The National Antimicrobial Resistance Monitoring System

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Center for Veterinary Medicine Strategy

Aimed at assessing relationships between antimicrobial use in food animals and the potential human health consequences

Multi-pronged approach that includes:

- Education/outreach activities
- Expanded research activities
- Revised safety assessment process (GFI #152) 2003
- Revised judicious use guidance (GFI #209) 2012
- Industry guidance on phasing out production uses (GFI #213)
- Update on veterinary feed directive
- Enhanced surveillance activities (NARMS) 1996
- Better antimicrobial use information (ANPRM)
- Participation in international activities (WHO, PAHO, OIE, Codex)

Challenges of Integrated Surveillance for Antimicrobial Resistance

- Gathering accurate information is expensive and laborious
- Burden of illness and food consumption data are needed for design and prioritization of pathogens and commodities
- Sound sampling scheme along the food chain is critical
- Cooperation of, and good communication between, agriculture and public health sectors
- Collaboration and information sharing between laboratorians, epidemiologists, industry and public health officials within and across sectors

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National Antimicrobial Resistance Monitoring System
FDA CDC USDA

Challenges of Integrated Surveillance for Antimicrobial Resistance

- Political/financial support - Requires recognition of the public health issues and the need for ongoing risk assessments
- Establish a process for review and enhancement
- Remain flexible in order to stay current
- Understanding the implications of the data and the need for research
- Publishing findings to different audiences in a timely manner
- Using the data to formulate sound public health policy
- International harmonization and cooperation

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NARMS Objectives

1. Monitor trends in antimicrobial resistance among foodborne bacteria from humans, retail meats, and animals

2. Disseminate timely information on antimicrobial resistance to promote interventions that reduce resistance among foodborne bacteria

3. Conduct research to better understand the emergence, persistence, and spread of antimicrobial resistance

4. Assist the FDA in making decisions related to the approval of safe and effective antimicrobial drugs for animals

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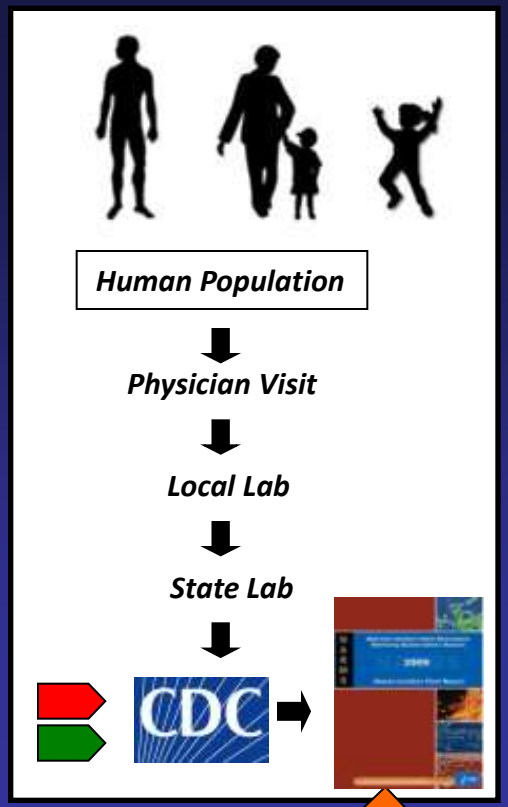
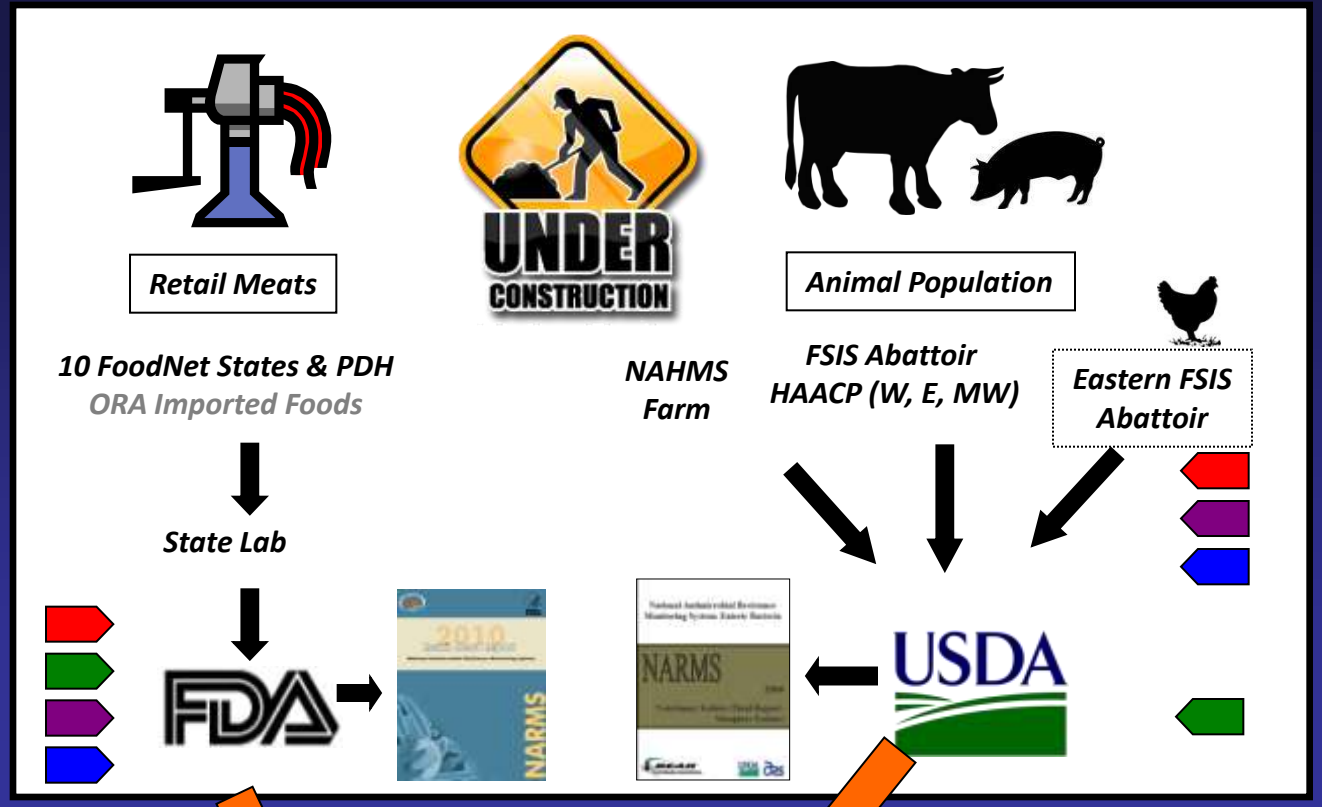




