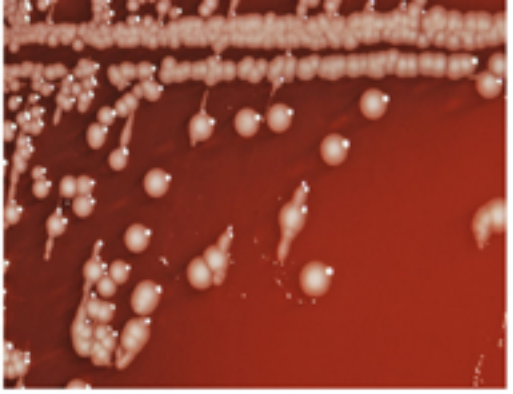


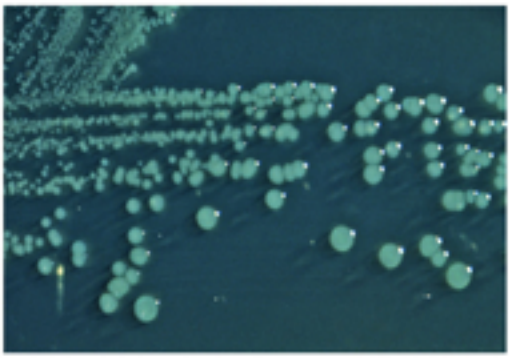
NARMS

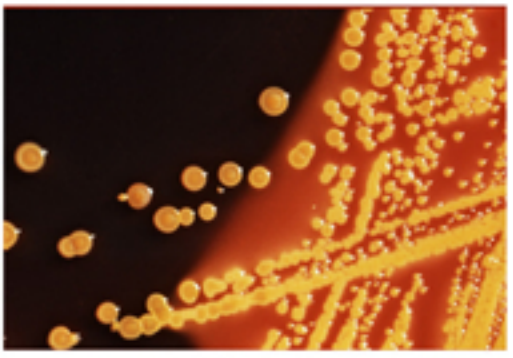
National Antimicrobial Resistance Monitoring System: Enteric Bacteria

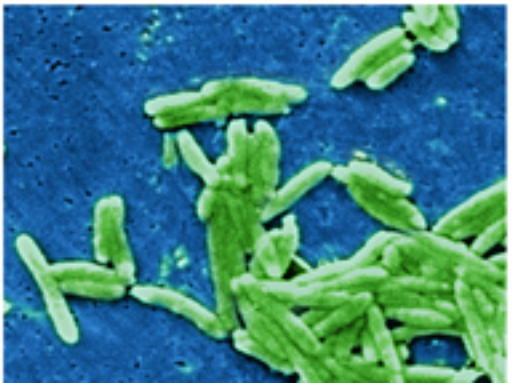
NARMS

2004

Human Isolates Final Report







DEPARTMENT OF HEALTH & HUMAN SERVICES • USA

CDC

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INFORMATION AVAILABLE ON-LINE

All CDC NARMS Annual Reports and additional information about NARMS are posted on the CDC NARMS website: http://www.cdc.gov/narms.

Additional general information about the NARMS surveillance program is posted on the Food and Drug Administration's Center for Veterinary Medicine website: http://www.fda.gov/cvm/narms_pg.html.

Information about animal isolates in NARMS is available on the U.S. Department of Agriculture–-Agricultural Research Service website: http://www.ars-grin.gov/ars/SoAtlantic/Athens/arru/narms.html.

General information about antimicrobial resistance is posted on the CDC website: http://www.cdc.gov/drugresistance.

Information regarding CDC's Get Smart program is available at http://www.cdc.gov/drugresistance/community.

General information about CDC's Foodborne Diseases Active Surveillance Network (FoodNet) is available at http://www.cdc.gov/foodnet.

General information about the National Molecular Subtyping Network for Foodborne Disease Surveillance (PulseNet) is available at http://www.cdc.gov/pulsenet.

General information about the World Health Organization Global Salm-Surv is available at http://www.who.int/salmsurv/en.

CDC *Salmonella* Annual Summaries are posted on the PHLIS website: http://www.cdc.gov/ncidod/dbmd/phlisdata/salmonella.htm.

CDC *Shigella* Annual Summaries also posted on the PHLIS website: http://www.cdc.gov/ncidod/dbmd/phlisdata/shigella.htm.

General information about the Foodborne and Diarrheal Diseases Branch at CDC is available at http://www.cdc.gov/foodborne/

INTRODUCTION

The National Antimicrobial Resistance Monitoring System (NARMS) for Enteric Bacteria is a collaboration among the Centers for Disease Control and Prevention (CDC), Food and Drug Administration (FDA), and U.S. Department of Agriculture (USDA). The primary purpose of NARMS at CDC is to monitor antimicrobial resistance among foodborne enteric bacteria isolated from humans. Other components of the interagency NARMS program include surveillance for resistance in human enteric bacterial pathogens isolated from foods, conducted by the FDA Center for Veterinary Medicine (http://www.fda.gov/cvm/narms_pg.html), and resistance in human enteric pathogens isolated from animals, conducted by the USDA Agricultural Research Services (http://www.ars-grin.gov/ars/SoAtlantic/Athens/arru/narms.html).

Many NARMS activities are conducted within the framework of CDC's Emerging Infections Program (EIP), Epidemiology and Laboratory Capacity (ELC) Program, and the Foodborne Diseases Active Surveillance Network (FoodNet). In addition to surveillance of resistance in enteric pathogens, the NARMS program at CDC also includes public health research into the mechanisms of resistance, education efforts to promote prudent use of antimicrobial agents, and studies of resistance in commensal organisms.

Before NARMS was established, CDC monitored antimicrobial resistance in *Salmonella, Shigella*, and *Campylobacter* through periodic surveys of isolates from a panel of sentinel counties. NARMS at CDC began in 1996 with prospective monitoring of antimicrobial resistance among human non-Typhi *Salmonella* and *Escherichia coli* O157 isolates in 14 sites. In 1997, testing of human *Campylobacter* isolates was initiated in the five sites participating in FoodNet. Testing of human *Salmonella* Typhi and *Shigella* isolates was added in 1999. Since 2003, all 50 states have been forwarding a representative sample of non-Typhi *Salmonella, Salmonella* Typhi, *Shigella*, and *E. coli* O157 isolates to NARMS for antimicrobial susceptibility testing, and 10 FoodNet states have been participating in *Campylobacter* surveillance.

This annual report includes CDC's human surveillance data for 2004 for non-Typhi *Salmonella, Salmonella* Typhi, *Shigella*, and *E. coli* O157. Resistance trends and comparisons to previous years are included when appropriate. Antimicrobial subclasses defined by the Clinical and Laboratory Standards Institute (CLSI) are used in data presentation and analysis. CLSI subclasses constitute major classifications of antimicrobial agents, e.g., aminoglycosides and cephalosporins.

This report also includes a section on the Enterococci Resistance Study, which is part of NARMS surveillance on commensal bacteria. Data from the 2004 Enterococci Resistance Study are presented, as are 2001–2003 data when reference to previous years is appropriate. In addition, Appendix A summarizes the *Escherichia coli* Resistance Surveillance Pilot Study conducted in 2004.

Additional NARMS data and more information about NARMS activities are available at http://www.cdc.gov/narms.

SUMMARY OF NARMS 2004 SURVEILLANCE DATA

POPULATION

In 2004, all 50 states participated in NARMS, representing approximately 294 million persons (Table I). Surveillance for antimicrobial resistance included non-Typhi *Salmonella, Salmonella* Typhi, *Shigella*, and *Escherichia coli* O157. *Campylobacter* resistance to antimicrobial agents was monitored in 10 states that also participated in the Foodborne Diseases Active Surveillance Network (FoodNet), representing approximately 45 million persons (15% of the U.S. population).

CLINICALLY IMPORTANT RESISTANCE

In the United States, certain quinolones (e.g., the fluoroquinolone ciprofloxacin) and third-generation cephalosporins (e.g., ceftriaxone) are antimicrobial agents commonly used to treat severe *Campylobacter* and *Salmonella* infections, including *Salmonella* serotype Typhi, the organism that causes Typhoid fever. Nalidixic acid is an elementary quinolone; resistance to nalidixic acid correlates with decreased susceptibility to ciprofloxacin and possible treatment failure. Ceftiofur is a third-generation cephalosporin used in food animals in the United States; resistance to ceftiofur correlates with decreased susceptibility to ceftriaxone. A substantial proportion of isolates tested by NARMS in 2004 demonstrated resistance to these clinically important antimicrobial agents, as follows:

- 19.0% (66/347) of *Campylobacter* isolates were resistant to the fluoroquinolone ciprofloxacin, compared with 12.9% (28/217) in 1997 (OR=1.6, 95% CI [1.0, 2.6]) (Table II).
    - 30.8% (8/26) of *Campylobacter coli* isolates were resistant to ciprofloxacin.
    - 18.1% (58/320) of *Campylobacter jejuni* isolates were resistant to ciprofloxacin.
- 2.6% (47/1793) of non-Typhi *Salmonella* isolates were resistant to the quinolone nalidixic acid, compared with 0.4% (5/1324) in 1996 (OR=9.2, 95% CI [3.6, 23.8]) (Table II).
    - *Salmonella* Enteritidis was the most common serotype among nalidixic acid-resistant non-Typhi *Salmonella* isolates: 38.3% (18/47) of quinolone-resistant isolates were serotype Enteritidis.
    - Nalidixic acid resistance in *Salmonella* Enteritidis was 6.6% (18/271) in 2004, compared with 0.9% (3/351) in 1996 (OR 95% CI [2.3, 49.3]) (Table II).
- 3.4% (61/1793) of non-Typhi *Salmonella* isolates were resistant to the third-generation cephalosporin ceftiofur, compared with 0.2% (2/1324) in 1996 (OR=34.5, 95% CI [8.3, 142.7]) (Table II).
    - *Salmonella* Newport was the most common serotype among ceftiofur-resistant non-Typhi *Salmonella* isolates: 47.5% (29/61) of ceftiofur-resistant isolates were serotype Newport.
- 41.7% (127/304) of *Salmonella* Typhi isolates were resistant to the quinolone nalidixic acid, compared with 18.7% (31/166) in 1999 (OR=3.1, 95% CI [1.9, 4.9]) (Table II).

MULTIDRUG RESISTANCE

- Multidrug resistance is described in NARMS by the number of antimicrobial subclasses or specific coresistant phenotypes. Antimicrobial subclasses are used as defined by the CLSI (Table III). For non-Typhi *Salmonella*, the most common multidrug-resistant phenotypes in 2004 were as follows: resistance to at least ampicillin, chloramphenicol, streptomycin, sulfamethoxazole/sulfisoxazole, and tetracycline (R-Type ACSSuT) and resistance to at least ampicillin, chloramphenicol, streptomycin, sulfamethoxazole/sulfisoxazole, tetracycline, amoxicillin-clavulanic acid, and ceftiofur, and decreased susceptibility to ceftriaxone (minimum inhibitory concentration ≥2 μg/mL) (MDR-AmpC).

- 15.0% (269/1793) of non-Typhi *Salmonella* isolates were resistant to two or more CLSI subclasses, and 8.1% (146/1793) were resistant to five or more CLSI subclasses.
    - 17.4% (33/190) of *Salmonella* Newport isolates were resistant to two or more CLSI subclasses, and 14.7% (28/190) were resistant to five or more CLSI subclasses.
    - 37.2% (142/382) of *Salmonella* Typhimurium isolates were resistant to two or more CLSI subclasses, and 24.3% (93/382) were resistant to five or more CLSI subclasses.
    - 3.0% (8/271) of *Salmonella* Enteritidis isolates were resistant to two or more CLSI subclasses, and 0.7% (2/271) were resistant to five or more CLSI subclasses.

- 7.1% (128/1793) of non-Typhi *Salmonella* isolates had R-Type ACSSuT, compared with 8.8% (116/1324) in 1996 (Table 1.3).
    - 23.3% (89/382) of *Salmonella* Typhimurium isolates were R-Type ACSSuT, compared with 33.7% (103/306) in 1996(OR=0.6, 95% CI [0.4, 0.8]) (Table II).
    - 14.7% (28/190) of *Salmonella* Newport isolates were R-Type ACSSuT, compared with 5.9% (3/51) in 1996.
- 2.3% (42/1793) of non-Typhi *Salmonella* isolates had the MDR-AmpC phenotype. These isolates consisted of five different serotypes. In 1996, MDR-AmpC resistance was not detected in any serotype.
    - 14.7% (28/189) of *Salmonella* Newport isolates were at least MDR-AmpC resistant, compared with none (0/51) in 1996 (95% CI [3.4, infinity]) (Table II).
    - 2.6% (10/382) of *Salmonella* Typhimurium isolates were at least MDR-AmpC resistant.

Table I: Population size and number of isolates tested, by site, NARMS, 2004

State/Site	Population Size*	Non-Typhi *Salmonella*		*Salmonella* Typhi		*Shigella*		*E. coli* O157		Campylobacter†	
		N	(%)	N	(%)	N	(%)	N	(%)	N	(%)
Alabama	4,530,182	36	(2.0%)	1	(0.3%)	9	(2.8%)	1	(0.6%)	N/A	
Alaska	655,435	2	(0.1%)	0	(0.0%)	1	(0.3%)	1	(0.6%)	N/A	
Arizona	5,743,834	28	(1.6%)	2	(0.7%)	8	(2.5%)	0	(0.0%)	N/A	
Arkansas	2,752,629	22	(1.2%)	0	(0.0%)	4	(1.3%)	3	(1.8%)	N/A	
California‡	32,056,400	109	(6.1%)	65	(21.4%)	1	(0.3%)	7	(4.1%)	27	(7.8%)
Colorado	4,601,403	23	(1.3%)	4	(1.3%)	6	(1.9%)	2	(1.2%)	33	(9.5%)
Connecticut	3,503,604	26	(1.5%)	9	(3.0%)	4	(1.3%)	5	(3.0%)	40	(11.5%)
Delaware	830,364	8	(0.4%)	1	(0.3%)	0	(0.0%)	0	(0.0%)	N/A	
District of Columbia	553,523	0	(0.0%)	0	(0.0%)	0	(0.0%)	0	(0.0%)	N/A	
Florida	17,397,161	54	(3.0%)	10	(3.3%)	0	(0.0%)	0	(0.0%)	N/A	
Georgia	8,829,383	111	(6.2%)	3	(1.0%)	24	(7.6%)	20	(11.8%)	45	(13.0%)
Hawaii	1,262,840	18	(1.0%)	7	(2.3%)	3	(0.9%)	0	(0.0%)	N/A	
Houston, Texas§	2,011,119	33	(1.8%)	0	(0.0%)	0	(0.0%)	0	(0.0%)	N/A	
Idaho	1,393,262	9	(0.5%)	0	(0.0%)	1	(0.3%)	3	(1.8%)	N/A	
Illinois	12,713,634	74	(4.1%)	14	(4.6%)	19	(6.0%)	5	(3.0%)	N/A	
Indiana	6,237,569	35	(2.0%)	1	(0.3%)	2	(0.6%)	2	(1.2%)	N/A	
Iowa	2,954,451	14	(0.8%)	0	(0.0%)	0	(0.0%)	0	(0.0%)	N/A	
Kansas	2,735,502	16	(0.9%)	0	(0.0%)	3	(0.9%)	1	(0.6%)	N/A	
Kentucky	4,145,922	20	(1.1%)	3	(1.0%)	4	(1.3%)	0	(0.0%)	N/A	
Los Angeles¶	3,837,399	60	(3.3%)	22	(7.2%)	7	(2.2%)	0	(0.0%)	N/A	
Louisiana	4,515,770	46	(2.6%)	0	(0.0%)	4	(1.3%)	0	(0.0%)	N/A	
Maine	1,317,253	5	(0.3%)	1	(0.3%)	1	(0.3%)	1	(0.6%)	N/A	
Maryland	5,558,058	44	(2.5%)	16	(5.3%)	8	(2.5%)	3	(1.8%)	22	(6.3%)
Massachusetts	6,416,505	58	(3.2%)	16	(5.3%)	8	(2.5%)	4	(2.4%)	N/A	
Michigan	10,112,620	40	(2.2%)	9	(3.0%)	7	(2.2%)	4	(2.4%)	N/A	
Minnesota	5,100,958	33	(1.8%)	6	(2.0%)	2	(0.6%)	5	(3.0%)	53	(15.3%)
Mississippi	2,902,966	43	(2.4%)	0	(0.0%)	1	(0.3%)	0	(0.0%)	N/A	
Missouri	5,754,618	43	(2.4%)	1	(0.3%)	9	(2.8%)	6	(3.6%)	N/A	
Montana	926,865	5	(0.3%)	0	(0.0%)	1	(0.3%)	1	(0.6%)	N/A	
Nebraska	1,747,214	12	(0.7%)	2	(0.7%)	8	(2.5%)	5	(3.0%)	N/A	
Nevada	2,334,771	12	(0.7%)	2	(0.7%)	4	(1.3%)	2	(1.2%)	N/A	
New Hampshire	1,299,500	8	(0.4%)	0	(0.0%)	0	(0.0%)	1	(0.6%)	N/A	
New Jersey	8,698,879	44	(2.5%)	17	(5.6%)	9	(2.8%)	10	(5.9%)	N/A	
New Mexico	1,903,289	19	(1.1%)	0	(0.0%)	8	(2.5%)	0	(0.0%)	21	(6.1%)
New York4	11,062,382	66	(3.7%)	10	(3.3%)	14	(4.4%)	9	(5.3%)	50	(14.4%)
New York City**	8,164,706	56	(3.1%)	29	(9.5%)	6	(1.9%)	3	(1.8%)	N/A	
North Carolina	8,541,221	86	(4.8%)	4	(1.3%)	7	(2.2%)	8	(4.7%)	N/A	
North Dakota	634,366	3	(0.2%)	0	(0.0%)	1	(0.3%)	1	(0.6%)	N/A	
Ohio	11,459,011	58	(3.2%)	5	(1.6%)	5	(1.6%)	5	(3.0%)	N/A	
Oklahoma	3,523,553	20	(1.1%)	0	(0.0%)	26	(8.2%)	4	(2.4%)	N/A	
Oregon	3,594,586	19	(1.1%)	1	(0.3%)	4	(1.3%)	3	(1.8%)	29	(8.4%)
Pennsylvania	12,406,292	80	(4.5%)	8	(2.6%)	6	(1.9%)	10	(5.9%)	N/A	
Rhode Island	1,080,632	9	(0.5%)	2	(0.7%)	0	(0.0%)	1	(0.6%)	N/A	
South Carolina	4,198,068	3	(0.2%)	0	(0.0%)	3	(0.9%)	0	(0.0%)	N/A	
South Dakota	770,883	10	(0.6%)	0	(0.0%)	6	(1.9%)	9	(5.3%)	N/A	
Tennessee	5,900,962	38	(2.1%)	4	(1.3%)	23	(7.3%)	2	(1.2%)	27	(7.8%)
Texas††	20,478,903	48	(2.7%)	11	(3.6%)	22	(7.0%)	1	(0.6%)	N/A	
Utah	2,389,039	12	(0.7%)	1	(0.3%)	1	(0.3%)	3	(1.8%)	N/A	
Vermont	621,394	2	(0.1%)	1	(0.3%)	1	(0.3%)	0	(0.0%)	N/A	
Virginia	7,459,827	57	(3.2%)	7	(2.3%)	4	(1.3%)	1	(0.6%)	N/A	
Washington	6,203,788	38	(2.1%)	6	(2.0%)	6	(1.9%)	8	(4.7%)	N/A	
West Virginia	1,815,354	30	(1.7%)	0	(0.0%)	1	(0.3%)	1	(0.6%)	N/A	
Wisconsin	5,509,026	43	(2.4%)	3	(1.0%)	13	(4.1%)	5	(3.0%)	N/A	
Wyoming	506,529	5	(0.3%)	0	(0.0%)	1	(0.3%)	3	(1.8%)	N/A	
Total	**293,655,404**	**1793**	**(100.0%)**	**304**	**(100.0%)**	**316**	**(100.0%)**	**169**	**(100.0%)**	**347**	**(100.0%)**

* US Census Bureau, 2004

† *Campylobacter* isolates were submitted only from FoodNet sites; total population size of FoodNet sites was 44,531,182

‡ Excluding Los Angeles County

§ Houston City

¶ Los Angeles County

4 Excluding New York City

** Five burroughs of New York City (Bronx, Brooklyn, Manhattan, Queens, Staten Island)

†† Excluding Houston, Texas

Table II: Summary of trend analysis of the proportion of specific resistance phenotypes among *Campylobacter*, non-Typhi *Salmonella*, and *Salmonella* Typhi isolates, 2004

Resistance Phenotype	Reference Year	Odds Ratio*	95% CI*
Ciprofloxacin resistance in *Campylobacter*	1997	1.6	1.0–2.6
Nalidixic acid resistance in non-Typhi *Salmonella*	1996	9.2	3.6–23.8
Nalidixic acid resistance in *Salmonella* Enteritidis	1996	–[†]	2.3–49.3[†]
Ceftiofur resistance in non-Typhi *Salmonella*	1996	34.5	8.3–142.7
Nalidixic acid resistance in *Salmonella* Typhi	1999	3.1	1.9–4.9
ACSSuT resistance in *Salmonella* Typhimurium[‡]	1996	0.6	0.4–0.8
MDR-AmpC resistance in *Salmonella* Newport[§]	1996	–[†]	3.4–infinity[†]

* For logistic regression models that adjusted for site, odds ratios (ORs) (2004 vs. reference year) and 95% confidence intervals (CIs) were calculated using unconditional maximum likelihood estimation.
[†] Model included only year. In the analysis, the maximum likelihood estimate of the OR did not exist; only the 95% CIs, calculated using unconditional exact methods, are reported.
[‡] Resistance to at least ampicillin, chloramphenicol, streptomycin, sulfamethoxazole/sulfisoxazole, and tetracycline.
[§] Resistance to at least ampicillin, chloramphenicol, streptomycin, sulfamethoxazole/sulfisoxazole, tetracycline, amoxicillin-clavulanic acid, and ceftiofur, and decreased susceptibility to ceftriaxone (minimum inhibitory concentration ≥2 μg/mL).

SURVEILLANCE AND LABORATORY TESTING METHODS

SURVEILLANCE SITES AND ISOLATE SUBMISSION

In 2004, NARMS conducted nationwide surveillance among the population of approximately 294 million persons (2004 U.S. Census Bureau estimates). Public health laboratories systematically selected every 20th non-Typhi *Salmonella* (i.e., all *Salmonella* serotypes except serotype Typhi)*, Shigella*, and *Escherichia coli* O157 isolate and every *Salmonella* Typhi isolate received at their laboratories and forwarded these isolates to CDC for antimicrobial susceptibility testing.

Public health laboratories of the 10 state health departments that participated in CDC's Foodborne Diseases Active Surveillance Network (FoodNet) during 2004 forwarded *Campylobacter* isolates to CDC for susceptibility testing. The FoodNet sites, representing approximately 45 million persons (2004 U.S. Census Bureau estimates), comprised California, Colorado, Connecticut, Georgia, Maryland, Minnesota, New Mexico, New York, Oregon, and Tennessee. *Campylobacter* isolates submitted to NARMS were selected in one of several ways. In Maryland, Minnesota, New Mexico, New York, and Tennessee, one isolate a week was selected (usually the first isolate received each week was selected, but otherwise isolates were randomly selected) from the collection of isolates sent to the state health department laboratory from almost all clinical laboratories in a geographic area (statewide in Maryland, Minnesota, New Mexico, and Tennessee, and metro Albany and Rochester areas in New York). In Georgia, all *Campylobacter* isolates received at the state laboratory from the Metropolitan Statistical Area (metro Atlanta area) were submitted to CDC. For that state, one isolate a week was selected at CDC (usually the first isolate received each week was selected, but otherwise isolates were randomly selected) from the collection of isolates from almost all clinical laboratories in metro Atlanta. In California, Colorado, Connecticut, and Oregon, one isolate a week was selected (usually the first isolate received each week was selected, but otherwise isolates were randomly selected) from one sentinel clinical laboratory. Sentinel clinical laboratories followed routine isolation practices for *Campylobacter*. No more than 53 *Campylobacter* isolates per state were included in the analyses; if more than one isolate was received in a week from a site, only the first isolate was included.

TESTING OF *SALMONELLA, SHIGELLA*, AND *ESCHERICHIA COLI* O157

Antimicrobial Susceptibility Testing

Salmonella, *Shigella*, and *E. coli* O157 isolates were tested using broth microdilution (Sensititre®, Trek Diagnostics, Westlake, OH) to determine the minimum inhibitory concentration (MIC) for each of 15 antimicrobial agents: amikacin, ampicillin, amoxicillin-clavulanic acid, cefoxitin, ceftiofur, ceftriaxone, chloramphenicol, ciprofloxacin, gentamicin, kanamycin, nalidixic acid, streptomycin, sulfisoxazole, tetracycline, and trimethoprim-sulfamethoxazole (Table III). Before 2004, sulfamethoxazole was used instead of sulfisoxazole to represent the sulfonamides. Interpretive criteria defined by the Clinical and Laboratory Standards Institute (CLSI) were used when available.[1] The resistance breakpoint for amikacin, according to CLSI guidelines, is an MIC of 64 µg/mL. For isolates that grew in all amikacin dilutions on the Sensititre® panel (MIC>4 µg/mL), E-Test (AB BIODISK, Solna, Sweden) was performed to determine amikacin MIC. The amikacin E-Test strip range of dilutions is 0.016–256 µg/mL.

