OneUSDA  “Do right and feed everyone”

Food Safety and Inspection Service
Protecting Public Health and Preventing Foodborne Illness
Antimicrobial Resistance Surveillance and Reporting at Food Safety and Inspection Service (FSIS)

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Overview

- FSIS and Data Analysis
  - FSIS and Antimicrobial Resistance (AMR)
  - Outcome of AMR Data
  - Software Tools

- NARMS
  - Antimicrobial Resistance Efforts
  - History
  - Workgroups

- NARMS Driven Investigations
  - $bla_{CTX-M-65}$, Linezolid Resistance, ECOFF Study, $mcr-1$
The Food Safety and Inspection Service (FSIS) is the public health agency in the U.S. Department of Agriculture (USDA) and is responsible for ensuring that meat, poultry, and processed egg products are safe, wholesome, and accurately labeled.

- Regulates more than 6,000 slaughter and processing establishments nationwide.
- Verifies safety of approximately 100 billion pounds of products annually.
Food Safety and Inspection Service: Intro slide on FSIS and Mission (cont. if necessary)

- Pulsed-Field Gel Electrophoresis
- Antimicrobial Susceptibility Testing
- *Salmonella* Molecular Serotyping
- Whole Genome Sequencing
FSIS and Antimicrobial Resistance Data Analysis

- FSIS and in AMR
- Outcome AMR Data
- Data Analysis Tools/Software
AMR: Antimicrobial Resistance
The general concept of the resistance of an organism to antimicrobial compounds

AST: Antimicrobial Susceptibility Testing
The laboratory testing method used to determine antimicrobial resistance in an organism
Food Safety and Inspection Service
Two Sources of Samples from Food Animals

FSIS Sampling Sources

Pathogen Reduction/Hazard Analysis and Critical Control Point (PR/HACCP) Program (1997-Present)

Cecal Sampling Program (2013-Present)

- Salmonella - Campylobacter
- Salmonella – Campylobacter – E.coli – Enterococcus

Samples are collected from federally inspected slaughter and processing plants throughout the United States

- The Cecal sampling program is non-regulatory
  - Results not used for enforcement but to understand AMR microflora in FSIS products
Organisms screened for Antimicrobial Resistance (AMR):

- *Salmonella, Campylobacter, E. coli, Enterococcus*

Antimicrobial susceptibility testing (AST) targets a combination of antimicrobial drugs used in human and veterinary medicine and for their utility as epidemiological markers for the movement of resistant bacteria and genes between environments
The AST method performed at Eastern Laboratory is a semi-automated broth micro dilution method that provides antimicrobial resistance (AMR) data in the form of minimal inhibitory concentrations (MICs) for specific antimicrobials.

The antimicrobials used in the AST panels and protocols used were designed by the NARMS interagency workgroups and detailed in the NARMS Manual of Laboratory Methods (Third Edition 2016).

An integral part of antimicrobial susceptibility testing is interpreting the results in order to categorize bacteria as susceptible, intermediate, or resistant.

FSIS uses interpretative criteria defined by NARMS, which uses breakpoints established by the Clinical Laboratory Standards Institute (CLSI) for Salmonella, E. coli, and Enterococcus, or the epidemiological cut-off values (ECOFFs) for Campylobacter, established by the European Committee on AST (EUCAST).
Antimicrobial Susceptibility Testing

\[ \text{MIC values} + \text{CLSI/ECOFF Breakpoints} = \text{Interpretation} \rightarrow \text{Phenotype} \]

Whole Genome Sequencing

WGS Data \[\rightarrow\] ResFinder

NCBI \[\rightarrow\] Genotype

PointFinder

Publication of integrated survey reports that consolidate phenotype and genotype data from all sources into an interactive format
Food Safety and Inspection Service:
FSIS AMR Data: Workflow

1. MIC Results
2. Transfer of MIC Results (operator & numerical value)
3. All AMR raw and calculated values to produce interactive visualizations
4. Interprettive Calculations (SIR)
   - MDR Calculations
   - NARMS Specific Fields
   - WGS | AMR Genotype

Link
Food Safety and Inspection Service: What AMR Data Provides

- Understand the emergence, prevalence, and distribution of antimicrobial resistance
- To monitor antimicrobial resistance trends in enteric bacteria among food animals
- Report data to help promote the reduction of antimicrobial resistance in foodborne bacteria
National Antimicrobial and Antimicrobial Resistance Monitoring System (NARMS)

- Antimicrobial Resistance Efforts
- History
- Workgroups
Antimicrobial resistance is truly a “One Health” issue, encompassing human use of antimicrobials, use in food production, and use in companion animals.

Antimicrobial resistance includes resistance to antifungals, antivirals, and anti-parasitic drugs as well as antibiotics.

Multiple national and international efforts are underway to minimize and contain antimicrobial resistance.
USDA Antimicrobial Resistance (AMR) Action Plan

- An approach to address knowledge gaps and develop practical mitigation strategies

- A plan for gathering science-based information about antibiotic drug use and its potential role in development of resistance in food-producing animals
A national public surveillance system established in 1996 which monitors changes in the antimicrobial susceptibility of enteric bacteria found in ill people (CDC), retail meats (FDA), and food animals (USDA) in the United States

### Purpose

- Monitor antimicrobial resistance trends
- Disseminate timely information
- Conduct research
- Assist FDA in making regulatory decisions
Food Safety and Inspection Service:
FSIS's Role in NARMS structure

NARMS Structure

Human
- State Laboratories
- Local Laboratories
- General Practice
- Centers for Disease Control & Prevention

Animal
- Random sampling of national production at slaughter
- US Department of Agriculture

