

N A R M S

National Antimicrobial Resistance Monitoring System: Enteric Bacteria

2005

Human Isolates Final Report



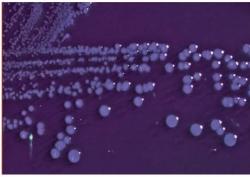








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Information Available Online

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

Information on CDC's National Surveillance Team of the Enteric Diseases Epidemiology Branch is available at http://www.cdc.gov/nationalsurveillance

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.usda.gov/Main/docs.htm?docid=14491

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

Information regarding CDC's Get Smart on the Farm program is available at http://www.cdc.gov/narms/get_smart.htm

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/enterics

What is New in the 2005 NARMS Report?

A New Look to NARMS

NARMS has a new look. Blue headline boxes differentiate between sections to facilitate navigating the annual report. Boxes in a blue double line border are at the beginning of each section, which consist of the major take home points of the NARMS 2005 Annual report.

NARMS gets interactive. The table of contents, list of tables, list of figures and all referenced tables and figures in the text are interactive, allowing guick access to tables and figures.

Antimicrobial Agents of Critical Importance

In May 2007, experts selected by the World Health Organization met in an expert consultation in Copenhagen to evaluate critically important antimicrobial agents for human medicine. The report from this meeting defines two criteria for antimicrobial agents important in human medicine: Criterion 1 is that the antimicrobial agent is the sole therapy or one of few alternatives to treat serious human disease. Criterion 2 is that the antimicrobial agent is used to treat diseases caused by organisms that may be transmitted via non-human sources or diseases caused by organisms that may acquire resistant genes from non-human sources. "Critically Important" antimicrobial agents are those that meet both criteria. "Highly Important" antimicrobial agents are those that meet one criteria. "Important" antimicrobial agents are those that meet neither criteria one nor two. The antimicrobial agents in the NARMS annual report tables are ordered using these criteria (Table I).

Antimicrobial Resistance in Humans

A separate list of antimicrobial agents used for susceptibility testing is shown for *Campylobacter*, instead of an overall list showing antimicrobial agents for *Campylobacter*, *Salmonella*, *Shigella*, and *E. coli* O157 used in previous reports. The new *Campylobacter* table consists of 10 antimicrobial agents, of which two agents, florfenicol and telithromycin, were added in 2005. Minimum inhibitory concentrations (MICs) are interpreted using criteria established by the Clinical and Laboratory Standards Institute (CLSI) when available. For agents tested in NARMS for *Campylobacter*, CLSI breakpoints have only been published for erythromycin, ciprofloxacin, and tetracycline. If CLSI breakpoints are not available, we used breakpoints from the CDC-NARMS counterpart at the Food and Drug Administration (FDA) Center for Veterinary Medicine.

An explanation on "how to read a table," showing the distribution of MICs for antimicrobial agents tested, which we refer to as "squashtogram", has been provided to assist the reader with the different parts of each table (Figure 1.01).

Proportional figures are new additions that visually display data from squashtograms for an immediate comparative summary of resistance in specific pathogens and serotypes. These figures are a categorical visual aid for the interpretation of MIC values. For most antimicrobial agents tested, three categories (susceptible, intermediate, and resistant) are used to interpret MICs. The proportion representing each category is shown in a horizontal proportional bar chart (Figure 1.02).

¹World Health Organization. Critically Important Antimicrobials for Human Medicine: Categorization for the Development of Risk Management Strategies to contain Antimicrobial Resistance due to Non-Human Antimicrobial Use. Report of the second WHO Expert Meeting Copenhagen, 29-31 May 2007.

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.usda.gov/main/site_main.htm?modecode=66-12-05-08).

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 clinical non-Typhi *Salmonella* and *Escherichia coli* O157 isolates in 14 sites. In 1997, testing of clinical *Campylobacter* isolates was initiated in the five sites participating in FoodNet. Testing of clinical *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 surveillance data for 2005 for clinical non-Typhi *Salmonella*, *Salmonella* Typhi, *Shigella*, and *E. coli* O157 isolates. Resistance trends and comparisons with previous years are included when appropriate. Antimicrobial subclasses defined by 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 data from the *Escherichia coli* Resistance Study, which is part of NARMS surveillance on commensal bacteria. Appendix A summarizes the *Escherichia coli* Resistance Surveillance Pilot Study conducted in 2005. Appendix B provides some examples of how the NARMS MIC distributions of *Escherichia coli* compare with the distributions defined by the European Committee on Antimicrobial Susceptibility Testing (EUCAST).

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

Summary of NARMS 2005 Surveillance Data

Population

In 2005, all 50 states participated in NARMS, representing approximately 296 million persons (<u>Table II</u>). 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 44.9 million persons (15.2% of the U.S. population).

Clinically Important Antimicrobial Resistance Patterns

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 2005 demonstrated resistance to these clinically important antimicrobial agents, as follows:

- 21.7% (193/890) of *Campylobacter* isolates were resistant to the fluoroquinolone ciprofloxacin, compared with 12.9% (28/217) in 1997 (OR=2.2, 95% CI [1.4, 3.4]).
 - o 23.5% (23/98) of Campylobacter coli isolates were resistant to ciprofloxacin.
 - o 21.5% (170/791) of Campylobacter jejuni isolates were resistant to ciprofloxacin.
- 2.9% (59/2052) of non-Typhi *Salmonella* isolates were resistant to the quinolone nalidixic acid, compared with 0.4% (5/1324) in 1996 (OR=8.1, 95% CI [3.2, 20.5]).
 - o Salmonella Enteritidis was the second most common serotype among nalidixic acid-resistant non-Typhi Salmonella isolates: 36.0% (18/50) of quinolone-resistant isolates were serotype Enteritidis.
 - o Nalidixic acid resistance in *Salmonella* Enteritidis was 4.7% (18/383) in 2005, compared with 0.9% (3/351) in 1996 (OR 95% CI [1.6, 30.5]).
- 2.9% (60/2052) of non-Typhi *Salmonella* isolates were resistant to the third-generation cephalosporin ceftiofur, compared with 0.2% (2/1324) in 1996 (OR=24.4, 95% CI [5.9, 100.2]).
 - o Salmonella Newport was the most common serotype among ceftiofur-resistant non-Typhi Salmonella isolates: 43.3% (26/60) of ceftiofur-resistant isolates were serotype Newport.
- 48.4% (154/318) of *Salmonella* Typhi isolates were resistant to the quinolone nalidixic acid, compared with 19.2% (32/167) in 1999 (OR=4.0, 95% CI [2.5, 6.3]).

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 Clinical and Laboratory Standards Institute (CLSI) (Table III). Multidrug resistance by the number of antimicrobial subclasses is defined as resistance to two or more CLSI subclasses. For non-Typhi Salmonella, common multidrug-resistant phenotypes in 2005 include resistance to at least ampicillin, chloramphenicol, streptomycin, sulfamethoxazole/sulfisoxazole, and tetracycline (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 $\geq 2 \mu g/mL$) (MDR-AmpC).

- 14.8% (304/2052) of non-Typhi *Salmonella* isolates were resistant to two or more CLSI subclasses, and 7.6% (156/2052) were resistant to five or more CLSI subclasses.
 - o 15.0% (31/207) of *Salmonella* Newport isolates were resistant to two or more CLSI subclasses, and 12.6% (26/207) were resistant to five or more CLSI subclasses.
 - o 33.2% (145/437) of Salmonella Typhimurium isolates were resistant to two or more CLSI subclasses, and 23.6% (103/437) were resistant to five or more CLSI subclasses.

- 3.7% (14/383) of Salmonella Enteritidis isolates were resistant to two or more CLSI subclasses, and 0.5% (2/383) were resistant to five or more CLSI subclasses.
- 6.9% (141/2052) of non-Typhi Salmonella isolates had the ACSSuT resistance pattern, compared with 8.8% (116/1324) in 1996 (Table II).
 - 22.2% (97/437) of Salmonella Typhimurium isolates were ACSSuT, compared with 33.7% (103/306) in 1996(OR=0.6, 95% CI [0.4, 0.8]).
 - 12.6% (26/207) of Salmonella Newport isolates were ACSSuT, compared with 5.9% (3/51) in 1996.
- 2.0% (41/2052) of non-Typhi *Salmonella* isolates had the MDR-AmpC phenotype (<u>Table III</u>). These isolates consisted of five different serotypes. In 1996, MDR-AmpC was not detected in any serotype.
 - 12.6% (26/207) of Salmonella Newport isolates were MDR-AmpC, compared with none (0/51) in 1996 (95% CI [1.8, infinity]).
 - o 1.8% (8/437) of Salmonella Typhimurium isolates were MDR-AmpC.

Table I: World Health Organization's categorization of antimicrobials of critical importance to human medicine¹

Critical Importance	CLSI Subclass	Antimicrobial Agent	Categorization of Antimicrobials
		Amikacin	Critically important ²
	Aminoglycosides	Gentamicin	Critically important
		Streptomycin	Critically important
	Aminopenicillins	Ampicillin	Critically important
	β-Lactamase inhibitor combinations	Amoxicillin-Clavulanic acid	Critically important
1	Cephalosporins (3 rd generation)	Ceftriaxone ⁵	Critically important
	Ketolides	Telithromycin	Critically important
	Macrolides	Azithromycin	Critically important
	iviaciondes	Erythromycin	Critically important
	Quinolones	Ciprofloxacin	Critically important
	Quinolones	Nalidixic acid	Critically important
	Aminoglycosides	Kanamycin	Highly important ³
	Cephalosporin (1 st generation)	Cephalothin	Highly important
	Cephamycins	Cefoxitin	Highly important
П	Folate pathway inhibitors	Trimethoprim- Sulfamethoxazole	Highly important
	Phenicols	Chloramphenicol ⁶	Highly important
	Sulfonamides [¶]	Sulfamethoxazole	Highly important
	Sullonamilues	Sulfisoxazole	Highly important
	Tetracyclines	Tetracycline	Highly important
III	Lincosamides	Clindamycin	Important ⁴

¹World Health Organization. Critically Important Antimicrobials for Human Medicine: Categorization for the Development of Risk Management Strategies to contain Antimicrobial Resistance due to Non-Human Antimicrobial Use. Report of the second WHO Expert Meeting Copenhagen, 29-31 May 2007.

²Both Criteria 1 and 2 met

³Either criteria 1 or 2 met but not both

⁴Neither criteria 1 or 2 met

Criteria 1 – the antimicrobial is the sole or one of few agents available for treatment of serious infections

Criteria 2 – Agent used to treat diseases caused by bacteria that may be transmitted from non-human sources to humans.

⁵Ceftiofur, a third-generation cephalosporin used in veterinary medicine is included in the panel of drugs.

⁶ Florfenicol, a phenicol used in veterinary medicine has replaced chloramphenicol in 2005.

Table II: Population size and number of isolates received and tested, by site, NARMS, 2005

Table II: Popul	Non-Typhi Salmonella		lesi			NAKIVIS, Z					
State/Site	Population Size*	Sal	n-Typhi monella		Typhi		higella		coli O157		npylobacter [†]
		N	(%)	N	(%)	N	(%)	N	(%)	N	(%)
Alabama	4,539,611	46	(2.2%)	2	(0.6%)	13	(3.3%)	2	(1.0%)	N/A	
Alaska	669,411	5	(0.2%)	1	(0.3%)	1	(0.3%)	1	(0.5%)	N/A	
Arizona	5,952,083	37	(1.8%)	4	(1.3%)	17	(4.3%)	2	(1.0%)	N/A	
Arkansas	2,772,152	39	(1.9%)	0	(0.0%)	0	(0.0%)	6	(3.1%)	N/A	
California [‡]	32,143,253	143	(7.0%)	37	(11.6%)	2	(0.5%)	4	(2.1%)	71	(8.0%)
Colorado	4,673,724	30	(1.5%)	7	(2.2%)	2	(0.5%)	4	(2.1%)	110	(12.4%)
Connecticut	3,486,490	31	(1.5%)	8	(2.5%)	3	(0.8%)	2	(1.0%)	55	(6.2%)
Delaware	840,558	8	(0.4%)	3	(0.9%)	1	(0.3%)	2	(1.0%)	N/A	
District of Columbia	582,049	0	(0.0%)	0	(0.0%)	0	(0.0%)	0	(0.0%)	N/A	
Florida	17,736,027	52	(2.5%)	12	(3.8%)	0	(0.0%)	0	(0.0%)	N/A	
Georgia	9,107,719	108	(5.3%)	8	(2.5%)	26	(6.6%)	27	(13.9%)	163	(18.3%)
Hawaii	1,267,581	16	(0.8%)	11	(3.5%)	1	(0.3%)	1	(0.5%)	N/A	
Houston, Texas [§]	2,117,937	28	(1.4%)	6	(1.9%)	1	(0.3%)	0	(0.0%)	N/A	
Idaho	1,425,894	8	(0.4%)	0	(0.0%)	1	(0.3%)	1	(0.5%)	N/A	
Illinois	12,719,550	92	(4.5%)	23	(7.2%)	21	(5.3%)	6	(3.1%)	N/A	
Indiana	6,257,121	35	(1.7%)	3	(0.9%)	2	(0.5%)	3	(1.5%)	N/A	
lowa	2,955,587	18	(0.9%)	2	(0.6%)	3	(0.8%)	3	(1.5%)	N/A	
Kansas	2,741,665	15	(0.7%)	0	(0.0%)	8	(2.0%)	2	(1.0%)	N/A	
Kentucky	4,171,016	24	(1.2%)	4	(1.3%)	14	(3.5%)	1	(0.5%)	N/A	
Los Angeles [¶]	3,847,059	68	(3.3%)	23	(7.2%)	5	(1.3%)	0	(0.0%)	N/A	
Louisiana	4,495,670	40	(1.9%)	0	(0.0%)	1	(0.3%)	0	(0.0%)	N/A	
Maine	1,312,222	9	(0.4%)	2	(0.6%)	1	(0.3%)	2	(1.0%)	N/A	
Maryland	5,573,163	30	(1.5%)	11	(3.5%)	11	(2.8%)	25	(12.9%)	64	(7.2%)
Massachusetts	6,429,137	57	(2.8%)	14	(4.4%)	10	(2.5%)	2	(1.0%)	N/A	
Michigan	10,107,940	42	(2.0%)	5	(1.6%)	7	(1.8%)	3	(1.5%)	N/A	
Minnesota	5,113,824	33	(1.6%)	6	(1.9%)	4	(1.0%)	5	(2.6%)	146	(16.4%)
Mississippi	2,900,456	38	(1.9%)	2	(0.6%)	2	(0.5%)	0	(0.0%)	N/A	
Missouri	5,787,885	59	(2.9%)	1	(0.3%)	44	(11.1%)	7	(3.6%)	N/A	
Montana	935,784	6	(0.3%)	0	(0.0%)	1	(0.3%)	1	(0.5%)	N/A	
Nebraska	1,754,042	13	(0.6%)	0	(0.0%)	9	(2.3%)	4	(2.1%)	N/A	
Nevada	2,408,948	14	(0.7%)	1	(0.3%)	4	(1.0%)	4	(2.1%)	N/A	
New Hampshire	1,303,112	8	(0.4%)	0	(0.0%)	1	(0.3%)	1	(0.5%)	N/A	
New Jersey	8,657,445	49	(2.4%)	20	(6.3%)	10	(2.5%)	12	(6.2%)	N/A	
New Mexico	1,916,331	12	(0.6%)	1	(0.3%)	8	(2.0%)	1	(0.5%)	40	(4.5%)
New York ⁴	11,048,706	91	(4.4%)	8	(2.5%)	9	(2.3%)	6	(3.1%)	116	(13.0%)
New York City**	8,213,839	76	(3.7%)	30	(9.4%)	20	(5.1%)	5	(2.6%)	N/A	,
North Carolina	8,679,089	90	(4.4%)	5	(1.6%)	6	(1.5%)	2	(1.0%)	N/A	
North Dakota	635,938	5	(0.2%)	0	(0.0%)	5	(1.3%)	1	(0.5%)	N/A	
Ohio	11,459,776	65	(3.2%)	1	(0.3%)	5	(1.3%)	7	(3.6%)	N/A	
Oklahoma	3,535,926	23	(1.1%)	1	(0.3%)	31	(7.8%)	3	(1.5%)	N/A	
Oregon	3,629,959	23	(1.1%)	4	(1.3%)	5	(1.3%)	5	(2.6%)	74	(8.3%)
Pennsylvania	12,367,276	89	(4.3%)	6	(1.9%)	6	(1.5%)	4	(2.1%)	N/A	(3 3 3)
Rhode Island	1,066,721	7	(0.3%)	1	(0.3%)	1	(0.3%)	0	(0.0%)	N/A	
South Carolina	4,254,989	32	(1.6%)	0	(0.0%)	3	(0.8%)	1	(0.5%)	N/A	
South Dakota	780,046	8	(0.4%)	0	(0.0%)	3	(0.8%)	2	(1.0%)	N/A	
Tennessee	5,989,309	34	(1.7%)	2	(0.6%)	25	(6.3%)	2	(1.0%)	51	(5.7%)
Texas ^{††}	20,726,062	55	(2.7%)	18	(5.7%)	14	(3.5%)	0	(0.0%)	N/A	\- ·-/
Utah	2,505,013	16	(0.8%)	1	(0.3%)	2	(0.5%)	3	(1.5%)	N/A	
Vermont	619,736	4	(0.2%)	0	(0.0%)	0	(0.0%)	1	(0.5%)	N/A	
Virginia	7,557,588	65	(3.2%)	16	(5.0%)	4	(1.0%)	3	(1.5%)	N/A	
Washington	6,270,838	45	(2.2%)	4	(1.3%)	11	(2.8%)	8	(4.1%)	N/A	
West Virginia	1,805,626	54	(2.6%)	0	(0.0%)	0	(0.0%)	0	(0.0%)	N/A	
Wisconsin	5,540,473	48	(2.3%)	4	(1.3%)	11	(2.8%)	5	(2.6%)	N/A	
Wyoming	506,541	9	(0.4%)	0	(0.0%)	1	(0.3%)	2	(1.0%)	N/A	
Total	295,895,897	2052	(100.0%)	318	(100.0%)	396	(100.0%)	194	(100.0%)	890	(100.0%)
* LIS Conque Bureau 20		2002	(100.070)	010	(100.070)	530	(100.070)	134	(100.070)	000	(130.070)

[™] US Census Bureau, 2005

[™] Campylobacter isolates are submitted only from FoodNet sites; total population size of FoodNet sites was 44,531,182

[™] Excluding Los Angeles County

[™] Houston City

[™] Los Angeles County

[™] Excluding New York City

[™] Excluding New York City (Bronx, Brooklyn, Manhattan, Queens, Staten Island)

[™] Excluding Houston, Texas

Table III: Summary of trend analysis of the proportion of specific resistance phenotypes among *Campylobacter*, non-Typhi *Salmonella*, and *Salmonella* Typhi isolates, 2005

Resistance Phenotype	Reference Year	Odds Ratio	[95% CI]*
Ciprofloxacin resistance in Campylobacter	1997	2.2	[1.4–3.4]
Nalidixic acid resistance in non-Typhi Salmonella	1996	8.1	[3.2–20.5]
Nalidixic acid resistance in <i>Salmonella</i> Enteritidis	1996	_†	[1.6–30.5] [†]
Ceftiofur resistance in non-Typhi Salmonella	1996	24.4	[5.9–100.2]
Nalidixic acid resistance in <i>Salmonella</i> Typhi	1999	4.0	[2.5–6.3]
ACSSuT resistance in <i>Salmonella</i> Typhimurium [‡]	1996	0.6	[0.4–0.8]
MDR-AmpC resistance in Salmonella Newport§	1996	_†	[1.8–infinity] [†]

^{*} For logistic regression models that adjusted for site, odds ratios (ORs) (2005 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, amoxicillinclavulanic acid, and ceftiofur, and decreased susceptibility to ceftriaxone (minimum inhibitory concentration) ≥2 μg/mL.

Surveillance and Laboratory Testing Methods

Surveillance Sites and Isolate Submissions

In 2005, NARMS conducted nationwide surveillance among the population of approximately 296 million persons (2005 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.

In 2005, a new scheme for *Campylobacter* isolate submission was initiated. Public health laboratories of the 10 state health departments that participated in CDC's Foodborne Diseases Active Surveillance Network (FoodNet) forwarded a representative sample of *Campylobacter* isolates to CDC for susceptibility testing. The FoodNet sites, representing approximately 45 million persons (2005 U.S. Census Bureau estimates), comprised California, Colorado, Connecticut, Georgia, Maryland, Minnesota, New Mexico, New York, Oregon, and Tennessee. There were three methods of selecting a representative sample of isolates for submission to CDC: all isolates received by Georgia, Maryland, New Mexico, Oregon, and Tennessee; every other isolate from California, Colorado, Connecticut, and New York; and every fifth isolate from Minnesota. From 1997 to 2004, one *Campylobacter* isolate each week from participating FoodNet sites was submitted to NARMS. This submission scheme was described in the 2004 report⁴.

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 IV). 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 available¹. The resistance breakpoint for amikacin, according to CLSI guidelines, is ≥64 μg/mL. In 2002 and 2003, a truncated broth microdilution series was used for amikacin testing (0.5-4 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 was 0.016-256 μg/mL. Since 2004, amikacin had a full range of dilutions (0.5-64 μg/mL) on the Sensititre panel (CMV1AGNF).

Table IV: Antimicrobial agents used for susceptibility testing for *Salmonella*, *Shigella*, and *Escherichia coli* O157 isolates, NARMS, 2005

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

[‡] Cephalothin was not tested in 2004 and 2005 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.

Additional Testing of Salmonella strains

Cephalosporin Retesting of isolates from 1996-1998

Review of *Salmonella* isolates tested in NARMS during 1996–1998 gave conflicting cephalosporin susceptibility results. In particular, 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 suggested that some previously reported results were inaccurate, 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 were first included in the 2003 and 2004 NARMS annual reports.

Serotype Confirmation/Categorization

To distinguish serotypes Paratyphi B and Paratyphi B var L(+) tartrate+ (formerly *Salmonella* Java), tartrate testing was performed at CDC on all *Salmonella* Paratyphi B isolates isolated from 1996 to 2005 for which the tartrate result was not reported or was reported to be negative. 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+. Confirmation of other biochemical reactions or somatic and flagellar antigens was not performed at CDC.

Salmonella serotype was accepted as reported with few exceptions. 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 1996–2005 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 Salmonella I 4,[5],12:i:- (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 serogroup B serotypes. Such isolates tested in NARMS in 2005 were similarly reviewed and reported as Salmonella I 4,[5],12:i:- when appropriate.

Testing of Campylobacter

Changes in testing methods in 2005

In 2005, there were two major changes in the methodology for *Campylobacter*. A scheme for selecting a representative sample of *Campylobacter* isolates for submission by FoodNet sites was initiated in 2005, which changed from a scheme that selected one *Campylobacter* isolate each week for submission during 1997 to 2004. In 2005, *Campylobacter* isolates were susceptibility tested using Sensititre; isolates were tested by E-test from 1997 to 2004. In addition, florfenicol replaced chloramphenicol and telithromycin was added to the NARMS panel of agents tested in 2005.

Identification/Speciation and Antimicrobial Susceptibility Testing

In 2005, isolates were confirmed as *Campylobacter* by dark-field microscopy, catalase, 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 polymerase chain reaction (PCR) as *C. jejuni* using a hippuricase gene-based PCR assay², or as *C. coli* using a *C. coli*-specific *ceuE* PCR³. Isolates determined to be neither *C. jejuni* nor *C. coli* were identified by alternative PCR methods⁴. The same methodology was used during 1997–2003.

In 2004, putative *Campylobacter* isolates were identified as *Campylobacter jejuni* or *Campylobacter coli* by 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.

In 2005, the broth microdilution methodology (Sensititre®, Trek Diagnostics, Westlake, OH) was used to determine the MICs for nine antimicrobial agents: azithromycin, ciprofloxacin, clindamycin, erythromycin, florfenicol, gentamicin, nalidixic acid, telithromycin, and tetracycline (Table V). Florfenicol replaced chloramphenicol in the NARMS panel to represent the phenicol antimicrobial subclass. Similar to the 2004 report, CLSI interpretive criteria for erythromycin, ciprofloxacin, and tetracycline (published in 2006) and revised NARMS criteria for azithromycin were used for all years in this report^{5,6}. In annual reports published before 2004, 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. In addition, revised NARMS interpretive criteria, adopted from the FDA arm of NARMS, have been used for clindamycin, gentamicin, and nalidixic acid since 2004. From 1997 to 2004, E-test was used for susceptibility testing of *Campylobacter* isolates⁴.

Table V: Antimicrobial agents used for susceptibility testing for *Campylobacter* isolates, NARMS, 1996-2005

CLSI Subclass	Antimiorabial Accept	Antimicrobial Agent Concentration		Breakpoints		
CLSI Subciass	Antimicrobial Agent	Range (µg/mL)	Susceptible Intermediate Reserve ≤4 8 ≤0.5 1-2 ≤4 8 ≤8 16 ≤4 ≤ ≤8 16 ≤4 ≤1 2 ≤16	Resistant		
Aminoglycosides	Gentamicin	0.25–16 0.016–256 [*]	≤4	4 8		
Lincosamides	Clindamycin	0.016–256 [*]	≤0.5	1–2	≥4	
	Azithromycin	0.016–256 [*]	≤4	8	≥16	
Macrolides Erythromycin Telithromycin [†]	Erythromycin	0.016–256 [*]	≤8	16	≥32	
	Telithromycin [†]	0.016-8	≤4		≥16	
Dhoniagle	Chloramphenicol [‡]	2–32	≤8	16	≥32	
Phenicols	Florfenicol [§]	0.03-64	≤4			
Ovinalanaa	Ciprofloxacin	0.015–4 0.002–32 [*]	≤1	2	≥4	
Quinolones	Nalidixic acid	0.5–32 0.016–256 [*]	≤16		≥32	
Tetracyclines	Tetracycline	4–32 0.016–256 [*]	≤4	8	≥16	

^{*}E-test dilution range used.