Table III: Antimicrobial agents used for susceptibility testing for *Salmonella*, *Shigella*, *Escherichia coli* O157, and *Campylobacter* isolates, NARMS, 2004

CLSI Subclass	Antimicrobial Agent	Antimicrobial Agent Concentration Range (μg/mL)	MIC Breakpoints (μg/mL)		
			Resistant	Intermediate	Susceptible
Aminoglycosides	Amikacin	0.5–4*	≥64	32	≤16
	Gentamicin	0.25–16 0.016–256[†]	≥16 ≥8**	8 4**	≤4 ≤2**
	Kanamycin	8–64	≥64	32	≤16
	Streptomycin	32–64	≥64		≤32
Aminopenicillins	Ampicillin	1–32	≥32	16	≤8
β-Lactamase inhibitor combinations	Amoxicillin-Clavulanic acid	1/0.5–32/16	≥32 / ≥16	16/8	≤8 / ≤4
Cephalosporin (1st generation)	Cephalothin[‡]	2–32	≥32	16	≤8
Cephalosporins (3rd generation)	Ceftiofur[§]	0.12–8	≥8	4	≤2
	Ceftriaxone	0.25–64	≥64	16–32	≤8
Cephamycins	Cefoxitin	0.5–16	≥32	16	≤8
Folate pathway inhibitors	Trimethoprim-Sulfamethoxazole	0.12/2.4–4/76	≥4 / ≥76		≤2 / ≤38
Lincosamides	Clindamycin	0.016–256[†]	≥8	4	≤2
Macrolides	Azithromycin	0.016–256[†]	≥8	4	≤2
	Erythromycin	0.016–256[†]	≥32	16	≤8
Phenicols	Chloramphenicol	2–32 0.016–256[†]	≥32	16	≤8
Quinolones	Ciprofloxacin	0.015–4 0.002–32[†]	≥4	2	≤1
	Nalidixic acid	0.5–32 0.016–256[†]	≥32 ≥64**	 32**	≤16 ≤16**
Sulfonamides[¶]	Sulfamethoxazole	16–512	≥512		≤256
	Sulfisoxazole	16–512	≥512		≤256
Tetracyclines	Tetracycline	4–16 0.016–256[†]	≥16	8	≤4

* The resistance breakpoint for amikacin, according to Clinical and Laboratory Standards Institute (CLSI) guidelines, is 64 μg/mL. For isolates that grew in all amikacin dilutions on the Sensititre® panel (minimum inhibitory concentration [MIC] >4 μg/mL), E-Test (AB BIODISK, Solna, Sweden) was performed to determine amikacin MIC. The amikacin E-Test strip range of dilutions is 0.016–256 μg/mL.
[†] E-test dilution range used for testing *Campylobacter.*
[‡] Cephalothin was not tested in 2004 but was tested in earlier years for *Salmonella*, *Shigella*, and *E. coli* O157.
[§] No CLSI breakpoints; resistance breakpoint used in NARMS is 8 μg/mL.
[¶] Sulfamethoxazole, which was tested during 1996–2003 to represent sulfonamides, was replaced by sulfisoxazole in 2004.
**Breakpoints for *Campylobacter* only

Additional Testing of Salmonella

Cephalosporin Retesting

Review of *Salmonella* isolates tested in NARMS during 1996–1998 gave conflicting cephalosporin susceptibility results. That is, some isolates previously reported in NARMS as ceftiofur-resistant exhibited a low ceftriaxone MIC and, in some cases, did not exhibit an elevated MIC to other β-lactams. Because these findings indicated that

some previously reported ceftiofur-resistant results were spurious, we retested, using the 2003 NARMS Sensititre® plate, isolates of *Salmonella* tested in NARMS during 1996–1998 that exhibited an MIC ≥2 µg/mL to ceftiofur or ceftriaxone. The retest results first were included in the 2003 NARMS annual report. Totals reported here also reflect the retest results.

Serotype Confirmation/Categorization

To distinguish serotypes Paratyphi B and Paratyphi B var L(+) tartrate-positive (formerly *Salmonella* Java), tartrate testing was performed at CDC on all *Salmonella* Paratyphi B isolates from 1996 to 2004 for which the tartrate result was not reported. Jordan's tartrate test was used to determine tartrate fermentation, and Kauffman's tartrate test subsequently was performed on isolates negative for tartrate fermentation by Jordan's tartrate test. Isolates negative for tartrate fermentation by both assays were categorized as serotype Paratyphi B. Isolates that were positive for tartrate fermentation by either assay were categorized as serotype Paratyphi B var L(+) tartrate-positive and in this report are referred to as serotype Java. Confirmation of other biochemical reactions or somatic and flagellar antigens was not performed at CDC.

Salmonella serotype was accepted as reported with few exceptions. As described above, tartrate testing was performed on all *Salmonella* Paratyphi B isolates for which the tartrate result was not reported. Because of increased submissions of *Salmonella* Typhimurium isolates lacking the second phase flagellar antigen (i.e., *Salmonella* I 4,[5],12:i:-), reports of such isolates tested in NARMS during 1996–2004 were reviewed, and isolates identified as serogroup B that exhibited first-phase flagellar antigen "I" but lacked a second phase are referred to in this report as "monophasic Typhimurium." Serogroup B isolates for which the first-phase flagellar antigen was not reported were not included in this category because they could be one of several other common serogroup B serotypes.

Testing of *Campylobacter*

Identification/Speciation and Antimicrobial Susceptibility Testing

In 2004, putative *Campylobacter* isolates were identified as *Campylobacter jejuni* or *Campylobacter coli* by polymerase chain reaction (PCR) using species-specific BAX® primers according to the manufacturer's instructions (DuPont Qualicon, Wilmington, DE). Isolates not identified as *C. jejuni* or *C. coli* were further characterized in conjunction with the CDC *Campylobacter* Reference Laboratory.

During 1996–2003, isolates were confirmed as *Campylobacter* by dark-field microscopy and oxidase test. Identification of *C. jejuni* was performed using the hippurate hydrolysis test. Hippurate-positive isolates were identified as *C. jejuni*. Hippurate-negative isolates were identified by PCR as *C. jejuni* using a hippuricase gene-based PCR assay,[2] or as *C. coli* using a *C. coli*-specific *ceuE* PCR.[3] Isolates determined to be neither *C. jejuni* nor *C. coli* were referred for identification to the CDC National *Campylobacter* Reference Laboratory. The methodology used during 1996–2003 was described in the 2003 annual report.[4]

In 2004, the E-test methodology (AB Biodisk, Solna, Sweden) was used to determine the MICs for eight antimicrobial agents: azithromycin, chloramphenicol, ciprofloxacin, clindamycin, erythromycin, gentamicin, nalidixic acid, and tetracycline (Table IIII). In this report, new CLSI interpretive criteria for erythromycin and revised NARMS criteria for azithromycin were used for 1997–2004.[5] In previous annual reports, these CLSI interpretive criteria were not available, and NARMS used resistance breakpoints for azithromycin and erythromycin that were lower than the new and revised breakpoints used in this report.[4] In addition, revised NARMS interpretive criteria, adopted from the FDA arm of NARMS, were used for clindamycin, gentamicin, and nalidixic acid.

Retesting

Known mechanisms of quinolone resistance in *Campylobacter* are expected to confer equivalent susceptibilities to nalidixic acid and ciprofloxacin. Similarly, known mechanisms of macrolide resistance are expected to confer equivalent susceptibilities to erythromycin and azithromycin. Confirmatory testing of isolates with conflicting results was performed by E-test (AB Biodisk, Solna, Sweden). Totals reported here reflect the retest results.

Data Analysis

For all pathogens in this report, MICs were categorized as resistant, intermediate susceptibility (if applicable), and susceptible. Analysis was restricted to one isolate (per pathogen) per patient. Where established, CLSI interpretive criteria were used; ceftiofur resistance was defined as MIC ≥8 μg/mL (Table III). The 95% confidence interval (CI) for the percentage of resistant isolates are included in the MIC distribution tables. The 95% CI was calculated using the Clopper-Pearson exact method.[6] Multidrug resistance by CLSI antimicrobial subclass was defined as resistance to two or more subclasses.

When describing results for several years, multidrug resistance for *Salmonella* and *E. coli* O157 isolates was limited to the 13 agents tested in all years from 1996 through 2004 (amoxicillin-clavulanic acid, ampicillin, ceftiofur, ceftriaxone, chloramphenicol, ciprofloxacin, gentamicin, kanamycin, nalidixic acid, streptomycin, sulfamethoxazole, tetracycline, and trimethoprim-sulfamethoxazole). For *Salmonella* Typhi and *Shigella,* results for several years included 14 agents tested in all years from 1999 through 2004 (13 antimicrobial agents mentioned above and amikacin). Similarly, when describing multidrug resistance for several years for *Campylobacter* isolates, multidrug resistance was limited to the six agents tested in all years from 1997 through 2004 (chloramphenicol, ciprofloxacin, clindamycin, erythromycin, nalidixic acid, and tetracycline).

Logistic regression was performed to compare the change in antimicrobial resistance among *Salmonella* and *Campylobacter* isolates tested in NARMS during 2004 with that of previous years for the following:

1. Non-Typhi *Salmonella*: resistance to nalidixic acid, resistance to ceftiofur, resistance to one or more CLSI subclass.
2. *Salmonella* Typhimurium: resistance to at least ampicillin, chloramphenicol, streptomycin, sulfamethoxazole, and tetracycline (R-Type ACSSuT).
3. *Salmonella* Enteritidis: resistance to nalidixic acid.
4. *Salmonella* Newport: resistance to at least ACSSuT, amoxicillin-clavulanic acid, and ceftiofur, with decreased susceptibility to ceftriaxone (MDR-AmpC).
5. *Salmonella* Typhi: resistance to nalidixic acid.
6. *Campylobacter* species: resistance to ciprofloxacin.
7. *Campylobacter jejuni*: resistance to ciprofloxacin.

The final regression models for non-Typhi *Salmonella,* and final models for serotypes Typhimurium and Typhi, adjusted for site using the nine Public Health Service geographic regions described in the Public Health Laboratory Information System (PHLIS [http://www.cdc.gov/ncidod/dbmd/phlisdata/]) based on the patient's state of residence. The PHLIS regions are East North Central, East South Central, Mid-Atlantic, Mountain, New England, Pacific, South Atlantic, West North Central, and West South Central. For all regression models that adjusted for site, odds ratios (ORs) and 95% confidence intervals (CIs) were calculated using unconditional maximum likelihood estimation. In the final regression models for serotypes Enteritidis and Newport, which included only year and used unconditional exact methods, the maximum likelihood estimate of the OR did not exist; only the 95% CIs are reported. For *Campylobacter*, the final regression models adjusted for site using four aggregated regions based on patient's state of residence. All analyses included observations from only those state and local health departments that had submitted isolates for at least 3 years. The adequacy of model fit was assessed in several ways. The significance of the main effect of year was assessed using the likelihood ratio test. The likelihood ratio test was also used to test for significance of interaction between site and year, although the power of the test to detect a single site-specific interaction was low. The Hosmer and Lemeshow goodness-of-fit test also was used.[7] Finally, residual analysis was performed to examine the influence of individual observations. ORs that did not include 1.0 in the 95% CI were reported as significant.

RESULTS FOR 2004

1. NON-TYPHI *SALMONELLA*

In 2004, CDC received 1832 non-Typhi *Salmonella* isolates, of which 1808 (98.7%) were viable and tested for antimicrobial susceptibility. Of these 1808 isolates, 15 isolates were excluded from the analysis because they were submissions from the same patient, leaving 1793 isolates for analysis. (Table I).

Fluoroquinolones (e.g., ciprofloxacin) and third-generation cephalosporins (e.g., ceftriaxone) are commonly used to treat severe *Salmonella* infections. Nalidixic acid is an elementary quinolone; resistance to nalidixic acid correlates with decreased susceptibility to ciprofloxacin and possible treatment failure. Ceftiofur is a third-generation cephalosporin used in food animals in the United States; resistance to ceftiofur correlates with decreased susceptibility to ceftriaxone. In 2004, the prevalence of resistance among *Salmonella* isolates was 2.6% for quinolones (represented by nalidixic acid) and 3.4% for third-generation cephalosporins (represented by ceftiofur) (Table 1.1).

The antimicrobial agents with the highest prevalence of resistance were tetracycline (13.5%), sulfisoxazole (13.2%), ampicillin (12.0%), and streptomycin (11.8%). (Sulfisoxazole replaced sulfamethoxazole to represent the sulfonamides in the 2004 NARMS panel.)

The prevalence of nalidixic acid resistance increased from 0.4% (5/1324) in 1996 to 2.6% (47/1793) in 2004 (Table 1.2); a statistically significant increase (OR=9.2, 95% CI [3.6, 23.8]). The prevalence of ceftiofur resistance increased from 0.2% (2/1324) in 1996 to 3.4% (61/1793) in 2004; a statistically significant increase (OR=34.5, 95% CI [8.3, 142.7]).

The proportion of resistance to most of the agents tested in 2004 was lower than in 2003, including ampicillin, amoxicillin-clavulanic acid, ceftiofur, cefoxitin, chloramphenicol, tetracycline, and streptomycin. However, for ceftiofur, resistance increased since 1996.

Of the 1783 non-Typhi *Salmonella* isolated in 2004, 79.6% (1427) had no detected resistance, a slight increase from the 77.7% in 2003 (Table 1.3). In 2004, 366 (20.4%) were resistant to one or more CLSI subclass; 269 (15.0%), to two or more subclasses; 210 (11.7%), to three or more subclasses; 168 (9.4%), to four or more subclasses; and 146 (8.1%), to five or more subclasses. There was a statistically significant decline in resistance to one or more subclass from 33.8% in 1996 to 20.4% in 2004 (OR=0.6, 95% CI [0.5, 0.7]) (Table 1.3).

In 2004, the most common multidrug-resistant phenotype (7.1%) among non-Typhi *Salmonella* isolates was resistance to at least ampicillin, chloramphenicol, streptomycin, sulfamethoxazole/sulfisoxazole, and tetracycline (R-Type ACSSuT). The proportion of isolates with R-Type ACSSuT was lower in 2004 than in 2003. Overall, however, the prevalence of R-Type ACSSuT did not change among non-Typhi *Salmonell*a isolates from 1996 to 2004. Another common multidrug-resistant phenotype among non-Typhi *Salmonell*a isolates was resistance to at least ACSSuT, amoxicillin-clavulanic acid, and ceftiofur and decreased susceptibility to ceftriaxone (MIC ≥2 µg/mL) (MDR-AmpC) (2.3%). The prevalence of MDR-AmpC increased from 0% (0/1324) in 1996 to 2.3% (42/1793) in 2004. Seven (0.4%) isolates were resistant to a quinolone (nalidixic acid) and third-generation cephalosporin (ceftiofur) (Table 1.3); this pattern was first detected in 1997.

Serotypes were identified for a higher proportion of isolates in NARMS (95.8%) than in the Public Health Laboratory Information System (PHLIS) (90.4%) (Table 1.4). The 20 most common serotypes accounted for 81.1% of isolates in NARMS and for 75.1% in PHLIS. The five most common serotypes accounted for 58.1% of isolates in NARMS and 53.0% in PHLIS.

Table 1.1: Minimum inhibitory concentrations (MICs) and resistance of non-Typhi *Salmonella* isolates to antimicrobial agents, 2004 (N=1793)

Antibiotic		% of isolates			Percent of all isolates with MIC (µg/mL)[§]														
		%I[*]	%R[†]	[95% CI][‡]	0.015	0.03	0.06	0.125	0.25	0.50	1	2	4	8	16	32	64	128	256	512
Aminoglycosides	Amikacin	0.0	0.0	[0.0–0.2]						7.8	69.5	20.0	2.5	0.2						
	Gentamicin	0.4	1.3	[0.9–2.0]					68.4	27.7	2.0	0.2	0.1	0.4	0.6	0.8				
	Kanamycin	0.2	2.8	[2.1–3.7]										96.7	0.3	0.2	0.2	2.6		
	Streptomycin	NA	11.8	[10.4–13.4]												88.2	5.7	6.1		
Aminopenicillins	Ampicillin	0.1	12.0	[10.6–13.6]							60.4	25.8	1.7		0.1	0.1	12.0			
β-lactamase inhibitor	Amoxicillin-clavulanic acid	5.7	3.7	[2.9–4.7]							83.8	3.8	0.4	2.5	5.7	0.8	2.9			
Cephalosporins (3rd generation)	Ceftiofur	0.3	3.4	[2.6–4.3]				0.6	1.5	76.2	17.6	0.4	0.3	0.1	3.3					
	Ceftriaxone	2.6	0.6	[0.3–1.0]					96.4	0.2		0.1		0.2	1.4	1.2	0.5	0.1		
Cephamycins	Cefoxitin	0.3	3.5	[2.7–4.4]						0.2	25.5	56.1	12.7	1.8	0.3	1.3	2.1			
Folate pathway inhibitors	Trimethoprim-sulfamethoxazole	NA	1.8	[1.2–2.5]				76.4	21.0	0.6	0.1	0.2	0.1	1.7						
Phenicols	Chloramphenicol	0.9	7.6	[6.4–8.9]								2.1	45.1	44.3	0.9		7.6			
Quinolones	Ciprofloxacin	0.1	0.2	[0.1–0.6]	95.8	1.4	0.1	1.1	0.9	0.4		0.1		0.2						
	Nalidixic Acid	NA	2.6	[1.9–3.5]						0.1	0.4	26.0	69.2	1.5	0.2	0.2	2.5			
Sulfonamides	Sulfamethoxazole/Sulfisoxazole	NA	13.2	[11.7–14.9]											19.3	55.7	11.5	0.2	0.1	13.2
Tetracyclines	Tetracycline	0.3	13.5	[11.9–15.2]									86.2	0.3	1.4	4.5	7.6			

[*]Percent of isolates with intermediate susceptibility, NA if no MIC range of intermediate susceptibility exists

[†]Percent of isolates that were resistant

[‡]95% confidence intervals (CI) for percent resistant (%R) were calculated using the Clopper-Pearson exact method

[§]The unshaded areas indicate the dilution range of the Sensititre plates used to test isolates. Single vertical bars indicate the breakpoints for susceptibility, while double vertical bars indicate breakpoints for resistance. Numbers in the shaded areas indicate the percentages of isolates with MICs greater than the highest concentrations on the Sensititre plate. Numbers listed for the lowest tested concentrations represent the precentages of isolates with MICs equal to or less than the lowest tested concentration. CLSI breakpoints were used when available.

Table 1.2: Percentage and number of non-Typhi *Salmonella* isolates resistant to antimicrobial agents, 1996–2004

Year		1996	1997	1998	1999	2000	2001	2002	2003	2004
Total Isolates		1324	1301	1460	1497	1377	1419	2008	1864	1793
Subclass	Antibiotic (Resistance breakpoint)									
Aminoglycosides	Amikacin (MIC ≥ 64)	Not Tested	0.0% 0	0.0% 0	0.1% 1	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0
	Gentamicin (MIC ≥ 16)	4.8% 63	2.9% 38	2.8% 41	2.1% 32	2.7% 37	1.9% 27	1.3% 27	1.4% 26	1.3% 24
	Kanamycin (MIC ≥ 64)	5.0% 66	5.1% 67	5.7% 83	4.3% 65	5.6% 77	4.8% 68	3.8% 76	3.4% 64	2.8% 50
	Streptomycin (MIC ≥ 64)	20.6% 273	21.4% 278	18.6% 272	16.8% 251	16.3% 224	17.0% 241	13.2% 265	15.0% 279	11.8% 212
Aminopenicillins	Ampicillin (MIC ≥ 32)	20.7% 274	18.3% 238	16.5% 241	15.6% 233	15.9% 219	17.4% 247	12.9% 259	13.6% 254	12.0% 216
β-lactamase inhibitor combinations	Amoxicillin-clavulanic acid (MIC ≥ 32)	1.1% 15	1.0% 13	1.7% 25	2.3% 35	3.9% 54	4.7% 66	5.3% 106	4.6% 86	3.7% 67
Cephalosporin (1st generation)	Cephalothin (MIC ≥ 32)	2.9% 39	2.2% 29	2.3% 33	3.6% 54	4.0% 55	4.0% 57	5.0% 101	5.4% 100	Not Tested
Cephalosporins (3rd generation)	Ceftiofur (MIC ≥ 8)	0.2% 2	0.5% 6	0.8% 12	2.0% 30	3.2% 44	4.1% 58	4.3% 87	4.5% 83	3.4% 61
	Ceftriaxone (MIC ≥ 64)	0.0% 0	0.1% 1	0.0% 0	0.3% 5	0.0% 0	0.0% 0	0.2% 4	0.4% 8	0.6% 10
Cephamycins	Cefoxitin (MIC ≥ 32)	Not Tested	Not Tested	Not Tested	Not Tested	3.2% 44	3.4% 48	4.3% 86	4.2% 79	3.5% 62
Folate pathway inhibitors	Trimethoprim-sulfamethoxazole (MIC ≥ 4)	3.9% 51	1.8% 24	2.3% 34	2.1% 31	2.1% 29	2.0% 28	1.4% 28	1.9% 36	1.8% 32
Phenicols	Chloramphenicol (MIC ≥ 32)	10.6% 140	10.1% 131	9.9% 145	9.2% 138	10.1% 139	11.6% 164	8.6% 172	10.0% 187	7.6% 136
Quinolones	Ciprofloxacin (MIC ≥ 4)	0.0% 0	0.0% 0	0.1% 1	0.1% 1	0.4% 5	0.2% 3	0.0% 1	0.2% 3	0.2% 4
	Nalidixic Acid (MIC ≥ 32)	0.4% 5	0.9% 12	1.4% 20	1.0% 15	2.5% 34	2.6% 37	1.8% 36	2.3% 42	2.6% 47
Sulfonamides	Sulfamethoxazole/Sulfisoxazole[*] (MIC ≥ 512)	20.3% 269	22.8% 297	19.4% 283	18.0% 270	17.1% 235	17.7% 251	12.8% 258	15.0% 280	13.2% 237
Tetracyclines	Tetracycline (MIC ≥ 16)	24.2% 320	21.7% 282	20.2% 295	19.4% 290	18.6% 256	19.7% 280	14.9% 299	16.3% 303	13.5% 242

[*]Sulfamethoxazole, which was tested during 1996-2003 to represent sulfonamides, was replaced by sulfisoxazole in 2004.

Table 1.3: Resistance patterns of non-Typhi *Salmonella* isolates, 1996–2004

Year	1996	1997	1998	1999	2000	2001	2002	2003	2004
Total Isolates	**1324**	**1301**	**1460**	**1497**	**1377**	**1419**	**2008**	**1864**	**1793**
	%	%	%	%	%	%	%	%	%
	n	n	n	n	n	n	n	n	n
No resistance detected	66.2%	68.4%	72.9%	74.1%	74.4%	72.3%	79.0%	77.7%	79.6%
	876	890	1064	1109	1024	1026	1586	1449	1427
Resistance ≥1CLSI subclass*	33.8%	31.6%	27.1%	25.9%	25.6%	27.7%	21.0%	22.3%	20.4%
	448	411	396	388	353	393	422	415	366
Resistance ≥2 CLSI subclasses*	27.0%	24.1%	22.6%	20.4%	20.2%	22.1%	15.8%	17.7%	15.0%
	358	314	330	306	278	314	318	330	269
Resistance ≥3 CLSI subclasses*	18.1%	17.7%	16.7%	15.1%	15.6%	16.8%	12.2%	14.3%	11.7%
	240	230	244	226	215	239	244	266	210
Resistance ≥4 CLSI subclasses*	13.7%	13.7%	13.1%	12.3%	12.9%	14.2%	9.9%	11.6%	9.4%
	181	178	191	184	178	202	199	216	168
Resistance ≥5 CLSI subclasses*	10.0%	9.9%	10.1%	8.7%	9.9%	10.5%	8.3%	9.9%	8.1%
	132	129	147	130	137	149	167	185	146
At least ACSSuT[†]	8.8%	9.5%	8.9%	8.4%	8.9%	10.0%	7.8%	9.3%	7.1%
	116	124	130	126	122	142	156	173	128
At least ACSuTm[‡]	0.8%	0.4%	0.9%	1.0%	1.0%	0.5%	1.0%	1.2%	0.6%
	10	5	13	15	14	7	21	23	10
At least ACSSuTAuCf[§]	0.0%	0.3%	0.3%	1.5%	2.6%	2.5%	3.3%	3.2%	2.3%
	0	4	5	23	36	36	67	60	42
At least MDR-AmpC[¶]	0.0%	0.3%	0.3%	1.5%	2.6%	2.5%	3.3%	3.2%	2.3%
	0	4	5	23	36	36	67	60	42
Resistance to quinolone and cephalosporin (3rd generation)	0.0%	0.2%	0.1%	0.1%	0.3%	0.3%	0.2%	0.2%	0.4%
	0	2	1	1	4	4	5	4	7

*CLSI: Clinical and Laboratory Standards Institute

[†]ACSSuT: resistance to ampicillin, chloramphenicol, streptomycin, sulfamethoxazole/sulfisoxazole, tetracycline

[‡]ACSuTm: resistance to ampicillin, chloramphenicol, trimethoprim-sulfamethoxazole

[§]ACSSuTAuCf: resistance to ACSSuT + amoxicillin-clavulanic acid, ceftiofur

[¶]MDR-AmpC: resistance to ACSSuTAuCf + decreased susceptibility to ceftriaxone (MIC ≥2 µg/mL)

Table 1.4: Twenty most common non-Typhi *Salmonella* serotypes in NARMS and the Public Health Laboratory Information System, 2004

NARMS			
		Isolates	
Rank	**Serotype**	**N**	**(%)**
1	Typhimurium	382	(21.3%)
2	Enteritidis	271	(15.1%)
3	Newport	190	(10.6%)
4	Javiana	106	(5.9%)
5	Heidelberg	93	(5.2%)
6	Montevideo	50	(2.8%)
7	I 4,[5],12:i:- (monophasic Typhimurium)	36	(2.0%)
8	Braenderup	33	(1.8%)
9	Oranienburg	32	(1.8%)
10	Muenchen	32	(1.8%)
11	Saintpaul	32	(1.8%)
12	Paratyphi B var. L(+) tartrate+	30	(1.7%)
13	Infantis	29	(1.6%)
14	Thompson	26	(1.5%)
15	Mississippi	24	(1.3%)
16	Agona	24	(1.3%)
17	Hartford	18	(1.0%)
18	Anatum	16	(0.9%)
19	Berta	14	(0.8%)
20	Mbandaka	14	(0.8%)
	Subtotal	**1452**	**(81.0%)**
	All Other serotypes	266	(14.8%)
	Unknown serotype	16	(0.9%)
	Partially serotyped	23	(1.3%)
	Rough/Nonmotile isolates	36	(2.0%)
	Subtotal	**341**	**(19.0%)**
	Grand Total	**1793**	**(100.0%)**

PHLIS			
		Isolates	
Rank	**Serotype**	**N**	**(%)**
1	Typhimurium	6855	(19.4%)
2	Enteritidis	5028	(14.2%)
3	Newport	3329	(9.4%)
4	Javiana	1776	(5.0%)
5	Heidelberg	1758	(5.0%)
6	Montevideo	874	(2.5%)
7	I 4,[5],12:i:- (monophasic Typhimurium)	739	(2.1%)
8	Muenchen	739	(2.1%)
9	Saintpaul	695	(2.0%)
10	Braenderup	684	(1.9%)
11	Infantis	588	(1.7%)
12	Mississippi	558	(1.6%)
13	Oranienburg	495	(1.4%)
14	Thompson	494	(1.4%)
15	Berta	409	(1.2%)
16	Agona	407	(1.2%)
17	Paratyphi B var. L(+) tartrate+	354	(1.0%)
18	Hadar	277	(0.8%)
19	Anatum	250	(0.7%)
20	Paratyphi B	239	(0.7%)
	Subtotal	**26548**	**(75.1%)**
	All Other serotypes	5423	(15.3%)
	Unknown serotype	1999	(5.7%)
	Partially serotyped	1324	(3.7%)
	Rough/Nonmotile isolates	61	(0.2%)
	Subtotal	**8807**	**(24.9%)**
	Grand Total	**35355**	**(100.0%)**

A. *Salmonella* Typhimurium

In 2004, Typhimurium was the most common *Salmonella* serotype in NARMS, accounting for 21.3% (382/1793) of non-Typhi *Salmonella* isolates (Table 1.5). Of the 382 *Salmonella* Typhimurium isolates tested, resistance was highest to sulfisoxazole (35.9%), ampicillin (31.9%), streptomycin (31.7%), tetracycline (30.1%), and chloramphenicol (24.1%). The prevalence of resistance among clinically important antimicrobial subclasses was 0.5% for quinolones (represented by nalidixic acid) and 4.5% for third-generation cephalosporins (represented by ceftiofur).

The most dramatic increase over time occurred with ceftiofur resistance—from no resistance in 1996 to 4.5% in 2004 (Table 1.6). Resistance to many of the other antimicrobial agents decreased since 1996 (Table 1.6). Resistance to tetracycline decreased from 49.3% in 1996 to 30.1% in 2004; ampicillin, from 50.0% to 31.9%; streptomycin, from 51.6% to 31.7%; chloramphenicol, from 39.9% to 24.1%; and gentamicin, from 4.2% to 2.1%.

