Pre-harvest:

1. What Happened in 2007 – Hypotheses
2. Pre-harvest Opportunities for Control of *E. coli O157:H7*

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West Texas A&M University
Canyon, Texas

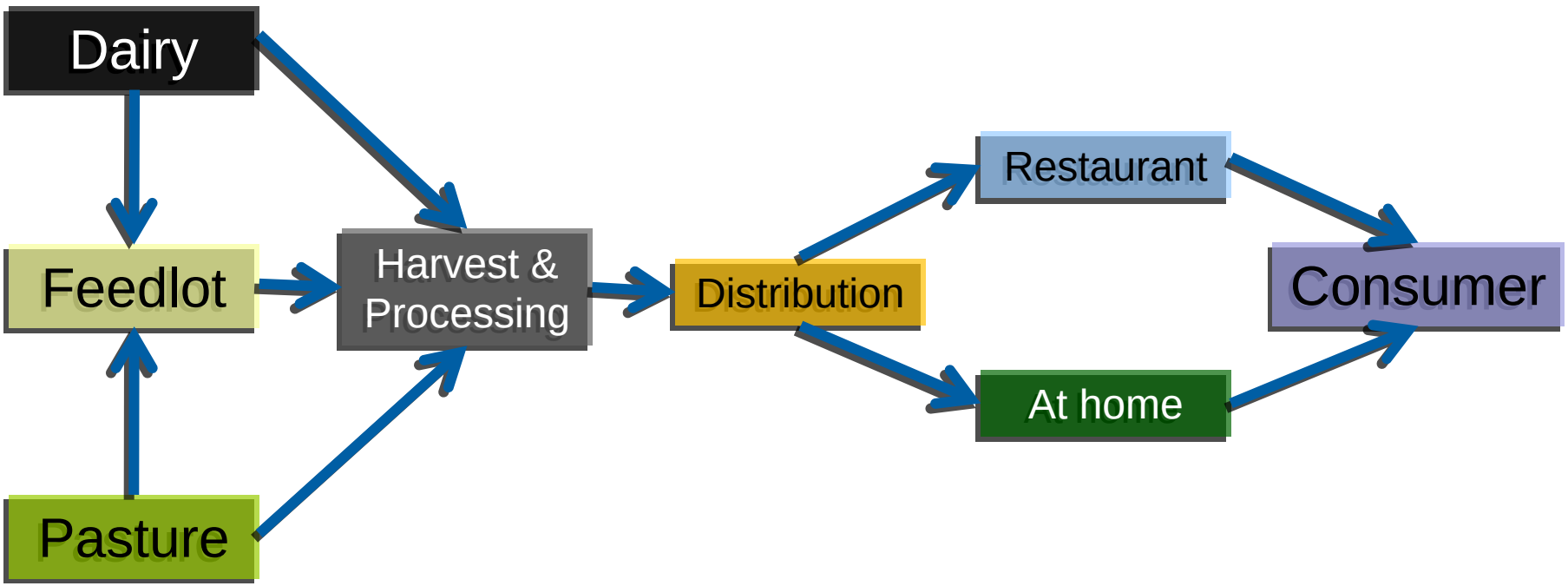
FSIS Public Meeting: Shiga Toxin-Producing *E. coli*: Addressing the Challenges, Moving Forward With Solutions
April 10, 2008, Washington, DC

Outline of Presentation

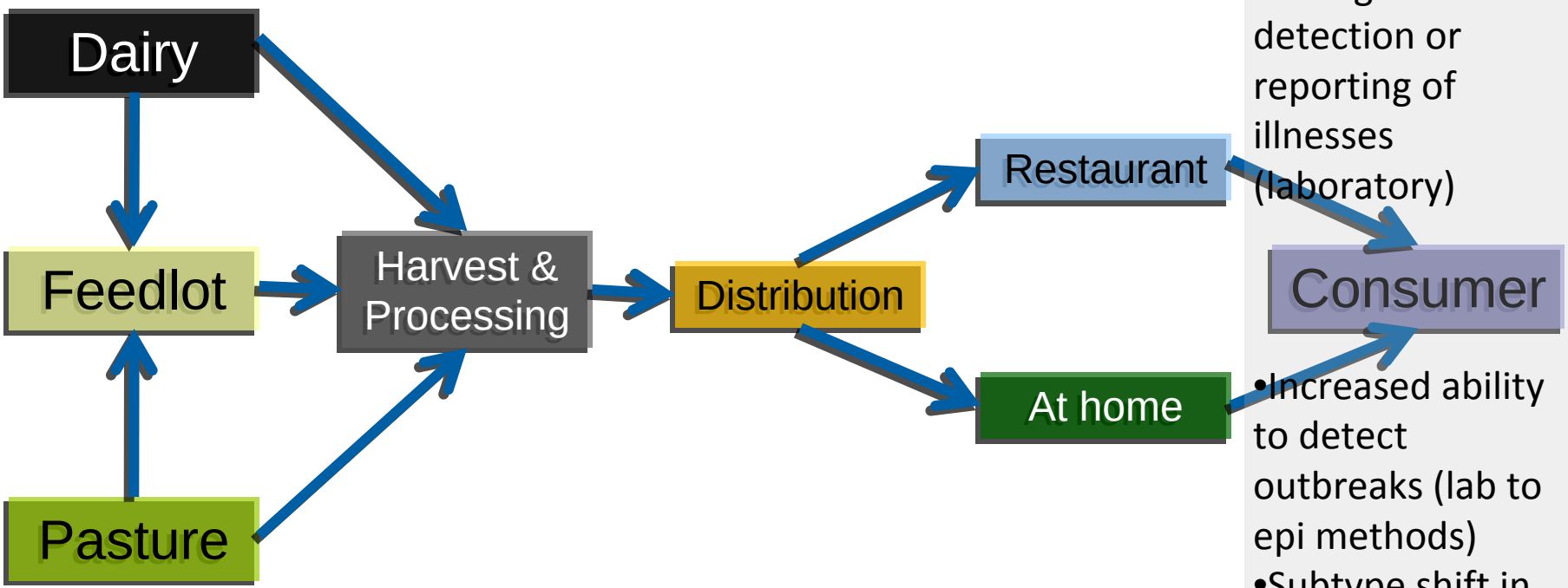
1. What factors could change pre-harvest *E. coli* O157 burden thereby explaining increased recalls and illnesses during 2007
   - Will we ever know?
2. Opportunities for control of *E. coli* O157 in the pre-harvest environment
   - What is the purpose of pre-harvest interventions
   - *Field efficacy* data of candidate pre-harvest interventions and Summary
3. Summary

Beef Production/Consumption Continuum

- Many potential sites at which changes could lead to increased recalls and illnesses

