Update On Antimicrobial Resistance In Beef Production

Terrance M. Arthur, Tommy L. Wheeler, John W. Schmidt*

john.w.schmidt@ars.usda.gov

Meat Safety and Quality Research Unit
U.S. Meat Animal Research Center
Clay Center, Nebraska

US Dept. of Agriculture - Agricultural Research Service

Nebraska One Health Stakeholder Meeting
December 6, 2017 - Omaha, NE
Is Food-Animal Production Antimicrobial-Use a “Substantial Driver” of Antimicrobial Resistance, esp. Human “Clinical”? 

This conclusion is largely based on the greater mass of antimicrobials consumed by food-animals.
Food-animal production accounts for 70% to 80% of US AM-use by mass.

**Animal**

2015

**SUMMARY REPORT**

On

*Antimicrobials Sold or Distributed for Use in Food-Producing Animals*

- Includes companion animals
- Until 2016 no breakdown by species

**Human**

- 2010/2011 Human use
- IMS Health proprietary use data (no yearly updates)
For Several AM Classes Human Use > Animal Use (by mass)

**Animals**
- 44% Tetracyclines
- 38% “NCMI” Mostly Ionophores
- 6% Penicillins
- 4% Macrolides
- 4% Sulfas
- 2% Aminoglycosides

**Humans**
- 44% Penicillins
- 15% Cephalosporins
- 15% Sulfa & COT
- 8.5% Quinolones
- 5% Macrolides
- 4% Tetracyclines
- 0.4% (Carba)penems
- 0.2% Aminoglycosides
AMR Should Be Studied In “Proper Context”

Frequently conclusions are made on the basis of isolation of ARB or ARG in a food-animal environment with no or improper comparisons.
Impact of “Raised without Antibiotics” Beef Cattle Production Practices on Occurrences of Antimicrobial Resistance


U.S. Department of Agriculture, Agricultural Research Service, Roman L. Hruska U.S. Meat Animal Research Center, Clay Center, Nebraska, USA; Department of Animal Sciences, Colorado State University, Fort Collins, Colorado, USA; Department of Clinical Sciences, College of Veterinary Medicine, Colorado State University, Fort Collins, Colorado, USA.

ABSTRACT The specific antimicrobial resistance (AMR) decreases that can be expected from reducing antimicrobial (AM) use in U.S. beef production have not been defined. To address this data gap, feces were recovered from 36 lots of “raised without antibiotics” (RWA) and 36 lots of “conventional” (CONV) beef cattle. Samples from both RWA and CONV cattle were assayed for the presence of various AMs and AMR genes. Fecal samples were assayed using culture-based and culture-independent methods. There were no significant differences in AMR between RWA and CONV cattle. The results of this study suggest that reducing AM use in beef cattle production has no measurable impact on AMR.
Rationale

- Feces are primary source of “product (beef)” contamination and “environmental” contamination.

- What impact does “Raised Without Antibiotics” (RWA) have on Antimicrobial Resistance (AMR) at the source?

**Objective:** To determine the impact of typical antimicrobial use during cattle production on fecal occurrence of antimicrobial resistance by culture, quantitative PCR, and metagenomic sequencing.
Impact of RWA Beef Cattle Production on AMR

Samples:
• 72 lots. 36 Raised Without Antibiotics (RWA), 36 Conventional (CONV).
• Once each month over a year a processing plant was visited.
• Each month 6 lots were sampled: 3 RWA, 3 CONV.
• For each lot 10 colons sampled. >10 grams feces recovered from each colon.

Criteria for RWA (“Natural Cattle”, “Never-Ever Cattle”):
1. No antimicrobials, including ionophores.
2. No supplemental hormones.
3. No steroids or beta-agonists.
4. No animal-derived feedstuffs.
**Methods**

**Bacteria cultured, both enumeration and enrichment (N = 719):**
- *E. coli*-TET<sup>r</sup>, COT<sup>r</sup>, 3GC<sup>r</sup>.
- *Salmonella*- NAL<sup>r</sup>, 3GC<sup>r</sup>.
- *Enterococcus*- ERY<sup>r</sup>.

**qPCR (N = 72):**
- Aminoglycoside - *aac(6’)-le-aph(2’’)-la, aadA1*.
- β-lactam - *bla<sub>CMY-2</sub>, bla<sub>CTX-M</sub>, bla<sub>KPC-2</sub>, mecA*.
- MLS - *erm(B)*.
- Tetracycline - *tet(A), tet(B), tet(M)*.