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 broth microdilution methods (Sensititre, Trek Diagnostics, Westlake, OH). Totals reported here reflect the retest results.

Data Analysis

For all pathogens, MICs were categorized as resistant, intermediately susceptible (if applicable), or susceptible. Analysis was restricted to one isolate (per genus under surveillance) per patient. Where established, CLSI interpretive criteria were used; ceftiofur resistance was defined as MIC \geq 8 µg/mL (Table IV). The 95% confidence intervals (CI) for the percentage of resistant isolates are included in the MIC distribution tables. The 95% CI was calculated using the Clopper-Pearson exact method⁷. 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 nine CLSI subclasses tested in all years from 1996 through 2005 represented by 13 agents: amoxicillin-clavulanic acid, ampicillin, ceftiofur, ceftriaxone, chloramphenicol, ciprofloxacin, gentamicin, kanamycin, nalidixic acid, streptomycin, sulfamethoxazole/sulfisoxazole, tetracycline, and trimethoprim-sulfamethoxazole. For *Salmonella* serotype Typhi and *Shigella*, results for several years included the nine CLSI subclasses tested in all years from 1999 through 2005 represented by 14 agents (13 antimicrobial agents mentioned above and amikacin). Similarly, when describing multidrug resistance for several years for *Campylobacter* isolates, multidrug resistance was limited to the five CLSI subclasses tested in all years from 1997 through 2004, represented by ciprofloxacin, chloramphenicol/florfenicol, clindamycin, erythromycin, nalidixic acid, and tetracycline.

[†]Telithromycin added to NARMS panel in 2005.

[‡]Chloramphenicol, tested from 1996-2004, was replaced by florfenicol in 2005.

[§]Currently only a susceptible breakpoint has been established. In this report isolates with a MIC ≥8 μg/mL are categorized as resistant.

Logistic regression was performed to compare the change in antimicrobial resistance among *Salmonella* and *Campylobacter* isolates tested in NARMS during 2005 with that of previous years for the following:

- Non-Typhi Salmonella: resistance to nalidixic acid, resistance to ceftiofur, resistance to one or more CLSI subclasses.
- 2. Salmonella Typhimurium: resistance to at least ampicillin, chloramphenicol, streptomycin, sulfamethoxazole, and tetracycline (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 patient's state of residence. 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. Finally, residual analysis was performed to examine the influence of individual observations. Odds ratios that did not include 1.0 in the 95% CI were reported as significant.

Results for 2005

1. Non-Typhi Salmonella

In non-Typhi *Salmonella*, an increase in resistance to two clinically important subclasses, quinolones (represented by nalidixic acid) and third-generation cephalosporins (represented by ceftiofur), was observed from 1996 to 2005. Nalidixic acid resistance increased from 0.4% to 2.4% and ceftiofur resistance increased from 0.2% to 2.9%.

In 2005, CDC received 2090 non-Typhi *Salmonella* isolates, of which 2052 (98.2%) were viable and tested for antimicrobial susceptibility (<u>Table II</u>).

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 2005, the prevalence of resistance among non-Typhi *Salmonella* isolates was 2.4% for quinolones (represented by nalidixic acid) and 2.9% for third-generation cephalosporins (represented by ceftiofur) (Table 1.01).

The antimicrobial agents with the highest prevalence of resistance were tetracycline (13.7%), followed by sulfisoxazole (12.5%), ampicillin (11.3%), and streptomycin (11.0%).

The prevalence of nalidixic acid resistance increased from 0.4% (5/1324) in 1996 to 2.4% (50/2052) in 2005 (Table 1.02), a statistically significant increase (OR=8.1, 95% CI [3.2, 20.5]). The prevalence of ceftiofur resistance increased from 0.2% (2/1324) in 1996 to 2.9% (60/2052) in 2005, a statistically significant increase (OR=24.4, 95% CI [5.9, 100.2]). The proportion of resistance to most of the agents tested in 2005 was lower than in 2004, including ampicillin, amoxicillin-clavulanic acid, ceftiofur, cefoxitin, chloramphenicol, tetracycline, and streptomycin.

Of the 2052 non-Typhi *Salmonella* isolated in 2005, 80.6% (1654) showed no resistance to the drugs tested, a slight increase from the 79.6% in 2004 (<u>Table 1.03</u>). In 2005, 398 (19.4%) were resistant to one or more CLSI subclass, 304 (14.8%) to two or more subclasses, 247 (12.0%) to three or more subclasses, 186 (9.1%) to four or more subclasses, and 156 (7.6%) to five or more subclasses. There was a statistically significant decline in resistance to one or more subclass from 33.8% in 1996 to 19.4% in 2005 (OR=0.6, 95% CI [0.5, 0.7]) (<u>Table 1.04</u>).

In 2005, resistance to at least ampicillin, chloramphenicol, streptomycin, sulfamethoxazole/sulfisoxazole, and tetracycline (ACSSuT) was among the most common multidrug-resistant phenotype (6.9%) among non-Typhi *Salmonella* isolates, but was lower than in 2004 (7.1%), and 1996 (8.8%). Another common multidrug-resistant phenotype among non-Typhi *Salmonella* isolates was to at least ACSSuT, amoxicillin-clavulanic acid,, and ceftiofur, and decreased susceptibility to ceftriaxone (MIC \geq 2 µg/mL); this pattern is called MDR-AmpC and 2.0% of isolates had this pattern. The prevalence of MDR-AmpC increased from 0% (0/1324) in 1996 to 2.0% (41/2052) in 2005. Seven (0.3%) isolates were resistant to nalidixic acid and ceftiofur (<u>Table 1.03</u>); this pattern was first detected in 1997.

In 2005, serotypes were identified for a higher proportion of isolates in NARMS (98.9%) than in the Public Health Laboratory Information System (PHLIS) (92.1%) (<u>Table 1.04</u>). The 20 most common serotypes accounted for 82.5% of isolates in NARMS and 77.2% in PHLIS. The same five most common serotypes were reported in NARMS and PHILIS, which accounted for 59.9% of isolates in NARMS and 56.5% in PHLIS. In NARMS; 1.1% of isolates were not completely serotyped in 2005, which was a decline compared with 4.2% in 2004.

Figure 1.01: How to read a squashtogram

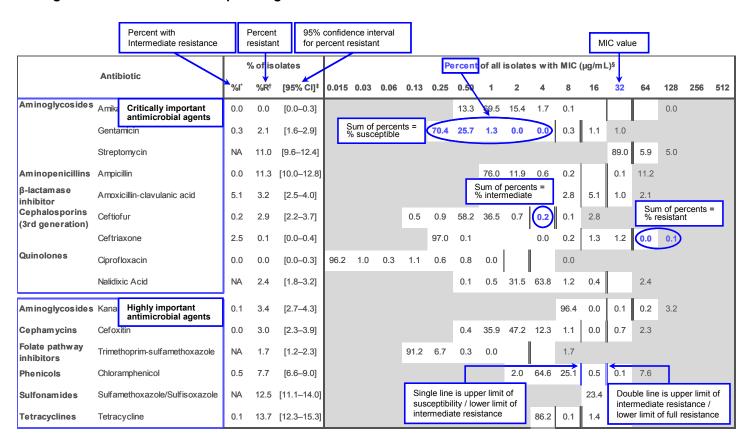


Figure 1.02: Proportional chart, a categorical graph of a squashtogram Percent of all isolates with MIC (µg/mL)§ Antibiotic %I^{*} %R[†] [95% CI][‡] 0.015 0.03 0.06 0.125 0.25 0.50 2 128 256 512 Aminoglycosides Amikacin 0.0 0.1 [0.0-0.3] 69.1 15.3 1.6 0.1 1.3 0.0 0.0 0.3 1.1 1.0 Gentamicin 0.3 2.1 [1.6-2.9] 25.6 Streptomycin NA 11.0 [9.6-12.4] 89.0 5.9 Ampicillin 0.0 11.3 [10.0-12.7] 75.6 12.3 0.6 0.1 11.2 Aminopenicillins β-lactamase 3.3 2.8 1.0 2.1 Amoxicillin-clavulanic acid 5.0 3.2 [2.4-4.0] 0.8 inhibitor Cephalosporins 0.7 0.2 0.1 Ceftiofur 0.2 2.9 [2.2-3.7] 0.5 0.9 58.0 36.8 (3rd generation) 0.0 Ceftriaxone 2.5 0.1 [0.0-0.4]97.0 0.1 0.2 1.3 1.2 0.0 Quinolones 0.0 Ciprofloxacin 0.0 0.0 [0.0-0.3]1.0 0.3 1.1 0.6 1.2 0.0 Nalidixic Acid NA 2.9 [2.2-3.7] 0.1 0.5 31.4 63.5 1.2 0.4 Aminoglycosides Kanamycin 0.1 3.4 [2.7-4.3] 96.4 0.0 0.2 Cephamycins 0.0 3.0 [2.3-3.8] 35.7 47.0 12.7 1.1 0.0 2.3 Folate pathway NA 1.7 91.2 6.7 Trimethoprim-sulfamethoxazole [1.2-2.4] 1.7 inhibitors Phenicols 0.5 7.8 [6.6-9.0] 2.0 64.2 25.4 0.5 Chloramphenicol Sulfonamides Sulfamethoxazole/Sulfisoxazole NA 12.5 [11.1-14.0] 23.7 0.7 0.1 12.5 86.2 0.1 Tetracyclines [12.3-15.3 Tetracycline 0.1 13.7 1.4 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 the 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. **Antimicrobial Agent** Susceptible, Intermediate, and Resistant Proportion Amikacin Gentamicin Streptomycin Ampicillin Amoxicillin/Clavulanic Acid Ceftiofur Ceftriaxone Ciprofloxacin Nalidixic Acid Kanamycin Cefoxitin Trimethoprim/Sulfamethoxazole Chloramphenicol Sulfameth/Sulfiz Tetracycline



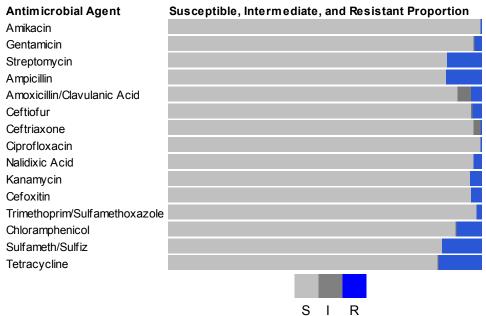
Table 1.01: Minimum inhibitory concentrations (MICs) and resistance of non-Typhi Salmonella isolates to

antimicrobial agents, 2005 (N=2052)

	Antibiotic		% of is	olates						Percei	nt of all	isolate	s with	MIC (µ	g/mL) [§]					
	Antibiotic	%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	[0.0-0.3]						13.3	69.5	15.4	1.7	0.1				0.0		
	Gentamicin	0.3	2.1	[1.6–2.9]					70.4	25.7	1.3	0.0	0.0	0.3	1.1	1.0				
	Streptomycin	NA	11.0	[9.6–12.4]												89.0	5.9	5.0		
Aminopenicillins	Ampicillin	0.0	11.3	[10.0–12.8]							76.0	11.9	0.6	0.2		0.1	11.2			
β-lactamase inhibitor	Amoxicillin-clavulanic acid	5.1	3.2	[2.5-4.0]							85.2	2.9	0.8	2.8	5.1	1.0	2.1			
Cephalosporins (3rd generation)	Ceftiofur	0.2	2.9	[2.2–3.7]				0.5	0.9	58.2	36.5	0.7	0.2	0.1	2.8					
(* · 3 · · · · ,	Ceftriaxone	2.5	0.1	[0.0-0.4]					97.0	0.1			0.0	0.2	1.3	1.2	0.0	0.1		
Quinolones	Ciprofloxacin	0.0	0.0	[0.0-0.3]	96.2	1.0	0.3	1.1	0.6	0.8	0.0			0.0						
	Nalidixic Acid	NA	2.4	[1.8–3.2]						0.1	0.5	31.5	63.8	1.2	0.4		2.4			
Aminoglycosides	Kanamycin	0.1	3.4	[2.7-4.3]										96.4	0.0	0.1	0.2	3.2		
Cephamycins	Cefoxitin	0.0	3.0	[2.3–3.9]						0.4	35.9	47.2	12.3	1.1	0.0	0.7	2.3			
Folate pathway inhibitors	Trimethoprim-sulfamethoxazole	NA	1.7	[1.2–2.3]				91.2	6.7	0.3	0.0			1.7						
Phenicols	Chloramphenicol	0.5	7.7	[6.6–9.0]								2.0	64.6	25.1	0.5	0.1	7.6			
Sulfonamides	Sulfamethoxazole/Sulfisoxazole	NA	12.5	[11.1–14.0]											23.4	48.7	14.6	0.7	0.1	12.5
Tetracyclines	Tetracycline	0.1	13.7	[12.3–15.3]									86.2	0.1	1.4	4.4	8.0		,	

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

Figure 1.03: Antimicrobial resistance pattern for non-Typhi Salmonella, 2005



[†]Percent of isolates that were resistant

 $^{^{\}text{\tiny{$1$}}}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 1.02: Percentage and number of non-Typhi *Salmonella* isolates resistant to antimicrobial agents, 1996–2005

1990-2005 Year		1996	1997	1998	1999	2000	0004	2002	2003	2004	2005
							2001				
Total Isolates	IAntibiotic	1324	1301	1460	1495	1377	1419	2008	1864	1793	2052
Outstand	(Resistance breakpoint)										
Subclass											
Aminoglycosides	Amikacin	Not	0.0%	0.0%	0.1%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
	(MIC ≥ 64)	Tested	0	0	1	0	0	0	0	0	1
	Gentamicin	4.8%	2.9%	2.8%	2.1%	2.7%	1.9%	1.3%	1.4%	1.3%	2.1%
	(MIC ≥ 16)	63	38	41	32	37	27	27	26	24	44
	Streptomycin	20.6%	21.4%	18.6%	16.7%	16.3%	17.0%	13.2%	15.0%	11.8%	11.0%
	(MIC ≥ 64)	273	278	272	250	224	241	265	279	212	225
Aminopenicillins	Ampicillin	20.7%	18.3%	16.5%	15.5%	15.9%	17.4%	12.9%	13.6%	12.0%	11.3%
	(MIC ≥ 32)	274	238	241	232	219	247	259	254	216	232
β-lactamase inhibitor combinations	Amoxicillin-clavulanic acid	1.1%	1.0%	1.7%	2.3%	3.9%	4.7%	5.3%	4.6%	3.7%	3.2%
	(MIC ≥ 32)	15	13	25	34	54	66	106	86	67	65
Cephalosporins (3 rd generation)	Ceftiofur	0.2%	0.5%	0.8%	2.0%	3.2%	4.1%	4.3%	4.5%	3.4%	2.9%
	(MIC ≥ 8)	2	6	12	30	44	58	87	83	61	60
	Ceftriaxone	0.0%	0.1%	0.0%	0.3%	0.0%	0.0%	0.2%	0.4%	0.6%	0.1%
	(MIC ≥ 64)	0	1	0	5	0	0	4	8	10	3
Quinolones	Ciprofloxacin	0.0%	0.0%	0.1%	0.1%	0.4%	0.2%	0.0%	0.2%	0.2%	0.0%
	(MIC ≥ 4)	0	0	1	1	5	3	1	3	4	1
	Nalidixic Acid	0.4%	0.9%	1.4%	0.9%	2.5%	2.6%	1.8%	2.3%	2.6%	2.4%
	(MIC ≥ 32)	5	12	20	14	34	37	36	42	47	50
Aminoglycosides	Kanamycin	5.0%	5.1%	5.7%	4.3%	5.6%	4.8%	3.8%	3.4%	2.8%	3.4%
	(MIC ≥ 64)	66	67	83	65	77	68	76	64	50	70
Cephalosporin (1 st generation)	Cephalothin	2.9%	2.2%	2.3%	3.5%	4.0%	4.0%	5.0%	5.4%	Not	Not
gonoration,	(MIC ≥ 32)	39	29	33	53	55	57	101	100	Tested	Tested
Cephamycins	Cefoxitin	Not	Not	Not	Not	3.2%	3.4%	4.3%	4.2%	3.5%	3.0%
, ,	(MIC ≥ 32)	Tested	Tested	Tested	Tested	44	48	86	79	62	62
Folate pathway inhibitors	Trimethoprim-sulfamethoxazole	3.9%	1.8%	2.3%	2.0%	2.1%	2.0%	1.4%	1.9%	1.8%	1.7%
, ,	(MIC ≥ 4)	51	24	34	30	29	28	28	36	32	34
Phenicols	Chloramphenicol	10.6%	10.1%	9.9%	9.2%	10.1%	11.6%	8.6%	10.0%	7.6%	7.7%
	(MIC ≥ 32)	140	131	145	137	139	164	172	187	136	159
Sulfonamides	Sulfamethoxazole/Sulfisoxazole*	20.3%	22.8%	19.4%	18.0%	17.1%	17.7%	12.8%	15.0%	13.2%	12.5%
	(MIC ≥ 512)	269	297	283	269	235	251	258	280	237	256
Tetracyclines	Tetracycline	24.2%	21.7%	20.2%	19.3%	18.6%	19.7%	14.9%	16.3%	13.5%	13.7%
	(MIC ≥ 16)	320	282	295	289	256	280	299	303	242	282

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

Table 1.03: Resistance patterns of non-Typhi Salmonella isolates, 1996–2005

Year	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005
Total Isolates	1324	1301	1460	1495	1377	1419	2008	1864	1793	2052
	%	%	%	%	%	%	%	%	%	%
	n	n	n	n	n	n	n	n	n	n
No resistance detected	66.2%	68.4%	72.9%	74.2%	74.4%	72.3%	79.0%	77.7%	79.6%	80.6%
	876	890	1064	1109	1024	1026	1586	1449	1427	1654
Resistance ≥1CLSI subclass*	33.8%	31.6%	27.1%	25.8%	25.6%	27.7%	21.0%	22.3%	20.4%	19.4%
	448	411	396	386	353	393	422	415	366	398
Resistance ≥2 CLSI subclasses*	27.0%	24.1%	22.6%	20.4%	20.2%	22.1%	15.8%	17.7%	15.0%	14.8%
	358	314	330	305	278	314	318	330	269	304
Resistance ≥3 CLSI subclasses*	18.1%	17.7%	16.7%	15.1%	15.6%	16.8%	12.2%	14.3%	11.7%	12.0%
	240	230	244	225	215	239	244	266	210	247
Resistance ≥4 CLSI subclasses*	13.7%	13.7%	13.1%	12.2%	12.9%	14.2%	9.9%	11.6%	9.4%	9.1%
	181	178	191	183	178	202	199	216	168	186
Resistance ≥5 CLSI subclasses*	10.0%	9.9%	10.1%	8.6%	9.9%	10.5%	8.3%	9.9%	8.1%	7.6%
	132	129	147	129	137	149	167	185	146	156
At least ACSSuT [†]	8.8%	9.5%	8.9%	8.4%	8.9%	10.0%	7.8%	9.3%	7.1%	6.9%
	116	124	130	125	122	142	156	173	128	141
At least ACSuTm [‡]	0.8%	0.4%	0.9%	0.9%	1.0%	0.5%	1.0%	1.2%	0.6%	0.9%
	10	5	13	14	14	7	21	23	10	18
At least ACSSuTAuCf [§]	0.0%	0.3%	0.3%	1.5%	2.6%	2.5%	3.3%	3.2%	2.3%	2.0%
	0	4	5	23	36	36	67	60	42	41
At least MDR-AmpC [¶]	0.0%	0.3%	0.3%	1.5%	2.6%	2.5%	3.3%	3.2%	2.3%	2.0%
· · · · · · · · · · · · · · · · · · ·	0	4	5	23	36	36	67	60	42	41
Resistance to quinolone and cephalosporin (3 rd generation)	0.0%	0.2%	0.1%	0.1%	0.3%	0.3%	0.2%	0.2%	0.4%	0.3%
reconstance to quincione and cophalosponii (o generation)	0	2	1	1	4	4	5	4	7	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 1.04: Twenty most common non-Typhi Salmonella serotypes in NARMS and the Public Health

Laboratory Information System, 2005

Labo	ratory information System, 2005	<u>, </u>	
	NARMS	1	-1-4
Danle	Comptime		olates
Rank	Serotype	N 407	(%)
1	Typhimurium	437	(21.3%)
2	Enteritidis	383	(18.7%)
3	Newport	207	(10.1%)
4	Heidelberg	125	(6.1%)
5	Javiana	75	(3.7%)
6	Montevideo	48	(2.3%)
7	Braenderup	47	(2.3%)
8	Muenchen	44	(2.1%)
9	Saintpaul	41	(2.0%)
10	Paratyphi B var. L(+) tartrate+	38	(1.9%)
11	Mississippi	37	(1.8%)
12	I 4,[5],12:i:- (monophasic Typhimurium)	33	(1.6%)
13	Oranienburg	33	(1.6%)
14	Infantis	30	(1.5%)
15	Thompson	26	(1.3%)
16	Agona	22	(1.1%)
17	Poona	19	(0.9%)
18	Stanley	17	(0.8%)
19	Mbandaka	17	(0.8%)
20	Berta	13	(0.6%)
	Subtotal	1692	(82.5%)
	All Other serotypes	336	(16.4%)
	Unknown serotype	1	(0.0%)
	Partially serotyped	21	(1.0%)
	Rough/Nonmotile isolates	2	(0.1%)
	Subtotal	360	(17.5%)
	Grand Total	2052	(100.0%)

	PHLIS		
		Iso	olates
Rank	Serotype	N	(%)
1	Typhimurium	6982	(19.5%)
2	Enteritidis	6730	(18.8%)
3	Newport	3295	(9.2%)
4	Heidelberg	1903	(5.3%)
5	Javiana	1324	(3.7%)
6	I 4,[5],12:i:- (monophasic Typhimurium)	822	(2.3%)
7	Montevideo	809	(2.3%)
8	Muenchen	733	(2.0%)
9	Saintpaul	683	(1.9%)
10	Braenderup	603	(1.7%)
11	Oranienburg	590	(1.6%)
12	Mississippi	565	(1.6%)
13	Infantis	505	(1.4%)
14	Paratyphi B var. L(+) tartrate+	460	(1.3%)
15	Thompson	428	(1.2%)
16	Agona	367	(1.0%)
17	Hartford	239	(0.7%)
18	Stanley	224	(0.7%)
19	Berta	209	(0.6%)
20	Hadar	205	(0.6%)
	Subtotal	27676	(77.2%)
	All Other serotypes	5324	(14.9%)
	Unknown serotype	1113	(3.1%)
	Partially serotyped	1684	(4.7%)
	Rough/Nonmotile isolates	39	(0.1%)
	Subtotal	8160	(22.8%)
	Grand Total	35836	(100.0%)

A. Salmonella Typhimurium

In 2005, Typhimurium was the most common non-Typhi *Salmonella* serotype in NARMS. ACSSuT in *Salmonella* Typhimurium decreased from 33.7% in 1996 to 22.2% in 2005.

In 2005, Typhimurium was the most common non-Typhi *Salmonella* serotype in NARMS, accounting for 21.3% (437/2052) of non-Typhi *Salmonella* isolates (<u>Table 1.05</u>). Of the 437 *Salmonella* Typhimurium isolates tested, resistance was highest to sulfisoxazole (31.8%), tetracycline (30.2%), ampicillin (28.8%), streptomycin (27.9%), and chloramphenicol (24.3%). The prevalence of resistance among clinically important antimicrobial subclasses was 0.9% for quinolones (represented by nalidixic acid) and 2.5% for third-generation cephalosporins (represented by ceftiofur).

Resistance to many of the other antimicrobial agents decreased since 1996 (<u>Table 1.06</u>). Resistance to tetracycline decreased from 49.3% in 1996 to 30.2% in 2005; ampicillin, from 50.0% to 28.8%; streptomycin, from 51.6% to 27.9%; chloramphenicol, from 39.9% to 24.3%; and gentamicin, from 4.2% to 1.8%.

Of the 437 *Salmonella* Typhimurium isolates tested during 2005, 65.2% (285) had no detected resistance, a slight increase from the 60.7% of isolates in 2004 (<u>Table 1.07</u>). In 2005, 33.2% (145/437) were resistant to two or more CLSI subclasses, compared with 37.2% in 2004. Similarly, in 2005, 23.6% (103/437) were resistant to at least five subclasses, compared with 24.3% in 2004.

In 2005, the most common multidrug-resistant phenotype among *Salmonella* Typhimurium was ACSSuT (22.2% of isolates). For *Salmonella* Typhimurium, ACSSuT commonly is associated with definitive phage type 104. Since 1996, the prevalence of ACSSuT among *Salmonella* Typhimurium decreased from 33.7% to 22.2%. In the logistic regression model, this decrease is statistically significant (OR=0.6, 95% CI [0.4, 0.8]).

One (0.2%) serotype Typhimurium isolate was resistant to both quinolones and third-generation cephalosporins in 2005. Since 1996, seven *Salmonella* Typhimurium isolates have shown this multidrug resistance pattern.

