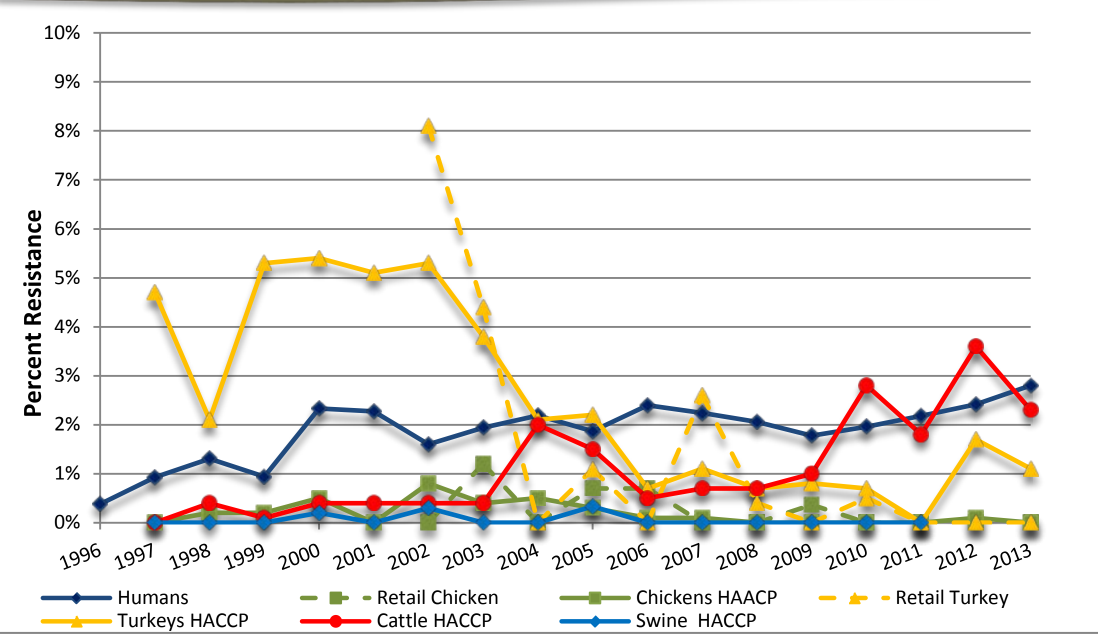
Quinolone Resistance

In the United States, fluoroquinolones (*e.g.*, ciprofloxacin) are critically important antimicrobials for treating severe *Salmonella* infections in adults. Other 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. Since the FDA withdrawal of enrofloxacin for poultry in 2005, fluoroquinolones are no longer approved for use in this animal species. The extra-label use of fluoroquinolones in food-producing animals also has been prohibited since 1997.

Ciprofloxacin non-susceptibility for *Salmonella* has been below 10% since 1996 when the NARMS program began. Resistance to nalidixic acid correlates with decreased susceptibility to ciprofloxacin. Although nalidixic acid resistance remains low overall, it has steadily increased in *Salmonella* isolates from human clinical cases from 0.4% in 1996 to a peak of 2.8% in 2013 (**Figure 4**). This trend is driven mainly by an increase in nalidixic acid resistance among serotype

Enteritidis, the most common serotype in human illness. Many of these infections were likely acquired during foreign travel (see more here). In addition, nalidixic acid has increased in cattle isolates from 0% in 1997 to 2.3% in 2013, and decreased among turkey isolates from 5.3% in 2002 to 1.1% in 2013.

Figure 4. Nalidixic Acid Resistance in Non-typhoidal *Salmonella*



Cephalosporin Resistance

Extended-spectrum cephalosporins like 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 (Animal Drugs @ FDA). Resistance to one compound results in cross-resistance to the other.

Ceftriaxone resistance increased in *Salmonella* from turkey sources and retail chicken meat between 2002 and 2010 and declined slightly in isolates from cattle and swine (**Figure 5** and **Figure 6**). The increases were often present as part of a multidrug resistance pattern (see below). 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. The cephalosporin order of prohibition went into effect in April 2012.

Figure 5. Ceftriaxone Resistance in Non-typhoidal *Salmonella* from Poultry and Humans

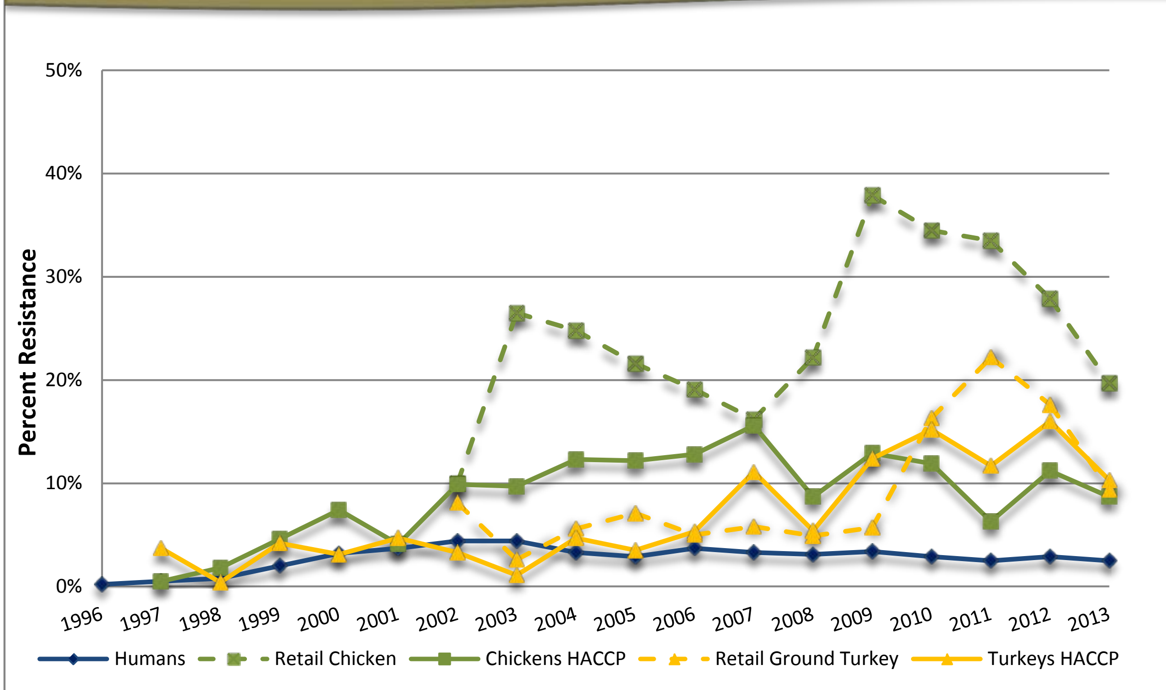
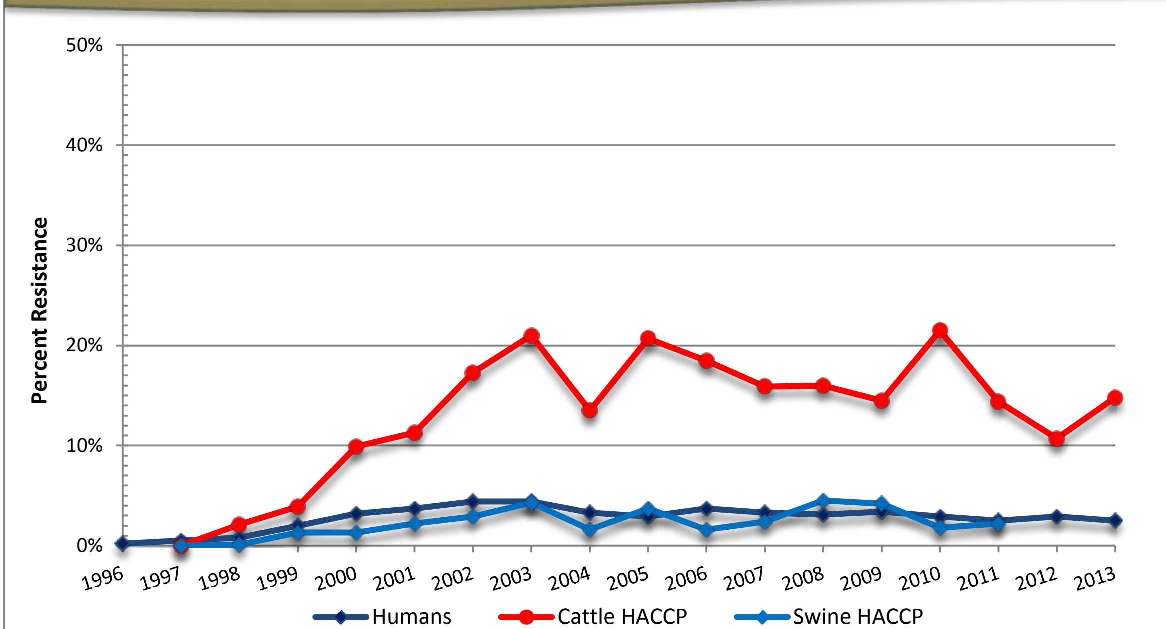


Figure 6. Ceftriaxone Resistance in Non-typhoidal *Salmonella* from Cattle, Swine, and Humans



Although resistance to ceftriaxone appears to be declining among non-typhoidal *Salmonella*, its prevalence varies by serotype and source. Among human isolates, the proportion of *Salmonella* showing ceftriaxone resistance declined from 3.4% in 2009 to 2.5% in 2013. This was paralleled by a decline in resistance from 38% to 20% in retail chicken isolates during the same time frame (**Figure 5**). Among retail ground turkey isolates, resistance showed a continued decline to 9.4% after peaking at 22% in 2011 (**Figure 5**).

The proportion of human S*almonella* serotype Heidelberg resistant to ceftriaxone was 15% in 2013, down from a peak of 24% in 2010. In Heidelberg isolates from retail chicken, resistance was 0% in 2013, after peaking to 32% in 2009. Among retail ground turkey isolates, ceftriaxone resistance declined to 29% on 2013 after reaching a peak of 39% in 2011.

Among human isolates of serotype Typhimurium, ceftriaxone resistance is < 7% since testing began in 1996. In retail chicken isolates, however, resistance has ranged between 33% and 64% since testing began in 2002; in 2013, 50% of the isolates were resistant.

High ceftriaxone resistance among serotypes associated with cattle sources (**Figure 6**), is mainly due to serotype Newport, and has declined slightly since 2002. In contrast, ceftriaxone resistance has appeared in an increasing proportion of strains of serotype Dublin from cattle sources (see TEXT BOX 1). While Dublin is not a common cause of human infection, it is more likely to result in bacteremia than other serotypes. It is also a challenge in veterinary medicine as a common cause of neonatal calf diarrhea.

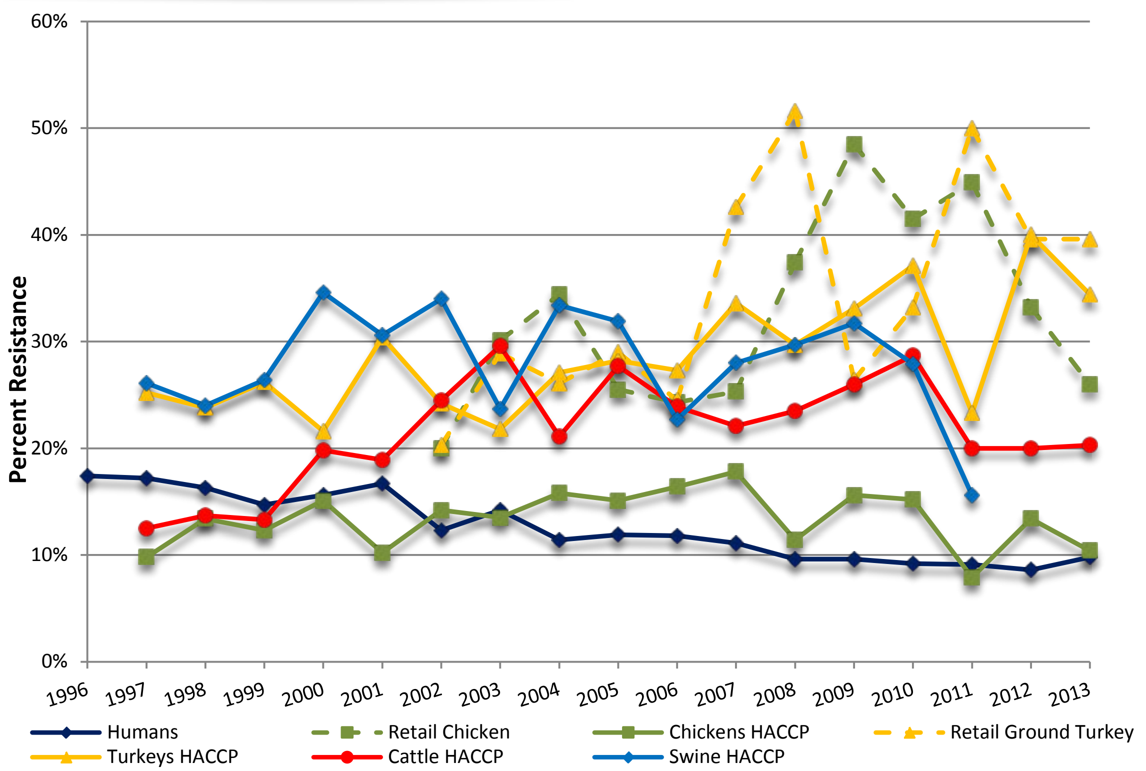
More information on ceftriaxone resistance in other serotypes is presented in the complete data tables associated with this report.