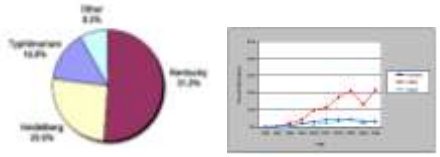
Campylobacter

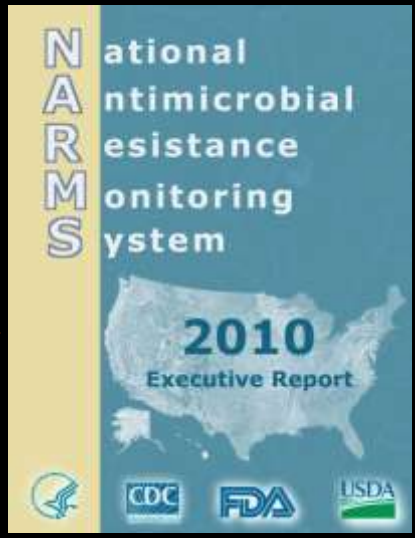
Salmonella

Enterococcus

E. coli

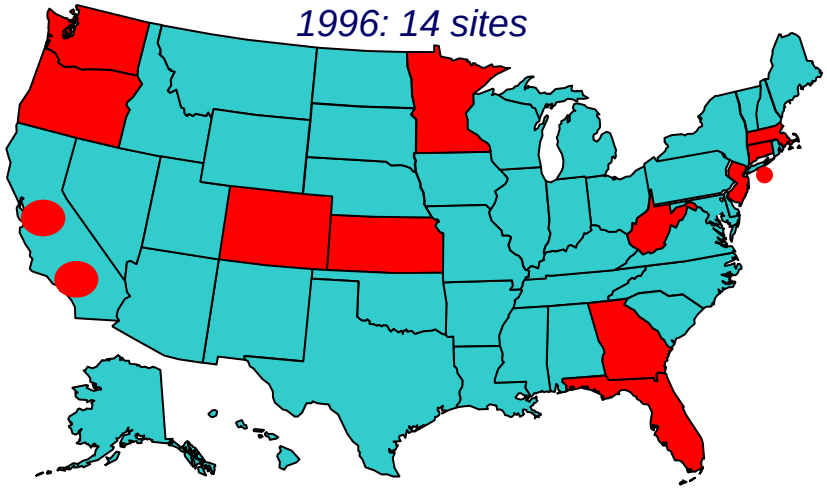
Data Integration



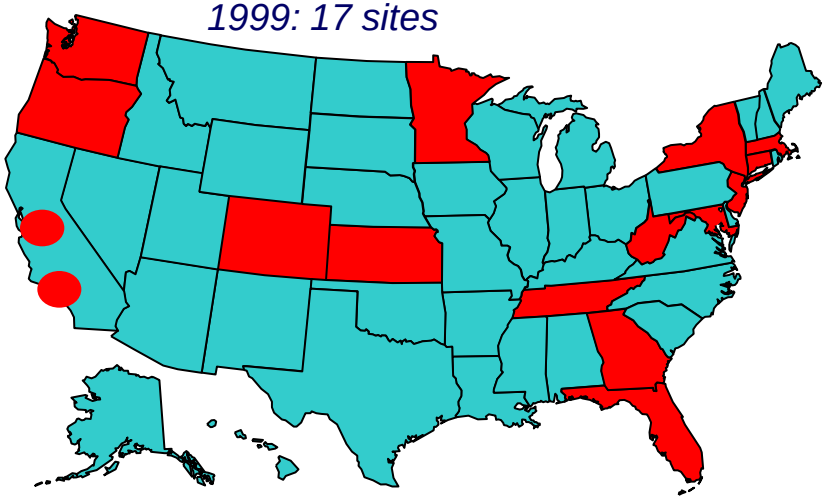


*Human Salmonella Surveillance Sites**

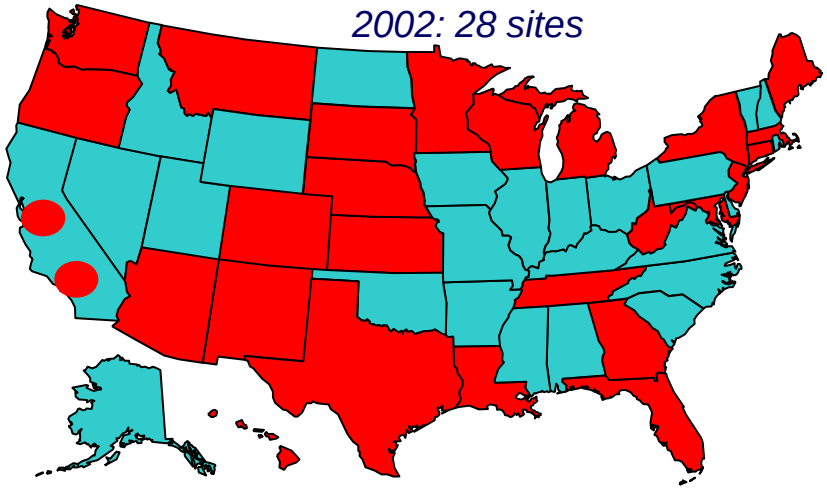
1996: 14 sites



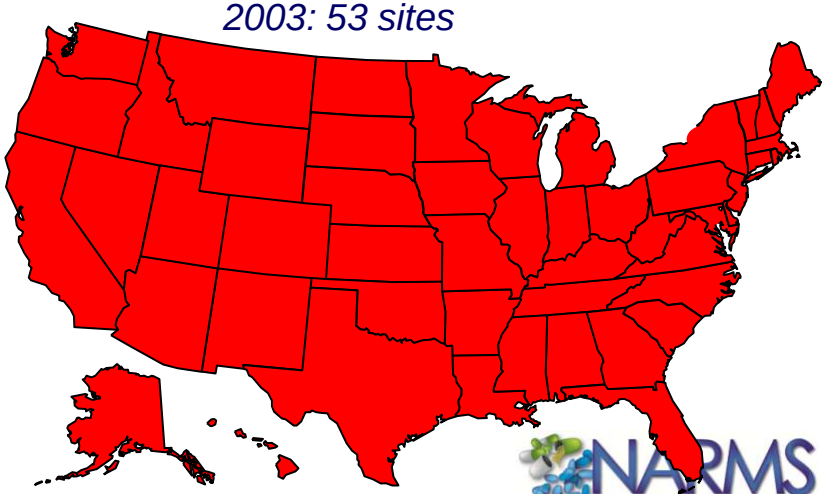
1999: 17 sites



2002: 28 sites



2003: 53 sites



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Human *Campylobacter* Surveillance Sites

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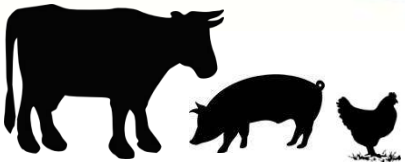
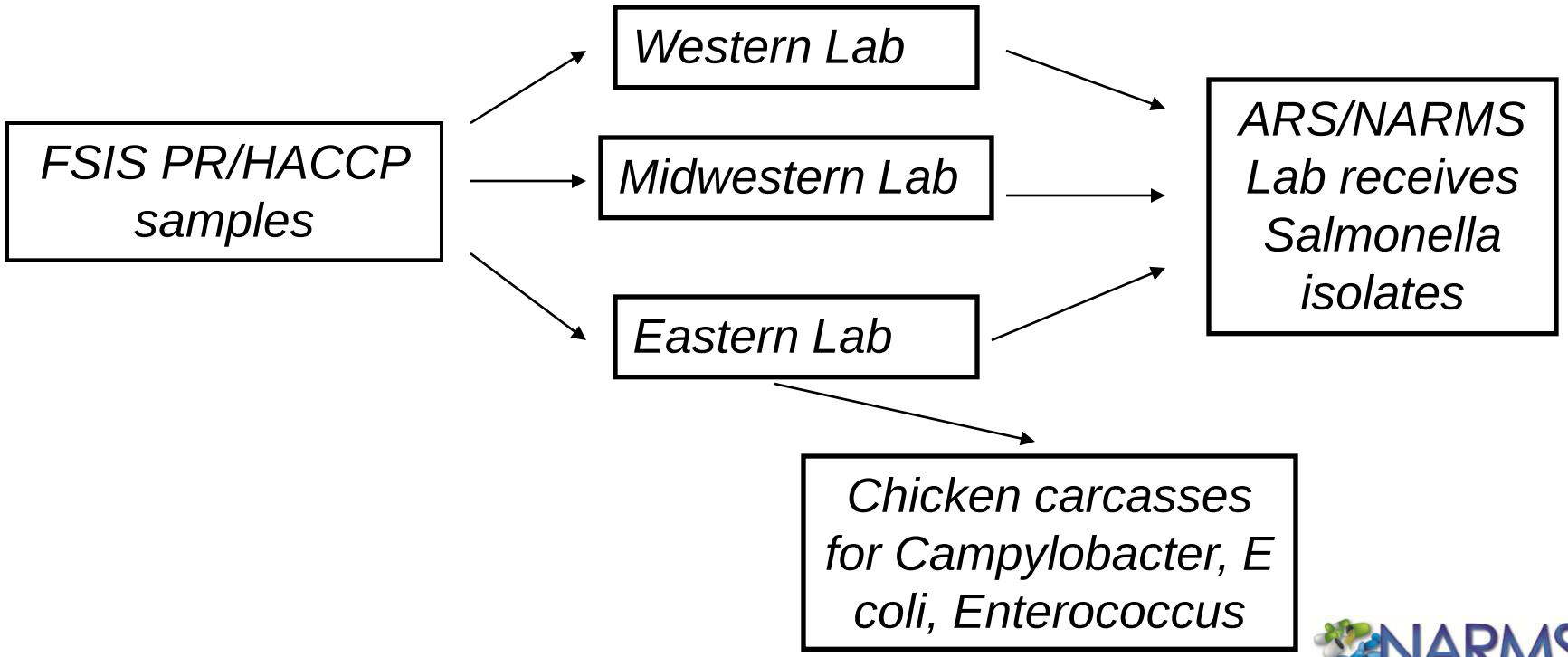


Animal Source of Isolates



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FDA Science Board Review

April 10-11, 2007

1. Are there inherent biases in the sampling strategies employed in NARMS? If so, how can they be improved to ensure that the data and our interpretation are scientifically sound given current resources?
2. Are there epidemiological and/or microbiological research studies that would better serve the goals of NARMS and the regulatory work of FDA?
3. Are our current plans for data harmonization and reporting appropriate? If not, what would you consider the top priorities for advancing harmonized reporting?
4. Are the current NARMS international activities adequate to address the worldwide spread of antimicrobial-resistant foodborne bacteria?

Focus Areas and Key Findings

1. Research studies
   - Encouraged further development and expansion
   - Emphasis on hypothesis-driven and collaborative research

2. Data harmonization and reporting
   - Need for an integrated database and timely reporting

3. International activities
   - Strongly endorsed continuation and expansion of international activities, including training

4. Sampling strategies
   - Use national, random sampling when possible
     - When not feasible, further stratify data or use a more targeted sampling strategy

1. Laboratory Method Meeting
Sep 10-12, 2008. Athens GA

- Revised NARMS Goals
- Sample and isolate processing
- Established research working groups (Lab, Epi, Mol.)
- Serotyping and species identification
- QC organisms and susceptibility testing
- Criteria for repeat testing
- PFGE updates
- Microarray and Luminex
- ARIS vs. manual AST for *Enterococcus*
- Other laboratory methods issues
  - Developed a laboratory methods manual

2. Data Management Meeting
Aug 5-7, 2009. Rockville MD

- NARMS integrated database and analytical tools
  - Currently in Phase III of B/A contract
- Linking NARMS with other programs (e.g., PulseNet)
- NARMS Working Group breakouts
- Sampling
- Strategic Planning
  - Developed 5Y Strategic Plan

3. International Partners Meeting
July 15-16, 2010 Atlanta GA

- International
  - WHO, EFSA, OIE, PAHO, PHAC, Korean, China, Denmark, Africa, IFAH
- Research
  - Molecular biology of resistance
  - Genomic typing tools
- Presented draft 5Y Strategic Plan

4. Sampling Meeting
July 2011, St. Louis, MO

- Revising animal and retail meat sampling
- Including industry stakeholders, academic experts and consumer representatives
- Explored potential partnerships to obtain samples
- Discussed best use of resources to meet public health goals

- Sept 2012 – meeting of the retail meat sites at White Oak

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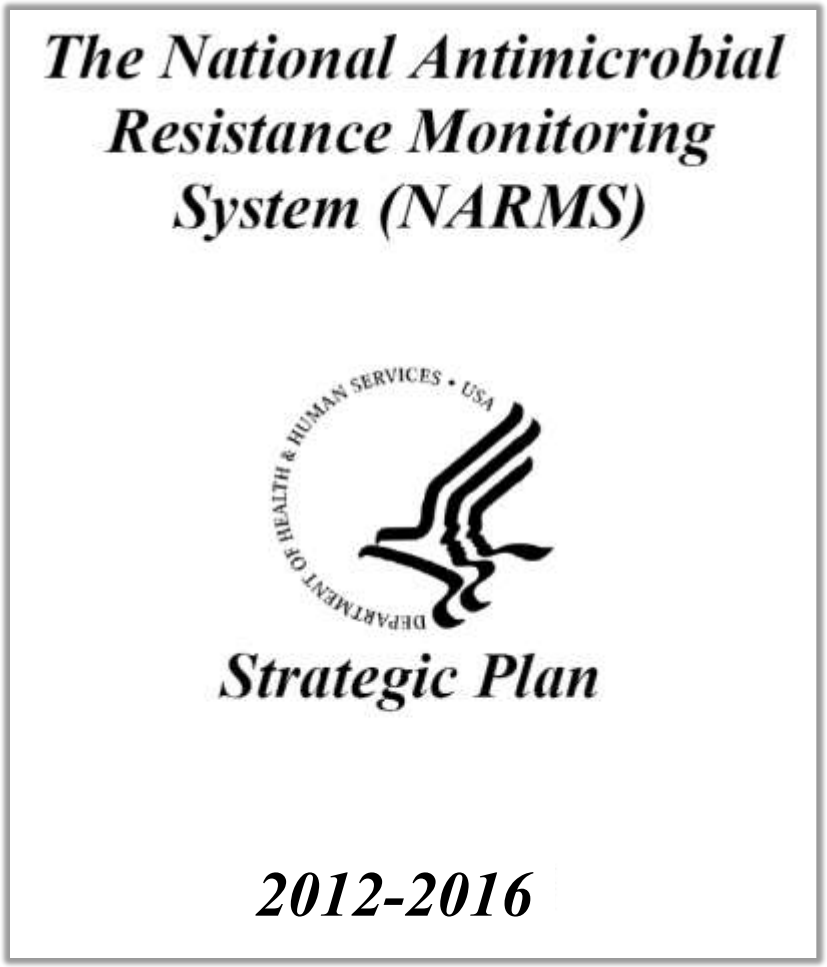
NARMS Strategic Plan



