



United States Department of Agriculture

One Team, One Purpose



Food Safety and Inspection Service

Protecting Public Health and Preventing Foodborne Illness



FSIS OPHS Update for NCC

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Food Safety and Inspection Service

FSIS OPHS Update: Presentation Outline

- ❑ Laboratory Accreditation/Industry Data
- ❑ About nBPW
- ❑ Cecal/NARMS Sampling
 - ❑ Focus on MDR and Serotypes and MDR I 4,[5],12:i:-, Outbreak
- ❑ WGS Activities
 - ❑ Distribution of an ESBL gene ctx-M-65 in Salmonella Infantis
 - ❑ WGS Discriminatory Power Compared to PFGE
 - ❑ Matches using NCBI Pathogen Detection Pipeline

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FSIS OPHS Update: About Laboratory Accreditation

ISO Standards Definition

- ❑ Standards are documented agreements containing technical specifications or other precise criteria to be used consistently as rules, guidelines, or definitions of characteristics, to ensure that materials, products, processes and services are fit for their purpose.

- ❑ **About FSIS Laboratory Accreditation (Not Certification):** When we speak of FSIS accreditation we mean specifically - ISO 17025, ALACC (AOAC), and our own quality system requirements.

Certification vs. Accreditation

- ❑ Certification
 - ❑ a written quality system
 - ❑ no demonstration of competence
- ❑ Accreditation
 - ❑ a written quality system
 - ❑ qualified, trained staff
 - ❑ adequate facilities

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FSIS OPHS Update: About Laboratory Accreditation and Goals

☐ Why seek Accreditation?

- ☐ Documents what you do and creates complete records
- ☐ Makes you design a Quality System
- ☐ Enhances uniformity
- ☐ Enhances training and proficiency
- ☐ Assigns responsibilities and accountability
- ☐ Credibility
- ☐ International recognition

☐ Goals of Laboratory Accreditation are summarized in the “Mission Statement” found in our quality manual

- ☐ **Quality statement:** The laboratories support the mission of the United States Department of Agriculture, Food Safety and Inspection Service, by performing analyses of meat, poultry, and egg products. The laboratory personnel are committed to performing quality activities to assure integrity, accuracy, reliability, and timeliness of the data.

- ☐ **American Association for Laboratory Accreditation audits FSIS labs**

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FSIS Update: Neutralizing Buffered Peptone Water (nBPW) Poultry Carcass Rinse – Background and Study Design

Background

- ❑ Academic/industry researchers shared data regarding the potential of anti-microbial intervention carry-over to impact FSIS poultry carcass *Salmonella* monitoring results (June 2013)
 - ❑ Concern that intervention carry-over could reduce survival of pathogens in Buffered Peptone Water (BPW) carcass rinsates that are subsequently analyzed by FSIS labs.
- ❑ ARS-FSIS initiate collaboration to investigate/validate the potential for intervention carry-over to impact FSIS poultry carcass poultry monitoring results (July 2013)

Study Design

- ❑ Phase I
 - ❑ Determine the potential volume of intervention chemical solution carry-over to carcass rinsates
- ❑ Phase II
 - ❑ Determine if antimicrobial intervention carry-over has the potential to impact *Salmonella* monitoring
- ❑ Phase III
 - ❑ Identify neutralizing agent(s) → improved carcass rinsate to negate the potential impact of carry-over on *Salmonella* recovery.

FSIS Update: Neutralizing Buffered Peptone Water (nBPW) Poultry Carcass Rinse – Research Outcome and FSIS Adoption

Research Outcome

☐ Laboratory Performance of Neutralizing Buffered Peptone Water (nBPW)

- ☐ nBPW recovery of Salmonella was superior to BPW for all interventions evaluated.
- ☐ nBPW recovery of Salmonella was not significantly different than control (no intervention) for all interventions evaluated.

FSIS Adoption of nBPW

- ☐ In July 2016, FSIS implemented the use of neutralizing buffered peptone water (nBPW) as a sampling and transport medium for carcass rinsate and carcass sponge samples.
- ☐ Monitoring Salmonella prevalence on poultry carcasses continues.