Multidrug Resistance

Multidrug resistance (MDR) is defined as resistance to 3 or more classes of antimicrobials. This categorization makes no distinction among the classes based on their importance to human medicine. Evidence shows, however, that patients with MDR *Salmonella* infections may have more severe clinical disease and a greater likelihood of hospitalization (Krueger AL, et al 2014; Varma JK, et al. 2005b).

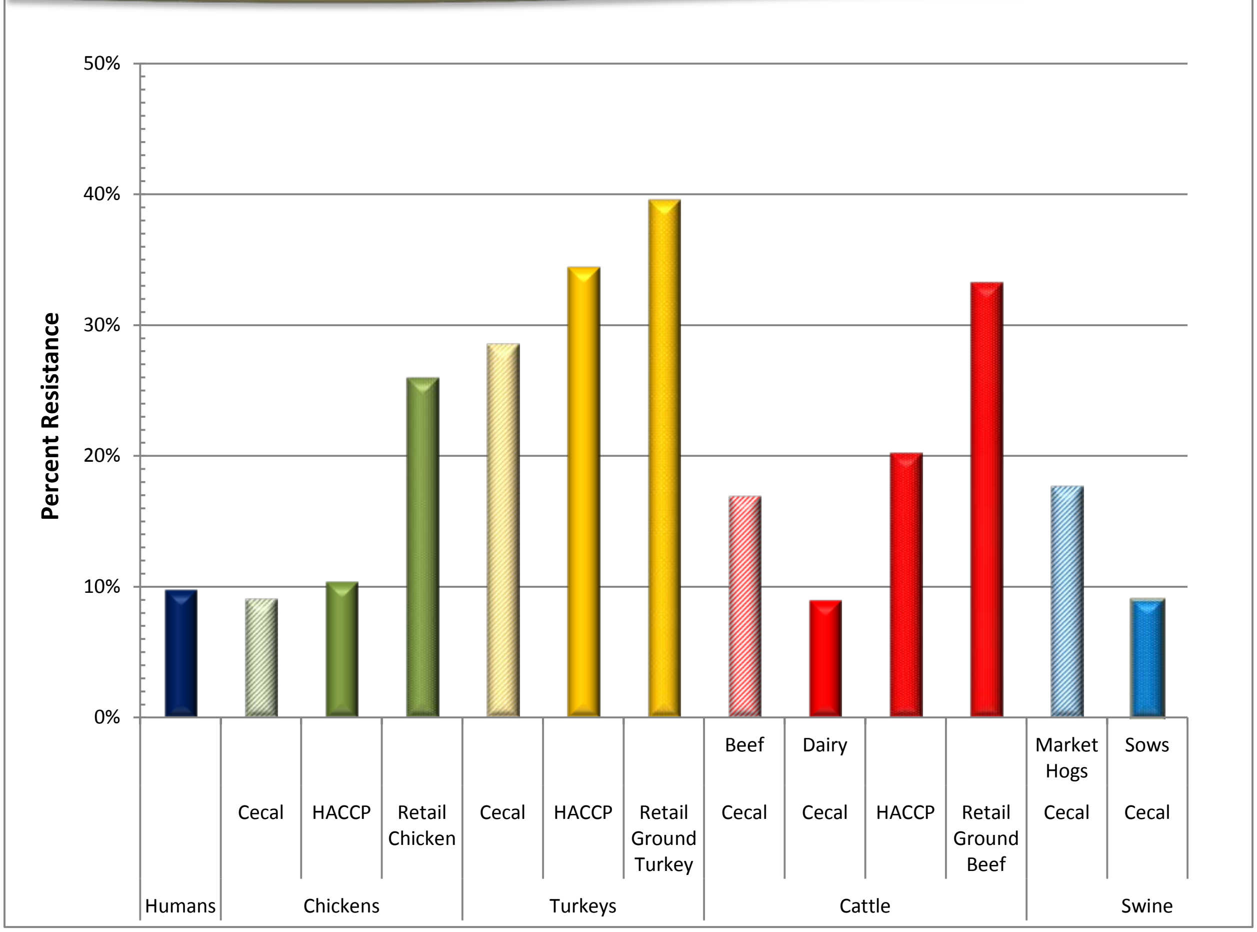
MDR among human *Salmonella* isolates declined from 17% in 1996 to 9.6% in 2008, and has remained stable since, appearing in 9.8% of human isolates in 2013

Figure 7. Non-typhoidal *Salmonella* Resistant to 3 or More Classes of Antimicrobials



In 2013 PR/HACCP isolates, MDR was more common in turkey (34%) and ground beef (20%) isolates than chicken (10%) isolates (**Figure 7**). MDR was high among all retail foods, ranging from 26% to 40%. Interestingly, PR/HACCP and retail meat isolates are significantly more likely to exhibit MDR than are animal or human isolates (**Figure 8**). The reasons for this are not known. Since this is the first year of cecal testing, it remains to be seen whether the tendency for the proportion of *Salmonella* isolates with resistance to increase from earlier to later stages of processing will be a consistent finding over time. For chicken isolates, a higher proportion of MDR and ceftriaxone-resistance in retail versus PR/HACCP isolates has been apparent since food testing began in 2002.

Figure 8. Non-typhoidal *Salmonella* Resistant to 3 or More Classes of Antimicrobials in 2013



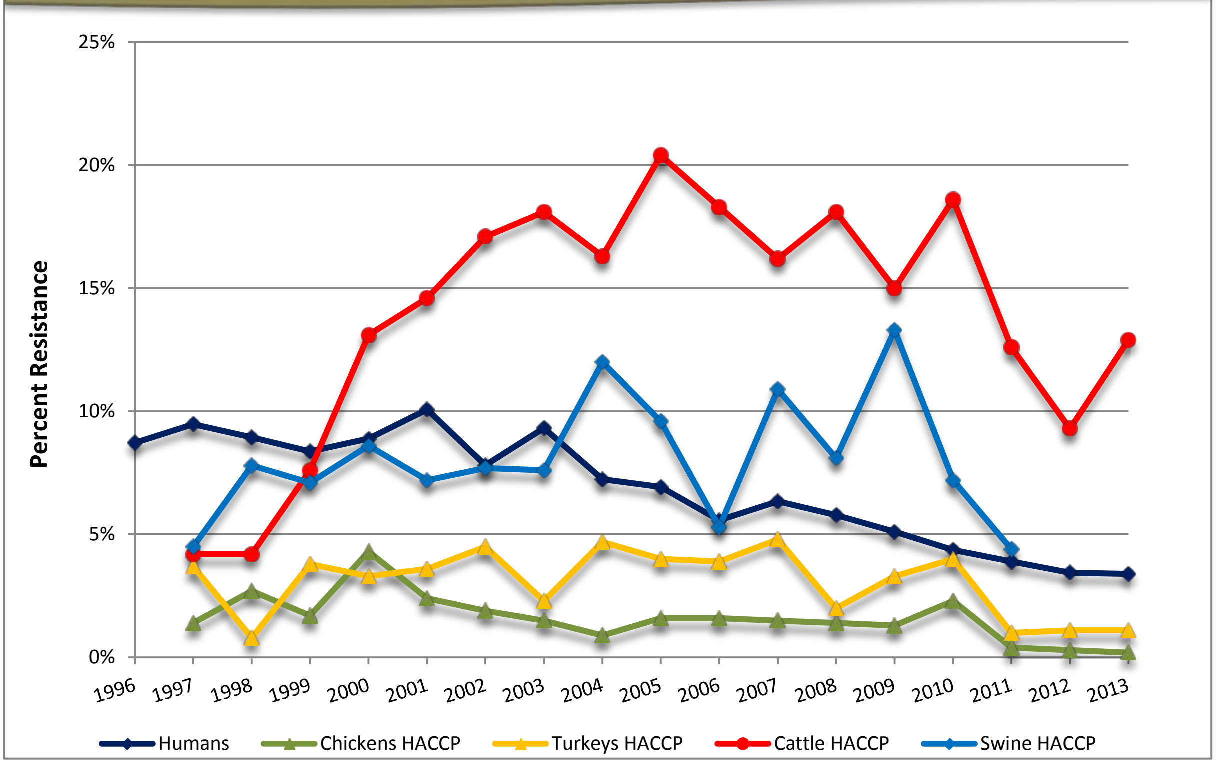
*No PR/HACCP sampling of Swine was performed in 2013.

Among new developments is the emergence of MDR in *Salmonella* serotype Dublin in recent years. While the incidence of human infections is relatively low, it is among the top 4 serotypes isolated from retail ground beef and PR/HACCP ground beef. The few human serotype Dublin isolates tested annually have high levels of MDR, along with frequent resistance to quinolones and cephalosporins. Nalidixic acid resistance was found in 30% (9/30) of Dublin PR/HACCP isolates obtained from cattle in 2012 and in 19% (4/21) in 2013. Ceftriaxone resistance was present in 11/12 human isolates in 2013.

An important MDR pattern in *Salmonella* is the combined resistance to ampicillin, chloramphenicol, streptomycin, sulfonamides, and tetracycline (ACSSuT). Among all serotypes, the percentage of human isolates resistant to at least ACSSuT declined to 3.4%, the lowest since testing began in 1996 (**Figure 9**). This MDR pattern is most common in cattle isolates, and was present in 13% of the PR/HACCP ground beef strains in 2013, a slight increase from 2012 (9.3%). In poultry strains of *Salmonella*, ACSSuT resistance has been consistently <5%.

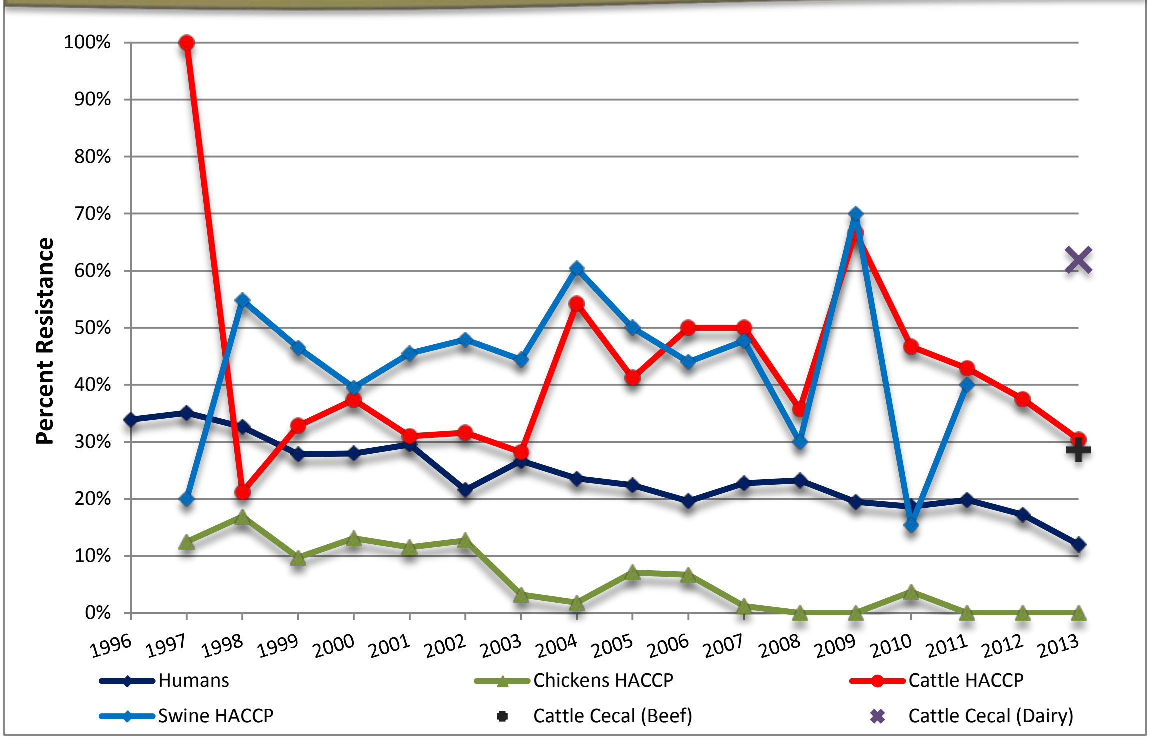
The ACSSuT resistance pattern is an integral feature in *Salmonella* Typhimurium DT104, a clone that emerged in humans and animals in the 1980s and became globally distributed in the 1990s (Threlfall, 2000). In human *Salmonella* Typhimurium, the percentage of isolates resistant to at least ACSSuT has steadily declined since 1996, reaching 12% in 2013, its lowest recorded level in NARMS (**Figure 10**). Similarly, ACSSuT resistance in cattle PR/HACCP isolates declined from 67% in 2009 to 30% in 2013. The levels of ACSSuT resistance in beef (29%) and dairy (62%) cattle cecal isolates indicate that cattle are an important source of this MDR *Salmonella*.