Goal 1: To develop, implement and optimize a shared database, with advanced data acquisition and reporting tools

Goal 2: To make sampling more representative and more applicable to trend analysis

Goal 3: To strengthen collaborative research projects to address high risk food safety issues

Goal 4: To support international activities which promote food safety, and mitigate the spread of antimicrobial resistance

NARMS Initiatives - FY2011

CDC

- **Expand Outbreak Isolate Testing.** CDC will expand antimicrobial susceptibility testing of isolates from *Salmonella* outbreaks. This additional testing will allow CDC to more fully use the rich epidemiologic data that is typically available from outbreak investigations.

- **Link Foodborne Disease Surveillance Data.** Link NARMS data with information in other surveillance systems (FoodNet, PulseNet, OutbreakNet). Currently, this type of linking is very labor-intensive and it must be redone whenever up-to-date information is needed.

USDA

- **ARS is coordinating 5 on-farm pilot studies:** dairy cattle, beef cattle, swine, broilers and turkeys. Will include surveys to assess antibiotic use in sampled animals.
- **FSIS** is working with NARMS to establish long-term in plant sampling of animals, slated to begin in mid-late 2012

FDA

- **Adding 3 retail testing sites in 2012 (MO, LA, WA). T**o expand the number of samples collected will improve the ability to determine trends in different strain subtypes
- **Database development**

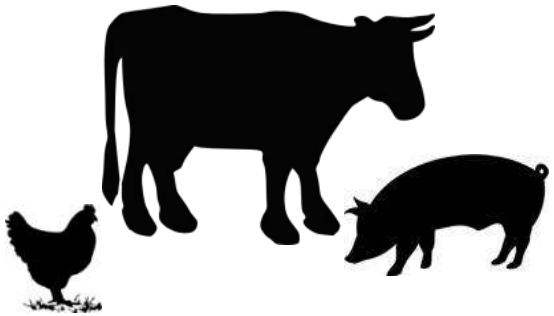
Science Board Comments on Animal Sampling

- Sampling needs to be nationally representative
- Sampling biases occur as processing plants are not randomly selected
  - USDA encouraged to assess HACCP sampling to see if modifications can make the sample more representative
  - Alternatively, consider an ongoing “baseline” sampling scheme
- On-farm data are essential in understanding movement of resistance from farm to fork

New NARMS Animal Component-2 parts

1. On-Farm

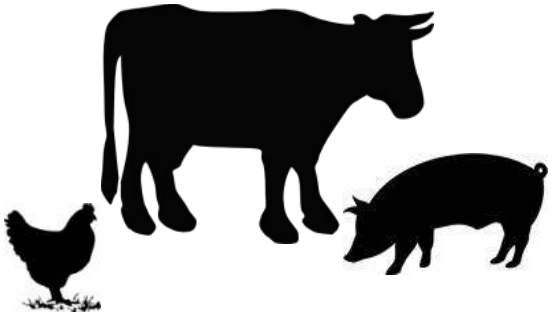
- Collaboration with USDA- Agricultural Research Service (ARS) and University partners
- Randomized nationally representative selection of farms
- Fecal samples
- Drug use information



New NARMS Animal Component-2 parts

2. In-plant

- Collaboration with USDA-Food Safety Inspection Service (FSIS)
- Randomized nationally representative selection of slaughterhouses
- Cecal samples will be added to HACCP samples to better reflect consequences of veterinary antimicrobial use and less confounding by plant contamination



In Plant Sampling

- Finalized an interagency agreement with FSIS to acquire intestinal samples at slaughter
- Goal is to include all plant sizes
- Testing all four bacteria from 6 production classes
  - Beef, dairy, hogs, sows, broilers, turkeys
- HACCP testing will continue
- Goal is a random representative and sustainable animal sampling scheme with benchmarking to baseline studies and comparison with farm data
- Coupled with on farm studies, we will meet the SB recommendations and better serve the goals of the program

New NARMS Animal Component

Old system

	Swine	Cattle	Chicken	Turkeys
Campylobacter			x	
Salmonella	x	x	x	x
E. coli			x	
Enterococcus			x	

New system

	Swine	Cattle	Chicken	Turkeys
Campylobacter	x	x	x	x
Salmonella	x	x	x	x
E. coli	x	x	x	x
Enterococcus	x	x	x	x

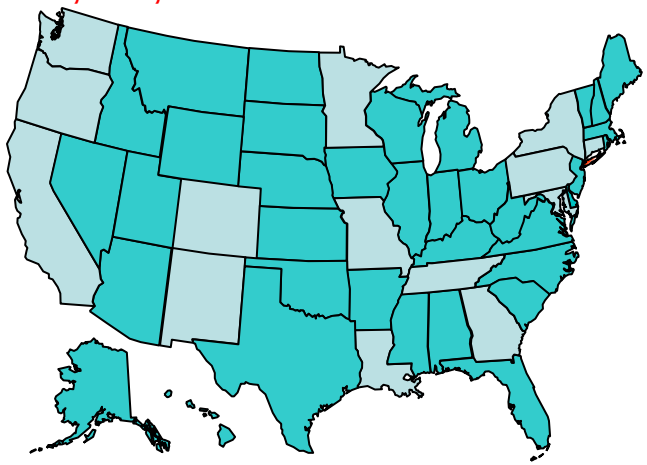
NARMS Retail Meat Surveillance

Partnership with state FoodNet Sites

- CT, GA, MD, MN, TN — 1/2002
- CT, GA, MD, MN, TN, OR — 9/2002
- CT, GA, MD, MN, TN, OR NY, CA — 1/2003
- CT, GA, MD, MN, TN, OR NY, CA, CO, NM — 1/2004
- CT, GA, MD, MN, TN, OR NY, CA, CO, NM, PA — 1/2008
- CT, GA, MD, MN, TN, OR NY, CA, CO, NM, PA, WA, LA, MO — 0/2012

Sampling scheme

- Each site purchases 10 packages each of chicken breasts, pork chops, ground turkey, ground beef per month
- All 11 sites culture for *Salmonella* and *Campylobacter*
- In addition, 3-4 sites (GA, OR, TN, ±MD) culture for *E. coli* and *Enterococcus*
- In 2005, changed from convenience to randomized sampling



Retail Food Testing Sites

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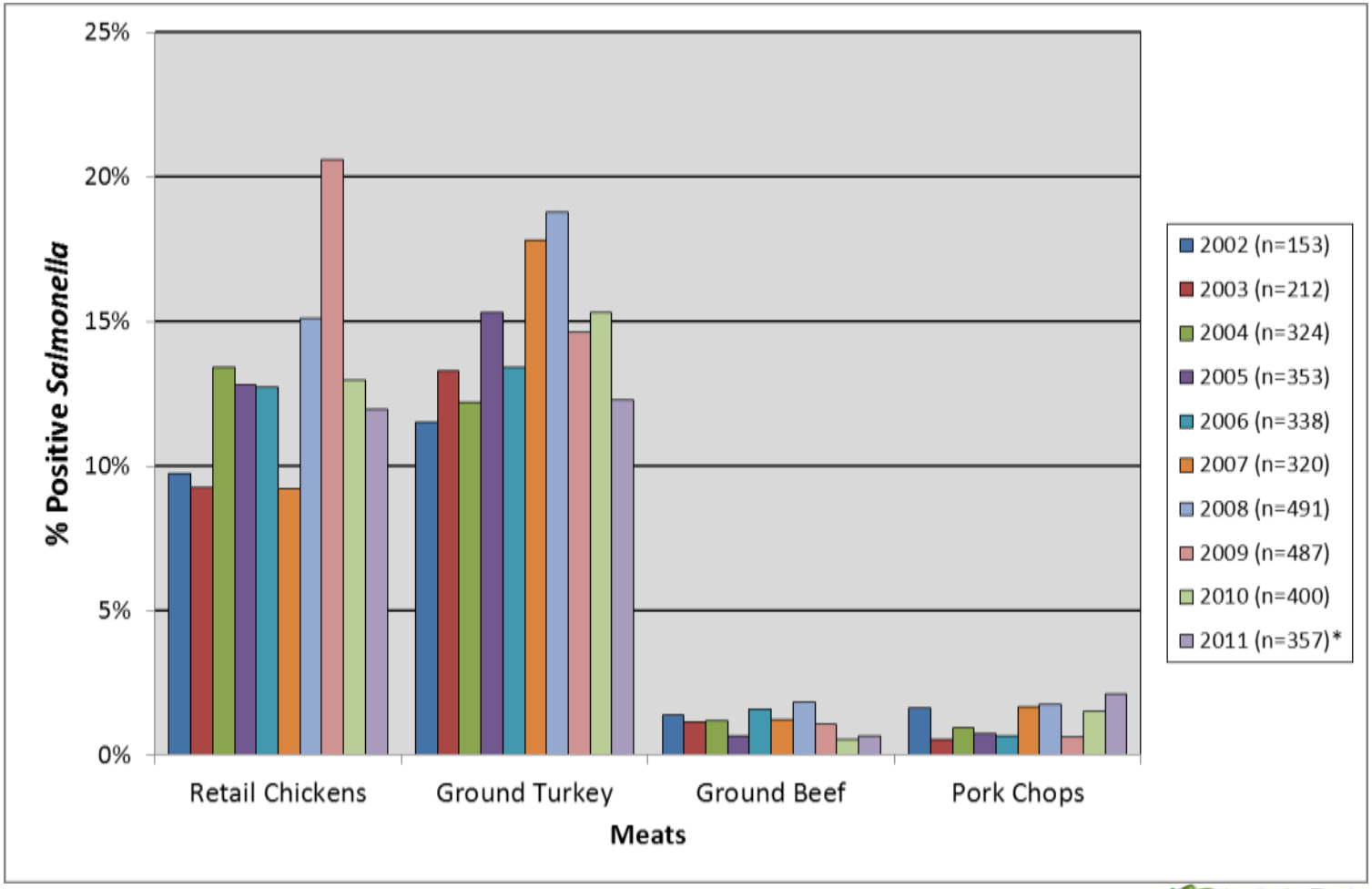
Number of Meat Samples Tested