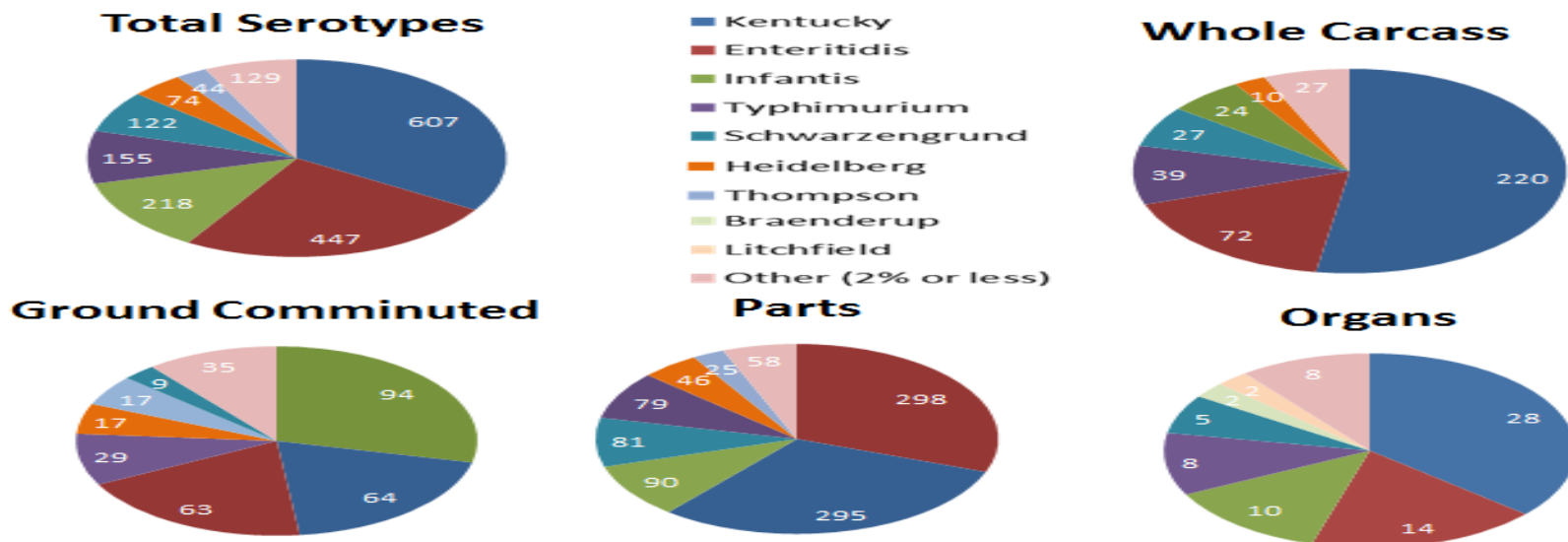
A Twelve Month Evaluation of nBPW

- ❑ The volume-weighted average used to calculate the carcass performance standard in 2011 was **4.58%**
- ❑ The volume-weighted average from the first 12 months of nBPW was **4.74%**
- ❑ Using the new nBPW data in the Performance Standard Model with the same predicted reduction in illnesses, the standard would result in the same 5 positives allowed out of the set of 51
- ❑ Note:
 - ❑ The aggregate data indicates that the prevalence of Salmonella on carcasses pre and post nBPW is significantly different, but not significantly different in chicken parts

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FSIS Update - NARMS: *Salmonella* in Chicken and Serotype Distribution

	2014			2015			2016 ¹		
	Samples	Isolates	% Positive	Samples	Isolates	% Positive	Samples	Isolates	% Positive
HACCP	10,446	936	9.0%	11,453	1,491	13.0%	16,973	1,857	10.9%
Cecal	575	103	17.9%	553	130	23.5%	568	133	23.4%

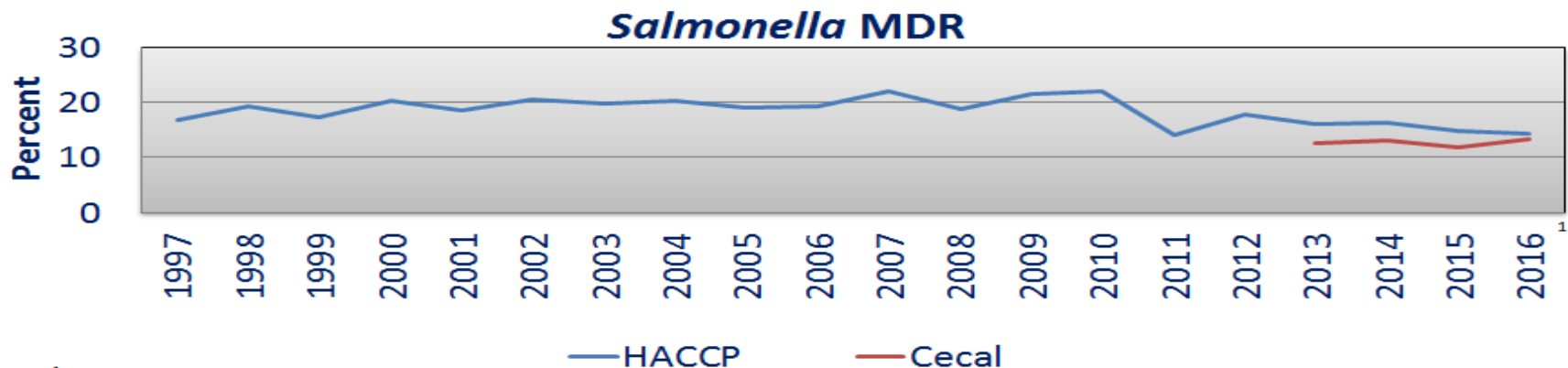


¹Preliminary 2016 Data

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FSIS Update - NARMS: MDR *Salmonella* and Serotypes – HACCP and Cecal, All Sources

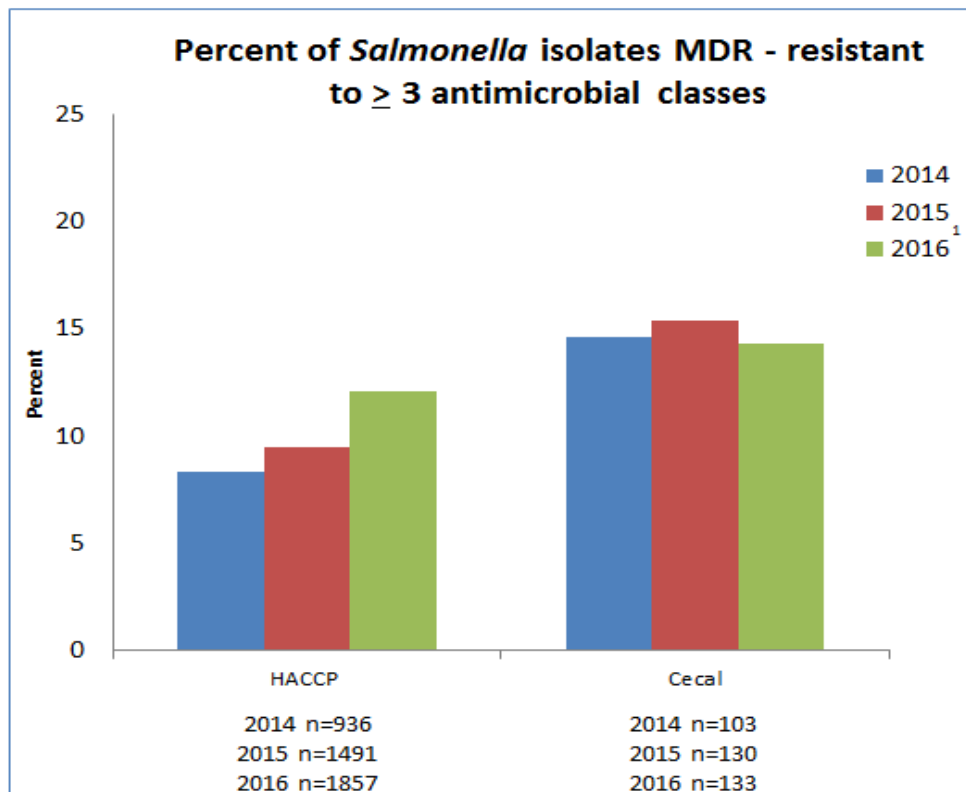
	HACCP (1997-2016)	Cecal (2013-2016)
Total No. of Isolates Tested	41,145	4,319
Total No. of MDR	7643	548
Total Percent MDR	18.6%	12.7%