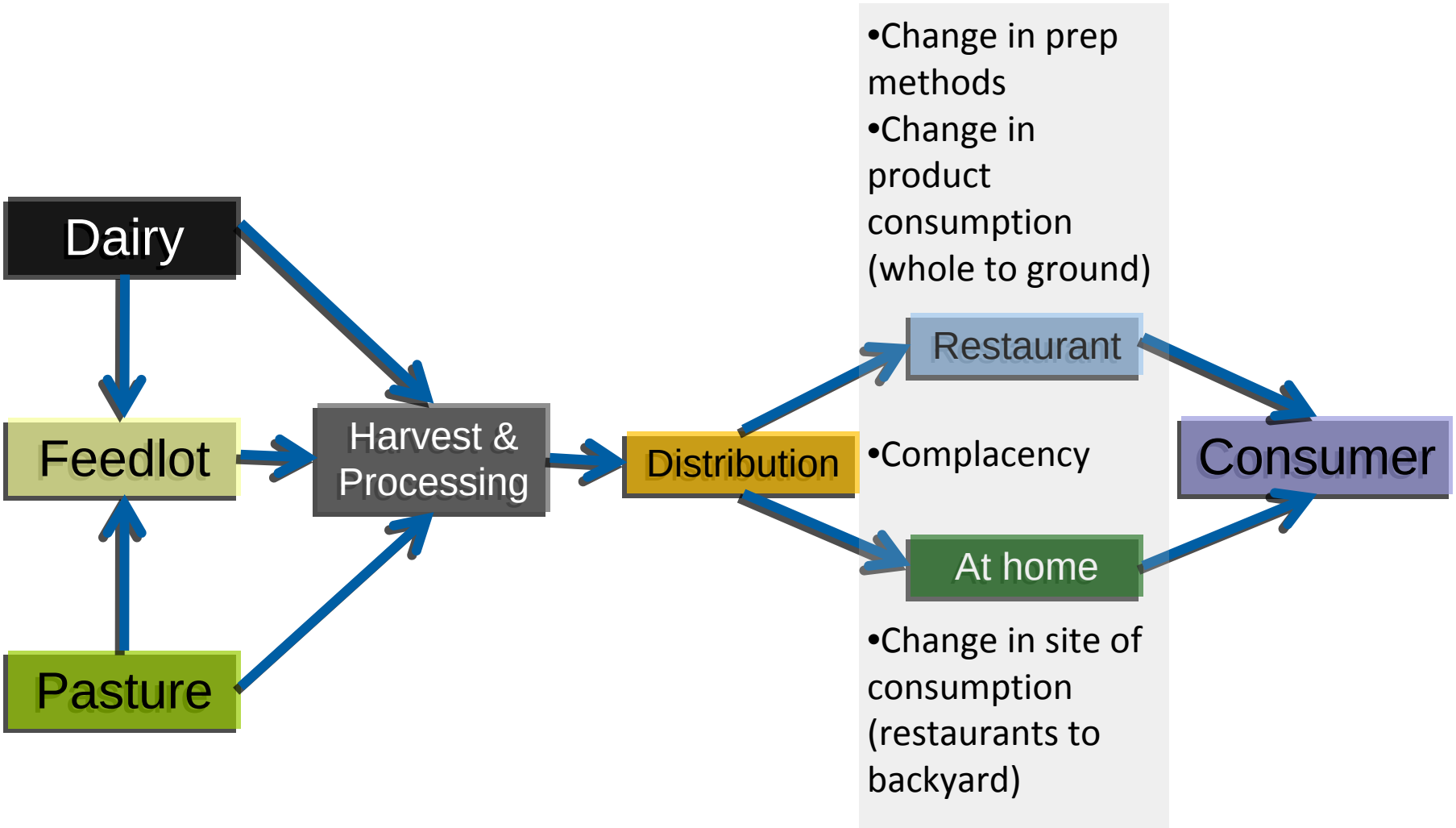


Beef Production/Consumption Continuum



- Change in reporting of illnesses (patient)
- Change in detection or reporting of illnesses (laboratory)
- Increased ability to detect outbreaks (lab to epi methods)
- Subtype shift in *E. coli* O157

Beef Production/Consumption Continuum



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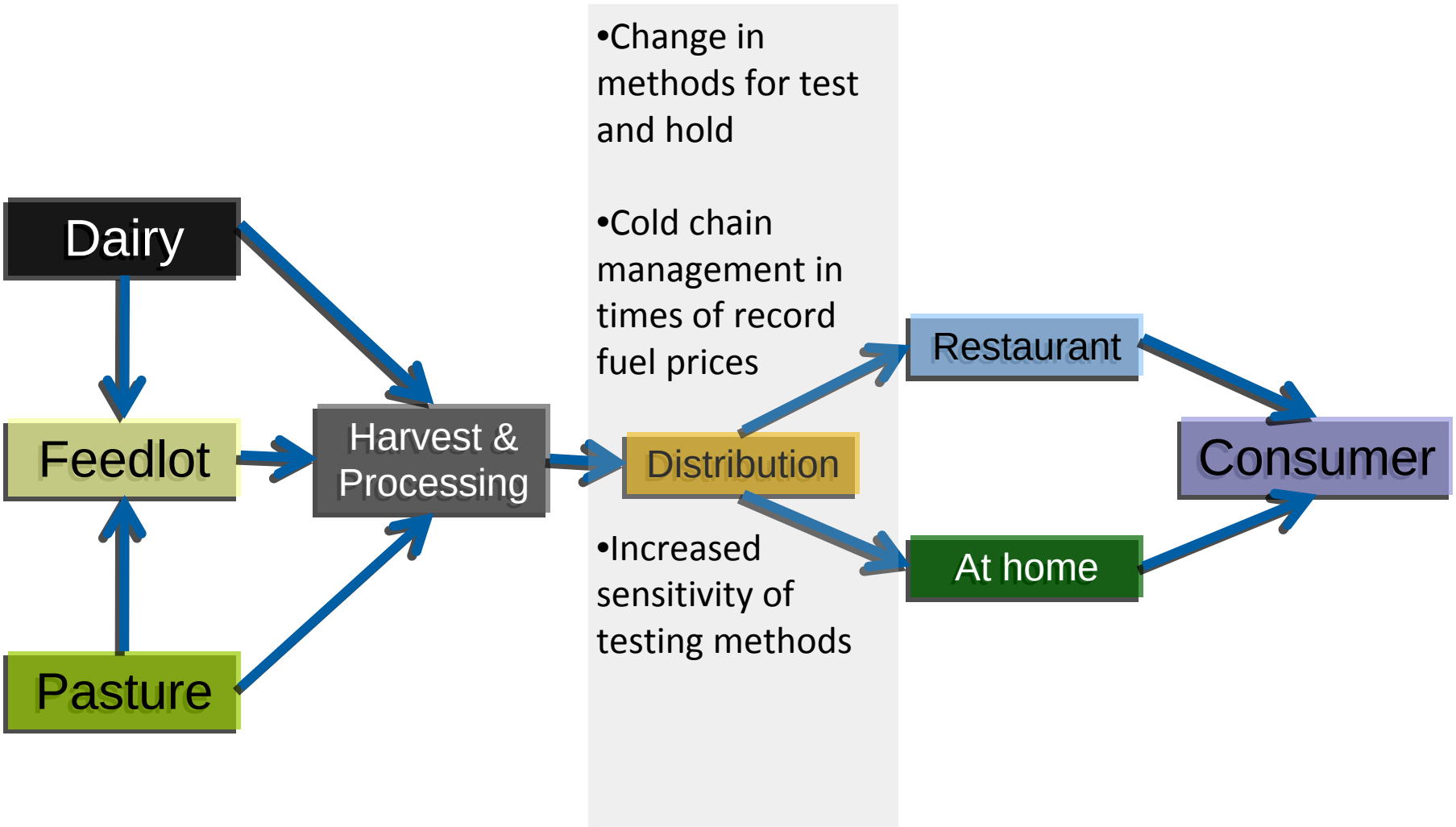

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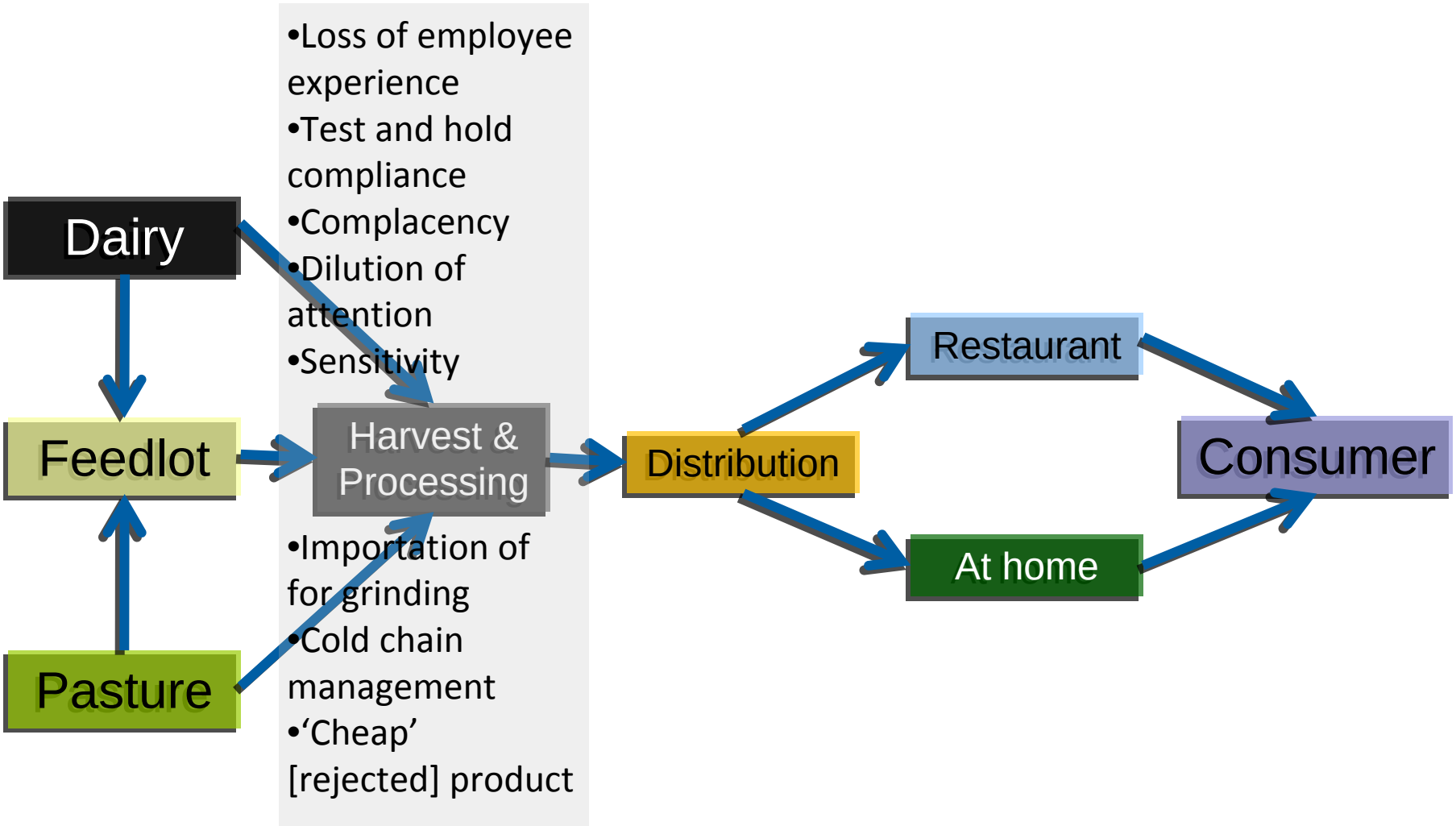