Of the 382 *Salmonella* Typhimurium isolates tested during 2004, 60.7% (232) had no detected resistance, a slight increase from the 55.3% of isolates in 2003 (Table 1.7). In 2004, 37.2% (142/382) were resistant to two or more CLSI subclasses, compared with 40.9% in 2003. Similarly, in 2004, 24.3% (93/382) were resistant to at least five subclasses, compared with 27.5% in 2003.

In 2004, the most common multidrug-resistant phenotype among *Salmonella* Typhimurium was R-Type ACSSuT (23.3% of isolates). For *Salmonella* Typhimurium, R-Type ACSSuT commonly is associated with definitive phage type 104. Since 1996, the prevalence of R-Type ACSSuT among *Salmonella* Typhimurium decreased from 33.7% to 23.3%. In the logistic regression model, this decrease was statistically significant (OR=0.6, 95% CI [0.4, 0.8]).

One (0.3%) serotype Typhimurium isolate was resistant to both quinolones and third-generation cephalosporins in 2004. Since 1996, six *Salmonella* Typhimurium isolates have shown this multidrug resistance pattern.

Table 1.5: Minimum inhibitory concentrations (MICs) and resistance of *Salmonella* Typhimurium isolates to antimicrobial agents, 2004 (N=382)

Antibiotic		% of isolates			Percent of all isolates with MIC (µg/mL)§														
		%I*	%R†	[95% CI]‡	0.015	0.03	0.06	0.125	0.25	0.50	1	2	4	8	16	32	64	128	256	512
Aminoglycosides	Amikacin	0.0	0.0	[0.0–1.0]						1.8	74.3	21.7	2.1							
	Gentamicin	0.0	2.1	[0.9–4.1]					64.1	32.5	1.0	0.3			0.5	1.6				
	Kanamycin	0.0	5.8	[3.6–8.6]										93.7	0.5		0.3	5.5		
	Streptomycin	NA	31.7	[27.0–36.6]												68.3	20.4	11.3		
Aminopenicillins	Ampicillin	0.0	31.9	[27.3–36.9]							43.2	23.3	1.6				31.9			
β-lactamase inhibitor	Amoxicillin-clavulanic acid	21.2	4.7	[2.8–7.3]							66.2	2.1		5.8	21.2	0.3	4.5			
Cephalosporins (3rd generation)	Ceftiofur	0.0	4.5	[2.6–7.0]				0.3	1.0	77.2	16.2	0.8			4.5					
	Ceftriaxone	3.4	0.8	[0.2–2.3]					95.5					0.3	2.9	0.5	0.8			
Cephamycins	Cefoxitin	0.3	4.7	[2.8–7.3]						0.3	19.6	66.2	6.5	2.4	0.3	2.6	2.1			
Folate pathway inhibitors	Trimethoprim-sulfamethoxazole	NA	2.6	[1.3–4.8]				63.4	33.5	0.3	0.3			2.6						
Phenicols	Chloramphenicol	0.3	24.1	[19.9–28.7]								1.8	38.2	35.6	0.3		24.1			
Quinolones	Ciprofloxacin	0.0	0.0	[0.0–1.0]	97.9	1.3		0.5	0.3											
	Nalidixic Acid	NA	0.5	[0.1–1.9]							0.5	24.6	72.8	1.3	0.3		0.5			
Sulfonamides	Sulfamethoxazole/Sulfisoxazole	NA	35.9	[31.0–40.9]											11.8	49.2	2.9	0.3		35.9
Tetracyclines	Tetracycline	0.0	30.1	[25.5–35.0]									69.9		5.2	15.2	9.7			

*Percent of isolates with intermediate susceptibility, NA if no MIC range of intermediate susceptibility exists

†Percent of isolates that were resistant

‡95% confidence intervals (CI) for percent resistant (%R) were calculated using the Clopper-Pearson exact method

§The unshaded areas indicate the dilution range of the Sensititre plates used to test isolates. Single vertical bars indicate the breakpoints for susceptibility, while double vertical bars indicate breakpoints for resistance. Numbers in the shaded areas indicate the percentages of isolates with MICs greater than the highest concentrations on the Sensititre plate. Numbers listed for the lowest tested concentrations represent the precentages of isolates with MICs equal to or less than the lowest tested concentration. CLSI breakpoints were used when available.

Table 1.6: Percentage and number of *Salmonella* Typhimurium isolates resistant to antimicrobial agents, 1996–2004

Year		1996	1997	1998	1999	2000	2001	2002	2003	2004
Total Isolates		306	328	377	362	303	325	393	403	382
Subclass	Antibiotic (Resistance breakpoint)									
Aminoglycosides	Amikacin (MIC ≥ 64)	Not Tested	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0
	Gentamicin (MIC ≥ 16)	4.2% 13	4.6% 15	3.7% 14	2.2% 8	2.6% 8	1.5% 5	2.3% 9	2.0% 8	2.1% 8
	Kanamycin (MIC ≥ 64)	14.4% 44	15.5% 51	15.9% 60	13.0% 47	13.2% 40	8.3% 27	7.6% 30	7.2% 29	5.8% 22
	Streptomycin (MIC ≥ 64)	51.6% 158	55.2% 181	47.2% 178	43.1% 156	39.3% 119	40.0% 130	31.8% 125	35.0% 141	31.7% 121
Aminopenicillins	Ampicillin (MIC ≥ 32)	50.0% 153	50.3% 165	45.1% 170	41.2% 149	41.9% 127	42.5% 138	33.6% 132	35.5% 143	31.9% 122
β-lactamase inhibitor combinations	Amoxicillin-clavulanic acid (MIC ≥ 32)	2.6% 8	3.4% 11	4.5% 17	2.8% 10	6.3% 19	6.2% 20	7.6% 30	5.2% 21	4.7% 18
Cephalosporin (1st generation)	Cephalothin (MIC ≥ 32)	2.0% 6	4.3% 14	4.0% 15	4.4% 16	4.3% 13	3.1% 10	5.6% 22	6.0% 24	Not Tested
Cephalosporins (3rd generation)	Ceftiofur (MIC ≥ 8)	0.0% 0	1.5% 5	1.9% 7	1.9% 7	3.6% 11	3.1% 10	4.3% 17	4.7% 19	4.5% 17
	Ceftriaxone (MIC ≥ 64)	0.0% 0	0.3% 1	0.0% 0	0.3% 1	0.0% 0	0.0% 0	0.3% 1	0.2% 1	0.8% 3
Cephamycins	Cefoxitin (MIC ≥ 32)	Not Tested	Not Tested	Not Tested	Not Tested	3.6% 11	3.1% 10	4.3% 17	4.2% 17	4.7% 18
Folate pathway inhibitors	Trimethoprim-sulfamethoxazole (MIC ≥ 4)	4.6% 14	3.0% 10	4.5% 17	2.8% 10	3.6% 11	2.5% 8	2.3% 9	3.5% 14	2.6% 10
Phenicols	Chloramphenicol (MIC ≥ 32)	39.9% 122	36.0% 118	33.4% 126	28.7% 104	30.7% 93	31.7% 103	23.2% 91	27.5% 111	24.1% 92
Quinolones	Ciprofloxacin (MIC ≥ 4)	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.3% 1	0.0% 0	0.0% 0	0.0% 0
	Nalidixic Acid (MIC ≥ 32)	0.3% 1	0.9% 3	0.5% 2	0.0% 0	1.3% 4	0.6% 2	1.3% 5	1.2% 5	0.5% 2
Sulfonamides	Sulfamethoxazole/Sulfisoxazole* (MIC ≥ 512)	53.3% 163	56.7% 186	49.6% 187	45.6% 165	45.2% 137	43.1% 140	32.1% 126	38.2% 154	35.9% 137
Tetracyclines	Tetracycline (MIC ≥ 16)	49.3% 151	52.4% 172	45.9% 173	41.7% 151	43.2% 131	43.4% 141	31.8% 125	37.7% 152	30.1% 115

*Sulfamethoxazole, which was tested during 1996-2003 to represent sulfonamides, was replaced by sulfisoxazole in 2004.

Table 1.7: Resistance patterns of *Salmonella* Typhimurium isolates, 1996–2004

Year	1996	1997	1998	1999	2000	2001	2002	2003	2004
Total Isolates	306	328	377	362	303	325	393	403	382
	% n	% n	% n	% n	% n	% n	% n	% n	% n
No resistance detected	37.9% 116	39.0% 128	46.9% 177	50.6% 183	49.5% 150	49.2% 160	60.3% 237	55.3% 223	60.7% 232
Resistance ≥1CLSI subclass*	62.1% 190	61.0% 200	53.1% 200	49.4% 179	50.5% 153	50.8% 165	39.7% 156	44.7% 180	39.3% 150
Resistance ≥2 CLSI subclasses*	56.2% 172	56.7% 186	50.9% 192	46.1% 167	46.9% 142	48.0% 156	36.1% 142	40.9% 165	37.2% 142
Resistance ≥3 CLSI subclasses*	51.0% 156	52.4% 172	47.2% 178	43.1% 156	43.2% 131	41.8% 136	32.3% 127	36.5% 147	31.4% 120
Resistance ≥4 CLSI subclasses*	45.4% 139	47.9% 157	42.7% 161	38.4% 139	39.6% 120	38.2% 124	28.5% 112	31.8% 128	28.0% 107
Resistance ≥5 CLSI subclasses*	35.6% 109	36.0% 118	34.0% 128	27.9% 101	30.4% 92	29.8% 97	23.4% 92	27.5% 111	24.3% 93
At least ACSSuT†	33.7% 103	35.1% 115	31.8% 120	27.6% 100	27.7% 84	29.5% 96	21.4% 84	25.8% 104	23.3% 89
At least ACSuTm‡	2.0% 6	0.6% 2	2.7% 10	2.2% 8	1.7% 5	0.9% 3	2.0% 8	3.2% 13	1.6% 6
At least ACSSuTAuCf§	0.0% 0	1.2% 4	1.1% 4	0.6% 2	2.0% 6	1.2% 4	1.8% 7	2.2% 9	2.6% 10
At least MDR-AmpC¶	0.0% 0	1.2% 4	1.1% 4	0.6% 2	2.0% 6	1.2% 4	1.8% 7	2.2% 9	2.6% 10
Resistance to quinolone and cephalosporin (3rd generation)	0.0% 0	0.3% 1	0.0% 0	0.0% 0	0.3% 1	0.3% 1	0.5% 2	0.0% 0	0.3% 1

*CLSI: Clinical and Laboratory Standards Institute

†ACSSuT: resistance to ampicillin, chloramphenicol, streptomycin, sulfamethoxazole/sulfisoxazole, tetracycline

‡ACSuTm: resistance to ampicillin, chloramphenicol, trimethoprim-sulfamethoxazole

§ACSSuTAuCf: resistance to ACSSuT + amoxicillin-clavulanic acid, ceftiofur

¶MDR-AmpC: resistance to ACSSuTAuCf + decreased susceptibility to ceftriaxone (MIC ≥2 µg/mL)

B. *Salmonella* Enteritidis

In 2004, *Salmonella* Enteritidis was the second most common serotype identified in NARMS, accounting for 15.1% (271/1793) of non-Typhi *Salmonella* isolates (Table 1.8). Among *Salmonella* Enteritidis isolates tested in 2004, resistance was uncommon. The most dramatic increase occurred with nalidixic acid. There was a statistically significant increase in nalidixic acid resistance from 0.9% in 1996 to 6.6% in 2004 (95% CI [2.3, 49.3]) (Table 1.9). *Salmonella* Enteritidis was the most prevalent (38.3%) non-Typhi *Salmonella* serotype that had resistance to nalidixic acid (Table 1.14).

Most (87.1%) of the *Salmonella* Enteritidis isolates tested in 2004 had no detected resistance (Table 1.10). Multidrug resistance was uncommon.

Table 1.8: Minimum inhibitory concentrations (MICs) and resistance of *Salmonella* Enteriditis isolates to antimicrobial agents, 2004 (N=271)

Antibiotic		% of isolates			Percent of all isolates with MIC (µg/mL)§														
		%I*	%R†	[95% CI]‡	0.015	0.03	0.06	0.125	0.25	0.50	1	2	4	8	16	32	64	128	256	512
Aminoglycosides	Amikacin	0.0	0.0	[0.0–1.4]						23.6	64.9	9.2	2.2							
	Gentamicin	0.0	0.4	[0.0–2.0]					85.2	12.9	1.1		0.4			0.4				
	Kanamycin	0.0	0.7	[0.1–2.6]										99.3				0.7		
	Streptomycin	NA	2.2	[0.8–4.8]												97.8	1.5	0.7		
Aminopenicillins	Ampicillin	0.0	4.1	[2.0–7.1]							57.2	38.4	0.4			0.4	3.7			
β-lactamase inhibitor	Amoxicillin-clavulanic acid	1.5	0.0	[0.0–1.4]							91.9	4.4	0.7	1.5	1.5					
Cephalosporins (3rd generation)	Ceftiofur	0.4	0.0	[0.0–1.4]				1.1	0.7	66.1	31.7		0.4							
	Ceftriaxone	0.0	0.0	[0.0–1.4]					99.6	0.4										
Cephamycins	Cefoxitin	0.0	0.0	[0.0–1.4]						0.4	23.2	69.4	5.9	1.1						
Folate pathway inhibitors	Trimethoprim-sulfamethoxazole	NA	0.0	[0.0–1.4]				81.2	18.1	0.7										
Phenicols	Chloramphenicol	0.4	0.4	[0.0–2.0]								1.8	51.3	46.1	0.4		0.4			
Quinolones	Ciprofloxacin	0.4	0.0	[0.0–1.4]	93.0	0.4		3.3	3.0			0.4								
	Nalidixic Acid	NA	6.6	[4.0–10.3]						0.4	0.4	11.1	80.4	1.1		0.4	6.3			
Sulfonamides	Sulfamethoxazole/Sulfisoxazole	NA	1.8	[0.6–4.3]											15.9	77.1	4.8	0.4		1.8
Tetracyclines	Tetracycline	1.1	3.3	[1.5–6.2]									95.6	1.1	0.4		3.0			

*Percent of isolates with intermediate susceptibility, NA if no MIC range of intermediate susceptibility exists

†Percent of isolates that were resistant

‡95% confidence intervals (CI) for percent resistant (%R) were calculated using the Clopper-Pearson exact method

§The unshaded areas indicate the dilution range of the Sensititre plates used to test isolates. Single vertical bars indicate the breakpoints for susceptibility, while double vertical bars indicate breakpoints for resistance. Numbers in the shaded areas indicate the percentages of isolates with MICs greater than the highest concentrations on the Sensititre plate. Numbers listed for the lowest tested concentrations represent the precentages of isolates with MICs equal to or less than the lowest tested concentration. CLSI breakpoints were used when available.

Table 1.9: Percentage and number of *Salmonella* Enteritidis isolates resistant to antimicrobial agents, 1996–2004

Year		1996	1997	1998	1999	2000	2001	2002	2003	2004
Total Isolates		351	301	244	269	319	276	337	257	271
Subclass	Antibiotic (Resistance breakpoint)									
Aminoglycosides	Amikacin (MIC ≥ 64)	Not Tested	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0
	Gentamicin (MIC ≥ 16)	4.8% 17	0.3% 1	0.4% 1	0.0% 0	0.3% 1	0.0% 0	0.3% 1	0.4% 1	0.4% 1
	Kanamycin (MIC ≥ 64)	0.0% 0	0.7% 2	0.4% 1	0.4% 1	0.3% 1	0.7% 2	0.3% 1	0.0% 0	0.7% 2
	Streptomycin (MIC ≥ 64)	2.0% 7	4.3% 13	1.6% 4	2.2% 6	0.0% 0	1.4% 4	1.8% 6	1.2% 3	2.2% 6
Aminopenicillins	Ampicillin (MIC ≥ 32)	20.5% 72	11.3% 34	6.1% 15	10.8% 29	7.5% 24	8.7% 24	7.1% 24	2.3% 6	4.1% 11
β-lactamase inhibitor combinations	Amoxicillin-clavulanic acid (MIC ≥ 32)	0.6% 2	0.0% 0	0.0% 0	0.4% 1	0.0% 0	1.4% 4	0.6% 2	0.0% 0	0.0% 0
Cephalosporin (1st generation)	Cephalothin (MIC ≥ 32)	4.0% 14	1.3% 4	0.0% 0	1.9% 5	0.9% 3	1.1% 3	0.6% 2	1.2% 3	Not Tested
Cephalosporins (3rd generation)	Ceftiofur (MIC ≥ 8)	0.0% 0	0.3% 1	0.0% 0	0.4% 1	0.0% 0	2.2% 6	0.0% 0	0.0% 0	0.0% 0
	Ceftriaxone (MIC ≥ 64)	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0
Cephamycins	Cefoxitin (MIC ≥ 32)	Not Tested	Not Tested	Not Tested	Not Tested	0.0% 0	0.4% 1	0.0% 0	0.0% 0	0.0% 0
Folate pathway inhibitors	Trimethoprim-sulfamethoxazole (MIC ≥ 4)	6.6% 23	1.3% 4	0.8% 2	0.7% 2	0.0% 0	0.7% 2	0.6% 2	0.8% 2	0.0% 0
Phenicols	Chloramphenicol (MIC ≥ 32)	0.0% 0	0.7% 2	0.0% 0	0.4% 1	0.0% 0	0.0% 0	0.6% 2	0.4% 1	0.4% 1
Quinolones	Ciprofloxacin (MIC ≥ 4)	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0
	Nalidixic Acid (MIC ≥ 32)	0.9% 3	1.7% 5	2.0% 5	2.2% 6	2.2% 7	4.3% 12	3.9% 13	4.7% 12	6.6% 18
Sulfonamides	Sulfamethoxazole/Sulfisoxazole* (MIC ≥ 512)	8.5% 30	9.0% 27	2.0% 5	3.0% 8	0.9% 3	2.2% 6	1.8% 6	1.2% 3	1.8% 5
Tetracyclines	Tetracycline (MIC ≥ 16)	16.8% 59	9.6% 29	6.6% 16	8.2% 22	1.9% 6	1.8% 5	4.5% 15	1.6% 4	3.3% 9

*Sulfamethoxazole, which was tested during 1996-2003 to represent sulfonamides, was replaced by sulfisoxazole in 2004.

Table 1.10: Resistance patterns of *Salmonella* Enteritidis isolates, 1996–2004

Year	1996	1997	1998	1999	2000	2001	2002	2003	2004
Total Isolates	351	301	244	269	319	276	337	257	271
	% n	% n	% n	% n	% n	% n	% n	% n	% n
No resistance detected	73.5% 258	77.4% 233	87.7% 214	83.6% 225	89.0% 284	86.6% 239	87.2% 294	91.8% 236	87.1% 236
Resistance ≥1CLSI subclass*	26.5% 93	22.6% 68	12.3% 30	16.4% 44	11.0% 35	13.4% 37	12.8% 43	8.2% 21	12.9% 35
Resistance ≥2 CLSI subclasses*	19.1% 67	9.6% 29	6.6% 16	8.6% 23	1.9% 6	4.7% 13	4.2% 14	2.3% 6	3.0% 8
Resistance ≥3 CLSI subclasses*	8.0% 28	3.0% 9	0.8% 2	1.1% 3	0.3% 1	2.9% 8	2.4% 8	0.8% 2	1.1% 3
Resistance ≥4 CLSI subclasses*	4.6% 16	1.3% 4	0.0% 0	0.7% 2	0.0% 0	1.8% 5	1.5% 5	0.4% 1	0.7% 2
Resistance ≥5 CLSI subclasses*	1.7% 6	0.7% 2	0.0% 0	0.4% 1	0.0% 0	0.0% 0	0.3% 1	0.4% 1	0.7% 2
At least ACSSuT†	0.0% 0	0.3% 1	0.0% 0	0.4% 1	0.0% 0	0.0% 0	0.3% 1	0.4% 1	0.4% 1
At least ACSuTm‡	0.0% 0	0.3% 1	0.0% 0	0.4% 1	0.0% 0	0.0% 0	0.0% 0	0.4% 1	0.0% 0
At least ACSSuTAuCf§	0.0% 0	0.0% 0	0.0% 0	0.4% 1	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0
At least MDR-AmpC¶	0.0% 0	0.0% 0	0.0% 0	0.4% 1	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0
Resistance to quinolone and cephalosporin (3rd generation)	0.0% 0	0.3% 1	0.0% 0	0.0% 0	0.3% 1	0.0% 0	0.0% 0	0.4% 1	0.0% 0

*CLSI: Clinical and Laboratory Standards Institute

†ACSSuT: resistance to ampicillin, chloramphenicol, streptomycin, sulfamethoxazole/sulfisoxazole, tetracycline

‡ACSuTm: resistance to ampicillin, chloramphenicol, trimethoprim-sulfamethoxazole

§ACSSuTAuCf: resistance to ACSSuT + amoxicillin-clavulanic acid, ceftiofur

¶MDR-AmpC: resistance to ACSSuTAuCf + decreased susceptibility to ceftriaxone (MIC ≥2 µg/mL)

C. *Salmonella* Newport

In 2004, Newport was the third most commonly isolated *Salmonella* serotype in NARMS, accounting for 10.5% (189/1793) of non-Typhi *Salmonella* isolates (Table 1.11). Of the 190 *Salmonella* Newport isolates, resistance was highest to sulfisoxazole (16.8%), tetracycline (16.8%), ampicillin (15.8%), streptomycin (15.8%), amoxicillin-clavulanic acid (15.3%), ceftiofur (15.3%), cefoxitin (15.3%), and chloramphenicol (15.3%). The prevalence of resistance among clinically important antimicrobial subclasses was 0.5% for quinolones (represented by nalidixic acid) and 15.3% for third-generation cephalosporins (represented by ceftiofur).

Ceftiofur resistance was first noted in one isolate (1.3%) in 1998; it increased to 18.2% in 1999, peaked at 27.4% in 2001, and declined to 15.3% in 2004 (Table 1.12). *Salmonella* Newport was the most prevalent (47.5%) non-Typhi *Salmonella* serotype that had resistance to ceftiofur (Table 1.14).

In contrast to other common serotypes, the percentage of *Salmonella* Newport isolates with no detected resistance declined from 86.3% in 1996 and 74.2% in 2003 (Table 1.13). However, the percentage of *Salmonella* Newport isolates with no detected resistance was higher in 2004 (82.1%) than in 2003 (73.9%). In addition, resistance to at least five subclasses of antimicrobial agents increased from 5.9% in 1996 to 14.7% in 2004, but decreased from the peak in 2001, similar to the trend in ceftiofur resistance.

In 2004, the most common multidrug-resistant phenotype among serotype Newport isolates was MDR-AmpC; (14.7% of isolates). This phenotype has increased since 1996, similar to the trend in ceftiofur resistance (Table 1.13). In the logistic regression model, the increase in MDR-AmpC from 1996 to 2004 was statistically significant (95% CI [3.4, infinity]).

Table 1.11: Minimum inhibitory concentrations (MICs) and resistance of *Salmonella* Newport itsolates to antimicrobial agents, 2004 (N=190)

Antibiotic		% of isolates			Percent of all isolates with MIC (µg/mL)[§]														
		%I[*]	%R[†]	[95% CI][‡]	0.015	0.03	0.06	0.125	0.25	0.50	1	2	4	8	16	32	64	128	256	512
Aminoglycosides	Amikacin	0.0	0.0	[0.0–1.9]						6.8	72.1	17.9	2.6	0.5						
	Gentamicin	0.0	0.5	[0.0–2.9]					78.4	19.5	1.6					0.5				
	Kanamycin	0.0	2.6	[0.9–6.0]										97.4				2.6		
	Streptomycin	NA	15.8	[10.9–21.8]												84.2		15.8		
Aminopenicillins	Ampicillin	0.0	15.8	[10.9–21.8]							57.4	25.8	1.1				15.8			
β-lactamase inhibitor	Amoxicillin-clavulanic acid	0.0	15.3	[10.5–21.2]							81.1	2.1	0.5	1.1		3.7	11.6			
Cephalosporins (3rd generation)	Ceftiofur	0.0	15.3	[10.5–21.2]				0.5	0.5	73.7	10.0			0.5	14.7					
	Ceftriaxone	12.1	2.6	[0.9–6.0]					84.2	1.1					4.7	7.4	2.1	0.5		
Cephamycins	Cefoxitin	0.0	15.3	[10.5–21.2]							23.7	55.8	3.7	1.6		3.2	12.1			
Folate pathway inhibitors	Trimethoprim-sulfamethoxazole	NA	2.1	[0.6–5.3]				73.2	23.2	0.5	0.5	0.5		2.1						
Phenicols	Chloramphenicol	0.0	15.3	[10.5–21.2]								2.1	54.7	27.9			15.3			
Quinolones	Ciprofloxacin	0.0	0.0	[0.0–1.9]	98.4	1.1		0.5												
	Nalidixic Acid	NA	0.5	[0.0–2.9]							1.1	34.7	62.1	1.6			0.5			
Sulfonamides	Sulfamethoxazole/Sulfisoxazole	NA	16.8	[11.8–22.9]											5.8	42.1	34.7	0.5		16.8
Tetracyclines	Tetracycline	0.0	16.8	[11.8–22.9]									83.2			4.2	12.6			

[*]Percent of isolates with intermediate susceptibility, NA if no MIC range of intermediate susceptibility exists

[†]Percent of isolates that were resistant

[‡]95% confidence intervals (CI) for percent resistant (%R) were calculated using the Clopper-Pearson exact method

§The unshaded areas indicate the dilution range of the Sensititre plates used to test isolates. Single vertical bars indicate the breakpoints for susceptibility, while double vertical bars indicate breakpoints for resistance. Numbers in the shaded areas indicate the percentages of isolates with MICs greater than the highest concentrations on the Sensititre plate. Numbers listed for the lowest tested concentrations represent the precentages of isolates with MICs equal to or less than the lowest tested concentration. CLSI breakpoints were used when available.