**QIAGEN 84 ARG Array (N = 72)**

**Metagenomic sequencing (N = 72):**
- Mean depth: $7.60 \times 10^7$ raw reads; $6.86 \times 10^7$ trimmed and filtered.
- Queried MEGARes. Mean aligned reads = $9.02 \times 10^4$ (0.1%).
3rd Gen. Cephalosporin-Resistant (3GC<sup>r</sup>) E. coli


### Production system % Prevalence

<table>
<thead>
<tr>
<th>Production system</th>
<th>% Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>CONV</td>
<td>47.5</td>
</tr>
<tr>
<td>RWA</td>
<td>34.8</td>
</tr>
<tr>
<td>Difference</td>
<td>12.7</td>
</tr>
</tbody>
</table>

### Factor P-value

<table>
<thead>
<tr>
<th>Factor</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Production system</td>
<td>0.04</td>
</tr>
<tr>
<td>Season</td>
<td>1.03 × 10⁻⁹</td>
</tr>
<tr>
<td>Prod. sys. × Season</td>
<td>0.86</td>
</tr>
</tbody>
</table>

- Lower limit of detection was 0.1 CFU/g.
- Only 2.8% of samples (20/719) had enumerable (≥ 200 CFU/g) 3GC<sup>r</sup> E. coli.
E. coli AMR Populations


### Table 1: Log_{10} CFU/g conc. for E. coli

<table>
<thead>
<tr>
<th></th>
<th>CONV</th>
<th>RWA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Generic</td>
<td>6.03</td>
<td>6.18</td>
</tr>
<tr>
<td>TET&lt;sup&gt;r&lt;/sup&gt;</td>
<td>5.22</td>
<td>4.98</td>
</tr>
<tr>
<td>COT&lt;sup&gt;r&lt;/sup&gt;</td>
<td>0.47</td>
<td>0.10</td>
</tr>
<tr>
<td>3GC&lt;sup&gt;r&lt;/sup&gt;</td>
<td>-0.64</td>
<td>-1.05</td>
</tr>
</tbody>
</table>

**Log_{10} CFU/g conc.**

Generic and TET<sup>r</sup> E. coli conc. strongly corr. Spearman’s rho = 0.72, P = 6.56 × 10<sup>-8</sup>

Only 19.8% enumerated
**Salmonella**


- *Salmonella* enumerated in only 1.7% of samples.

<table>
<thead>
<tr>
<th>Production system</th>
<th>% Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>CONV</td>
<td>11.7</td>
</tr>
<tr>
<td>RWA</td>
<td>15.9</td>
</tr>
<tr>
<td>Difference</td>
<td>-4.2</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Factor</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Production system</td>
<td>0.42</td>
</tr>
<tr>
<td>Season</td>
<td>$7.96 \times 10^{-6}$</td>
</tr>
<tr>
<td>Prod. sys. × Season</td>
<td>0.76</td>
</tr>
</tbody>
</table>

- **3GC** *Salmonella* prevalence = 0.3% CONV, 0.0% RWA (1 positive CONV sample).

- **NAL** *Salmonella* not detected.
• Erythromycin-resistant (ERYr) *Enterococcus* spp. concentration was higher in CONV (P < 0.01). Erythromycin and tylosin are macrolides.
qPCR


Not Detected

aac(6′')-le-aph(2′′')-Ia
mecA

Log₂ fold change | 3.8 | 0.6 | 0.8 | -0.1 | 2.6 | 1.3 | 1.9 | 1.9
P-value         | < 0.01 | 0.05 | 0.02 | 0.48 | < 0.01 | 0.01 | < 0.01 | < 0.01
**Methods**


**Bacteria cultured, both enumeration and enrichment (N = 719):**

- *E. coli*-TET\(^r\), COT\(^r\), 3GC\(^r\).
- *Salmonella*- NAL\(^r\), 3GC\(^r\).
- *Enterococcus*- ERY\(^r\).

**qPCR (N = 72):**

- Aminoglycoside - *aac(6’)-le-aph(2”)-la, aadA1*.
- β-lactam - *bla\(_{CMY-2}\), bla\(_{CTX-M}\), bla\(_{KPC-2}\), mecA*.
- MLS - *erm(B)*.
- Tetracycline - *tet(A), tet(B), tet(M)*.