Table 1.05: Minimum inhibitory concentrations (MICs) and resistance of Salmonella Typhimurium isolates

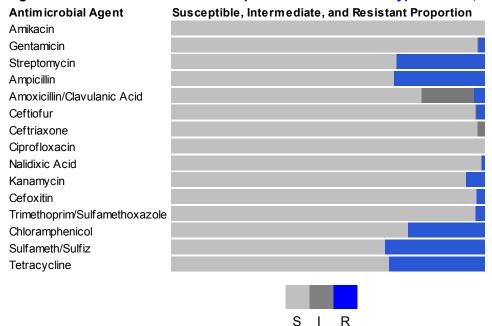
to antimicrobial agents, 2005 (N=437)

	Antibiotic		% of is	olates						Percei	nt of all	isolate	es with	MIC (µ	ıg/mL) [§]					
	Antibiotic	%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	[8.0–0.8]						3.9	75.3	17.6	3.2							
	Gentamicin	0.2	1.8	[0.8–3.6]					66.1	29.7	2.1			0.2	1.1	0.7				
	Streptomycin	NA	27.9	[23.8–32.4]												72.1	18.3	9.6		
Aminopenicillins	Ampicillin	0.0	28.8	[24.6–33.3]							63.4	7.6	0.2				28.8			
β-lactamase inhibitor	Amoxicillin-clavulanic acid	19.0	3.2	[1.8–5.3]							68.9	2.1	0.5	6.4	19.0	1.1	2.1			
Cephalosporins (3rd generation)	Ceftiofur	0.2	2.5	[1.3–4.5]				0.2	0.7	60.2	35.2	0.9	0.2		2.5					
,	Ceftriaxone	2.1	0.0	[8.0–0.8]					97.5			,		0.5	1.1	0.9				
Quinolones	Ciprofloxacin	0.0	0.0	[8.0–0.8]	97.3	1.4		0.7	0.2	0.2	0.2									
	Nalidixic Acid	NA	0.9	[0.2–2.3]						0.2	0.5	37.3	59.7	0.9	0.5		0.9			
Aminoglycosides	Kanamycin	0.0	5.7	[3.7–8.3]										94.1	0.2		0.5	5.3		
Cephamycins	Cefoxitin	0.0	2.5	[1.3–4.5]							34.3	54.5	7.3	1.4		0.5	2.1			
Folate pathway inhibitors	Trimethoprim-sulfamethoxazole	NA	2.7	[1.4–4.7]				78.5	18.1	0.7				2.7	•					
Phenicols	Chloramphenicol	0.2	24.3	[20.3–28.6]								1.4	55.6	18.5	0.2	0.5	23.8			
Sulfonamides	Sulfamethoxazole/Sulfisoxazole	NA	31.8	[27.5–36.4]											20.1	43.5	4.3	0.2		31.8
Tetracyclines	Tetracycline	0.2	30.2	[25.9–34.7]									69.6	0.2	5.5	14.6	10.1			

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

\$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.

Figure 1.04: Antimicrobial resistance pattern for Salmonella Typhimurium, 2005



[†]Percent of isolates that were resistant

 $^{^{\}ddagger}95\%$ confidence intervals (CI) for percent resistant (%R) were calculated using the Clopper-Pearson exact method

Table 1.06: Percentage and number of *Salmonella* Typhimurium isolates resistant to antimicrobial agents, 1996–2005

Year		1996	1997	1998	1999	2000	2001	2002	2003	2004	2005
Total Isolates		306	328	379	362	304	325	393	406	382	437
	Antibiotic							ĺ			
Subclass	(Resistance breakpoint)										
Aminoglycosides	Amikacin	Not	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
• /	(MIC ≥ 64)	Tested	0	0	0	0	0	0	0	0	0
	Gentamicin	4.2%	4.6%	3.7%	2.2%	2.6%	1.5%	2.3%	2.0%	2.1%	1.8%
	(MIC ≥ 16)	13	15	14	8	8	5	9	8	8	8
	Streptomycin	51.6%	55.2%	47.5%	43.1%	39.5%	40.0%	31.8%	35.2%	31.7%	27.9%
	(MIC ≥ 64)	158	181	180	156	120	130	125	143	121	122
Aminopenicillins	Ampicillin	50.0%	50.3%	45.4%	41.2%	42.1%	42.5%	33.6%	36.0%	31.9%	28.8%
•	(MIC ≥ 32)	153	165	172	149	128	138	132	146	122	126
β-lactamase inhibitor combinations	Amoxicillin-clavulanic acid	2.6%	3.4%	4.5%	2.8%	6.3%	6.2%	7.6%	5.4%	4.7%	3.2%
	(MIC ≥ 32)	8	11	17	10	19	20	30	22	18	14
Cephalosporins (3 rd generation)	Ceftiofur	0.0%	1.5%	1.8%	1.9%	3.6%	3.1%	4.3%	4.9%	4.5%	2.5%
o opinancia (o generania)	(MIC ≥ 8)	0	5	7	7	11	10	17	20	17	11
	Ceftriaxone	0.0%	0.3%	0.0%	0.3%	0.0%	0.0%	0.3%	0.2%	0.8%	0.0%
	(MIC ≥ 64)	0	1	0	1	0	0	1	1	3	0
Quinolones	Ciprofloxacin	0.0%	0.0%	0.0%	0.0%	0.0%	0.3%	0.0%	0.0%	0.0%	0.0%
	(MIC ≥ 4)	0	0	0	0	0	1	0	0	0	0
	Nalidixic Acid	0.3%	0.9%	0.5%	0.0%	1.3%	0.6%	1.3%	1.2%	0.5%	0.9%
	(MIC ≥ 32)	1	3	2	0	4	2	5	5	2	4
Aminoglycosides	Kanamycin	14.4%	15.5%	15.8%	13.0%	13.2%	8.3%	7.6%	7.1%	5.8%	5.7%
	(MIC ≥ 64)	44	51	60	47	40	27	30	29	22	25
Cephalosporin (1 st generation)	Cephalothin	2.0%	4.3%	4.0%	4.4%	4.3%	3.1%	5.6%	6.2%	Not	Not
(· g((MIC ≥ 32)	6	14	15	16	13	10	22	25	Tested	Tested
Cephamycins	Cefoxitin	Not	Not	Not	Not	3.6%	3.1%	4.3%	4.4%	4.7%	2.5%
	(MIC ≥ 32)	Tested	Tested	Tested	Tested	11	10	17	18	18	11
Folate pathway inhibitors	Trimethoprim-sulfamethoxazole	4.6%	3.0%	4.5%	2.8%	3.6%	2.5%	2.3%	3.4%	2.6%	2.7%
	(MIC ≥ 4)	14	10	17	10	11	8	9	14	10	12
Phenicols	Chloramphenicol	39.9%	36.0%	33.8%	28.7%	30.9%	31.7%	23.2%	27.8%	24.1%	24.3%
	(MIC ≥ 32)	122	118	128	104	94	103	91	113	92	106
Sulfonamides	Sulfamethoxazole/Sulfisoxazole*	53.3%	56.7%	49.9%	45.6%	45.4%	43.1%	32.1%	38.4%	35.9%	31.8%
	(MIC ≥ 512)	163	186	189	165	138	140	126	156	137	139
Tetracyclines	Tetracycline	49.3%	52.4%	46.2%	41.7%	43.4%	43.4%	31.8%	37.9%	30.1%	30.2%
, i	(MIC ≥ 16)	151	172	175	151	132	141	125	154	115	132

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

Table 1.07: Resistance patterns of Salmonella Typhimurium isolates, 1996–2005

Variable 1.07. Resistance patterns of Samione							2002	2002	2004	2005
Year	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005
Total Isolates	306	328	379	362	304	325	393	406	382	437
	%	%	%	%	%	%	%	%	%	%
	n	n	n	n	n	n	n	n	n	n
No resistance detected	37.9%	39.0%	46.7%	50.6%	49.3%	49.2%	60.3%	54.9%	60.7%	65.2%
	116	128	177	183	150	160	237	223	232	285
Resistance ≥1CLSI subclass*	62.1%	61.0%	53.3%	49.4%	50.7%	50.8%	39.7%	45.1%	39.3%	34.8%
	190	200	202	179	154	165	156	183	150	152
Resistance ≥2 CLSI subclasses*	56.2%	56.7%	51.2%	46.1%	47.0%	48.0%	36.1%	41.4%	37.2%	33.2%
	172	186	194	167	143	156	142	168	142	145
Resistance ≥3 CLSI subclasses*	51.0%	52.4%	47.5%	43.1%	43.4%	41.8%	32.3%	36.9%	31.4%	30.0%
	156	172	180	156	132	136	127	150	120	131
Resistance ≥4 CLSI subclasses*	45.4%	47.9%	43.0%	38.4%	39.8%	38.2%	28.5%	32.0%	28.0%	27.2%
	139	157	163	139	121	124	112	130	107	119
Resistance ≥5 CLSI subclasses*	35.6%	36.0%	34.3%	27.9%	30.6%	29.8%	23.4%	27.8%	24.3%	23.6%
	109	118	130	101	93	97	92	113	93	103
At least ACSSuT [†]	33.7%	35.1%	32.2%	27.6%	28.0%	29.5%	21.4%	26.1%	23.3%	22.2%
	103	115	122	100	85	96	84	106	89	97
At least ACSuTm [‡]	2.0%	0.6%	2.6%	2.2%	1.6%	0.9%	2.0%	3.2%	1.6%	2.1%
7 (1000 (7 10 0 0 1 1 11 1	6	2	10	8	5	3	8	13	6	9
At least ACSSuTAuCf [§]	0.0%	1.2%	1.1%	0.6%	2.0%	1.2%	1.8%	2.2%	2.6%	1.8%
At least Accountact	0.070	4	4	2	6	4	7	9	10	8
At least MDR-AmpC [¶]	0.0%	1.2%	1.1%	0.6%	2.0%	1.2%	1.8%	2.2%	2.6%	1.8%
At least MDR-Allipo	0.078	4	4	2	6	4	7	9	10	8
	_				_			_		
Resistance to quinolone and cephalosporin (3 rd generation)	0.0%	0.3%	0.0%	0.0%	0.3%	0.3%	0.5%	0.0%	0.3%	0.2%
	0	I 1	0	0	I 1	I 1	2	0	I 1	1 1

^{*}CLSI: Clinical and Laboratory Standards Institute

 $^{^{\}dagger} ACSSuT: resistance \ to \ ampicillin, \ chloramphenicol, \ streptomycin, \ sulfamethoxazole/sulfisoxazole, \ tetracycline$

 $^{^{\}ddagger}$ ACSuTm: resistance to ampicillin, chloramphenicol, trimethoprim-sulfamethoxazole

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

 $^{^{\}P}$ MDR-AmpC: resistance to ACSSuTAuCf + decreased susceptibility to ceftriaxone (MIC ≥2 μg/mL)

B. Salmonella Enteritidis

In 2005, Enteritidis was the second most common non-Typhi *Salmonella* serotype in NARMS. Most *Salmonella* Enteritidis isolates had no detected resistance. However, nalidixic acid resistance increased from 0.9% in 1996 to 4.7% in 2005.

In 2005, Enteritidis was the second most common non-Typhi *Salmonella* serotype identified in NARMS, accounting for 18.6% (383/2052) of non-Typhi *Salmonella* isolates (<u>Table 1.04</u>). Among *Salmonella* Enteritidis isolates tested in 2005, resistance was rare. The most dramatic increase occurred with nalidixic acid. There is a statistically significant increase in nalidixic acid resistance from 0.9% in 1996 to 4.7% in 2005 (95% CI [1.6, 30.5]) (<u>Table 1.09</u>). *Salmonella* Enteritidis was the second most prevalent (30.5%) non-Typhi *Salmonella* serotype that had resistance to nalidixic acid (<u>Table 1.20</u>).

Most (91.9%) of the *Salmonella* Enteritidis isolates tested in 2005 had no detected resistance (<u>Table 1.10</u>). Multidrug resistance was rare.

Table 1.08: Minimum inhibitory concentrations (MICs) and resistance of Salmonella Enteritidis isolates to

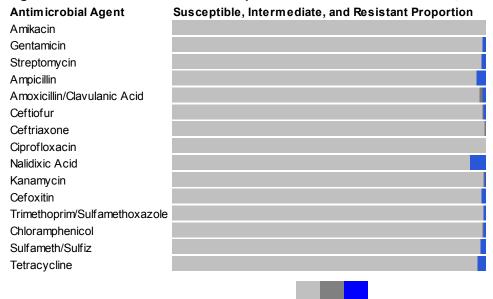
antimicrobial agents, 2005 (N=383)

	Antibiotic		% of iso	olates						Perce	nt of all	isolate	s with	МІС (μ	ig/mL) [§]					
	Antibiotic	%l [⁺]	%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]						30.5	61.1	8.4								
	Gentamicin	0.0	0.8	[0.2–2.3]					86.2	13.1					0.5	0.3				
	Streptomycin	NA	1.0	[0.3–2.7]												99.0	0.3	0.8		
Aminopenicillins	Ampicillin	0.0	2.9	[1.4–5.1]							72.1	24.3	0.5	0.3		0.3	2.6			
β-lactamase inhibitor	Amoxicillin-clavulanic acid	1.0	8.0	[0.2-2.3]							93.5	3.1	0.5	1.0	1.0	0.5	0.3			
Cephalosporins (3rd generation)	Ceftiofur	0.3	0.5	[0.1–1.9]				0.3	0.8	36.3	61.6	0.3	0.3	0.3	0.3					
(· · 3 · · · · · ,	Ceftriaxone	0.3	0.0	[0.0-1.0]					99.5	0.3			•	•		0.3				
Quinolones	Ciprofloxacin	0.0	0.0	[0.0-1.0]	94.5	0.5	1.0	3.1	0.8						•	•				
	Nalidixic Acid	NA	4.7	[2.8–7.3]								14.1	78.6	2.6			4.7			
Aminoglycosides	Kanamycin	0.3	0.3	[0.0-1.4]										99.5		0.3		0.3		
Cephamycins	Cefoxitin	0.0	1.0	[0.3–2.7]						0.5	34.2	59.0	4.7	0.5		0.5	0.5			
Folate pathway inhibitors	Trimethoprim-sulfamethoxazole	NA	0.5	[0.1–1.9]				97.7	1.6	0.3				0.5						
Phenicols	Chloramphenicol	0.3	0.5	[0.1–1.9]								1.0	77.3	20.9	0.3		0.5			
Sulfonamides	Sulfamethoxazole/Sulfisoxazole	NA	1.6	[0.6–3.4]											22.2	63.4	12.0	0.5	0.3	1.6
Tetracyclines	Tetracycline	0.0	2.3	[1.1-4.4]									97.7				2.3			

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

\$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.

Figure 1.05: Antimicrobial resistance pattern for Salmonella Enteritidis, 2005



SI

[†]Percent of isolates that were resistant

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

Table 1.09: Percentage and number of *Salmonella* Enteritidis isolates resistant to antimicrobial agents, 1996–2005

1990-2005 Year		1996	1997	1998	1999	2000	2001	2002	2003	2004	2005
Total Isolates		351	301	244	269	319	277	337	257	271	383
Total isolates	Antibiotic	331	301	244	209	313	211	331	237	2/1	303
Subclass	(Resistance breakpoint)										
Aminoglycosides	Amikacin	Not	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
3,	(MIC ≥ 64)	Tested	0	0	0	0	0	0	0	0	0
	Gentamicin	4.8%	0.3%	0.4%	0.0%	0.3%	0.0%	0.3%	0.4%	0.4%	0.8%
	(MIC ≥ 16)	17	1	1	0	1	0	1	1	1	3
	Streptomycin	2.0%	4.3%	1.6%	2.2%	0.0%	1.4%	1.8%	1.2%	2.2%	1.0%
	(MIC ≥ 64)	7	13	4	6	0	4	6	3	6	4
Aminopenicillins	Ampicillin	20.5%	11.3%	6.1%	10.8%	7.5%	8.7%	7.1%	2.3%	4.1%	2.9%
•	(MIC ≥ 32)	72	34	15	29	24	24	24	6	11	11
β-lactamase inhibitor combinations	Amoxicillin-clavulanic acid	0.6%	0.0%	0.0%	0.4%	0.0%	1.4%	0.6%	0.0%	0.0%	0.8%
	(MIC ≥ 32)	2	0	0	1	0	4	2	0	0	3
Cephalosporins (3 rd generation)	Ceftiofur	0.0%	0.3%	0.0%	0.4%	0.0%	2.2%	0.0%	0.0%	0.0%	0.5%
, , ,	(MIC ≥ 8)	0	1	0	1	0	6	0	0	0	2
	Ceftriaxone	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
	(MIC ≥ 64)	0	0	0	0	0	0	0	0	0	0
Quinolones	Ciprofloxacin	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
	(MIC ≥ 4)	0	0	0	0	0	0	0	0	0	0
	Nalidixic Acid	0.9%	1.7%	2.0%	2.2%	2.2%	4.3%	3.9%	4.7%	6.6%	4.7%
	(MIC ≥ 32)	3	5	5	6	7	12	13	12	18	18
Aminoglycosides	Kanamycin	0.0%	0.7%	0.4%	0.4%	0.3%	0.7%	0.3%	0.0%	0.7%	0.3%
	(MIC ≥ 64)	0	2	1	1	1	2	1	0	2	1
Cephalosporin (1st generation)	Cephalothin	4.0%	1.3%	0.0%	1.9%	0.9%	1.1%	0.6%	1.2%	Not	Not
, , , ,	(MIC ≥ 32)	14	4	0	5	3	3	2	3	Tested	Tested
Cephamycins	Cefoxitin	Not	Not	Not	Not	0.0%	0.4%	0.0%	0.0%	0.0%	1.0%
	(MIC ≥ 32)	Tested	Tested	Tested	Tested	0	1	0	0	0	4
Folate pathway inhibitors	Trimethoprim-sulfamethoxazole	6.6%	1.3%	0.8%	0.7%	0.0%	0.7%	0.6%	0.8%	0.0%	0.5%
	(MIC ≥ 4)	23	4	2	2	0	2	2	2	0	2
Phenicols	Chloramphenicol	0.0%	0.7%	0.0%	0.4%	0.0%	0.0%	0.6%	0.4%	0.4%	0.5%
	(MIC ≥ 32)	0	2	0	1	0	0	2	1	1	2
Sulfonamides	Sulfamethoxazole/Sulfisoxazole*	8.5%	9.0%	2.0%	3.0%	0.9%	2.2%	1.8%	1.2%	1.8%	1.6%
	(MIC ≥ 512)	30	27	5	8	3	6	6	3	5	6
Tetracyclines	Tetracycline	16.8%	9.6%	6.6%	8.2%	1.9%	1.8%	4.5%	1.6%	3.3%	2.3%
	(MIC ≥ 16)	59	29	16	22	6	5	15	4	9	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, 1996–2005

Year	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005
Total Isolates	351	301	244	269	319	277	337	257	271	383
	%	%	%	%	%	%	%	%	%	%
	n	n	n	n	n	n	n	n	n	n
No resistance detected	73.5%	77.4%	87.7%	83.6%	89.0%	86.6%	87.2%	91.8%	87.1%	91.9%
	258	233	214	225	284	240	294	236	236	352
Resistance ≥1CLSI subclass*	26.5%	22.6%	12.3%	16.4%	11.0%	13.4%	12.8%	8.2%	12.9%	8.1%
	93	68	30	44	35	37	43	21	35	31
Resistance ≥2 CLSI subclasses*	19.1%	9.6%	6.6%	8.6%	1.9%	4.7%	4.2%	2.3%	3.0%	3.7%
	67	29	16	23	6	13	14	6	8	14
Resistance ≥3 CLSI subclasses*	8.0%	3.0%	0.8%	1.1%	0.3%	2.9%	2.4%	0.8%	1.1%	2.1%
	28	9	2	3	1	8	8	2	3	8
Resistance ≥4 CLSI subclasses*	4.6%	1.3%	0.0%	0.7%	0.0%	1.8%	1.5%	0.4%	0.7%	0.8%
	16	4	0	2	0	5	5	1	2	3
Resistance ≥5 CLSI subclasses*	1.7%	0.7%	0.0%	0.4%	0.0%	0.0%	0.3%	0.4%	0.7%	0.5%
	6	2	0	1	0	0	1	1	2	2
At least ACSSuT [†]	0.0%	0.3%	0.0%	0.4%	0.0%	0.0%	0.3%	0.4%	0.4%	0.5%
	0	1	0	1	0	0	1	1	1	2
At least ACSuTm [‡]	0.0%	0.3%	0.0%	0.4%	0.0%	0.0%	0.0%	0.4%	0.0%	0.0%
	0	1	0	1	0	0	0	1	0	0
At least ACSSuTAuCf [§]	0.0%	0.0%	0.0%	0.4%	0.0%	0.0%	0.0%	0.0%	0.0%	0.3%
	0	0	0	1	0	0	0	0	0	1
At least MDR-AmpC ¹	0.0%	0.0%	0.0%	0.4%	0.0%	0.0%	0.0%	0.0%	0.0%	0.3%
r -	0	0	0	1	0	0	0	0	0	1
Resistance to quinolone and cephalosporin (3 rd generation)	0.0%	0.3%	0.0%	0.0%	0.3%	0.0%	0.0%	0.4%	0.0%	0.3%
. toolotanoo to quinosono ana oopilaloopoilii (o gorioration)	0	1	0	0	1	0	0	1	0	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)

C. Salmonella Newport

In 2005, Newport was the third most common non-Typhi *Salmonella* serotype in NARMS. MDR-AmpC in *Salmonella* Newport increased from 1996 to 2005, which was similar to the trend in ceftiofur resistance. MDR-AmpC was first noted in 1998, increased to 18.2% in 1999, peaked at 25.0% in 2001, and declined to 12.6% in 2005.

In 2005, Newport was the third most commonly isolated non-Typhi *Salmonella* serotype in NARMS, accounting for 10.0% (207/2052) of non-Typhi *Salmonella* isolates (<u>Table 1.04</u>). The highest proportions of the *Salmonella* Newport isolates tested were resistant to sulfisoxazole (15.5%), tetracycline (14.5%), ampicillin (14.0%), streptomycin (14.0%), chloramphenicol (13.5%) amoxicillin-clavulanic acid (12.6%), ceftiofur (12.6%), and cefoxitin (12.6%). The prevalence of resistance among clinically important antimicrobial subclasses was 0.0% for quinolones (represented by nalidixic acid) and 12.6% 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 12.6% in 2005 (<u>Table 1.12</u>). Salmonella Newport was the most prevalent (43.3%) non-Typhi Salmonella serotype that had resistance to ceftiofur (<u>Table 1.20</u>).

In contrast to other common serotypes, the percentage of *Salmonella* Newport isolates with no detected resistance declined from 86.3% in 1996 and 73.5% in 2003 (<u>Table 1.13</u>). However, the percentage of *Salmonella* Newport isolates with no detected resistance was higher in 2005 (84.1%) than in 2004 (82.2%). In addition, resistance to at least five subclasses of antimicrobial agents increased from 5.9% in 1996 to 12.6% in 2005; it peaked in 2001, similar to the trend in ceftiofur resistance.

In 2005, MDR-AmpC was among the most common multidrug-resistant phenotype in serotype Newport (12.6% of isolates). MDR-AmpC increased since 1996, which was similar to the trend in ceftiofur resistance (<u>Table 1.13</u>); it was first noted in 1998, increased to 18.2% in 1999, peaked at 25.0% in 2001, and declined to 12.6% in 2005. In the logistic regression model, the increase from 1996 to 2005 was statistically significant (95% CI [1.8, infinity]).

Table 1.11: Minimum inhibitory concentrations (MICs) and resistance of *Salmonella* Newport isolates to antimicrobial agents, 2005 (N=207)

	Antibiotic		% of is	olates						Percei	nt of al	l isolate	es with	МІС (μ	g/mL) [§]					
	Antibiotic	%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	[0.0–1.8]						8.2	75.4	13.0	3.4							
	Gentamicin	1.0	1.0	[0.1–3.4]					75.8	21.7	0.5			1.0	1.0					
	Streptomycin	NA	14.0	[9.6–19.5]												86.0	1.0	13.0		
Aminopenicillins	Ampicillin	0.0	14.0	[9.6–19.5]							82.1	3.4	0.5				14.0			
β-lactamase inhibitor	Amoxicillin-clavulanic acid	0.0	12.6	[8.4–17.9]							85.0	0.5	0.5	1.4		4.3	8.2			
Cephalosporins (3rd generation)	Ceftiofur	0.0	12.6	[8.4–17.9]				0.5		58.9	27.5	0.5			12.6					
, ,	Ceftriaxone	11.1	1.4	[0.3-4.2]					87.4						4.3	6.8	0.5	1.0		
Quinolones	Ciprofloxacin	0.0	0.0	[0.0–1.8]	100.0															
	Nalidixic Acid	NA	0.0	[0.0–1.8]							1.4	33.8	64.7							
Aminoglycosides	Kanamycin	0.0	1.9	[0.5-4.9]										98.1				1.9		
Cephamycins	Cefoxitin	0.0	12.6	[8.4–17.9]						0.5	41.1	42.5	2.4	1.0		1.0	11.6			
Folate pathway inhibitors	Trimethoprim-sulfamethoxazole	NA	1.9	[0.5-4.9]				94.7	3.4					1.9						
Phenicols	Chloramphenicol	0.0	13.5	[9.2–19.0]								5.3	75.4	5.8			13.5			
Sulfonamides	Sulfamethoxazole/Sulfisoxazole	NA	15.5	[10.8–21.1]											4.8	44.0	33.8	1.9		15.5
Tetracyclines	Tetracycline	0.0	14.5	[10.0–20.0]									85.5			3.4	11.1			

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.

