Twenty Years of the National Antimicrobial Resistance Monitoring System (NARMS)
Where Are We And What Is Next?

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Center for Veterinary Medicine
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NARMS Structure

State Laboratories

Local Laboratories

General Practice

Random sampling of national production at slaughter

Random stratified sampling of chicken, turkey, beef and pork in 21 States

Centers for Disease Control & Prevention

US Department of Agriculture

Food & Drug Administration

Annual Drug Sales & Distribution Data

www.fda.gov
The Purpose of NARMS

1. Monitor resistance trends
2. Disseminate timely information
3. Conduct research
4. Prioritize outbreaks
5. Assist the FDA in making regulatory decisions
NARMS Strategic Plan

**Goal 1:** Develop a sampling strategy that is more representative of food animal production and consumption and more applicable to trend analysis

**Goal 2:** Optimize data acquisition, analysis, and reporting

**Goal 3:** Strengthen collaborative research projects

**Goal 4:** Collaborate with international institutions that promote food safety, especially those focused on mitigating the spread of antimicrobial-resistant bacteria
NARMS Strategic Plan 2012-2016

Objective 1.1: Improve the geographic representativeness of retail meat testing and increase the total number of retail meat isolates recovered in order to better assess trends (14-21 states)

Objective 1.2: Modify animal slaughter sampling to establish a statistically designed scheme that allows an unbiased national estimate of resistance prevalence in target organisms
Objective 1.1: Improve the geographic representativeness of retail meat testing and increase the total number of retail meat isolates recovered in order to better assess trends (14-21 states)

Sampling Scheme:
Sampling: 80 pkgs/mo.
- 40 retail chicken
- 20 ground turkey
- 10 ground beef
- 10 pork chops

Sample size increased from 6,720 in 2016 to 19,200 in 2018

Partnership with States
- CT, GA, MD, MN, TN, OR, NY, CA, CO, NM, PA 2008
- CT, GA, MD, MN, TN, OR, NY, CA, CO, NM, PA, WA, LA, MO 2013
- GA, MD, MN, TN, OR, NY, CA, CO, NM, PA, WA, LA, MO, IA KS, SC, SD (ND), TX (OKC) 2017
- GA, MD, MN, TN, OR, NY, CA, CO, NM, PA, WA, LA, MO, IA. KS, SC, SD (ND), TX (OKC), UC-Davis, NC 2018
**Objective 1.2:** Modify animal slaughter sampling to establish a statistically designed scheme that allows an unbiased national estimate of resistance prevalence in target organisms

**Old System (HACCP)**

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Swine</th>
<th>Cattle</th>
<th>Chicken</th>
<th>Turkeys</th>
</tr>
</thead>
<tbody>
<tr>
<td>Campylobacter</td>
<td></td>
<td></td>
<td>x</td>
<td></td>
</tr>
<tr>
<td>Salmonella</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>E. coli</td>
<td></td>
<td>x</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Enterococcus</td>
<td></td>
<td>x</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**New System (Cecal)**

- Led by USDA-Food Safety Inspection Service
- Cecal samples better reflect animal status and less confounded by plant events
- A randomized, nationally representative testing of slaughterhouses
- Ability to distinguish production classes
- Complete microbiology for all animal species
- Began in late 2013
Objective 2.1: Develop and launch an integrated database that will allow data sharing among NARMS partners and stakeholders in a secure environment, and provide tools for efficient exploration and analysis of data across sample sources.
New Objective 2.1: Publish annual surveillance reports that make the surveillance findings more accessible to a broad range of stakeholders

https://www.fda.gov/AnimalVeterinary/SafetyHealth/AntimicrobialResistance/NationalAntimicrobialResistanceMonitoringSystem/ucm059103.htm

www.fda.gov
Objective 3.2: Evaluate and apply existing research tools, and develop new ones, to enhance surveillance of antimicrobial-resistant bacteria