¹ Preliminary 2015 & 2016 data

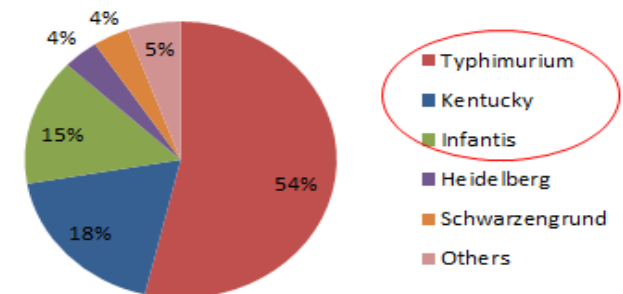
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FSIS Update - NARMS: MDR *Salmonella* and Serotypes – HACCP and Cecal Chicken Sources

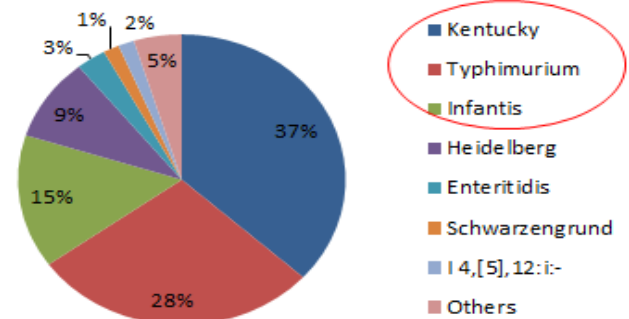


¹Preliminary 2016 Data

Cecal Chicken – MDR Serotypes



HACCP Chicken – MDR Serotypes



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FSIS Update - NARMS: MDR *Salmonella* involved in an Outbreak

2016-2017 West Coast *Salmonella* I 4,[5],12:i:- Investigation Associated with Rotisserie Chicken

- ❑ 63 case-patients from 13 states (West Coast focus)
 - ❑ Illness onset: 7/5/16 – 1/24/17
 - ❑ 27% hospitalized
 - ❑ 88% case-patients report consuming chicken, including 60% case-patients who reported consuming rotisserie chicken products from 11 chain B locations
- ❑ **WGS ResFinder indicates ASSuT (ampicillin, streptomycin, sulfamethoxazole and tetracycline resistance)**

FSIS Actions

- ❑ On 10/9/16, FSIS issued a public health alert for rotisserie chicken salad produced from 8/26/16 to 9/2/16 from a WA retail chain B location
- ❑ In December 2016, FSIS personnel visited 4 chain B stores for observation of practices
 - ❑ Noted opportunities for undercooking and cross-contamination
- ❑ Findings shared with chain B corporate personnel
- ❑ Chain B retrained employees on temperature measurement and log keeping
- ❑ Adjust holding temperatures in coolers to minimize ice on chicken so starting temperatures for cooking are more consistent
- ❑ Worked with suppliers to standardize chicken size
- ❑ Explore use of wireless thermometer system
- ❑ **FSIS plans to submit best practices to CFP as guideline to avoid undercooking and cross-contamination during preparation of rotisserie chicken**