Figure 1.06: Antimicrobial resistance pattern for Salmonella Newport, 2005

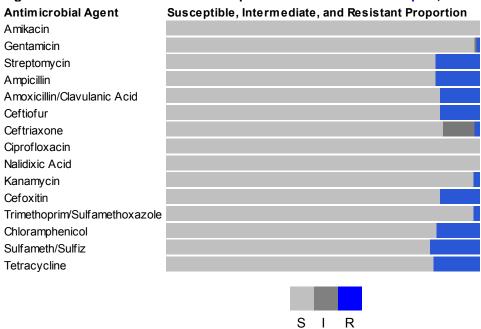


Table 1.12: Percentage and number of *Salmonella* Newport isolates resistant to antimicrobial agents, 1996–2005

Year Total Isolates		1996 51	1997 46	1998 77	1999 99	2000 121	2001 124	2002 241	2003 223	2004 191	2005 207
Total lociates	Antibiotic	Ų.		•••			12-7			101	
Subclass	(Resistance breakpoint)										
Aminoglycosides	Amikacin	Not	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
0,	(MIC ≥ 64)	Tested	0	0	0	0	0	0	0	0	0
	Gentamicin	5.9%	4.3%	0.0%	0.0%	2.5%	3.2%	3.3%	3.1%	0.5%	1.0%
	(MIC ≥ 16)	3	2	0	0	3	4	8	7	1	2
	Streptomycin	7.8%	4.3%	2.6%	19.2%	24.0%	31.5%	25.3%	24.2%	15.7%	14.0%
	(MIC ≥ 64)	4	2	2	19	29	39	61	54	30	29
Aminopenicillins	Ampicillin	5.9%	6.5%	2.6%	18.2%	23.1%	29.8%	24.9%	22.9%	15.7%	14.0%
	(MIC ≥ 32)	3	3	2	18	28	37	60	51	30	29
β-lactamase inhibitor combinations	Amoxicillin-clavulanic acid	2.0%	0.0%	2.6%	18.2%	22.3%	26.6%	22.8%	21.5%	15.2%	12.6%
	(MIC ≥ 32)	1	0	2	18	27	33	55	48	29	26
Cephalosporins (3 rd generation)	Ceftiofur	0.0%	0.0%	1.3%	18.2%	22.3%	27.4%	22.8%	22.0%	15.2%	12.6%
3 ,	(MIC ≥ 8)	0	0	1	18	27	34	55	49	29	26
	Ceftriaxone	0.0%	0.0%	0.0%	3.0%	0.0%	0.0%	0.8%	1.8%	2.6%	1.4%
	(MIC ≥ 64)	0	0	0	3	0	0	2	4	5	3
Quinolones	Ciprofloxacin	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
	(MIC ≥ 4)	0	0	0	0	0	0	0	0	0	0
	Nalidixic Acid	0.0%	0.0%	0.0%	0.0%	0.8%	0.0%	0.8%	0.4%	0.5%	0.0%
	(MIC ≥ 32)	0	0	0	0	1	0	2	1	1	0
Aminoglycosides	Kanamycin	2.0%	0.0%	1.3%	1.0%	5.0%	7.3%	10.0%	4.5%	2.6%	1.9%
	(MIC ≥ 64)	1	0	1	1	6	9	24	10	5	4
Cephalosporin (1st generation)	Cephalothin	3.9%	4.3%	2.6%	18.2%	22.3%	26.6%	22.8%	22.4%	Not	Not
(· g)	(MIC ≥ 32)	2	2	2	18	27	33	55	50	Tested	Tested
Cephamycins	Cefoxitin	Not	Not	Not	Not	22.3%	25.8%	22.4%	21.5%	15.2%	12.6%
•	(MIC ≥ 32)	Tested	Tested	Tested	Tested	27	32	54	48	29	26
Folate pathway inhibitors	Trimethoprim-sulfamethoxazole	3.9%	4.3%	1.3%	2.0%	4.1%	1.6%	4.1%	0.9%	2.1%	1.9%
	(MIC ≥ 4)	2	2	1	2	5	2	10	2	4	4
Phenicols	Chloramphenicol	5.9%	4.3%	2.6%	18.2%	23.1%	28.2%	25.3%	22.4%	15.2%	13.5%
	(MIC ≥ 32)	3	2	2	18	28	35	61	50	29	28
Sulfonamides	Sulfamethoxazole/Sulfisoxazole*	11.8%	4.3%	3.9%	22.2%	23.1%	32.3%	25.7%	24.7%	16.8%	15.5%
	(MIC ≥ 512)	6	2	3	22	28	40	62	55	32	32
Tetracyclines	Tetracycline	7.8%	4.3%	2.6%	19.2%	23.1%	30.6%	25.7%	24.2%	16.8%	14.5%
/ -	(MIC ≥ 16)	4	2	2	19	28	38	62	54	32	30

^{*}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, 1996–2005

					2001	2002	2003	2004	2005
									2003
, ,			, -	, •	, -	, -		, ,	%
									n
									84.1%
44	43	73	75	91	81	174	164	157	174
13.7%	6.5%	5.2%	24.2%	24.8%	34.7%	27.8%	26.5%	17.8%	15.9%
7	3	4	24	30	43	67	59	34	33
7.8%	4.3%	2.6%	18.2%	23.1%	32.3%	25.7%	25.1%	17.3%	15.0%
4	2	2	18	28	40	62	56	33	31
5.9%	4.3%	2.6%	18.2%	23.1%	31.5%	25.3%	23.3%	16.8%	14.5%
3	2	2	18	28	39	61	52	32	30
5.9%	4.3%	2.6%	18.2%	23.1%	31.5%	25.3%	22.9%	15.7%	14.0%
3	2	2	18	28	39	61	51	30	29
5.9%	4.3%	2.6%	18.2%	23.1%	27.4%	23.7%	22.4%	14.7%	12.6%
3	2	2	18	28	34	57	50	28	26
5.9%	4.3%	1.3%	18.2%	23.1%	25.8%	23.7%	22.0%	14.7%	12.6%
3	2	1	18	28	32	57	49	28	26
3.9%	4.3%	1.3%	2.0%	4.1%	0.8%	3.7%	0.9%	1.0%	1.9%
2	2	1	2	5	1	9	2	2	4
0.0%	0.0%	1.3%	18.2%	22.3%	25.0%	22.8%	21.1%	14.7%	12.6%
0	0	1		27			47	28	26
0.0%	0.0%	1.3%		22.3%				14 7%	12.6%
0	0	1	18	27	31	55	47	28	26
0.0%	0.0%	1.3%							0.0%
		1				1		1	0.070
	1996 51 % n 86.3% 44 13.7% 7 7.8% 4 5.9% 3 5.9% 3 5.9% 3 3.9% 2 0.0% 0	1996	1996 1997 1998 51 46 77 % % % n n n 86.3% 93.5% 94.8% 44 43 73 13.7% 6.5% 5.2% 7 3 4 7.8% 4.3% 2.6% 4 2 2 5.9% 4.3% 2.6% 3 2 2 5.9% 4.3% 2.6% 3 2 2 5.9% 4.3% 2.6% 3 2 2 5.9% 4.3% 1.3% 3 2 1 0.0% 0.0% 1.3% 2 1 1.3% 3 2 1 0.0% 0.0% 1.3% 0 0 1 0.0% 0.0% 1.3% 0 0 1 0	1996 1997 1998 1999 51 46 77 99 % % % % n n n n 86.3% 93.5% 94.8% 75.8% 44 43 73 75 13.7% 6.5% 5.2% 24.2% 7 3 4 24 7.8% 4.3% 2.6% 18.2% 4 2 2 18 5.9% 4.3% 2.6% 18.2% 3 2 2 18 5.9% 4.3% 2.6% 18.2% 3 2 2 18 5.9% 4.3% 2.6% 18.2% 3 2 2 18 5.9% 4.3% 2.6% 18.2% 3 2 1 18 5.9% 4.3% 1.3% 18.2% 3 2 1 18	51 46 77 99 121 % % % % % n n n n n 86.3% 93.5% 94.8% 75.8% 75.2% 44 43 73 75 91 13.7% 6.5% 5.2% 24.2% 24.8% 7 3 4 24 30 7.8% 4.3% 2.6% 18.2% 23.1% 4 2 2 18 28 5.9% 4.3% 2.6% 18.2% 23.1% 3 2 2 18 28 5.9% 4.3% 2.6% 18.2% 23.1% 3 2 2 18 28 5.9% 4.3% 2.6% 18.2% 23.1% 3 2 2 18 28 5.9% 4.3% 1.3% 18.2% 23.1% 3 2 1 <t< td=""><td>1996 1997 1998 1999 2000 2001 51 46 77 99 121 124 % % % % % % n n n n n n 86.3% 93.5% 94.8% 75.8% 75.2% 65.3% 44 43 73 75 91 81 13.7% 6.5% 5.2% 24.2% 24.8% 34.7% 7 3 4 24 30 43 7.8% 4.3% 2.6% 18.2% 23.1% 32.3% 4 2 2 18 28 40 5.9% 4.3% 2.6% 18.2% 23.1% 31.5% 3 2 2 18 28 39 5.9% 4.3% 2.6% 18.2% 23.1% 27.4% 3 2 2 18 28 39 5.9%<td>1996 1997 1998 1999 2000 2001 2002 51 46 77 99 121 124 241 % % % % % % % n n n n n n n n 86.3% 93.5% 94.8% 75.8% 75.2% 65.3% 72.2% 44 43 73 75 91 81 174 13.7% 6.5% 5.2% 24.2% 24.8% 34.7% 27.8% 27.8% 4 24 30 43 67 7.8% 4.3% 2.6% 18.2% 23.1% 32.3% 25.7% 25.3% 4 22 18 28 40 62 25.3% 3 2 2 18 28 40 62 25.3% 3 2 2 18 28 39 61 5.9% 4.3% 2.6% 18.2% 23.1% 31.5% 25.3%</td></td></t<> <td>1996 1997 1998 1999 2000 2001 2002 2003 51 46 77 99 121 124 241 223 % % % % % % % % n n n n n n n n 86.3% 93.5% 94.8% 75.8% 75.2% 65.3% 72.2% 73.5% 44 43 73 75 91 81 174 164 13.7% 6.5% 5.2% 24.2% 24.8% 34.7% 27.8% 26.5% 7 3 4 24 30 43 67 59 7.8% 4.3% 2.6% 18.2% 23.1% 32.3% 25.7% 25.1% 4 2 2 18 28 40 62 56 5.9% 4.3% 2.6% 18.2% 23.1% 31.5% 25.3% 22.9%<td>1996 1997 1998 1999 2000 2001 2002 2003 2004 51 46 77 99 121 124 241 223 191 % % % % % % % % n n n n n n n n 86.3% 93.5% 94.8% 75.8% 75.2% 65.3% 72.2% 73.5% 82.2% 44 43 73 75 91 81 174 164 157 13.7% 6.5% 5.2% 24.2% 24.8% 34.7% 27.8% 26.5% 17.8% 7 3 4 24 30 43 67 59 34 7.8% 4.3% 2.6% 18.2% 23.1% 32.3% 25.7% 25.1% 17.3% 4 2 2 18 28 40 62 56.9% 13.3%</td></td>	1996 1997 1998 1999 2000 2001 51 46 77 99 121 124 % % % % % % n n n n n n 86.3% 93.5% 94.8% 75.8% 75.2% 65.3% 44 43 73 75 91 81 13.7% 6.5% 5.2% 24.2% 24.8% 34.7% 7 3 4 24 30 43 7.8% 4.3% 2.6% 18.2% 23.1% 32.3% 4 2 2 18 28 40 5.9% 4.3% 2.6% 18.2% 23.1% 31.5% 3 2 2 18 28 39 5.9% 4.3% 2.6% 18.2% 23.1% 27.4% 3 2 2 18 28 39 5.9% <td>1996 1997 1998 1999 2000 2001 2002 51 46 77 99 121 124 241 % % % % % % % n n n n n n n n 86.3% 93.5% 94.8% 75.8% 75.2% 65.3% 72.2% 44 43 73 75 91 81 174 13.7% 6.5% 5.2% 24.2% 24.8% 34.7% 27.8% 27.8% 4 24 30 43 67 7.8% 4.3% 2.6% 18.2% 23.1% 32.3% 25.7% 25.3% 4 22 18 28 40 62 25.3% 3 2 2 18 28 40 62 25.3% 3 2 2 18 28 39 61 5.9% 4.3% 2.6% 18.2% 23.1% 31.5% 25.3%</td>	1996 1997 1998 1999 2000 2001 2002 51 46 77 99 121 124 241 % % % % % % % n n n n n n n n 86.3% 93.5% 94.8% 75.8% 75.2% 65.3% 72.2% 44 43 73 75 91 81 174 13.7% 6.5% 5.2% 24.2% 24.8% 34.7% 27.8% 27.8% 4 24 30 43 67 7.8% 4.3% 2.6% 18.2% 23.1% 32.3% 25.7% 25.3% 4 22 18 28 40 62 25.3% 3 2 2 18 28 40 62 25.3% 3 2 2 18 28 39 61 5.9% 4.3% 2.6% 18.2% 23.1% 31.5% 25.3%	1996 1997 1998 1999 2000 2001 2002 2003 51 46 77 99 121 124 241 223 % % % % % % % % n n n n n n n n 86.3% 93.5% 94.8% 75.8% 75.2% 65.3% 72.2% 73.5% 44 43 73 75 91 81 174 164 13.7% 6.5% 5.2% 24.2% 24.8% 34.7% 27.8% 26.5% 7 3 4 24 30 43 67 59 7.8% 4.3% 2.6% 18.2% 23.1% 32.3% 25.7% 25.1% 4 2 2 18 28 40 62 56 5.9% 4.3% 2.6% 18.2% 23.1% 31.5% 25.3% 22.9% <td>1996 1997 1998 1999 2000 2001 2002 2003 2004 51 46 77 99 121 124 241 223 191 % % % % % % % % n n n n n n n n 86.3% 93.5% 94.8% 75.8% 75.2% 65.3% 72.2% 73.5% 82.2% 44 43 73 75 91 81 174 164 157 13.7% 6.5% 5.2% 24.2% 24.8% 34.7% 27.8% 26.5% 17.8% 7 3 4 24 30 43 67 59 34 7.8% 4.3% 2.6% 18.2% 23.1% 32.3% 25.7% 25.1% 17.3% 4 2 2 18 28 40 62 56.9% 13.3%</td>	1996 1997 1998 1999 2000 2001 2002 2003 2004 51 46 77 99 121 124 241 223 191 % % % % % % % % n n n n n n n n 86.3% 93.5% 94.8% 75.8% 75.2% 65.3% 72.2% 73.5% 82.2% 44 43 73 75 91 81 174 164 157 13.7% 6.5% 5.2% 24.2% 24.8% 34.7% 27.8% 26.5% 17.8% 7 3 4 24 30 43 67 59 34 7.8% 4.3% 2.6% 18.2% 23.1% 32.3% 25.7% 25.1% 17.3% 4 2 2 18 28 40 62 56.9% 13.3%

^{*}CLSI: Clinical and Laboratory Standards Institute

D. Salmonella Heidelberg

In 2005, Heidelberg was the fourth most commonly isolated non-Typhi *Salmonella* serotype in NARMS, accounting for 6.1% (125/2052) of non-Typhi *Salmonella* isolates (<u>Table 1.04</u>). The highest proportions of the *Salmonella* Heidelberg isolates tested were resistant to ampicillin (20.0%), tetracycline (18.4%), streptomycin (13.6%), kanamycin (12.8%) amoxicillin-clavulanic acid, ceftiofur, and cefoxitin (8.8%) and sulfisoxazole (8.0%). The prevalence of resistance among clinically important antimicrobial subclasses was 1.7% for quinolones (represented by nalidixic acid) and 18.3% for third-generation cephalosporins (represented by ceftiofur) (<u>Table 1.20</u>).

Ceftiofur resistance was first noted in one isolate (1.3%) in 1996; it increased to 9.7% in 2004 and decreased to 8.8% in 2005 (<u>Table 1.15</u>). *Salmonella* Heidelberg was the second most common serotype (18.3%), tied with Typhimurium, among ceftiofur-resistant non-Typhi *Salmonella* (<u>Table 1.20</u>).

In contrast to other common serotypes, the percentage of *Salmonella* Heidelberg isolates with no detected resistance increased from 54.1% in 1996 and 62.4% in 2005 (<u>Table 1.16</u>). In addition, resistance to at least five subclasses of antimicrobial agents decreased from 3.2% in 2004 to 2.4% in 2005.

In 2005, one Salmonella Heidelberg isolate was found to have the combination of quinolone and third-generation cephalosporin resistance (Table 1.16).

[†]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)

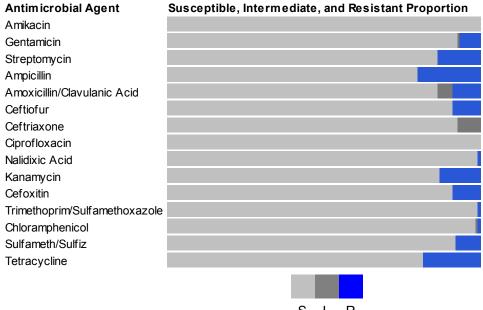
Table 1.14: Minimum inhibitory concentrations (MICs) and resistance of Salmonella Heidelberg isolates to

antimicrobial agents, 2005 (N=125)

	Antibiotic		% of is	olates		•			•	Percei	nt of all	isolate	s with	MIC (μ	g/mL) [§]	•				
	Antibiotic	%l [⁺]	%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	[0.0-2.9]						26.4	63.2	8.8	0.8	0.8						
	Gentamicin	0.8	6.4	[2.8–12.2]					73.6	16.0	2.4	0.8		0.8	3.2	3.2	l.			
	Streptomycin	NA	13.6	[8.1–20.9]												86.4	7.2	6.4		
Aminopenicillins	Ampicillin	0.0	20.0	[13.4–28.1]							62.4	16.8	0.8				20.0			
β-lactamase inhibitor	Amoxicillin-clavulanic acid	4.8	8.8	[4.5–15.2]							77.6	1.6	0.8	6.4	4.8	2.4	6.4			
Cephalosporins (3rd generation)	Ceftiofur	0.0	8.8	[4.5–15.2]					1.6	73.6	15.2	0.8			8.8					
, ,	Ceftriaxone	7.2	0.0	[0.0-2.9]					91.2					1.6	6.4	0.8				
Quinolones	Ciprofloxacin	0.0	0.0	[0.0-2.9]	99.2					8.0										
	Nalidixic Acid	NA	8.0	[0.0-4.4]							,	20.8	77.6	0.8			0.8			
Aminoglycosides	Kanamycin	0.0	12.8	[7.5–20.0]										87.2	•			12.8		
Cephamycins	Cefoxitin	0.0	8.8	[4.5–15.2]							59.2	26.4	4.0	1.6		4.8	4.0			
Folate pathway inhibitors	Trimethoprim-sulfamethoxazole	NA	8.0	[0.0-4.4]				96.0	3.2					0.8						
Phenicols	Chloramphenicol	0.8	8.0	[0.0-4.4]								0.8	61.6	36.0	0.8		0.8			
Sulfonamides	Sulfamethoxazole/Sulfisoxazole	NA	0.0	[3.9–14.2]											50.4	37.6	4.0		8.0	
Tetracyclines	Tetracycline	0.0	18.4	[12.0–26.3]									81.6			1.6	16.8		,	

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

Figure 1.07: Antimicrobial resistance pattern for Salmonella Heidelberg, 2005



[†]Percent of isolates that were resistant

 $^{^{\}ddagger}95\%$ 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 1.15: Percentage and number of *Salmonella* Heidelberg isolates resistant to antimicrobial agents, 1996–2005

Table 1.15: Percentage and number of Salmonella Heidelberg isolates resistant to antimicrobial agents, 1996–2005

Year		1996	1997	1998	1999	2000	2001	2002	2003	2004	2005
Total Isolates		74	75	101	88	79	102	105	96	93	125
	Antibiotic										
Subclass	(Resistance breakpoint)										
Aminoglycosides	Amikacin	Not	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
	(MIC ≥ 64)	Tested	0	0	0	0	0	0	0	0	0
	Gentamicin	23.0%	17.3%	16.8%	14.8%	8.9%	7.8%	3.8%	5.2%	4.3%	6.4%
	(MIC ≥ 16)	17	13	17	13	7	8	4	5	4	8
	Streptomycin	40.5%	24.0%	30.7%	23.9%	22.8%	25.5%	17.1%	12.5%	15.1%	13.6%
	(MIC ≥ 64)	30	18	31	21	18	26	18	12	14	17
Aminopenicillins	Ampicillin	14.9%	13.3%	16.8%	6.8%	10.1%	9.8%	12.4%	10.4%	25.8%	20.0%
•	(MIC ≥ 32)	11	10	17	6	8	10	13	10	24	25
β-lactamase inhibitor combinations	Amoxicillin-clavulanic acid	2.7%	1.3%	1.0%	1.1%	3.8%	2.9%	9.5%	5.2%	10.8%	8.8%
	(MIC ≥ 32)	2	1	1	1	3	3	10	5	10	11
Cephalosporins (3 rd generation)	Ceftiofur	1.4%	0.0%	0.0%	0.0%	3.8%	2.9%	7.6%	5.2%	9.7%	8.8%
generality (c. generality)	(MIC ≥ 8)	1	0	0	0	3	3	8	5	9	11
	Ceftriaxone	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
	(MIC ≥ 64)	0	0	0	0	0	0	0	0	0	0
Quinolones	Ciprofloxacin	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
	(MIC ≥ 4)	0	0	0	0	0	0	0	0	0	0
	Nalidixic Acid	0.0%	0.0%	1.0%	1.1%	1.3%	0.0%	0.0%	1.0%	0.0%	0.8%
	(MIC ≥ 32)	0	0	1	1	1	0	0	1	0	1
Aminoglycosides	Kanamycin	14.9%	8.0%	12.9%	9.1%	15.2%	19.6%	10.5%	8.3%	8.6%	12.8%
	(MIC ≥ 64)	11	6	13	8	12	20	11	8	8	16
Cephalosporin (1 st generation)	Cephalothin	6.8%	2.7%	5.9%	3.4%	5.1%	3.9%	10.5%	7.3%	Not	Not
	(MIC ≥ 32)	5	2	6	3	4	4	11	7	Tested	Tested
Cephamycins	Cefoxitin	Not	Not	Not	Not	2.5%	2.9%	8.6%	5.2%	8.6%	8.8%
, ,	(MIC ≥ 32)	Tested	Tested	Tested	Tested	2	3	9	5	8	11
Folate pathway inhibitors	Trimethoprim-sulfamethoxazole	0.0%	0.0%	2.0%	1.1%	1.3%	2.0%	1.0%	2.1%	0.0%	0.8%
, ,	(MIC ≥ 4)	0	0	2	1	1	2	1	2	0	1
Phenicols	Chloramphenicol	1.4%	0.0%	1.0%	1.1%	1.3%	1.0%	1.0%	0.0%	1.1%	0.8%
	(MIC ≥ 32)	1	0	1	1	1	1	1	0	1	1
Sulfonamides	Sulfamethoxazole/Sulfisoxazole*	17.6%	21.3%	21.8%	18.2%	11.4%	8.8%	6.7%	7.3%	7.5%	8.0%
	(MIC ≥ 512)	13	16	22	16	9	9	7	7	7	10
Tetracyclines	Tetracycline	20.3%	12.0%	19.8%	18.2%	21.5%	24.5%	19.0%	16.7%	19.4%	18.4%
	(MIC ≥ 16)	15	9	20	16	17	25	20	16	18	23

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

Table 1.16: Resistance patterns of Salmonella Heidelberg isolates, 1996–2005

Year	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005
Total Isolates	74	75	101	88	79	102	105	96	93	125
	%	%	%	%	%	%	%	%	%	%
	n	n	n	n	n	n	n	n	n	n
No resistance detected	54.1%	66.7%	56.4%	68.2%	63.3%	64.7%	67.6%	68.8%	55.9%	62.4%
	40	50	57	60	50	66	71	66	52	78
Resistance ≥1CLSI subclass*	45.9%	33.3%	43.6%	31.8%	36.7%	35.3%	32.4%	31.3%	44.1%	37.6%
	34	25	44	28	29	36	34	30	41	47
Resistance ≥2 CLSI subclasses*	33.8%	26.7%	33.7%	26.1%	26.6%	29.4%	25.7%	17.7%	23.7%	24.8%
	25	20	34	23	21	30	27	17	22	31
Resistance ≥3 CLSI subclasses*	12.2%	12.0%	13.9%	10.2%	7.6%	7.8%	11.4%	10.4%	14.0%	15.2%
	9	9	14	9	6	8	12	10	13	19
Resistance ≥4 CLSI subclasses*	4.1%	1.3%	4.0%	4.5%	3.8%	2.0%	1.9%	2.1%	4.3%	4.8%
	3	1	4	4	3	2	2	2	4	6
Resistance ≥5 CLSI subclasses*	2.7%	1.3%	1.0%	0.0%	3.8%	2.0%	1.9%	0.0%	3.2%	2.4%
	2	1	1	0	3	2	2	0	3	3
At least ACSSuT [†]	1.4%	0.0%	0.0%	0.0%	1.3%	1.0%	1.0%	0.0%	1.1%	0.0%
	1	0	0	0	1	1	1	0	1	0
At least ACSuTm [‡]	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	1.0%	0.0%	0.0%	0.0%
	0	0	0	0	0	0	1	0	0	0
At least ACSSuTAuCf [§]	0.0%	0.0%	0.0%	0.0%	1.3%	1.0%	1.0%	0.0%	0.0%	0.0%
	0	0	0	0	1	1	1	0	0	0
At least MDR-AmpC [¶]	0.0%	0.0%	0.0%	0.0%	1.3%	1.0%	1.0%	0.0%	0.0%	0.0%
į. ·	0	0	0	0	1	1	1	0	0	0
Resistance to quinolone and cephalosporin (3 rd generation)	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.8%
. toolotanoo to quinono and sopridiooponii (o gonoralion)	0	0	0	0	0	0	0	0	0	1

^{*}CLSI: Clinical and Laboratory Standards Institute

 $^{^{\}dagger} ACSSuT: resistance \ to \ ampicillin, \ chloramphenicol, \ streptomycin, \ sulfamethoxazole/sulfisoxazole, \ tetracycline$

 $^{^{\}ddagger} ACSuTm. \ resistance \ to \ ampicillin, \ chloramphenicol, \ trimethoprim-sulfamethoxazole$

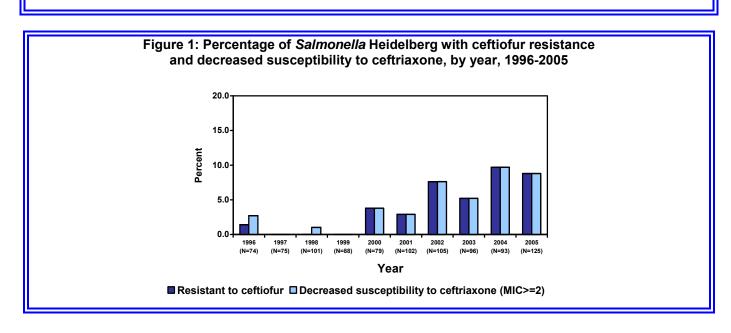
 $^{^{\}S} ACSSuTAuCf:$ resistance to ACSSuT + amoxicillin-clavulanic acid, ceftiofur

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

Salmonella Heidelberg is one of the leading non-Typhi Salmonella serotypes. In 2005, it ranked 5th among human non-Typhi Salmonella isolates tested by the National Antimicrobial Resistance Monitoring (NARMS) and among culture-confirmed infections reported to National Salmonella Surveillance System at CDC (http://www.cdc.gov/ncidod/dbmd/phlisdata/default.htm). It is one of the most common serotypes among non-Typhi Salmonella isolates reported from retail poultry (http://www.fda.gov/cvm/2005NARMSAnnualRpt.htm) and food animals (http://www.ars.usda.gov/Main/docs.htm?docid=16598). Ceftriaxone, a third-generation cephalosporin used to treat invasive Salmonella infections in children, is closely related to ceftiofur, a third-generation cephalosporin used in food animals in the United States. Ceftiofur resistance has been associated with decreased susceptibility to ceftriaxone (Medalla et al., ICEID 2006). Molecular biological analyses of extended-spectrum cephalosporin-resistant strains of Salmonella have revealed that resistance is primarily associated with plasmids (designated types A, B, C, and D) that carry the bla_{CMY-2} gene. These data suggest that the bla_{CMY-2} gene has been disseminated among Salmonella strains primarily through plasmid transfer (Carattoli et al., Antimicrob Agents Chemother 2004, 48:2845-52).