<table>
<thead>
<tr>
<th>Methods</th>
<th>Results</th>
<th>Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Human Animal Food Environmental Pure Culture</td>
<td>Identification → Genus, species</td>
<td>Slow and piecemeal</td>
</tr>
<tr>
<td></td>
<td>Serotyping → Serotype</td>
<td>Low resolution typing</td>
</tr>
<tr>
<td></td>
<td>Antibiotic Susceptibility → Resistance pattern</td>
<td>Multiple assays and reagents</td>
</tr>
<tr>
<td></td>
<td>PFGE → Genetic relationship</td>
<td>Limited drug coverage</td>
</tr>
<tr>
<td></td>
<td>Molecular study → Genetic mechanisms</td>
<td>Limited resistance mechanisms</td>
</tr>
</tbody>
</table>

Traditional

- Identification
- Serotyping
- Antibiotic Susceptibility
- PFGE
- Molecular study

WGS

- Metagenomic Sample → DNA → WGS
- Identification Serotype Resistance genes Genetic relationships Virulence properties Phage type

- Rapid and comprehensive
- Highest resolution typing
- Single assay/instrument/output
- Extensive drug coverage
- Detect all known genes
- Details on genetic context
- Computation intensive
- Lower costs
- Requires new standards
NARMS Genotype-Phenotype Correlations

Whole-Genome Sequencing for Detecting Antimicrobial Resistance in Nontyphoidal Salmonella

Patrick F. McDermott, Gregory H. Tyson, Claudine Kabera, Yruansha Chen, Cong Li, Jason P. Folster, Sherry L. Ayers, Claudia Lam, Heather P. Tate, Shaohua Zhao

Whole-Genome Sequencing Analysis Accurately Predicts Antimicrobial Resistance Phenotypes in Campylobacter spp.

S. Zhao, G. H. Tyson, Y. Chen, C. Li, S. Mukherjee, S. Young, C. Lam, J. P. Folster, J. M. Whichard, P. F. McDermott

J Antimicrob Chemother 2015; 70: 2763–2769

WGS accurately predicts antimicrobial resistance in Escherichia coli

Gregory H. Tyson, Patrick F. McDermott, Cong Li, Yruansha Chen, Daniel A. Tadesse, Sampa Mukherjee, Sonya Bodeis-Jones, Claudine Kabera, Stuart A. Gaines, Guy H. Loneragan, Tom S. Edrington, Mary Torrence, Dayna M. Harhay and Shaohua Zhao
Metagenomic Surveillance
Resistance Genes by Animal Origin


- Eight different GenR genes were found.
- Six for the first time in Campylobacter

WGS gives new answers to old questions

- Recent descent from a well-preserved plasmid backbone
- Resistance to compounds not tested
- Reveals new possible drivers of AMR
Plasmid-Mediated Colistin Resistance

- Colistin is used as a last-resort drug to treat patients with multidrug-resistant infections, including CRE

- The \textit{mcr-1} (mobile colistin resistance) gene was the first plasmid-mediated resistance mechanisms discovered. First reported in China, November 2015

- Without opening a freezer door, we screened over 155,000 bacterial genomes, about 7,000 from NARMS, and none contained the gene

- By selective culture enrichment, our partners at USDA found \textit{mcr-1} in \textit{E. coli} isolates collected from the intestines of two pigs (out of 2,000 samples tested)

- Metagenomic analysis of blinded samples also detected the \textit{mcr-1} gene.

\textbf{Bacteria that resist last-resort antibiotics were found in China two months ago, now they're everywhere}
RESISTOMOME TRACKER
Salmonella

**NARMS Isolates are marked by green squares.** *Note: Some NARMS isolates do not have corresponding NARMS biosample IDs and therefore are not marked with green squares. Biosamples may have more than one entry because there is more than one SRA number per Biosample.*