Table 1.12: Percentage and number of *Salmonella* Newport isolates resistant to antimicrobial agents, 1996–2004

Year		1996	1997	1998	1999	2000	2001	2002	2003	2004
Total Isolates		51	46	77	99	121	124	239	221	190
Subclass	Antibiotic (Resistance breakpoint)									
Aminoglycosides	Amikacin (MIC ≥ 64)	Not Tested	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0
	Gentamicin (MIC ≥ 16)	5.9% 3	4.3% 2	0.0% 0	0.0% 0	2.5% 3	3.2% 4	3.3% 8	3.2% 7	0.5% 1
	Kanamycin (MIC ≥ 64)	2.0% 1	0.0% 0	1.3% 1	1.0% 1	5.0% 6	7.3% 9	9.6% 23	4.5% 10	2.6% 5
	Streptomycin (MIC ≥ 64)	7.8% 4	4.3% 2	2.6% 2	19.2% 19	24.0% 29	31.5% 39	24.7% 59	23.5% 52	15.8% 30
Aminopenicillins	Ampicillin (MIC ≥ 32)	5.9% 3	6.5% 3	2.6% 2	18.2% 18	23.1% 28	29.8% 37	24.3% 58	22.2% 49	15.8% 30
β-lactamase inhibitor combinations	Amoxicillin-clavulanic acid (MIC ≥ 32)	2.0% 1	0.0% 0	2.6% 2	18.2% 18	22.3% 27	26.6% 33	22.2% 53	21.3% 47	15.3% 29
Cephalosporin (1st generation)	Cephalothin (MIC ≥ 32)	3.9% 2	4.3% 2	2.6% 2	18.2% 18	22.3% 27	26.6% 33	22.2% 53	21.7% 48	Not Tested
Cephalosporins (3rd generation)	Ceftiofur (MIC ≥ 8)	0.0% 0	0.0% 0	1.3% 1	18.2% 18	22.3% 27	27.4% 34	22.2% 53	21.7% 48	15.3% 29
	Ceftriaxone (MIC ≥ 64)	0.0% 0	0.0% 0	0.0% 0	3.0% 3	0.0% 0	0.0% 0	0.8% 2	1.8% 4	2.6% 5
Cephamycins	Cefoxitin (MIC ≥ 32)	Not Tested	Not Tested	Not Tested	Not Tested	22.3% 27	25.8% 32	22.2% 53	21.3% 47	15.3% 29
Folate pathway inhibitors	Trimethoprim-sulfamethoxazole (MIC ≥ 4)	3.9% 2	4.3% 2	1.3% 1	2.0% 2	4.1% 5	1.6% 2	4.2% 10	0.9% 2	2.1% 4
Phenicols	Chloramphenicol (MIC ≥ 32)	5.9% 3	4.3% 2	2.6% 2	18.2% 18	23.1% 28	28.2% 35	24.7% 59	21.7% 48	15.3% 29
Quinolones	Ciprofloxacin (MIC ≥ 4)	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0
	Nalidixic Acid (MIC ≥ 32)	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.8% 1	0.0% 0	0.8% 2	0.0% 0	0.5% 1
Sulfonamides	Sulfamethoxazole/Sulfisoxazole* (MIC ≥ 512)	11.8% 6	4.3% 2	3.9% 3	22.2% 22	23.1% 28	32.3% 40	25.1% 60	24.0% 53	16.8% 32
Tetracyclines	Tetracycline (MIC ≥ 16)	7.8% 4	4.3% 2	2.6% 2	19.2% 19	23.1% 28	30.6% 38	25.1% 60	23.5% 52	16.8% 32

*Sulfamethoxazole, which was tested during 1996-2003 to represent sulfonamides, was replaced by sulfisoxazole in 2004.

Table 1.13: Resistance patterns of *Salmonella* Newport isolates, 1996–2004

Year	1996	1997	1998	1999	2000	2001	2002	2003	2004
Total Isolates	51	46	77	99	121	124	239	221	190
	% n	% n	% n	% n	% n	% n	% n	% n	% n
No resistance detected	86.3% 44	93.5% 43	94.8% 73	75.8% 75	75.2% 91	65.3% 81	72.8% 174	74.2% 164	82.1% 156
Resistance ≥1CLSI subclass*	13.7% 7	6.5% 3	5.2% 4	24.2% 24	24.8% 30	34.7% 43	27.2% 65	25.8% 57	17.9% 34
Resistance ≥2 CLSI subclasses*	7.8% 4	4.3% 2	2.6% 2	18.2% 18	23.1% 28	32.3% 40	25.1% 60	24.4% 54	17.4% 33
Resistance ≥3 CLSI subclasses*	5.9% 3	4.3% 2	2.6% 2	18.2% 18	23.1% 28	31.5% 39	24.7% 59	22.6% 50	16.8% 32
Resistance ≥4 CLSI subclasses*	5.9% 3	4.3% 2	2.6% 2	18.2% 18	23.1% 28	31.5% 39	24.7% 59	22.2% 49	15.8% 30
Resistance ≥5 CLSI subclasses*	5.9% 3	4.3% 2	2.6% 2	18.2% 18	23.1% 28	27.4% 34	23.0% 55	21.7% 48	14.7% 28
At least ACSSuT†	5.9% 3	4.3% 2	1.3% 1	18.2% 18	23.1% 28	25.8% 32	23.0% 55	21.3% 47	14.7% 28
At least ACSuTm‡	3.9% 2	4.3% 2	1.3% 1	2.0% 2	4.1% 5	0.8% 1	3.8% 9	0.9% 2	1.1% 2
At least ACSSuTAuCf§	0.0% 0	0.0% 0	1.3% 1	18.2% 18	22.3% 27	25.0% 31	22.2% 53	20.8% 46	14.7% 28
At least MDR-AmpC¶	0.0% 0	0.0% 0	1.3% 1	18.2% 18	22.3% 27	25.0% 31	22.2% 53	20.8% 46	14.7% 28
Resistance to quinolone and cephalosporin (3rd generation)	0.0% 0	0.0% 0	1.3% 1	0.0% 0	0.0% 0	0.0% 0	0.4% 1	0.0% 0	0.5% 1

*CLSI: Clinical and Laboratory Standards Institute

†ACSSuT: resistance to ampicillin, chloramphenicol, streptomycin, sulfamethoxazole/sulfisoxazole, tetracycline

‡ACSuTm: resistance to ampicillin, chloramphenicol, trimethoprim-sulfamethoxazole

§ACSSuTAuCf: resistance to ACSSuT + amoxicillin-clavulanic acid, ceftiofur

¶MDR-AmpC: resistance to ACSSuTAuCf + decreased susceptibility to ceftriaxone (MIC ≥2 µg/mL)

D. Specific Phenotypes

The multidrug-resistant phenotypes ACSSuT and MDR-AmpC, and resistance to nalidixic acid and ceftiofur, were detected in several other serotypes in 2004 (Table 1.14).

In 2004, 128 non-Typhi *Salmonella* isolates were resistant to at least ACSSuT. Of these isolates, 69.5% were serotype Typhimurium, 21.9% Newport, and 0.8% each Agona, Anatum, Enteritidis, Heidelberg, and "monophasic Typhimurium."

Forty-two non-Typhi *Salmonella* isolates were at least MDR-AmpC. Of these isolates, 66.7% were serotype Newport, 23.8% Typhimurium, 2.4% Agona, and 2.4% Anatum.

Forty-seven non-Typhi *Salmonella* isolates were nalidixic acid-resistant. Of these isolates, 38.3% were serotype Enteritidis, 4.3% Typhimurium, and 2.1% each Agona, Infantis, Javiana, Montevideo, "monophasic Typhimurium," Newport, and Saintpaul.

Sixty-one non-Typhi *Salmonella* isolates were ceftiofur-resistant. Of these isolates, 47.5% were serotype Newport, 27.9% Typhimurium, 14.8% Heidelberg, and 1.6% each Agona, Anatum, and monophasic Typhimurium."

Table 1.14: Number and percentage of ACSSuT-, MDR-AmpC-, nalidixic acid-, and ceftiofur-resistant isolates among the 20 most common non-Typhi *Salmonella* serotypes isolated in NARMS, 2004

			ACSSuT*		MDRAmpC†		Nalidixic Acid		Ceftiofur	
Rank	**Serotype**	**N**	**n**	**(%)**	**n**	**(%)**	**n**	**(%)**	**n**	**(%)**
1	Typhimurium	382	**89**	**(69.5%)**	**10**	**(23.8%)**	**2**	**(4.3%)**	**17**	**(27.9%)**
2	Enteritidis	271	**1**	**(0.8%)**	0	**(0.0%)**	**18**	**(38.3%)**	0	(0.0%)
3	Newport	190	**28**	**(21.9%)**	**28**	**(66.7%)**	**1**	**(2.1%)**	**29**	**(47.5%)**
4	Javiana	106	0	(0.0%)	0	(0.0%)	**1**	**(2.1%)**	0	(0.0%)
5	Heidelberg	93	**1**	**(0.8%)**	0	(0.0%)	0	(0.0%)	**9**	(14.8%)
6	Montevideo	50	0	(0.0%)	0	(0.0%)	**1**	**(2.1%)**	0	(0.0%)
7	I 4,[5],12:i:- (monophasic Typhimurium)	36	**1**	**(0.8%)**	0	(0.0%)	**1**	**(2.1%)**	**1**	**(1.6%)**
8	Braenderup	33	0	(0.0%)	0	(0.0%)	0	(0.0%)	0	(0.0%)
9	Oranienburg	32	0	(0.0%)	0	(0.0%)	0	(0.0%)	0	(0.0%)
10	Muenchen	32	0	(0.0%)	0	(0.0%)	0	(0.0%)	0	(0.0%)
11	Saintpaul	32	0	(0.0%)	0	(0.0%)	**1**	**(2.1%)**	0	(0.0%)
12	Infantis	30	0	(0.0%)	0	(0.0%)	**1**	**(2.1%)**	0	(0.0%)
13	Paratyphi B var. L(+) tartrate+	29	0	(0.0%)	0	(0.0%)	0	(0.0%)	0	(0.0%)
14	Thompson	26	0	(0.0%)	0	(0.0%)	0	(0.0%)	0	(0.0%)
15	Mississippi	24	0	(0.0%)	0	(0.0%)	0	(0.0%)	0	(0.0%)
16	Agona	24	**1**	**(0.8%)**	**1**	**(2.4%)**	**1**	**(2.1%)**	**1**	**(1.6%)**
17	Hartford	18	0	(0.0%)	0	(0.0%)	0	(0.0%)	0	(0.0%)
18	Anatum	16	**1**	(0.8%)	**1**	**(2.4%)**	0	(0.0%)	**1**	**(1.6%)**
19	Berta	14	0	(0.0%)	0	(0.0%)	0	(0.0%)	0	(0.0%)
20	Mbandaka	14	0	(0.0%)	0	(0.0%)	0	(0.0%)	0	(0.0%)
	Subtotal	**1452**	**122**	**(95.3%)**	**40**	**(95.2%)**	**27**	**(57.4%)**	**58**	**(95.1%)**
	All Other Serotypes	341	6	(4.7%)	2	(4.8%)	20	(42.6%)	3	(4.9%)
	Total	**1793**	**128**	**(100.0%)**	**42**	**(100.0%)**	**47**	**(100.0%)**	**61**	**(100.0%)**

*ACSSuT: resistance to ampicillin, chloramphenicol, streptomycin, sulfamethoxazole/sulfisoxazole, tetracycline
† MDR-AmpC: resistance to ACSSuT + amoxicillin-clavulanic acid, ceftiofur + decreased susceptibility to ceftriaxone (MIC ≥2µg/mL)

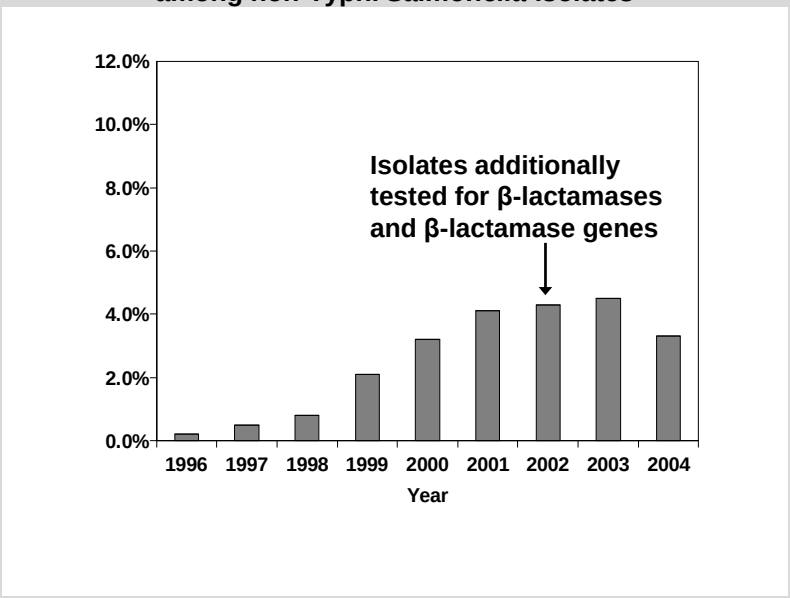
Molecular Characterization of β-Lactamase Resistance Genes among NARMS *Salmonella* and *Shigella* Isolates, 2002

Extended-spectrum cephalosporins are important for treating persons with severe *Salmonella* infections [Hohmann EL. Nontyphoidal salmonellosis. Clin Infect Dis 2001;32:263–9]. This drug class is particularly important for pediatric therapy because fluoroquinolones are not approved for use in children. In 2004, 34% (11,976/35,661) of laboratory-confirmed *Salmonella* cases reported to CDC occurred in children <10 years of age [CDC. PHLIS *Salmonella* 2004 Annual Summary. Division of Bacterial and Mycotic Diseases. 2005. Available at http://www.cdc.gov/ncidod/dbmd/phlisdata/salmtab/2004/SalmonellaTable2_2004.pdf]. NARMS conducts surveillance for resistance to two extended-spectrum cephalosporins: ceftriaxone (approved for use in humans) and ceftiofur (approved for use in food animals). The prevalence of resistance to ceftiofur among non-Typhi *Salmonella* isolates tested in NARMS increased from 1996 to 2004 (Figure 1.1).

To facilitate an understanding of this increase in resistance, isolates that exhibited a ceftriaxone minimum inhibitory concentration (MIC) of ≥2 µg/mL or a ceftiofur MIC of ≥2 µg/mL also were tested for extended-spectrum cephalosporin-resistance mechanisms. Of the 2629 non-Typhi *Salmonella* and *Shigella* isolates tested in 2002, 95 (3.6%) isolates, including 94 *Salmonella* and one *Shigella*, met these criteria for additional testing. This included susceptibility testing of additional β-lactams, such as ceftazidime and cefotaxime, and molecular characterization of β-lactamases and β-lactamase genes. Ninety-two percent (87/95) of the isolates exhibited a ceftazidime or cefotaxime MIC that was intermediate or resistant; 76% (72/95) exhibited a ceftazidime or cefotaxime MIC that was resistant.

Isoelectric focusing was performed for β-lactamases and polymerase chain reaction (PCR) for bla_{CMY}, bla_{SHV} and bla_{TEM} genes. Of the 95 isolates, 93 (92 *Salmonella* and one *Shigella*) were positive by isoelectric focusing for one or more β-lactams. Of the 92 *Salmonella* isolates with one or more β-lactams, 53 (58%) were *Salmonella* Newport; 19 (21%) were *Salmonella* Typhimurium; and eight (9%) were *Salmonella* Heidelberg; six (7%) isolates were cultured from blood. Among these 92 isolates, 86 (93%) were positive by PCR for a CMY mechanism, 12 (13%) were positive for a TEM mechanism, and one (1%) was positive for a SHV mechanism. Ten (11%) isolates were positive for both CMY and TEM. The *Shigella* isolate was positive by isoelectric focusing and PCR for a TEM mechanism.

Figure 1.1: Prevalence of resistance to ceftiofur among non-Typhi *Salmonella* isolates



2. *SALMONELLA* TYPHI

In 2004, CDC received 349 *Salmonella* Typhi isolates, of which 341 (97.7%) were viable and tested for antimicrobial susceptibility. Of these 341 isolates, 37 isolates were excluded from the analysis because they were submissions from the same patient, leaving 304 isolates for analysis (Table I). Antimicrobial agents with the highest prevalence of resistance were nalidixic acid (41.8%), trimethoprim-sulfamethoxazole (13.2%), chloramphenicol (13.2%), ampicillin (11.8%), streptomycin (11.8%), and sulfisoxazole (11.8%).

Resistance decreased from 2003 to 2004 to most of the antimicrobial agents tested (Table 2.2). However, nalidixic acid resistance increased from 18.7% in 1999 to 41.8% in 2004; a statistically significant increase (OR=3.1, 95% CI [1.9, 4.9]).

In 1999, 12.0% of *Salmonella* Typhi isolates were resistant to at least ampicillin, chloramphenicol, and trimethoprim-sulfamethoxazole (ACSuTm), which increased to 15.6% in 2003 but declined to 11.8% in 2004 (Table 2.3).

Table 2.1: Minimum inhibitory concentrations (MICs) and resistance of *Salmonella* Typhi isolates to antimicrobial agents, 2004 (N=304)

Antibiotic		% of isolates			Percent of all isolates with MIC (µg/mL)[§]														
		%I[*]	%R[†]	[95% CI][‡]	0.015	0.03	0.06	0.125	0.25	0.50	1	2	4	8	16	32	64	128	256	512
Aminoglycosides	Amikacin	0.0	0.0	[0.0–1.2]						28.0	68.4	3.6								
	Gentamicin	0.0	0.0	[0.0–1.2]					96.1	3.9										
	Kanamycin	0.0	0.0	[0.0–1.2]										100.0						
	Streptomycin	NA	11.8	[8.4–16.0]												88.2	0.3	11.5		
Aminopenicillins	Ampicillin	0.0	11.8	[8.4–16.0]							72.4	15.8					11.8			
β-lactamase inhibitor	Amoxicillin-clavulanic acid	0.3	0.0	[0.0–1.2]							87.5	0.7	3.9	7.6	0.3					
Cephalosporins (3rd generation)	Ceftiofur	0.0	0.0	[0.0–1.2]				2.3	18.8	75.0	3.9									
	Ceftriaxone	0.0	0.0	[0.0–1.2]					100.0											
Cephamycins	Cefoxitin	0.7	0.0	[0.0–1.2]						3.9	45.4	9.9	28.0	12.2	0.7					
Folate pathway inhibitors	Trimethoprim-sulfamethoxazole	NA	13.2	[9.6–17.5]				77.3	9.5					13.2						
Phenicols	Chloramphenicol	0.0	13.2	[9.6–17.5]								3.3	74.3	9.2			13.2			
Quinolones	Ciprofloxacin	0.0	0.0	[0.0–1.2]	53.6	0.3	3.6	15.1	26.0	1.3										
	Nalidixic Acid	NA	41.8	[36.2–47.5]							1.3	50.0	3.6	3.3		1.0	40.8			
Sulfonamides	Sulfamethoxazole/Sulfisoxazole	NA	11.8	[8.4–16.0]											53.6	30.6	3.6	0.3		11.8
Tetracyclines	Tetracycline	0.0	8.9	[5.9–12.7]									91.1				8.9			

[*]Percent of isolates with intermediate susceptibility, NA if no MIC range of intermediate susceptibility exists

[†]Percent of isolates that were resistant

[‡]95% confidence intervals (CI) for percent resistant (%R) were calculated using the Clopper-Pearson exact method

§The unshaded areas indicate the dilution range of the Sensititre plates used to test isolates. Single vertical bars indicate the breakpoints for susceptibility, while double vertical bars indicate breakpoints for resistance. Numbers in the shaded areas indicate the percentages of isolates with MICs greater than the highest concentrations on the Sensititre plate. Numbers listed for the lowest tested concentrations represent the precentages of isolates with MICs equal to or less than the lowest tested concentration. CLSI breakpoints were used when available.

Table 2.2: Percentage and number of *Salmonella* Typhi isolates resistant to antimicrobial agents, 1999–2004

Year Total Isolates		1999 166	2000 177	2001 197	2002 195	2003 334	2004 304
Subclass	Antibiotic (Resistance breakpoint)						
Aminoglycosides	Amikacin (MIC ≥ 64)	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0
	Gentamicin (MIC ≥ 16)	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0
	Kanamycin (MIC ≥ 64)	0.0% 0	0.0% 0	0.5% 1	0.0% 0	0.0% 0	0.0% 0
	Streptomycin (MIC ≥ 64)	13.3% 22	9.0% 16	20.3% 40	7.2% 14	14.4% 48	11.8% 36
Aminopenicillins	Ampicillin (MIC ≥ 32)	12.7% 21	9.0% 16	20.3% 40	5.6% 11	16.2% 54	11.8% 36
β-lactamase inhibitor combinations	Amoxicillin-clavulanic acid (MIC ≥ 32)	0.6% 1	0.0% 0	0.0% 0	0.0% 0	0.3% 1	0.0% 0
Cephalosporin (1st generation)	Cephalothin (MIC ≥ 32)	2.4% 4	1.1% 2	0.5% 1	1.5% 3	0.6% 2	Not Tested
Cephalosporins (3rd generation)	Ceftiofur (MIC ≥ 8)	0.6% 1	0.0% 0	0.0% 0	0.0% 0	0.6% 2	0.0% 0
	Ceftriaxone (MIC ≥ 64)	0.6% 1	0.0% 0	0.0% 0	0.0% 0	0.3% 1	0.0% 0
Cephamycins	Cefoxitin (MIC ≥ 32)	Not Tested	0.6% 1	0.5% 1	0.0% 0	0.9% 3	0.0% 0
Folate pathway inhibitors	Trimethoprim-sulfamethoxazole (MIC ≥ 4)	12.7% 21	9.0% 16	20.8% 41	6.7% 13	16.8% 56	13.2% 40
Phenicols	Chloramphenicol (MIC ≥ 32)	12.0% 20	10.7% 19	20.8% 41	6.2% 12	16.5% 55	13.2% 40
Quinolones	Ciprofloxacin (MIC ≥ 4)	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.3% 1	0.0% 0
	Nalidixic Acid (MIC ≥ 32)	18.7% 31	22.0% 39	29.9% 59	23.6% 46	37.7% 126	41.8% 127
Sulfonamides	Sulfamethoxazole/Sulfisoxazole* (MIC ≥ 512)	16.3% 27	11.3% 20	20.8% 41	6.2% 12	17.1% 57	11.8% 36
Tetracyclines	Tetracycline (MIC ≥ 16)	9.0% 15	9.6% 17	20.8% 41	6.7% 13	15.6% 52	8.9% 27

*Sulfamethoxazole, which was tested during 1999-2003 to represent sulfonamides, was replaced by sulfisoxazole in 2004.

Table 2.3: Resistance patterns of *Salmonella* Typhi isolates, 1999–2004

Year Total Isolates	1999 166	2000 177	2001 197	2002 195	2003 334	2004 304
	% n	% n	% n	% n	% n	% n
No resistance detected	71.7% 119	72.9% 129	59.4% 117	74.4% 145	56.6% 189	56.6% 172
Resistance ≥1CLSI subclass*	28.3% 47	27.1% 48	40.6% 80	25.6% 50	43.4% 145	43.4% 132
Resistance ≥2 CLSI subclasses*	14.5% 24	10.7% 19	22.8% 45	7.2% 14	18.0% 60	13.2% 40
Resistance ≥3 CLSI subclasses*	12.7% 21	9.6% 17	22.8% 45	6.7% 13	17.7% 59	12.8% 39
Resistance ≥4 CLSI subclasses*	12.7% 21	9.0% 16	21.8% 43	6.7% 13	16.8% 56	12.5% 38
Resistance ≥5 CLSI subclasses*	12.0% 20	9.0% 16	18.8% 37	5.6% 11	15.9% 53	11.8% 36
At least ACSSuT[†]	9.0% 15	7.9% 14	16.8% 33	5.6% 11	12.6% 42	7.9% 24
At least ACSuTm[‡]	12.0% 20	9.0% 16	17.8% 35	5.6% 11	15.6% 52	11.8% 36
At least ACSSuTAuCf[§]	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0
At least MDR-AmpC[¶]	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0
Resistance to quinolone and cephalosporin (3rd generation)	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.3% 1	0.0% 0

*CLSI: Clinical and Laboratory Standards Institute

[†]ACSSuT: resistance to ampicillin, chloramphenicol, streptomycin, sulfamethoxazole/sulfisoxazole, tetracycline

[‡]ACSuTm: resistance to ampicillin, chloramphenicol, trimethoprim-sulfamethoxazole

[§]ACSSuTAuCf: resistance to ACSSuT + amoxicillin-clavulanic acid, ceftiofur

[¶]MDR-AmpC: resistance to ACSSuTAuCf + decreased susceptibility to ceftriaxone (MIC ≥2 µg/mL)

3. *SHIGELLA*

In 2004, CDC received 367 *Shigella* isolates, of which 320 (87.2%) were viable and tested for antimicrobial susceptibility. Of these 320 isolates, three submissions from the same patient and two isolates identified as not *Shigella* were excluded, leaving 315 isolates for analysis. (Table I). Of the 315 isolates tested, 241 (76.5%) were *S. sonnei*; 61 (19.4%), *S. flexneri*; nine (2.9%), *S. boydii*; and two (0.6%), *S. dysenteriae* (Table 3.1). Resistance was highest to ampicillin (77.8%), streptomycin (61.0%), sulfisoxazole (52.4%), trimethoprim-sulfamethoxazole (51.4%), and tetracycline (49.2%) (Table 3.2).

Shigella flexneri isolates showed a higher prevalence of resistance to most antimicrobial agents than did *Shigella sonnei* (Tables 3.3 and 3.4). Important differences between the species include the prevalence of tetracycline resistance (95.1% in *S. flexneri*, compared with 36.1% in *S. sonnei*) and chloramphenicol resistance (60.7% in *S. flexneri*, compared with 2.5% in *S. sonnei*).

The percentage of *S. sonnei* isolates resistant to trimethoprim-sulfamethoxazole increased from 38.5% in 2003 to 53.1% in 2004 (Table 3.6), a rate similar to that during 1999–2000 (53.1–54.9%). Ampicillin resistance among *S. sonnei* isolates remained high (79.3%). Tetracycline resistance also increased from 22.1% in 2003 to 36.1% in 2004. One *S. sonnei* isolate was resistant to ceftriaxone; this is the first ceftriaxone-resistant *Shigella* isolate detected since NARMS began testing *Shigella* in 1999.

Resistance of *S. flexneri* isolates to trimethoprim-sulfamethoxazole also apparently increased from the low of 28.8% in 2002 to 45.9% in 2004 (Table 3.7). However, nalidixic acid resistance was 1.6% in 2004, compared with 5.9% in 2003. Resistance to streptomycin and tetracycline was higher in 2004 (72.1% and 95.1%, respectively) than during 1999–2003. In 2004, chloramphenicol resistance among *S. flexneri* isolates was the lowest of the 6-year period (60.7%).

In all years from 1999 to 2004, more than 90% of *Shigella* isolates tested were resistant to at least one CLSI subclass. A total of 40.5% were resistant to at least five subclasses in 1999, compared with 27.6% in 2004 (Table 3.8).

For both *S. sonnei* and *S. flexneri*, resistance to multiple antimicrobial classes and specific combinations changed from 1999 to 2004 (Tables 3.9 and 3.10). One *Shigella* (*S. sonnei*) isolate was resistant to nalidixic acid and ceftiofur. This is the first *S. sonnei* isolate with this phenotype reported in NARMS. The first reported *Shigella* isolate with this phenotype in NARMS was a *S. flexneri* isolated in 2003. The nalidixic acid- and ceftiofur-resistant *S. sonnei* isolate is also the first ceftriaxone-resistant *Shigella* isolate reported in NARMS. Combined resistance to ampicillin and trimethoprim-sulfamethoxazole (ASuTm) was present in more than 40% of isolates from 1999 through 2001, declined to 30.2% in 2002, but increased to 33.6% in 2003 and 39.4% in 2004. Resistance to both agents is clinically relevant, particularly for children for whom treatment with fluoroquinolones in this age group is not recommended.