Meat Type	Year										
	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011*	2013
Retail Chickens	616	897	1172	1194	1196	1072	1310	1320	1320	1320	
Ground Turkey	642	857	1165	1195	1185	1066	1309	1320	1320	1320	
Ground Beef	642	880	1186	1196	1196	1071	1310	1320	1320	1320	
Pork Chops	613	899	1176	1196	1192	1073	1307	1320	1320	1320	
Total	**2513**	**3533**	**4699**	**4781**	**4769**	**4282**	**5236**	**5280**	**5280**	**5280**	**6720**

**2011 data is preliminary*

N=45,653

Prevalence of *Salmonella*

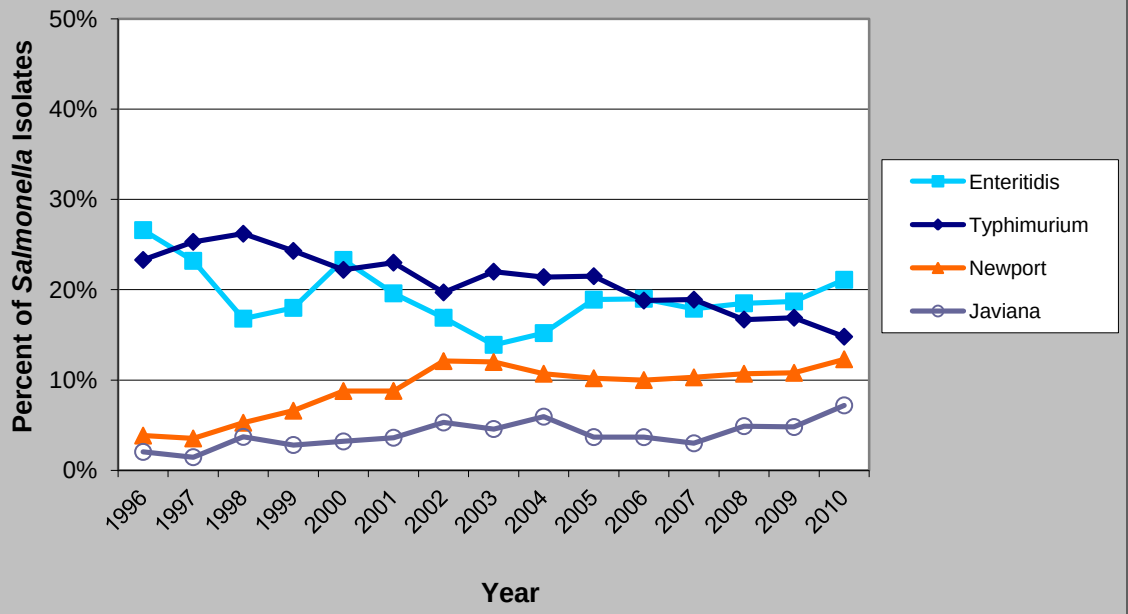


*2011 data is preliminary

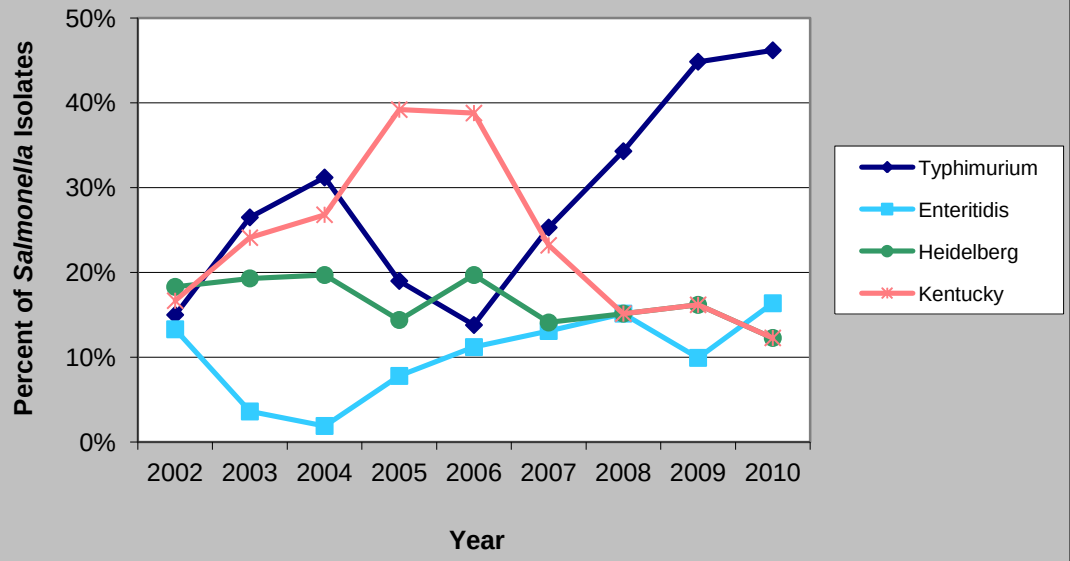
Salmonella Serotype Distributions

Humans	Chicken Breast	Ground Turkey	Cattle	Swine
Enteritidis	Typhimurium	Saintpaul	Montevideo	Typhimurium
Typhimurium	Enteritidis	Heidelberg	Typhimurium	Saintpaul
Newport	Heidelberg	Typhimurium	Infantis	Infantis
Javiana	Infantis	Infantis	Saintpaul	Heidelberg
I 4,[5],12:i:-	I 4,[5],12:i:-	Newport	Heidelberg	I 4,[5],12:i:-
Heidelberg	Branderup	Montevideo	Javiana	
Montevideo			Enteritidis	
Saintpaul				
Braenderup				
Infantis				