Figure 9. ACSSuT Resistant Non-typhoidal *Salmonella*



The ACSSuT pattern can occur with resistance to additional beta-lactam drugs, such as ceftriaxone and amoxicillin-clavulanic acid. This phenotype (abbreviated as MDR-AmpC or ACSSuTAuCx) has been observed in *Salmonella* from all NARMS sample sources. The ACSSuTAuCx resistance pattern is most common in cattle isolates, where resistance among PR/HACCP strains ranges from 6.8% to 17% with no apparent trends.

Figure 10. ACSSuT Resistance in *Salmonella* Typhimurium 1996-2013



Extremely Drug Resistant (XDR) *Salmonella*

For the purposes of this report, XDR is defined as resistance to all, or all but one, antimicrobial class. In 2012, 5 XDR *Salmonella* strains were identified in the NARMS sampling scheme for human isolate testing: 2 isolates were *Salmonella* serotype Typhimurium and 3 isolates were other serotypes. These isolates were resistant to all agents except azithromycin. Four XDR *Salmonella* Dublin isolates from PR/HACCP cattle samples exhibited the same phenotype.

In the 2013 subset of human isolate tested in NARMS, 2 *Salmonella* were identified that were resistant to all 15 drugs assayed. Among cattle sources, 7 isolates showed resistance to all drugs except azithromycin. Five of the 7 isolates were recovered from PR/HACCP ground beef samples: 2 Typhimurium and 3 Dublin. One isolate each was recovered from beef and dairy cecal samples. Three isolates from swine cecal sources were identified as XDR: 1 from market hogs and 2 from sows. Among food sources, the majority of the XDR isolates came from cattle No isolates from poultry sources were XDR.

TEXT BOX 1

Ceftriaxone Resistance in *Salmonella* serotype Dublin from Humans and Cattle

Salmonella enterica serotype Dublin is a host-adapted serotype causing enteric and systemic disease in cattle. Infections also occur in other animals and in humans. In humans, *Salmonella* Dublin infection can result in more severe illness than other non-typhoidal *Salmonella.*[1,2] A 1996-2006 FoodNet study found that among non-typhoidal serotypes with more than 50 isolates, *Salmonella* Dublin had the highest proportion of invasive infections (64%), hospitalizations (67%), and deaths (3%).[2] Antimicrobial agents commonly used to treat invasive *Salmonella* infections include ceftriaxone (children and adults) and ciprofloxacin (adults).[3] Over the past decade and a half, ceftriaxone resistance among NARMS Dublin isolates from humans and cattle (FSIS-PR/HACCP samples) has increased from 0% to 92% and from 0% to 86%, respectively. Such an increase in ceftriaxone resistance in a serotype that is highly invasive in humans is a significant public health concern.

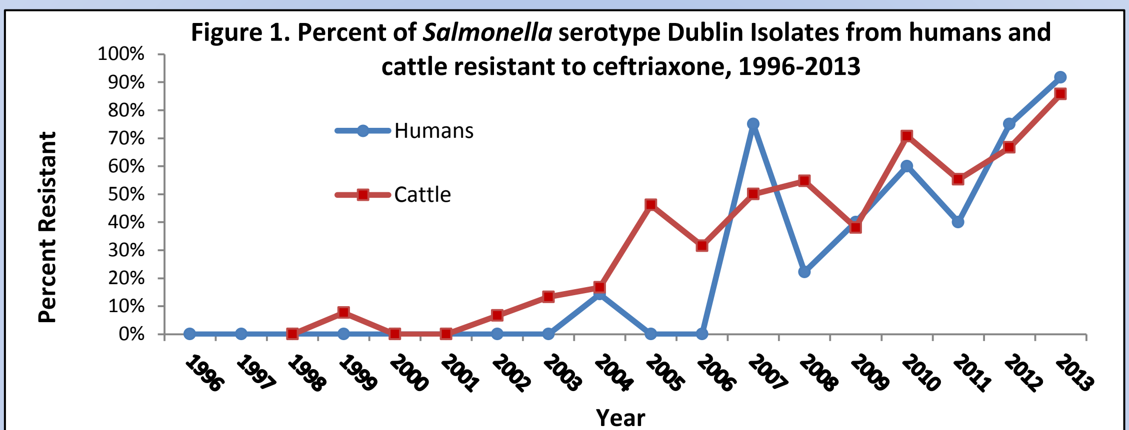


Table 1. Number and percent of *Salmonella* serotype Dublin isolates from humans and cattle resistant to ceftriaxone, 1996-2013

Year	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013
Human Isolates	5	2	4	5	5	2	7	4	7	5	3	4	9	5	5	10	8	12
Number resistant	0	0	0	0	0	0	0	0	1	0	0	3	2	2	3	4	6	11
Percent resistant	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	14.3	0.0	0.0	75.0	22.2	40.0	60.0	40.0	75.0	91.7
Cattle Isolates		0	1	26	21	14	15	30	30	13	19	40	53	21	41	38	30	21
Number resistant			0	2	0	0	1	4	5	6	6	20	29	8	29	21	20	18
Percent resistant			0.0	7.7	0.0	0.0	6.7	13.3	16.7	46.2	31.6	50.0	54.7	38.1	70.7	55.3	66.7	85.7

References:

1. Blaser MJ, Feldman, RA. From the Centers for Disease Control. *Salmonella* bacteremia: reports to the Centers for Disease Control, 1968-1979. *J Infect Dis* 1981; 143:743-746.
2. Jones TF, et al. Salmonellosis outcomes differ substantially by serotype. *J Infect Dis* 2008; 198:109-114.
3. Hohmann EL. Nontyphoidal salmonellosis. *Clin Infect Dis* 2001; 32:263-269.

TEXT BOX 2

Continued Rise of ASSuT Resistance in *Salmonella* ser. I 4,[5],12:i:- Infections in the United States

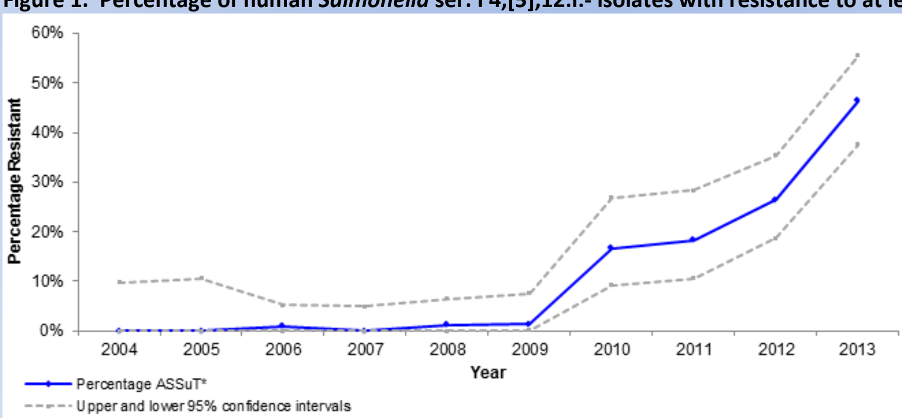
In 2013, NARMS continued to observe an increase of human *Salmonella* ser. I 4,[5],12:i:- isolates with resistance to at least ampicillin, streptomycin, sulfonamide, and tetracycline (ASSuT) but not chloramphenicol. As previously reported, NARMS detected this emergence in 2010 when the percentage of resistant isolates increased to nearly 17% from historically low levels.1 Over the next three years, ASSuT resistance among serotype I 4,[5],12:i:- isolates increased to 18.3% (15/82) in 2011, 26.5% (31/117) in 2012, and 45.5% (59/127) in 2013 (**Figure 1**).

Salmonella serotype I 4,[5],12:i:- is a monophasic variant of serotype Typhimurium (I 4,[5],12:i:1,2). Resistance to ASSuT has also been observed among NARMS isolates of serotype Typhimurium; however, the majority of Typhimurium isolates resistant to these four agents showed additional resistance to chloramphenicol. In 2013, 90.7% (39/43) of Typhimurium isolates resistant to at least ASSuT were also chloramphenicol resistant (ACSSuT), compared to only 1.7% (1/60) of ASSuT I 4,[5],12:i:- isolates. Among all non-typhoidal *Salmonella* isolates tested by NARMS in 2013, 74 (3.4%) were resistant to ASSuT (not chloramphenicol); 59 (79.7%) of these were serotype I 4,[5],12:i:- while the next most common serotype was Typhimurium with 4 (5.4%) isolates.

In Europe, a notable increase of *Salmonella* ser. I 4,[5],12:i:- infections with resistance to ASSuT has been observed since the early 2000s, predating emergence in the United States. The European emergence was caused by a clonal group of I 4,[5],12:i:- ASSuT strains commonly belonging to definitive phage type DT193, with resistance conferred by blaTEM-1, strA/B, sul2, and tet(B) genes on the chromosome.2,3 Similar to ACSSuT in DT104, ASSuT in DT193 is due to a *Salmonella* Genomic Island (SGI) located in the chromosome; however, the SGI type and location differ between the two strains. Infections with the DT193 "European clone" have frequently been associated with swine and pork products.[2]

In the United States since 2010, CDC has investigated multiple outbreaks and clusters associated with ASSuT-resistant serotype I 4,[5],12:i- with pulsed-field gel electrophoresis (PFGE) pattern JPXX01.1314 (identical to DT193) and resistance determinates blaTEM-1, strA/B, sul2, and tet(B). Frequently, these events have been associated with animal exposure or consumption of pork, lamb or beef, including meats purchased from live animal markets.[4] The presence of this strain in swine cecal samples suggests that swine may also be an important source of infections in the U.S. The increase of ASSuT-resistant serotype I 4,[5],12:i- in the U.S. is likely due to clonal expansion, given the uniformity of the PFGE patterns and the resistance determinants likely being chromosomal, limiting horizontal transfer. These characteristics parallel the spread of DT193 that occurred in Europe.

Figure 1. Percentage of human *Salmonella* ser. I 4,[5],12:i:- isolates with resistance to at least ASSuT*,2004–2013



*Resistance to ampicillin, streptomycin, sulfonamides, tetracycline

1. CDC. National Antimicrobial Resistance Monitoring System for Enteric Bacteria (NARMS): Human Isolates Final Report, 2011. Atlanta, Georgia: U.S. Department of Health and Human Services, CDC, 2013
2. Hopkins KL,et al. Salmonella enterica serovar 4,[5],12:i:- in Europe: a new pandemic strain?. Euro Surveill. 2010; 15(22):19580.
3. Lucarelli C, et al. Nucleotide sequence of the chromosomal region conferring multidrug resistance (R-type ASSuT) in *Salmonella* Typhimurium and monophasic *Salmonella* Typhimurium strains. JAC 2012;67(1):pp111–4.
4. Imanishi M, et al. Salmonellosis and Meat Purchased at Live-Bird and Animal-Slaughter Markets, United States, 2007–2012. Emerging infectious diseases 2014; 20(1): 16

Campylobacter

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* get diarrhea, abdominal pain and fever. Approximately 90% of human infections are caused by *Campylobacter jejuni* and 10% by *Campylobacter coli*. Case-control studies have shown poultry to be a major food source of these infections. Physicians rely on drugs such as erythromycin and ciprofloxacin for treating patients with severe *Campylobacter* infection.

Prevalence of *Campylobacter*

A total of 3,986 *Campylobacter* isolates tested in 2012 and 3,143 isolates were tested in 2013. The distribution of *Campylobacter* species by source is shown in **Figure 11**.

For retail meat testing in 2013, *Campylobacter* was isolated from 38% of retail chicken and 0.7% of retail ground turkey (**Figure 12**). The prevalence in retail chicken has declined steadily, down 27% (from 52% to 38%) since 2003. For cecal samples, *Campylobacter* was isolated from 22% of chickens, 9.5% of turkeys, 42% of beef cattle, 43% of dairy cattle, 31% of market hogs and 32% of sows (**Figure 13**).