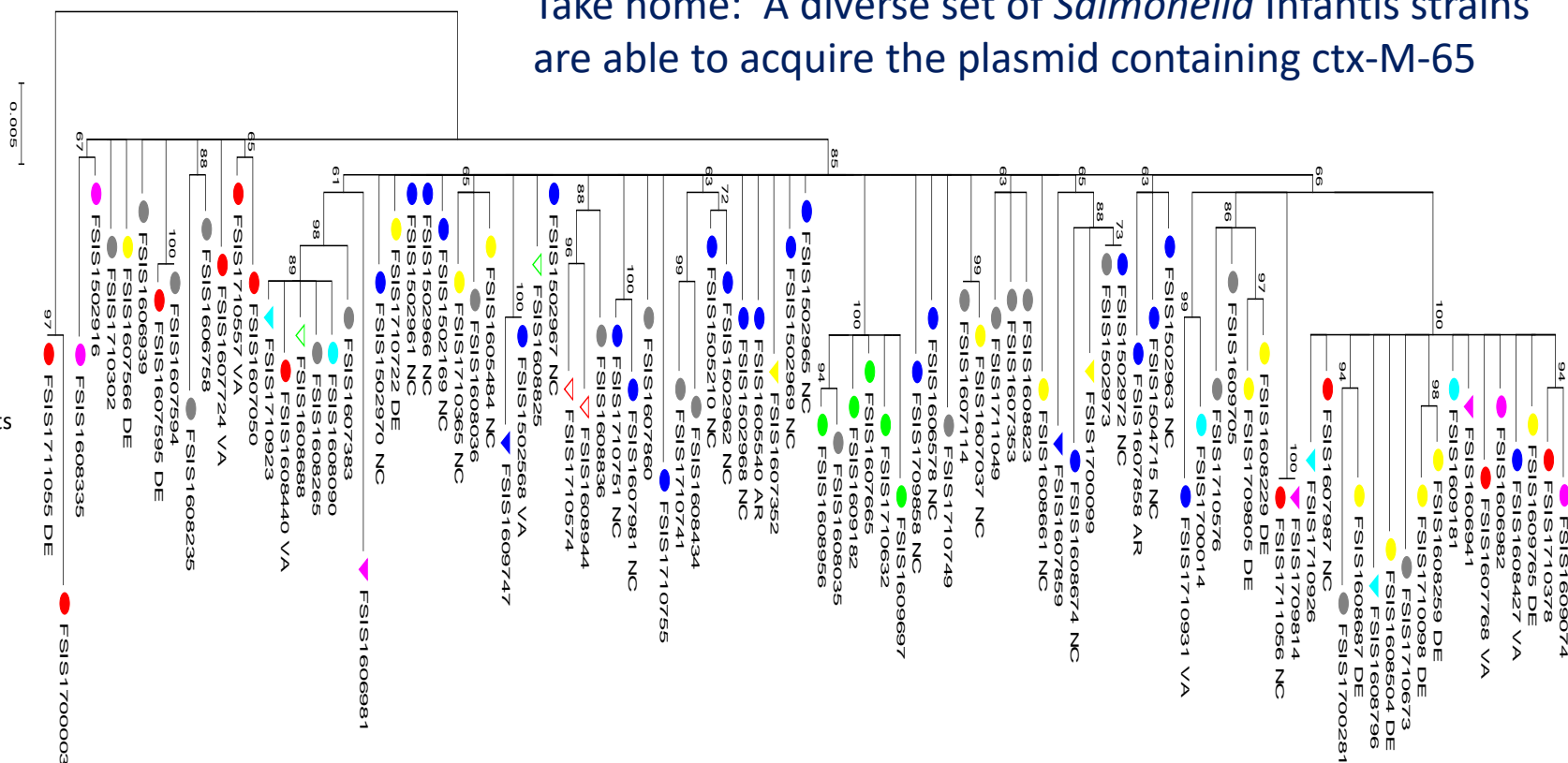
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FSIS Update: NARMS – Summary and Future Direction

- ❑ Cecal sampling has further strengthened NARMS surveillance by adding another sampling point and additional ~ 5000 samples
- ❑ Launched a FSIS NARMS Webpage to share FSIS AMR information in a timely manner
- ❑ Successfully sequenced and uploaded into NCBI all the NARMS *Salmonella* and *Campylobacter* isolates in near-real-time
- ❑ Initiated a process to inform the FSIS regulated entities about unusual AMR findings (Ex. ctx-M-65, Locus of Heat Resistance –LHR etc.)
- ❑ Continue to work with NARMS partners to -
 - ❑ Develop a new strategic plan based on the recommendations from Science board
 - ❑ Host a NARMS Public Meeting (Oct 24th and 25th)
 - ❑ Reminder: FSIS will also host a WGS Public Meeting (Oct 26th and 27th)
 - ❑ Understand the potential for the application of resistome and mobilome approaches in FSIS environment
 - ❑ Adopt the new Tableau system for data handling, processing and visualization of FSIS NARMS data

Food Safety and Inspection Service: FSIS Update – WGS: Analyses of MDR *Salmonella* Infantis with ctx-M-65 Gene

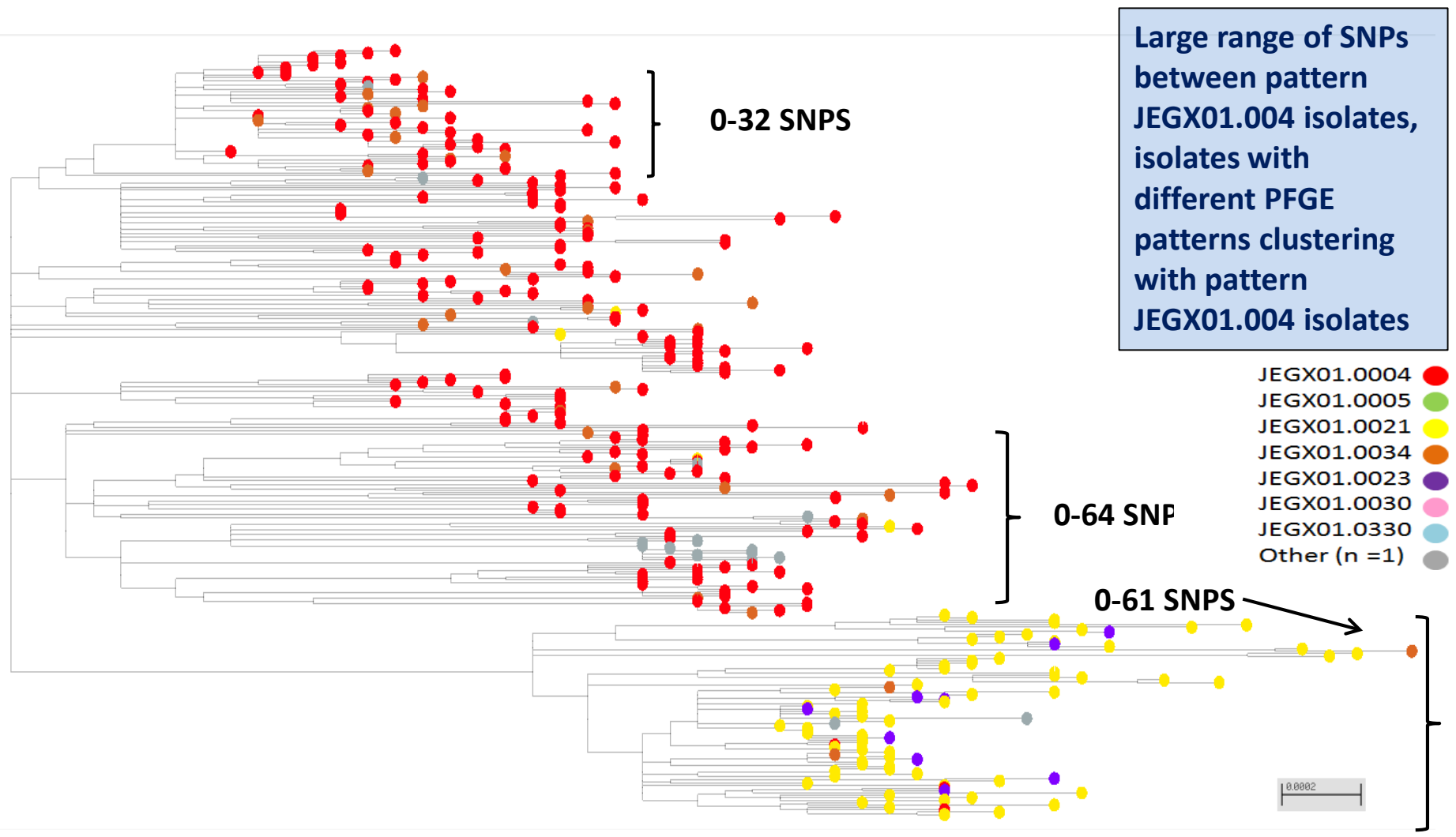
Take home: A diverse set of *Salmonella* Infantis strains are able to acquire the plasmid containing ctx-M-65