Although ceftriaxone resistance is rare among non-Typhi *Salmonella* submitted to NARMS, an increase in ceftiofur resistance since 1996 has been seen. This increase was mainly driven by an increase in the so-called "MDR-AmpC" phentoype in serotype Newport (Gupta et al., J Infect Dis 2003, 188:1707-16). MDR-AmpC is defined as resistance to at least ampicillin, chloramphenicol, streptomycin, sulfonamide, tetracycline, amoxicillin-clavulanic acid, and ceftiofur, and decreased susceptibility to ceftriaxone (MIC ≥2 µg/mL). From 1996 to 2005, MDR-AmpC was noted in 12 serotypes in addition to Newport. Here we describe the trend in ceftiofur resistance in *Salmonella* Heidelberg in NARMS from 1996-2005. Isolate submission and testing are described in the methods section of this report.

From 1996-2005, 938 (5.8%) of 16,093 non-Typhi *Salmonella* isolates were serotype Heidelberg. Of 938 Heidelberg isolates, 40 (4.3%) were ceftiofur-resistant. Ceftiofur resistance increased from 1.4% in 1996 to 8.8% in 2005 [Figure 1]. Decreased susceptibility to ceftriaxone (MIC \geq 2 µg/mL) showed the same trend [Figure 1]. In contrast to an increase in MDR-AmpC observed with the emergence of extended-spectrum cephalosporin resistance among serotype Newport, only 3 of the ceftiofur-resistant Heidelberg isolates were MDR-AmpC. NARMS is characterizing the genetic elements involved in the dissemination of the bla_{CMY} genes that confer extended-spectrum cephalosporin resistance in Salmonella Heidelberg.



E. Salmonella I 4,[5],12:i:-

In 2005, I 4,[5],12:i:- was the twelfth most common non-Typhi *Salmonella* serotype in NARMS. Most *Salmonella* I 4,[5],12:i:- isolates had no detected resistance. Multidrug resistance was not common in this serotype.

In 2005, I 4,[5],12:i:- was the twelfth most commonly isolated non-Typhi *Salmonella* serotype in NARMS, accounting for 1.6% (33/2052) of non-Typhi *Salmonella* isolates (<u>Table 1.04</u>). The highest proportions of the *Salmonella* I 4,[5],12:i:- isolates tested were resistant to ampicillin (6.1%), tetracycline, streptomycin, amoxicillin-clavulanic acid, ceftiofur, and cefoxitin (3.0%). The prevalence of resistance among clinically important antimicrobial subclasses was 0.0% for quinolones (represented by nalidixic acid) and 1.7% for third-generation cephalosporins (represented by ceftiofur) (<u>Table 1.20</u>).

Ceftiofur resistance was first noted in one isolate (7.1%) in 2001; it decreased to 2.8% in 2004 and rose again to 3.0% in 2005 (<u>Table 1.18</u>).

Most *Salmonella* I 4,[5],12:i:- isolates had no detected resistance. In contrast to other common serotypes, the percentage of *Salmonella* I 4,[5],12:i:- isolates with no detected resistance increased from 80.6% in 2004 to 87.9% in 2005 (<u>Table 1.19</u>). In addition, resistance to at least three subclasses of antimicrobial agents decreased from 11.1% in 2004 to 3.0% in 2005.

Multidrug-resistance was not common in *Salmonella* I 4,[5],12:i:- (<u>Table 1.19</u>). Resistance to at least ampicillin, chloramphenicol, streptomycin, sulfamethoxazole/sulfisoxazole, and tetracycline (ACSSuT) and resistance to at least ampicillin, chloramphenicol, and trimethoprim-sulfamethoxazole (ACSuTm) were first reported in 2001.

Table 1.17: Minimum inhibitory concentrations (MICs) and resistance of *Salmonella* I 4,[5],12:i:- isolates to antimicrobial agents. 2005 (N=33)

	Antibiotic		% of is	olates						Perce	nt of al	isolate	s with	МІС (μ	g/mL) [§]					
	Antibiotic	%l [*]	%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	[0.0–10.6]						9.1	75.8	15.2								
	Gentamicin	0.0	0.0	[0.0–10.6]					72.7	27.3										
	Streptomycin	NA	3.0	[0.1–15.8]												97.0	3.0			
Aminopenicillins	Ampicillin	0.0	6.1	[0.7–20.2]							78.8	15.2				•	6.1			
β-lactamase inhibitor	Amoxicillin-clavulanic acid	0.0	3.0	[0.1–15.8]							81.8	9.1	3.0	3.0			3.0			
Cephalosporins (3rd generation)	Ceftiofur	0.0	3.0	[0.1–15.8]						78.8	18.2				3.0					
(3 ,	Ceftriaxone	3.0	0.0	[0.0–10.6]					97.0			,	,	•	3.0					
Quinolones	Ciprofloxacin	0.0	0.0	[0.0–10.6]	100.0															
	Nalidixic Acid	NA	0.0	[0.0–10.6]								60.6	36.4	3.0						
Aminoglycosides	Kanamycin	0.0	0.0	[0.0–10.6]										100.0						
Cephamycins	Cefoxitin	0.0	3.0	[0.1–15.8]							42.4	51.5	3.0	'			3.0			
Folate pathway inhibitors	Trimethoprim-sulfamethoxazole	NA	0.0	[0.0–10.6]				93.9	6.1											
Phenicols	Chloramphenicol	0.0	0.0	[0.0–10.6]									81.8	18.2						
Sulfonamides	Sulfamethoxazole/Sulfisoxazole	NA	0.0	[0.0-10.6]											15.2	66.7	18.2			
Tetracyclines	Tetracycline	0.0	3.0	[0.1–15.8]									97.0			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.

Figure 1.08: Antimicrobial resistance pattern for Salmonella I 4,[5],12:i:-, 2005

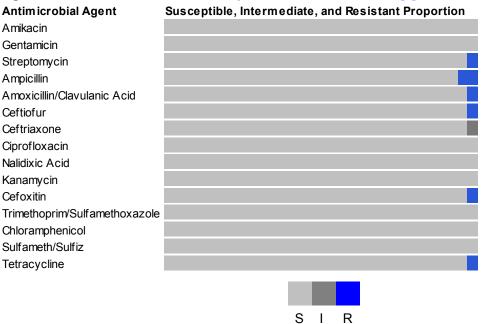


Table 1.18: Percentage and number of *Salmonella* I 4,[5],12:i:- isolates resistant to antimicrobial agents, 1996–2005

Year		1996	1997	1998	1999	2000	2001	2002	2003	2004	2005
Total Isolates		3	3	0	8	13	14	35	37	36	33
Subclass	Antibiotic (Resistance breakpoint)										
Aminoglycosides	Amikacin	Not	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
0,7	(MIC ≥ 64)	Tested	0	0	0	0	0	0	0	0	0
	Gentamicin	0.0%	0.0%	0.0%	0.0%	0.0%	7.1%	0.0%	5.4%	5.6%	0.0%
	(MIC ≥ 16)	0	0	0	0	0	1	0	2	2	0
	Streptomycin	0.0%	66.7%	0.0%	0.0%	7.7%	14.3%	2.9%	8.1%	5.6%	3.0%
	(MIC ≥ 64)	0	2	0	0	1	2	1	3	2	1
Aminopenicillins	Ampicillin	0.0%	0.0%	0.0%	0.0%	7.7%	7.1%	8.6%	8.1%	5.6%	6.1%
·	(MIC ≥ 32)	0	0	0	0	1	1	3	3	2	2
β-lactamase inhibitor combinations	Amoxicillin-clavulanic acid	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	2.9%	5.4%	2.8%	3.0%
	(MIC ≥ 32)	0	0	0	0	0	0	1	2	1	1
Cephalosporins (3 rd generation)	Ceftiofur	0.0%	0.0%	0.0%	0.0%	0.0%	7.1%	2.9%	5.4%	2.8%	3.0%
spreadornes (or generalist)	(MIC ≥ 8)	0	0	0	0	0	1	1	2	1	1
	Ceftriaxone	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	2.8%	0.0%
	(MIC ≥ 64)	0	0	0	0	0	0	0	0	1	0
Quinolones	Ciprofloxacin	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
	(MIC ≥ 4)	0	0	0	0	0	0	0	0	0	0
	Nalidixic Acid	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	2.7%	2.8%	0.0%
	(MIC ≥ 32)	0	0	0	0	0	0	0	1	1	0
Aminoglycosides	Kanamycin	0.0%	0.0%	0.0%	0.0%	0.0%	7.1%	0.0%	0.0%	0.0%	0.0%
	(MIC ≥ 64)	0	0	0	0	0	1	0	0	0	0
Cephalosporin (1 st generation)	Cephalothin	0.0%	0.0%	0.0%	0.0%	0.0%	7.1%	2.9%	5.4%	Not	Not
3 ,	(MIC ≥ 32)	0	0	0	0	0	1	1	2	Tested	Tested
Cephamycins	Cefoxitin	Not	Not	Not	Not	Not	0.0%	2.9%	5.4%	2.8%	3.0%
	(MIC ≥ 32)	Tested	Tested	Tested	Tested	Tested	0	1	2	1	1
Folate pathway inhibitors	Trimethoprim-sulfamethoxazole	0.0%	0.0%	0.0%	0.0%	0.0%	7.1%	2.9%	0.0%	2.8%	0.0%
	(MIC ≥ 4)	0	0	0	0	0	1	1	0	1	0
Phenicols	Chloramphenicol	0.0%	0.0%	0.0%	0.0%	0.0%	7.1%	2.9%	0.0%	2.8%	0.0%
	(MIC ≥ 32)	0	0	0	0	0	1	11	0	11	0
Sulfonamides	Sulfamethoxazole/Sulfisoxazole	0.0%	100.0%	0.0%	12.5%	0.0%	14.3%	2.9%	5.4%	11.1%	0.0%
	(MIC ≥ 512)	0	3	0	1	0	2	1	2	4	0
Tetracyclines	Tetracycline	0.0%	0.0%	0.0%	0.0%	7.7%	7.1%	5.7%	0.0%	11.1%	3.0%
•	(MIC ≥ 16)	0	0	0	0	1	1	2	0	4	1

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

Table 1.19: Resistance patterns of Salmonella I 4,[5],12:i:- isolates, 1996-2005

Table 1.19: Resistance patterns of Salmone									
Year	1996	1997	1999	2000	2001	2002	2003	2004	2005
Total Isolates	3	3	8	13	14	35	37	36	33
	%	%	%	%	%	%	%	%	%
	n	n	n	n	n	n	n	n	n
No resistance detected	100.0%	0.0%	87.5%	92.3%	78.6%	91.4%	78.4%	80.6%	87.9%
	3	0	7	12	11	32	29	29	29
Resistance ≥1CLSI subclass*	0.0%	100.0%	12.5%	7.7%	21.4%	8.6%	21.6%	19.4%	12.1%
	0	3	1	1	3	3	8	7	4
Resistance ≥2 CLSI subclasses*	0.0%	66.7%	0.0%	7.7%	14.3%	8.6%	10.8%	13.9%	3.0%
	0	2	0	1	2	3	4	5	1
Resistance ≥3 CLSI subclasses*	0.0%	0.0%	0.0%	7.7%	7.1%	5.7%	5.4%	11.1%	3.0%
	0	0	0	1	1	2	2	4	1
Resistance ≥4 CLSI subclasses*	0.0%	0.0%	0.0%	0.0%	7.1%	2.9%	0.0%	2.8%	0.0%
	0	0	0	0	1	1	0	1	0
Resistance ≥5 CLSI subclasses*	0.0%	0.0%	0.0%	0.0%	7.1%	2.9%	0.0%	2.8%	0.0%
	0	0	0	0	1	1	0	1	0
At least ACSSuT [†]	0.0%	0.0%	0.0%	0.0%	7.1%	2.9%	0.0%	2.8%	0.0%
	0	0	0	0	1	1	0	1	0
At least ACSuTm [‡]	0.0%	0.0%	0.0%	0.0%	7.1%	2.9%	0.0%	0.0%	0.0%
	0	0	0	0	1	1	0	0	0
At least ACSSuTAuCf [§]	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
7 (1000 (7 100 G (17 100 f	0	0	0	0	0	0	0	0	0
At least MDR-AmpC ¹	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
A Cloud Children Ampo	0.070	0.070	0.070	0.070	0.070	0.070	0.070	0.070	0.070
Resistance to quinolone and cephalosporin (3 rd generation)	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Resistance to quinotone and dephalosponii (3 generation)									
	0	0	0	0	0	0	0	0	0

^{*}CLSI: Clinical and Laboratory Standards Institute

F. Specific Phenotypes

The multidrug-resistant phenotypes ACSSuT and MDR-AmpC, and resistance to nalidixic acid and ceftiofur, were detected in several other serotypes in 2005 (Table 1.20).

In 2005, 141 (6.9%) non-Typhi *Salmonella* isolates were resistant to at least ACSSuT. Of these isolates, 68.8% were serotype Typhimurium; 18.4% were Newport; and 2.8% were serotype Java [Paratyphi B var. L(+) tartrate+]; 2.1% were serotype Agona; 1.4% were serotype Enteritidis, and 0.7% were serotype Mbandaka (<u>Table 1.20</u>). Forty-one (1.9%) non-Typhi *Salmonella* isolates were at least MDR-AmpC, of which 63.4% were serotype Newport, 19.5% Typhimurium; 7.3%, Agona; 2.4%, Enteritidis and 2.4%, Mbandaka. Fifty (2.4%) non-Typhi *Salmonella* isolates were nalidixic acid resistant, 36.0% of which were Enteritidis; 8.0%, Typhimurium; 4.0% Javiana, and 2.0%, Agona, Infantis, Heidelberg Muenchen, and Thompson. Sixty (2.9%) non-Typhi *Salmonella* isolates were ceftiofur resistant, of which 43.3% were serotype Newport; 18.3% were Typhimurium; 18.3% were Heidelberg; and 5.0% were Agona, 3.3% were Enteritidis, and 1.7% were Mbandaka, and "monophasic Typhimurium."

[†]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 1.20: 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. 2005

	anong the 20 most common non			CSSuT*	_			idixic Acid		eftiofur
Rank	Serotype	N	n	(%)	n	(%)	n	(%)	n	(%)
1	Typhimurium	437	97	(68.8%)	8	(19.5%)	4	(8.0%)	11	(18.3%)
2	Enteritidis	383	2	(1.4%)	1	(2.4%)	18	(36.0%)	2	(3.3%)
3	Newport	207	26	(18.4%)	26	(63.4%)	0	(0.0%)	26	(43.3%)
4	Heidelberg	125	0	(0.0%)	0	(0.0%)	1	(2.0%)	11	(18.3%)
5	Javiana	75	0	(0.0%)	0	(0.0%)	2	(4.0%)	0	(0.0%)
6	Montevideo	48	0	(0.0%)	0	(0.0%)	0	(0.0%)	0	(0.0%)
7	Braenderup	47	0	(0.0%)	0	(0.0%)	0	(0.0%)	0	(0.0%)
8	Muenchen	44	0	(0.0%)	0	(0.0%)	1	(2.0%)	0	(0.0%)
9	Saintpaul	41	0	(0.0%)	0	(0.0%)	0	(0.0%)	0	(0.0%)
10	Paratyphi B var. L(+) tartrate+	38	4	(2.8%)	0	(0.0%)	0	(0.0%)	0	(0.0%)
11	Mississippi	37	0	(0.0%)	0	(0.0%)	0	(0.0%)	0	(0.0%)
12	I 4,[5],12:i:- (monophasic Typhimurium)	33	0	(0.0%)	0	(0.0%)	0	(0.0%)	1	(1.7%)
13	Oranienburg	33	0	(0.0%)	0	(0.0%)	0	(0.0%)	0	(0.0%)
14	Infantis	30	0	(0.0%)	0	(0.0%)	1	(2.0%)	0	(0.0%)
15	Thompson	26	0	(0.0%)	0	(0.0%)	1	(2.0%)	0	(0.0%)
16	Agona	22	3	(2.1%)	3	(7.3%)	1	(2.0%)	3	(5.0%)
17	Poona	19	0	(0.0%)	0	(0.0%)	0	(0.0%)	0	(0.0%)
18	Stanley	17	0	(0.0%)	0	(0.0%)	0	(0.0%)	0	(0.0%)
19	Mbandaka	17	1	(0.7%)	1	(2.4%)	0	(0.0%)	1	(1.7%)
20	Berta	13	0	(0.0%)	0	(0.0%)	0	(0.0%)	0	(0.0%)
	Subtotal	1692	133	(94.3%)	39	(95.1%)	29	(58.0%)	55	(91.7%)
	All Other Serotypes	360	8	(5.7%)	2	(4.9%)	21	(42.0%)	5	(8.3%)
	Total	2052	141	(100.0%)	41	(100.0%)	50	(100.0%)	60	(100.0%)

^{*}ACSSuT: ampicillin, chloramphenicol, streptomycin, sulfamethoxazole/sulfisoxazole, tetracycline † MDR-AmpC: ACSSuTAuCf + decreased susceptibility to ceftriaxone (MIC ≥2µg/mL)

2. Salmonella Typhi

Among *Salmonella* Typhi isolates, resistance to nalidixic acid increased from 19.2% in 1996 to 48.4% in 2005. Resistance increased from 2004 to 2005 to most of the antimicrobial agents tested. The percentage of isolates with no detected resistance decreased from 56.6% in 2004 to 48.1% in 2005.

During 2005, CDC received 418 *Salmonella* Typhi isolates, of which 382 (91.3%) were viable and tested for antimicrobial susceptibility; of these isolates, 64 (1.4%) were not included in the analysis because they were duplicate submissions from the same patient, leaving 318 isolates for analysis (<u>Tables II</u> and <u>2.01</u>). Antimicrobial agents with the highest prevalence of resistance were nalidixic acid (48.4%), trimethoprim-sulfamethoxazole (14.2%), sulfisoxazole (14.2%), and chloramphenicol, streptomycin and ampicillin (13.2%).

Resistance increased from 2004 to 2005 to most of the antimicrobial agents tested (<u>Table 2.02</u>). Nalidixic acid resistance increased from 19.2% in 1999 to 48.4% in 2005; a statistically significant increase (OR=4.0, 95% CI [2.5, 6.3]).

The percentage of isolates with no detected resistance decreased from 56.6% in 2004 to 48.1% in 2005. In 1999, 12.6% 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 12.9% in 2005 (Table 2.03).

Table 2.01: Minimum inhibitory concentrations (MICs) and resistance of Salmonella Typhi isolates to

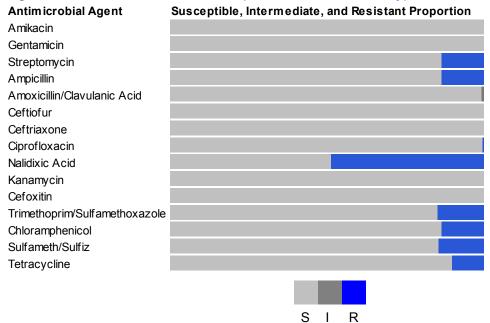
antimicrobial agents, 2005 (N=318)

	Antibiotic		% of is	olates						Percei	nt of all	isolate	s with	MIC (µ	ıg/mL) [§]					
	Antibiotic	%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]						34.9	57.9	6.3	0.9							
	Gentamicin	0.0	0.0	[0.0–1.2]					94.0	6.0										
	Streptomycin	NA	13.2	[9.7–17.4]												86.8		13.2		
Aminopenicillins	Ampicillin	0.0	13.2	[9.7–17.4]							69.2	17.6					13.2			
β-lactamase inhibitor	Amoxicillin-clavulanic acid	0.6	0.0	[0.0–1.2]							86.8		4.1	8.5	0.6					
Cephalosporins (3rd generation)	Ceftiofur	0.0	0.0	[0.0–1.2]				2.2	11.0	77.7	9.1									
, ,	Ceftriaxone	0.0	0.0	[0.0–1.2]					100.0					•						
Quinolones	Ciprofloxacin	0.0	0.3	[0.0–1.7]	48.4	1.3	2.2	15.7	29.6	2.5				0.3						
	Nalidixic Acid	NA	48.4	[42.8–54.1]							1.3	43.1	5.3	1.9		0.6	47.8			
Aminoglycosides	Kanamycin	0.0	0.0	[0.0–1.2]										100.0						
Cephamycins	Cefoxitin	0.0	0.0	[0.0–1.2]						4.7	38.1	11.6	33.3	12.3						
Folate pathway inhibitors	Trimethoprim-sulfamethoxazole	NA	14.5	[10.8–18.8]				76.4	9.1					14.5	•					
Phenicols	Chloramphenicol	0.0	13.2	[9.7–17.4]								5.3	73.0	8.5			13.2			
Sulfonamides	Sulfamethoxazole/Sulfisoxazole	NA	14.2	[10.5–18.5]											50.3	22.3	11.3	1.9		14.2
Tetracyclines	Tetracycline	0.0	10.1	[7.0–13.9]									89.9				10.1			

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

\$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.