Figure 11. *Campylobacter* species distribution by source, 2012-2013

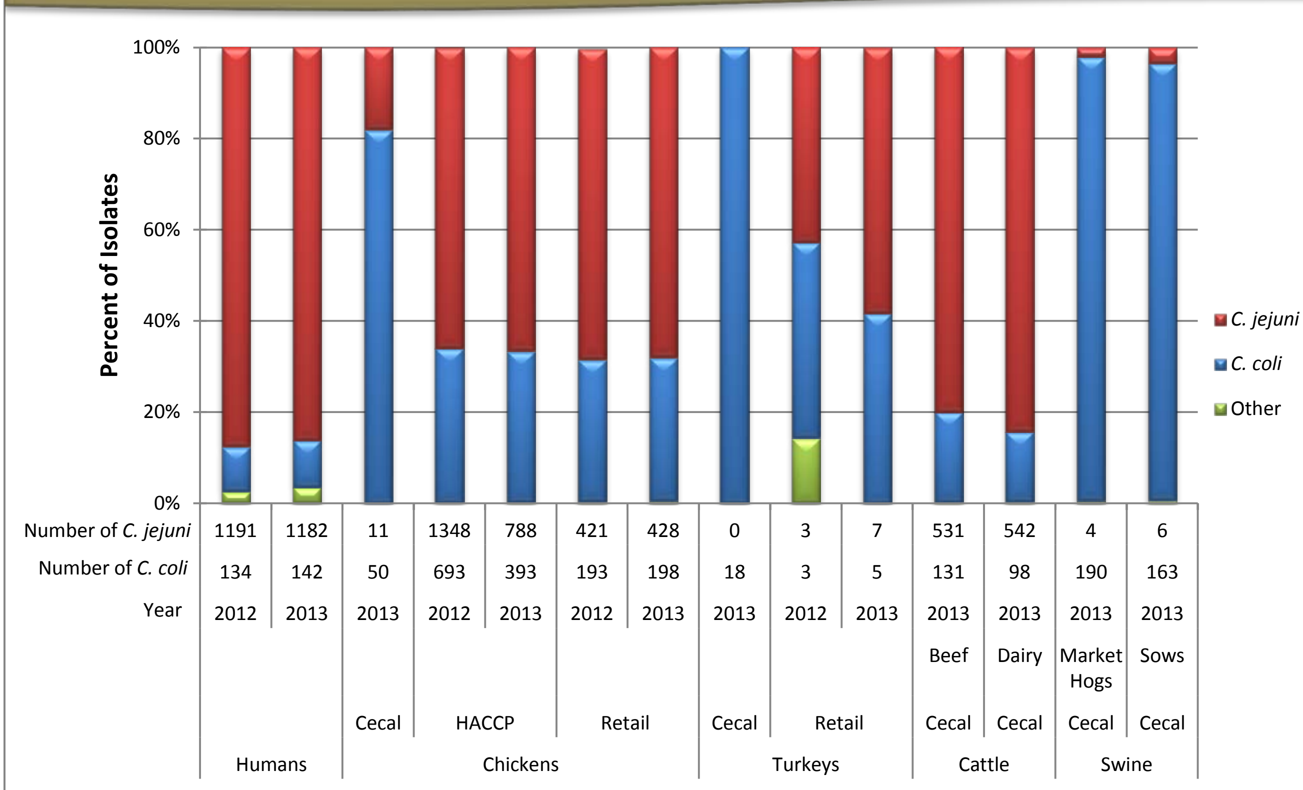


Figure 12. Prevalence of *Campylobacter* in Retail Meat Samples

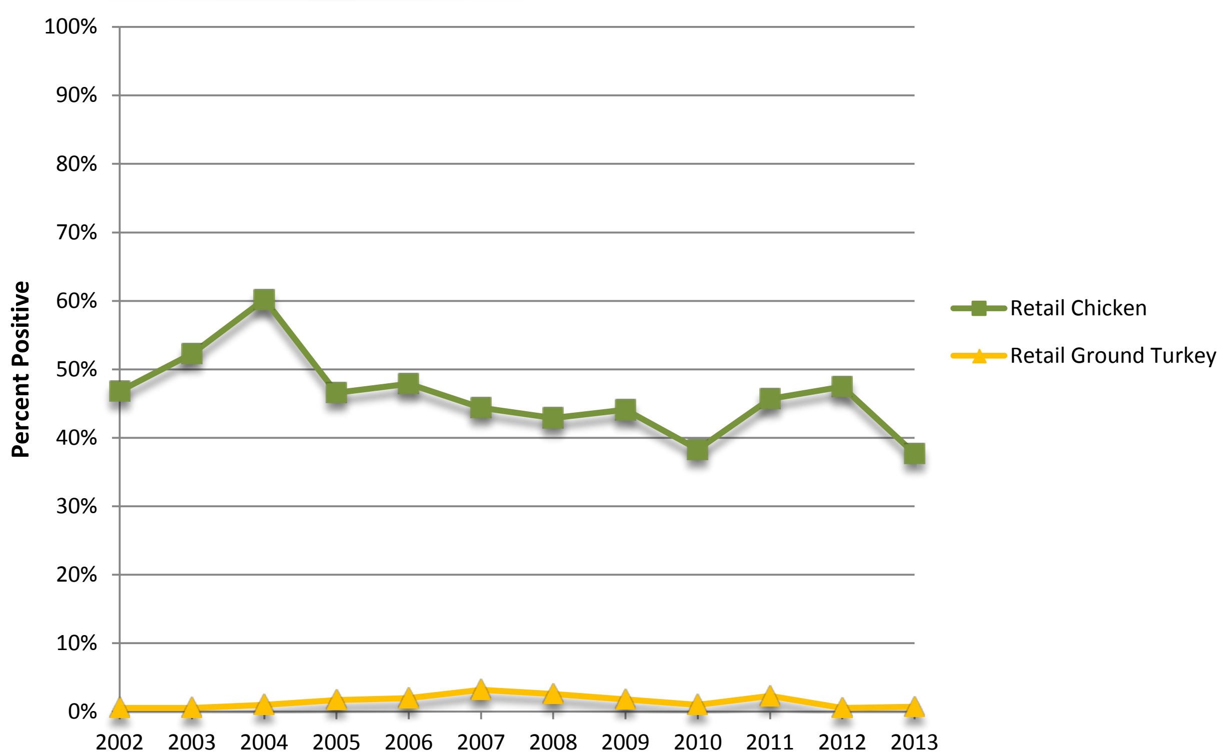
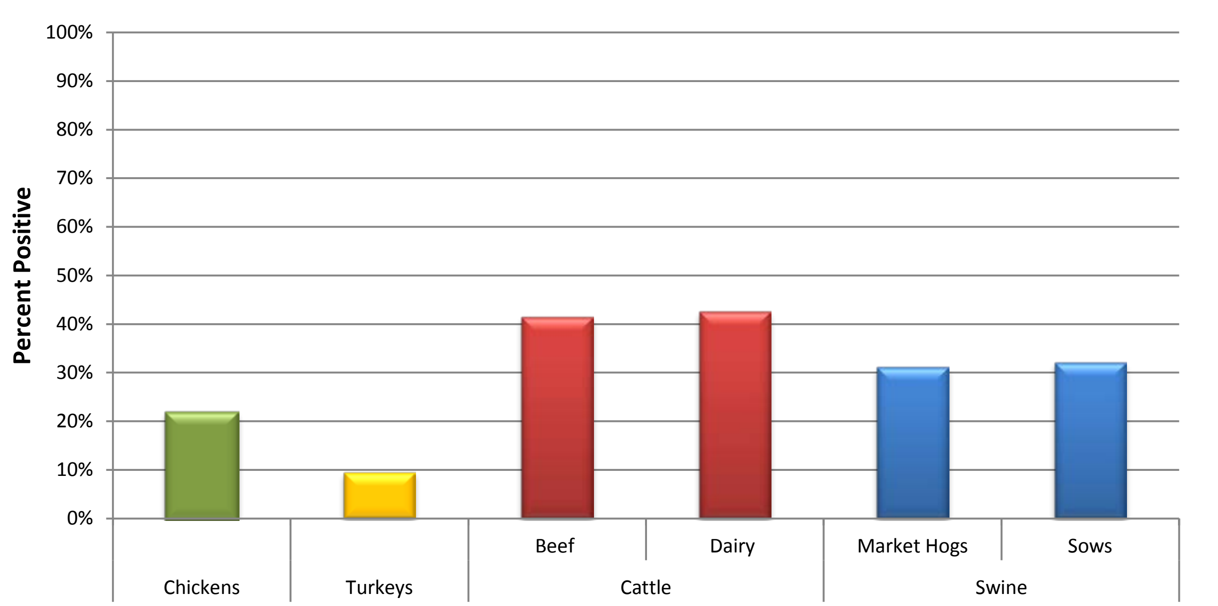


Figure 13. Prevalence of *Campylobacter* in Animal Cecal Samples , 2013



Antimicrobial Resistance in *Campylobacter*

Macrolide Resistance

The macrolide erythromycin is a drug of choice for the treatment of severe campylobacteriosis in humans (Allos and Blaser, 2010). Macrolides also are authorized for use in all major classes of food-producing animals (Animal Drugs @ FDA).

C. jejuni from both human and chicken sources have exhibited erythromycin resistance rates of less than 4% since NARMS testing began (**Figure 14**). In 2012-2013, erythromycin resistance in *C. jejuni* remained below 3% in isolates from all sources except for sows (2/6; 33%). Among *C. jejuni* cecal isolates from cattle, erythromycin resistance was not detected in beef cattle and was very low (0.4%) in dairy isolates (**Figure 15**).

Figure 14. Erythromycin Resistance in *C. jejuni* from Poultry and Humans

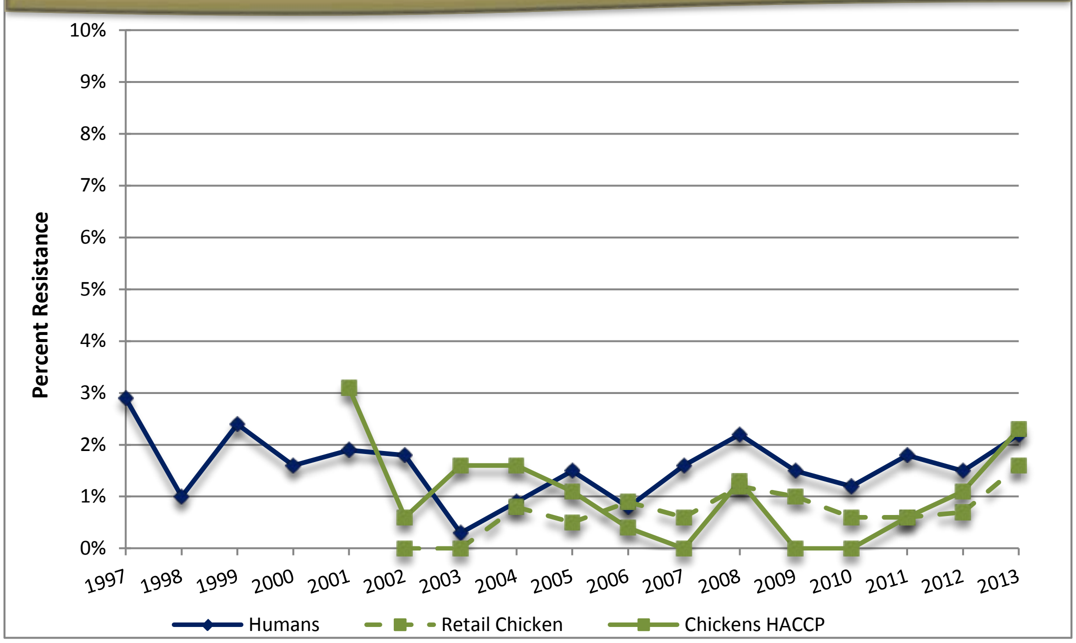
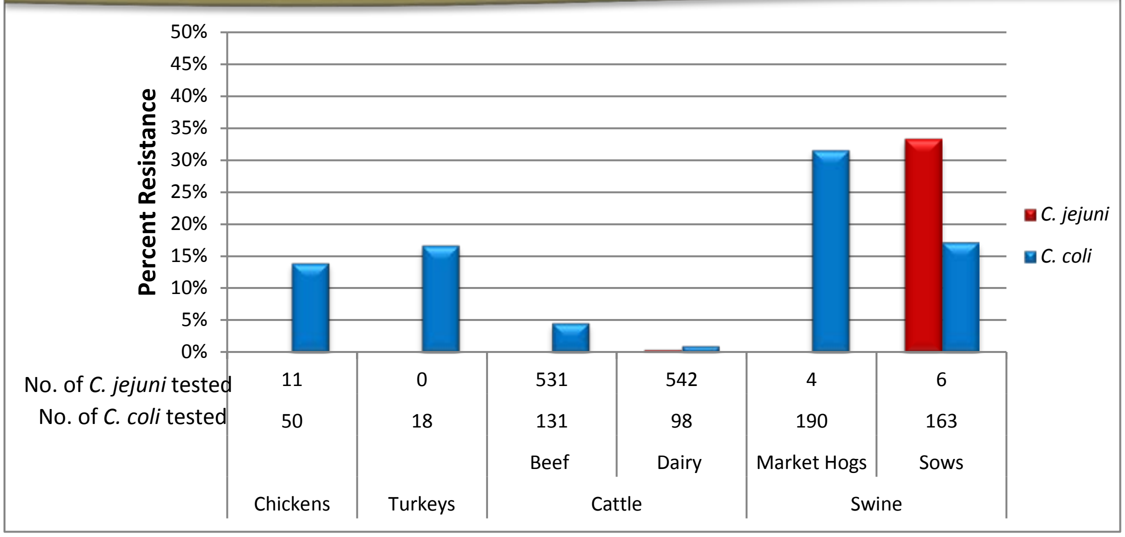
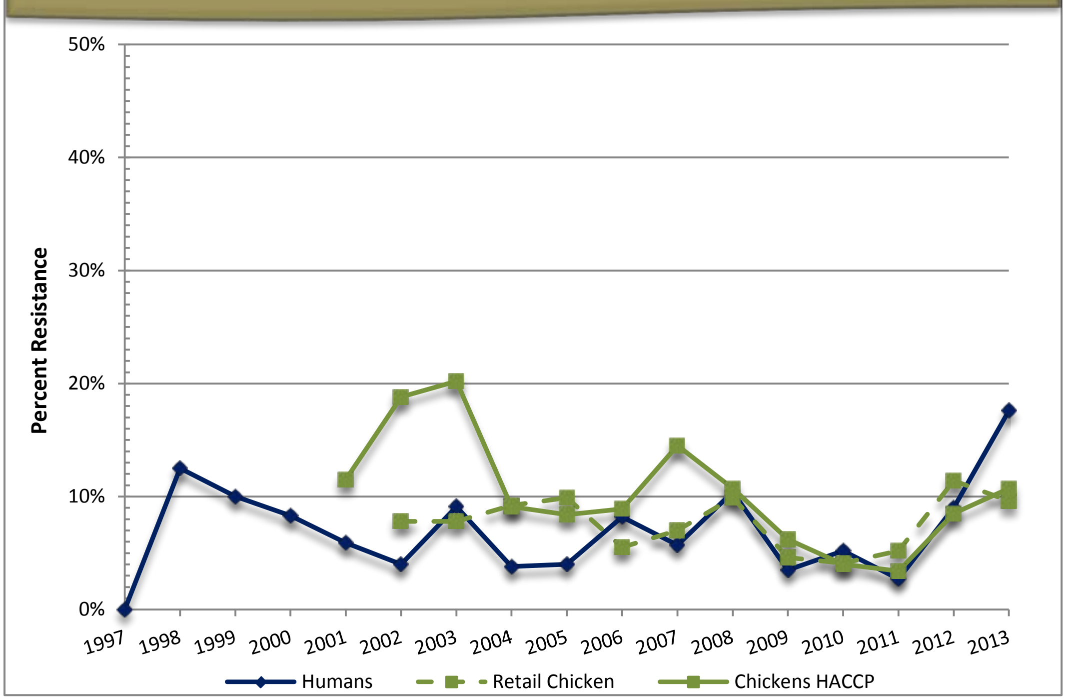