Retail
- Random stratified sampling of chicken, turkey, beef and pork in 21 States
- Food & Drug Administration
- Annual Drug Sales & Distribution Data

Source: FDA
NARMS at USDA FSIS: A Collaborative Program

**ARS**

1996

NARMS antimicrobial susceptibility testing (AST) on PR/HACCP isolates conducted by ARS

1997

FSIS conducts AST for PR/HACCP and cecal isolates

2012

Cecal sampling begins: culture, subtyping, and AST conducted by FDA/CVM

2013

FDA: Whole Genome Sequencing (WGS) for *Salmonella* isolates from cecal samples

2014

FSIS: WGS for all *Salmonella* and *Campylobacter* from cecal samples

2015

FSIS begins WGS on selected cecal *Salmonella* and *Campylobacter*

2016

FSIS: WGS for all *Salmonella* and *Campylobacter*

2017

FSIS: WGS for select *Enterococcus* and *E. coli* from cecal samples

2018

FSIS PR/HACCP verification sampling begins
The United States NARMS program helps us meet critically important data needs as required by:

- **FDA regulatory needs and the Science Advisory Board Recommendations**
  - NARMS to continue AMR surveillance from farm-to-fork and its use as an important tool in the decision-making process for antimicrobial drug approval and use in food animals.

- **WHO**
  - Integrated AMR surveillance in foodborne bacteria through a coordinated effort in sampling and testing of bacteria from food animals, foods, and clinically ill humans

- **CARB**
  - One of the 5 Goals focused on strengthening national one-Health surveillance efforts to combat resistance.

- **White House, WHO/FAO/OIE**
  - One Health AMR data needs

- **USDA AMR Action Plan**
  - Objective 2 focuses on monitor antibiotic drug susceptibilities of selected bacterial organisms in food-producing animals, production environments, and meat and poultry

- The other entities include OIG, GAO and different international country forums such as G8/7, APEC, PAHO etc.
AMR Driven Investigations

- $bla_{CTX-M-65}$ Salmonella Infantis
- Linezolid Resistance
- Epidemiological Cut-off Values (ECOFFs)
- Prevalence of $mcr-1$
Food Safety and Inspection Service: NARMS Workgroups

Molecular Workgroups
- All aspects of molecular methods/plans for AMR
- Harmonization of methods and their uses by NARMS
  - WGS methods
    - Gene length cutoff
  - AMR Workflows
    - Read mapping hits
    - Mutational workflows
      - Databases
      - Targets
  - Reporting
    - Predicted resistance vs. phenotype results
    - Comparison of predicted resistance to phenotype results for antimicrobials without established breakpoints

Epidemiology Workgroups
- Emerging AMR trends
  - Increase in multi-drug resistance (MDR)
    - bla_{CTX-M-65} S. Infantis
  - Decreased susceptibility/resistance to Ciprofloxacin in Salmonella, E. coli and Campylobacter
    - Increase in I 4,[5],12:i:-
- Reporting
  - MDR definition/calculations
  - Changes in antimicrobials/concentrations tested

Laboratory Workgroups
- Discuss laboratory methods/NARMS Manual
- Allow for uniformity across agencies
- Discuss quality control activities
- Discuss changes in antimicrobial panel formats
- Discuss AMR laboratory issues

FDA/CDC Reports

NARMS Integrated Report
Food Safety and Inspection Service: AMR Driven Investigations: $bla_{CTX-M-65}$ *S. Infantis*

- Sequenced the genomes of 10 *S. Infantis* isolates containing $bla_{CTX-M-65}$

- Isolates collected through NARMS Chicken, Cattle and Human surveillance and product sampling programs

- First report of the $bla_{CTX-M-65}$ gene and a pESI-like megaplasmid from *S. Infantis* in the U.S.

- Resistance profiles include ampicillin, chloramphenicol, sulfisoxazole, tetracycline, ceftriaxone, ceftiofur, nalidixic acid, trimethoprim/sulfamethoxazole and decreased susceptibility to ciprofloxacin

- Concerns regarding MDR *S. Infantis* have been communicated to industry
First identification of Linezolid resistance in the U.S. in bacteria isolated from food animals

Linezolid resistance gene *optrA* in 3 Enterococcus isolates from cecal content

An additional linezolid resistance gene *cfr* identified on the same plasmid for one of the isolates

Other resistance markers on these plasmids may indicate that use of other antimicrobials may co-select for these plasmids

Horizontal transmission into bacterial populations that cause human infections is of concern

*Pending publication*
Food Safety and Inspection Service:

AMR Driven Investigations: Epidemiological Cut-off Values (ECOFFs) for Salmonella

- ECOFFs divide bacteria into wild-type and non-wild-type strains based on their MIC distributions
- ECOFFs better suited to detect emerging resistance and correlate with genotypically detectable resistance mechanisms
- Ceftriaxone, cefepime and colistin are currently lacking values
- Diverse set of 500 Salmonella enterica isolates tested from various animal, food, and clinical sources
- Proposed ECOFFs will be valuable additions to AMR surveillance

Pending publication in Foodborne Pathogens and Disease
The plasmid-borne gene *mcr-1* confers resistance to polymyxin E (colistin) in *Escherichia coli*

Survey of 2,003 cecal content samples from chickens, turkeys, cattle and swine in 2016

Two cecal samples from swine had *Escherichia coli* with IncI2 plasmids bearing the *mcr-1* gene

First report of *mcr-1* bearing IncI2 plasmid from swine cecal contents

The gene appears to be phylogenetically young and rapidly spreading
Questions?

One Team, One Purpose
Protecting Public Health and Preventing Foodborne Illness