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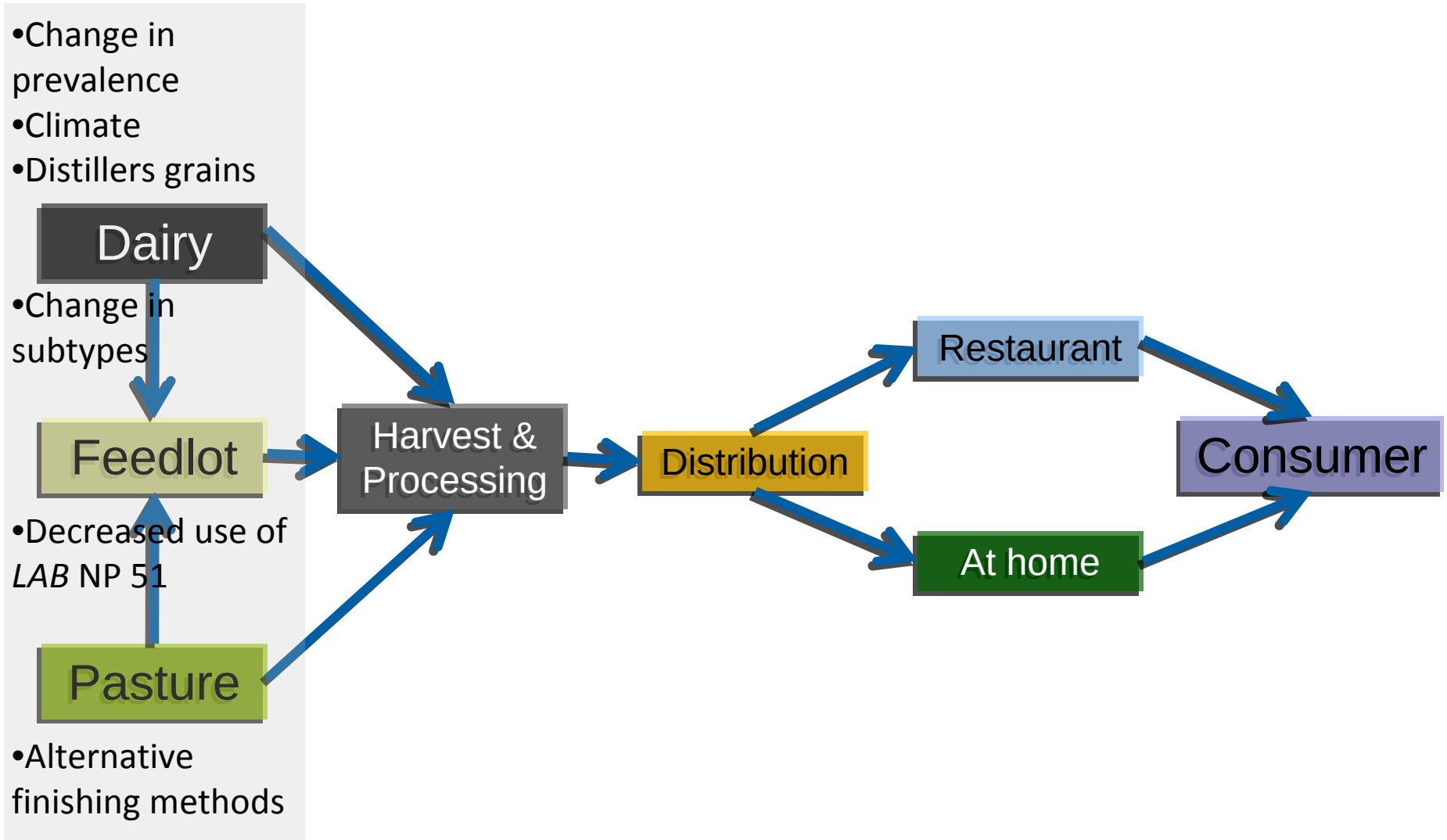
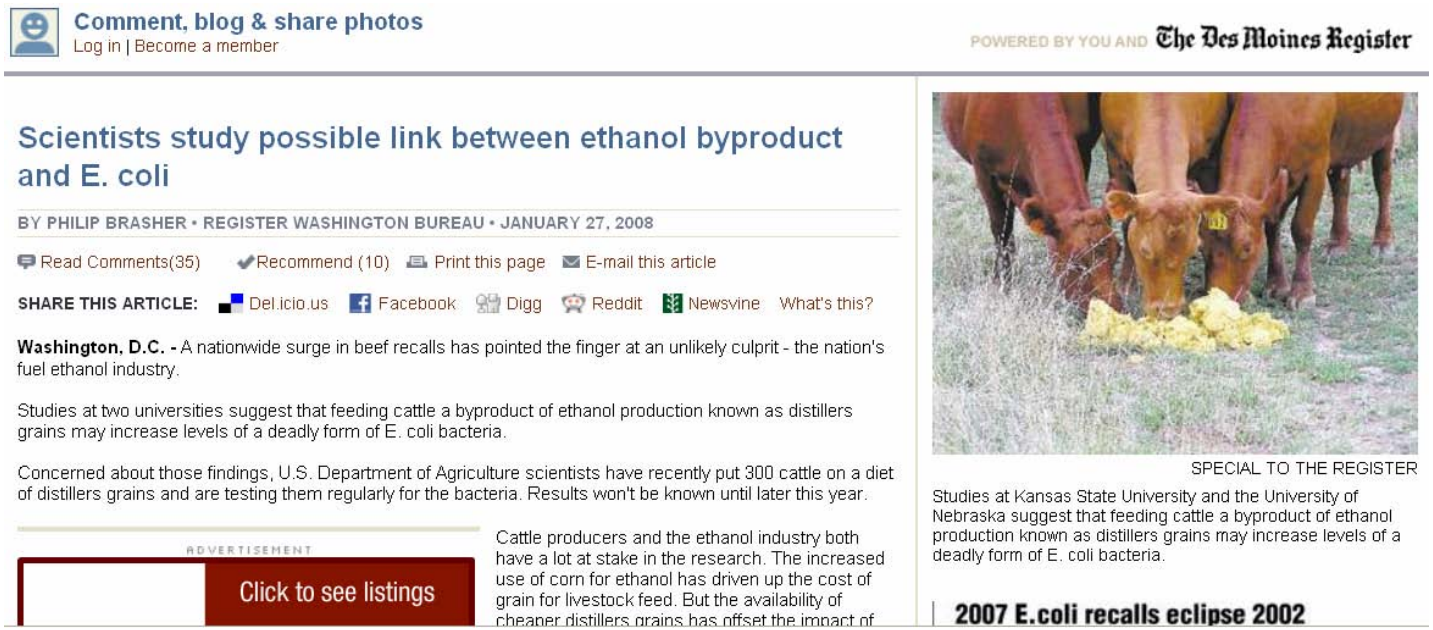


Pre-Harvest Hypotheses

- Use of Distiller's grains in cattle rations
  - Some evidence in published research
  - Dewell et al., *Foodborne Pathog Dis*. 2005;2(1):70
  - Jacob et al., *Appl Environ Microbiol*. 2008 Jan;74(1):38



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Scientists study possible link between ethanol byproduct and E. coli

BY PHILIP BRASHER • REGISTER WASHINGTON BUREAU • JANUARY 27, 2008

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SHARE THIS ARTICLE: Del.icio.us Facebook Digg Reddit Newsvine What's this?