Table 3.1: Frequency of *Shigella* species isolated in NARMS, 2004

Species	2004	
	N	(%)
Shigella sonnei	241	(76.5%)
Shigella flexneri	61	(19.4%)
Shigella boydii	9	(2.9%)
Shigella dysenteriae	2	(0.6%)
Other	2	(0.6%)
Total	**315**	**(100.0%)**

Table 3.2: Minimum inhibitory concentrations (MICs) and resistance of *Shigella* isolates to antimicrobial agents, 2004 (N=316)

Antibiotic		% of isolates			Percent of all isolates with MIC (µg/mL)[§]														
		%I[*]	%R[†]	[95% CI][‡]	0.015	0.03	0.06	0.125	0.25	0.50	1	2	4	8	16	32	64	128	256	512
Aminoglycosides	Amikacin	0.0	0.0	[0.0–1.2]							4.1	54.9	37.8	2.9	0.3					
	Gentamicin	0.0	0.0	[0.0–1.2]					1.9	44.8	51.7	1.6								
	Kanamycin	0.0	0.0	[0.0–1.2]										100.0						
	Streptomycin	NA	61.0	[55.3–66.4]												39.0	20.3	40.6		
Aminopenicillins	Ampicillin	0.3	77.8	[72.8–82.2]							3.8	9.8	6.0	2.2	0.3	0.6	77.1			
β-lactamase inhibitor	Amoxicillin-clavulanic acid	24.8	1.6	[0.5–3.7]							0.6	3.8	16.8	52.4	24.8	1.0	0.6			
Cephalosporins (3rd generation)	Ceftiofur	0.0	0.3	[0.0–1.8]				34.9	59.7	4.8	0.3				0.3					
	Ceftriaxone	0.0	0.3	[0.0–1.8]					99.4	0.3								0.3		
Cephamycins	Cefoxitin	0.3	0.3	[0.0–1.8]						0.3	10.8	67.0	19.7	1.6	0.3	0.3				
Folate pathway inhibitors	Trimethoprim-sulfamethoxazole	NA	51.4	[45.8–57.1]				32.4	10.2	2.2	1.9	1.9	2.5	48.9						
Phenicols	Chloramphenicol	4.4	14.9	[11.2–19.3]								11.1	63.5	6.0	4.4	2.2	12.7			
Quinolones	Ciprofloxacin	0.0	0.0	[0.0–1.2]	98.1	0.3	0.6	1.0												
	Nalidixic Acid	NA	1.6	[0.5–3.7]						0.3	60.6	35.9	1.6			0.6	1.0			
Sulfonamides	Sulfamethoxazole/Sulfisoxazole	NA	52.4	[46.7–58.0]											44.4	3.2				52.4
Tetracyclines	Tetracycline	0.3	49.2	[43.6–54.9]									50.5	0.3		9.5	39.7			

[*]Percent of isolates with intermediate susceptibility, NA if no MIC range of intermediate susceptibility exists
[†]Percent of isolates that were resistant
[‡]95% confidence intervals (CI) for percent resistant (%R) were calculated using the Clopper-Pearson exact method
§The unshaded areas indicate the dilution range of the Sensititre plates used to test isolates. Single vertical bars indicate the breakpoints for susceptibility, while double vertical bars indicate breakpoints for resistance. Numbers in the shaded areas indicate the percentages of isolates with MICs greater than the highest concentrations on the Sensititre plate. Numbers listed for the lowest tested concentrations represent the precentages of isolates with MICs equal to or less than the lowest tested concentration. CLSI breakpoints were used when available.

Table 3.3: Minimum inhibitory concentrations (MICs) and resistance of *Shigella* sonnei isolates to antimicrobial agents, 2004 (N=241)

Antibiotic		% of isolates			Percent of all isolates with MIC (µg/mL)[§]														
		%I[*]	%R[†]	[95% CI][‡]	0.015	0.03	0.06	0.125	0.25	0.50	1	2	4	8	16	32	64	128	256	512
Aminoglycosides	Amikacin	0.0	0.0	[0.0–1.5]							4.6	62.7	30.7	2.1						
	Gentamicin	0.0	0.0	[0.0–1.5]					2.1	47.7	48.5	1.7								
	Kanamycin	0.0	0.0	[0.0–1.5]										100.0						
	Streptomycin	NA	58.1	[51.6–64.4]												41.9	21.2	36.9		
Aminopenicillins	Ampicillin	0.4	79.3	[73.6–84.2]							0.8	10.4	6.2	2.9	0.4	0.8	78.4			
β-lactamase inhibitor	Amoxicillin-clavulanic acid	16.6	1.7	[0.5–4.2]							0.4	1.2	17.0	63.1	16.6	0.8	0.8			
Cephalosporins (3rd generation)	Ceftiofur	0.0	0.4	[0.0–2.3]				27.4	66.4	5.4	0.4				0.4					
	Ceftriaxone	0.0	0.4	[0.0–2.3]					99.2	0.4								0.4		
Cephamycins	Cefoxitin	0.4	0.4	[0.0–2.3]						0.4	12.9	73.0	12.0	0.8	0.4	0.4				
Folate pathway inhibitors	Trimethoprim-sulfamethoxazole	NA	53.1	[46.6–59.5]				33.2	7.9	1.7	2.1	2.1	3.3	49.8						
Phenicols	Chloramphenicol	5.4	2.5	[0.9–5.3]								3.3	81.3	7.5	5.4	0.4	2.1			
Quinolones	Ciprofloxacin	0.0	0.0	[0.0–1.5]	98.3		0.8	0.8												
	Nalidixic Acid	NA	1.7	[0.5–4.2]						0.4	60.6	35.7	1.7			0.8	0.8			
Sulfonamides	Sulfamethoxazole/Sulfisoxazole	NA	49.0	[42.5–55.5]											46.9	4.1				49.0
Tetracyclines	Tetracycline	0.4	36.1	[30.0–42.5]									63.5	0.4		8.3	27.8			

[*]Percent of isolates with intermediate susceptibility, NA if no MIC range of intermediate susceptibility exists
[†]Percent of isolates that were resistant
[‡]95% confidence intervals (CI) for percent resistant (%R) were calculated using the Clopper-Pearson exact method
§The unshaded areas indicate the dilution range of the Sensititre plates used to test isolates. Single vertical bars indicate the breakpoints for susceptibility, while double vertical bars indicate breakpoints for resistance. Numbers in the shaded areas indicate the percentages of isolates with MICs greater than the highest concentrations on the Sensititre plate. Numbers listed for the lowest tested concentrations represent the precentages of isolates with MICs equal to or less than the lowest tested concentration. CLSI breakpoints were used when available.

Table 3.4: Minimum inhibitory concentrations (MICs) and resistance of *Shilgella* flexneri isolates to antimicrobial agents, 2004 (N=61)

Antibiotic		% of isolates			Percent of all isolates with MIC (µg/mL)[§]														
		%I[*]	%R[†]	[95% CI][‡]	0.015	0.03	0.06	0.125	0.25	0.50	1	2	4	8	16	32	64	128	256	512
Aminoglycosides	Amikacin	0.0	0.0	[0.0–5.9]							3.3	27.9	60.7	6.6	1.6					
	Gentamicin	0.0	0.0	[0.0–5.9]					1.6	36.1	60.7	1.6								
	Kanamycin	0.0	0.0	[0.0–5.9]										100.0						
	Streptomycin	NA	72.1	[59.2–82.9]												27.9	19.7	52.5		
Aminopenicillins	Ampicillin	0.0	82.0	[70.0–90.6]							14.8	1.6	1.6				82.0			
β-lactamase inhibitor	Amoxicillin-clavulanic acid	55.7	1.6	[0.0–8.8]							1.6	13.1	6.6	21.3	55.7	1.6				
Cephalosporins (3rd generation)	Ceftiofur	0.0	0.0	[0.0–5.9]				55.7	41.0	3.3										
	Ceftriaxone	0.0	0.0	[0.0–5.9]					100.0											
Cephamycins	Cefoxitin	0.0	0.0	[0.0–5.9]							1.6	45.9	49.2	3.3						
Folate pathway inhibitors	Trimethoprim-sulfamethoxazole	NA	45.9	[33.1–59.2]				31.1	16.4	4.9	1.6			45.9						
Phenicols	Chloramphenicol	1.6	60.7	[47.3–72.9]								34.4	3.3		1.6	8.2	52.5			
Quinolones	Ciprofloxacin	0.0	0.0	[0.0–5.9]	96.7	1.6		1.6												
	Nalidixic Acid	NA	1.6	[0.0–8.8]							60.7	36.1	1.6				1.6			
Sulfonamides	Sulfamethoxazole/Sulfisoxazole	NA	65.6	[52.3–77.3]											34.4					65.6
Tetracyclines	Tetracycline	0.0	95.1	[86.3–99.0]									4.9			13.1	82.0			

[*]Percent of isolates with intermediate susceptibility, NA if no MIC range of intermediate susceptibility exists

[†]Percent of isolates that were resistant

[‡]95% confidence intervals (CI) for percent resistant (%R) were calculated using the Clopper-Pearson exact method

§The unshaded areas indicate the dilution range of the Sensititre plates used to test isolates. Single vertical bars indicate the breakpoints for susceptibility, while double vertical bars indicate breakpoints for resistance. Numbers in the shaded areas indicate the percentages of isolates with MICs greater than the highest concentrations on the Sensititre plate. Numbers listed for the lowest tested concentrations represent the precentages of isolates with MICs equal to or less than the lowest tested concentration. CLSI breakpoints were used when available.

Table 3.5: Percentage and number of *Shigella* isolates resistant to antimicrobial agents, 1999–2004

Year Total Isolates		1999 375	2000 450	2001 344	2002 620	2003 495	2004 315
Subclass	Antibiotic (Resistance breakpoint)						
Aminoglycosides	Amikacin (MIC ≥ 64)	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0
	Gentamicin (MIC ≥ 16)	0.3% 1	0.2% 1	0.0% 0	0.2% 1	0.0% 0	0.0% 0
	Kanamycin (MIC ≥ 64)	0.5% 2	1.3% 6	0.6% 2	0.8% 5	0.4% 2	0.0% 0
	Streptomycin (MIC ≥ 64)	55.7% 209	57.1% 257	53.2% 183	54.4% 337	57.0% 282	61.0% 192
Aminopenicillins	Ampicillin (MIC ≥ 32)	77.6% 291	79.1% 356	79.7% 274	76.6% 475	79.4% 393	77.8% 245
β-lactamase inhibitor combinations	Amoxicillin-clavulanic acid (MIC ≥ 32)	1.1% 4	2.2% 10	4.4% 15	2.6% 16	1.4% 7	1.6% 5
Cephalosporin (1st generation)	Cephalothin (MIC ≥ 32)	3.2% 12	8.0% 36	9.0% 31	6.6% 41	9.3% 46	Not Tested
Cephalosporins (3rd generation)	Ceftiofur (MIC ≥ 8)	0.0% 0	0.0% 0	0.0% 0	0.2% 1	0.2% 1	0.3% 1
	Ceftriaxone (MIC ≥ 64)	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.3% 1
Cephamycins	Cefoxitin (MIC ≥ 32)	Not Tested	0.2% 1	1.2% 4	0.3% 2	0.0% 0	0.3% 1
Folate pathway inhibitors	Trimethoprim-sulfamethoxazole (MIC ≥ 4)	51.5% 193	52.9% 238	46.8% 161	37.3% 231	38.6% 191	51.4% 162
Phenicols	Chloramphenicol (MIC ≥ 32)	17.3% 65	14.0% 63	21.5% 74	7.6% 47	8.5% 42	14.9% 47
Quinolones	Ciprofloxacin (MIC ≥ 4)	0.0% 0	0.0% 0	0.3% 1	0.0% 0	0.0% 0	0.0% 0
	Nalidixic Acid (MIC ≥ 32)	1.6% 6	0.9% 4	1.7% 6	1.6% 10	1.0% 5	1.6% 5
Sulfonamides	Sulfamethoxazole/Sulfisoxazole* (MIC ≥ 512)	56.0% 210	55.8% 251	56.4% 194	31.8% 197	33.9% 168	52.4% 165
Tetracyclines	Tetracycline (MIC ≥ 16)	57.3% 215	44.9% 202	59.3% 204	30.6% 190	29.1% 144	49.2% 155

*Sulfamethoxazole, which was tested during 1999-2003 to represent sulfonamides, was replaced by sulfisoxazole in 2004.

Table 3.6: Percentage and number of *Shigella sonnei* isolates resistant to antimicrobial agents, 1999–2004

Year Total Isolates		1999 275	2000 366	2001 239	2002 536	2003 434	2004 241
Subclass	Antibiotic (Resistance breakpoint)						
Aminoglycosides	Amikacin (MIC ≥ 64)	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0
	Gentamicin (MIC ≥ 16)	0.4% 1	0.3% 1	0.0% 0	0.0% 0	0.0% 0	0.0% 0
	Kanamycin (MIC ≥ 64)	0.7% 2	1.6% 6	0.4% 1	0.4% 2	0.0% 0	0.0% 0
	Streptomycin (MIC ≥ 64)	52.0% 143	56.0% 205	54.0% 129	55.4% 297	56.5% 245	58.1% 140
Aminopenicillins	Ampicillin (MIC ≥ 32)	79.6% 219	80.6% 295	82.8% 198	77.6% 416	79.7% 346	79.3% 191
β-lactamase inhibitor combinations	Amoxicillin-clavulanic acid (MIC ≥ 32)	0.4% 1	1.9% 7	4.6% 11	2.2% 12	1.4% 6	1.7% 4
Cephalosporin (1st generation)	Cephalothin (MIC ≥ 32)	2.9% 8	8.7% 32	12.6% 30	7.3% 39	10.1% 44	Not Tested
Cephalosporins (3rd generation)	Ceftiofur (MIC ≥ 8)	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.4% 1
	Ceftriaxone (MIC ≥ 64)	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.4% 1
Cephamycins	Cefoxitin (MIC ≥ 32)	Not Tested	0.3% 1	1.7% 4	0.4% 2	0.0% 0	0.4% 1
Folate pathway inhibitors	Trimethoprim-sulfamethoxazole (MIC ≥ 4)	53.1% 146	54.9% 201	50.6% 121	37.9% 203	38.5% 167	53.1% 128
Phenicols	Chloramphenicol (MIC ≥ 32)	1.8% 5	2.7% 10	1.3% 3	0.2% 1	1.2% 5	2.5% 6
Quinolones	Ciprofloxacin (MIC ≥ 4)	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0
	Nalidixic Acid (MIC ≥ 32)	1.5% 4	1.1% 4	0.8% 2	1.5% 8	0.5% 2	1.7% 4
Sulfonamides	Sulfamethoxazole/Sulfisoxazole* (MIC ≥ 512)	54.5% 150	56.0% 205	54.4% 130	29.9% 160	31.3% 136	49.0% 118
Tetracyclines	Tetracycline (MIC ≥ 16)	46.2% 127	34.4% 126	44.8% 107	23.5% 126	22.1% 96	36.1% 87

*Sulfamethoxazole, which was tested during 1999-2003 to represent sulfonamides, was replaced by sulfisoxazole in 2004.

Table 3.7: Percentage and number of *Shigella flexneri* isolates resistant to antimicrobial agents, 1999–2004

Year Total Isolates		1999 87	2000 75	2001 91	2002 73	2003 51	2004 61
Subclass	Antibiotic (Resistance breakpoint)						
Aminoglycosides	Amikacin (MIC ≥ 64)	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0
	Gentamicin (MIC ≥ 16)	0.0% 0	0.0% 0	0.0% 0	1.4% 1	0.0% 0	0.0% 0
	Kanamycin (MIC ≥ 64)	0.0% 0	0.0% 0	1.1% 1	4.1% 3	3.9% 2	0.0% 0
	Streptomycin (MIC ≥ 64)	63.2% 55	61.3% 46	47.3% 43	43.8% 32	60.8% 31	72.1% 44
Aminopenicillins	Ampicillin (MIC ≥ 32)	77.0% 67	77.3% 58	72.5% 66	75.3% 55	84.3% 43	82.0% 50
β-lactamase inhibitor combinations	Amoxicillin-clavulanic acid (MIC ≥ 32)	3.4% 3	4.0% 3	4.4% 4	5.5% 4	2.0% 1	1.6% 1
Cephalosporin (1st generation)	Cephalothin (MIC ≥ 32)	4.6% 4	2.7% 2	1.1% 1	2.7% 2	3.9% 2	Not Tested
Cephalosporins (3rd generation)	Ceftiofur (MIC ≥ 8)	0.0% 0	0.0% 0	0.0% 0	1.4% 1	2.0% 1	0.0% 0
	Ceftriaxone (MIC ≥ 64)	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0
Cephamycins	Cefoxitin (MIC ≥ 32)	Not Tested	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0
Folate pathway inhibitors	Trimethoprim-sulfamethoxazole (MIC ≥ 4)	48.3% 42	42.7% 32	34.1% 31	28.8% 21	39.2% 20	45.9% 28
Phenicols	Chloramphenicol (MIC ≥ 32)	64.4% 56	69.3% 52	74.7% 68	63.0% 46	68.6% 35	60.7% 37
Quinolones	Ciprofloxacin (MIC ≥ 4)	0.0% 0	0.0% 0	1.1% 1	0.0% 0	0.0% 0	0.0% 0
	Nalidixic Acid (MIC ≥ 32)	1.1% 1	0.0% 0	3.3% 3	2.7% 2	5.9% 3	1.6% 1
Sulfonamides	Sulfamethoxazole/Sulfisoxazole* (MIC ≥ 512)	58.6% 51	53.3% 40	57.1% 52	41.1% 30	52.9% 27	65.6% 40
Tetracyclines	Tetracycline (MIC ≥ 16)	92.0% 80	92.0% 69	94.5% 86	78.1% 57	82.4% 42	95.1% 58

*Sulfamethoxazole, which was tested during 1999-2003 to represent sulfonamides, was replaced by sulfisoxazole in 2004.

Table 3.8: Resistance patterns of *Shigella* isolates, 1999–2004

Year Total Isolates	1999 375	2000 450	2001 344	2002 620	2003 495	2004 315
	% n	% n	% n	% n	% n	% n
No resistance detected	9.1% 34	7.3% 33	4.9% 17	8.2% 51	8.5% 42	4.4% 14
Resistance ≥1CLSI subclass*	90.9% 341	92.7% 417	95.1% 327	91.8% 569	91.5% 453	95.6% 301
Resistance ≥2 CLSI subclasses*	63.7% 239	64.7% 291	69.8% 240	55.3% 343	57.8% 286	66.7% 210
Resistance ≥3 CLSI subclasses*	61.1% 229	62.0% 279	61.3% 211	41.8% 259	41.4% 205	62.2% 196
Resistance ≥4 CLSI subclasses*	54.1% 203	56.7% 255	54.1% 186	31.0% 192	32.5% 161	52.1% 164
Resistance ≥5 CLSI subclasses*	40.5% 152	26.2% 118	36.0% 124	20.5% 127	22.4% 111	27.6% 87
At least ACSSuT[†]	8.5% 32	5.6% 25	6.4% 22	1.8% 11	3.2% 16	6.0% 19
At least ACSuTm[‡]	9.9% 37	6.9% 31	7.0% 24	2.7% 17	3.6% 18	6.7% 21
At least ASuTm[§]	44.3% 166	44.4% 200	37.5% 129	29.8% 185	33.7% 167	37.8% 119
At least ANSuTm[¶]	0.3% 1	0.0% 0	0.6% 2	0.3% 2	0.8% 4	0.6% 2
At least ACSSuTAuCf**	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0
At least MDR-AmpC[††]	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0
Resistance to quinolone and cephalosporin (3rd generation)	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.2% 1	0.3% 1

*CLSI: Clinical and Laboratory Standards Institute

[†]ACSSuT: resistance to ampicillin, chloramphenicol, streptomycin, sulfamethoxazole/sulfisoxazole, tetracycline

[‡]ACSuTm: resistance to ampicillin, chloramphenicol, trimethoprim-sulfamethoxazole

[§]ASuTm: resistance to ampicillin, trimethoprim-sulfamethoxazole

[¶]ANSuTm: resistance to ASuTm + naladixic acid

**ACSSuTAuCf: resistance to ACSSuT + amoxicillin-clavulanic acid, ceftiofur

[††]MDR-AmpC: resistance to ACSSuTAuCf + decreased susceptibility to ceftriaxone (MIC ≥2 µg/mL)

Table 3.9: Resistance patterns of *Shigella sonnei* isolates, 1999–2004

Year Total Isolates	1999 275	2000 366	2001 239	2002 536	2003 434	2004 241
	% n	% n	% n	% n	% n	% n
No resistance detected	10.5% 29	7.7% 28	5.4% 13	7.1% 38	8.5% 37	5.0% 12
Resistance ≥1CLSI subclass*	89.5% 246	92.3% 338	94.6% 226	92.9% 498	91.5% 397	95.0% 229
Resistance ≥2 CLSI subclasses*	56.0% 154	60.7% 222	60.7% 145	52.1% 279	54.1% 235	59.8% 144
Resistance ≥3 CLSI subclasses*	54.5% 150	57.7% 211	53.1% 127	36.6% 196	36.2% 157	54.4% 131
Resistance ≥4 CLSI subclasses*	50.5% 139	54.1% 198	49.0% 117	26.7% 143	28.6% 124	46.5% 112
Resistance ≥5 CLSI subclasses*	38.5% 106	23.5% 86	36.0% 86	19.4% 104	20.0% 87	24.9% 60
At least ACSSuT[†]	0.4% 1	0.8% 3	0.0% 0	0.0% 0	0.2% 1	0.0% 0
At least ACSuTm[‡]	1.8% 5	1.9% 7	0.8% 2	0.2% 1	0.9% 4	1.7% 4
At least ASuTm[§]	45.1% 124	46.2% 169	41.0% 98	30.2% 162	33.6% 146	39.4% 95
At least ANSuTm[¶]	0.0% 0	0.0% 0	0.0% 0	0.2% 1	0.2% 1	0.8% 2
At least ACSSuTAuCf**	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0
At least MDR-AmpC[††]	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0
Resistance to quinolone and cephalosporin (3rd generation)	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.4% 1

*CLSI: Clinical and Laboratory Standards Institute

[†]ACSSuT: resistance to ampicillin, chloramphenicol, streptomycin, sulfamethoxazole/sulfisoxazole, tetracycline

[‡]ACSuTm: resistance to ampicillin, chloramphenicol, trimethoprim-sulfamethoxazole

[§]ASuTm: resistance to ampicillin, trimethoprim-sulfamethoxazole

[¶]ANSuTm: resistance to ASuTm + naladixic acid

**ACSSuTAuCf: resistance to ACSSuT + amoxicillin-clavulanic acid, ceftiofur

[††]MDR-AmpC: resistance to ACSSuTAuCf + decreased susceptibility to ceftriaxone (MIC ≥2 µg/mL)

Table 3.10: Resistance patterns of *Shigella flexneri* isolates, 1999–2004

Year	1999	2000	2001	2002	2003	2004
Total Isolates	**87**	**75**	**91**	**73**	**51**	**61**
	%	%	%	%	%	%
	n	n	n	n	n	n
No resistance detected	4.6%	4.0%	3.3%	15.1%	7.8%	0.0%
	4	3	3	11	4	0
Resistance ≥1CLSI subclass*	95.4%	96.0%	96.7%	84.9%	92.2%	100.0%
	83	72	88	62	47	61
Resistance ≥2 CLSI subclasses*	83.9%	82.7%	90.1%	76.7%	86.3%	93.4%
	73	62	82	56	44	57
Resistance ≥3 CLSI subclasses*	80.5%	81.3%	80.2%	75.3%	82.4%	91.8%
	70	61	73	55	42	56
Resistance ≥4 CLSI subclasses*	67.8%	69.3%	65.9%	58.9%	64.7%	75.4%
	59	52	60	43	33	46
Resistance ≥5 CLSI subclasses*	49.4%	40.0%	31.9%	28.8%	45.1%	41.0%
	43	30	29	21	23	25
At least ACSSuT[†]	33.3%	29.3%	22.0%	15.1%	29.4%	27.9%
	29	22	20	11	15	17
At least ACSuTm[‡]	34.5%	32.0%	23.1%	21.9%	27.5%	24.6%
	30	24	21	16	14	15
At least ASuTm[§]	44.8%	38.7%	25.3%	27.4%	37.3%	36.1%
	39	29	23	20	19	22
At least ANSuTm[¶]	1.1%	0.0%	1.1%	1.4%	5.9%	0.0%
	1	0	1	1	3	0
At least ACSSuTAuCf**	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
	0	0	0	0	0	0
At least MDR-AmpC[††]	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
	0	0	0	0	0	0
Resistance to quinolone and cephalosporin (3rd generation)	0.0%	0.0%	0.0%	0.0%	2.0%	0.0%
	0	0	0	0	1	0

*CLSI: Clinical and Laboratory Standards Institute

[†]ACSSuT: resistance to ampicillin, chloramphenicol, streptomycin, sulfamethoxazole/sulfisoxazole, tetracycline

[‡]ACSuTm: resistance to ampicillin, chloramphenicol, trimethoprim-sulfamethoxazole

[§]ASuTm: resistance to ampicillin, trimethoprim-sulfamethoxazole

[¶]ANSuTm: resistance to ASuTm + naladixic acid

**ACSSuTAuCf: resistance to ACSSuT + amoxicillin-clavulanic acid, ceftiofur

[††]MDR-AmpC: resistance to ACSSuTAuCf + decreased susceptibility to ceftriaxone (MIC ≥2 µg/mL)

4. *ESCHERICHIA COLI* O157

In 2004, CDC received a total of 177 *Escherichia coli* O157 isolates, of which 170 (96.0%) were viable and tested for antimicrobial susceptibility. Of these 170 isolates, one isolate was excluded from the analysis because it was a duplicate submission, leaving 169 isolates for analysis (Table I). Antimicrobial agents with the highest prevalence of resistance were nalidixic acid (1.8%), sulfisoxazole (1.8%), streptomycin (1.8%), and tetracycline (1.8%) (Table 4.2). Ampicillin resistance decreased from 3.2% in 2003 to 1.2% in 2004 (Table 4.2). Cefoxitin and chloramphenicol resistance decreased to 0.6% in 2004, down from 1.3% in 2003. No isolates in 2004 were resistant to ceftiofur, whereas two isolates were resistant in 2003 (Table 4.2).

Isolates resistant to at least one CLSI subclass decreased from 9.6% in 2003 to 4.7% in 2004 (Table 4.3). Resistance to at least two CLSI subclasses decreased from 5.1% in 2003 to 1.2% in 2004. No isolates were resistant to at least five subclasses in 2004, but one (0.6%) was resistant in 2003.

Antimicrobial treatment of *E. coli* O157 infections is not recommended, but resistance changes, particularly appearance of third-generation cephalosporin resistance, might prove useful in understanding exchange of mobile resistance elements in bovine production settings.