Figure 15. Erythromycin Resistance in *Campylobacter* from Animal Ceca, 2013



It is well known that *C. coli* isolates are more likely to be resistant to erythromycin and other agents than is *C. jejuni*. In 2011, erythromycin resistance in *C. coli* from humans and PR/HACCP chickens dropped to the lowest levels in several years (2.7% and 3.4%, respectively). In contrast, erythromycin resistance was detected in 18% of human *C. coli* isolates in 2013, about a five-fold increase above 2011 levels (**Figure 16**). Similarly, erythromycin resistance in PR/HAACP chicken *C. coli* isolates resistance rose to 11%.

Figure 16. Erythromycin Resistance in *C. coli* from Poultry and Humans



TEXT BOX 3

Increased Campylobacter Resistance to Macrolides, Ketolides, and Lincosamides

Macrolides are considered first-line therapies for laboratory-confirmed cases of human campylobacteriosis. Macrolides (erythromycin, azithromycin) and ketolides (telithromycin) differ in their chemical structures but function similarly by binding reversibly to the bacterial ribosome and inhibiting protein synthesis. Macrolides are used commonly in veterinary medicine to treat and control infections in chickens, turkeys, cattle and swine.

Between 2011 and 2013, macrolide resistance more than doubled among human isolates of *C. coli*. Comparable macrolide resistance trends have been observed in *C. coli* from chicken sources collected during this same time frame. While swine are thought to be a major source of macrolide resistant *C. coli* infections (Gibreel and Taylor, 2006), NARMS data from this source are only available since 2013. Approximately 32% of *C. coli* from market hogs were resistant to erythromycin in 2013.

Increased macrolide resistance also corresponds with increased resistance to clindamycin, a lincosamide antimicrobial approved to treat enteric and respiratory disease in cattle, chickens, and swine. Lincosamides are currently approved for increased weight gain and improve feed efficiency in chickens and swine, although these uses are targeted for withdrawal under FDA Guidance for Industry #213. Lincosamides exhibit a spectrum of activity similar to that of macrolides, and both drug classes target 23S ribosomal RNA, inhibiting protein synthesis. Mutations in the 23S ribosomal RNA that confer resistance to macrolides also confer resistance to lincosamides. Therefore both macrolide and lincosamide use may select for macrolide-resistant *Campylobacter*.

Preliminary genetic data indicate that resistance is due to common mutations in the ribosome and not to the presence of transmissible macrolide resistance genes that have appeared in *Campylobacter* from other countries (Wang et al., 2014). Additional testing is underway to determine the relatedness of the resistant bacteria recovered from human, chicken, and swine sources and to give clues to their origins.

Reference:

AnimalDrugs@FDA. Available at: http://www.accessdata.fda.gov/scripts/animaldrugsatfda/

Gibreel, A. and Taylor, D.E. Macrolide resistance in *Campylobacter jejuni* and *Campylobacter coli*. J. *Antimicrob. Chemother.* (2006) 58 (2): 243-255.

Wang Y, Zhang M, Deng F,et al. Emergence of multidrug-resistant Campylobacter species isolates with a horizontally acquired rRNA methylase. Antimicrob Agents Chemother. 2014 Sep;58(9):5405-12.

Among the 2013 cecal samples collected at slaughter, macrolide resistance was found in 17% of *C. coli* isolates from sows, 32% from market hogs, 14% from chickens, and 17% from turkeys (**Figure 15**). NARMS will continue to monitor macrolide resistance (see TEXT BOX 3). In addition, it is expected that these new sampling sources will lead to new insights on the animal origins of human *Campylobacter* infections, including those caused by antimicrobial resistant strains.

Fluoroquinolone Resistance

The 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 certain classes of cattle, and off-label uses are prohibited.

Ciprofloxacin resistance among *Campylobacter* from humans was high in 2013 for *C. jejuni* (22%), remaining unchanged from levels seen in 2005 (22%). In 2013, ciprofloxacin resistance in *C. jejuni* strains from retail chicken dropped to an all-time low in NARMS of 11% (**Figure 17**). There was no corresponding resistance decline in PR/HACCP chicken isolates (24%), and levels were high in the first year of testing chicken cecal strains (36%). In cattle, ciprofloxacin resistance was detected in *C. jejuni* recovered from dairy (8.5%) and beef (14%) cattle (**Figure 18**). Isolate numbers are too low to evaluate the new swine cecal samples.

Ciprofloxacin resistance in *Campylobacter* from humans was high for *C. coli* (35%), up from 25% in 2005 **(Figure 19).** Similar to the trend in *C. jejuni*, ciprofloxacin resistance was down in retail chicken *C. coli* isolates between 2005 (30%) and 2013 (20%), without a corresponding change in PR/HACCP chicken isolates where it has remained at 22% during the same time frame. Among the new sample sources, fluoroquinolone resistance was found in 67% of turkey cecal strains *C. coli* isolates, and comparably low in swine cecal isolates (3.7% to 7.4%). Fluoroquinolone resistance was found in 53% of beef and 31% of dairy cecal *C. coli* **(Figure 18).**

Figure 17. Ciprofloxacin Resistance in *C. jejuni* from Poultry and Humans

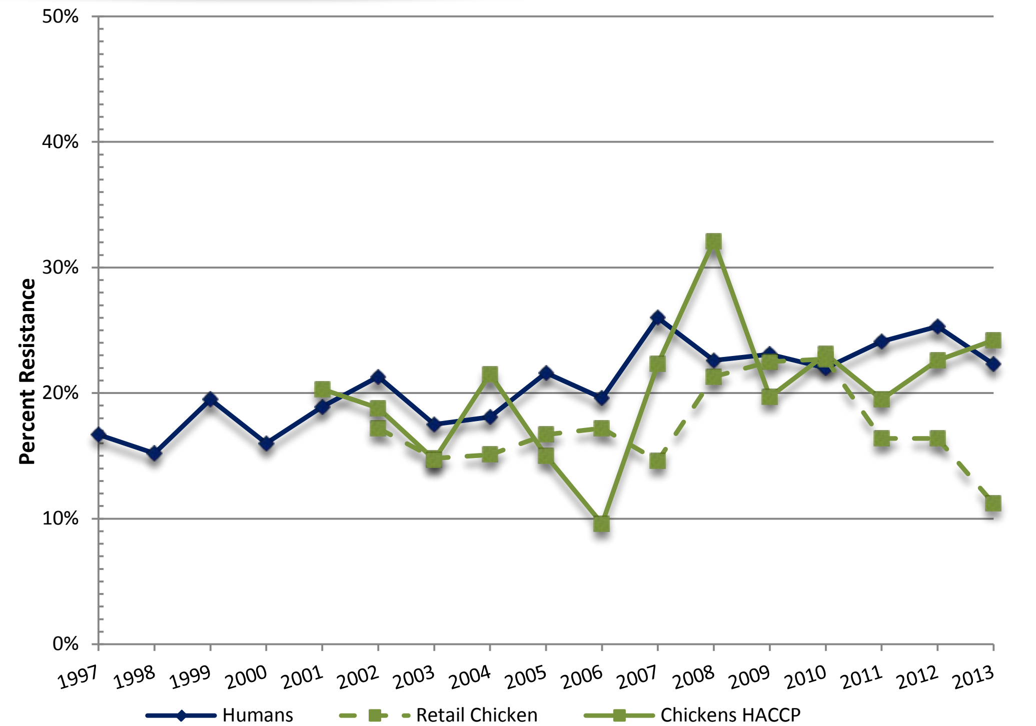
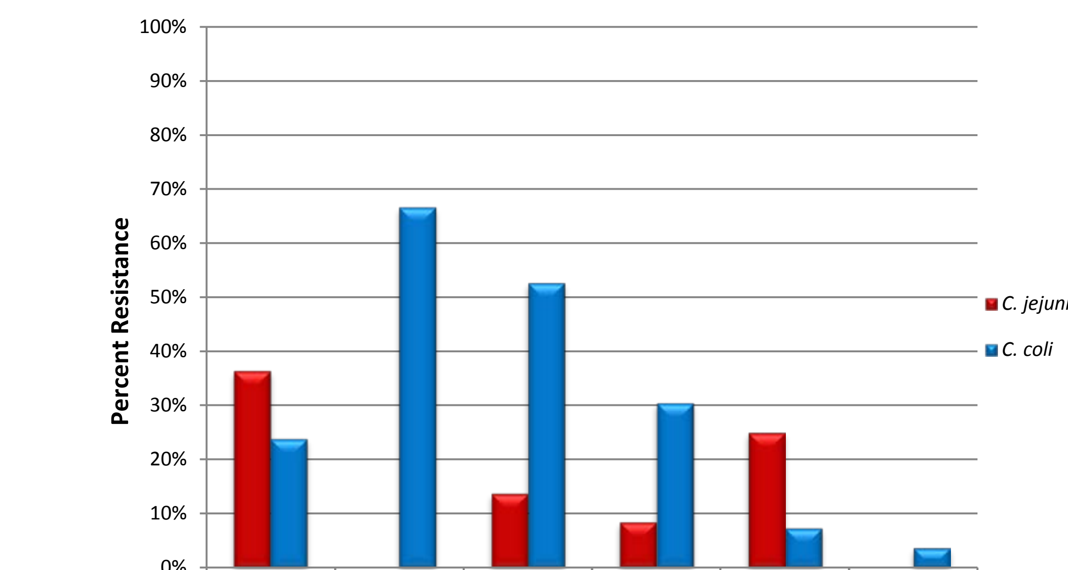
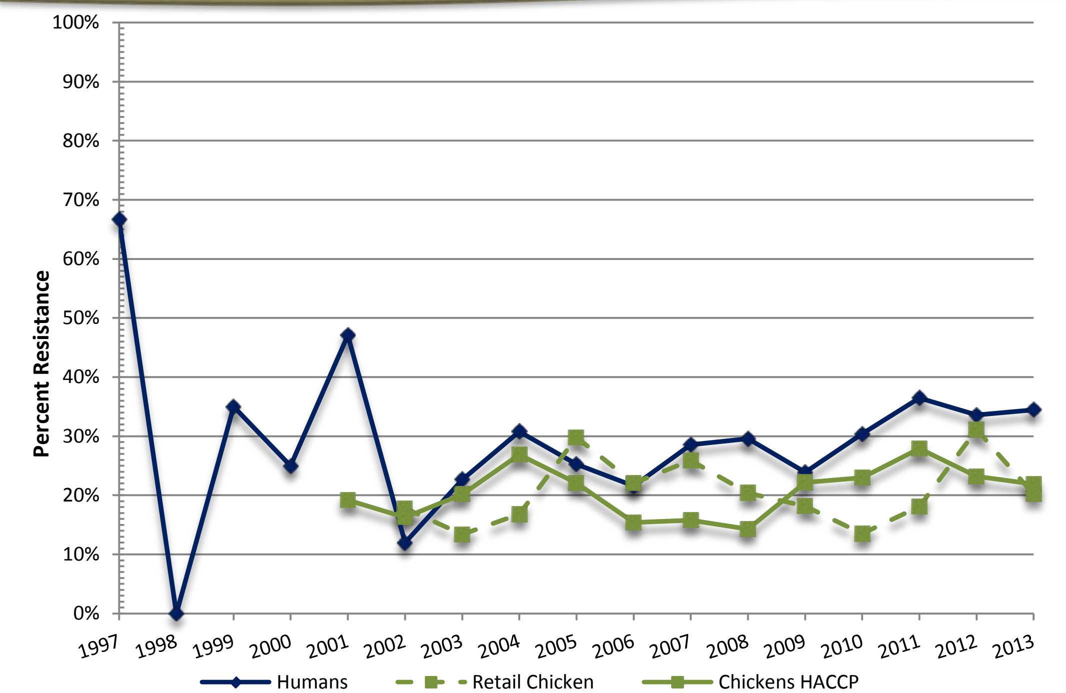