Washington, D.C. - A nationwide surge in beef recalls has pointed the finger at an unlikely culprit - the nation's fuel ethanol industry.

Studies at two universities suggest that feeding cattle a byproduct of ethanol production known as distillers grains may increase levels of a deadly form of E. coli bacteria.

Concerned about those findings, U.S. Department of Agriculture scientists have recently put 300 cattle on a diet of distillers grains and are testing them regularly for the bacteria. Results won't be known until later this year.

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Cattle producers and the ethanol industry both have a lot at stake in the research. The increased use of corn for ethanol has driven up the cost of grain for livestock feed. But the availability of cheaper distillers grains has offset the impact of

SPECIAL TO THE REGISTER

Studies at Kansas State University and the University of Nebraska suggest that feeding cattle a byproduct of ethanol production known as distillers grains may increase levels of a deadly form of E. coli bacteria.

2007 E.coli recalls eclipse 2002

Pre-Harvest Hypotheses

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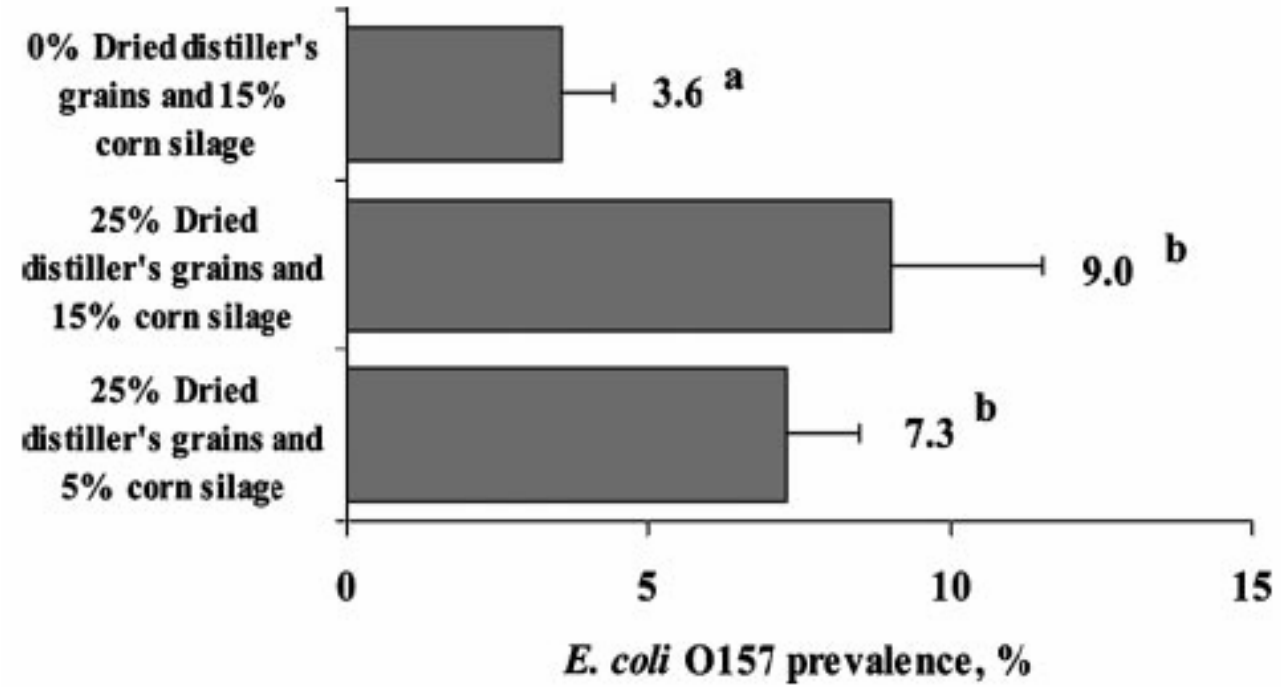

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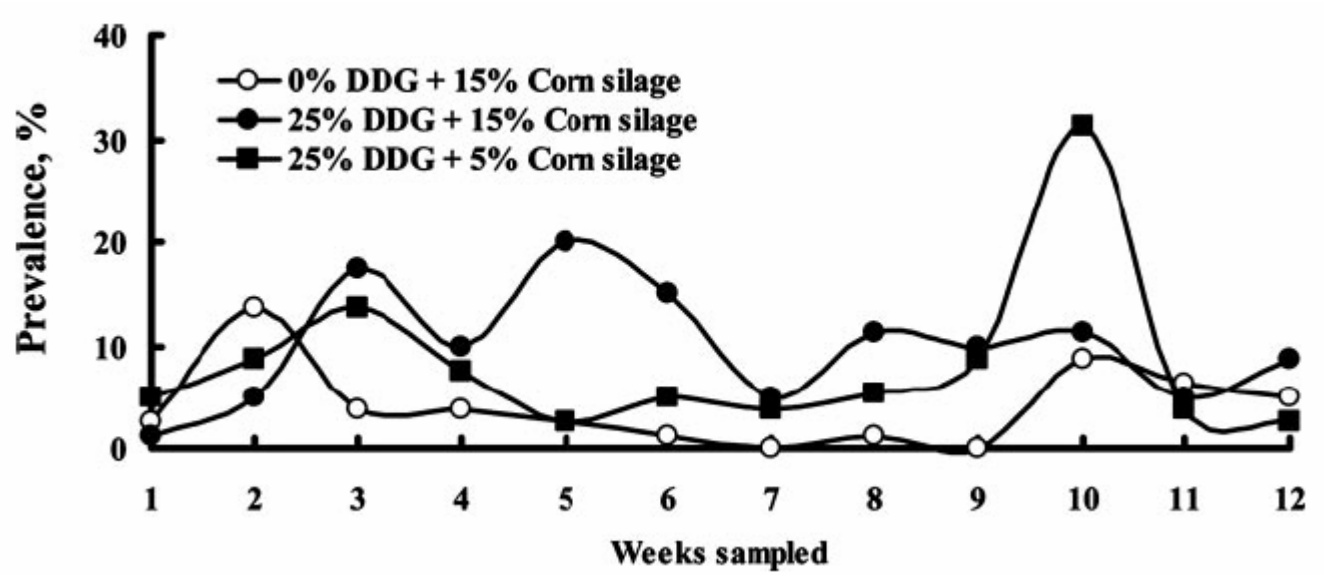