Table 4.1: Minimum inhibitory concentrations (MICs) and resistance of *Escherichia coli* O157 isolates to antimicrobial agents, 2004 (N=169)

Antibiotic		% of isolates			Percent of all isolates with MIC (µg/mL)§														
		%I*	%R†	[95% CI]‡	0.015	0.03	0.06	0.125	0.25	0.50	1	2	4	8	16	32	64	128	256	512
Aminoglycosides	Amikacin	0.0	0.0	[0.0–2.2]						5.9	68.0	22.5	3.6							
	Gentamicin	0.0	0.6	[0.0–3.3]					57.4	37.3	4.7					0.6				
	Kanamycin	0.0	0.0	[0.0–2.2]										100.0						
	Streptomycin	NA	1.8	[0.4–5.1]												98.2	0.6	1.2		
Aminopenicillins	Ampicillin	0.0	1.2	[0.1–4.2]							5.3	59.2	31.4	3.0			1.2			
β-lactamase inhibitor	Amoxicillin-clavulanic acid	0.6	0.0	[0.0–2.2]							3.6	6.5	88.2	1.2	0.6					
Cephalosporins (3rd generation)	Ceftiofur	0.0	0.0	[0.0–2.2]				2.4	43.2	52.1	2.4									
	Ceftriaxone	0.0	0.0	[0.0–2.2]					100.0											
Cephamycins	Cefoxitin	1.2	0.6	[0.0–3.3]						0.6	3.0	5.9	70.4	18.3	1.2	0.6				
Folate pathway inhibitors	Trimethoprim-sulfamethoxazole	NA	0.0	[0.0–2.2]				94.1	5.9											
Phenicols	Chloramphenicol	0.6	0.6	[0.0–3.3]								1.8	46.2	50.9	0.6		0.6			
Quinolones	Ciprofloxacin	0.0	0.0	[0.0–2.2]	97.6	0.6		0.6	1.2											
	Nalidixic Acid	NA	1.8	[0.4–5.1]							2.4	75.7	19.5	0.6			1.8			
Sulfonamides	Sulfamethoxazole/Sulfisoxazole	NA	1.8	[0.4–5.1]											92.9	5.3				1.8
Tetracyclines	Tetracycline	0.0	1.8	[0.4–5.1]									98.2		0.6		1.2			

*Percent of isolates with intermediate susceptibility, NA if no MIC range of intermediate susceptibility exists

†Percent of isolates that were resistant

‡95% confidence intervals (CI) for percent resistant (%R) were calculated using the Clopper-Pearson exact method

§The unshaded areas indicate the dilution range of the Sensititre plates used to test isolates. Single vertical bars indicate the breakpoints for susceptibility, while double vertical bars indicate breakpoints for resistance. Numbers in the shaded areas indicate the percentages of isolates with MICs greater than the highest concentrations on the Sensititre plate. Numbers listed for the lowest tested concentrations represent the precentages of isolates with MICs equal to or less than the lowest tested concentration. CLSI breakpoints were used when available.

Table 4.2: Percentage and number of *Escherichia coli* O157 isolates resistant to antimicrobial agents, 1996–2004

Year Total Isolates		1996 201	1997 161	1998 318	1999 292	2000 407	2001 277	2002 399	2003 157	2004 169
Subclass	Antibiotic (Resistance breakpoint)									
Aminoglycosides	Amikacin (MIC ≥ 64)	Not Tested	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0
	Gentamicin (MIC ≥ 16)	0.0% 0	0.0% 0	0.0% 0	0.3% 1	0.5% 2	0.4% 1	0.0% 0	0.0% 0	0.6% 1
	Kanamycin (MIC ≥ 64)	0.0% 0	0.0% 0	0.3% 1	0.7% 2	1.0% 4	0.0% 0	0.5% 2	0.0% 0	0.0% 0
	Streptomycin (MIC ≥ 64)	2.0% 4	2.5% 4	1.9% 6	2.7% 8	5.2% 21	1.8% 5	2.3% 9	1.9% 3	1.8% 3
Aminopenicillins	Ampicillin (MIC ≥ 32)	1.5% 3	0.0% 0	2.5% 8	1.4% 4	2.7% 11	2.2% 6	1.5% 6	3.2% 5	1.2% 2
Beta-lactamase inhibitor combinations	Amoxicillin-clavulanic acid (MIC ≥ 32)	0.0% 0	0.0% 0	0.0% 0	0.3% 1	1.0% 4	0.7% 2	0.0% 0	1.3% 2	0.0% 0
Cephalosporin (1st Gen.)	Cephalothin (MIC ≥ 32)	1.5% 3	2.5% 4	0.0% 0	0.7% 2	1.2% 5	1.4% 4	1.5% 6	2.5% 4	Not Tested
Cephalosporins (3rd Gen.)	Ceftiofur (MIC ≥ 8)	0.0% 0	0.0% 0	0.0% 0	0.0% 0	1.0% 4	1.1% 3	0.0% 0	1.3% 2	0.0% 0
	Ceftriaxone (MIC ≥ 64)	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0
Cephamycins	Cefoxitin (MIC ≥ 32)	Not Tested	Not Tested	Not Tested	Not Tested	1.0% 4	0.7% 2	0.0% 0	1.3% 2	0.6% 1
Folate pathway inhibitors	Trimethoprim-sulfamethoxazole (MIC ≥ 4)	0.0% 0	0.0% 0	0.6% 2	1.4% 4	0.7% 3	0.7% 2	0.5% 2	0.6% 1	0.0% 0
Phenicols	Chloramphenicol (MIC ≥ 32)	0.5% 1	0.0% 0	0.3% 1	0.0% 0	3.7% 15	1.4% 4	1.3% 5	1.3% 2	0.6% 1
Quinolones	Ciprofloxacin (MIC ≥ 4)	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0
	Nalidixic acid (MIC ≥ 32)	0.0% 0	0.0% 0	0.0% 0	0.7% 2	0.5% 2	1.1% 3	1.0% 4	0.6% 1	1.8% 3
Sulfonamides	Sulfamethoxazole/Sulfisoxazole* (MIC ≥ 512)	11.9% 24	9.9% 16	5.7% 18	8.2% 24	5.9% 24	5.1% 14	3.5% 14	3.8% 6	1.8% 3
Tetracyclines	Tetracycline (MIC ≥ 16)	5.0% 10	3.1% 5	4.4% 14	3.4% 10	7.1% 29	5.4% 15	3.0% 12	5.7% 9	1.8% 3

*Sulfamethoxazole, which was tested during 1996-2003 to represent sulfonamides, was replaced by sulfisoxazole in 2004.

Table 4.3: Resistance patterns of *Escherichia coli* O157 isolates, 1996–2004

Year Total Isolates	1996 201	1997 161	1998 318	1999 292	2000 407	2001 277	2002 399	2003 157	2004 169
	% n	% n	% n	% n	% n	% n	% n	% n	% n
No resistance detected	86.6% 174	88.8% 143	92.8% 295	89.7% 262	90.4% 368	91.3% 253	94.0% 375	90.4% 142	95.3% 161
Resistance ≥1CLSI subclass*	13.4% 27	11.2% 18	7.2% 23	10.3% 30	9.6% 39	8.7% 24	6.0% 24	9.6% 15	4.7% 8
Resistance ≥2 CLSI subclasses*	5.0% 10	3.7% 6	5.3% 17	3.4% 10	6.6% 27	5.4% 15	3.8% 15	5.1% 8	1.2% 2
Resistance ≥3 CLSI subclasses*	1.5% 3	0.6% 1	1.9% 6	3.1% 9	4.7% 19	2.2% 6	2.0% 8	3.2% 5	0.6% 1
Resistance ≥4 CLSI subclasses*	0.5% 1	0.0% 0	0.9% 3	1.0% 3	3.7% 15	1.8% 5	1.0% 4	1.3% 2	0.6% 1
Resistance ≥5 CLSI subclasses*	0.5% 1	0.0% 0	0.0% 0	0.7% 2	1.5% 6	0.7% 2	0.3% 1	0.6% 1	0.0% 0
At least ACSSuT†	0.5% 1	0.0% 0	0.0% 0	0.0% 0	1.2% 5	0.4% 1	0.0% 0	0.0% 0	0.0% 0
At least ACSuTm‡	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.2% 1	0.0% 0	0.0% 0	0.0% 0	0.0% 0
At least ACSSuTAuCf§	0.0% 0	0.0% 0	0.0% 0	0.0% 0	1.0% 4	0.4% 1	0.0% 0	0.0% 0	0.0% 0
At least MDR-AmpC¶	0.0% 0	0.0% 0	0.0% 0	0.0% 0	1.0% 4	0.4% 1	0.0% 0	0.0% 0	0.0% 0
Resistance to quinolone and cephalosporin (3rd generation)	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0

*CLSI: Clinical and Laboratory Standards Institute

†ACSSuT: resistance to ampicillin, chloramphenicol, streptomycin, sulfamethoxazole/sulfisoxazole, tetracycline

‡ACSuTm: resistance to ampicillin, chloramphenicol, trimethoprim-sulfamethoxazole

§ACSSuTAuCf: resistance to ACSSuT + amoxicillin-clavulanic acid, ceftiofur

¶MDR-AmpC: resistance to ACSSuTAuCf + decreased susceptibility to ceftriaxone (MIC ≥2 µg/mL)

5. *CAMPYLOBACTER*

In 2004, CDC received 449 *Campylobacter* isolates, of which 431 isolates (95.9%) were viable and tested for antimicrobial susceptibility. Of these 431 isolates, 70 isolates that were not part of the sampling scheme, eight isolates that were not *Campylobacter*, and six submissions from patients residing outside the catchment area were excluded, leaving 347 isolates for analysis (Table I). A total of 320 (92.2%) were *C. jejuni* and 26 (7.5%) were *C. coli* (Table 5.1).

For the *Campylobacter* isolates tested in 2004, resistance was highest to tetracycline (46.1%), nalidixic acid (19.6%), and ciprofloxacin (19.0%) (Table 5.3). Of these isolates tested, 1.4% were resistant to chloramphenicol.

The percentage of *Campylobacter* isolates resistant to ciprofloxacin increased from 12.9% in 1997 and peaked at 20.1% in 2002 (Table 5.3). (This significant increase was reported in previous annual reports.) The percentage of *Campylobacter* isolates resistant to ciprofloxacin was 19.0% in 2004, which is not a statistically significant increase from 1997 (OR=1.6, 95% CI [1.0, 2.6]). Resistance to erythromycin remained low at 0.3% in 2004.

In 2004, 53.9% of *Campylobacter* isolates were resistant to one or more CLSI subclass, compared with 48.8% in 2003 (Table 5.4). In 2004, 14.1% of *Campylobacter* isolates were resistant to two or more subclasses, compared with 8.5% in 2003.

The antimicrobial agent with the highest prevalence of resistance among the 320 *C. jejuni* isolates was tetracycline (46.9%), followed by nalidixic acid (18.4%) and ciprofloxacin (18.1%) (Table 5.6). Of note, 0.3% and 1.6% of *C. jejuni* isolates were resistant to gentamicin and chloramphenicol, respectively.

The percentage of *C. jejuni* isolates resistant to ciprofloxacin increased from 12.4% in 1997 to 18.1% in 2004 (Table 5.6), but the increase was not statistically significant (OR=1.6, 95% CI [0.9, 2.6]). Resistance to erythromycin remained low at 0.3% in 2004.

The highest levels of resistance among the 26 *C. coli* isolates were to tetracycline (38.5%), nalidixic acid (34.6%), and ciprofloxacin (30.8%) (Table 5.8). The percentage of *C. coli* isolates resistant to ciprofloxacin was 33.3% in 1997 and 30.8% in 2004 (Table 5.8). Resistance to erythromycin, which was 12.5% in 1998 and 4.0%–10.0% during 1999–2003, was not detected in 2004.

Table 5.1: Frequency of *Campylobacter* species isolated in NARMS, 2004

Species	2004	
	N	(%)
Campylobacter jejuni	320	(92.2%)
Campylobacter coli	26	(7.5%)
Other	1	(0.3%)
Total	**347**	**(100.0%)**

Table 5.2: Minimum inhibitory concentrations (MICs) and resistance of *Campylobacter* isolates to antimicrobial agents, 2004 (N=347)

Antibiotic		% of isolates			Percent of all isolates with MIC (µg/mL)[§]															
		%I[*]	%R[†]	[95% CI][‡]	0.015	0.03	0.06	0.125	0.25	0.50	1	2	4	8	16	32	64	128	256	512
Aminoglycosides	Gentamicin	2.0	0.3	[0.0–1.6]			0.3		9.2	44.4	29.7	14.1	2.0							0.3
Lincosamides	Clindamycin	0.3	2.0	[0.8–4.1]		0.6	2.0	23.3	48.7	18.2	3.2	1.7	0.3	0.3	1.2		0.6			
Macrolides	Azithromycin	1.4	0.6	[0.1–2.1]			5.5	39.8	44.7	6.1	1.4	0.6	1.4				0.3			0.3
	Erythromycin	0.6	0.3	[0.0–1.6]			0.6	0.9	10.4	48.4	27.7	9.2	1.7	0.3	0.6					0.3
Phenicols	Chloramphenicol	2.9	1.4	[0.5–3.3]					0.6	2.3	42.9	35.7	10.7	3.5	2.9	1.4				
Quinolones	Ciprofloxacin	0.0	19.0	[15.0–23.6]	0.6	36.3	36.0	6.6	1.2	0.3				0.3	1.4		17.3			
	Nalidixic Acid	0.6	19.6	[15.6–24.2]						0.6	11.0	38.0	21.3	6.9	2.0	0.6	0.3			19.3
Tetracyclines	Tetracycline	0.3	46.1	[40.8–51.5]		2.0	20.7	22.8	6.1	1.2	0.6		0.3	0.3	1.4	4.6	5.8	5.8	1.2	27.4

[*]Percent of isolates with intermediate susceptibility

[†]Percent of isolates that were resistant

[‡]95% confidence intervals (CI) for percent resistant (%R) were calculated using the Clopper-Pearson exact method

[§]The unshaded areas indicate the range of dilutions tested for each antimicrobial agent. Single vertical bars indicate the breakpoints for susceptibility, while double vertical bars indicate breakpoints for resistance. Numbers in the shaded areas indicate the percentages of isolates with MICs greater than the highest tested concentrations. Numbers listed for the lowest tested concentrations represent the precentages of isolates with MICs equal to or less than the lowest tested concentration. CLSI breakpoints were used when available.

Table 5.3: Percentage and number of Campylobacter isolates resistant to antimicrobial agents, 1997–2004

Year Total Isolates		1997 217	1998 310	1999 317	2000 324	2001 384	2002 354	2003 328	2004 347
Subclass	Antibiotic (Resistance breakpoint)								
Aminoglycosides	Gentamicin (MIC ≥ 8)	Not Tested	0.3% 1	0.0% 0	0.3% 1	0.0% 0	0.0% 0	0.3% 1	0.3% 1
Lincosamides	Clindamycin (MIC ≥ 8)	1.8% 4	1.3% 4	1.3% 4	0.9% 3	2.1% 8	2.0% 7	0.6% 2	2.0% 7
Macrolides	Azithromycin (MIC ≥ 8)	Not Tested	0.6% 2	2.2% 7	1.9% 6	2.1% 8	2.0% 7	0.9% 3	0.6% 2
	Erythromycin (MIC ≥ 32)	1.8% 4	1.0% 3	1.9% 6	1.2% 4	2.1% 8	1.4% 5	0.9% 3	0.3% 1
Phenicols	Chloramphenicol (MIC ≥ 32)	5.1% 11	2.9% 9	0.6% 2	0.0% 0	0.3% 1	0.3% 1	0.0% 0	1.4% 5
Quinolones	Ciprofloxacin (MIC ≥ 4)	12.9% 28	13.9% 43	18.3% 58	14.8% 48	19.5% 75	20.1% 71	17.7% 58	19.0% 66
	Nalidixic acid (MIC ≥ 64)	14.3% 31	16.8% 52	21.1% 67	16.7% 54	20.3% 78	20.6% 73	18.9% 62	19.6% 68
Tetracyclines	Tetracycline (MIC ≥ 16)	47.9% 104	45.5% 141	43.8% 139	38.3% 124	40.9% 157	41.2% 146	38.4% 126	46.1% 160

Table 5.4: Resistance patterns of *Campylobacter* isolates, 1997–2004

Year Total Isolates	1997 217	1998 310	1999 317	2000 324	2001 384	2002 354	2003 328	2004 347
	% n	% n	% n	% n	% n	% n	% n	% n
No resistance detected	47.0% 102	45.2% 140	47.3% 150	52.2% 169	49.2% 189	48.3% 171	50.9% 167	46.1% 160
Resistance ≥1CLSI subclass*	53.0% 115	54.8% 170	52.7% 167	47.8% 155	50.8% 195	51.7% 183	49.1% 161	53.9% 187
Resistance ≥2 CLSI subclasses*	15.7% 34	9.7% 30	13.6% 43	8.0% 26	13.3% 51	12.7% 45	8.5% 28	14.1% 49
Resistance ≥3 CLSI subclasses*	1.8% 4	2.6% 8	1.6% 5	0.9% 3	1.6% 6	1.1% 4	0.9% 3	1.2% 4
Resistance ≥4 CLSI subclasses*	0.5% 1	0.3% 1	0.9% 3	0.3% 1	0.3% 1	0.0% 0	0.3% 1	0.3% 1
Resistance ≥5 CLSI subclasses*	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0

*CLSI: Clinical and Laboratory Standards Institute

Table 5.5: Minimum inhibitory concentrations (MICs) and resistance of *Campylobacter jejuni* isolates to antimicrobial agents, 2004 (N=320)

Antibiotic		% of isolates			Percent of all isolates with MIC (µg/mL)[§]														
		%I[*]	%R[†]	[95% CI][‡]	0.015	0.03	0.06	0.125	0.25	0.50	1	2	4	8	16	32	64	128	256	512
Aminoglycosides	Gentamicin	1.9	0.3	[0.0–1.7]			0.3		9.4	45.3	28.8	14.1	1.9							0.3
Lincosamides	Clindamycin	0.3	2.2	[0.9–4.5]		0.6	2.2	25.3	48.1	18.1	2.2	0.9	0.3	0.3	1.3		0.6			
Macrolides	Azithromycin	1.6	0.6	[0.1–2.2]			5.9	40.3	44.4	5.3	1.6	0.3	1.6				0.3			0.3
	Erythromycin	0.3	0.3	[0.0–1.7]			0.6	0.9	10.0	49.7	28.4	7.8	1.6	0.3	0.3					0.3
Phenicols	Chloramphenicol	3.1	1.6	[0.5–3.6]					0.6	2.5	45.9	35.3	8.4	2.5	3.1	1.6				
Quinolones	Ciprofloxacin	0.0	18.1	[14.1–22.8]	0.6	36.9	37.8	5.6	0.9						1.6		16.6			
	Nalidixic Acid	0.6	18.4	[14.3–23.1]						0.6	11.9	39.4	20.6	6.9	1.6	0.6	0.3			18.1
Tetracyclines	Tetracycline	0.3	46.9	[41.3–52.5]		2.2	22.2	21.3	5.3	1.3	0.3		0.3	0.3	1.6	4.7	5.6	5.6	1.3	28.1

[*]Percent of isolates with intermediate susceptibility

[†]Percent of isolates that were resistant

[‡]95% confidence intervals (CI) for percent resistant (%R) were calculated using the Clopper-Pearson exact method

[§]The unshaded areas indicate the range of dilutions tested for each antimicrobial agent. Single vertical bars indicate the breakpoints for susceptibility, while double vertical bars indicate breakpoints for resistance. Numbers in the shaded areas indicate the percentages of isolates with MICs greater than the highest tested concentrations. Numbers listed for the lowest tested concentrations represent the precentages of isolates with MICs equal to or less than the lowest tested concentration. CLSI breakpoints were used when available.

Table 5.6: Percentage and number of Campylobacter jejuni isolates resistant to antimicrobial agents, 1997–2004

Year Total Isolates		1997 209	1998 297	1999 293	2000 306	2001 365	2002 329	2003 303	2004 320
Subclass	Antibiotic (Resistance breakpoint)								
Aminoglycosides	Gentamicin (MIC ≥ 8)	Not Tested	0.3% 1	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.3% 1
Lincosamides	Clindamycin (MIC ≥ 8)	1.0% 2	1.0% 3	0.7% 2	0.7% 2	1.9% 7	1.8% 6	0.0% 0	2.2% 7
Macrolides	Azithromycin (MIC ≥ 8)	Not Tested	0.3% 1	1.7% 5	1.6% 5	1.9% 7	1.8% 6	0.3% 1	0.6% 2
	Erythromycin (MIC ≥ 32)	1.4% 3	0.7% 2	1.4% 4	1.0% 3	1.9% 7	1.2% 4	0.3% 1	0.3% 1
Phenicols	Chloramphenicol (MIC ≥ 32)	3.8% 8	1.0% 3	0.7% 2	0.0% 0	0.3% 1	0.3% 1	0.0% 0	1.6% 5
Quinolones	Ciprofloxacin (MIC ≥ 4)	12.4% 26	13.8% 41	17.7% 52	14.7% 45	18.4% 67	20.7% 68	17.2% 52	18.1% 58
	Nalidixic acid (MIC ≥ 64)	13.4% 28	15.5% 46	20.1% 59	16.0% 49	18.9% 69	21.3% 70	17.8% 54	18.4% 59
Tetracyclines	Tetracycline (MIC ≥ 16)	47.8% 100	46.1% 137	45.4% 133	39.2% 120	40.3% 147	41.3% 136	38.3% 116	46.9% 150

Table 5.7: Minimum inhibitory concentrations (MICs) and resistance of *Campylobacter coli* isolates to antimicrobial agents, 2004 (N=26)

Antibiotic		% of isolates			Percent of all isolates with MIC (µg/mL)[§]														
		%I[*]	%R[†]	[95% CI][‡]	0.015	0.03	0.06	0.125	0.25	0.50	1	2	4	8	16	32	64	128	256	512
Aminoglycosides	Gentamicin	3.8	0.0	[0.0–13.2]					7.7	30.8	42.3	15.4	3.8							
Lincosamides	Clindamycin	0.0	0.0	[0.0–13.2]					53.8	19.2	15.4	11.5								
Macrolides	Azithromycin	0.0	0.0	[0.0–13.2]				34.6	46.2	15.4		3.8								
	Erythromycin	3.8	0.0	[0.0–13.2]					15.4	34.6	15.4	26.9	3.8		3.8					
Phenicols	Chloramphenicol	0.0	0.0	[0.0–13.2]							7.7	38.5	38.5	15.4						
Quinolones	Ciprofloxacin	0.0	30.8	[14.3–51.8]		26.9	15.4	19.2	3.8	3.8				3.8			26.9			
	Nalidixic Acid	0.0	34.6	[17.2–55.7]								19.2	30.8	7.7	7.7					34.6
Tetracyclines	Tetracycline	0.0	38.5	[20.2–59.4]				42.3	15.4		3.8					3.8	7.7	7.7		19.2

[*]Percent of isolates with intermediate susceptibility

[†]Percent of isolates that were resistant

[‡]95% confidence intervals (CI) for percent resistant (%R) were calculated using the Clopper-Pearson exact method

§The unshaded areas indicate the range of dilutions tested for each antimicrobial agent. Single vertical bars indicate the breakpoints for susceptibility, while double vertical bars indicate breakpoints for resistance. Numbers in the shaded areas indicate the percentages of isolates with MICs greater than the highest tested concentrations. Numbers listed for the lowest tested concentrations represent the precentages of isolates with MICs equal to or less than the lowest tested concentration. CLSI breakpoints were used when available.

Table 5.8: Percentage and number of *Campylobacter coli* isolates resistant to antimicrobial agents, 1997–2004

Year Total Isolates		1997 6	1998 8	1999 20	2000 12	2001 17	2002 25	2003 22	2004 26
Subclass	Antibiotic (Resistance breakpoint)								
Aminoglycosides	Gentamicin (MIC ≥ 8)	Not Tested	0.0% 0	0.0% 0	8.3% 1	0.0% 0	0.0% 0	4.5% 1	0.0% 0
Lincosamides	Clindamycin (MIC ≥ 8)	16.7% 1	12.5% 1	10.0% 2	8.3% 1	5.9% 1	4.0% 1	9.1% 2	0.0% 0
Macrolides	Azithromycin (MIC ≥ 8)	Not Tested	12.5% 1	10.0% 2	8.3% 1	5.9% 1	4.0% 1	9.1% 2	0.0% 0
	Erythromycin (MIC ≥ 32)	0.0% 0	12.5% 1	10.0% 2	8.3% 1	5.9% 1	4.0% 1	9.1% 2	0.0% 0
Phenicols	Chloramphenicol (MIC ≥ 32)	50.0% 3	37.5% 3	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0	0.0% 0
Quinolones	Ciprofloxacin (MIC ≥ 4)	33.3% 2	0.0% 0	30.0% 6	25.0% 3	47.1% 8	12.0% 3	22.7% 5	30.8% 8
	Nalidixic acid (MIC ≥ 64)	50.0% 3	50.0% 4	30.0% 6	25.0% 3	47.1% 8	12.0% 3	22.7% 5	34.6% 9
Tetracyclines	Tetracycline (MIC ≥ 16)	66.7% 4	50.0% 4	30.0% 6	25.0% 3	58.8% 10	40.0% 10	45.5% 10	38.5% 10

Limitations to NARMS Campylobacter *Surveillance*

Three limitations are evident in NARMS *Campylobacter* surveillance; the use of sentinel clinical laboratories in some states, the sampling scheme, and the limited geographic area under surveillance. In four states that participated in NARMS *Campylobacter* surveillance during 2004 (California, Colorado, Connecticut, and Oregon), *Campylobacter* isolates were submitted to NARMS from one sentinel clinical laboratory. In Georgia, Maryland, Minnesota, New Mexico, New York, and Tennessee, the *Campylobacter* isolates submitted were selected from all *Campylobacter* isolates from most clinical laboratories within a specific geographic area (metro Atlanta area in Georgia; statewide in Maryland, Minnesota, New Mexico, and Tennessee; and the metro Albany and Rochester areas in New York). In California, Colorado, Connecticut, and Oregon, the sentinel clinical laboratory selected the first *Campylobacter* isolate isolated each week for submission to NARMS; if no isolate was isolated in a week, then no isolate was submitted from that laboratory. Because none of the sentinel clinical laboratories used an isolation procedure that was more or less likely than the procedure of other clinical laboratories in their respective states to yield antimicrobial-resistant *Campylobacter* isolates, use of a sentinel clinical laboratory is unlikely to be associated with a change of antimicrobial resistance among *Campylobacter* isolates submitted to NARMS.

In 2004, the NARMS participating public health laboratories in Georgia, Maryland, Minnesota, New Mexico, New York, and Tennessee, and sentinel clinical laboratories in all other FoodNet sites, selected one *Campylobacter* isolate each week and forwarded the isolate to CDC. When the isolates were selected, the antimicrobial resistance pattern of the isolates was not known. Therefore, the antimicrobial resistance pattern of an isolate is unlikely to influence submission of the isolate to NARMS. However, the one-a-week sampling scheme could result in oversampling or undersampling of antimicrobial-resistant isolates if the prevalence of such resistance is not uniform throughout the year. The impact of oversampling or undersampling can vary among states.

Campylobacter isolates were forwarded to CDC by 10 states participating in FoodNet during 2004, representing approximately 45 million persons (15% of the U.S. population). Because NARMS 2004 *Campylobacter* surveillance was not nationwide, generalization of findings to the U.S. population should be done with caution because of possible regional differences in the prevalence of antimicrobial resistance among *Campylobacter*.

6. SUMMARY OF LONG-TERM CHANGES

Non-Typhi *Salmonella*, 1979–2004

For non-Typhi *Salmonella*, sentinel counties were surveyed during 1979–80, 1984–85, 1989–90, and 1994–95.[8-11] CDC tested isolates by disk diffusion. NARMS began testing *Salmonella* in 1996 with 14 participating sites, and by 2003 had expanded nationwide. From 1996 to 2002, participating sites forwarded every 10th non-Typhi *Salmonella* received at their public health laboratories to CDC. Since 2003, sites have forwarded every 20th isolate. In 2004, isolates were tested by broth microdilution to determine minimal inhibitory concentrations (MICs) to 15 antimicrobial agents.