**QIAGEN 84 ARG Array (N = 72)**

**Metagenomic sequencing (N = 72):**

- Mean depth: 7.60 × 10\(^7\) raw reads; 6.86 × 10\(^7\) trimmed and filtered.
- Queried MEGARes. Mean aligned reads = 9.02 × 10\(^4\) (0.1%).
- 175 ARG sequences “hits”.
- 95 ARGs, 27 resistance mechs., 12 AM classes.
- After removing “structural genes” 43 ARGs.
Metagenomics - AM Class Abundances

All Log2 Fold Change < 1.0
11 Most Abundant ARGs, No Difference


All Log₂ Fold Change < 1.0
12th to 17th Abundant ARGs Higher in CONV


<table>
<thead>
<tr>
<th>ARG</th>
<th>Log2 Fold Change</th>
<th>% detected</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ant(6)-I</td>
<td>1.0</td>
<td>100.0</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>tet(X)</td>
<td>2.8</td>
<td>91.7</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>tet(M)</td>
<td>2.5</td>
<td>84.7</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>erm(Q)</td>
<td>1.7</td>
<td>97.2</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>erm(F)</td>
<td>2.8</td>
<td>93.1</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>bla_AcI</td>
<td>1.4</td>
<td>98.6</td>
<td>&lt; 0.01</td>
</tr>
</tbody>
</table>
Similar CONV and RWA Microbiomes


16S rRNA V1-V3

Percent relative abundance

CONV  RWA

Firmicutes  Bacteroidetes  Tenericutes  Proteobacteria  Spirochaetes  Actinobacteria  Cyanobacteria  Verrucomicrobiota  Fibrobacteres  Lentisphaerae  Fusobacteria  TM7  Others

NMDS1  NMDS2  NMDS3

CONV  RWA

Metagenomic Seq.

Enterobacteriales  Bacteroidales  Clostridiales  Lactobacillales  Spirochaetales  Bifidobacteriales  Others

CONV  RWA
Impact of RWA Beef Cattle Production on AMR Conclusions


• Consistent differences (higher in CONV) were limited to:
  - MLS\textsubscript{B} esp. ERY\textsuperscript{r} Enterococcus and erm(B).
  - Tetracyclines esp. tet(M).

• Human and environmental exposures may not differ because:
  • erm(B), tet(M), and ERY\textsuperscript{r} Enterococcus are ubiquitous, esp. in fecal and fecal impacted samples.

  • RWA cattle are fed for approximately 7 more weeks than CONV cattle.

  • Processing removes much ARB and ARG.

Applied and Environmental Microbiology

Occurrence of Antimicrobial-Resistant Escherichia coli and Salmonella enterica in the Beef Cattle Production and Processing Continuum

© John W. Schmidt, Getahun E. Agga, Joseph M. Bosilevac, Dayna M. Brichta-Harhay, Steven D. Shackelford, Rong Wang, Tommy L. Wheeler, Terrance M. Arthur
U.S. Department of Agriculture, Agricultural Research Service, Roman L. Hruska U.S. Meat Animal Research Center, Clay Center, Nebraska, USA
AMR in CONV and RWA Ground Beef

- CONV and RWA feces are similar and processing interventions are effective, AMR in CONV and RWA ground beef likely do not differ.
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Public believes that RWA meats harbor less AMR.

CDC materials imply that AM use increases AMR that is transmitted to humans by meats.
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• CDC materials imply that AM use increases AMR that is transmitted to humans by meats.
• CONV and RWA feces are similar and processing interventions are effective, AMR in CONV and RWA ground beef likely do not differ.

• Public believes that RWA meats harbor less AMR.

• CDC materials imply that AM use increases AMR that is transmitted to humans by meats.

• Review articles (some highly cited) make similar claims.
AMR in CONV and RWA Ground Beef (3)

- CONV and RWA feces are similar and processing interventions are effective, AMR in CONV and RWA ground beef likely do not differ.
- Public believes that RWA meats harbor less AMR.
- CDC materials imply that AM use increases AMR that is transmitted to humans by meats.
- Review articles (some highly cited) make similar claims.

Hoelzer et al. *BMC Veterinary Research* (2017) 13:211
DOI 10.1186/s12917-017-1131-3

**Antimicrobial drug use in food-producing animals and associated human health risks: what, and how strong, is the evidence?**
Karin Hoelzer, Nora Wong, Joe Thomas, Kathy Talkington, Elizabeth Jungman and Allan Coukell
AMR in CONV and RWA Ground Beef (4)

**Objective:** To determine if AMR levels (ARB and ARGs) differ between RWA and CONV ground beef. Also, to determine the concentrations of ARB and ARG to inform risk modeling and assessments.