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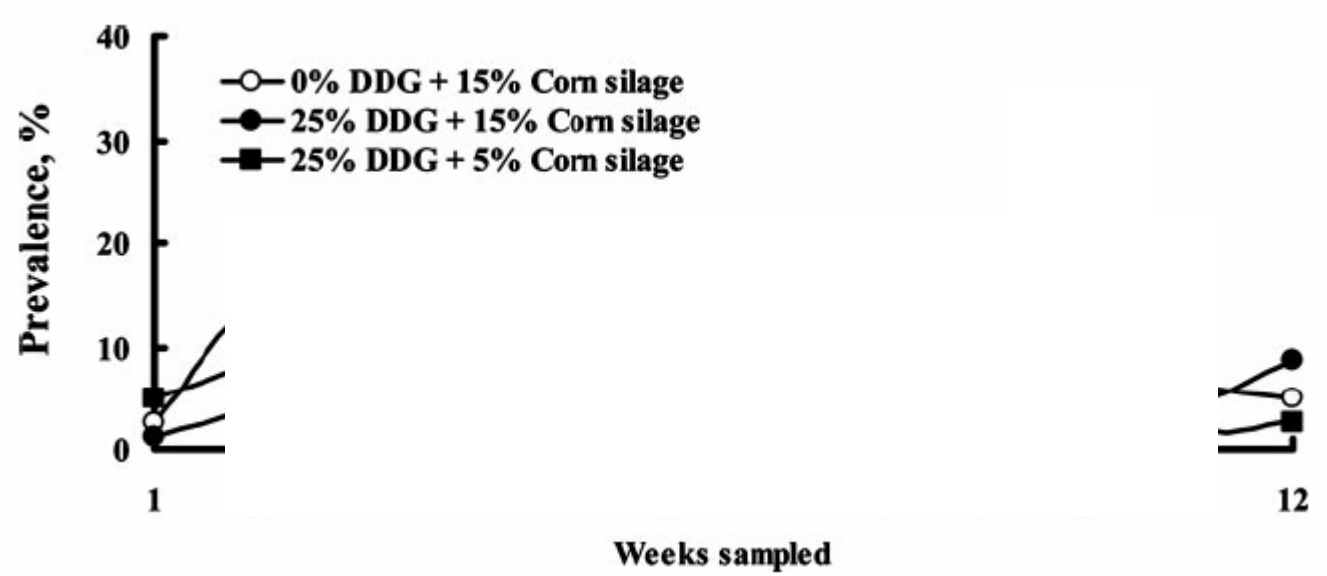
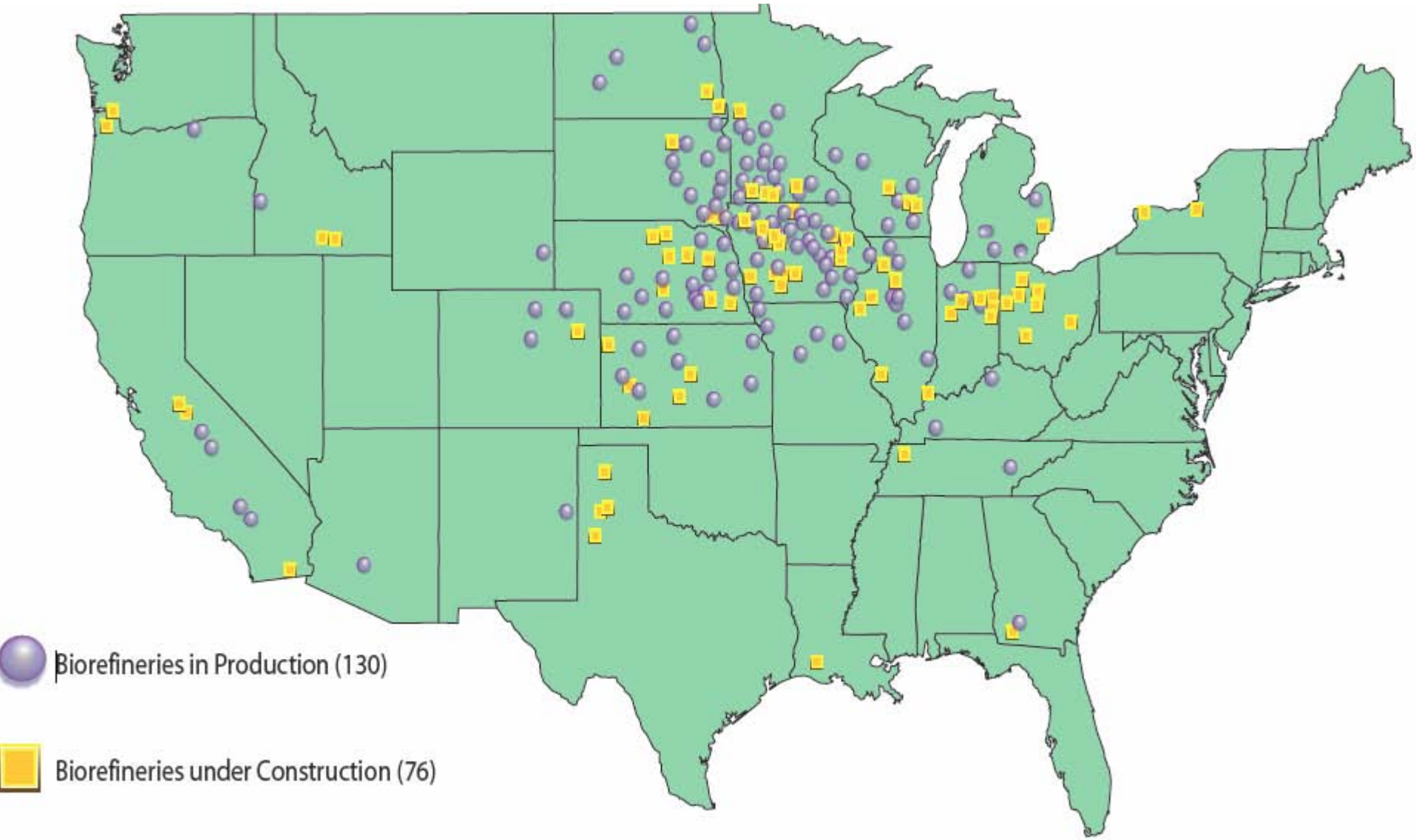


