IS VACCINATION OF CATTLE THE ANSWER?
WHAT’S THE EVIDENCE?

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E. coli Webinar
Washington State University
University of Nebraska-Lincoln

NEW VACCINE!!!
-We stand at the doorway to pre-harvest control of STEC O157...

... but should we step inside?
Rates of human STEC O157 illness differ by season

2004 FoodNet Final Report, CDC

Rates of ground beef contamination differ by season

Season explains the prevalence of fecal shedding in commercial feedyards

Summer *E. coli* O157:H7
- 4,952 cattle, 44 pens
  - 1,501 culture positive (30%)
  - EVERY pen (100%)
  - Variable prevalence (1-80%)

Winter *E. coli* O157:H7
- 2,941 cattle, 30 pens
  - 179 culture positive (6.1%)
  - 16/30 pens (53%)
  - Variable prevalence (0-56%)
  - Significant difference by season

Smith DR, et al. 2001. J Food Prot 64 (12) 1899-1903

This project was supported by the National Research Initiative of the USDA Cooperative State Research, Education and Extension Service, grant number #0002501.
What are the key determinants of human STEC infection?

Seasonal variation for human STEC O157 illness, prevalence of STEC O157 in cattle and ground beef, and ground beef supply (expressed as a percentage of the mean)

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**Seasonal variation for human STEC O157 illness**, prevalence of STEC O157 in cattle and ground beef, and ground beef supply (expressed as a percentage of the mean)

Live cattle serve as an important reservoir for human *E. coli* O157:H7 exposure
There is a positive correlation between carcass contamination and pre-harvest carriage of O157:H7 by cattle

“The association between fecal prevalence and carcass contamination indicates a role for control of EHEC O157 in cattle on the farm toward reducing the risk of human infection from ingestion of undercooked beef or cross-contamination of other foods. Obviously, such a control program would also reduce the risk of environmental contamination, another potential source of human infection.”


See also: Arthur et al. 2004. J Food Prot, 67(4) 658–665
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TIME and E. coli O157:H7

Longitudinal study
Research Feedyard

Conditions of natural O157:H7 exposure

Feces from 100 steers (10 pens of 10) cultured each week

*E. coli* O157:H7 recovered every week and at least once from every animal

Conclusions

*E. coli* O157:H7 is ubiquitous to cattle populations

Variable in prevalence by TIME and PLACE

Bacterial ecology: what affects the probability for cattle to shed *E. coli* O157:H7?

1) a **pen environment** when it favors bacterial survival and fecal-oral transmission, and/or

2) a **gut environment** when it favors its colonization and replication

• Smith et al. *J Food Prot.* 2001, 64 (12) 1899-1903.


• Smith et al. *Foodborne Pathogens and Disease.* 2005, 2(1):50-60
What can we do about it?

Strategies for intervention:

- Limiting direct environmental exposure
  - Seasonal differences

- Reducing the duration of infection
  - Target of interventions
Making the gut unfavorable to STEC infection

Primary Sites of *E. coli* O157:H7 colonization:

- **rumen**
  - (Brown et al. 1997)

- **colon**
  - (Cray & Moon, 1995)
  - (Grauke et al. 2002)

- **terminal rectum**
  - (Naylor et al. 2003)
  - (Argenzio, 1993)

Enterohemorrhagic *E. coli* colonization and infection of calf rectum

Feed components
Chemicals
Competing microflora
Immune modulation

News Flash!

World’s First Cattle Vaccine to Reduce E. coli O157 Threat Receives Full Licensing Approval in Canada
Econiche™ now available to reduce risk of food and water contamination

BELLEVILLE, ON, October 27, 2008 – Bioniche Life Sciences Inc. (TSX: BNC), a research-based, technology-driven Canadian biopharmaceutical company, today announced that Econiche™, the world’s first vaccine designed to reduce the shedding by cattle of Escherichia coli (E. coli) O157:H7, has received full licensing approval from the Canadian Food Inspection Agency (CFIA). Econiche is now available for unrestricted use by Canadian cattle producers and their veterinarians.

Beef safety takes a new step
By Drovers news source | Wednesday, March 11, 2009

Production-level food safety interventions have been a long time in coming, but a conditional license for an E. coli vaccine may be a step in the right direction. The United States Department of Agriculture has granted a conditional license to Epitopix, LLC for an E. coli O157 vaccine. The new vaccine is labeled for use in cattle to reduce the prevalence of the E. coli O157-carrier state and for reduction in the amount of E. coli O157 shed in feces to minimize E. coli exposure and infection of herd-mates. Although the product license is conditional while additional efficacy studies are completed, USDA approval allows Epitopix to make the vaccine immediately available for use by the beef industry.
Vaccination as a strategy to reduce shedding of *E. coli* O157:H7 in cattle populations

Stimulate immunity against type III secreted proteins that mediate bacterial attachment to intestinal cells

Marketed in Canada as Econiche™ by Bioniche Life Sciences

Courtesy Dr. Brett Finlay
Siderophore Receptor Porin Protein (SRP) vaccines

Epitopix

When iron is in short supply, bacteria develop siderophore receptors, specialized proteins that steal iron from the host. SRPs in the vaccine cause antibodies to be developed as part of the normal immune response.