- ❑ WGS data from 97 *Salmonella* Infantis isolates carrying ctx-M-65 were analyzed
- ❑ 0-63 SNP across all isolates
- ❑ ctx-M-65 identified in diverse group of Infantis strains
- ❑ This gene confers extended spectrum beta-lactamase resistance

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FSIS Update – WGS: *Salmonella* Enteritidis from Chicken commodities for FY17- Discriminatory Power of WGS vs. PFGE

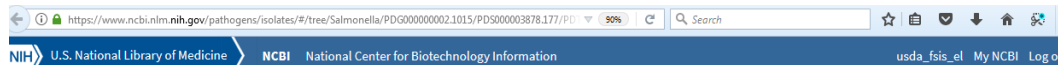


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FSIS Update - WGS: FY17 Salmonella Isolates from Chicken Commodities and NCBI Pathogen Detection Pipeline

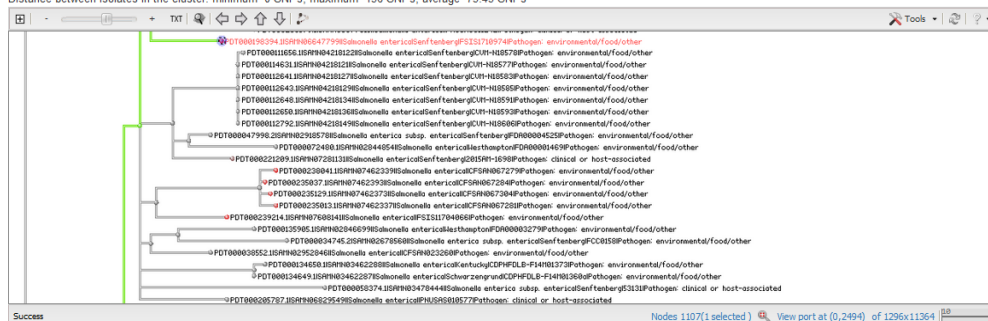
Product	Serotype	Total #	% in SNP cluster (#)	% w/in 20 SNPs of clinical	% w/in 10 SNPs of clinical
Total Serotypes	Enteritidis	447	99.8% (446)	98.9% (442)	90.6% (405)
	Kentucky	607	99.8% (606)	0% (0)	0% (0)
	Heidelberg	74	98.6% (73)	98.6% (73)	86.4% (64)
	Schwarzengrund	122	100% (122)	47.5% (58)	7.3% (9)
	Infantis	218	94.5% (206)	92.2% (201)	50.9% (111)
	Typhimurium	155	96.8% (150)	30.3% (47)	10.3% (16)

- Using NCBI's pathogen detection pipeline food commodity isolates can be placed in a clinical context: So what does this really mean and how can this information be useful?



Health > Pathogen Detection > Isolates Browser > SNP Tree for PD0000003878.177

Distance between isolates in the cluster: minimum=0 SNPs, maximum=156 SNPs, average=73.45 SNPs



#	Organism Group	Strain	Serovar	Isolate	Create I	Location	Isolation	Host	SNP cluster	Min+	Min-	BioSampl	Assembly	K-mer group	AST phenotypes	AMR genotypes
1	Salmonella enterica	FSIS171	Sentinel	PD000018394	2017-03	USA, FL	communitie	environment	PD0000003878	26	31	SAMN0864		PD000000002		

- Of the 1734 Salmonella isolates analyzed, 773 isolates (44.58%) were pan-susceptible and had no resistance genes
- The most common combination of genes detected (strA, strB, tet(B)) was found in 290 isolates (16.72%)

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FSIS WGS Update: Summary and Future Directions

- ❑ **FSIS' new strategic plan is focused on the use of new technology to preventing foodborne illnesses and protect public health protection**
 - ❑ Based on Healthy People 2020 (soon 2030) our pathogen reduction goals and our challenges are well defined
- ❑ **With the acquisition of 12 Sequencers, FSIS has build sufficient capacity for conducting WGS on all FSIS isolates and in FY 2017 FSIS will have sequenced around 7282 isolates with the future targets of ~ 10,000 isolates/year**
- ❑ **In FY 2017 FSIS initiated WGS data analysis beyond its use in outbreak investigations and in FY 2018 FSIS will focus on further understanding the occurrence, trend and patterns of genotypes of public health concern in FSIS regulated products**
- ❑ **FSIS continues to engage with National and International partners to stay at the cutting-edge of utilizing WGS technology**
 - ❑ Work with National Antimicrobial Resistance Monitoring System (NARMS) partners (FDA, CDC) to understand the occurrence or introduction of antimicrobial resistance genes in pathogens and indicators
 - ❑ The WGS interagency collaboration Gen-FS will have an operational charter in early FY 2018
- ❑ **In October 2017 with its Gen-FS and NARMS partners, FSIS will conduct two Public Meetings to seek stakeholder input**
 - ❑ **WGS Public Meeting led by FSIS will be held on Oct 26th and 27th**
 - ❑ The focus of the WGS meeting is to understand the scope, applicability and perception, associated with the application of WGS in a regulatory setting
 - ❑ **Reminder: NARMS Public Meeting led by the FDA will be held on Oct 24th and 25th**
- ❑ **Note: In our investigative decision making we utilize WGS findings/interpretations - as a part of the totality of available evidence**