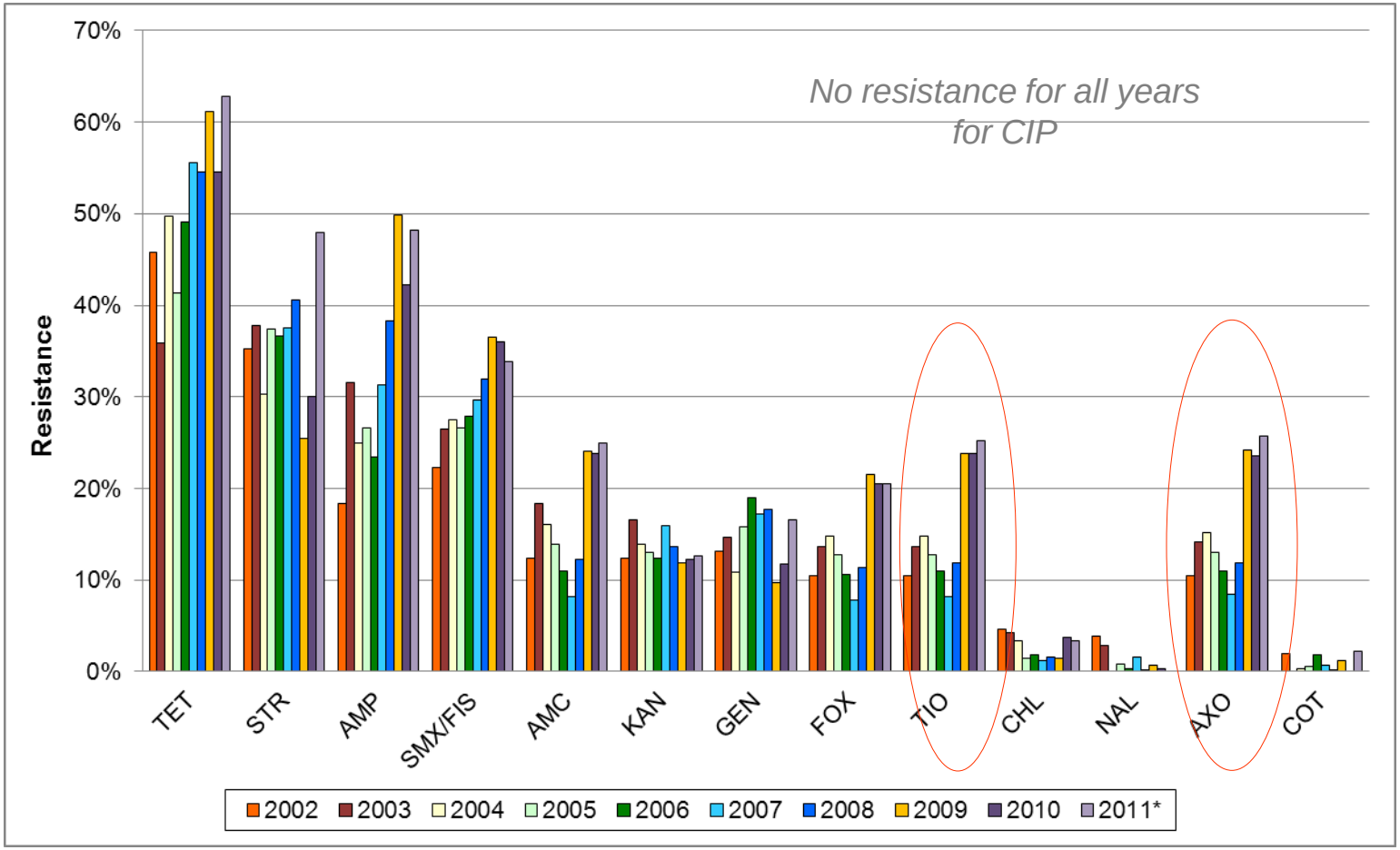
Humans



Chicken Breasts



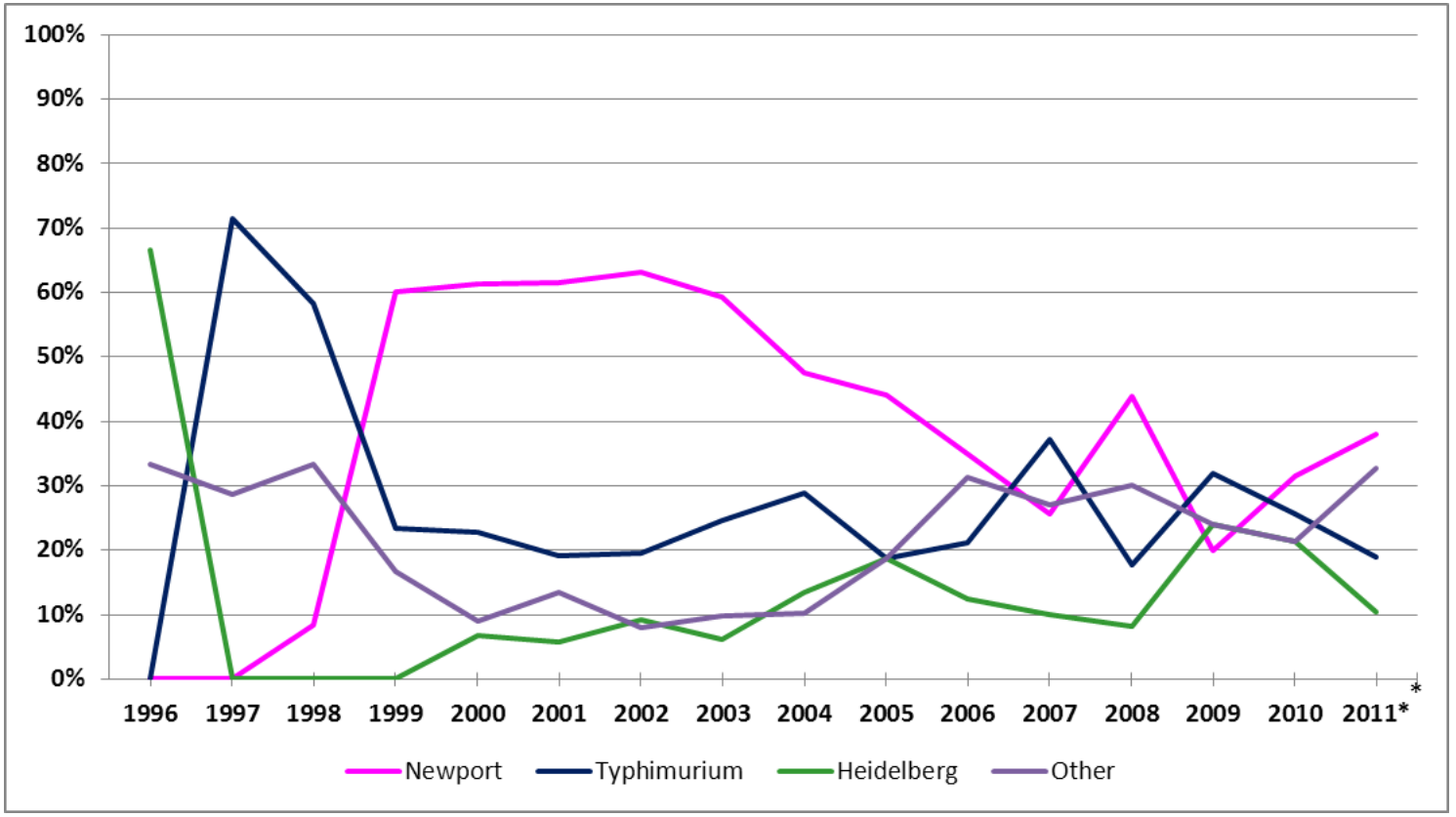
Antimicrobial Resistance Phenotypes



-In 2011 AMI was removed from the NARMS panel and AZI was added.

**2011 data is preliminary*

Ceftriaxone Resistance by Serotype



*2011 is preliminary

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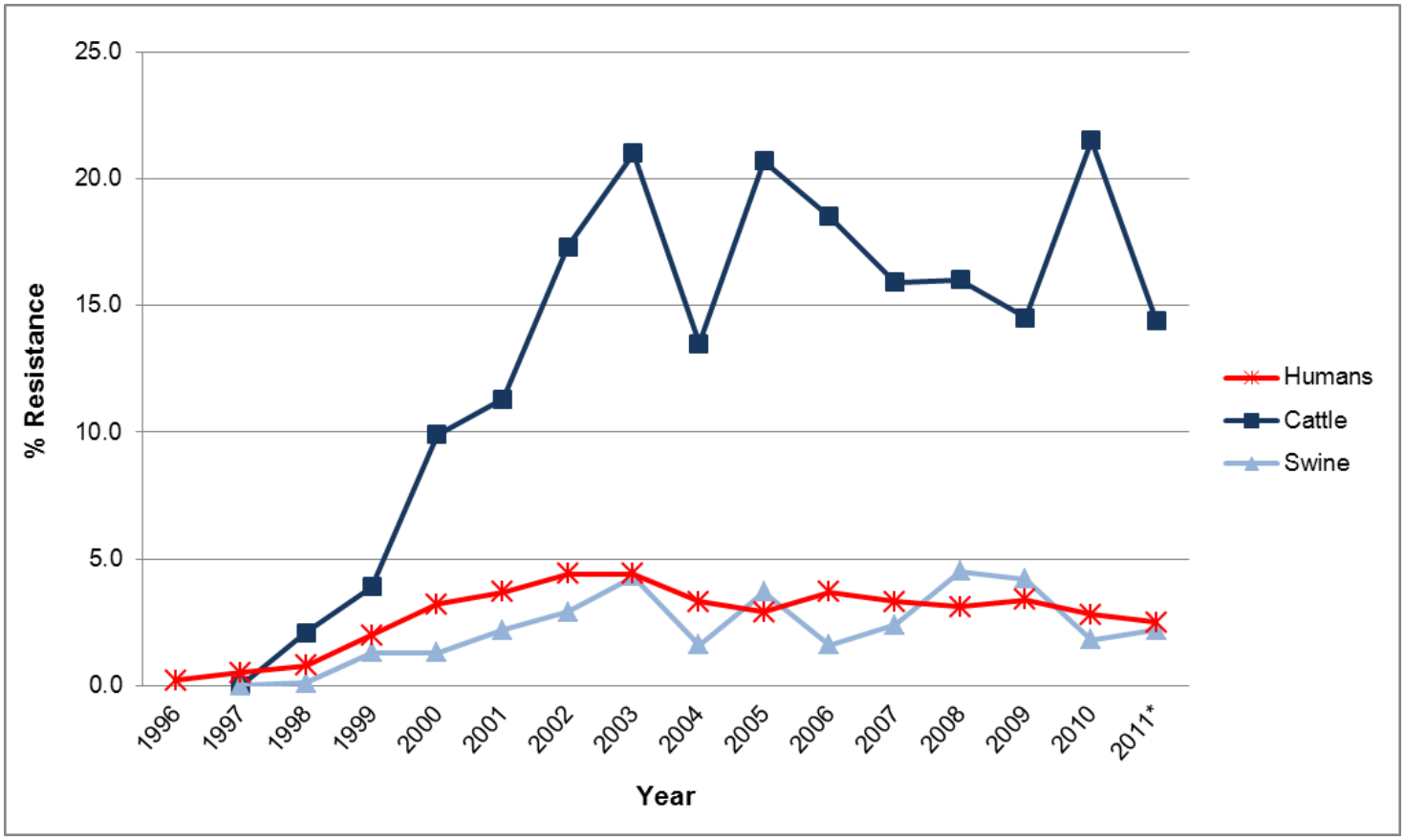
Salmonella Resistance to Ceftriaxone: 1996-2011*



*2011 data is preliminary

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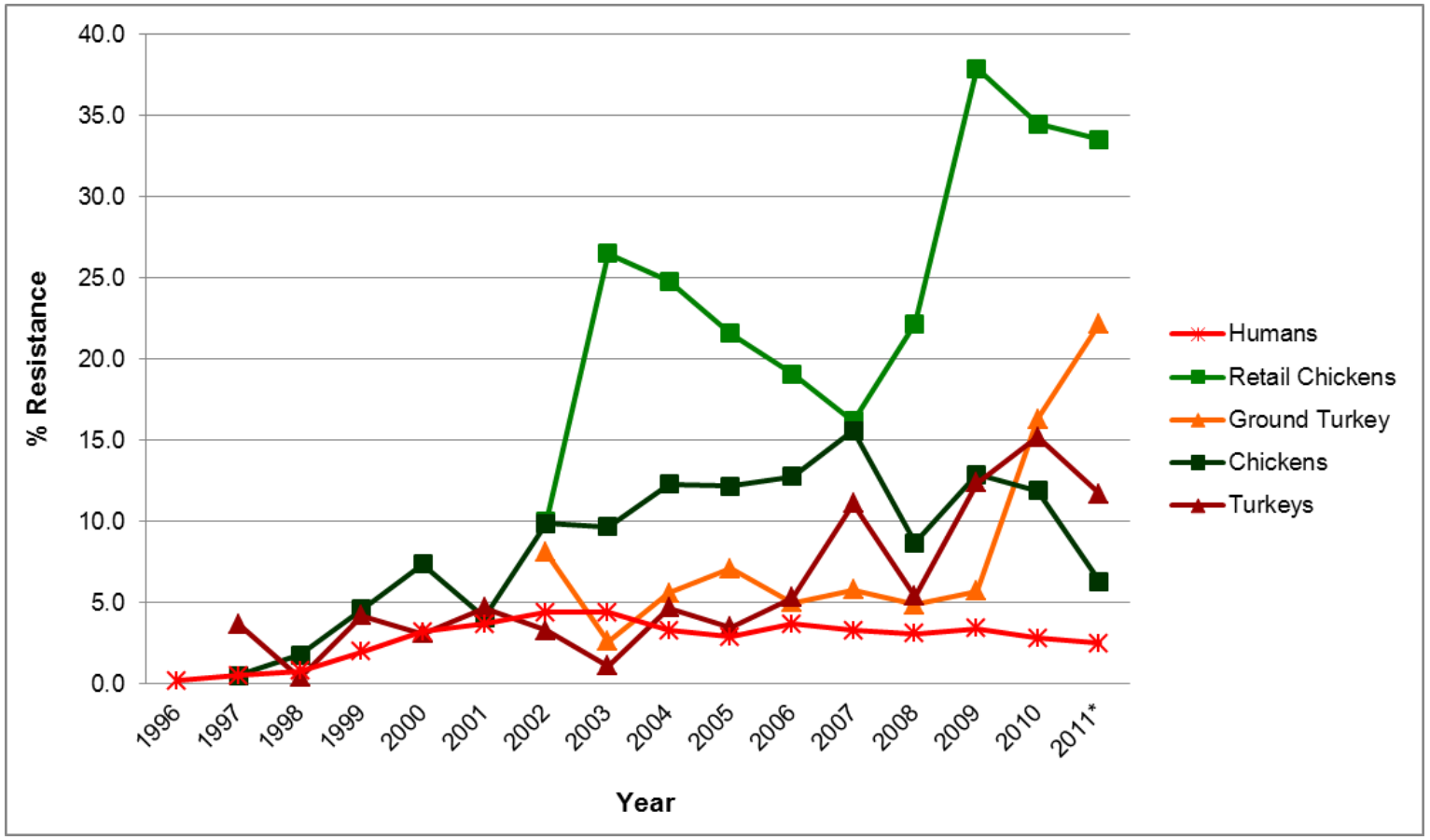
Salmonella Resistance to Ceftriaxone: 1996-2011*