Figure 2.01: Antimicrobial resistance pattern for Salmonella Typhi, 2005



[†]Percent of isolates that were resistant

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

Table 2.02: Percentage and number of *Salmonella* Typhi isolates resistant to antimicrobial agents, 1999–2005

Year		1999	2000	2001	2002	2003	2004	2005
Total Isolates		167	177	197	195	334	304	318
	Antibiotic	1						
Subclass	(Resistance breakpoint)							
Aminoglycosides	Amikacin	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
	(MIC ≥ 64)	0	0	0	0	0	0	0
	Gentamicin	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
	(MIC ≥ 16)	0	0	0	0	0	0	0
	Streptomycin	13.8%	9.0%	20.3%	7.2%	14.4%	11.8%	13.2%
	(MIC ≥ 64)	23	16	40	14	48	36	42
Aminopenicillins	Ampicillin	13.2%	9.0%	20.3%	5.6%	16.2%	11.8%	13.2%
	(MIC ≥ 32)	22	16	40	11	54	36	42
β-lactamase inhibitor combinations	Amoxicillin-clavulanic acid	0.6%	0.0%	0.0%	0.0%	0.3%	0.0%	0.0%
	(MIC ≥ 32)	1	0	0	0	1	0	0
Cephalosporins (3 rd generation)	Ceftiofur	0.6%	0.0%	0.0%	0.0%	0.6%	0.0%	0.0%
Coprimitor (or generalist)	(MIC ≥ 8)	1	0	0	0	2	0	0
	Ceftriaxone	0.6%	0.0%	0.0%	0.0%	0.3%	0.0%	0.0%
	(MIC ≥ 64)	1	0	0	0	1	0	0
Quinolones	Ciprofloxacin	0.0%	0.0%	0.0%	0.0%	0.3%	0.0%	0.3%
	(MIC ≥ 4)	0	0	0	0	1	0	1
	Nalidixic Acid	19.2%	22.0%	29.9%	23.6%	37.7%	41.8%	48.4%
	(MIC ≥ 32)	32	39	59	46	126	127	154
Aminoglycosides	Kanamycin	0.0%	0.0%	0.5%	0.0%	0.0%	0.0%	0.0%
	(MIC ≥ 64)	0	0	1	0	0	0	0
Cephalosporin (1 st generation)	Cephalothin	2.4%	1.1%	0.5%	1.5%	0.6%	Not	Not
(3: :::: ,	(MIC ≥ 32)	4	2	1	3	2	Tested	Tested
Cephamycins	Cefoxitin	Not	0.6%	0.5%	0.0%	0.9%	0.0%	0.0%
	(MIC ≥ 32)	Tested	1	1	0	3	0	0
Folate pathway inhibitors	Trimethoprim-sulfamethoxazole	13.2%	9.0%	20.8%	6.7%	16.8%	13.2%	14.5%
	(MIC ≥ 4)	22	16	41	13	56	40	46
Phenicols	Chloramphenicol	12.6%	10.7%	20.8%	6.2%	16.5%	13.2%	13.2%
	(MIC ≥ 32)	21	19	41	12	55	40	42
Sulfonamides	Sulfamethoxazole/Sulfisoxazole*	16.8%	11.3%	20.8%	6.2%	17.1%	11.8%	14.2%
	(MIC ≥ 512)	28	20	41	12	57	36	45
Tetracyclines	Tetracycline	9.6%	9.6%	20.8%	6.7%	15.6%	8.9%	10.1%
	(MIC ≥ 16)	16	17	41	13	52	27	32

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

Table 2.03: Resistance patterns of Salmonella Typhi isolates, 1999–2005

Year	1999	2000	2001	2002	2003	2004	2005
Total Isolates	167	177	197	195	334	304	318
Total Isolates	%	%	%	%	%	%	%
	l n	n /0	n 70	n /0	n /0	n 70	n
No resistance detected	71.3%	72.9%	59.4%	74.4%	56.6%	56.6%	48.1%
140 resistance detected	119	129	117	145	189	172	153
Resistance ≥1CLSI subclass*	28.7%	27.1%	40.6%	25.6%	43.4%	43.4%	51.9%
1.0000000000000000000000000000000000000	48	48	80	50	145	132	165
Resistance ≥2 CLSI subclasses*	15.0%	10.7%	22.8%	7.2%	18.0%	13.2%	14.5%
	25	19	45	14	60	40	46
Resistance ≥3 CLSI subclasses*	13.2%	9.6%	22.8%	6.7%	17.7%	12.8%	13.8%
	22	17	45	13	59	39	44
Resistance ≥4 CLSI subclasses*	13.2%	9.0%	21.8%	6.7%	16.8%	12.5%	12.9%
	22	16	43	13	56	38	41
Resistance ≥5 CLSI subclasses*	12.6%	9.0%	18.8%	5.6%	15.9%	11.8%	11.9%
	21	16	37	11	53	36	38
At least ACSSuT [†]	9.6%	7.9%	16.8%	5.6%	12.6%	7.9%	9.1%
	16	14	33	11	42	24	29
At least ACSuTm [‡]	12.6%	9.0%	17.8%	5.6%	15.6%	11.8%	12.9%
	21	16	35	11	52	36	41
At least ACSSuTAuCf [§]	0.0%	0.0%	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	0	0	0
Resistance to quinolone and cephalosporin (3 rd generation)	0.0%	0.0%	0.0%	0.0%	0.3%	0.0%	0.0%
, , , , , , , , , , , , , , , , , , , ,	0	0	0	0	1	0	0

^{*}CLSI: Clinical and Laboratory Standards Institute

3. Shigella

There were differences in resistance to antimicrobial agents between *Shigella sonnei* and *Shigella flexneri*. In 2005, *Shigella sonnei* isolates showed a higher prevalence of resistance to streptomycin and trimethoprim-sulfamethoxazole, *while S. flexneri* showed a higher prevalence of resistance to tetracycline and chloramphenicol. The percentage of isolates with no detected resistance was low in *S. sonnei* (4.4%) and *S. flexneri* (5.8%).

During 2005, CDC received 436 *Shigella* isolates, of which 398 (91.3%) were viable and tested for antimicrobial susceptibility; two (0.5%) isolates were determined to be duplicate submissions from the same patient and were removed from analysis, leaving 396 (90.8%) isolates for analysis (<u>Table II</u>). Of the 396 isolates tested, 340 (85.9%) were *S. sonnei*, 52 (13.1%), *S. flexneri*; three (0.8%), *S. boydii*, and one (0.3%), *S. dysenteriae* (<u>Table 3.01</u>). Resistance was highest to ampicillin (70.7%), streptomycin (68.7%), trimethoprim-sulfamethoxazole (58.6%), sulfisoxazole (57.6%), and tetracycline (38.4%) (<u>Table 3.02</u>).

In 2005, there were differences in resistance to antimicrobial agents between *Shigella sonnei* and *Shigella flexneri* (Tables 3.03 and 3.04). *Shigella sonnei* isolates showed a higher prevalence of resistance to streptomycin and trimethoprim-sulfamethoxazole than *Shigella flexneri*: 70.3% streptomycin resistance in *S. sonnei*, compared with 57.7% in *S. flexneri*; 61.2% trimethoprim-sulfamethoxazole resistance in *S.sonnei*, compared with 44.2% in *S. flexneri*. However, *S. flexneri* showed a higher prevalence of resistance to tetracycline and chloramphenicol than *S. sonnei*: 94.2% tetracycline resistance in *S. flexneri*, compared with 29.4% in *S. sonnei*; 65.4% chloramphenicol resistance in *S. flexneri*, compared with 2.4% in *S. sonnei*.

The percentage of *S. sonnei* isolates resistant to trimethoprim-sulfamethoxazole increased from 53.1% in 2004 to 61.2% in 2005 (Tables 3.05 and 3.06), a rate similar to that during 1999–2000 (53.1–54.9%). Ampicillin resistance

[†]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)

among *S. sonnei* isolates remained high (70.3%). Tetracycline resistance also decreased from 36.1% in 2004 to 29.4% in 2005. Two *S. sonnei* isolates were resistant to ceftriaxone in 2005 and one in 2004; these are the first three ceftriaxone-resistant *Shigella* isolates detected since NARMS began testing *Shigella* in 1999.

Resistance of *S. flexneri* isolates to trimethoprim-sulfamethoxazole also increased from 28.8% in 2002 to 44.2% in 2005 (<u>Tables 3.05</u> and <u>3.07</u>). Nalidixic acid resistance was 1.6% in 2004, compared with 3.8% in 2005. Resistance to streptomycin and tetracycline was higher in 2004 (72.1% and 95.1%, respectively) than in 2005 (57.7% and 94.2%, respectively).

Among all *Shigella* spp. isolates tested in all years from 1999 to 2005, more than 90% of isolates, which ranged from 90.9% to 95.6%, were resistant to at least one CLSI subclass. However, resistance to at least five CLSI subclasses declined from 1999 to 2005: 40.5% were resistant to at least five subclasses in 1999, compared with 15.7% in 2005 (Table 3.08).

In all years from 1999 to 2005, resistance to at least ampicilin, chloramphenicol, streptomycin, sulfamethoxazole/sulfisoxazole, and tetracycline (ACSSuT) and resistance to at least ampicillin, chloramphenicol, and trimethoprim-sulfamethoxazole (ACSuTm) were higher in *S. flexneri* compared with *S. sonnei* (Tables 3.09 and 3.10). The percentage of isolates with no detected resistance among *S. sonnei* and *S. flexneri* remained low in all years from 1999 to 2005; it was 4.4% in *S. sonnei* and 5.8% in *S. flexneri* in 2005.

For both *S. sonnei* and *S. flexneri*, resistance to clinically important antimicrobial classes and specific combinations changed from 1999 to 2005 (<u>Tables 3.09</u> and <u>3.10</u>). One *Shigella* (*S. sonnei*) isolate was resistant to nalidixic acid and ceftiofur. This was the second *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. Combined resistance to ampicillin and trimethoprim-sulfamethoxazole was present in more than 40% of isolates from 1999 through 2001, declined to 30.2% in 2002, but increased to 39.4% in 2004 and 40.6% in 2005. Resistance to both agents is clinically relevant, particularly for children for whom treatment with fluoroquinolones is not recommended.

Table 3.01: Frequency of Shigella species isolated in NARMS, 2005

		2005
Species	N	(%)
Shigella sonnei	340	(85.9%)
Shigella flexneri	52	(13.1%)
Shigella boydii	3	(0.8%)
Shigella dysenteriae	1	(0.3%)
Other	0	(0.0%)
Total	396	(100.0%)

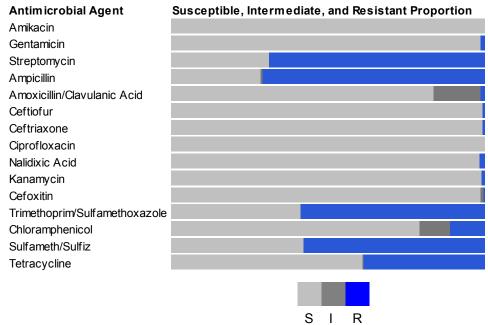
Table 3.02: Minimum inhibitory concentrations (MICs) and resistance of Shigella isolates to antimicrobial

agents, 2005 (N=396)

	Antibiotic		% of is	olates						Perce	nt of all	isolate	es with	MIC (µ	ıg/mL) [§]					
	Antibiotic	%l⁺	%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	0.3	0.0	[0.0-0.9]						0.3	5.3	51.5	39.6	3.0		0.3				
	Gentamicin	0.0	1.0	[0.3–2.6]					2.3	32.1	61.1	3.3	0.3			1.0				
	Streptomycin	NA	68.7	[63.9–73.2]												31.3	37.4	31.3		
Aminopenicillins	Ampicillin	0.8	70.7	[66.0–75.1]							4.5	18.9	4.5	0.5	0.8	1.3	69.4			
β-lactamase inhibitor	Amoxicillin-clavulanic acid	16.9	1.0	[0.3–2.6]							1.8	5.3	22.0	53.0	16.9	1.0				
Cephalosporins (3rd generation)	Ceftiofur	0.0	0.5	[0.1–1.8]				15.2	76.3	6.6	1.5				0.5					
,	Ceftriaxone	0.0	0.5	[0.1–1.8]					99.0	0.5		,		•				0.5		
Quinolones	Ciprofloxacin	0.0	0.0	[0.0-0.9]	98.2		0.5	1.0	0.3											
	Nalidixic Acid	NA	1.5	[0.6–3.3]						0.8	72.2	24.0	1.5			0.5	1.0			
Aminoglycosides	Kanamycin	0.0	0.8	[0.2–2.2]										98.2	1.0			0.8		
Cephamycins	Cefoxitin	0.8	0.3	[0.0-1.4]							17.9	68.9	11.9	0.3	0.8	•	0.3			
Folate pathway inhibitors	Trimethoprim-sulfamethoxazole	NA	58.6	[53.6–63.5]				24.2	5.1	2.0	4.0	6.1	4.3	54.3						
Phenicols	Chloramphenicol	10.6	10.9	[8.0–14.3]								10.9	56.8	10.9	10.6	1.5	9.3			
Sulfonamides	Sulfamethoxazole/Sulfisoxazole	NA	57.6	[52.5–62.5]											39.1	2.8	0.5			57.6
Tetracyclines	Tetracycline	0.3	38.4	[33.6–43.4]									61.4	0.3	2.5	11.9	24.0			

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

Figure 3.01: Antimicrobial resistance pattern for Shigella, 2005



[†]Percent of isolates that were resistant

 $^{^{\}ddagger}95\%$ 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.

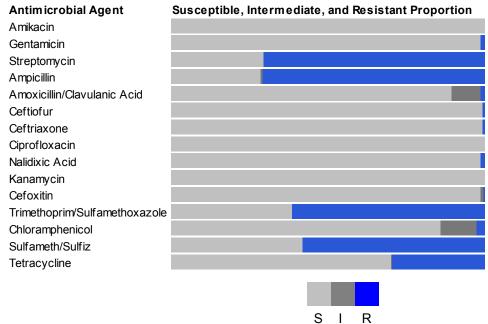
Table 3.03: Minimum inhibitory concentrations (MICs) and resistance of Shigella sonnei isolates to

antimicrobial agents, 2005 (N=340)

	Antibiotic		% of is	olates						Percei	nt of all	isolate	s with	MIC (µ	ıg/mL) [§]	i				
	Antibiotic	%l [*]	%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	[0.0–1.1]						0.3	5.9	56.8	36.2	0.9						
	Gentamicin	0.0	1.2	[0.3–3.0]					2.1	34.4	60.3	2.1				1.2				
	Streptomycin	NA	70.3	[65.1–75.1]										•		29.7	40.3	30.0		
Aminopenicillins	Ampicillin	0.9	70.6	[65.4–75.4]							1.8	20.9	5.3	0.6	0.9	1.5	69.1			
β-lactamase inhibitor	Amoxicillin-clavulanic acid	9.7	1.2	[0.3–3.0]							0.9	3.5	24.1	60.6	9.7	1.2				
Cephalosporins (3rd generation)	Ceftiofur	0.0	0.6	[0.1–2.1]				11.5	80.0	6.5	1.5				0.6					
, ,	Ceftriaxone	0.0	0.6	[0.1–2.1]					98.8	0.6		,	•					0.6		
Quinolones	Ciprofloxacin	0.0	0.0	[0.0–1.1]	98.5		0.3	1.2												
	Nalidixic Acid	NA	1.2	[0.3–3.0]						0.9	74.7	21.8	1.5			0.3	0.9			
Aminoglycosides	Kanamycin	0.0	0.0	[0.0–1.1]										98.8	1.2					
Cephamycins	Cefoxitin	0.9	0.3	[0.0-1.6]							19.7	71.5	7.6		0.9		0.3			
Folate pathway inhibitors	Trimethoprim-sulfamethoxazole	NA	61.2	[55.8–66.4]				22.1	4.1	0.9	4.7	7.1	5.0	56.2						
Phenicols	Chloramphenicol	12.4	2.4	[1.0-4.6]								7.1	65.6	12.6	12.4	0.9	1.5			
Sulfonamides	Sulfamethoxazole/Sulfisoxazole	NA	57.9	[52.5–63.2]											38.2	3.2	0.6			57.9
Tetracyclines	Tetracycline	0.3	29.4	[24.6–34.6]									70.3	0.3	2.4	12.6	14.4			

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

Figure 3.02: Antimicrobial resistance pattern for Shigella sonnei, 2005



[†]Percent of isolates that were resistant

 $^{^{\}ddagger}95\%$ 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.

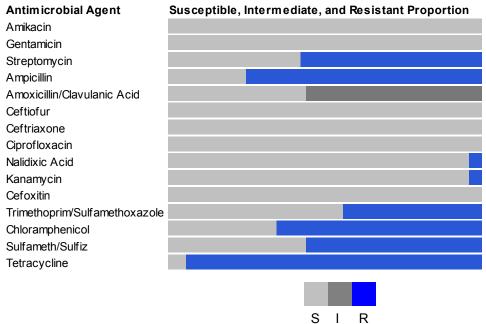
Table 3:04: Minimum inhibitory concentrations and resistance of Shigella flexneri isolates to antimicrobial

agents, 2005 (N=52)

	Antibiotic		% of is	olates						Perce	nt of all	isolate	es with	MIC (µ	g/mL) [§]					
	Antibiotic	%l [*]	%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	1.9	0.0	[0.0–6.8]							1.9	19.2	59.6	17.3		1.9				
	Gentamicin	0.0	0.0	[0.0-6.8]					3.8	19.2	63.5	11.5	1.9							
	Streptomycin	NA	57.7	[43.2–71.3]												42.3	19.2	38.5		
Aminopenicillins	Ampicillin	0.0	75.0	[61.1–86.0]							21.2	3.8					75.0			
β-lactamase inhibitor	Amoxicillin-clavulanic acid	65.4	0.0	[0.0–6.8]							5.8	17.3	3.8	7.7	65.4					
Cephalosporins (3rd generation)	Ceftiofur	0.0	0.0	[0.0–6.8]				36.5	55.8	5.8	1.9									
,	Ceftriaxone	0.0	0.0	[0.0-6.8]					100.0					•						
Quinolones	Ciprofloxacin	0.0	0.0	[0.0–6.8]	96.2		1.9		1.9											
	Nalidixic Acid	NA	3.8	[0.5–13.2]							55.8	38.5	1.9			1.9	1.9			
Aminoglycosides	Kanamycin	0.0	3.8	[0.5–13.2]										96.2		Ĭ		3.8		
Cephamycins	Cefoxitin	0.0	0.0	[0.0–6.8]							5.8	53.8	38.5	1.9						
Folate pathway inhibitors	Trimethoprim-sulfamethoxazole	NA	44.2	[30.5–58.7]				38.5	9.6	7.7				44.2						
Phenicols	Chloramphenicol	0.0	65.4	[50.9–78.0]								30.8	3.8			5.8	59.6			
Sulfonamides	Sulfamethoxazole/Sulfisoxazole	NA	55.8	[41.3–69.5]											44.2					55.8
Tetracyclines	Tetracycline	0.0	94.2	[84.1–98.8]									5.8		1.9	7.7	84.6			

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

Figure 3.03: Antimicrobial resistance pattern for Shigella flexneri, 2005



[†]Percent of isolates that were resistant

 $^{^{\}ddagger}95\%$ 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 3.05: Percentage and number of Shigella isolates resistant to antimicrobial agents, 1999–2005

Year		1999	2000	2001	2002	2003	2004	2005
Total Isolates		375	450	344	620	495	315	396
	Antibiotic							
Subclass	(Resistance breakpoint)							
Aminoglycosides	Amikacin	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
3,	(MIC ≥ 64)	0	0	0	0	0	0	0
	Gentamicin	0.3%	0.2%	0.0%	0.2%	0.0%	0.0%	1.0%
	(MIC ≥ 16)	1	1	0	1	0	0	4
	Streptomycin	55.7%	57.1%	53.2%	54.4%	57.0%	61.0%	68.7%
	(MIC ≥ 64)	209	257	183	337	282	192	272
Aminopenicillins	Ampicillin	77.6%	79.1%	79.7%	76.6%	79.4%	77.8%	70.7%
	(MIC ≥ 32)	291	356	274	475	393	245	280
β-lactamase inhibitor combinations	Amoxicillin-clavulanic acid	1.1%	2.2%	4.4%	2.6%	1.4%	1.6%	1.0%
•	(MIC ≥ 32)	4	10	15	16	7	5	4
Cephalosporins (3 rd generation)	Ceftiofur	0.0%	0.0%	0.0%	0.2%	0.2%	0.3%	0.5%
copilalospoliilo (o golioralioni)	(MIC ≥ 8)	0	0	0	1	1	1	2
	Ceftriaxone	0.0%	0.0%	0.0%	0.0%	0.0%	0.3%	0.5%
	(MIC ≥ 64)	0	0	0	0	0	1	2
Quinolones	Ciprofloxacin	0.0%	0.0%	0.3%	0.0%	0.0%	0.0%	0.0%
	(MIC ≥ 4)	0	0	1	0	0	0	0
	Nalidixic Acid	1.6%	0.9%	1.7%	1.6%	1.0%	1.6%	1.5%
	(MIC ≥ 32)	6	4	6	10	5	5	6
Aminoglycosides	Kanamycin	0.5%	1.3%	0.6%	0.8%	0.4%	0.0%	0.8%
	(MIC ≥ 64)	2	6	2	5	2	0	3
Cephalosporin (1 st generation)	Cephalothin	3.2%	8.0%	9.0%	6.6%	9.3%	Not	Not
copilatopetiii (i generation)	(MIC ≥ 32)	12	36	31	41	46	Tested	Tested
Cephamycins	Cefoxitin	Not	0.2%	1.2%	0.3%	0.0%	0.3%	0.3%
•	(MIC ≥ 32)	Tested	1	4	2	0	1	1
Folate pathway inhibitors	Trimethoprim-sulfamethoxazole	51.5%	52.9%	46.8%	37.3%	38.6%	51.4%	58.6%
	(MIC ≥ 4)	193	238	161	231	191	162	232
Phenicols	Chloramphenicol	17.3%	14.0%	21.5%	7.6%	8.5%	14.9%	10.9%
	(MIC ≥ 32)	65	63	74	47	42	47	43
Sulfonamides	Sulfamethoxazole/Sulfisoxazole*	56.0%	55.8%	56.4%	31.8%	33.9%	52.4%	57.6%
	(MIC ≥ 512)	210	251	194	197	168	165	228
Tetracyclines	Tetracycline	57.3%	44.9%	59.3%	30.6%	29.1%	49.2%	38.4%
,	(MIC ≥ 16)	215	202	204	190	144	155	152

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

Table 3.06: Percentage and number of *Shigella sonnei* isolates resistant to antimicrobial agents, 1999–2005

Year		1999	2000	2001	2002	2003	2004	2005
Total Isolates		275	366	239	536	434	241	340
	Antibiotic							
Subclass	(Resistance breakpoint)							
Aminoglycosides	Amikacin	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
0,1	(MIC ≥ 64)	0	0	0	0	0	0	0
	Gentamicin	0.4%	0.3%	0.0%	0.0%	0.0%	0.0%	1.2%
	(MIC ≥ 16)	1	1	0	0	0	0	4
	Streptomycin	52.0%	56.0%	54.0%	55.4%	56.5%	58.1%	70.3%
	(MIC ≥ 64)	143	205	129	297	245	140	239
Aminopenicillins	Ampicillin	79.6%	80.6%	82.8%	77.6%	79.7%	79.3%	70.6%
·	(MIC ≥ 32)	219	295	198	416	346	191	240
β-lactamase inhibitor combinations	Amoxicillin-clavulanic acid	0.4%	1.9%	4.6%	2.2%	1.4%	1.7%	1.2%
	(MIC ≥ 32)	1	7	11	12	6	4	4
Cephalosporins (3 rd generation)	Ceftiofur	0.0%	0.0%	0.0%	0.0%	0.0%	0.4%	0.6%
generalist (or generalism)	(MIC ≥ 8)	0	0	0	0	0	1	2
	Ceftriaxone	0.0%	0.0%	0.0%	0.0%	0.0%	0.4%	0.6%
	(MIC ≥ 64)	0	0	0	0	0	1	2
Quinolones	Ciprofloxacin	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
	(MIC ≥ 4)	0	0	0	0	0	0	0
	Nalidixic Acid	1.5%	1.1%	0.8%	1.5%	0.5%	1.7%	1.2%
	(MIC ≥ 32)	4	4	2	8	2	4	4
Aminoglycosides	Kanamycin	0.7%	1.6%	0.4%	0.4%	0.0%	0.0%	0.0%
	(MIC ≥ 64)	2	6	1	2	0	0	0
Cephalosporin (1 st generation)	Cephalothin	2.9%	8.7%	12.6%	7.3%	10.1%	Not	Not
	(MIC ≥ 32)	8	32	30	39	44	Tested	Tested
Cephamycins	Cefoxitin	Not	0.3%	1.7%	0.4%	0.0%	0.4%	0.3%
	(MIC ≥ 32)	Tested	1	4	2	0	1	1
Folate pathway inhibitors	Trimethoprim-sulfamethoxazole	53.1%	54.9%	50.6%	37.9%	38.5%	53.1%	61.2%
	(MIC ≥ 4)	146	201	121	203	167	128	208
Phenicols	Chloramphenicol	1.8%	2.7%	1.3%	0.2%	1.2%	2.5%	2.4%
	(MIC ≥ 32)	5	10	3	1	5	6	8
Sulfonamides	Sulfamethoxazole/Sulfisoxazole*	54.5%	56.0%	54.4%	29.9%	31.3%	49.0%	57.9%
	(MIC ≥ 512)	150	205	130	160	136	118	197
Tetracyclines	Tetracycline	46.2%	34.4%	44.8%	23.5%	22.1%	36.1%	29.4%
	(MIC ≥ 16)	127	126	107	126	96	87	100

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

Table 3.07: Percentage and number of *Shigella flexneri* isolates resistant to antimicrobial agents, 1999–2005

Year Total Isolates		1999 87	2000 75	2001 91	2002 73	2003 51	2004 61	2005 52
	Antibiotic							
Subclass	(Resistance breakpoint)							
Aminoglycosides	Amikacin	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
3,	(MIC ≥ 64)	0	0	0	0	0	0	0
	Gentamicin	0.0%	0.0%	0.0%	1.4%	0.0%	0.0%	0.0%
	(MIC ≥ 16)	0	0	0	1	0	0	0
	Streptomycin	63.2%	61.3%	47.3%	43.8%	60.8%	72.1%	57.7%
	(MIC ≥ 64)	55	46	43	32	31	44	30
Aminopenicillins	Ampicillin	77.0%	77.3%	72.5%	75.3%	84.3%	82.0%	75.0%
•	(MIC ≥ 32)	67	58	66	55	43	50	39
β-lactamase inhibitor combinations	Amoxicillin-clavulanic acid	3.4%	4.0%	4.4%	5.5%	2.0%	1.6%	0.0%
	(MIC ≥ 32)	3	3	4	4	1	1	0
Cephalosporins (3 rd generation)	Ceftiofur	0.0%	0.0%	0.0%	1.4%	2.0%	0.0%	0.0%
generalist (or generalism)	(MIC ≥ 8)	0	0	0	1	1	0	0
	Ceftriaxone	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
	(MIC ≥ 64)	0	0	0	0	0	0	0
Quinolones	Ciprofloxacin	0.0%	0.0%	1.1%	0.0%	0.0%	0.0%	0.0%
	(MIC ≥ 4)	0	0	1	0	0	0	0
	Nalidixic Acid	1.1%	0.0%	3.3%	2.7%	5.9%	1.6%	3.8%
	(MIC ≥ 32)	1	0	3	2	3	1	2
Aminoglycosides	Kanamycin	0.0%	0.0%	1.1%	4.1%	3.9%	0.0%	3.8%
	(MIC ≥ 64)	0	0	1	3	2	0	2
Cephalosporin (1 st generation)	Cephalothin	4.6%	2.7%	1.1%	2.7%	3.9%	Not	Not
generalist,	(MIC ≥ 32)	4	2	1	2	2	Tested	Tested
Cephamycins	Cefoxitin	Not	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
	(MIC ≥ 32)	Tested	0	0	0	0	0	0
Folate pathway inhibitors	Trimethoprim-sulfamethoxazole	48.3%	42.7%	34.1%	28.8%	39.2%	45.9%	44.2%
	(MIC ≥ 4)	42	32	31	21	20	28	23
Phenicols	Chloramphenicol	64.4%	69.3%	74.7%	63.0%	68.6%	60.7%	65.4%
	(MIC ≥ 32)	56	52	68	46	35	37	34
Sulfonamides	Sulfamethoxazole/Sulfisoxazole*	58.6%	53.3%	57.1%	41.1%	52.9%	65.6%	55.8%
	(MIC ≥ 512)	51	40	52	30	27	40	29
Tetracyclines	Tetracycline	92.0%	92.0%	94.5%	78.1%	82.4%	95.1%	94.2%
	(MIC ≥ 16)	80	69	86	57	42	58	49