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FSIS Update: NARMS – Summary and Future Direction

Discussion

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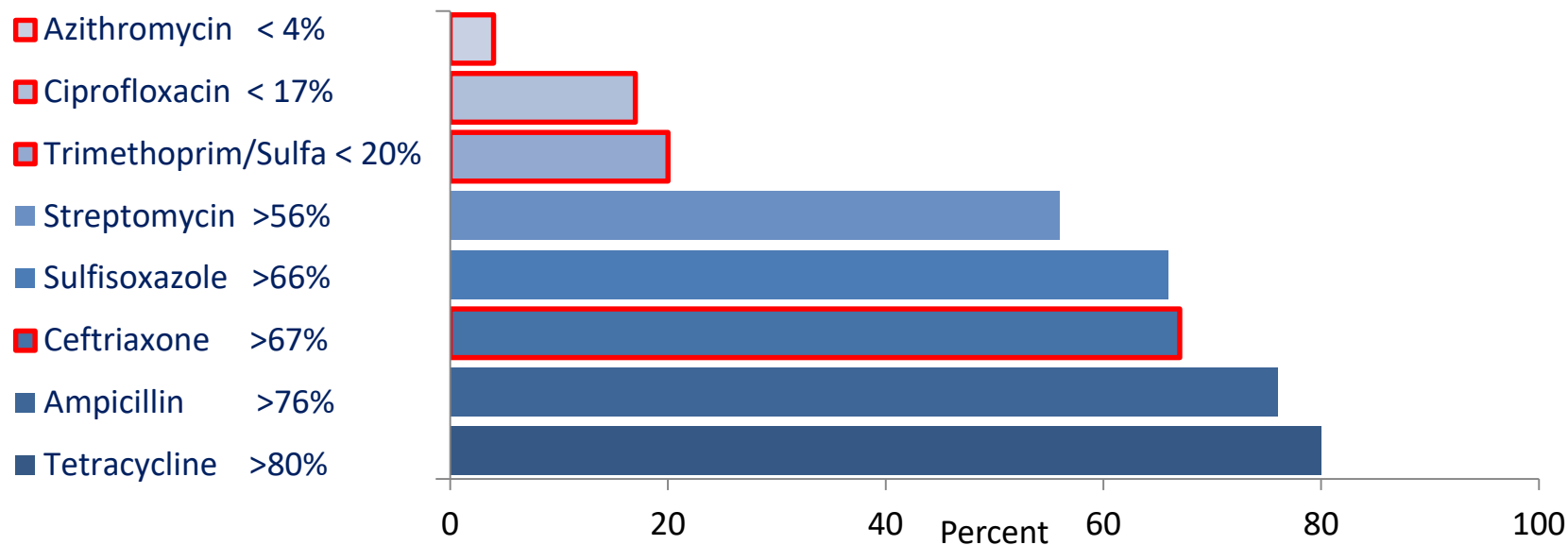
FSIS Update: NARMS – Summary and Future Direction

Back-up Slides

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FSIS Update - NARMS: Multi-Drug Resistance (MDR) in *Salmonella* from Chickens

MDR – Which antimicrobial drugs are involved?