**Design:** For each month, for 13 months, from three foodservice suppliers (Pacific, West South Central, South Atlantic) 5 CONV samples and 5 RWA samples were obtained. $N_{\text{CONV}} = 191$, $N_{\text{RWA}} = 179$.

<table>
<thead>
<tr>
<th>Table S5 Distribution of ground beef samples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Month</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Oct. 2015</td>
</tr>
<tr>
<td>Nov. 2015</td>
</tr>
<tr>
<td>Dec. 2015</td>
</tr>
<tr>
<td>Jan. 2016</td>
</tr>
<tr>
<td>Feb. 2016</td>
</tr>
<tr>
<td>Mar. 2016</td>
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<tr>
<td>Apr. 2016</td>
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<tr>
<td>May 2016</td>
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<tr>
<td>Jun. 2016</td>
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<tr>
<td>Jul. 2016</td>
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<tr>
<td>Aug. 2016</td>
</tr>
<tr>
<td>Sep. 2016</td>
</tr>
<tr>
<td>Oct. 2016</td>
</tr>
</tbody>
</table>
Methods

Bacteria cultured, both enumeration and enrichment ($N = 370$):
- *E. coli*-TET\textsuperscript{r}, 3GC\textsuperscript{r}.
- *Salmonella*- TET\textsuperscript{r}, 3GC\textsuperscript{r}.
- *Enterococcus*- TET\textsuperscript{r}, ERY\textsuperscript{r}.
- *S. aureus*- MRSA

qPCR ($N = 75$):
- Aminoglycoside - *aac(6’)-le-aph(2’’)-la*, *aadA1*.
- β-lactam - *bla\textsubscript{CMY-2}, bla\textsubscript{CTX-M},* *bla\textsubscript{KPC-2}, mecA*.
- MLS - *erm(B)*.
- Tetracycline - *tet(A), tet(B), tet(M)*.
**TET<sup>r</sup> *E. coli* Higher in CONV**


<table>
<thead>
<tr>
<th></th>
<th>CONV</th>
<th>RWA</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>% detection</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Generic E. coli</strong></td>
<td>![Graph]</td>
<td>![Graph]</td>
</tr>
<tr>
<td><strong>TET&lt;sup&gt;r&lt;/sup&gt; E. coli</strong></td>
<td>![Graph]</td>
<td>![Graph]</td>
</tr>
<tr>
<td><strong>3GC&lt;sup&gt;r&lt;/sup&gt; E. coli</strong></td>
<td>![Graph]</td>
<td>![Graph]</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>CONV</th>
<th>RWA</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>% detection</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Generic Sal.</strong></td>
<td>![Graph]</td>
<td>![Graph]</td>
</tr>
<tr>
<td><strong>TET&lt;sup&gt;r&lt;/sup&gt; Sal.</strong></td>
<td>![Graph]</td>
<td>![Graph]</td>
</tr>
<tr>
<td><strong>3GC&lt;sup&gt;r&lt;/sup&gt; Sal.</strong></td>
<td>![Graph]</td>
<td>![Graph]</td>
</tr>
<tr>
<td><strong>NAL&lt;sup&gt;r&lt;/sup&gt; Sal.</strong></td>
<td>![Graph]</td>
<td>![Graph]</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>CONV</th>
<th>RWA</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>% detection</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Generic Enterococcus</strong></td>
<td>![Graph]</td>
<td>![Graph]</td>
</tr>
<tr>
<td><strong>TET&lt;sup&gt;r&lt;/sup&gt; Enterococcus</strong></td>
<td>![Graph]</td>
<td>![Graph]</td>
</tr>
<tr>
<td><strong>ERY&lt;sup&gt;r&lt;/sup&gt; Enterococcus</strong></td>
<td>![Graph]</td>
<td>![Graph]</td>
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</table>

<table>
<thead>
<tr>
<th></th>
<th>CONV</th>
<th>RWA</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>% detection</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Generic S. aureus</strong></td>
<td>![Graph]</td>
<td>![Graph]</td>
</tr>
<tr>
<td><strong>MRSA</strong></td>
<td>![Graph]</td>
<td>![Graph]</td>
</tr>
</tbody>
</table>
Supplier 2 - *E. coli*, TET-*E. coli*, and *Sal.*