Figure 18. Ciprofloxacin Resistance in *Campylobacter* from Animal Ceca, 2013



	Chickens	Turkeys	Cattle: Beef	Cattle: Dairy	Swine: Market Hogs	Swine: Sows
No. of *C. jejuni* tested	11	0	531	542	4	6
No. of *C. coli* tested	50	18	131	98	190	163

Figure 19. Ciprofloxacin Resistance in *C. coli* from Poultry and Humans

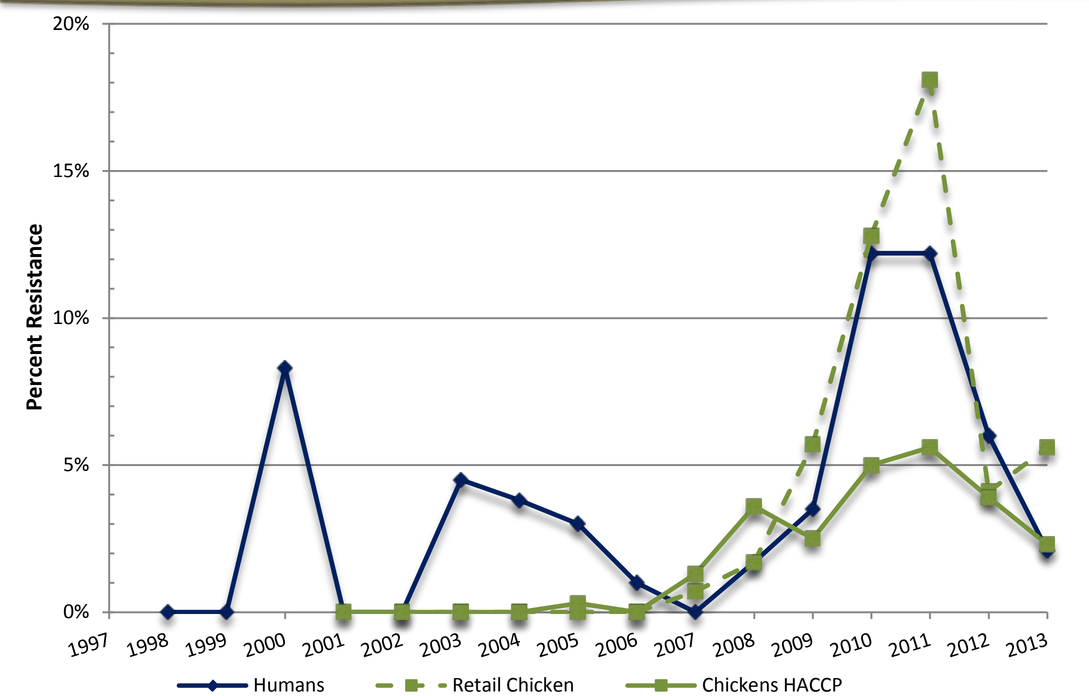


Aminoglycosides

Gentamicin is categorized as a highly important antimicrobial for human anti-infective therapy according to criteria outlined in FDA's Guidance 152. It is used in humans for the treatment of severe infections, including some *Campylobacter* infections (Allos and Blaser, 2010). Gentamicin is also approved for food animal use, including poultry, where it is approved for injection in day-old chicks and 1- to 3-day old turkey poults for the prevention of early mortality associated with bacterial infections (Animal Drugs @ FDA). Gentamicin is also approved as a dip for turkey eggs.

Between 2007 and 2011, gentamicin resistance increased sharply in *C. coli* from human and chicken sources (**Figure 20**). Gentamicin resistance rose from 0% to 12% in human strains, 0.7% to 18% among retail chicken strains, and from 1.3% to 5.6% among PR/HACCP chicken isolates. In 2012, resistance began a steep decline to <6% in isolates from human and food sources. Baseline cecal data show gentamicin resistance in 18% (chickens) to 22% (turkeys) of poultry samples at slaughter. The cause of the surge and decline is not known.

Figure 20. Gentamicin Resistance in *C. coli* from Poultry and Humans



Indicator Bacteria

Escherichia coli

Escherichia coli are monitored as an indicator organism for emerging resistance patterns and specific resistance genes that could be transferred to other pathogenic Gram-negative bacteria (e.g., *Salmonella*). *E. coli* isolates are tested for susceptibility to the same antimicrobials used in *Salmonella* testing. This report includes data on generic *E. coli* isolated from all four retail meat commodities, PR/HACCP chicken carcasses and from food animal cecal samples. Ongoing antimicrobial resistance surveillance is not conducted for indicator organisms from healthy human populations.

Prevalence of *E. coli*

E. coli is an indicator of fecal contamination and is commonly present in raw retail meat products. In 2012, a total 2,199 *E. coli* isolates from retail meats and PR/HACCP chicken carcasses were tested. In 2013, a total 2,033 were tested. Post-slaughter chicken carcasses were not tested in 2013. The prevalence of *E. coli* from the tested retail meat sources ranged between approximately 40% in pork chops to around 80% ground turkey in 2013 (**Figure 21**).

The addition of cecal samples to NARMS in 2013 marked the first time that *E. coli* isolates from all found food animals sources at slaughter were tested. As a normal constituent of the animal gut, *E. coli* was recovered from nearly every sample as expected (**Figure 22)**.

Figure 21. Prevalence of *E. coli* in Retail Meat Samples

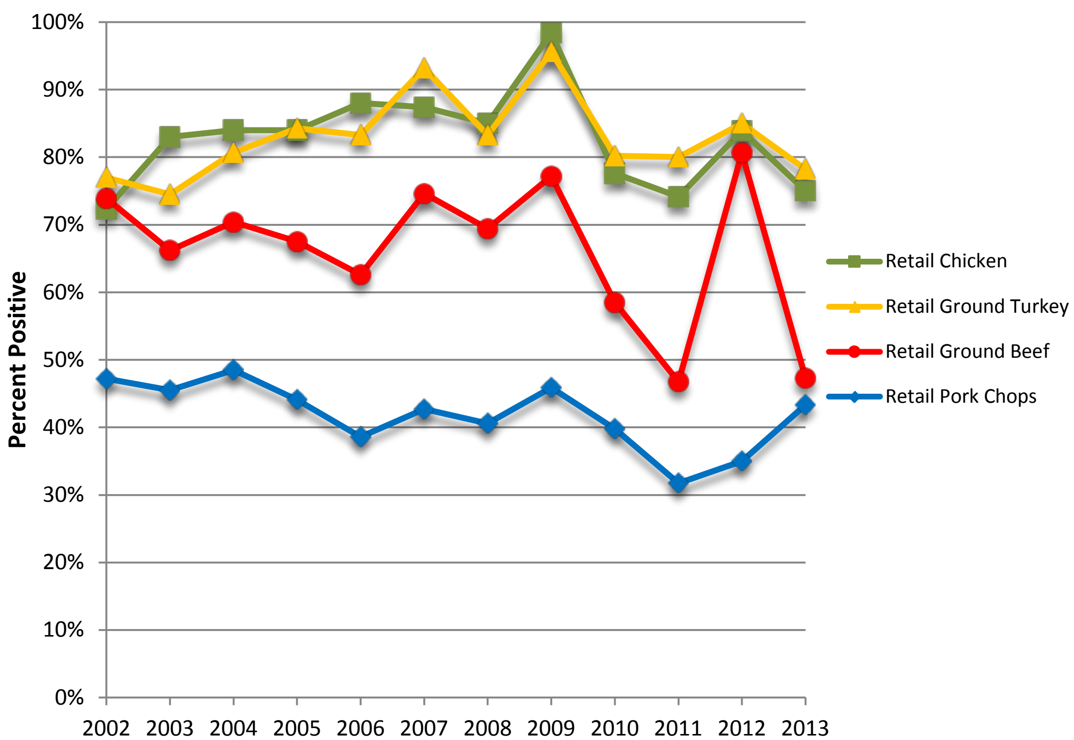
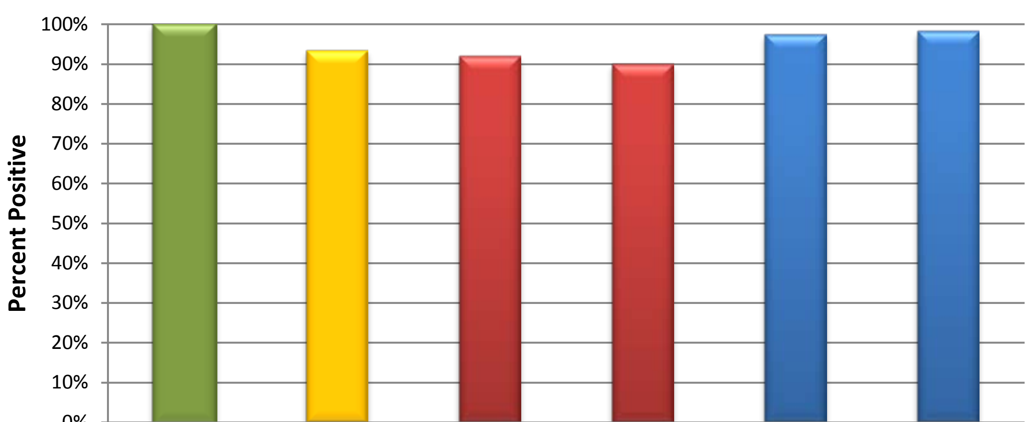


Figure 22. Prevalence of *E.coli* in Animal Cecal Samples, 2013



	Chickens	Turkeys	Cattle: Beef	Cattle: Dairy	Swine: Market Hogs	Swine: Sows
No. of *E. coli*	48	29	293	256	118	120
No. of samples tested	48	31	318	284	121	122

Antimicrobial Resistance in *Escherichia coli*

In 2013, *E. coli* showing resistance to at least one antimicrobial were most common among turkey sources (86% from ground turkey and 83% from turkey ceca) and least frequent in isolates from cattle sources (23% from ground beef, 27% from beef cattle and 17% from dairy cattle).

Quinolone Resistance

As with *Salmonella*, ciprofloxacin resistance in *E. coli* from retail meats, slaughtered chickens, and cecal samples from chicken, turkeys, beef and dairy cattle, market hogs and swine was absent or low (0 % to 1.7%).

Cephalosporin Resistance

Ceftriaxone resistance among *E. coli* from retail chickens decreased from 13% in 2011 to 4.4% in 2013. Retail turkey isolates showed a similar decrease during the same time period (from 10% to 6.7%). As noted above, this coincided with declines in ceftriaxone resistance among non-typhoidal *Salmonella* from retail poultry meats.

Important Multidrug Resistance Patterns

In 2013, isolates from turkey sources most commonly exhibited resistance to 3 or more drug classes (59% - 62%), followed by isolates from chicken (17% - 32%), swine (14% - 22%) and cattle sources (6.3% - 8.2%). The proportion of retail and slaughter isolates exhibiting ACSSuT and ACSSuTAuCx resistance patterns was either absent or low. There are no noteworthy trends in MDR among E.coli from PR/HACCP chicken samples or any of the retail food commodities.

Extremely Drug Resistant (XDR) *E. coli*

In 2012, there were 2 XDR retail isolates, both from turkeys. One isolate was resistant to all drug classes except phenicols. The other isolate showed resistance to all drug classes except amoxicillin/clavulanate. In 2013, there was one XDR isolate (from ground beef) that was resistant to all drug classes except quinolones.

Enterococcus

Enterococcus is a natural part of both animal and human intestinal microflora and is an indicator of fecal contamination. *Enterococcus* can be present in high numbers in food but they are not considered a major foodborne pathogen. Resistance in *Enterococcus* is monitored to understand how resistance occurs in Gram-positive bacteria.

As with *E. coli*, the NARMS Integrated Report includes data on *Enterococcus* from retail meat and food animals but not from human sources. The two species most commonly recovered are

Enterococcus faecalis and *Enterococcus faecium*. Results are reported by species because they differ in their ability to acquire and express resistance to various antimicrobials.

Prevalence of *Enterococcus*

Enterococcus is commonly recovered from retail meats, ranging in prevalence from 80% to 98% across commodities (**Figure 23**).