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

Table 3.08: Resistance patterns of Shigella isolates, 1999–2005

Year	1999	2000	2001	2002	2003	2004	2005
Total Isolates	375	450	344	620	495	315	396
	%	%	%	%	%	%	%
	n	n	n	n	n	n	n
No resistance detected	9.1%	7.3%	4.9%	8.2%	8.5%	4.4%	4.5%
	34	33	17	51	42	14	18
Resistance ≥1CLSI subclass*	90.9%	92.7%	95.1%	91.8%	91.5%	95.6%	95.5%
	341	417	327	569	453	301	378
Resistance ≥2 CLSI subclasses*	63.7%	64.7%	69.8%	55.3%	57.8%	66.7%	73.7%
	239	291	240	343	286	210	292
Resistance ≥3 CLSI subclasses*	61.1%	62.0%	61.3%	41.8%	41.4%	62.2%	62.9%
	229	279	211	259	205	196	249
Resistance ≥4 CLSI subclasses*	54.1%	56.7%	54.1%	31.0%	32.5%	52.1%	55.6%
	203	255	186	192	161	164	220
Resistance ≥5 CLSI subclasses*	40.5%	26.2%	36.0%	20.5%	22.4%	27.6%	15.7%
	152	118	124	127	111	87	62
At least ACSSuT [†]	8.5%	5.6%	6.4%	1.8%	3.2%	6.0%	4.0%
	32	25	22	11	16	19	16
At least ACSuTm [‡]	9.9%	6.9%	7.0%	2.7%	3.6%	6.7%	6.3%
	37	31	24	17	18	21	25
At least ASuTm [§]	44.3%	44.4%	37.5%	29.8%	33.7%	37.8%	39.9%
	166	200	129	185	167	119	158
At least ANSuTm [¶]	0.3%	0.0%	0.6%	0.3%	0.8%	0.6%	0.5%
	1	0	2	2	4	2	2
At least ACSSuTAuCf**	0.0%	0.0%	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	0	0	0
Resistance to quinolone and cephalosporin (3 rd generation)	0.0%	0.0%	0.0%	0.0%	0.2%	0.3%	0.3%
resolutions to quinolone and oophalooperin (o generation)	0.070	0.070	0.070	0.070	1	1	1

^{*}CLSI: Clinical and Laboratory Standards Institute

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

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

 $[\]mbox{\S}\mbox{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 3.09: Resistance patterns of **Shigella sonnei** isolates, 1999–2005

Year	1999	2000	2001	2002	2003	2004	2005
Total Isolates	275	366	239	536	434	241	340
	%	%	%	%	%	%	%
	n	n	n	n	n	n	n
No resistance detected	10.5%	7.7%	5.4%	7.1%	8.5%	5.0%	4.4%
	29	28	13	38	37	12	15
Resistance ≥1CLSI subclass*	89.5%	92.3%	94.6%	92.9%	91.5%	95.0%	95.6%
	246	338	226	498	397	229	325
Resistance ≥2 CLSI subclasses*	56.0%	60.7%	60.7%	52.1%	54.1%	59.8%	72.6%
	154	222	145	279	235	144	247
Resistance ≥3 CLSI subclasses*	54.5%	57.7%	53.1%	36.6%	36.2%	54.4%	60.0%
	150	211	127	196	157	131	204
Resistance ≥4 CLSI subclasses*	50.5%	54.1%	49.0%	26.7%	28.6%	46.5%	53.5%
	139	198	117	143	124	112	182
Resistance ≥5 CLSI subclasses*	38.5%	23.5%	36.0%	19.4%	20.0%	24.9%	11.5%
	106	86	86	104	87	60	39
At least ACSSuT [†]	0.4%	0.8%	0.0%	0.0%	0.2%	0.0%	0.3%
	1	3	0	0	1	0	1
At least ACSuTm [‡]	1.8%	1.9%	0.8%	0.2%	0.9%	1.7%	2.4%
	5	7	2	1	4	4	8
At least ASuTm [§]	45.1%	46.2%	41.0%	30.2%	33.6%	39.4%	40.6%
	124	169	98	162	146	95	138
At least ANSuTm [¶]	0.0%	0.0%	0.0%	0.2%	0.2%	0.8%	0.3%
	0	0	0	1	1	2	1
At least ACSSuTAuCf**	0.0%	0.0%	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	0	0	0
Resistance to quinolone and cephalosporin (3 rd generation)	0.0%	0.0%	0.0%	0.0%	0.0%	0.4%	0.3%
3010-04-01)	0	0	0	0	0	1	1

^{*}CLSI: Clinical and Laboratory Standards Institute

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

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

 $[\]mbox{\S}\mbox{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, 1999-2005

Year	1999	2000	2001	2002	2003	2004	2005
Total Isolates	87	75	91	73	51	61	52
	%	%	%	%	%	%	%
	n	n	n	n	n	n	n
No resistance detected	4.6%	4.0%	3.3%	15.1%	7.8%	0.0%	5.8%
	4	3	3	11	4	0	3
Resistance ≥1CLSI subclass*	95.4%	96.0%	96.7%	84.9%	92.2%	100.0%	94.2%
	83	72	88	62	47	61	49
Resistance ≥2 CLSI subclasses*	83.9%	82.7%	90.1%	76.7%	86.3%	93.4%	80.8%
	73	62	82	56	44	57	42
Resistance ≥3 CLSI subclasses*	80.5%	81.3%	80.2%	75.3%	82.4%	91.8%	80.8%
	70	61	73	55	42	56	42
Resistance ≥4 CLSI subclasses*	67.8%	69.3%	65.9%	58.9%	64.7%	75.4%	69.2%
	59	52	60	43	33	46	36
Resistance ≥5 CLSI subclasses*	49.4%	40.0%	31.9%	28.8%	45.1%	41.0%	44.2%
	43	30	29	21	23	25	23
At least ACSSuT [†]	33.3%	29.3%	22.0%	15.1%	29.4%	27.9%	28.8%
	29	22	20	11	15	17	15
At least ACSuTm [‡]	34.5%	32.0%	23.1%	21.9%	27.5%	24.6%	32.7%
	30	24	21	16	14	15	17
At least ASuTm [§]	44.8%	38.7%	25.3%	27.4%	37.3%	36.1%	38.5%
	39	29	23	20	19	22	20
At least ANSuTm [¶]	1.1%	0.0%	1.1%	1.4%	5.9%	0.0%	1.9%
A COUNTY TO A THI	1	0	1	1	3	0	1
At least ACSSuTAuCf**	0.0%	0.0%	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%
. C. Odde (III.) C. Alipo	0	0	0	0	0	0	0
Resistance to quinolone and cephalosporin (3 rd generation)	0.0%	0.0%	0.0%	0.0%	2.0%	0.0%	0.0%
resistance to quinolone and cephalosponin (5 generation)	0.070	0.070	0.070	0.070	1	0.070	0.070

^{*}CLSI: Clinical and Laboratory Standards Institute

4. Escherichia coli O157

In *E. coli* O157, resistance to antimicrobial agents was not common. From 1996 to 2005, there was no temporal trend in the percentage of isolates with no detected resistance, which ranged from 86.6% to 95.3%. Multidrug resistance was rare.

In 2005, CDC received a total of 214 *Escherichia coli* O157 isolates, of which 194 (90.7%) were viable and tested for antimicrobial susceptibility (<u>Table II</u>). Resistance to antimicrobial agents was not common. Antimicrobial agents with the highest prevalence of resistance were tetracycline (8.8%), sulfisoxazole (6.7%), ampicillin (4.1%), and streptomycin (2.1%). Ampicillin resistance decreased from 3.2% in 2003 to 1.2% in 2004 but increased again in 2005 to 4.1% (<u>Table 4.01</u>). Cefoxitin resistance decreased to 0.0% in 2005, down from 0.6% in 2004. No isolates in 2005 were resistant to ceftiofur, whereas two isolates were resistant in 2003 (<u>Table 4.02</u>).

Isolates resistant to at least one CLSI subclass increased from 4.7% in 2004 to 12.4% in 2005 (<u>Table 4.03</u>). Resistance to at least two CLSI subclasses increased from 1.2% in 2004 to 5.2% in 2005. No isolates were resistant to at least five subclasses in 2005. From 1996 to 2005, there was no temporal trend in the percentage of isolates with no detected resistance, which ranged from 86.6% to 95.3%. Multidrug resistance was rare.

[†]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)

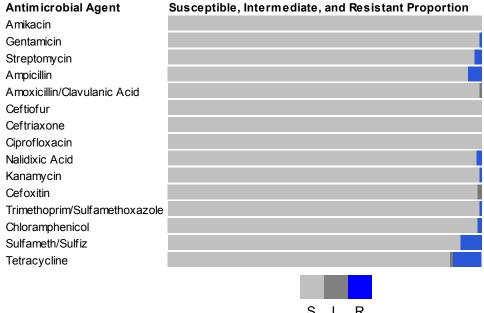
Antimicrobial treatment of *E. coli* O157 infections is not recommended. However, third-generation cephalosporin resistance surveillance might prove useful in understanding resistance mechanisms and the exchange of mobile resistance elements among enteric pathogens in bovine production settings.

Table 4.01: Minimum inhibitory concentrations (MICs) and resistance of *Escherichia coli* O157 isolates to antimicrobial agents, 2005 (N=194)

	Antibiotic		% of is	olates						Percer	nt of al	l isolat	es with	MIC (µ	g/mL) [§]					
	Antibiotic	%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]						5.2	73.2	19.1	2.6							
	Gentamicin	0.0	0.5	[0.0-2.8]					54.6	42.8	2.1				<u>'</u>	0.5				
	Streptomycin	NA	2.1	[0.6–5.2]											ll.	97.9	1.0	1.0		
Aminopenicillins	Ampicillin	0.0	4.1	[1.8–8.0]							4.6	72.7	17.0	1.5			4.1			
β-lactamase inhibitor	Amoxicillin-clavulanic acid	0.5	0.0	[0.0-1.9]							0.5	9.3	86.1	3.6	0.5					
Cephalosporins (3rd generation)	Ceftiofur	0.0	0.0	[0.0–1.9]				3.1	30.9	63.4	2.6									
	Ceftriaxone	0.0	0.0	[0.0-1.9]					100.0					•						
Quinolones	Ciprofloxacin	0.0	0.0	[0.0-1.9]	97.9	0.5		0.5	1.0											
	Nalidixic Acid	NA	1.5	[0.3-4.5]						0.5	2.6	77.3	18.0				1.5			
Aminoglycosides	Kanamycin	0.0	0.5	[0.0-2.8]										99.5				0.5		
Cephamycins	Cefoxitin	1.0	0.0	[0.0-1.9]							2.1	7.7	75.3	13.9	1.0					
Folate pathway inhibitors	Trimethoprim-sulfamethoxazole	NA	0.5	[0.0-2.8]				95.9	3.6					0.5						
Phenicols	Chloramphenicol	0.5	1.0	[0.1–3.7]								4.6	31.4	62.4	0.5		1.0			
Sulfonamides	Sulfamethoxazole/Sulfisoxazole	NA	6.7	[3.6–11.2]											87.1	5.7	0.5			6.7
Tetracyclines	Tetracycline	1.0	8.8	[5.2–13.7]									90.2	1.0	1.0	0.5	7.2			

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

Figure 4.01: Antimicrobial resistance pattern for *Escherichia coli* O157, 2005



[†]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 4.02: Percentage and number of *Escherichia coli* O157 isolates resistant to antimicrobial agents, 1996–2005

Year		1996	1997	1998	1999	2000	2001	2002	2003	2004	2005
Total Isolates		201	161	318	292	407	277	399	157	169	194
	Antibiotic										
Subclass	(Resistance breakpoint)										
Aminoglycosides	Amikacin	Not	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
	(MIC ≥ 64)	Tested	0	0	0	0	0	0	0	0	0
	Gentamicin	0.0%	0.0%	0.0%	0.3%	0.5%	0.4%	0.0%	0.0%	0.6%	0.5%
	(MIC ≥ 16)	0	0	0	1	2	1	0	0	1	1
	Streptomycin	2.0%	2.5%	1.9%	2.7%	5.2%	1.8%	2.3%	1.9%	1.8%	2.1%
	(MIC ≥ 64)	4	4	6	8	21	5	9	3	3	4
Aminopenicillins	Ampicillin	1.5%	0.0%	2.5%	1.4%	2.7%	2.2%	1.5%	3.2%	1.2%	4.1%
	(MIC ≥ 32)	3	0	8	4	11	6	6	5	2	8
Beta-lactamase inhibitor combinations	Amoxicillin-clavulanic acid	0.0%	0.0%	0.0%	0.3%	1.0%	0.7%	0.0%	1.3%	0.0%	0.0%
	(MIC ≥ 32)	0	0	0	1	4	2	0	2	0	0
Cephalosporins (3 rd Gen.)	Ceftiofur	0.0%	0.0%	0.0%	0.0%	1.0%	1.1%	0.0%	1.3%	0.0%	0.0%
	(MIC ≥ 8)	0	0	0	0	4	3	0	2	0	0
	Ceftriaxone	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
	(MIC ≥ 64)	0	0	0	0	0	0	0	0	0	0
Quinolones	Ciprofloxacin	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
	(MIC ≥ 4)	0	0	0	0	0	0	0	0	0	0
	Nalidixic acid	0.0%	0.0%	0.0%	0.7%	0.5%	1.1%	1.0%	0.6%	1.8%	1.5%
	(MIC ≥ 32)	0	0	0	2	2	3	4	1	3	3
Aminoglycosides	Kanamycin	0.0%	0.0%	0.3%	0.7%	1.0%	0.0%	0.5%	0.0%	0.0%	0.5%
	(MIC ≥ 64)	0	0	1	2	4	0	2	0	0	1
Cephalosporin (1st Gen.)	Cephalothin	1.5%	2.5%	0.0%	0.7%	1.2%	1.4%	1.5%	2.5%	Not	Not
(·)	(MIC ≥ 32)	3	4	0	2	5	4	6	4	Tested	Tested
Cephamycins	Cefoxitin	Not	Not	Not	Not	1.0%	0.7%	0.0%	1.3%	0.6%	0.0%
	(MIC ≥ 32)	Tested	Tested	Tested	Tested	4	2	0	2	1	0
Folate pathway inhibitors	Trimethoprim-sulfamethoxazole	0.0%	0.0%	0.6%	1.4%	0.7%	0.7%	0.5%	0.6%	0.0%	0.5%
	(MIC ≥ 4)	0	0	2	4	3	2	2	1	0	1
Phenicols	Chloramphenicol	0.5%	0.0%	0.3%	0.0%	3.7%	1.4%	1.3%	1.3%	0.6%	1.0%
	(MIC ≥ 32)	1	0	1	0	15	4	5	2	1	2
Sulfonamides	Sulfamethoxazole/Sulfisoxazole*	11.9%	9.9%	5.7%	8.2%	5.9%	5.1%	3.5%	3.8%	1.8%	6.7%
	(MIC ≥ 512)	24	16	18	24	24	14	14	6	3	13
Tetracyclines	Tetracycline	5.0%	3.1%	4.4%	3.4%	7.1%	5.4%	3.0%	5.7%	1.8%	8.8%
,	(MIC ≥ 16)	10	5	14	10	29	15	12	9	3	17

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

Table 4.03: Resistance patterns of Escherichia coli O157 isolates, 1996-2005

Year	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005
Total Isolates	201	161	318	292	407	277	399	157	169	194
	%	%	%	%	%	%	%	%	%	%
	n	n	n	n	n	n	n	n	n	n
No resistance detected	86.6%	88.8%	92.8%	89.7%	90.4%	91.3%	94.0%	90.4%	95.3%	87.6%
	174	143	295	262	368	253	375	142	161	170
Resistance ≥1CLSI subclass*	13.4%	11.2%	7.2%	10.3%	9.6%	8.7%	6.0%	9.6%	4.7%	12.4%
	27	18	23	30	39	24	24	15	8	24
Resistance ≥2 CLSI subclasses*	5.0%	3.7%	5.3%	3.4%	6.6%	5.4%	3.8%	5.1%	1.2%	5.2%
	10	6	17	10	27	15	15	8	2	10
Resistance ≥3 CLSI subclasses*	1.5%	0.6%	1.9%	3.1%	4.7%	2.2%	2.0%	3.2%	0.6%	1.0%
	3	1	6	9	19	6	8	5	1	2
Resistance ≥4 CLSI subclasses*	0.5%	0.0%	0.9%	1.0%	3.7%	1.8%	1.0%	1.3%	0.6%	0.5%
	1	0	3	3	15	5	4	2	1	1
Resistance ≥5 CLSI subclasses*	0.5%	0.0%	0.0%	0.7%	1.5%	0.7%	0.3%	0.6%	0.0%	0.0%
	1	0	0	2	6	2	1	1	0	0
At least ACSSuT [†]	0.5%	0.0%	0.0%	0.0%	1.2%	0.4%	0.0%	0.0%	0.0%	0.0%
	1	0	0	0	5	1	0	0	0	0
At least ACSuTm [‡]	0.0%	0.0%	0.0%	0.0%	0.2%	0.0%	0.0%	0.0%	0.0%	0.0%
	0	0	0	0	1	0	0	0	0	0
At least ACSSuTAuCf [§]	0.0%	0.0%	0.0%	0.0%	1.0%	0.4%	0.0%	0.0%	0.0%	0.0%
	0	0	0	0	4	1	0	0	0	0
At least MDR-AmpC ¹	0.0%	0.0%	0.0%	0.0%	1.0%	0.4%	0.0%	0.0%	0.0%	0.0%
·	0	0	0	0	4	1	0	0	0	0
Resistance to quinolone and cephalosporin (3 rd 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	0	0	0

^{*}CLSI: Clinical and Laboratory Standards Institute

 $^{^{\}dagger} ACSSuT: \ resistance \ to \ ampi cillin, \ chloramphenicol, \ streptomycin, \ sulfamethoxazole/sulfisoxazole, \ tetracycline$

[‡]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

Among all *Campylobacter* isolates tested, ciprofloxacin resistance increased from 12.9% in 1997 to 21.7 in 2005. Resistance to erythromycin remained low during 1997 to 2005. An increase in ciprofloxacin resistance in *C. jejuni* similar to the trend in all *Campylobacter* isolates was observed. The percentage of resistance to most agents tested, including ciprofloxacin and erythromycin, was higher in *C. coli* compared with *C. jejuni*.

In 2005, CDC received 998 *Campylobacter* isolates, of which 890 (89.2%) were viable and tested for antimicrobial susceptibility. A total of 791 (92.6%) were *C. jejuni* and 98 (11.5%) were *C. coli* (Table 5.01).

Of the *Campylobacter* isolates tested in 2005 (<u>Table II</u>), resistance was highest to tetracycline (40.6%), nalidixic acid (22.4%), and ciprofloxacin (21.7%) (<u>Table 5.02</u>). Of the isolates tested, 0.6% were resistant to florfenicol, which replaced chloramphenicol to represent the phenicol antimicrobial subclass.

The percentage of *Campylobacter* isolates resistant to ciprofloxacin increased from 12.9% in 1997 to 21.7% in 2005, which is a statistically significant increase (OR=2.2, 95% CI [1.4, 3.4]). Resistance to erythromycin remained low at 2.1% or less during 1997 to 2005. It increased from 0.3% in 2004 to 1.8% in 2005 (<u>Table 5.03</u>).

In 2005, 51.6% of *Campylobacter* isolates were resistant to one or more CLSI subclass, compared with 53.9% in 2004 (<u>Table 5.04</u>). In 2005, 13.6% of *Campylobacter* isolates were resistant to two or more subclasses, compared with 14.1% in 2004.

In 2005, the antimicrobial agent with the highest prevalence of resistance among the 791 *C. jejuni* isolates was tetracycline (41.8), followed by nalidixic acid (21.9%) and ciprofloxacin (21.5%) (<u>Table 5.05</u>). Of note, 0.5% and 1.6% of *C. jejuni* isolates were resistant to gentamicin and erythromycin, respectively.

The percentage of *C. jejuni* isolates resistant to ciprofloxacin increased from 12.4% in 1997 to 21.5% in 2005 (<u>Table 5.06</u>); this increase was statistically significant (OR=2.2, 95% CI [1.4, 3.5]). Erythromycin resistance was low at 1.9% or less during 1997 to 2005.

The percentage of resistance to most agents tested, including ciprofloxacin and erythromycin, was higher in *C. coli* compared with *C. jejuni*. In 2005, the highest levels of resistance among the 98 *C. coli* isolates were to tetracycline (30.6%), nalidixic acid (26.5%), and ciprofloxacin (23.5%) (Table 5.07). The percentage of *C. coli* isolates resistant to ciprofloxacin was 33.3% in 1997, not detected in 1998, but ranged from 12.0% to 47.1% from 1999 to 2005; it was 23.5% in 2005 (Table 5.08). Resistance to erythromycin was not detected in 1997, 12.5% in 1998, ranged from 4.0% to 10.0% during 1999 to 2003, decreased to 0.0% in 2004, and increased to 3.1% in 2005.

Table 5.01: Frequency of Campylobacter species isolated in NARMS, 2005

Species		2005
	N	(%)
Campylobacter jejuni	791	(92.6%)
Campylobacter coli	98	(11.5%)
Other	1	(0.1%)
Total	890	(104.2%)

Table 5.02: Minimum inhibition concentrations (MICs) and resistance of Campylobacter isolates to

antimicrobial agents, 2005 (N=890)

Antik	piotic		% of iso	olates					Perc	ent of	all isola	ates w	ith MIC	C (µg/ı	mL)§					
Andi	Jiotic	%I [*]	$%R^{\dagger}$	[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	0.0	0.6	[0.2–1.4]				6.4	34.7	52.6	5.2	0.6		0.1	0.1		0.4			
Ketolide	Telithromycin	0.7	0.8	[0.3–1.7]	0.1	0.2	0.4	1.2	11.2	39.6	28.3	13.8	3.6	0.7	0.8					
Macrolides	Azithromycin	0.1	1.9	[1.1–3.0]	4.4	24.8	43.5	19.3	4.9	0.1	0.9		0.1	0.3		0.1		1.5		
	Erythromycin	0.0	1.8	[1.0-2.9]			0.6	8.1	34.0	32.8	17.9	3.5	1.2	0.1			0.2	1.6		
Quinolones	Ciprofloxacin	0.0	21.7	[19.0–24.5]	0.6	3.1	34.7	30.0	7.2	2.4	0.3		1.9	9.6	5.5	2.6	1.9	0.2		
	Nalidixic Acid	0.7	22.4	[19.7–25.2]									52.6	20.0	4.4	0.7	3.3	19.1		
Phenicols	Florfenicol¶	N/A	0.5	[0.2-1.3]					0.2	19.4	61.5	13.4	4.9	0.3	0.2					
Tetracyclines	Tetracycline	0.8	40.6	[37.3-43.9]			6.5	24.7	16.0	6.5	3.8	0.7	0.4	0.8	0.7	4.2	12.7	23.0		
Lincosamides	Clindamycin	0.4	1.5	[0.8-2.5]		4.9	27.2	36.3	21.0	5.4	2.7	0.6	0.4	0.3	0.3	0.8				

Percent of isolates with intermediate susceptibility

Figure 5.01: Antimicrobial resistance pattern for *Campylobacter*, 2005 Antimicrobial

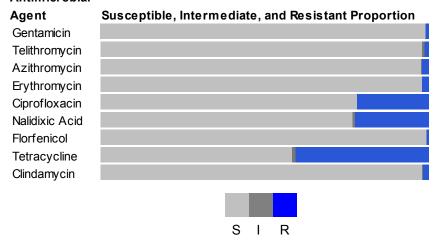


Table 5.03: Percentage and number of Campylobacter isolates resistant to antimicrobial agents, 1997–2005

Year		1997	1998	1999	2000	2001	2002	2003	2004	2005
Total Isolates		217	310	317	324	384	354	328	347	890
	Antibiotic									
Subclass	(Resistance breakpoint)									
Aminoglycosides	Gentamicin	Not	0.3%	0.0%	0.3%	0.0%	0.0%	0.3%	0.3%	0.7%
	(MIC ≥ 8)	Tested	1	0	1	0	0	1	1	6
Ketolides	Telithromycin	Not	1.0%							
	(MIC ≥ 16)	Tested	9							
Macrolides	Azithromycin	Not	0.6%	2.2%	1.9%	2.1%	2.0%	0.9%	0.6%	1.9%
	(MIC ≥ 8)	Tested	2	7	6	8	7	3	2	17
	Erythromycin	1.8%	1.0%	1.9%	1.2%	2.1%	1.4%	0.9%	0.3%	1.8%
	(MIC ≥ 32)	4	3	6	4	8	5	3	1	16
Quinolones	Ciprofloxacin	12.9%	13.9%	18.3%	14.8%	19.5%	20.1%	17.7%	19.0%	21.7%
	(MIC ≥ 4)	28	43	58	48	75	71	58	66	193
	Nalidixic acid	14.3%	16.8%	21.1%	16.7%	20.3%	20.6%	18.9%	19.6%	22.4%
	(MIC ≥ 64)	31	52	67	54	78	73	62	68	199
Phenicols	Chloramphenicol	5.1%	2.9%	0.6%	0.0%	0.3%	0.3%	0.0%	1.4%	Not
	(MIC ≥ 32)	11	9	2	0	1	1	0	5	Tested
	Florfenicol*	Not	0.6%							
	Susceptible breakpoint: (MIC < 4)	Tested	5							
Tetracyclines	Tetracycline	47.9%	45.5%	43.8%	38.3%	40.9%	41.2%	38.4%	46.1%	40.6%
	(MIC ≥ 16)	104	141	139	124	157	146	126	160	361
Lincosamides	Clindamycin	1.8%	1.3%	1.3%	0.9%	2.1%	2.0%	0.6%	2.0%	1.5%
	(MIC ≥ 8)	4	4	4	3	8	7	2	7	13

Only a susceptible breakpoint (≤ 4 µg/ml) has been established. In this report, isolates with an MIC ≥ 8 µg/ml are categorized as resistant

^TPercent 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.