*2011 data is preliminary

Ceftriaxone-Resistant *Salmonella* Serotypes - 2011*

Serotype	n	%
Typhimurium	22	37.9
Newport	11	19.0
Heidelberg	6	10.3
Dublin	4	6.9
I 4,[5],12:i:-	3	5.2
Agona	2	3.5
Senftenberg	2	3.5
Other	8	13.8
Total	58	100.0

- *In 2011, 58/2,344 (2.4%) NT Salmonella from humans were AxoR*

**2011 data is preliminary*

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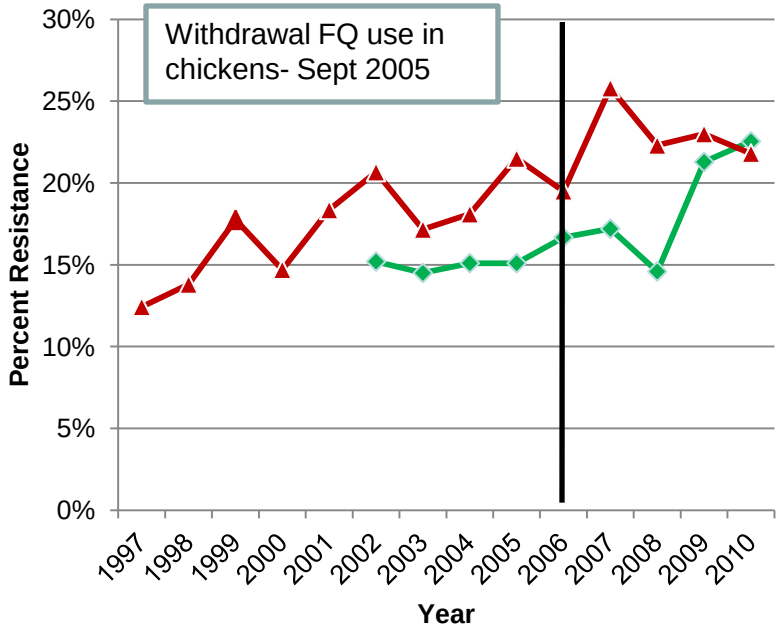
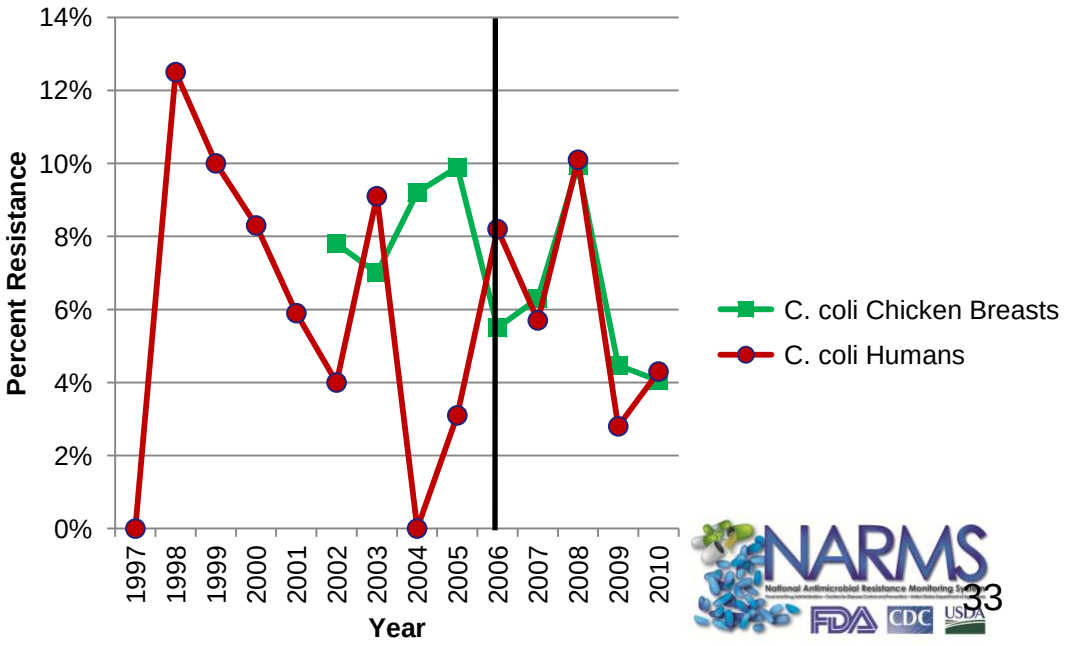
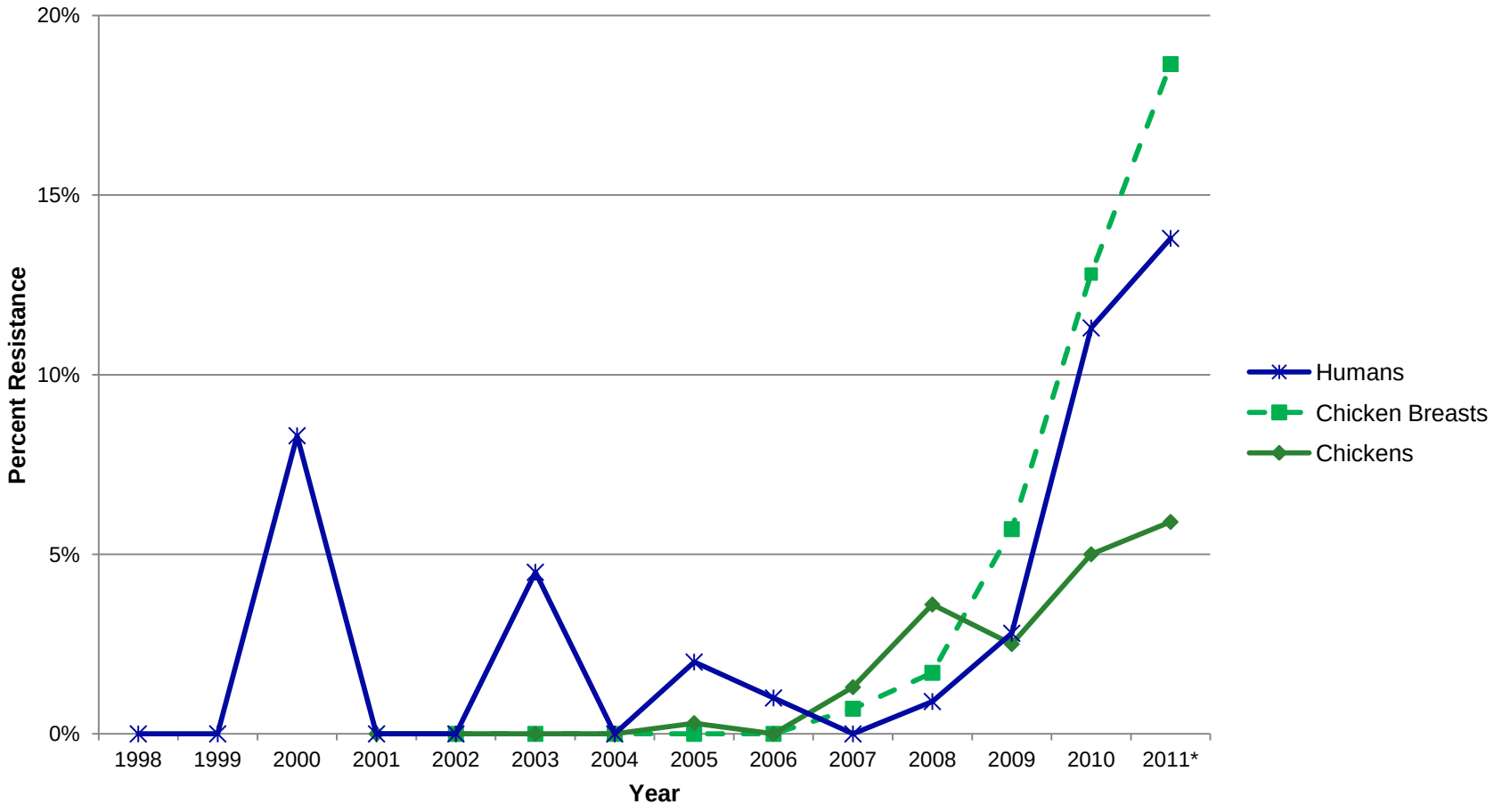
Fluoroquinolone Resistance in *Campylobacter*





Gentamicin Resistance among *Campylobacter coli* isolates



** Data are preliminary*

Antimicrobial Resistance among Non-typhoidal *Salmonella* Isolates from Humans, Retail Meats, and Food Animals, by Year, 1996-2009

NARMS

Select Antimicrobial

Antimicrobials

- Aminoglycosides
- β-Lactam/β-Lactamase Inhibitor Combination
- Cephems
- Folate Pathway Inhibitors
- Penicillins
- Phenicols
- Quinolones
- Tetracyclines

Auto-Scale Off

Select Source(s)