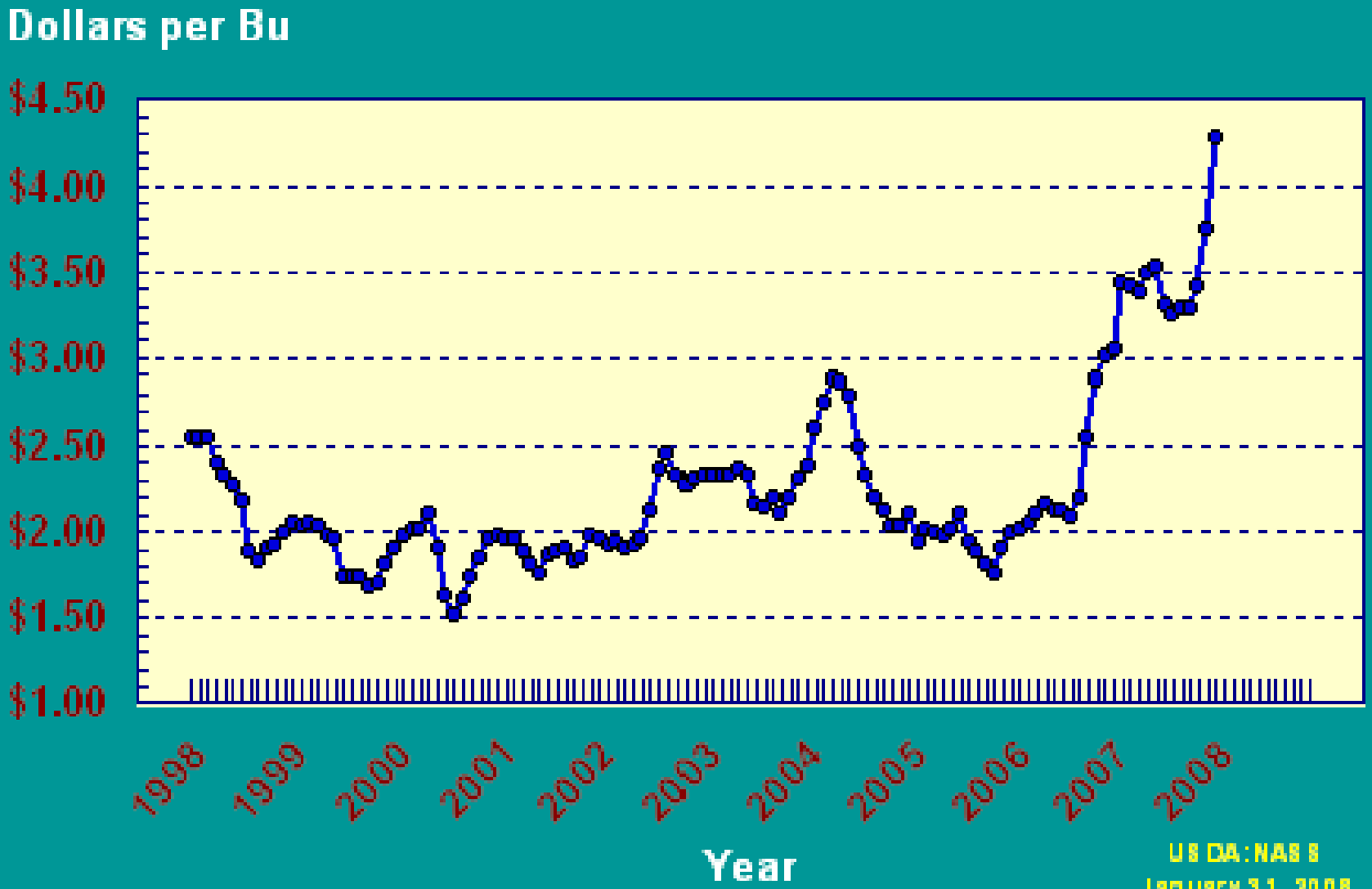
U.S. Ethanol Biorefinery Locations



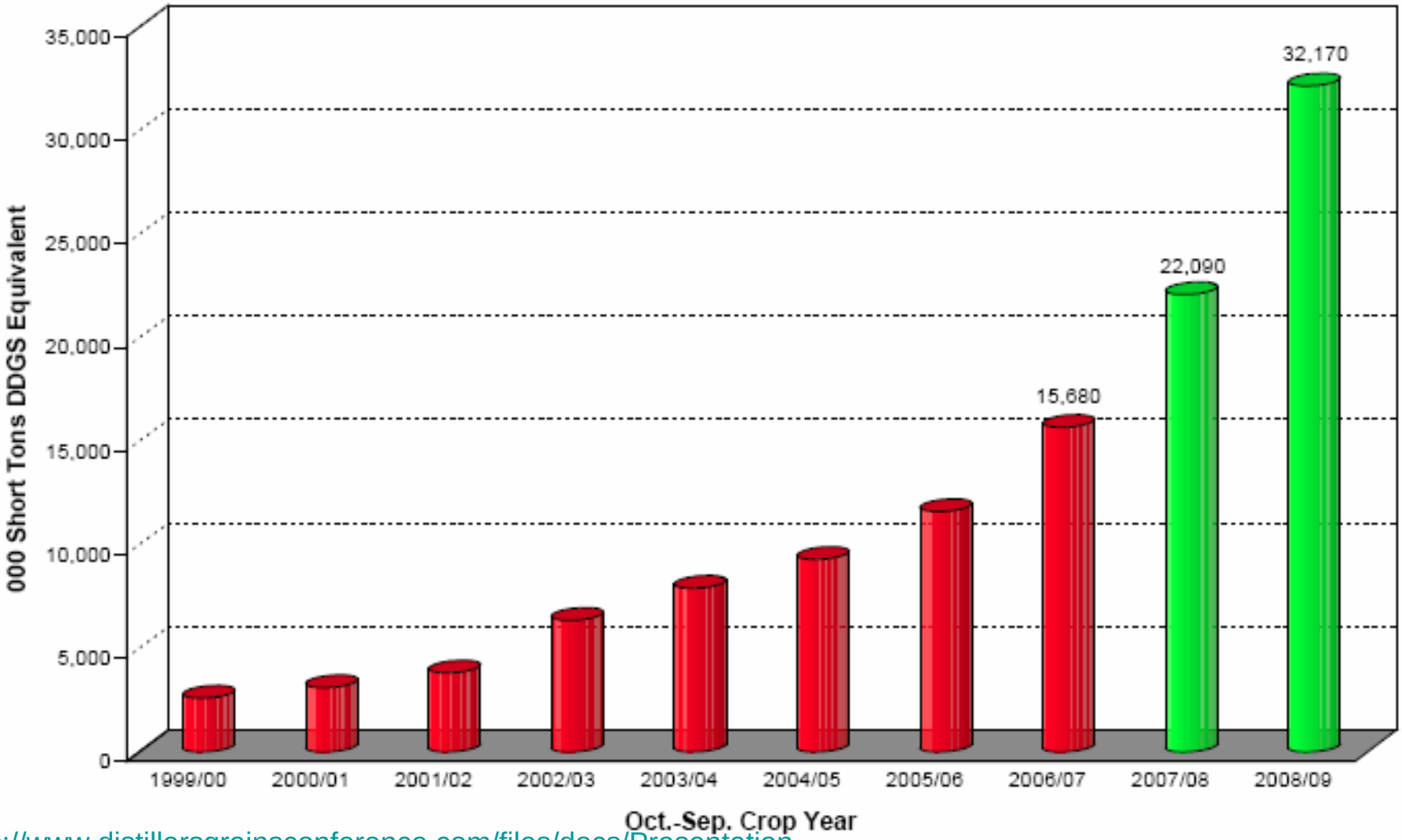
http://www.ethanolrfa.org/objects/douments/plantmap_oct_4_2007.pdf

Source: Renewable Fuels Association
10.4.07

Prices Received, Corn, US



Distillers Grains Production Will Increase Rapidly in Line With Ethanol Output



https://www.distillersgrainsconference.com/files/docs/Presentations/IDGC07-20071022-GS1-Richman.pdf

Source: Informa Economics

2006 NASS Ethanol Co-Products Used for Livestock Feed Released June 29, 2007

Operations Feeding and Not Feeding Co-Products

Item	% Feeding Co-Products	% Not Feeding but Considered Feeding	% Not Feeding, Not Considered Feeding
Dairy Cattle	38	22	40
Cattle on Feed	36	34	30
Beef Cattle	13	30	57

http://www.mnpork.com/producer/research/2007/EthFeed-06-29-2007%5B1%5D.pdf

Distiller's Grains and *E. coli* O157


The New York Times

Shift in Cow Feed May Make Beef Safer

By JANE E. BRODY
Published: September 11, 1998

Cornell University have found a way to virtually rid
of E. coli bacteria, including the bacteria that
have caused sickened thousands of consumers of
undercooked hamburgers.

- We were 'led to believe' that high-starch diets were the culprit
  - Diets with distiller's grains actually reduce starch content of diet
- I believe blaming distiller's grains is premature
  - More likely that distiller's grains has no or negligible effect
  - Highly publicized observations likely due to endemic instability of *E. coli* O157 shedding
- Compared to 0% distiller's grains
  - 10, 20 and 30% less likely to shed *E. coli* O157
  - 40 and 50% more likely to shed *E. coli* O157
    - Peterson et al., *J Food Prot*. 2007;70(11):2568

Distiller's Grains and *E. coli* O157

- Recent press release from K-State (same research team that reported link)
- Nagaraja reports: 'there was no significant effect of DDGS (P = 0.2)'

Feedstuffs
THE WEEKLY NEWSPAPER FOR AGRIBUSINESS

Feeding DDGs does not increase E. coli prevalence

printer friendly format email page

(3/25/2008)
Tim Lundeen

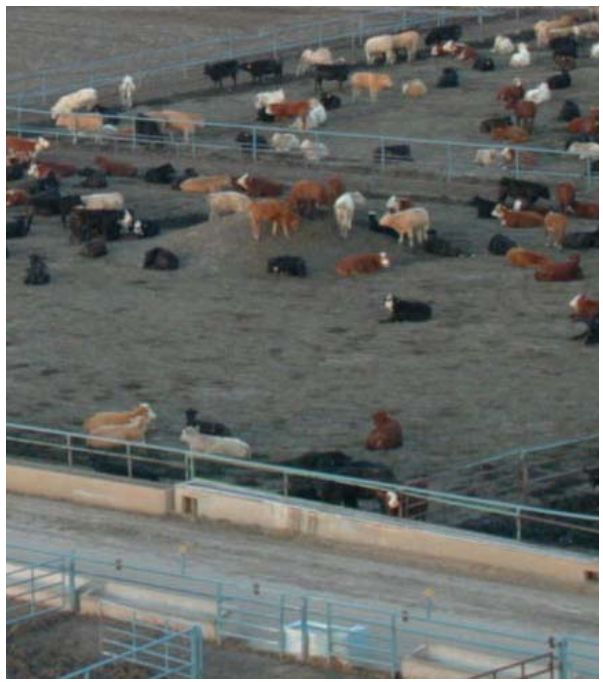
Research has shown no statistical difference in the prevalence of Escherichia coli O157:H7 or salmonella between cattle fed steam-flaked corn and those supplemented with dry distillers grain (DDG). The current study was funded by the Kansas Beef Council and conducted at Kansas State University. Previous research suggested that feeding DDGs increased E. coli O157:H7 shedding in fecal matter.

"Unlike our previous studies, we found no evidence to indicate that dietary inclusion of (DDGs) or corn processing methods have a significant effect on the prevalence of E. coli O157:H7 or salmonella in cattle feces," said Kansas State University professor of microbiology T.G. Nagaraja.