<table>
<thead>
<tr>
<th>Bio Sample</th>
<th>Genotype</th>
<th>Geographic Location</th>
<th>Serovar</th>
<th>Sources</th>
<th>Year of NCBI Release Date</th>
<th>Click Buttons for Links to NCBI</th>
</tr>
</thead>
<tbody>
<tr>
<td>SAMN02367912</td>
<td>aadA1 aac(3)-Ia sul1 sul2 tet(A)</td>
<td>USA: Connecticut</td>
<td>Typhimurium var. 5-</td>
<td>chicken breast</td>
<td>2016</td>
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</tr>
<tr>
<td>SAMN02367902</td>
<td>aac(3)-Ia strB aadA1 blaTEM-1B blaCMY-2 sul2 tet(A) tet(B)</td>
<td>USA: New Mexico</td>
<td>Litchfield</td>
<td>chicken breast</td>
<td>2016</td>
<td>Click Here</td>
</tr>
<tr>
<td>SAMN02368023</td>
<td>aac(3)-Ia aadA1 strB sul1 tet(C) tet(D)</td>
<td>USA: New Mexico</td>
<td>Kentucky</td>
<td>chicken wing</td>
<td>2016</td>
<td>Click Here</td>
</tr>
<tr>
<td>SAMN02699266</td>
<td>aadA1 dfrA15 sul1</td>
<td>USA: MN</td>
<td>Kentucky</td>
<td>chicken breast</td>
<td>2016</td>
<td>Click Here</td>
</tr>
</tbody>
</table>
### What *Salmonella* resistance genes appear for the first time in the NCBI dataset?

Note: list only goes back 6 months

<table>
<thead>
<tr>
<th>Day of NCBI Release Date</th>
<th>Gene</th>
<th>Class</th>
<th>Geographic Location</th>
<th>Sources</th>
<th>Bio Sample</th>
<th>Click Buttons for Links to NCBI</th>
</tr>
</thead>
<tbody>
<tr>
<td>10/5/2017</td>
<td>mcr5</td>
<td>Polymixin</td>
<td>Australia</td>
<td>faces</td>
<td>SAMN07739130</td>
<td><a href="#">Click Here</a></td>
</tr>
<tr>
<td>9/30/2017</td>
<td>blaTEM-29</td>
<td>Beta-lactam</td>
<td>United Kingdom</td>
<td>human</td>
<td>SAMN07719053</td>
<td><a href="#">Click Here</a></td>
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<tr>
<td>9/29/2017</td>
<td>blaTEM-138</td>
<td>Beta-lactam</td>
<td>United Kingdom</td>
<td>human</td>
<td>SAMN07717931</td>
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<tr>
<td>9/28/2017</td>
<td>blaCTX-M-114</td>
<td>Beta-lactam</td>
<td>Unknown</td>
<td>Null</td>
<td>SAMN07718851</td>
<td><a href="#">Click Here</a></td>
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<tr>
<td></td>
<td>blaTEM-77</td>
<td>Beta-lactam</td>
<td>Unknown</td>
<td>Null</td>
<td>SAMN07718910</td>
<td><a href="#">Click Here</a></td>
</tr>
<tr>
<td>9/27/2017</td>
<td>blaTEM-130</td>
<td>Beta-lactam</td>
<td>USA</td>
<td>missing</td>
<td>SAMN07667877</td>
<td><a href="#">Click Here</a></td>
</tr>
<tr>
<td></td>
<td>QnrB17-1</td>
<td>Quinolone</td>
<td>USA:MN</td>
<td>lung (porcine)</td>
<td>SAMN07420427</td>
<td><a href="#">Click Here</a></td>
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<tr>
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<td>blaTEM-122</td>
<td>Beta-lactam</td>
<td>United Kingdom</td>
<td>human</td>
<td>SAMN07655361</td>
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<tr>
<td></td>
<td>blaTEM-150</td>
<td>Beta-lactam</td>
<td>United Kingdom</td>
<td>human</td>
<td>SAMN07655269</td>
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</tr>
<tr>
<td>9/26/2017</td>
<td>mcr2</td>
<td>Polymixin</td>
<td>Belgium</td>
<td>pork carcassos</td>
<td>SAMEA104175516</td>
<td><a href="#">Click Here</a></td>
</tr>
</tbody>
</table>