During the last quarter-century, resistance among non-Typhi *Salmonella* has increased to a number of clinically important antimicrobial agents (Figures 6.1 and 6.2). Resistance to ampicillin and trimethoprim-sulfamethoxazole increased first, reaching 20.7% and 3.9%, respectively, in 1996. Resistance to third-generation cephalosporins (e.g., ceftriaxone) and quinolones (e.g., nalidixic acid) and ACSSuT increased more recently.

A public health concern raised by this resistance is loss of efficacious agents to treat serious *Salmonella* infections, especially in children. The clinical implications of current resistance levels are potential treatment failure, increased duration of illness, and increased length of hospitalization.[10,12,13] For more information about treatment of *Salmonella* see *Diagnosis and Management of Foodborne Illness: A Primer for Physicians*.[14]

Figure 6.1: Sentinel county studies: 1979–1980, 1984–1985, 1989–1990, and 1994–1995

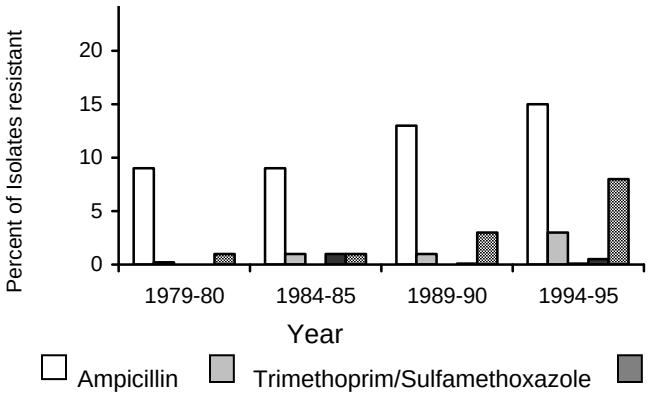
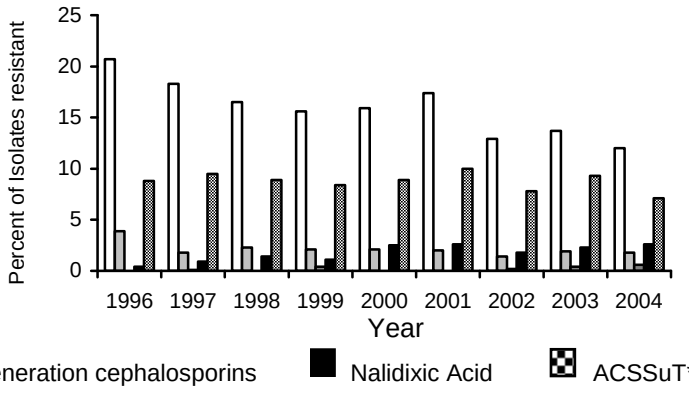
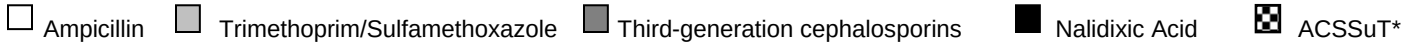


Figure 6.2: NARMS: 1996–2004





*ACSSuT = resistance to ampicillin, chloramphenicol, streptomycin, sulfamethoxazole, and tetracycline

Campylobacter jejuni, 1989–2004

For *Campylobacter jejuni*, sentinel counties were surveyed during 1989–90.[15] Isolates were received and tested at CDC. NARMS began testing *Campylobacter* in 1997 with five participating sites in 1997, seven in 1998, eight in 1999, nine in 2000–2002, and 10 in 2003–2004. In 2004, one *Campylobacter* isolate per week was forwarded to CDC and tested by E-test to determine MICs to eight antimicrobial agents.

During the last 16 years, *C. jejuni* resistance to a number of clinically important antimicrobial agents has changed (Figures 6.3 and 6.4). Resistance to tetracycline was already 42% in 1989–90 and has declined in more recent years. Resistance to ciprofloxacin has increased. No isolates resistant to ciprofloxacin were identified in 1989–90; 12.4% were resistant in 1997, 20.7% in 2002, 17.2% in 2003, and 18.1% in 2004. Using the new CLSI interpretive criteria for macrolides, resistance to erythromycin remained low, at less than 2% from 1997 to 2004. Because poultry is the primary reservoir for *C. jejuni*, this increasing ciprofloxacin resistance is likely to be related to use of fluoroquinolones, which in 1995 were approved for use in poultry farming. This resistance raised public health concern because of the threat it posed to the efficacy of fluoroquinolones for treating campylobacteriosis. The clinical implications of resistance to fluoroquinolones include increased duration of illness and potential treatment failure.[16] For more information about treatment of *Campylobacter*, see *Diagnosis and Management of Foodborne Illness: A Primer for Physicians*.[14]

Figure 6.3: Sentinel county study: 1989–90

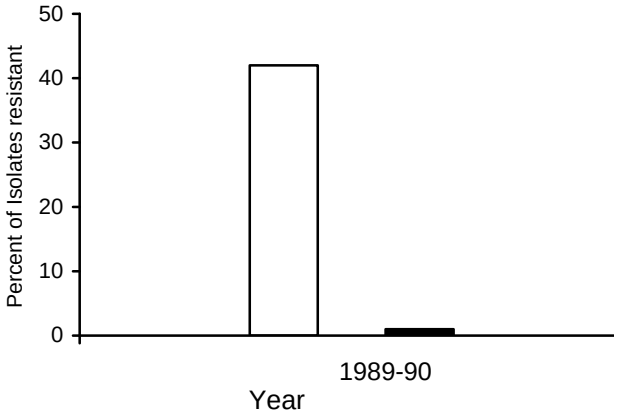
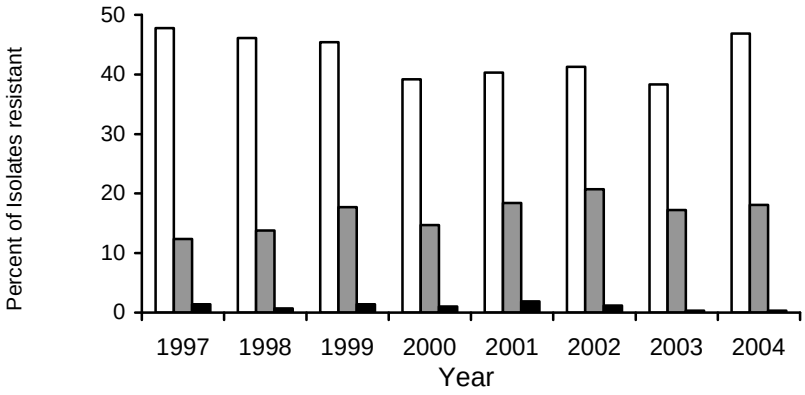
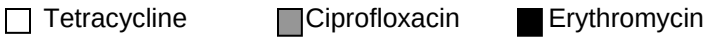


Figure 6.4: NARMS: 1997–2004





***Shigella*, 1985–2004**

For *Shigella*, sentinel counties were surveyed during 1985–86 and 1995–96.[17,18] Isolates were received and tested at CDC. Since NARMS began testing *Shigella* in 1999, every 10th *Shigella* isolate received at participating state public health laboratories was forwarded to CDC during 1999–2002 and every 20th isolate during 2003–2004. In 2004, isolates were tested by broth microdilution to determine MICs to 15 antimicrobial agents.

During the last 19 years, resistance among *Shigella* isolates has increased to a number of clinically important antimicrobial agents (Figures 6.5 and 6.6). Resistance to ampicillin, already 32% in 1985–86, increased to 67% by 1995. Resistance to nalidixic acid emerged more recently. One *Shigella* isolate resistant to nalidixic acid was identified during 1985–86. The percentage of *Shigella* isolates resistant to nalidixic acid increased to nearly 2% in 1999 but has remained at 2% or less. One isolate was resistant to ciprofloxacin in 2001. One ceftriaxone-resistant isolate was noted in 2004.

Because *Shigella* has no environmental or animal reservoir except humans, this resistance probably is related to the use of antimicrobials in human medicine. A public health concern raised by these resistances is the loss of efficacious agents to treat *Shigella* infections. The clinical implication of current resistance levels is potential treatment failure. This may be particularly important for infections related to international travel.[17,19] For more information about treatment of *Shigella*, see *Diagnosis and Management of Foodborne Illness: A Primer for Physicians*.[14]

Figure 6.5: Sentinel county studies: 1985–86 and 1995–96

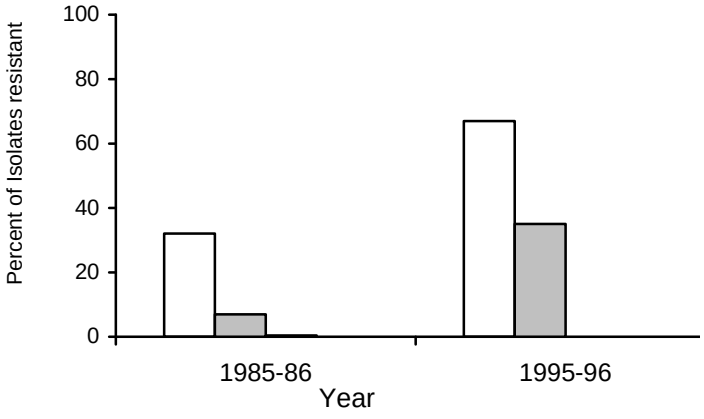
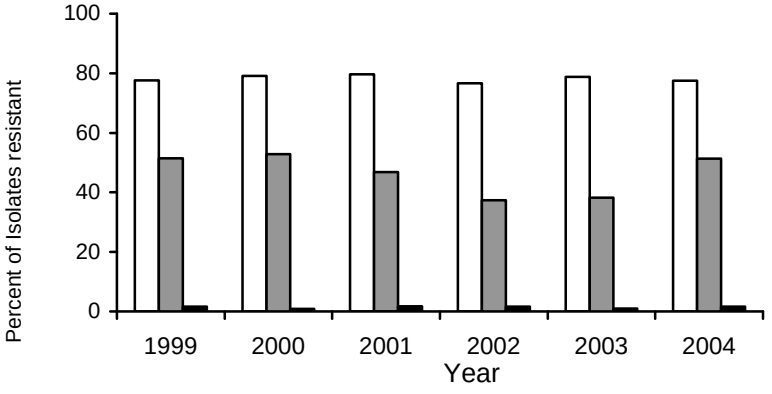


Figure 6.6: NARMS: 1999–2004



7. SUMMARY OF ENTEROCOCCI RESISTANCE SURVEILLANCE, 2004

Enterococci Working Group

Centers for Disease Control and Prevention

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INTRODUCTION

Enterococci are gram-positive cocci whose major habitat is the gastrointestinal tract of humans and other animals. Intestinal carriage of resistant enterococci in humans results is associated with hospitalization and antimicrobial use. However, carriage of enterococci resistant to certain antimicrobial agents has been documented among persons who have not been hospitalized or recently taken antimicrobial agents, suggesting a community source. Antimicrobial agents commonly are used for growth promotion, disease prevention, and therapy in food animals, such as chickens and pigs. Such use results in the selection of resistant enterococci in the intestinal tracts of animals, suggesting that use of antimicrobial agents in food animals creates selective pressure on enterococci among food animals and ultimately might contribute to the pool of resistant enterococci among humans. Therefore, monitoring resistance in commensals is important to determine the role of these bacteria as reservoirs of resistance determinants for human pathogens. The Enterococci Resistance Surveillance project was designed to determine the prevalence of clinically important antimicrobial-resistant enterococci in stool samples among persons in the community.

SUMMARY OF 2004 SURVEILLANCE DATA

Background

Enterococci resistance study began in 2001 to prospectively monitor the prevalence of antimicrobial resistance of human enterococci isolates from stool samples. The study includes five sites: Georgia, Maryland, Michigan, Minnesota, and Oregon.

Multidrug-resistant enterococci

- Multidrug resistance is described in NARMS by the number of antimicrobial subclasses or specific co-resistance phenotypes. Antimicrobial subclasses are used as defined by CLSI.
- 99.3% of *Enterococcus faecium* and 98.1% of *Enterococcus faecalis* isolates tested were resistant to two or more CLSI subclasses.
- 17.8% of *E. faecium* and 30.2% of *E. faecalis* isolates tested were resistant to five or more CLSI subclasses.

Clinically Important Resistance

The number of antimicrobial agents available to treat serious enterococcal infections in humans is limited, in part because of the intrinsic resistance of enterococci to many antimicrobials and the ease with which the bacteria acquire resistance. Concern exists that currently available antimicrobial agents also progressively are losing effectiveness because of resistance, complicating treatment or presenting with serious enterococci infection. In particular, resistance has developed to gentamicin, penicillin, quinupristin-dalfopristin (Synercid®), and vancomycin.

- 1.5% of *E. faecium* isolates and 6.2% of *E. faecalis* isolates were resistant to gentamicin.
- 5.9% of *E. faecium* isolates and 1.2% of *E. faecalis* isolates were resistant to penicillin.
- 3.7% of *E. faecium* isolates were resistant to quinupristin-dalfopristin. *E. faecalis* was not reported because of intrinsic resistance.
- 0.7% of *E. faecium* isolates were resistant to vancomycin. No *E. faecalis* isolates were resistant to vancomycin.

SURVEILLANCE AND LABORATORY TESTING METHODS

Stool samples from outpatients with diarrhea and healthy volunteers were collected by laboratories in Georgia, Maryland, Michigan, Minnesota, and Oregon. All presumptive enterococci were submitted to the NARMS lab for species identification and antimicrobial susceptibility testing. Ten stool samples per month were requested.

Predominant Enterococci

Predominant enterococci were selected by mixing 0.5 grams of each stool in 5 mL of bile-esculin azide broth and incubating at 35–37°C for 48 hours. After incubation, 10 μL from a black culture was streaked onto Columbia CNA[20] with 5% sheep blood and incubated at 35–37°C for 24 hours. A predominant colony with typical enterococci morphology were Gram stained and L-pyrrolidonyl-β-naphthylamide (PYR) spot-tested.

Enrichment for Vancomycin-Resistant Enterococci

Vancomycin-resistant enterococci (VRE) were selected as above with the addition of 10 μg/mL vancomycin and 10 μg/mL aztreonam to the bile-esculin azide broth. After incubation, 10 μl from a black culture was streaked onto Modified Ford agar[21] supplemented with 10 g/mL raffinose and incubated at 35–37 C for 24 hours. A red colony characteristic of *E. faecium* and *E. faecalis* (raffinose nonfermenters) were Gram stained and PYR spot-tested.

Enterococcus Species Identification and Antimicrobial Susceptibility Testing

On arrival at CDC, isolates were subcultured on trypticase soy agar at least two times to obtain isolated single colonies. All incubations were performed at 35° ± 1°C. A pure culture was selected for definitive identification, antimicrobial susceptibility testing, and freezing at –70°C for archival purposes. Enterococci were identified to the species level according to standard biochemical methods.[22] Antimicrobial susceptibility was tested by microbroth dilution using a custom Sensititre® panel, according to the manufacturer's instructions (Trek Diagnostics, Cleveland, OH). MICs of antimicrobials were read manually using the Sensititre® Sensitouch™ system in 2001. In 2002 and 2003, susceptibility results were read and interpreted using an automated system, ARIS™ by Trek Diagnostics. *Staphylococcus aureus* ATCC 29213, *Escherichia coli* ATCC 25922, *E. faecalis* ATCC 29212, and *E. faecalis* ATCC 51299 were used as quality controls for *Enterococcus* susceptibility testing according to CLSI guidelines.[1] MICs were determined for 17 antimicrobial agents: bacitracin, chloramphenicol, ciprofloxacin, daptomycin, erythromycin, flavomycin, gentamicin, kanamycin, lincomycin, linezolid, nitrofurantoin, penicillin, streptomycin, quinupristin/dalfopristin, tetracycline, tylosin, and vancomycin (Table 7.1).

Where established, CLSI interpretive criteria were used (Table 7.1). The 95% CIs for the percentage of resistant isolates calculated using the Clopper-Pearson exact method are included in the MIC distribution tables.[6] Similarly, multidrug resistance by CLSI antimicrobial subclass was defined as resistance two or more subclasses.

RESULTS

Predominant Enterococci

In 2004, CDC received 479 enterococci isolates, of which 474 (98.9%) were viable and tested for antimicrobial susceptibility (Table 7.2). Of the enterococci isolates tested, 54.4% (258/474) were *E. faecalis,* and 28.5% (135/474) were *E. faecium* (Table 7.3).

MICs for *E. faecium, E. faecalis*, and other enterococci species were determined for each of the 17 antimicrobial agents from 2004 (Table 7.4). Resistance to specific antimicrobial agents also was determined (Table 7.5).

E. faecium

Of the *E. faecium* isolates, 1.5% were resistant to gentamicin in 2004. Resistance to penicillin was 5.9% (Table 7.5), and resistance to quinupristin/dalfopristin was 3.7%. Vancomycin resistance among *E. faecium* isolates was 0.7% (Table 7.5).

E. faecalis

Of the *E. faecalis* isolates, 6.2% were resistant to gentamicin. Resistance to penicillin was 1.2% and 58.1% to tetracycline (Table 7.5).

In 2004, 99.3% of *E. faecium* isolates were resistant to two or more CLSI subclasses, and 17.8% were resistant to five or more CLSI subclasses (Table 7.6). *E. faecalis* isolates resistant to two or more CLSI subclasses was 98.1%, and resistance to five or more CLSI subclasses was 30.2% (Table 7.6).

Enrichment for Vancomycin-Resistant Enterococci (VRE)

In 2004, specimens from 13 patients yielded enterococci growth on VRE media. CDC received these isolates and tested them for antimicrobial susceptibility. Two isolates were confirmed *E. faecalis*, and neither were confirmed resistant to vancomycin. Five isolates were confirmed *E. faecium*, of which four were confirmed resistant to vancomycin.

Table 7.1: Antimicrobial agents used for susceptibility testing of Enterococci, NARMS, 2004

CLSI Subclass	Antimicrobial Agent	Antimicrobial Agent Concentration Range (µg/mL)	Breakpoints			Source of MIC
			Resistant	Intermediate	Susceptible	
Aminoglycoside	Gentamicin	128 - 1024	≥500		≤256	CLSI
	Kanamycin	128 - 1024	≥2048		≤1024	DanMap
	Streptomycin	512 - 2048	≥1000		≤512	CLSI
Glycopeptide	Vancomycin	0.5 - 32	32	8-16	≤4	CLSI
Lincosamides	Lincomycin	1 - 32	≥8		≤4	CASFM
Lipopeptides	Daptomycin	0.5 - 16	≥8		≤4	CLSI
Macrolide	Erythromycin	0.5 - 8	≥8	1-4	≤0.5	CLSI
	Tylosin	0.25 - 32	≥8		≤4	DanMap
Nitrofuran	Nitrofurantoin	2 - 64	≥128	64	≤32	CLSI
Oxazolidinones	Linezolid	0.5 - 8	≥8	4	≤2	CLSI
Penicillin	Penicillin	0.5 - 16	≥16		≤8	CLSI
Phenicol	Chloramphenicol	2 - 32	≥32	16	≤8	CLSI
Phosphoglycolipid	Flavomycin	1 - 32	≥16		≤8	DanMap
Polypeptide	Bacitracin	8 - 128	≥64		≤32	NORM-VET
Quinolone	Ciprofloxacin	0.12 - 4	≥4	2	≤1	CLSI
Streptogramin	Synercid QD	1 - 32	≥4	2	≤1	CLSI
Tetracycline	Tetracycline	4 - 32	≥16	8	≤4	CLSI

Table 7.2: Frequency of Enterococci isolated by site, NARMS, 2004

Site	2004 N	(%)
Georgia	78	(16.5%)
Maryland	99	(20.9%)
Michigan	111	(23.4%)
Minnesota	107	(22.6%)
Oregon	79	(16.7%)
Total	**474**	**(100.0%)**

Table 7.3: Enterococci speciation for isolates received in NARMS, 2004

Species	2004 N	(%)
Enterococcus faecalis	258	(54.4%)
Enterococcus faecium	135	(28.5%)
Enterococcus avium	31	(6.5%)
Enterococcus durans	14	(3.0%)
Enterococcus casseliflavus	9	(1.9%)
Enterococcus hirae	8	(1.7%)
Enterococcus raffinosus	6	(1.3%)
Enterococcus gallinarum	5	(1.1%)
Enterococcus spp.	4	(0.8%)
Enterococcus pseudoavium	3	(0.6%)
Enterococcus sanguinicola	1	(0.2%)
Total	**474**	**(100.0%)**

Table 7.4: Minimum inhibitory concentrations (MICs) and resistance of Enterococcus isolates to antimicrobial agents, 2004 (N=474)

Antibiotic		Species*	% of isolates			Percent of all isolates with MIC (µg/mL)¶														
			%I†	%R‡	[95% CI]§	0.12	0.25	0.5	1	2	4	8	16	32	64	128	256	512	1024	2048	4096
Aminoglycosides		ENTFM	NA	1.5	[0.2–5.3]											96.3	2.2	0.7		0.7	
	Gentamicin	ENTFS	NA	6.2	[3.6–9.9]											92.2	1.6	1.6	0.4	4.3	
		OTHER	NA	1.2	[0.0–6.8]											98.8			1.2		
		ENTFM	NA	2.2	[0.5–6.4]											73.3	22.2	2.2		2.2	
	Kanamycin	ENTFS	NA	17.8	[13.4–23.1]											79.8	2.3			17.8	
		OTHER	NA	2.5	[0.3–8.7]											96.3	1.2			2.5	
		ENTFM	NA	0.7	[0.0–4.1]													99.3		0.7	
	Streptomycin	ENTFS	NA	11.7	[8.0–16.2]													88.3	3.1	4.3	4.3
		OTHER	NA	11.1	[5.3–20.3]													88.9	1.2	8.6	1.2
		ENTFM	0.0	0.7	[0.0–4.1]			80.0	14.8	4.4					0.7						
Glycopeptides	Vancomycin	ENTFS	0.0	0.0	[0.0–1.4]			0.4	54.7	39.5	5.4										
		OTHER	3.7	0.0	[0.0–4.5]			65.4	17.3		13.6	2.5	1.2								
		ENTFM	NA	73.3	[64.8–80.4]				18.5	2.2	5.9	20.0	38.5	8.1	6.7						
Lincosamides	Lincomycin	ENTFS	NA	98.1	[95.5–99.4]						1.9	4.3	44.2	26.4	23.3						
		OTHER	NA	82.7	[72.4–90.1]				7.4		9.9	48.1	28.4		6.2						
		ENTFM	0.0	8.9	[4.7–15.1]			5.9	5.2	21.5	58.5	8.9									
Lipopeptides	Daptomycin	ENTFS	0.0	0.0	[0.0–1.4]			24.8	67.8	7.4											
		OTHER	0.0	1.2	[0.0–6.8]			40.7	34.6	11.1	12.3	1.2									
Macrolides		ENTFM	66.7	12.6	[7.6–19.5]			20.7	18.5	22.2	25.9	8.9	3.7								
	Erythromycin	ENTFS	41.1	25.2	[20.0–31.0]			33.7	34.5	5.0	1.6	2.7	22.5								
		OTHER	25.9	18.5	[9.9–27.6]			55.6	17.3	2.5	6.2	3.7	14.8								
		ENTFM	NA	37.8	[29.1–46.1]			0.7	9.6	19.3	32.6	27.4	7.4	0.7	2.2						
	Tylosin	ENTFS	NA	25.6	[20.4–31.4]				19.8	50.8	3.9	0.4	0.8		24.4						
		OTHER	NA	9.9	[4.4–18.8]		1.2	3.7	23.5	40.7	21.0	1.2			8.6						
		ENTFM	76.3	3.0	[0.5–6.4]							0.7	4.4	15.6	76.3	3.0					
Nitrofurans	Nitrofurantoin	ENTFS	0.0	0.0	[0.0–1.4]						1.9	59.7	35.7	2.7							
		OTHER	40.7	14.8	[8.0–24.7]						4.9	9.9	8.6	21.0	40.7	14.8					
		ENTFM	3.0	0.7	[0.0–2.7]			2.2	49.6	44.4	3.0	0.7									
Oxazolidinones	Linezolid	ENTFS	2.3	0.4	[0.0–2.1]			1.9	77.1	18.2	2.3	0.4									
		OTHER	2.5	1.2	[0.0–6.8]			18.5	27.2	50.6	2.5	1.2									
		ENTFM	NA	5.9	[2.1–10.5]			9.6	10.4	28.1	33.3	12.6	0.7	5.2							
Penicillins	Penicillin	ENTFS	NA	1.2	[0.2–3.4]			0.4		24.8	54.3	19.4	1.2								
		OTHER	NA	3.7	[0.8–10.6]			27.2	17.3	40.7	11.1		1.2	2.5							
		ENTFM	1.5	1.5	[0.2–5.3]					1.5	71.9	23.7	1.5	1.5							
Phenicols	Chloramphenicol	ENTFS	0.8	6.6	[3.9–10.3]					0.8	52.3	39.5	0.8	3.9	2.7						
		OTHER	2.5	7.4	[2.8–15.6]					14.8	38.3	37.0	2.5		7.4						
		ENTFM	NA	94.1	[88.6–97.4]					1.5	1.5	3.0	3.0	4.4	86.7						
Phosphoglycolipid	Flavomycin	ENTFS	NA	6.2	[3.6–9.9]				5.0	86.8	1.2	0.8	1.6	0.4	4.3						
		OTHER	NA	49.4	[38.6–61.4]				2.5	19.8	22.2	6.2	4.9	2.5	42.0						
		ENTFM	NA	91.1	[84.9–95.3]							3.0	0.7	5.2	25.9	52.6	12.6				
Polypeptide	Bacitracin	ENTFS	NA	92.2	[88.3–95.2]								1.2	6.6	27.5	54.7	10.1				
		OTHER	NA	84.0	[73.8–91.1]							4.9	6.2	4.9	29.6	46.9	7.4				
		ENTFM	18.5	20.0	[13.7–27.9]			14.1	47.4	18.5	13.3	6.7									
Quinolones	Ciprofloxacin	ENTFS	16.3	5.0	[2.7–8.5]			11.6	67.1	16.3		5.0									
		OTHER	33.3	9.9	[4.4–18.8]	1.2	4.9	19.8	30.9	33.3	1.2	8.6									
		ENTFM	53.3	3.7	[1.2–8.5]				43.0	53.3	0.7	0.7		1.5	0.7						
Streptogramins	Synercid QD	ENTFS**	NA	NA	NA																
		OTHER	21.0	3.7	[0.8–10.6]				75.3	21.0	1.2	1.2		1.2							
		ENTFM	3.0	24.4	[17.6–32.8]						72.6	3.0	5.2		19.3						
Tetracyclines	Tetracycline	ENTFS	1.6	58.1	[51.9–64.2]						40.3	1.6	6.6	36.8	14.7						
		OTHER	3.7	46.9	[35.0–57.8]						49.4	3.7	6.2	23.5	17.3						

*ENTFM: *Enterococcus faecium* (n=135), ENTFS: *Enterococcus faecalis* (n=258), OTHER: all other *Enterococcus* spp. (n=81)

†Percent of isolates with intermediate susceptibility, NA if no MIC range of intermediate susceptibility exists

‡Percent of isolates that were resistant

§95% confidence intervals (CI) for percent resistant (%R) were calculated using the Clopper-Pearson exact method

¶The unshaded areas indicate the dilution range of the Sensititre plates used to test isolates. Single vertical bars indicate the breakpoints for susceptibility, while double vertical bars indicate breakpoints for resistance. Numbers in the shaded areas indicate the percentages of isolates with MICs greater than the highest concentrations on the Sensititre plate. Numbers listed for the lowest tested concentrations represent the precentages of isolates with MICs equal to or less than the lowest tested concentration. CLSI breakpoints were used when available.