[¶]CLSI guidelines do not currently define a resistance-breakpoint for florfenicol.

Table 5.04: Resistance patterns of Campylobacter isolates, 2005

Year	1997	1998	1999	2000	2001	2002	2003	2004	2005
Total Isolates	217	310	317	324	384	354	328	347	890
	%	%	%	%	%	%	%	%	%
	n	n	n	n	n	n	n	n	n
No resistance detected	47.0%	45.2%	47.3%	52.2%	49.2%	48.3%	50.9%	46.1%	48.4%
	102	140	150	169	189	171	167	160	431
Resistance ≥1CLSI subclass*	53.0%	54.8%	52.7%	47.8%	50.8%	51.7%	49.1%	53.9%	51.6%
	115	170	167	155	195	183	161	187	459
Resistance ≥2 CLSI subclasses*	15.7%	9.7%	13.6%	8.0%	13.3%	12.7%	8.5%	14.1%	13.6%
	34	30	43	26	51	45	28	49	121
Resistance ≥3 CLSI subclasses*	1.8%	2.6%	1.6%	0.9%	1.6%	1.1%	0.9%	1.2%	1.5%
	4	8	5	3	6	4	3	4	13
Resistance ≥4 CLSI subclasses*	0.5%	0.3%	0.9%	0.3%	0.3%	0.0%	0.3%	0.3%	0.3%
	1	1	3	1	1	0	1	1	3
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	0	0	0

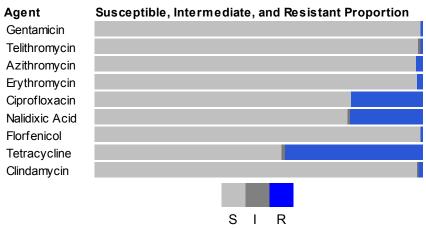
^{*}CLSI: Clinical and Laboratory Standards Institute

Table 5.05: Minimum inhibitory concentrations (MICs) and resistance of *Campylobacter jejuni* isolates to antimicrobial agents, 2005, (N=791)

antimicrobia	ii agoiito, ze	- 																		
Antib	viotic		% of iso	olates					Per	cent of	all isol	ates w	ith MI	C (µg/ı	mL)§					
Aitus	notic	%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	0.0	0.5	[0.1–1.3]				7.1	37.3	51.3	3.3	0.5		0.1			0.4			
Ketolide	Telithromycin	0.4	0.5	[0.1–1.3]		0.3	0.4	1.3	11.2	41.1	30.0	12.9	1.8	0.4	0.5					
Macrolides	Azithromycin	0.1	1.8	[1.0-3.0]	4.8	26.4	46.6	16.9	2.3		1.0		0.1	0.4		0.1		1.3		
	Erythromycin	0.0	1.6	[0.9–2.8]			0.5	8.7	36.9	33.6	16.2	2.0	0.3	0.1			0.3	1.4		
Quinolones	Ciprofloxacin	0.0	21.5	[18.7–24.5]	0.6	3.4	35.9	30.2	5.8	2.3	0.3		1.8	9.5	5.4	2.7	2.0	0.1		
	Nalidixic Acid	8.0	21.9	[19.0–24.9]									55.0	18.8	3.5	8.0	2.9	19.0		
Phenicols	Florfenicol¶	N/A	0.5	[0.1–1.3]					0.3	20.7	62.3	12.0	4.2	0.25	0.25					
Tetracyclines	Tetracycline	0.9	41.8	[38.4–45.4]			7.1	25.0	14.8	5.6	3.7	0.6	0.5	0.9	8.0	4.6	13.5	23.0		
Lincosamides	Clindamycin	0.5	1.1	[0.5–2.1]		5.2	29.6	38.4	19.6	3.8	1.5	0.3	0.5	·	0.3	0.9				

Percent of isolates with intermediate susceptibility

Figure 5.02: Antimicrobial resistance pattern for *Campylobacter jejuni*, 2005 Antimicrobial



[†]Percent of isolates that were resistant

 $^{^{\}ddagger}95\%$ 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.

 $[\]P{\hbox{\scriptsize CLSI guidelines do not currently define a resistance-breakpoint for florfenicol.}}$

Table 5.06: Percentage and number of *Campylobacter jejuni* isolates resistant to antimicrobial agents, 1997–2005

Year Total Isolates		1997 209	1998 297	1999 293	2000 306	2001 365	2002 329	2003 303	2004 320	2005 791
Out also	Antibiotic									
Subclass	(Resistance breakpoint)									
Aminoglycosides	Gentamicin	Not	0.3%	0.0%	0.0%	0.0%	0.0%	0.0%	0.3%	0.5%
	(MIC ≥ 8)	Tested	1	0	0	0	0	0	1	4
Ketolides	Telithromycin	Not	0.0%							
	(MIC ≥ 16)	Tested	0							
Macrolides	Azithromycin	Not	0.3%	1.7%	1.6%	1.9%	1.8%	0.3%	0.6%	1.8%
	(MIC ≥ 8)	Tested	1	5	5	7	6	1	2	14
	Erythromycin	1.4%	0.7%	1.4%	1.0%	1.9%	1.2%	0.3%	0.3%	1.6%
	(MIC ≥ 32)	3	2	4	3	7	4	1	1	13
Quinolones	Ciprofloxacin	12.4%	13.8%	17.7%	14.7%	18.4%	20.7%	17.2%	18.1%	21.5%
	(MIC ≥ 4)	26	41	52	45	67	68	52	58	170
	Nalidixic acid	13.4%	15.5%	20.1%	16.0%	18.9%	21.3%	17.8%	18.4%	21.9%
	(MIC ≥ 64)	28	46	59	49	69	70	54	59	173
Phenicols	Chloramphenicol	3.8%	1.0%	0.7%	0.0%	0.3%	0.3%	0.0%	1.6%	Not
	(MIC ≥ 32)	8	3	2	0	1	1	0	5	Tested
	Florfenicol*	Not	0.5%							
	Susceptible breakpoint: (MIC < 4)	Tested	4							
Tetracyclines	Tetracycline	47.8%	46.1%	45.4%	39.2%	40.3%	41.3%	38.3%	46.9%	41.8%
-	(MIC ≥ 16)	100	137	133	120	147	136	116	150	331
Lincosamides	Clindamycin	1.0%	1.0%	0.7%	0.7%	1.9%	1.8%	0.0%	2.2%	1.1%
	(MIC ≥ 8)	2	3	2	2	7	6	0	7	9

^{*}Only a susceptible breakpoint (≤ 4 µg/ml) has been established. In this report, isolates with an MIC ≥ 8 µg/ml are categorized as resistant

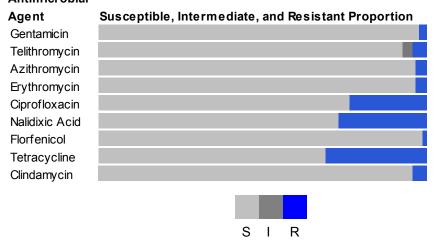
Table 5.07: Minimum inhibitory concentrations (MICs) and resistance of *Campylobacter coli* isolates to

antimicrobial agents, 2005 (N=98)

Antik	piotic		% of is	olates					Perd	ent of	all isol	ates w	ith MI	C (µg/	mL) [§]					
Andi	Jiotic	%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	0.0	1.1	[0.0-5.8]				1.1	12.8	63.8	20.2	1.1			1.1					
Ketolide	Telithromycin	3.2	3.2	[0.7-9.0]	1.1				11.7	26.6	14.9	21.3	18.1	3.2	3.2					
Macrolides	Azithromycin	0.0	3.1	[0.6-8.7]	1.0	11.2	18.4	38.8	26.5	1.0								3.1		
	Erythromycin	0.0	3.1	[0.6-8.7]			1.0	3.1	11.2	25.5	31.6	15.3	9.2	•				3.1		
Quinolones	Ciprofloxacin	0.0	23.5	[15.5–33.1]		1.0	25.5	27.6	18.4	3.1	1.0		3.1	10.2	6.1	2.0	1.0	1.0		
	Nalidixic Acid	0.0	26.5	[18.1–36.4]									32.7	29.6	11.2		6.1	20.4		
Phenicols	Florfenicol¶	N/A	1.0	[0.0-5.6]						9.2	54.1	24.5	11.2	1.0		•				
Tetracyclines	Tetracycline	0.0	30.6	[21.7-40.7]			2.0	21.4	25.5	14.3	5.1	1.0				1.0	6.1	23.5		
Lincosamides	Clindamycin	0.0	4.1	[1.1–10.1]		3.1	8.2	19.4	31.6	18.4	12.2	3.1		3.1	1.0					

Percent of isolates with intermediate susceptibility

Figure 5.03: Antimicrobial resistance pattern for *Campylobacter coli*, 2005 Antimicrobial



[†]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.

[¶]CLSI guidelines do not currently define a resistance-breakpoint for florfenicol.

Table 5.08: Percentage and number of *Campylobacter coli* isolates resistant to antimicrobial agents, 1997–2005

Vace		4007	4000	4000	2000	2004	2002	2002	2004	2005
Year		1997	1998	1999	2000	2001	2002	2003	2004	2005
Total Isolates		6	8	20	12	17	25	22	26	98
	Antibiotic									
Subclass	(Resistance breakpoint)									
Aminoglycosides	Gentamicin	Not	0.0%	0.0%	8.3%	0.0%	0.0%	4.5%	0.0%	2.0%
	(MIC ≥ 8)	Tested	0	0	1	0	0	1	0	2
Ketolides	Telithromycin	Not	4.1%							
	(MIC ≥ 16)	Tested	4							
Macrolides	Azithromycin	Not	12.5%	10.0%	8.3%	5.9%	4.0%	9.1%	0.0%	3.1%
	(MIC ≥ 8)	Tested	1	2	1	1	1	2	0	3
	Erythromycin	0.0%	12.5%	10.0%	8.3%	5.9%	4.0%	9.1%	0.0%	3.1%
	(MIC ≥ 32)	0	1	2	1	1	1	2	0	3
Quinolones	Ciprofloxacin	33.3%	0.0%	30.0%	25.0%	47.1%	12.0%	22.7%	30.8%	23.5%
	(MIC ≥ 4)	2	0	6	3	8	3	5	8	23
	Nalidixic acid	50.0%	50.0%	30.0%	25.0%	47.1%	12.0%	22.7%	34.6%	26.5%
	(MIC ≥ 64)	3	4	6	3	8	3	5	9	26
Phenicols	Chloramphenicol	50.0%	37.5%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	Not
	(MIC ≥ 32)	3	3	0	0	0	0	0	0	Tested
	Florfenicol*	Not	1.0%							
	Susceptible breakpoint: (MIC < 4)	Tested	1							
Tetracyclines	Tetracycline	66.7%	50.0%	30.0%	25.0%	58.8%	40.0%	45.5%	38.5%	30.6%
	(MIC ≥ 16)	4	4	6	3	10	10	10	10	30
Lincosamides	Clindamycin	16.7%	12.5%	10.0%	8.3%	5.9%	4.0%	9.1%	0.0%	4.1%
	(MIC ≥ 8)	1	1	2	1 1	1	1	2	0	4

^{*}Only a susceptible breakpoint (≤ 4 µg/ml) has been established. In this report, isolates with an MIC ≥ 8 µg/ml are categorized as resistant

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 implemented during 1997 to 2004, and the limited geographic area under surveillance.

In four states that participated in NARMS *Campylobacter* surveillance (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 from 1997 to 2004, 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. From the other six FoodNet sites, one *Campylobacter* isolate among isolates received from participating clinical laboratories was also selected each week. 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 was unlikely to be associated with a change of antimicrobial resistance among *Campylobacter* isolates submitted to NARMS.

From 1997 to 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 was unlikely to influence submission of the isolate to NARMS. However, the one-a-week sampling scheme could have resulted in oversampling or undersampling of antimicrobial-resistant isolates if the prevalence of such resistance was not uniform throughout the year. The impact of oversampling or undersampling can vary among states. In 2005, a representative sampling scheme was initiated in the 10 FoodNet sites.

Campylobacter isolates were forwarded to CDC by 10 states participating in FoodNet during 2005, representing approximately 45 million persons (15% of the U.S. population). Because NARMS 2005 Campylobacter surveillance was not nationwide, findings should be generalized to the U.S. population with caution because of possible regional differences in the prevalence of antimicrobial resistance among Campylobacter.

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- 3. Chiller T. Broadening your appropriate use program to agriculture; current data, trends, and importance of monitoring pathogens of public health concern. CDC's Conference on Antimicrobial Resistance Programs Building Bridges: Surveillance, Atlanta, GA, April 2005 (invited lecture).
- 4. Chiller T. Foodborne disease surveillance and antibiotic resistance. Pennsylvania Public Health Institute, State College, PA, May 2005 (invited lecture).
- 5. Chiller T. Household treatment of drinking water and hygiene reduce disease in developing country households. ASM Symposium on Drinking Water Treatment and Safe Storage for Households in Developing Countries, June 2005 (invited lecture).
- 6. Chiller T. Human NARMS surveillance. Public Health Agency for Canada's International Network on Integrated Surveillance of Antimicrobial Resistance Conference, Winnipeg, Canada, September 2005 (invited lecture).
- 7. Chiller T, May A, Lewis K, Gay K, Barrett T, and the NARMS Enterococci Working Group. Community associated vancomycin-resistant enterococci (VRE) from human stools in the United States. 2nd International ASM-FEMS Conference on Enterococci, Helsingor, Denmark, August 2005.
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APPENDIX A

Summary of Escherichia coli Resistance Surveillance Pilot Study, 2005

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 pathogens⁴. 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 2005 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

- 25.4% of 118 E. coli isolates tested were resistant to two or more subclasses of antimicrobial agents.
- 8.5% of 118 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.

- 0.8% of 118 E. coli isolates were resistant to ceftiofur (Table A.04).
- 7.6% of 118 E. coli isolates were resistant to ciprofloxacin (Table A.04).

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.01). The resistance breakpoint for amikacin, according to CLSI⁵ guidelines, is an MIC of 64 µg/mL.

Interpretive criteria from the Clinical Laboratory and Standards Institute (CLSI) were used (<u>Table A.01</u>). The 95% Cls 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 2005, CDC received and tested 118 viable *E. coli* isolates (<u>Table A.02</u>). Minimum Inhibitory Concentrations (MIC) was determined for *E. coli* isolates for 15 antimicrobial agents (<u>Table A.03</u>).

Of the *E. coli* isolates, 26.3% were resistant to ampicillin; 19.5% to tetracycline; 17.7%, to sulfamethoxazole; and 9.3% to nalidixic acid (Table A.04).

In 2005, 22.9% of *E. coli* isolates were resistant to two or more CLSI subclasses, and 7.6% were resistant to five or more CLSI subclasses (<u>Table A.05</u>). The level of *E. coli* resistance in this pilot study differs than that observed in NARMS 2004. Because of the different sampling methods between this study and NARMS, this observation requires further investigation.

There is a difference in the level of resistance among *E. coli* isolates in this study compared with *E. coli* O157 isolates submitted to NARMS in 2005. Because of the different sampling methods employed between this study and NARMS, this observation requires further investigation.

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Table A.01: Antimicrobial agents used for susceptibility testing of Escherichia coli, 2005

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

^{*} 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.02: Escherichia coli isolates received and tested at CDC, by site, 2005

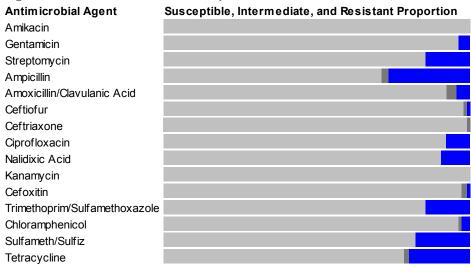
		2005
Site	N	(%)
Maryland	69	(58.5%)
Michigan	49	(41.5%)
Total	118	(100.0%)

Table A.03: Minimum inhibition concentrations (MICs) of Escherichia coli, 2005 (N=118)

	William Illinoidol				<u> </u>		<i>,,</i> 0.			01111		, -	-		,					
	Antibiotic		% of is	olates						Percei	nt of al	lisolate	s with	МІС (µ	g/mL) [§]					
	,	%l [*]	%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	[0.0–2.6]						0.8	44.1	50.8	4.2							
	Gentamicin	0.0	3.3	[2.2-8.3]					17.8	70.3	8.5				8.0	2.5				
	Streptomycin	NA	14.4	[9.6–19.2]												85.6	5.9	8.5		
Aminopenicillins	Ampicillin	2.5	26.3	[24.1–36.7]							7.6	44.1	16.9	2.5	2.5		26.3			
β-lactamase inhibitor	Amoxicillin-clavulanic acid	3.4	4.2	[1.6–7.2]							4.2	19.5	46.6	22.0	3.4	3.4	0.8			
Cephalosporins (3rd generation)	Ceftiofur	8.0	0.8	[0.0–2.6]				8.5	57.6	31.4	8.0		0.8	0.8						
	Ceftriaxone	8.0	0.0	[0.0–2.6]					98.3			0.8		•	0.8					
Quinolones	Ciprofloxacin	0.0	7.6	[5.7–13.9]	90.7				1.7				7.6							
	Nalidixic Acid	NA	9.3	[14.0–24.9]							22.9	61.0	6.8				9.3			
Aminoglycosides	Kanamycin	0.0	0.0	[0.8–5.3]										98.3	1.7					
Cephamycins	Cefoxitin	1.7	0.8	[1.3–6.6]							5.1	50.0	33.9	8.5	1.7		0.8			
Folate pathway inhibitors	Trimethoprim-sulfamethoxazole	NA	14.2	[11.2–21.3]				76.1	8.8		0.9			14.2						
Phenicols	Chloramphenicol	8.0	2.5	[0.5–4.7]								4.2	66.1	26.3	0.8		2.5			
Sulfonamides	Sulfamethoxazole/Sulfisoxazole	NA	17.7	[17.7–29.4]											73.5	8.8				17.7
Tetracyclines	Tetracycline	1.7	19.5	[12.4–22.8]									78.8	1.7		5.1	14.4			

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

Figure A.01: Antibiotic resistance pattern for Escherichia coli, 2005





[†]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.04: Escherichia coli isolates with antimicrobial resistance, 2005

Year		2004	2005
Total Isolates		151	118/113*
Subclass	Antibiotic (Resistance breakpoint)		
	1 /	0.00/	0.00/
Aminoglycosides	Amikacin	0.0%	0.0%
	(MIC ≥ 64)	0	0
	Gentamicin	2.0%	3.4%
	(MIC ≥ 16)	3	4
	Streptomycin	10.6%	14.4%
	(MIC ≥ 64)	16	17
Aminopenicillins	Ampicillin	24.5%	26.3%
	(MIC ≥ 32)	37	31
β-lactamase inhibitor combinations	Amoxicillin-clavulanic acid	2.6%	4.2%
	(MIC ≥ 32)	4	5
Cephalosporins (3 rd generation)	Ceftiofur	0.0%	0.8%
	(MIC ≥ 8)	0	1
	Ceftriaxone	0.0%	0.0%
	(MIC ≥ 64)	0	0
Quinolones	Ciprofloxacin	3.3%	7.6%
	(MIC ≥ 4)	5	9
	Nalidixic Acid	9.3%	9.3%
	(MIC ≥ 32)	14	11
Aminoglycosides	Kanamycin	2.0%	0.0%
	(MIC ≥ 64)	3	0
Cephamycins	Cefoxitin	2.6%	0.8%
•	(MIC ≥ 32)	4	1
Folate pathway inhibitors	Trimethoprim-sulfamethoxazole	11.3%	14.2%
, ,	(MIC ≥ 4)	17	16
Phenicols	Chloramphenicol	1.3%	2.5%
Sulfonamides	(MIC ≥ 32)	2	3
	Sulfamethoxazole/Sulfisoxazole	17.9%	17.7%
	(MIC ≥ 512)	27	20
Tetracyclines	Tetracycline	13.2%	19.5%
,	(MIC ≥ 16)	20	23

^{*}Five isolates do not have test results for Trimethoprim-sulfamethoxazole and Sulfamethoxazole/Sulfisoxazole.

Table A.05: Antimicrobial agents resistant to Escherichia coli, 2005

Year		2005
Total Isolates	2004	118
	%	%
	n	n
No resistance detected	62.9%	63.6%
	95	75
Resistance ≥1CLSI subclass*	37.7%	36.4%
	57	43
Resistance ≥2 CLSI subclasses*	17.9%	22.9%
	27	27
Resistance ≥3 CLSI subclasses*	9.9%	14.4%
	15	17
Resistance ≥4 CLSI subclasses*	5.3%	9.3%
	8	11
Resistance ≥5 CLSI subclasses*	3.3%	7.6%
	5	9
At least ACSSuT [†]	1.3%	0.8%
	2	1
At least ACSuTm [‡]	1.3%	0.8%
	2	1
At least ACSSuTAuCf [§]	0.0%	0.0%
	0	0
At least AAuC ¹	0.0%	0.0%
	0	0
At least A3C**	0.0%	0.0%
	0	0
At least MDR-AmpC ^{††}	0.0%	0.0%
'	0	0
Resistance to quinolone and cephalosporin (3 rd generation)	0.0%	0.0%
	0	0

^{*}CLSI: Clinical and Laboratory Standards Institute

Among isolates of commensal *E. coli* ceftiofur resistance has increased from 0.0% in 2004 to 0.8% in 2005. Ciprofloxacin resistance increased from 3.3% in 2004 to 7.6% in 2005. A decrease in detected resistance was observed for two drugs; cefoxitin (2.7% to 0.8%) and kanamycin (2.0 to 0.0%).

[†]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)

APPENDIX B: International Comparison of Antimicrobial MIC-Distributions

Several committees determine clinical antimicrobial MIC breakpoints. In the U.S., breakpoints have traditionally been determined by the Clinical Laboratory Standards Institute (CLSI, formerly NCCLS) and the FDA. In Europe, the ESCMID-formed authority EUCAST (European Committee on Antimicrobial Susceptibility Testing) has been tasked with harmonizing clinical breakpoints for existing drugs in Europe and to determine breakpoints for new antimicrobial agents as part of the regulatory process for approval of new drugs in Europe [1-3]. In addition to clinical breakpoints, EUCAST has introduced the concept of epidemiological cut-off values (ECOFFs) as a way of distinguishing bacteria without resistance mechanisms ("wild type") from those with mutational or acquired resistance [1, 4]. The ECOFF is expressed as WT \leq Xmg/L and will divide the distribution into two groups; those that are wild type (WT) and those that are non-wild type (NWT). Thus, ECOFFs do not relate to clinical efficacy-instead they were introduced to allow the sensitive measurement and comparison of resistance as a biological phenomenon.

The EUCAST webpage displays MIC wild type-distributions for many organism-drug combinations (http://www.eucast.org). An example of a wild type MIC distribution is shown in Figure 1. EUCAST's wild type distributions are based on MIC-data collected from all over the world and from various sources, including humans, animals and plants. The typical wild type MIC distribution spans over 3-5 dilution steps.

In theory, the wild type MIC-distributions should, for a given organism-drug combination, be the same irrespective of the origin of the isolates. Below are some examples of how the CDC distributions of *Escherichia coli* compare to the distributions defined by EUCAST (Figure 2). Even though the CDC-distributions do not represent full range MIC-distributions (hence leaving one or the other end of the distribution truncated) a good correlation between EUCAST and CDC distributions can be observed. This confirms that *E. coli* wild type distributions are similar regardless of origin and source. NARMS is currently participating in international discussions on how to harmonize antimicrobial resistance surveillance.

Figure 1. Wild type distribution for Escherichia coli and amikacin (www.eucast.org).

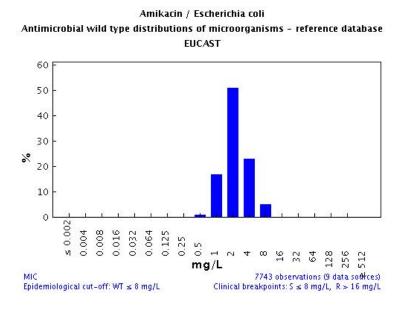
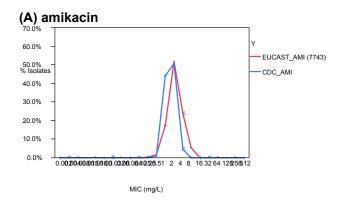
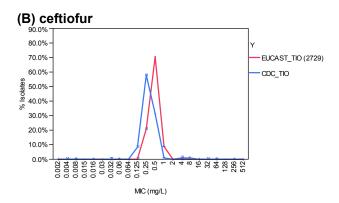


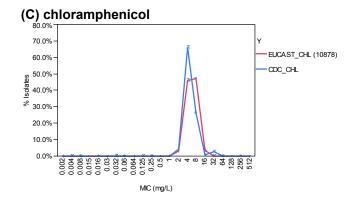
Figure 2 A-D. Comparison between NARMS E. coli MIC-distributions and EUCAST wild-type distributions.



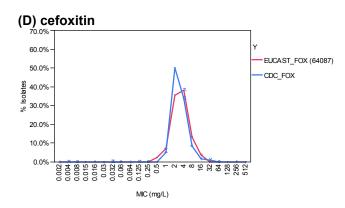
NARMS concentration test range: 0.5-64 mg/L



NARMS concentration test range: 0.125-8 mg/L



NARMS concentration test range: 2-32 mg/L



NARMS concentration test range: 0.5-32 mg/L

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APPENDIX C: 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