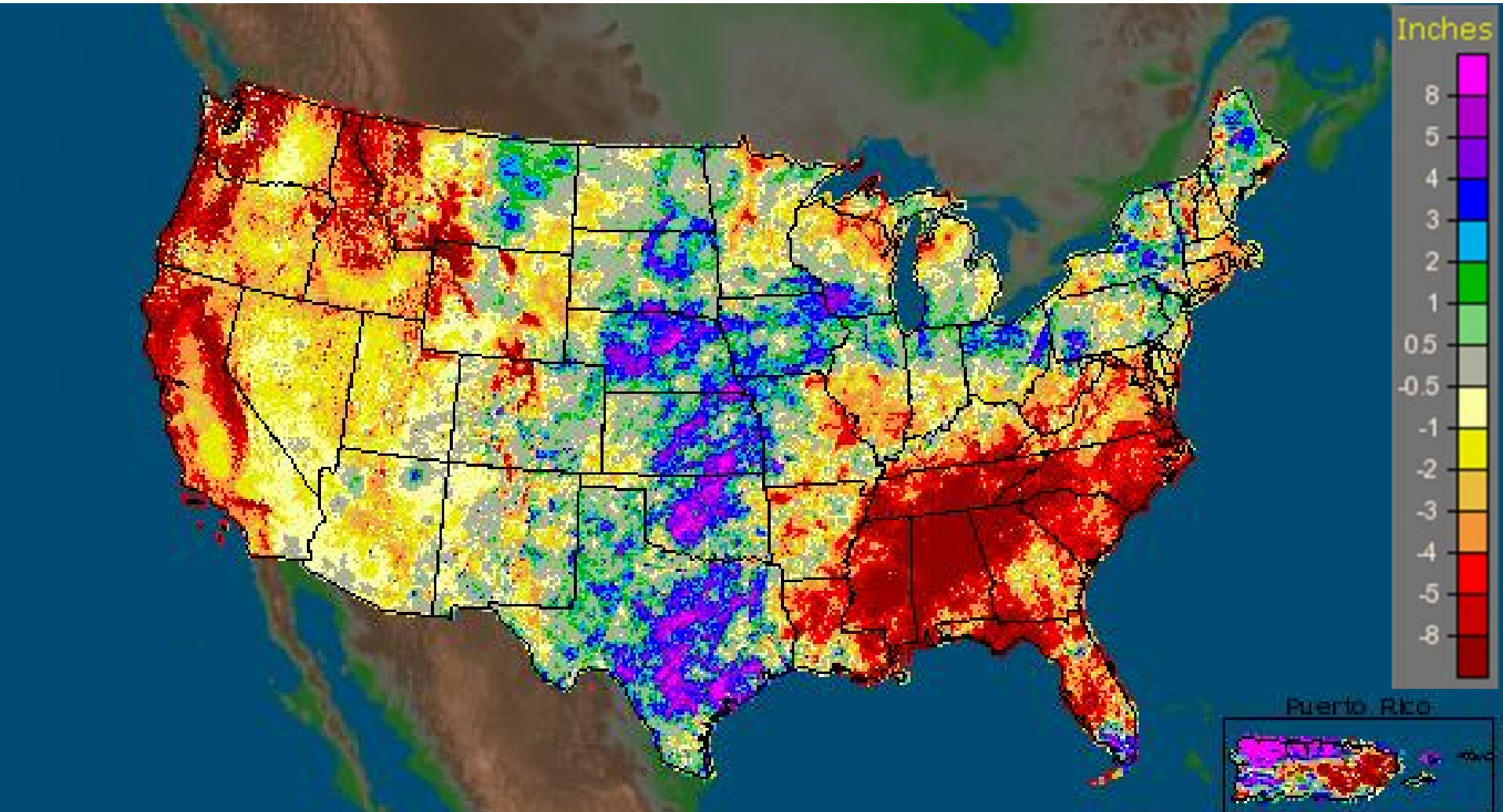
Nagaraja's previous research implicated DDG feeding in the prevalence of E. coli O157:H7 conflicted with research conducted at the University of Nebraska-Lincoln.

Climatic Events

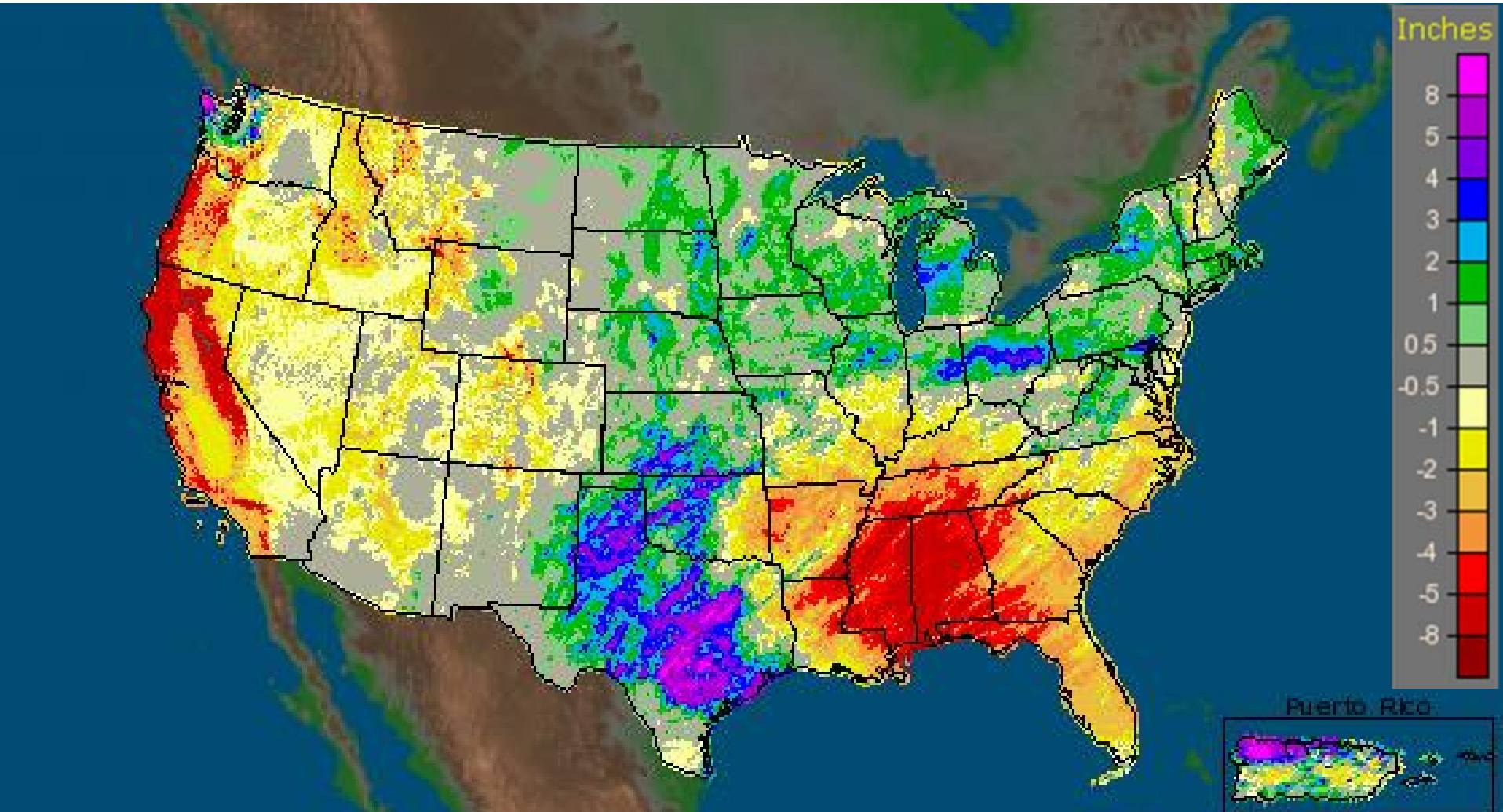
- *E. coli* O157 shedding is strongly seasonal in cattle
  - Macro-climatic change
- There is some evidence that condition of pen surface is associated with likelihood of shedding
  - Micro-climatic changes
  - Smith et al., *J Food Prot*. 2001;64(12):1899
  - Shedding associated with very wet or very dry pen surfaces