Sources

- Humans

Retail Meats

- Chicken Breast
- Ground Turkey
- Ground Beef
- Pork Chops

Food Animals

- Chickens
- Turkeys
- Cattle
- Swine

Number of Isolates Tested

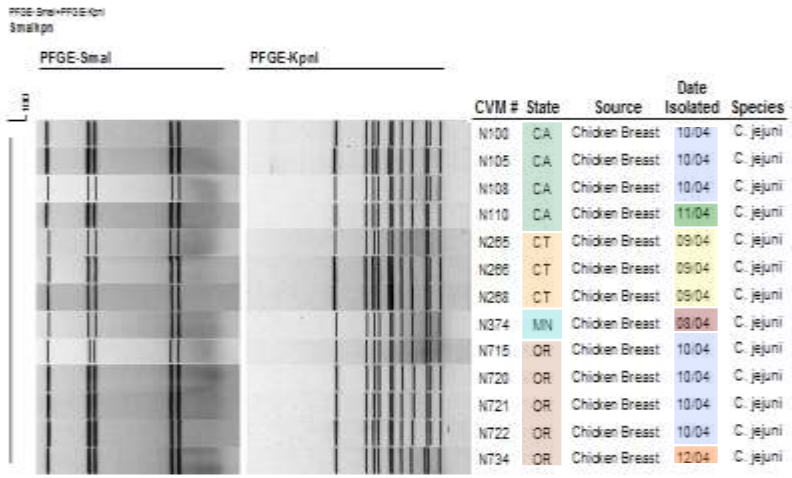
	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009
Humans	1318	1297	1455	1491	1372	1410	1998	1815	1782	2014	2171	2144	2380	2192
Chicken Breasts							60	81	157	151	152	98	199	277
Ground Turkey							74	114	142	181	253	190	245	190
Ground Beef							9	10	14	8	19	13	24	14
Pork Chops							30	5	11	9	8	18	23	8
Chickens		214	561	1438	1171	1107	1900	1158	1280	1983	1180	994	624	551
Turkeys		107	240	711	518	550	244	262	216	227	304	271	148	121
Cattle		24	284	1010	1188	893	1008	670	607	124	189	439	441	200
Swine		111	791	876	451	418	179	211	108	101	304	211	111	120

National Antimicrobial Resistance Monitoring System

FDA CDC USDA

NARMS/PulseNet

- *Salmonella* and *Campylobacter* isolates undergo further molecular characterization
  - PFGE analysis
    - Follow CDC guidelines for PFGE analysis
    - Data is shared with PulseNet
    - CVM PulseNet database has more than 12,000 data entries, including
      - 8,380 *Salmonella*
      - 3,439 *Campylobacter*
      - 547 *E. coli*
      - 69 *Vibrio*
    - Isolates can be used for future research projects
      - Attribution
      - Virulence studies
      - Antimicrobial resistance studies
      - Method development



Timeline of Events: Multistate Outbreak of *Salmonella* Heidelberg Infections Associated with Ground Turkey — United States, 2011

Outbreak Identification, Source Implication and Results of Product Testing

May 23
CDC PulseNet[1] identified multistate cluster of *Salmonella* Heidelberg infections (30 ill persons, 17 states) and began monitoring for additional illnesses. Investigators noted two ground turkey isolates matching the outbreak strain that were uploaded to PulseNet by MN on 4/11/2011 (Retail Sample 1) and NM on 5/11/2011 (Retail Sample 2) as part of NARMS[2] surveillance.

May 26
CDC began coordinating a multistate investigation. MN reported Retail Sample 1 was Brand A produced at establishment P-963.

June 16 – June 21
Exposure information from 19 ill persons revealed no single food that stood out as a likely source; 32% reported eating multiple brands and types of ground turkey.

June 21
CDC asked states to use a turkey-specific questionnaire to further characterize turkey exposures. NM reported Retail Sample 2 was Brand A produced at establishment P-963; another NARMS retail sample (Sample 3 uploaded to PulseNet by NM 6/8/2011) matching the outbreak strain was Brand B.

June 21 – July 7
Exposure information from turkey-specific questionnaires collected for 16 ill persons in 6 states: 33% reported consumption of multiple brands and types of ground turkey.

July 7
CDC asked states to use an expanded questionnaire to further examine other possible sources in addition to ground turkey.

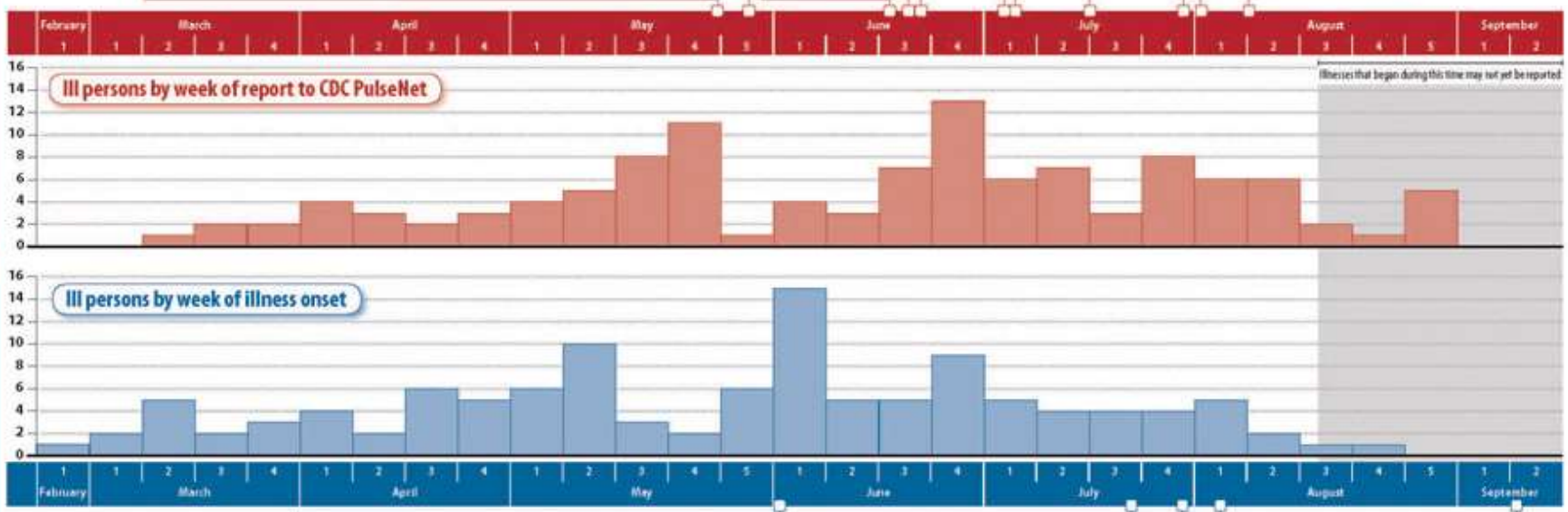
July 8 – August 2
23 ill persons interviewed with expanded questionnaire; 54% reported consumption of ground turkey.

July 15
OR reported first results from clinical laboratory indicating the outbreak strain was multidrug resistant.

July 29
Tests of leftover ground turkey from the home of an ill person in Ohio yielded *Salmonella* Heidelberg. Laboratory analysis identified two closely related DNA "fingerprint" patterns; one an exact match to the outbreak strain.

August 1
CDC posted initial web announcement about the investigation.

August 11
23 additional ill persons with *Salmonella* Heidelberg with a closely related DNA "fingerprint" pattern with illness since March included in total number of ill persons.



Traceback, Regulatory Actions and Recalls

June 1
CDC notified USDA-FSIS. Frequent discussions between both agencies continue throughout the investigation.

July 19
FSIS began first traceback investigation. Product was left over ground turkey from ill person's household; original packaging not available.

July 19 – August 2
FSIS continued traceback of ground turkey as shopper card details received; purchased from three ill persons linked to P963.

July 29
FSIS released a public health alert for frozen and fresh ground turkey products.

July 29
FSIS informed Cargill Meat Solutions Corporation about epidemiologic data, information from traceback of ground turkey products, and analysis of distribution records indicating establishment P-963 is a likely, but not definitive, source of this outbreak.

August 3
FSIS reported that the source of ground turkey for Brand B Retail Sample 3 was establishment P-963. 30 (54%) of 56 interviewed ill persons reported eating any ground turkey prepared at home in the week before illness.

August 3
Cargill Meat Solutions Corporation recalled approximately 36 million pounds of ground turkey products that may be contaminated with a multi-drug resistant strain of *Salmonella* Heidelberg.

September 11
Cargill Meat Solutions Corporation recalled approximately 185,000 pounds of ground turkey that may be contaminated with *Salmonella* Heidelberg based on sample results from an intensive in-plant investigation.

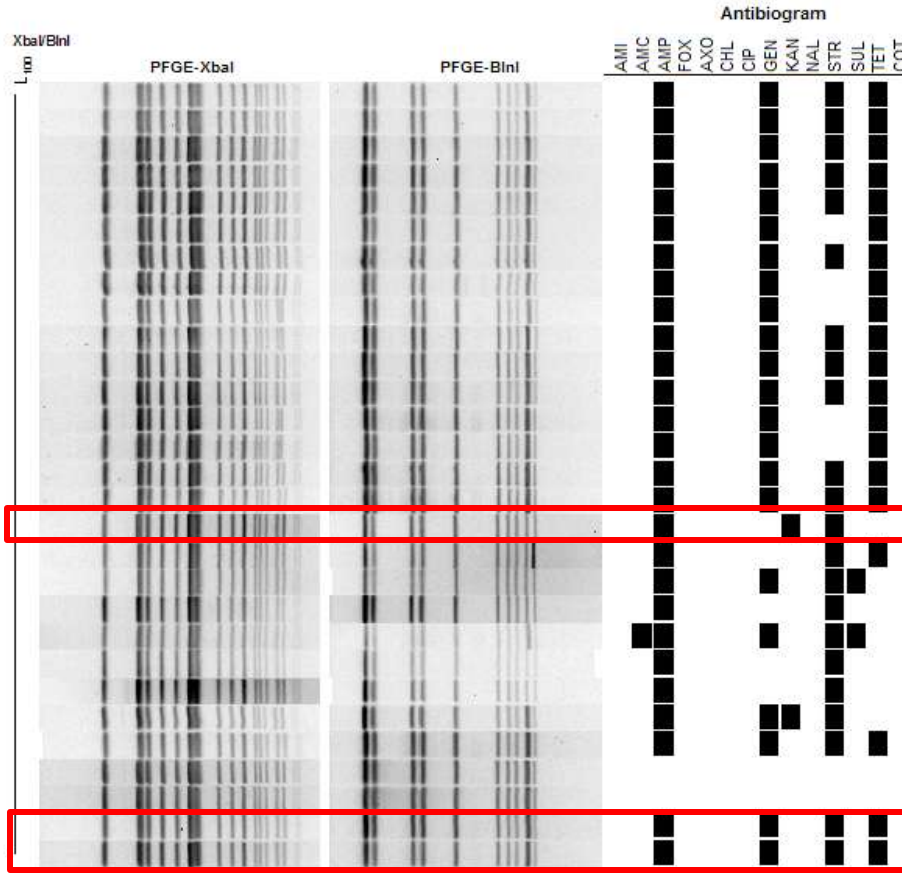
[1] PulseNet
[2] National Antimicrobial Resistance Monitoring System