### When was the first *Salmonella* isolate with the following resistance gene *collected*?

Gene: QnrA1

<table>
<thead>
<tr>
<th>Gene</th>
<th>Class</th>
<th>Collection Years</th>
<th>Geographic Location</th>
<th>Source</th>
<th>Bio Sample</th>
<th>Click Buttons for Links to NCBI</th>
</tr>
</thead>
<tbody>
<tr>
<td>QnrA1</td>
<td>Quinolone</td>
<td>2003</td>
<td>Malawi</td>
<td>blood</td>
<td>SAMEA1940373</td>
<td><a href="#">Click Here</a></td>
</tr>
</tbody>
</table>
Objective 3.4: Seek out new partnerships within and outside of government to leverage resources dedicated to microbial food safety and help prevent the development, persistence, and transmission of antimicrobial resistance
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*FDA, CDC, And USDA Announce 2017 Scientific Meeting Of The National Antimicrobial Resistance Monitoring System:* On September 20, 2017, FDA, along with its National Antimicrobial Resistance Monitoring System partners, the Centers for Disease Control and Prevention (CDC) and USDA, announced that it will be holding the 2017 Scientific Meeting of the National Antimicrobial Resistance Monitoring System (NARMS) on **October 24-25, 2017, from 8:30 a.m. to 5:00 p.m. (EST)** at the USDA’s South Building, in the Jefferson Auditorium, 14th & Independence Avenue S.W., Washington, DC 20250. The purpose of this public meeting will be to “summarize NARMS progress since the last public meeting in 2014, present recommendations made by the recent FDA Science Board review of NARMS in 2017, and to explore new possible directions for NARMS within a One Health paradigm.”
NARMS Looking Forward: From Integrated to One Health Surveillance

1. Add food animal pathogens.
2. Add appropriate on-farm testing.
3. Incorporate companion animal surveillance.
4. Develop an environmental surveillance piece to advance a One Health approach.
5. Develop methods of microbiome surveillance.
6. Broaden collaboration with other U.S. programs
7. Continue to work toward international harmonization and cooperation
Acknowledgements

• FDA (CVM, CFSAN, ORA)
• CDC (NCZEID)
• USDA (FSIS, ARS, APHIS)
• NIH/NCBI
• ANL/Univ Chicago
• State Public Health Labs, Universities

This communication is consistent with 21 CFR 10.85 (k) and constitutes an informal communication that represents my best judgment at this time but does not constitute an advisory opinion, does not necessarily represent the formal position of FDA, and does not bind or otherwise obligate or commit the agency to the views expressed.
What Have We Learned about Resistance to Critically-Important Antibiotics in Nontyphoidal *Salmonella* from Humans in the US
Resistance to Critically-Important Antibiotics in Human Nontyphoidal *Salmonella* from Select EU Countries, Norway and the USA

± Breakpoints used for interpreting MICs were derived from the EUCAST.
† Among critically-important drugs (defined here as macrolides, fluoroquinolones, extended-spectrum cephalosporins, and carbapenems), azithromycin, meropenem and colistin resistance were very rare and not reported in most countries.
‡ Percentage based on reporting of either cefotaxime or ceftazidime resistance from the EU or ceftriaxone from US.
Resistance to Critically-Important Antibiotics in Broiler Nontyphoidal *Salmonella* from Select EU Countries, Norway and the USA

Breakpoints used for interpreting MICs were derived from the EUCAST.

Among critically-important drugs (defined here as macrolides, fluoroquinolones, extended-spectrum cephalosporins, and carbapenems), azithromycin, meropenem and colistin resistance were very rare and not reported in most countries.

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*Percentage based on reporting of either cefotaxime or ceftazidime resistance from the EU or ceftriaxone from US.
Antibiotic Resistance in Human Nontyphoidal *Salmonella* from Select EU Countries, Norway and the USA

Breakpoints used for interpreting MICs were derived from the EUCAST.

# Breakpoints used for interpreting MICs were derived from the EUCAST.
Antibiotic Resistance in Broiler Nontyphoidal *Salmonella* from Select EU Countries, Norway and the USA

Breakpoints used for interpreting MICs were derived from the EUCAST.