In 2012, a total of 1,845 *Enterococcus* isolates from retail meats were tested for antimicrobial susceptibility. In 2013, a total of 2,542 *Enterococcus* were tested. In 2012 and 2013 there was no *Enterococcus* testing done on chickens collected through PR/HACCP.

With the advent of cecal sampling, however, 2013 was the first year that *Enterococcus* was recovered from all four food animal species at slaughter. A majority of the *Enterococcus* isolates were *E. faecalis*, with the exception of retail chickens where the majority of isolates were *E. faecium*. The prevalence of *Enterococcus* from the animal cecal samples is shown in **Figure 24**.

Figure 23. Prevalence of *Enterococcus* in Retail Meat Samples

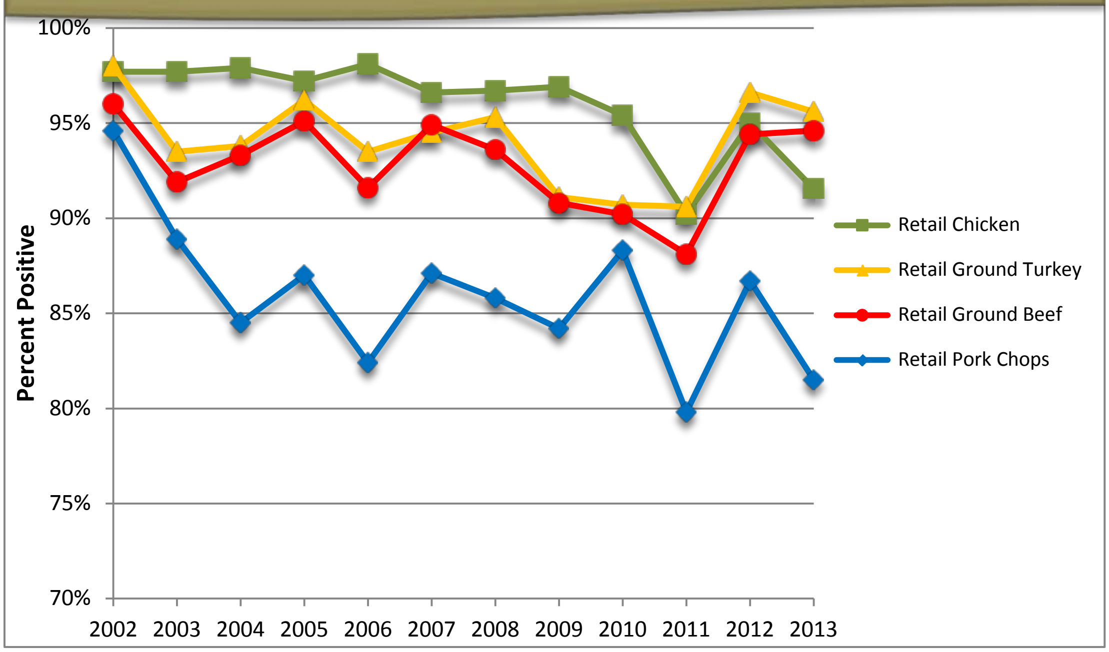
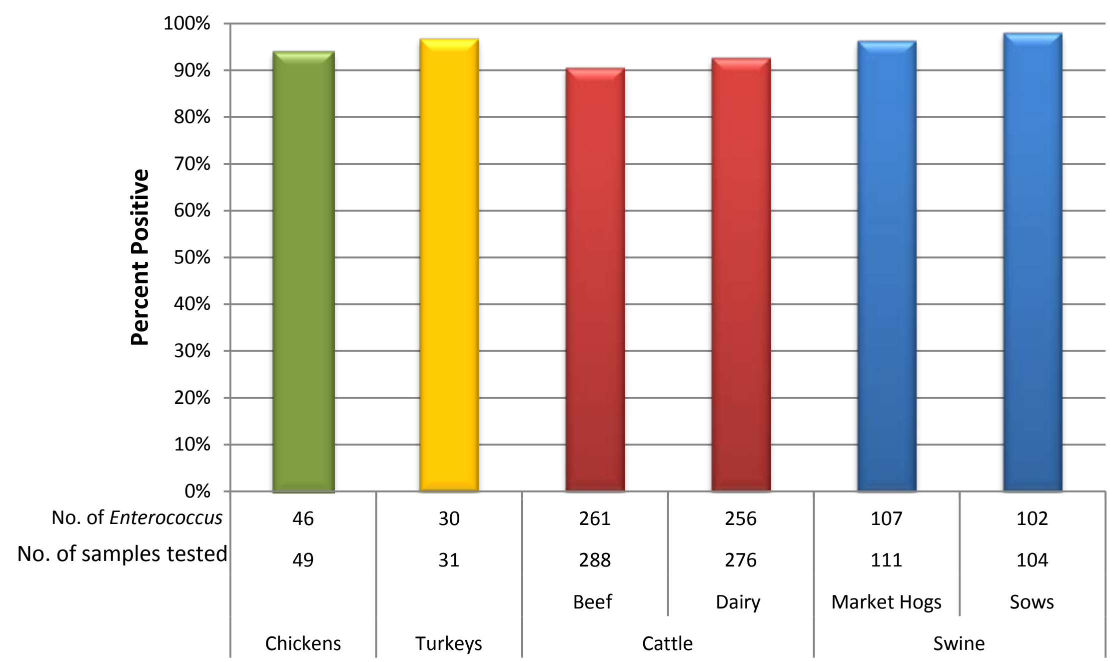


Figure 24. Prevalence of *Enterococcus* in Animal Cecal Samples, 2013



Antimicrobial Resistance in *Enterococcus*

A summary of resistance in *E. faecalis* and *E. faecium* is presented in **Table 3 and Table 4**, respectively. The majority (>90%) of *E. faecalis* and *E. faecium* isolates from all sources were resistant to at least one antimicrobial class during 2013 (see data tables 97, 101 and 105). Both retail chicken and turkey isolates of *Enterococcus* were more likely to exhibit resistance to at least one antimicrobial class than were isolates from ground beef or pork chops.

The aminopenicillin, ampicillin, alone or in combination with an aminoglycoside, is a treatment of choice for susceptible *E. faecalis* infection. Other treatment options for enterococcal infections include vancomycin, daptomycin and linezolid. Penicillin resistance, an indicator of ampicillin resistance, is generally very low (<1%) in *E. faecalis* isolates from all sources. In 2013, gentamicin resistance in retail chicken *E. faecalis* isolates (24%) was similar to levels seen in 2002 (22%) when testing began.

Vancomycin resistant *Enterococcus* has not been detected in any food or animal isolate. Linezolid, which may be used to treat vancomycin-resistant enterococcal infections, was detected in a single isolate of *E. faecium* recovered from a pig cecum at slaughter. Daptomycin is a lipopeptide antimicrobial used in the treatment of systemic and life-threatening infections caused by Gram-positive organisms including *Enterococcus faecalis*. Non-susceptibility to daptomycin has occurred in 5 isolates of *E. faecalis* in 10 years of testing. A summary of resistance findings for 2013 are shown in **Table 3 and Table 4**.

Important Multidrug Resistance Patterns

Among *E. faecium* and *E. faecalis* isolated from retail poultry, MDR has been consistently high. MDR in *E. faecium* from ground beef and pork chops has been less frequent (< 30% since 2005) with no consistent trend. Cecal isolates of *E. faecium* and *E. faecalis* from swine tended to exhibit much higher levels of MDR, when compared to retail swine. These differences will be monitored through ongoing cecal sampling.

Table 3. Resistance (%) among *Enterococcus faecalis* from retail meat and animals at slaughter, 2013

	Chickens		Turkeys		Cattle			Swine		
	Retail Chicken	Cecal	Retail Ground Turkey	Cecal	Retail Ground Beef	Cecal (Beef)	Cecal (Dairy)	Retail Pork Chops	Cecal (Market Hogs)	Cecal (Sows)
Antimicrobial agent	%	%	%	%	%	%	%	%	%	%
Gentamicin	24	46	34	39	0.7	2.8	0	0.9	9.1	17
Kanamycin	27	49	43	42	2.3	5.6	1.9	2.7	22	39
Streptomycin	17	11	26	31	3.6	5.6	1.9	4.9	27	27
Vancomycin	0	0	0	0	0	0	0	0	0	0
Tigecycline	0	0	0	0	0	0	0	0	0	0
Lincomycin	100	100	100	100	97	100	98	99	100	100
Daptomycin	0	0	0	0	0	0	1.9	0	0	0
Erythromycin	35	37	39	42	3.0	11	3.7	7.0	53	53
Tylosin	35	49	39	42	3.0	11	3.7	7.0	53	53
Nitrofurantoin	0	0	0	0	0	0	0	0	0	0
Linezolid	0	0	0	0	0	0	0	0	0	1.5
Penicillin	0	0	0	0	0	0	0	0	0	0
Chloramphenicol	0.5	0	0.7	0	0	2.8	0	2.1	15	21
Ciprofloxacin	0.5	0	0	0	0	0	3.7	0	0	0
Tetracycline	62	69	88	92	21	25	13	82	73	77
No Resistance Detected	0	0	0	0	3.3	0	1.9	0	0	0
Multidrug Resistance	38	46	58	58	3.6	14	5.6	8.2	56	59
No. of Isolates Tested	202	35	407	26	304	36	54	328	55	66

Table 4. Resistance (%) among *Enterococcus faecium* from retail meat and animals at slaughter, 2013

	Chickens		Turkeys		Cattle			Swine		
	Retail Chicken	Cecal	Retail Ground Turkey	Cecal	Retail Ground Beef	Cecal (Beef)	Cecal (Dairy)	Retail Pork Chops	Cecal (Market Hogs)	Cecal (Sows)
Antimicrobial agent	%	%	%	%	%	%	%	%	%	%
Gentamicin	7	0	8.3	0	0	0	0	0	0	0
Kanamycin	9.4	33	27	0	3.8	0	2.9	4	0	29
Streptomycin	17	0	38	0	2.5	0	2.9	4	25	43
Vancomycin	0	0	0	0	0	0	0	0	0	0
Tigecycline	0	0	0	0	0	0	0	0	0	0
Lincomycin	83	100	92	75	59	82	68	84	83	86
Erythromycin	30	17	40	0	7.5	3.7	0	4	17	14
Tylosin	28	17	21	0	5	0	0	4	8.3	14
Nitrofurantoin	23	0	29	0	20	0	0	16	0	0
Linezolid	0	0	0	0	0	0	0	0	0	0
Penicillin	9.9	0	54	0	5	0	0	4	0	43
Chloramphenicol	0	0	0	0	1.3	0	0	0	0	0
Ciprofloxacin	39	50	35	50	25	33	50	16	25	0
Quinupristin-Dalfopristin	28	33	42	0	19	30	8.8	8	25	29
Tetracycline	59	67	75	25	20	30	12	64	42	71
No Resistance Detected	6.6	0	2.1	0	15	0	0	6	8.3	14
Multidrug Resistance	64	67	79	25	16	19	15	18	42	71
No. of Isolates Tested	213	6	48	4	80	27	34	50	12	7

Changes in Antimicrobial Resistance: 2013 vs. 2004–2008 and 2008–2012

To understand changes in the prevalence of antimicrobial resistance among *Salmonella*, *Campylobacter*, *Escherichia coli*, and *Enterococcus* over time, annual data from 2004–2013 were modeled using logistic regression. Changes in resistance were calculated based on the prevalence in 2013 compared with the average prevalence of resistance from two reference periods, 2004–2008 and 2008–2012. The methods are described in more detail in the Methodology section of the report.