As of September 11, 2011

For more information, visit CDC's *Salmonella* website: **http://www.cdc.gov/salmonella**

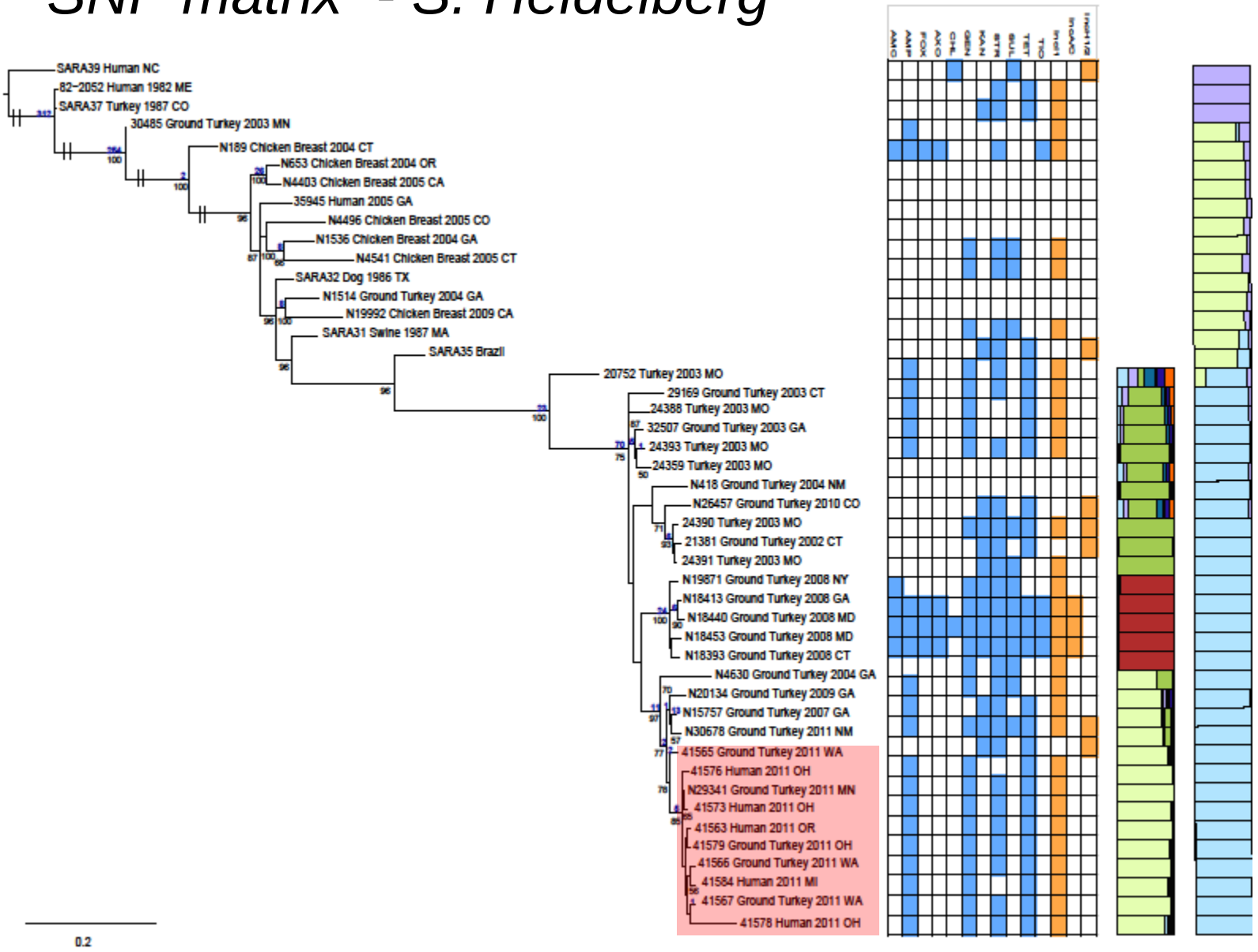
Multistate Outbreak of *S.* Heidelberg Infections

Associated with Ground Turkey - 2011



ID #	State	Source	Year	Serotype	PulseNet Pattern #
41563	OR	Clinical	2011	Heidelberg	JF6X01.0058
41564	MI	Clinical	2011	Heidelberg	JF6X01.0058
41567	OH	Ground Turkey	2011	Heidelberg	JF6X01.0058
41569	OH	Clinical	2011	Heidelberg	JF6X01.0058
41570	OH	Clinical	2011	Heidelberg	JF6X01.0058
41571	OH	Clinical	2011	Heidelberg	JF6X01.0058
41572	OH	Clinical	2011	Heidelberg	JF6X01.0058
41573	OH	Clinical	2011	Heidelberg	JF6X01.0058
41574	OH	Clinical	2011	Heidelberg	JF6X01.0058
41575	OH	Clinical	2011	Heidelberg	JF6X01.0058
41576	OH	Clinical	2011	Heidelberg	JF6X01.0058
41577	OH	Clinical	2011	Heidelberg	JF6X01.0058
41581	OH	Clinical	2011	Heidelberg	JF6X01.0058
41582	OH	Clinical	2011	Heidelberg	JF6X01.0058
41583	MI	Clinical	2011	Heidelberg	JF6X01.0058
41584	MI	Clinical	2011	Heidelberg	JF6X01.0058
N14653	MN	Ground Turkey	2007	Heidelberg	JF6X01.0058
N15787	NM	Ground Turkey	2007	Heidelberg	JF6X01.0058
N15835	CT	Ground Turkey	2007	Heidelberg	JF6X01.0057
N18399	GA	Ground Turkey	2008	Heidelberg	JF6X01.0058
N18415	GA	Ground Turkey	2008	Heidelberg	JF6X01.0058
N19753	CO	Ground Turkey	2008	Heidelberg	JF6X01.0058
N23760	MD	Ground Turkey	2010	Heidelberg	JF6X01.0058
N27399	NM	Ground Turkey	2010	Heidelberg	JF6X01.0058
N29341	MN	Ground Turkey	2011	Heidelberg	JF6X01.0058
N29368	NM	Ground Turkey	2011	Heidelberg	JF6X01.0058
N30644	GA	Ground Turkey	2011	Heidelberg	JF6X01.0058
N30667	NM	Ground Turkey	2011	Heidelberg	JF6X01.0058
N30684	NM	Ground Turkey	2011	Heidelberg	JF6X01.0058

SNP matrix - S. Heidelberg



NARMS Research to Support FDA's Mission

1. Determine the genetic diversity within bacterial populations to understand the movement of bacteria through the food chain

   Collaborations with CFSAN-MRC and CFSAN-College Park

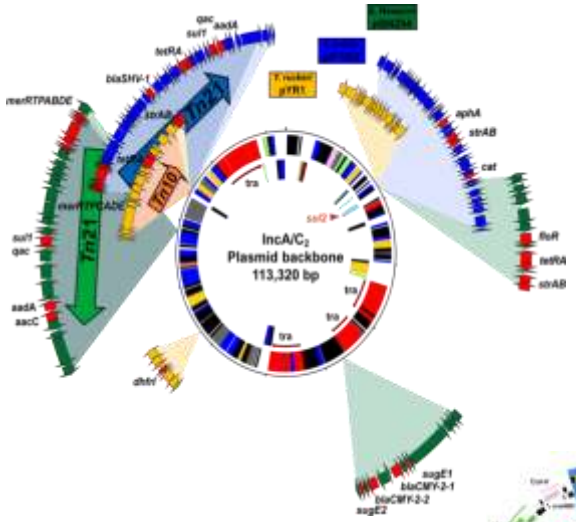
   US-EU consortium on NGS

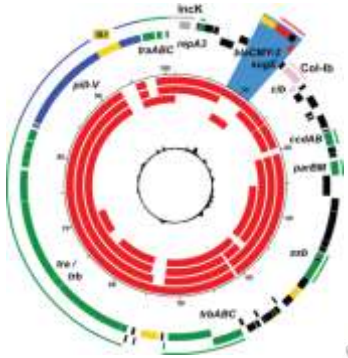
2. Characterize genetic mechanisms of resistance

   Collaborations with many partners at universities (Univ. MD) and government (CFSAN, CDC, USDA)

3. Examine the role of animal feeds in the ecology of resistance

   ORA - feeds and imports surveillance





NARMS
National Antimicrobial Resistance Monitoring System
FDA CDC USDA

Summary

- Comprehensive susceptibility data can be used for regulatory decision making, including pre-approval of new animal antibiotics
- Most extensive national program for integrated laboratory based surveillance of bacteria in foods
  - Only national program that provides routine isolates for analysis
  - Strong stakeholder support
- Leverages existing public health infrastructure
  - Partnership with FoodNet, PulseNet, USDA-FSIS & USDA-ARS
- Making improvements to overcome limitations based on original NARMS design
- Infrastructure in place for hypothesis-driven food hazard analyses
- Provides food safety officials with ongoing baseline data on the prevalence of specific pathogens in food supply
  - Provides bacterium/commodity data needed for attribution

NARMS National Antimicrobial Resistance Monitoring System
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Challenges & Future Needs

- Overcoming the inherent limitations because NARMS was built on existing infrastructure
  - Animal sampling –
    - Sampling at slaughter (FSIS): sustainable, representative, random, cost effective
    - Sampling on-farm with antibiotic use information in some cases (ARS): value added.
  - Adding 3 retail meat testing sites (WA, LA, MO)
- Examining other pathogens and commodities as needed without compromising core monitoring functions.
  - Seafood, feeds - MRSA, ESBLs
- Transitioning to WGS hardware and bioinformatics
- Need for detailed drug use information in food animals
- Continued database development
- Incorporating ORA data into NARMS
- Anticipating feed safety/security events with appropriate method development
- Environmental routes of dissemination

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http://www.fda.gov/AnimalVeterinary/SafetyHealth/AntimicrobialResistance/NationalAntimicrobialResistanceMonitoringSystem/default.htm

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