**Table:**

<table>
<thead>
<tr>
<th>Organism</th>
<th>Supplier 1</th>
<th>Supplier 2</th>
<th>Supplier 3</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>% detection</td>
<td>% detection</td>
<td>% detection</td>
</tr>
<tr>
<td><em>E. coli</em></td>
<td>CONV (n = 65)</td>
<td>RWA (n = 54)</td>
<td><em>P</em>-value</td>
</tr>
<tr>
<td>Generic</td>
<td>83.1</td>
<td>77.8</td>
<td>0.47</td>
</tr>
<tr>
<td>Tetracycline-resistant (TET^r) <em>E. coli</em></td>
<td>49.2</td>
<td>50.0</td>
<td>0.93</td>
</tr>
<tr>
<td>Third-generation cephalosporin (3GC^r) <em>E. coli</em></td>
<td>0.0</td>
<td>1.9</td>
<td>0.27</td>
</tr>
<tr>
<td><em>Sal.</em></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TET^r <em>Sal.</em></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3GC^r <em>Sal.</em></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
E. coli Concentrations

**Enterococcus Concentrations**

**S. aureus Concentrations**


---

**B**

<table>
<thead>
<tr>
<th></th>
<th>CONV</th>
<th>RWA</th>
<th>log$_{10}$ CFU/g</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Generic S. aureus</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(n = 191)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(n = 179)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>MRSA</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Black: $< -1.4$
- Light blue: -1.4 to 0.9
- Navy: 1.0 to 1.9
- Magenta: 2.0 to 2.9
qPCR — tet(A) & tet(B) Higher in RWA


Table 2 qPCR detection rates

<table>
<thead>
<tr>
<th>Gene</th>
<th>CONV (n = 38)</th>
<th>RWA (n = 37)</th>
</tr>
</thead>
<tbody>
<tr>
<td>16s rRNA</td>
<td>100.0</td>
<td>100.0</td>
</tr>
<tr>
<td>aac(6')-Ie-aph(2'')-Ia</td>
<td>7.9</td>
<td>2.7</td>
</tr>
<tr>
<td>aadA1</td>
<td>31.6</td>
<td>27.0</td>
</tr>
<tr>
<td>blacMY</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>blacCTX-M</td>
<td>15.8</td>
<td>2.7</td>
</tr>
<tr>
<td>blakPC2</td>
<td>13.2</td>
<td>0.0</td>
</tr>
<tr>
<td>mecA</td>
<td>2.6</td>
<td>5.4</td>
</tr>
<tr>
<td>erm(B)</td>
<td>50.0</td>
<td>46.0</td>
</tr>
<tr>
<td>tet(A)</td>
<td>36.8</td>
<td>40.5</td>
</tr>
<tr>
<td>tet(B)</td>
<td>13.2</td>
<td>13.5</td>
</tr>
<tr>
<td>tet(M)</td>
<td>84.2</td>
<td>86.5</td>
</tr>
</tbody>
</table>

Log₂ fold change

<table>
<thead>
<tr>
<th></th>
<th>-2.4</th>
<th>-1.0</th>
<th>-2.9</th>
<th>-5.6</th>
<th>-0.3</th>
</tr>
</thead>
<tbody>
<tr>
<td>P-value</td>
<td>0.20</td>
<td>0.06</td>
<td>0.04</td>
<td>0.03</td>
<td>0.39</td>
</tr>
</tbody>
</table>
Microbiomes Differ More By Supplier Than Production System


**PERMANOVA**

Production System = 0.14
Supplier < 0.01

### Figure A

![Graph showing percent relative abundance for different suppliers and production systems.]

### Figure B

![Bar chart showing percent relative abundance of different bacterial families across CONV and RWA for each supplier.]

PERMANOVA P Production System = 0.14
PERMANOVA P Supplier < 0.01
AMR in CONV and RWA Ground Beef Conclusions

- Similar levels of AMR in CONV and RWA ground beef.
  - TET\textsuperscript{r} *E. coli* higher in CONV.
  - *tet*(A) & *tet*(B) higher in RWA.

- Ground beef microbiomes varied more by supplier than by production system
  - ?Processing interventions \Rightarrow Similar carcass microbiome \Rightarrow product environmental exposure directs microbiome?
AM Use and AMR in Beef Cattle Conclusions

• Similar levels of AMR in CONV and RWA ground beef.
  ➢ TET\(^\text{r}\) E. coli higher in CONV.
  ➢ tet(A) & tet(B) higher in RWA.

• Ground beef microbiomes varied more by supplier than by production system
  ➢ ?Processing interventions ➔ Similar carcass microbiome ➔ product environmental exposure directs microbiome?