Antibodies prevent iron from passing through the SRPs in the cell's outer membrane. Bacteria are deprived of iron and die.

http://www.epitopix.com/srp_vaccines.asp (02/28/10)
Both vaccines have been efficacious in vaccine clinical trials.

<table>
<thead>
<tr>
<th>Significant findings (natural exposure):</th>
<th>Bioniche</th>
<th>Epitopix</th>
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<tbody>
<tr>
<td>Reduced probability for shedding in feces</td>
<td>x</td>
<td>x</td>
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<td>Reduced colonization (terminal rectum mucosa cells)</td>
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<tr>
<td>Reduced environmental detection/ oral exposure (ROPES)</td>
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<tr>
<td>Reduced probability to contaminate hides</td>
<td>x</td>
<td>x</td>
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<tr>
<td>Herd-immunity / group-regional dynamics</td>
<td>x</td>
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<tr>
<td>Dose-effect (3 doses have better efficacy than 2)</td>
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<td>Reduced CFU/g</td>
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<tr>
<td>Tested in commercial feedlots (&gt;50 head/pen)</td>
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A Systematic Review of Vaccinations to Reduce the Shedding of *Escherichia coli* O157 in the Faeces of Domestic Ruminants

K. G. Snedeker¹,², M. Campbell¹ and J. M. Sargeant¹,²

¹ Centre for Public Health and Zoonoses, Ontario Veterinary College, University of Guelph, Guelph, ON, Canada
² Department of Population Medicine, Ontario Veterinary College, University of Guelph, Guelph, ON, Canada

**Impacts**

- This study provides a meta-analysis of results from studies examining the effects of vaccination on prevalence of *E. coli* O157 in ruminant faeces.
- It suggests that Type III and SRP protein vaccines reduce statistically significantly the prevalence of *E. coli* O157 in beef cattle faeces.
- It suggests that further study is needed, particularly with regards to the SRP protein vaccine, to examine the effect of vaccines at feedlot pen densities.
Type III secreted protein vaccine

SRP vaccine
What needs to be discovered before action is taken?

- **Efficacy** – does the intervention have a biological effect?
- **Effectiveness** – will it be useful?
  - What level of efficacy is worthwhile?
  - To whom?
  - How best to use in commercial applications
    - Will it be useful in the food system?
    - How to implement, document, validate...
  - Transfer of value
Efficacy – does the intervention have a biological effect?

Effectiveness – will it be useful?
Economic assessment

- How much is it worth (to whom)?
  - Marginal costs vs marginal returns

Example: based on cost of human O157 illness

“For our purposes, a vaccination program is considered cost effective as long as the marginal cost of vaccination is no greater than the marginal benefit of a foregone human illness.”

“If the per unit vaccination cost is assumed to be $3.00, then it will be optimal to prevent approximately 21,000 human illnesses each year. This level of control will require vaccinating 22 million cattle intended for slaughter each year at a total cost of $66 million. The total benefits accrued as a result of foregoing 21,000 human illnesses is approximately $131 million (21,000 foregone cases $6256 per case)....”

Withee et al. 2009. Foodborne Pathogens and Disease 6(7)
Are pre-harvest efforts useful to the beef industry? – a systems process control approach
Process Control

- How might a pre-harvest intervention affect O157:H7 shedding compared to what we’ve observed in winter or summer?
- Winter serves as a benchmark for comparison
Modeling pre-harvest interventions in the context of existing seasonal differences

Treatment efficacy based on randomized clinical vaccine trials

- 58% reduction in fecal shedding – from Snedeker
- Lognormal distribution
- 5,000 pen simulations (@risk software)
- 500,000+ cattle
Modeling pre-harvest interventions in the context of existing seasonal differences

Seasonal Prevalence in Commercial Feedyards

- **Summer**
  - Lower risk
  - Higher risk

- **Winter**
  - Lower risk
  - Higher risk

**Post-Vaccination**

Predicted summer shedding after using an intervention with 58% efficacy
Conclusions

Protecting food safety and quality by taking action both pre-harvest and post-harvest has history and tradition in the US.
Conclusions

Science is beginning to deliver efficacious **pre-harvest** tools against STEC O157
Conclusions

The question of whether these tools will be useful remains unanswered

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