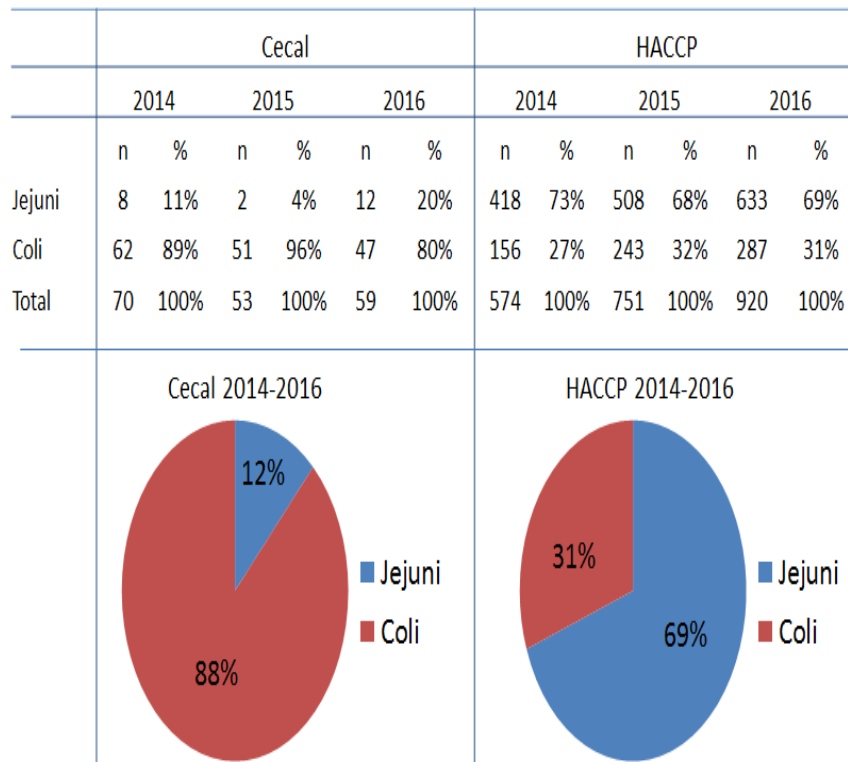
Extreme Drug Resistance (XDR) 2014-2016

- Two isolates from HACCP (1 Thompson, 1 Kentucky)
- None from Cecal

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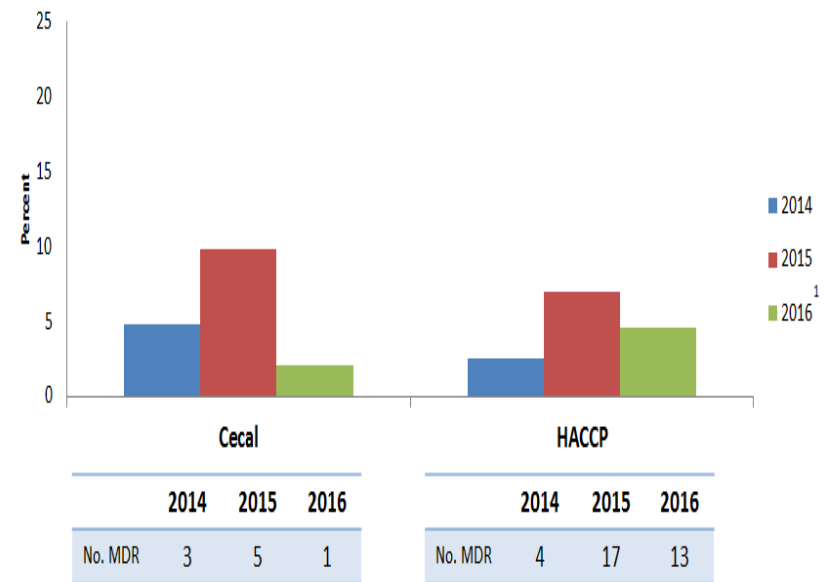
FSIS Update - NARMS: Focus on *Campylobacter jejuni* and *Campylobacter coli*

Campylobacter Species Distribution - Chickens¹



¹Preliminary 2016 Data

Percent of *C. Coli* isolates MDR - resistant to ≥ 3 antimicrobial classes



MDR in *C. Jejuni* was <2% for all commodities in both Cecal and HACCP

¹Preliminary 2016 Data

Note: Cecal samples show a much higher percentage of *C. coli* than *C. jejuni* which is the reverse of what is seen in HACCP samples

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FSIS Update: NARMS - Application of WGS and Detection of Novel Genes

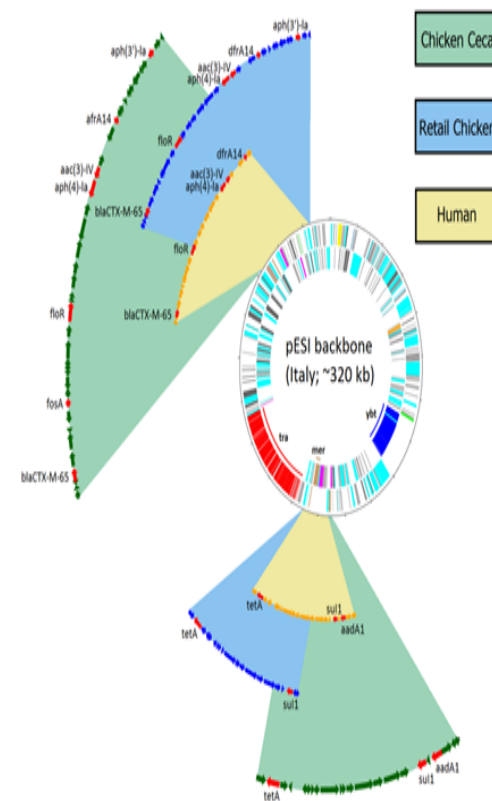
Genotypic screening for antimicrobial resistance using whole genome sequencing (WGS)



- Ability to rapidly identify new genes of concern
 - Work with NARMS and other partners in a real-time to identify the presence, magnitude and impact of undesirable gene(s)
 - Proactively work with stakeholders to start taking the necessary actions
- Examples of WGS application to novel gene detection and actions
 - ESBL *bla*_{CTX-M-65}
 - Colistin Resistance
 - Quinolone Resistance
 - Linezolid Resistance
 - Daptomycin Resistance

□ The *bla*_{CTX-m_65} gene is located in a multiresistance region and confers resistance to 5 other antimicrobial classes:

- Florfenicol/Chloramphenicol
- Sulfisoxazole, Trimethoprim/Sulfamethoxazole
- Tetracycline
- Fosfomycin
- Aminoglycosides



An FDA-CDC-FSIS Paper: [Antimicrob Agents Chemother](#). 2017 Jun 27;61(7). pii: e00488-17. doi: 10.1128/AAC.00488-17. Print 2017 Jul Press
Title: Comparative Analysis of Extended-Spectrum-β-Lactamase CTX-M-65-Producing *Salmonella enterica* Serovar Infantis Isolates from Humans, Food Animals, and Retail Chickens in the United States

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FSIS Update - NARMS: A New FSIS Web Page



The National Antimicrobial Resistance Monitoring System (NARMS) is an interagency, collaborative partnership with state and local public health departments, the U.S. Food and Drug Administration (FDA), the Centers for Disease Control and Prevention (CDC), and the U.S. Department of Agriculture (USDA). This national public health surveillance system tracks changes in antimicrobial susceptibility of select foodborne enteric bacteria found in ill people (CDC), retail meats (FDA), and food animals (USDA). The NARMS program at USDA focuses on two sampling points—samples collected from intestinal (cecal) content and carcass or food commodity samples.

Primary Objectives of NARMS

- Monitor trends in antimicrobial resistance among enteric bacteria from humans, retail meats, and animals.
- Disseminate timely information on antimicrobial resistance to promote interventions which reduce resistance among foodborne bacteria.
- Conduct research to achieve better understanding of emergence, persistence, and spread of antimicrobial resistance.
- Provide data that assists FDA in decision making involving the approval of safe and effective antimicrobial drugs for animals.