• **Further reductions in AM use unlikely to reduce AMR in meat.**

• **Beliefs and assumptions regarding AMR levels in RWA ground beef should be re-examined.**

Terrance M. Arthur, Tommy L. Wheeler, John W. Schmidt*

[john.w.schmidt@ars.usda.gov](mailto:john.w.schmidt@ars.usda.gov)

Meat Safety and Quality Research Unit
U.S. Meat Animal Research Center
Clay Center, Nebraska

US Dept. of Agriculture - Agricultural Research Service

Nebraska One Health Stakeholder Meeting
December 6, 2017 - Omaha, NE
Effects of 5-day CTC on AMR

Previous Results:
- No long term differences TET$^+$ E. coli in feces or pen surface material.
- No differences in 3GC$^+$ E. coli.

**TET$^+$ E. coli**

![Graph showing TET$^+$ E. coli concentration over time](image1)

**Generic E. coli**

![Graph showing generic E. coli concentration over time](image2)
New qPCR Results:
• No differences in 10 gene abundances by qPCR.
Compared AMR in 3 cattle feedlot ponds, 3 swine waste lagoons, and effluents from 3 municipal WWTPs.

- More diverse AMR in WWTP effluent.
- More macrolide resistance in cattle and swine wastes.
  - More macrolide use in animals.
- More β-lactam resistance (cephalosporin and carbapenem) in WWTP effluent.
  - More β-lactam use in humans.
- More fluoroquinolone resistance in WWTP effluent.
  - More fluoroquinolone use in humans.
Other Published AMR Studies

- Therapeutic ceftiofur (3GC) injections have no long term impact on ARB.
  - Feedlot cattle (only *E. coli* studied).
  - Pasture beef cows (*E. coli, Salmonella, Enterococcus*).

**References**


  Influence of Therapeutic Ceftiofur Treatments of Feedlot Cattle on Fecal and Hide Prevalences of Commensal *Escherichia coli* Resistant to Expanded-Spectrum Cephalosporins, and Molecular Characterization of Resistant Isolates

  John W. Schmidt, Dee Griffin, Larry A. Kuehn, Dayna M. Brichta-Harhay

  U.S. Department of Agriculture, Agricultural Research Service, Romal L. Hruska U.S. Meat Animal Research Center, Clay Center, Nebraska, USA; Great Plains Veterinary Educational Center, School of Veterinary Medicine and Biomedical Sciences, University of Nebraska—Lincoln, Clay Center, Nebraska, USA

  In the United States, the *bla*<sub>CMY-2</sub> gene contained within incompatibility type A/C (IncA/C) plasmids is frequently identified in


  Antimicrobial-Resistant Fecal Bacteria from Ceftiofur-Treated and Nonantimicrobial-Treated Comingled Beef Cows at a Cow–Calf Operation

  Getahun E. Agga, John W. Schmidt, and Terrance M. Arthur

  We compared the occurrences of 3rd-generation cephalosporin-resistant (3GC<sup>+</sup>), tetracycline-resistant (TET<sup>+</sup>), and...
Final Thoughts

- Reducing AM use in cattle production is still a good practice.

- However, further reductions in U.S. AM use during cattle production should not be expected to have relevant impacts on AMR levels or human health outcomes.
Ongoing Studies

• AMR in CONV & RWA pork.

• Tylosin impact on AMR, including shorter duration of in-feed tylosin.

• Comparison of AMR between Beef and Dairy Cattle since antimicrobial usage differs in dairies. Collaboration With Colorado State Univ.

• Culture, qPCR, metagenomic examination of 300 CONV and 300 RWA retail ground beef samples. Collaboration With Colorado State Univ.

• Presence of Carbapenem Resistant Bacteria (CRB) in food-animals.

• AMR impact of land application of cattle manure (CONV & RWA), swine manure (CONV & RWA), and WWTP bio-solids.

• Assessing the contribution of nutrient enrichment to the detection of AMR.
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john.w.schmidt@ars.usda.gov

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U.S. Meat Animal Research Center

- 35,000 acres
- 6,500 cattle
- 4,000 sheep
- 700 swine litters/year

- Genetics, Breeding, & Animal Health
- Nutrition & Environmental Management
- Meat Safety & Quality
- Reproduction

- ~45 Scientists
- ~7 Post-docs
- Summer Interns

Terrance M. Arthur, Microbiologist  Terrance.Arthur@ars.usda.gov
Tommy L. Wheeler, Meat Scientist  Tommy.Wheeler@ars.usda.gov
John W. Schmidt, Microbiologist  John.W.Schmidt@ars.usda.gov