Table 5. Changes in the percentage of clinically important resistance among nontyphoidal *Salmonella* and *Campylobacter* isolated from humans and retail meat: 2013 compared with 2004–2008*†

Pathogen	Resistance Pattern	Humans		Retail							
				Chicken		Ground Turkey		Ground Beef		Pork Chops	
		Change	2013	Change	2013	Change	2013	Change	2013	Change	2013
Nontyphoidal *Salmonella*	Ciprofloxacin‡	↑0.3	0.5	↔	0.0	↔	0.0	↔	0.0	↔	0.0
	Nalidixic Acid	↑0.6	2.8	↓0.3	0.0	↓0.8	0.0	↔	0.0	↔	0.0
	Ceftriaxone	↓0.7	2.5	↓1.1	19.7	↑3.7	9.4	↑22	26.7	↔	0.0
	Resistance to ≥1 class§	↑0.5	19.2	↑3.4	59.6	↓0.1	77.4	↑33	53.3	↓9.3	45.8
	Resistance to ≥3 classes§	↓1.4	9.8	↓3.4	26.0	↑4.9	39.6	↑19	33.3	↑16	33.3
Campylobacter jejuni	Ciprofloxacin	↑0.7	22.3	↓4.5	11	↓21	14.3				
	Erythromycin‡	↑0.8	2.2	↑0.8	1.6	↓3.0	0.0				
	Resistance to ≥1 class§	↓0.6	55.4	↓5.3	53.7	↓37	42.9				
Campylobacter coli	Ciprofloxacin	↑7.3	34.5	↓2.8	20.2	↓37	0.0				
	Erythromycin‡	↑11	17.6	↑1.4	9.6	↓5.5	0.0				
	Resistance to ≥1 class§	↑10	68.3	↓0.2	61.1	↓27	40.0				

* Odd ratios that do not include 1.0 in the 95% confidence intervals are reported as statistically significant

†Statistical analysis was not conducted on isolates collected from the HACCP verification program. The PR/HACCP Salmonella verification program was designed to evaluate the performance of FSIS regulated establishments using prescribed performance standards. Prior to 2006, FSIS sampling collection methods included both random and risked-based methods. In 2006, FSIS began to schedule establishment sampling based on criteria that are risk-based rather than random. This change in sample collection methods limits meaningful trend comparison between pre-2006 and post-2006. Similarly, these changes limit year-to-year comparisons post-2006

‡Testing for significant difference between 2013 and reference was not performed due to low number of resistant isolates and/or number tested

§Antimicrobial classes are defined using categories from the Clinical and Laboratory Standards Institute (CLSI)

Significant difference	(orange shading)
Decline in resistance	↓
Increase in resistance	↑
No change in resistance	↔

The differences between the prevalence of resistance in 2013 and the average prevalence of resistance in 2004–2008 (Table 5) were statistically significant for the following:

- *Salmonella*
  - Ground beef
    - Resistance to at least one antimicrobial class was higher in 2013 than in 2004–2008 (33% increase; OR=4.6, 95% confidence interval, 1.3–15.8)

- *Campylobacter*
  - *C. jejuni* from retail chicken
    - Resistance to at least one antimicrobial class was lower in 2013 than in 2004–2008 (5.3% decline; OR=0.4, 95% confidence interval, 0.2–0.8)

Table 6. Changes in the percentage of clinically important resistance among nontyphoidal *Salmonella* and *Campylobacter* isolated from humans and retail meat: 2013 compared with 2008–2012*†

Pathogen	Resistance Pattern	Humans		Retail							
				Chicken		Ground Turkey		Ground Beef		Pork Chops	
		Change	2013	Change	2013	Change	2013	Change	2013	Change	2013
Nontyphoidal *Salmonella*	Ciprofloxacin[‡]	↑0.3	0.5	↔	0.0	↔	0.0	↔	0.0	↔	0.0
	Nalidixic Acid	↑0.7	2.8	↓0.1	0.0	↓0.2	0.0	↓2.9	0.0	↔	0.0
	Ceftriaxone	↓0.4	2.5	↓12	19.7	↓3.9	9.4	↑11	26.7	↓6.4	0.0
	Resistance to ≥1 class[§]	↑3.5	19.2	↓5.5	59.6	↑3.6	77.4	↑17	53.3	↓13	45.8
	Resistance to ≥3 classes[§]	↑0.6	9.8	↓15	26.0	↓0.6	39.6	↑6.6	33.3	↓0.9	33.3
Campylobacter jejuni	Ciprofloxacin	↓1.1	22.3	↓8.2	11.2	↑30	14.3				
	Erythromycin[‡]	↑0.6	2.2	↑0.7	1.6	↓2.0	0.0				
	Resistance to ≥1 class[§]	↓4.2	55.4	↓3.4	53.7	↓53	42.9				
Campylobacter coli	Ciprofloxacin	↑3.7	34.5	↓0.1	20.2	↓53	0.0				
	Erythromycin[‡]	↑11	17.6	↑2.6	9.6	↓5.0	0.0				
	Resistance to ≥1 class[§]	↑7.2	68.3	↑2.7	61.1	↓51	40.0				

* Odd ratios that do not include 1.0 in the 95% confidence intervals are reported as statistically significant

†Statistical analysis was not conducted on isolates collected from the HACCP verification program. The PR/HACCP *Salmonella* verification program was designed to evaluate the performance of FSIS regulated establishments using prescribed performance standards. Prior to 2006, FSIS sampling collection methods included both random and risked-based methods. In 2006, FSIS began to schedule establishment sampling based on criteria that are risk-based rather than random. This change in sample collection methods limits meaningful trend comparison between pre-2006 and post-2006. Similarly, these changes limit year-to-year comparisons post-2006

[‡]Testing for significant difference between 2013 and reference was not performed due to low number of resistant isolates and/or number tested

[§]Antimicrobial classes are defined using categories from the Clinical and Laboratory Standards Institute (CLSI)

Significant difference
Decline in resistance ↓
Increase in resistance ↑
No change in resistance ↔

The differences between the prevalence of resistance in 2013 and the average prevalence of resistance in 2008–2012 (Table 6) were statistically significant for the following:

- *Salmonella*
  - Humans
    - Resistance to at least one antimicrobial class was higher in 2013 than in 2008–2012 (3.5% increase; OR=1.3, 95% confidence interval, 1.2–1.5)
  - Retail chicken
    - Ceftriaxone resistance was lower in 2013 than in 2008–2012 (12% decline; OR=0.6, 95% confidence interval, 0.4–0.9)
    - Resistance to three or more antimicrobial classes was lower in 2013 than in 2008–2012 (15% decline; OR= 0.6, 95% confidence interval, 0.4–0.8)
- *Campylobacter*
  - *C. jejuni* from retail chicken
    - Ciprofloxacin resistance was lower in 2013 than in 2008–2012 (8.2% decline; OR=0.6, 95% confidence interval, 0.4–0.8)

Table 7. Changes in the percentage of clinically important resistance among *E coli* and *Enteroccocus* isolated from retail meat: 2013 compared with 2004–2008*†

Pathogen	Resistance Pattern	Retail							
		Chicken		Ground Turkey		Ground Beef		Pork Chops	
		Change	2013	Change	2013	Change	2013	Change	2013
E. coli	Ciprofloxacin	↑0.6	0.6	↓0.1	0.3	↓0.1	0.0	↓0.1	0.0
	Nalidixic Acid	↓2.4	2.5	↓4.5	1.9	↓0.4	0.4	↓0.4	0.0
	Ceftriaxone	↓4.2	4.4	↑3.4	6.7	↑0.7	2.2	↑0.3	1.4
	Resistance to ≥1 class‡	↓5.3	69.2	↑0.1	85.6	↓1.7	23.3	↓1.8	53.8
	Resistance to ≥3 classes‡	↓7.4	31.4	↑3.2	59.4	↓1.6	7.9	↓3.3	13.9
Enterococcus faecalis	Linezolid§	↔	0.0	↔	0.0	↔	0.0	↔	0.0
	Daptomycin§	↔	0.0	↓0.1	0.0	↔	0.0	↓0.1	0.0
	Vancomycin§	↔	0.0	↔	0.0	↔	0.0	↔	0.0
	Pencillin	↔	0.0	↓0.4	0.0	↔	0.0	↓0.3	0.0
	Gentamcin	↑4.4	24.3	↑3.6	33.7	↓0.6	0.7	↓0.1	0.9
	Gentamcin and Penicillin§	↔	0.0	↓0.2	0.0	↔	0.0	↔	0.0
Enterococcus faecium	Linezolid§	↓0.1	0.0	↔	0.0	↔	0.0	↔	0.0
	Vancomycin§	↔	0.0	↔	0.0	↔	0.0	↔	0.0
	Pencillin	↓17	9.9	↓7.9	54.2	↑0.8	5.0	↑1.8	4.0
	Gentamicin	↓0.5	7.0	↓2.1	8.3	↓0.2	0.0	↓0.3	0.0
	Gentamicin and Penicillin	↓2.8	1.4	↓5.1	2.1	↔	0.0	↔	0.0

* Odd ratios that do not include 1.0 in the 95% confidence intervals are reported as statistically significant

†Statistical analysis was not conducted on isolates collected from the HACCP verification program. The PR/HACCP *Salmonella* verification program was designed to evaluate the performance of FSIS regulated establishments using prescribed performance standards. Prior to 2006, FSIS sampling collection methods included both random and risked-based methods. In 2006, FSIS began to schedule establishment sampling based on criteria that are risk-based rather than random. This change in sample collection methods limits meaningful trend comparison between pre-2006 and post-2006. Similarly, these changes limit year-to-year comparisons post-2006

‡Antimicrobial classes are defined using categories from the Clinical and Laboratory Standards Institute (CLSI)

§Testing for significant difference between 2013 and reference was not performed due to low number of resistant isolates and/or number tested

Significant difference	(orange shading)
Decline in resistance	↓
Increase in resistance	↑
No change in resistance	↔

The differences between the prevalence of resistance in 2013 and the average prevalence of resistance in 2004–2008 (Table 7) were statistically significant for the following:

- *E. coli*
  - Retail chicken
    - Ceftriaxone resistance was lower in 2013 than in 2004–2008 (4.2% decline; OR=0.4, 95% confidence interval, 0.2–0.7)
    - Resistance to at least one antimicrobial class was lower in 2013 than in 2004–2008 (5.3% decline; OR=0.7, 95% confidence interval, 0.6–0.9)
    - Resistance to three or more antimicrobial classes was lower in 2013 than in 2004–2008 (7.4% decline; p OR=0.7, 95% confidence interval, 0.6–0.9)
  - Retail ground turkey:
    - Nalidixic acid resistance was lower in 2013 than in 2004–2008 (4.5% decline; OR=0.3, 95% confidence interval, 0.1–0.7)
    - Ceftriaxone resistance was higher in 2013 than in 2004–2008 (3.4% increase; OR=2.5, 95% confidence interval, 1.5–4.1)

- *Enterococcus*
  - *E. faecium* from retail chicken
    - Penicillin resistance was lower in 2013 than in 2004–2008 (17% decline; OR=0.3, 95% confidence interval, 0.2–0.4)

Table 8. Changes in the percentage of clinically important resistance among *E coli* and *Enteroccocus* isolated from retail meat: 2013 compared with 2008–2012*†

Pathogen	Resistance Pattern	Retail							
		Chicken		Ground Turkey		Ground Beef		Pork Chops	
		Change	2013	Change	2013	Change	2013	Change	2013
E. coli	Ciprofloxacin	↑0.4	0.6	↔	0.3	↔	0.0	↔	0.0
	Nalidixic Acid	↓0.2	2.5	↓0.6	1.9	↔	0.4	↓0.1	0.0
	Ceftriaxone	↓5.6	4.4	↓1.2	6.7	↑1.4	2.2	↓0.9	1.4
	Resistance to ≥1 class‡	↑1.6	69.2	↓1.6	85.6	↓10.3	23.3	↑4.6	53.8
	Resistance to ≥3 classes‡	↓2.6	31.4	↓4.1	59.4	↓1.1	7.9	↓0.4	13.9
Enterococcus faecalis	Linezolid§	↔	0.0	↔	0.0	↔	0.0	↔	0.0
	Daptomycin§	↔	0.0	↓0.1	0.0	↔	0.0	↔	0.0
	Vancomycin§	↔	0.0	↔	0.0	↔	0.0	↔	0.0
	Pencillin	↓0.1	0.0	↓0.1	0.0	↓0.1	0.0	↓0.2	0.0
	Gentamicin	↓2.3	24.3	↓1.3	33.7	↔	0.7	↓0.4	0.9
	Gentamicin and Penicillin§	↔	0.0	↔	0.0	↔	0.0	↔	0.0
Enterococcus faecium	Linezolid§	↔	0.0	↔	0.0	↔	0.0	↔	0.0
	Vancomycin§	↔	0.0	↔	0.0	↔	0.0	↔	0.0
	Pencillin	↓11	9.9	↓11	54.2	↓0.3	5.0	↑0.7	4.0
	Gentamicin	↓1.2	7.0	↓3.4	8.3	↓0.3	0.0	↔	0.0
	Gentamicin and Penicillin	↓2.1	1.4	↓6.3	2.1	↓0.3	0.0	↔	0.0

* Odd ratios that do not include 1.0 in the 95% confidence intervals are reported as statistically significant

†Statistical analysis was not conducted on isolates collected from the HACCP verification program. The PR/HACCP *Salmonella* verification program was designed to evaluate the performance of FSIS regulated establishments using prescribed performance standards. Prior to 2006, FSIS sampling collection methods included both random and risked-based methods. In 2006, FSIS began to schedule establishment sampling based on criteria that are risk-based rather than random. This change in sample collection methods limits meaningful trend comparison between pre-2006 and post-2006. Similarly, these changes limit year-to-year comparisons post-2006

‡Antimicrobial classes are defined using categories from the Clinical and Laboratory Standards Institute (CLSI)

§Testing for significant difference between 2013 and reference was not performed due to low number of resistant isolates and/or number tested

Significant difference	(orange shading)
Decline in resistance	↓
Increase in resistance	↑
No change in resistance	↔

The differences between the prevalence of resistance in 2013 and the average prevalence of resistance in 2008–2012 (Table 8) were statistically significant for the following:

- *E. coli*
  - Retail chicken
    - Ceftriaxone resistance was lower in 2013 than in 2008–2012 (5.6% decline; OR=0.4, 95% confidence interval, 0.2–0.7)
- *Enterococcus*
  - *E. faecium* from retail chicken
    - Penicillin resistance was lower in 2013 than in 2008–2012 (11% decline; OR=0.3, 95% confidence interval, 0.2–0.6)

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