Data Collection

FDA, CDC, and USDA collect data from farm to fork to accomplish the NARMS objectives. These data are collected from three sources:

Food Animal Component

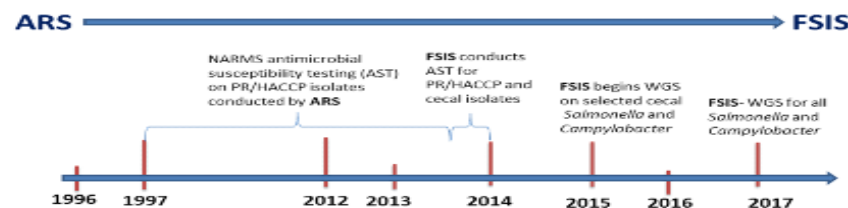
In 1997, NARMS began collecting data on food animals which was led by the USDA Agriculture Research Service (ARS) through 2013 (Figure 1). Antimicrobial susceptibility testing (AST) for non-typhoidal *Salmonella* began in 1997 on isolates collected from raw meat and poultry products at all slaughter facilities across the United States under the Pathogen Reduction Hazard Analysis and Critical Control Point (PR/HACCP) program. Sample types have changed over the years depending on FSIS directives: carcasses of cows/bulls, steers/heifers, market hogs¹, broilers (young chickens), ground beef, ground chicken and ground turkey. Testing later expanded to include *Campylobacter* (1998), *E. coli* (2000), and *Enterococcus* (2003) isolated from chicken carcasses.

ARS discontinued AST of *Enterococcus* in PR/HACCP chicken isolates in 2012 and *E. coli* in 2013. Those organisms are currently tested from food animal ceca and retail meat samples. In October 2013, FSIS assumed responsibility for the AST of NARMS PR/HACCP isolates.

In March 2013, NARMS began the cecal sampling program—a collaborative effort between the FDA's Center for Veterinary Medicine (CVM) and FSIS. Samples from cecal contents are collected at slaughter facilities of selected food animals and analyzed for *Salmonella*, *Campylobacter*, *Escherichia coli*, and *Enterococcus*. The food animals that are sampled include young chickens, young turkeys, dairy cattle, beef cattle, market hogs, and sows.

In 2014, the FDA began whole genome sequencing (WGS) on *Salmonella* isolates collected from the cecal program. Today, FSIS performs WGS on all *Salmonella* and *Campylobacter* isolates collected from both the PR/HACCP and cecal programs.

Figure 1. Transition of NARMS Program at USDA



Retail Meat Component

In 2002, NARMS began collecting retail meat samples. This component is led by FDA's Center for Veterinary Medicine (CVM). Retail meat surveillance is conducted in 18 states in partnerships with universities and public health departments. Participating sites purchase chicken, ground turkey, ground beef, and pork chops at retail outlets and culture them for nontyphoidal *Salmonella* and *Campylobacter*. Additionally, 11 sites also culture retail meats for *E. coli* and 9 sites culture for *Enterococcus*. Additional information on FDA NARMS is available at <https://www.fda.gov/AnimalVeterinary/SafetyHealth/AntimicrobialResistance/NationalAntimicrobialResistanceMonitoringSystem/> [5].

Human Component

In 1996, NARMS began collecting antibiotic resistance data from ill people on select enteric bacteria transmitted commonly through food. This component started within the framework of CDC's Emerging Infections Program and the Foodborne Diseases Active Surveillance Network (FoodNet). Human surveillance began in fourteen sites in 1996 and became nationwide in 2003. CDC performs AST on approximately 5000 human isolates per year. Additional information on CDC NARMS is available at <https://www.cdc.gov/narms/> [5].

NARMS Reporting

Each year, NARMS publishes an annual *Integrated Report* [5] that summarizes the most important resistance findings from the three participating Agencies for *Salmonella* and *Campylobacter*, as well as for *E. coli* and *Enterococcus*. This report includes summary data tables, isolate level information and *Interactive Tableau displays* [5] to enhance data visualization.

Antimicrobial Susceptibility Testing

The antimicrobial drugs selected for testing are based on their importance in human and veterinary medicine and for their utility as epidemiological markers for the movement of resistant bacteria and genes between environments. NARMS partners test for bacterial susceptibility to a range of antimicrobial drugs which include 15 antimicrobial drugs for *Salmonella* and *E. coli*, 9 for *Campylobacter* and 16 for *Enterococcus*. Selected antimicrobials/antimicrobial drug classes are also ranked, by FDA, as Critically Important, Highly Important and Important using similar criteria. The specific factors and the criteria to rank the importance of antimicrobial drugs are outlined in FDA's *Guidance - GFI #151* [5].

Whole Genome Sequencing

Whole genome sequencing (WGS) technology has become a routine part of NARMS surveillance to screen for resistance genes in enteric bacteria. Use of WGS can provide better isolate resolution including resistance genes and mobile elements and help link human and non-human resistance data.

¹Note: The FSIS NARMS report gives a description of antimicrobial resistance surveillance data in certain foodborne pathogens and assists the Agency and NARMS partners in making food safety and policy decisions. FSIS recommends that consumers keep their food safe and reduce the chance of illness at home by practicing four simple food safety tips: **clean, separate, cook, chill** [5].

NARMS Related Publications and Websites

- National Antimicrobial Resistance Monitoring System: Two Decades of Advancing Public Health Through Integrated Surveillance of Antimicrobial Resistance [5]
- Food and Drug Administration NARMS Website [5]
- Centers for Disease Control and Prevention [5]
- World Health Organization (WHO) Antimicrobial Resistance Website [5]
- President's Advisory Council on Combating Antimicrobial Resistant Bacteria [5] (PACCARB)
- Antimicrobial Resistance Overview (AMR) [5] (USDA)
- USDA One Health Website [5]

¹ FSIS suspended scheduling cows/bulls from sampling in 2011 and market hogs and steer/heifers in 2012 because of the low number