**Intrinsic resistance to Quinipristin-Dalfopristin

Table 7.5: Minimum inhibitory concentrations (MICs) and resistance of enterococci, by species, to antimicrobial agents, 2001–2004

Species		ENTFM*				ENTFS†				OTHER‡			
Year		2001	2002	2003	2004	2001	2002	2003	2004	2001	2002	2003	2004
Total Isolates		234	172	165	135	315	219	247	258	61	57	58	81
Subclass	Antibiotic (Resistance breakpoint)												
Aminoglycosides	Gentamicin	1.7%	0.6%	0.0%	1.5%	5.7%	6.4%	2.0%	6.2%	1.6%	0.0%	0.0%	1.2%
	(MIC >500)	4	1	0	2	18	14	5	16	1	0	0	1
	Kanamycin	8.5%	9.3%	2.4%	2.2%	14.9%	14.2%	8.9%	17.8%	4.9%	8.8%	3.4%	2.5%
	(MIC ≥2048)	20	16	4	3	47	31	22	46	3	5	2	2
	Streptomycin	4.3%	7.0%	2.4%	0.7%	14.6%	10.0%	7.7%	11.6%	11.5%	8.8%	3.4%	11.1%
	(MIC >1000)	10	12	4	1	46	22	19	30	7	5	2	9
Glycopeptides	Vancomycin	1.7%	2.3%	0.0%	0.7%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
	(MIC ≥32)	4	4	0	1	0	0	0	0	0	0	0	0
Ionophore coccidiostat	Salinomycin	0.0%	0.6%	0.0%	Not	0.0%	0.0%	0.0%	Not	0.0%	1.8%	0.0%	Not
	(MIC ≥16)	0	1	0	Tested	0	0	0	Tested	0	1	0	Tested
Lincosamides	Lincomycin	75.6%	69.8%	73.9%	73.3%	95.6%	98.6%	98.4%	98.1%	78.7%	86.0%	74.1%	82.7%
	(MIC ≥8)	177	120	122	99	301	216	243	253	48	49	43	67
Lipopeptides	Daptomycin	Not	Not	Not	8.9%	Not	Not	Not	0.0%	Not	Not	Not	1.2%
	(MIC ≥8)	Tested	Tested	Tested	12	Tested	tested	tested	0	Tested	Tested	Tested	1
Macrolides	Erythromycin	7.3%	15.1%	10.3%	12.6%	24.4%	19.2%	22.7%	25.2%	21.3%	21.1%	10.3%	18.5%
	(MIC ≥8)	17	26	17	17	77	42	56	65	13	12	6	15
	Tylosin	23.5%	20.3%	6.7%	37.8%	23.8%	20.1%	22.7%	25.6%	13.1%	10.5%	6.9%	9.9%
	(MIC ≥8)	55	35	11	51	75	44	56	66	8	6	4	8
Nitrofurans	Nitrofurantoin	14.1%	2.9%	0.0%	3.0%	0.3%	0.5%	0.0%	0.0%	13.1%	0.0%	0.0%	14.8%
	(MIC ≥128)	33	5	0	4	1	1	0	0	8	0	0	12
Oxazolidinones	Linezolid	0.0%	0.0%	0.0%	0.7%	0.0%	0.0%	0.0%	0.4%	0.0%	0.0%	0.0%	1.2%
	(MIC ≥8)	0	0	0	1	0	0	0	1	0	0	0	1
Penicillins	Penicillin	4.3%	7.6%	10.3%	5.9%	0.0%	2.3%	0.4%	1.2%	4.9%	8.8%	8.6%	3.7%
	(MIC ≥16)	10	13	17	8	0	5	1	3	3	5	5	3
Phenicols	Chloramphenicol	1.7%	0.0%	0.0%	1.5%	6.0%	7.3%	2.0%	6.6%	1.6%	0.0%	0.0%	7.4%
	(MIC ≥32)	4	0	0	2	19	16	5	17	1	0	0	6
Phosphoglycolipid	Flavomycin	79.9%	90.1%	90.3%	94.1%	2.5%	0.5%	0.0%	6.2%	42.6%	35.1%	50.0%	49.4%
	(MIC ≥16)	187	155	149	127	8	1	0	16	26	20	29	40
Polypeptide	Bacitracin	92.3%	93.6%	92.7%	91.1%	84.4%	90.4%	96.0%	92.2%	83.6%	87.7%	89.7%	84.0%
	(MIC ≥64)	216	161	153	123	266	198	237	238	51	50	52	68
Quinolones	Ciprofloxacin	15.0%	12.2%	18.2%	20.0%	4.4%	4.6%	3.2%	5.0%	1.6%	0.0%	1.7%	9.9%
	(MIC ≥4)	35	21	30	27	14	10	8	13	1	0	1	8
Streptogramins	Quinupristin-Dalfopristin	20.9%	2.3%	3.6%	3.7%	Not	Not	Not	Not	8.2%	3.5%	3.4%	3.7%
	(MIC ≥4)	49	4	6	5	Reported§	Reported§	Reported§	Reported§	5	2	2	3
	Virginiamycin	0.9%	Not	Not	Not	11.1%	Not	Not	Not	0.0%	Not	Not	Not
	(MIC ≥8)	2	Tested	Tested	Tested	35	Tested	Tested	Tested	0	Tested	Tested	Tested
Tetracyclines	Tetracycline	21.4%	18.0%	15.2%	24.4%	56.8%	57.5%	55.1%	58.1%	42.6%	47.4%	22.4%	46.9%
	(MIC ≥16)	50	31	25	33	179	126	136	150	26	27	13	38

*ENTFM = *Enterococcus faecium*

†ENTFS = *Enterococcus faecalis*

‡OTHER = *Enterococcus* spp.

§Intrinsic resistance to quinupristin-dalfopristin

Table 7.6: Resistance of enterococci, by species, to antimicrobial agents, 2001–2004

Species	ENTFM*				ENTFS†				OTHER‡			
Year	2001	2002	2003	2004	2001	2002	2003	2004	2001	2002	2003	2004
Total Isolates	234	172	165	135	315	219	247	258	61	57	58	81
	%	%	%	%	%	%	%	%	%	%	%	%
	n	n	n	n	n	n	n	n	n	n	n	n
No resistance detected	0.9%	1.7%	0.0%	0.0%	0.3%	0.5%	0.0%	0.0%	1.6%	0.0%	1.7%	1.2%
	2	3	0	0	1	1	0	0	1	0	1	1
Resistance ≥1CLSI subclass§	99.1%	98.3%	100.0%	100.0%	99.7%	99.5%	100.0%	100.0%	98.4%	100.0%	98.3%	98.8%
	232	169	165	135	314	218	247	258	60	57	57	80
Resistance ≥2 CLSI subclasses§	97.4%	96.5%	97.0%	99.3%	95.6%	96.8%	97.6%	98.1%	96.7%	98.2%	89.7%	92.6%
	228	166	160	134	301	212	241	253	59	56	52	75
Resistance ≥3 CLSI subclasses§	86.3%	80.2%	73.9%	83.7%	84.8%	84.5%	90.3%	90.7%	70.5%	61.4%	56.9%	74.1%
	202	138	122	113	267	185	223	234	43	35	33	60
Resistance ≥4 CLSI subclasses§	47.4%	38.4%	30.9%	48.1%	56.8%	50.2%	54.7%	58.5%	32.8%	28.1%	13.8%	38.3%
	111	66	51	65	179	110	135	151	20	16	8	31
Resistance ≥5 CLSI subclasses§	19.7%	11.6%	9.1%	17.8%	30.5%	21.5%	23.1%	30.2%	14.8%	12.3%	6.9%	16.0%
	46	20	15	24	96	47	57	78	9	7	4	13

*ENTFM = *Enterococcus faecium*

†ENTFS = *Enterococcus faecalis*

‡OTHER = *Enterococcus* spp.

§CLSI: Clinical and Laboratory Standards Institute

Molecular Characterization of Vancomycin-resistant enterococci isolated from persons in the community in the United States, 2001-2004

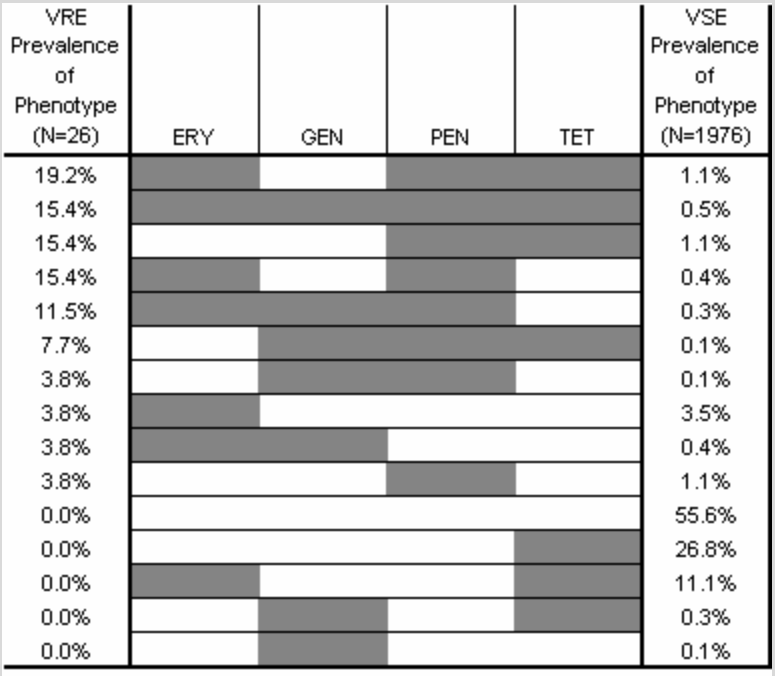
Vancomycin-resistant enterococci (VRE), a major cause of nosocomial infection, were isolated first in Europe in 1986 and in the United States in 1987 [Sahm DF, Kissinger J, Gilmore MS, et al. *In vitro* susceptibility studies of vancomycin-resistant *Enterococcus faecalis*. Antimicrob Agents Chemother 1989;33:1588–91]. Avoparcin, a glycopeptide related to vancomycin, was used for growth promotion of food animals in Europe during 1975–1997 [Casewell M, Friis C, Marco E,et al. The European ban on growth-promoting antibiotics and emerging consequences for human and animal health. Antimicrob Agents Chemother 2003;52:159–61]. The use of avoparcin in food animals resulted in a reservoir of VRE in food animals, and after transmission of VRE through the food supply, a reservoir of VRE in persons in the European community. In the United States, avoparcin was never approved for use in food animals, and confirmed reports of VRE in persons outside of a health-care setting are lacking. An aim of the NARMS Enterococci Resistance Surveillance is to investigate community-associated VRE in the United States.

As part of ongoing surveillance, stool samples from outpatients with diarrhea and healthy volunteers were collected by laboratories in Georgia, Maryland, Michigan, Minnesota, and Oregon. Beginning in 2001, stool samples were tested for enterococci. If present, one enterococci isolated from each sample was susceptibility tested for vancomycin.

VRE (MIC ≥32 mg/L) was screened by polymerase chain reaction (PCR) for *van*A, *van*B, *van*C, and *van*D [Clark NC, Cooksey RC, Hill BC, Swenson JM, Tenover FC. Characterization of glycopeptide-resistant enterococci from U.S. hospitals. Antimicrob Agents Chemother 1993;37:2311–7]. VRE also was tested by PCR for a macrolide-resistance determinant *ermB* [Tait-Kamradt A, Clancy J, Cronan M, et al. mefE is necessary for the erythromycin-resistant M phenotype in *Streptococcus pneumoniae*. Antimicrob Agents Chemother 1997;41:2251–5] and tetracycline resistance determinant *tetM* [Aarestrup FM, Agerso Y, Gerner-Smidt P, Madsen M, Jensen LB. Comparison of antimicrobial resistance phenotypes and resistance genes in *Enterococcus faecalis* and *Enterococcus faecium* from humans in the community, broilers, and pigs in Denmark. Diagn Microbiol Infect Dis 2000;37:127–37].

Of 2483 stool specimens tested during 2001–2004, 2002 (80.6%) yielded enterococci. Of 2002 enterococci isolates tested for susceptibility, 26 (1.3%) of the isolates were VRE, of which 24 (92.3%) were resistant to penicillin; 18 (69.2%), to erythromycin; 15 (57.7%), to tetracycline; and 11 (42.3%), to high-level gentamicin. Of the 23 VRE that were available for further characterization, 22 were *E. faecium* with vancomycin MICs ≥256 mg/L harboring *van*A, and one was *E. faecalis* with a vancomycin MIC of 64 mg/L with *van*B. All erythromycin- and tetracycline-resistant isolates contained *ermB* and *tetM*,, respectively.

Figure 7.1: Prevalence of co-resistant phenotypes among VRE and VSE: erythromycin, gentamicin, penicillin, and tetracycline



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APPENDIX A
SUMMARY OF *ESCHERICHIA COLI* RESISTANCE SURVEILLANCE PILOT STUDY, 2004

***E. COLI* WORKING GROUP**

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INTRODUCTION

Escherichia coli is a gram-negative rod that is part of the intestinal flora of humans and other animals. Because antimicrobial resistance genes commonly reside in mobile genetic elements that can be transferred horizontally to other bacteria, antimicrobial-resistant bacteria of the intestinal flora, including *E. coli*, constitute an important reservoir of resistance genes for pathogenic bacteria of humans and other animals. Furthermore, when introduced into a normally sterile site, *E. coli* is an important cause of infections, including septicemia, urinary tract infections, and wound infections. The human intestinal tract is the predominant source of *E. coli* causing these infections. Antimicrobial resistance among *E. coli* causing such infections complicates treatment options.

The use of antimicrobial agents creates a selective pressure for the emergence and dissemination of resistant bacteria. Use of antimicrobial agents in food animals selects resistant bacteria, including resistant *E. coli* in the intestinal tract of food animals. These resistant bacteria can be transmitted to humans through the food supply.[1,2,3] Therefore, monitoring resistance in *E. coli* isolated from the intestinal flora of humans and animals is important to determining the role of these bacteria as human pathogens and as reservoirs of resistance determinants for human pathogens.[4] The *E. coli* Resistance Surveillance Pilot is designed to determine the prevalence of resistance to clinically important antimicrobial agents among *E. coli* isolated from persons in the community.

SUMMARY OF 2004 SURVEILLANCE DATA

Background

Beginning in 2004, NARMS began to prospectively monitor the prevalence of antimicrobial resistance of *E. coli* isolated from human stool samples in two sites: Maryland and Michigan.

Multidrug-Resistant *E. coli*

- 24.8% of 218 *E. coli* isolates tested were resistant to two or more subclasses of antimicrobial agents.
- 6.9% of 218 *E. coli* isolates tested were resistant to five or more subclasses of antimicrobial agents.

Clinically Important Resistance

Antimicrobial agents commonly used to treat serious *E. coli* infections in humans include third-generation cephalosporins and fluoroquinolones.

- 0.9% of 218 *E. coli* isolates were resistant to ceftiofur (Table A.3).
- 9.3% of 218 *E. coli* isolates were resistant to ciprofloxacin (Table A.3).

SURVEILLANCE AND LABORATORY TESTING METHODS

Participating laboratories in Maryland and Michigan cultured 10 human stool samples each month for *E. coli* using Eosin Methylene Blue agar one *E. coli* isolate, if present, from each stool sample was sent to CDC for susceptibility testing to antimicrobial agents using broth microdilution (Sensititre®) to determine the minimum inhibitory concentration (MIC) for each of 15 antimicrobial agents: amikacin, ampicillin, amoxicillin-clavulanic acid, cefoxitin, ceftiofur, ceftriaxone, chloramphenicol, ciprofloxacin, gentamicin, kanamycin, nalidixic acid, streptomycin, sulfamethoxazole, tetracycline, and trimethoprim-sulfamethoxazole (Table A.1). The resistance breakpoint for amikacin, according to CLSI[5] guidelines, is an MIC of 64 µg/mL.

Interpretive criteria from the Clinical Laboratory and Standards Institute (CLSI) were used (Table A.1). The 95% CIs for the percentage of resistant isolates calculated using the Clopper-Pearson exact method, are included in the MIC distribution tables. Similarly, multiclass resistance by CLSI antimicrobial subclass was defined as resistance to two or more subclasses.

RESULTS

In 2004, CDC received and tested 218 viable *E. coli* isolates (Table A.2). MICs were determined for *E. coli* isolates for 15 antimicrobial agents (Table A.3).

Resistance also was determined to specific antimicrobial agents during 2004 (Table A.4). Of the *E. coli* isolates, 30.1% were resistant to ampicillin; 23.1%, to sulfamethoxazole; 19.0%, to nalidixic acid; and 17.1% to tetracycline (Table A-4).

In 2004, 24.8% of *E. coli* isolates were resistant to two or more CLSI subclasses, and 6.9% were resistant to five or more CLSI subclasses (Table A.5).

There is an apparent difference in the level of resistance among *E. coli* isolates in this study compared with *E. coli* O157 isolates submitted to NARMS in 2004. Because of the different sampling methods employed in this study and NARMS, this observation requires further investigation.

Table A.1: Antimicrobial agents used for susceptibility testing of *Escherichia coli* , NARMS, 2004

CLSI Subclass	Antimicrobial Agent	Antimicrobial Agent Concentration Range (µg/mL)	Breakpoints		
			Resistant	Intermediate	Susceptible
Aminoglycosides	Amikacin*	0.5 – 4*	>64	32	<16
	Gentamicin	0.25 – 16	>16	8	<4
	Kanamycin	8 – 64	>64	32	<16
	Streptomycin	32 – 64	>64		<32
Aminopenicillins	Ampicillin	1 – 32	>32	16	<8
β-lactamase inhibitor combinations	Amoxicillin–Clavulanic acid	1/0.5 – 32/16	>32/16	46/8	<8/4
Cephalosporins (3rd Gen.)	Ceftiofur	0.12– 8	>8	4	<2
	Ceftriaxone	0.25 – 64	>64	16-32	<8
Cephamycins	Cefoxitin	0.5 – 16	>32	16	≤8
Folate pathway inhibitors	Trimethoprim–Sulfamethoxazole	0.12/2.4 – 4/76	>4/76		<2/38
Phenicols	Chloramphenicol	2 – 32	>32	16	<8
Quinolones	Ciprofloxacin	0.015 – 4	>4	2	<1
	Nalidixic acid	0.5 – 32	>32		<16
Sulfonamides	Sulfisoxazole	16 – 512	>512		<256
Tetracyclines	Tetracycline	4 – 16	>16	8	<4

* The resistance breakpoint for amikacin, according to Clinical and Laboratory Standards Institute (CLSI) guidelines, is 64µg/mL. For isolates that grew in all amikacin dilutions on the Sensititre panel (minimum inhibitory concentration [MIC] >4 µg/mL), E-Test (AB BIODISK, Solna, Sweden) was performed in order to determine amikacin MIC. The amikacin E-Test strip range of dilutions is 0.016-256 µg/mL.

Table A.2: Frequency of *Escherichia coli* isolated by site, NARMS, 2004

Site	2004 N	(%)
Maryland	133	(61.0%)
Michigan	85	(39.0%)
Total	**218**	**(100.0%)**

Table A.3: Minimum inhibitory concentrations (MICs) and resistance of *Escherichia coli* isolates to antimicrobial agents, 2004 (N=216)

Antibiotic		% of isolates			Percent of all isolates with MIC (µg/mL)[§]														
		%I[*]	%R[†]	[95% CI][‡]	0.015	0.03	0.06	0.125	0.25	0.50	1	2	4	8	16	32	64	128	256	512
Aminoglycosides	Amikacin	0.0	0.5	[0.0–2.6]						0.9	37.5	54.6	5.6	0.9				0.5		
	Gentamicin	0.0	5.1	[2.2–8.3]					22.2	61.1	11.1	0.5				5.1				
	Kanamycin	0.0	2.8	[0.8–5.3]										94.4	2.8		0.5	2.3		
	Streptomycin	NA	14.4	[9.6–19.2]												85.6	3.7	10.6		
Aminopenicillins	Ampicillin	0.0	30.1	[24.1–36.7]							6.5	38.9	20.4	4.2		1.4	28.7			
β-lactamase inhibitor	Amoxicillin-clavulanic acid	2.3	3.7	[1.6–7.2]							3.7	17.6	45.8	26.9	2.3	3.2	0.5			
Cephalosporins (3rd generation)	Ceftiofur	0.0	0.9	[0.0–2.6]				10.2	69.0	17.6	2.3				0.9					
	Ceftriaxone	0.5	0.5	[0.0–2.6]					97.2	1.9						0.5		0.5		
Cephamycins	Cefoxitin	1.9	3.2	[1.3–6.6]							4.2	31.5	50.9	8.3	1.9	2.8	0.5			
Folate pathway inhibitors	Trimethoprim-sulfamethoxazole	NA	15.7	[11.2–21.3]				73.6	9.3	1.4				15.7						
Phenicols	Chloramphenicol	2.8	1.9	[0.5–4.7]								6.5	62.0	26.9	2.8		1.9			
Quinolones	Ciprofloxacin	0.0	9.3	[5.7–13.9]	79.2	1.9	1.4	4.2	3.7	0.5				9.3						
	Nalidixic Acid	NA	19.0	[14.0–24.9]							15.3	56.5	8.8	0.5		2.3	16.7			
Sulfonamides	Sulfamethoxazole/Sulfisoxazole	NA	23.1	[17.7–29.4]											66.2	10.2	0.5			23.1
Tetracyclines	Tetracycline	0.0	17.1	[12.4–22.8]									82.9			3.2	13.9			

[*]Percent of isolates with intermediate susceptibility, NA if no MIC range of intermediate susceptibility exists

[†]Percent of isolates that were resistant

[‡]95% confidence intervals (CI) for percent resistant (%R) were calculated using the Clopper-Pearson exact method

[§]The unshaded areas indicate the dilution range of the Sensititre plates used to test isolates. Single vertical bars indicate the breakpoints for susceptibility, while double vertical bars indicate breakpoints for resistance. Numbers in the shaded areas indicate the percentages of isolates with MICs greater than the highest concentrations on the Sensititre plate. Numbers listed for the lowest tested concentrations represent the precentages of isolates with MICs equal to or less than the lowest tested concentration. CLSI breakpoints were used when available.

Table A.4: *Escherichia coli* isolates with antimicrobial resistance, 2004

Year		**2004**
Total Isolates		**216**
Subclass	Antibiotic (Resistance breakpoint)	
Aminoglycosides	Amikacin (MIC ≥ 64)	0.5% 1
	Gentamicin (MIC ≥ 16)	4.6% 10
	Kanamycin (MIC ≥ 64)	2.3% 5
	Streptomycin (MIC ≥ 64)	13.9% 30
Aminopenicillins	Ampicillin (MIC ≥ 32)	30.1% 65
β-lactamase inhibitor combinations	Amoxicillin-clavulanic acid (MIC ≥ 32)	3.7% 8
Cephalosporin (1st generation)	Cephalothin (MIC ≥ 32)	Not Tested
Cephalosporins (3rd generation)	Ceftiofur (MIC ≥ 8)	0.5% 1
	Ceftriaxone (MIC ≥ 64)	0.5% 1
Cephamycins	Cefoxitin (MIC ≥ 32)	3.2% 7
Folate pathway inhibitors	Trimethoprim-sulfamethoxazole (MIC ≥ 4)	15.7% 34
Phenicols	Chloramphenicol (MIC ≥ 32)	1.9% 4
Quinolones	Ciprofloxacin (MIC ≥ 4)	9.3% 20
	Nalidixic Acid (MIC ≥ 32)	19.0% 41
Sulfonamides	Sulfamethoxazole/Sulfisoxazole (MIC ≥ 512)	23.1% 50
Tetracyclines	Tetracycline (MIC ≥ 16)	17.1% 37

Table A.5: Antimicrobial agents resistant to *Escherichia coli* , 2004

Year Total Isolates	2004 216
	% n
No resistance detected	55.6% 120
Resistance ≥1CLSI subclass*	45.4% 98
Resistance ≥2 CLSI subclasses*	25.0% 54
Resistance ≥3 CLSI subclasses*	16.2% 35
Resistance ≥4 CLSI subclasses*	9.7% 21
Resistance ≥5 CLSI subclasses*	6.9% 15
At least ACSSuT[†]	1.4% 3
At least ACSuTm[‡]	1.9% 4
At least ACSSuTAuCf[§]	0.0% 0
At least AAuC[¶]	0.0% 0
At least A3C**	0.0% 0
At least MDR-AmpC[††]	0.0% 0
Resistance to quinolone and cephalosporin (3rd generation)	0.5% 1

*CLSI: Clinical and Laboratory Standards Institute

[†]ACSSuT: resistance to ampicillin, chloramphenicol, streptomycin, sulfamethoxazole/sulfisoxazole, tetracycline

[‡]ACSuTm: resistance to ampicillin, chloramphenicol, trimethoprim-sulfamethoxazole

[§]ACSSuTAuCf: resistance to ACSSuT + amoxicillin-clavulanic acid, ceftiofur

[¶]AAuC: resistance to ampicillin, amoxicillin-clavulanic acid, ceftiofur

**A3C: resistance to amikacin, ampicillin, amoxicillin-clavulanic acid

[††]MDR-AmpC: resistance to ACSSuTAuCf + decreased susceptibility to ceftriaxone (MIC ≥2 µg/mL)

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APPENDIX B:
LIST OF ABBREVIATIONS

ACSSuT	Resistance to at least ampicillin, chloramphenicol, streptomycin, sulfamethoxazole/sulfisoxazole, and tetracycline
ACSSuTAuC	Resistance to at least ACSSuT , amoxicillin-clavulanic acid, and ceftiofur
ACSuTm	Resistance to at least ampicillin, chloramphenicol, and trimethoprim-sulfamethoxazole
CDC	Centers for Disease Control and Prevention
CI	Confidence interval
CLSI	Clinical and Laboratory Standards Institute
EIP	Emerging Infections Program
ELC	Epidemiology and Laboratory Capacity
EMB	Eosin methylene blue
ENTFM	*Enterococcus faecium*
ENTFS	*Enterococcus faecalis*
ERS	Enterococci Resistance Surveillance
FDA	Food and Drug Administration
FoodNet	Foodborne Diseases Active Surveillance Network
MDR-AmpC	Resistance to at least ACSSuT, amoxicillin-clavulanic acid, and ceftiofur, and decreased susceptibility to ceftriaxone (MIC ≥ 2 µg/mL)
MIC	Minimum inhibitory concentration
NARMS	National Antimicrobial Resistance Monitoring System for Enteric Bacteria
OR	Odds ratio
PCR	Polymerase chain reaction
PHLIS	Public Health Laboratory Information System
VRE	Vancomycin-resistant enterococci