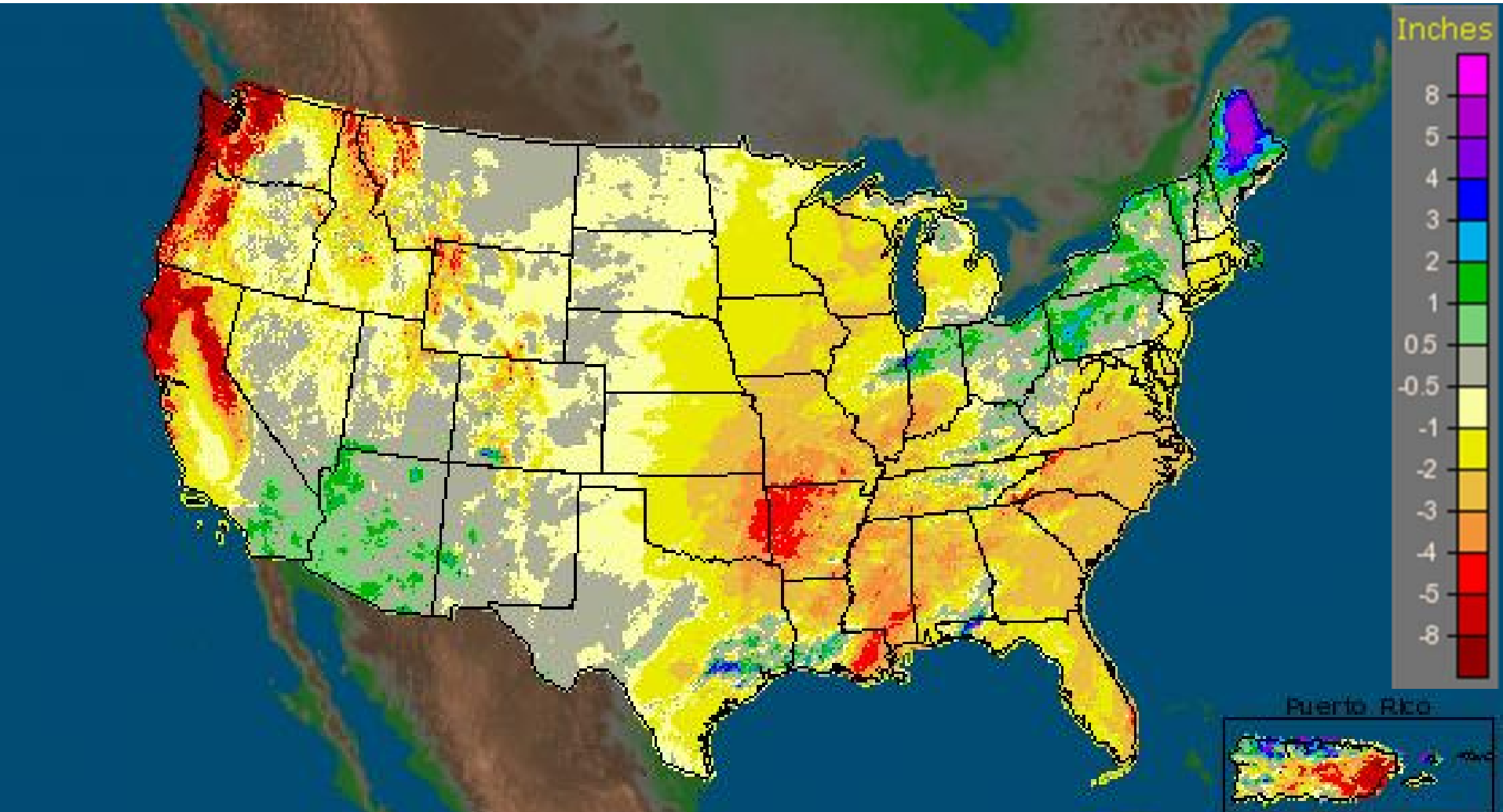
Precipitation for Year-2007 Departure from Normal



Precipitation March-2007 Departure from Normal



Precipitation November-2007
Departure from Normal



Climatic Events

- Hypotheses that some macro-climatic change was associated with a) change in prevalence and b) increased recalls during 2007
- Interesting concept and potential evidence to support this (at least in a very limited way)
- Challenging, however, to develop and implement testable hypotheses
  - Not just to test this putative etiology BUT to other proposed *causes* as well

Did Prevalence Even Change in 2007?

- It may be premature to speculate about (and where possible test) possible pre-harvest 'causes' of increased recalls during 2007
- No systematic evidence that prevalence (or bacterial subtype carried) in cattle presented for harvest actually changed
- In our research from 2001 to 2006, we averaged 20 to 25% prevalence during warm months
  - Prevalence in our 2007 field study was 7.3% and never exceeded 12%
    - Very similar to 2006 in the same feedlot in SW Kansas

Did Prevalence Even Change in 2007?

- We will likely never know if prevalence in cattle presented for slaughter changed
  - No systematical monitoring system designed to generate precise and accurate estimates of prevalence
- Highlights the opportunity for a purpose-designed sampling scheme to estimate prevalence of *E. coli* O157 on cattle presented for harvest
  - Purpose to look for marco changes in prevalence

Outline of Presentation

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   - Will we ever know?
2. Opportunities for control of *E. coli* O157 in the pre-harvest environment
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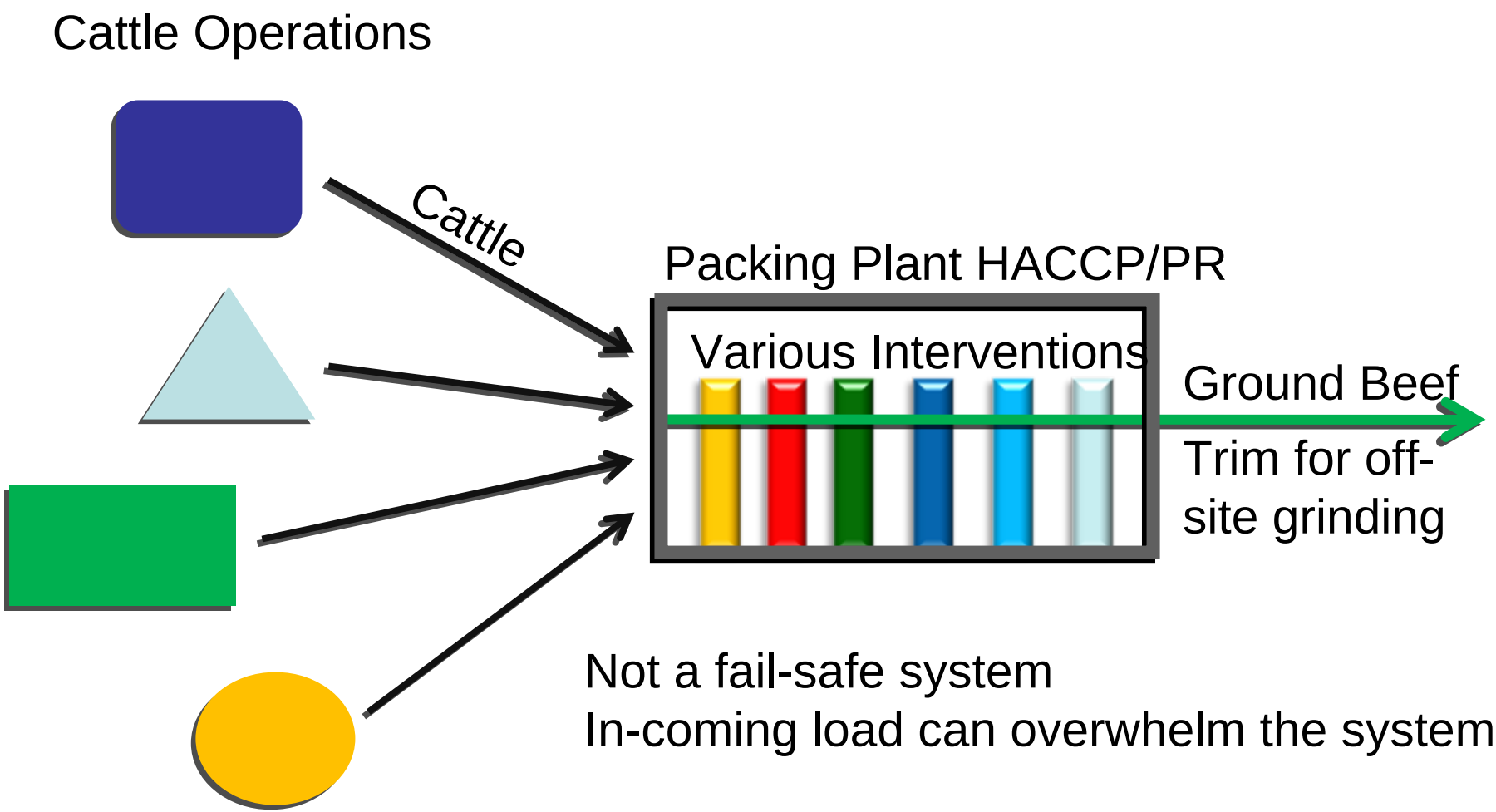
Purpose of a Pre-Harvest Intervention?

- Really measuring *PREVALENCE* of cattle carrying *E. coli* O157 to harvest
  - Prevalence = proportion of population with an attribute at a particular time
  - Still applicable even if talk about load (cfu/unit)
- Prevalence a function of both incidence and duration of infection
  - Can target either incidence or duration and will reduce PREVALENCE
- Not important which one is targeted as the outcome is the same
  - Reduce burden
    - Reduce burden to an *acceptable* level
  - Provides opportunities for R&D

Purpose of a Pre-Harvest Intervention?

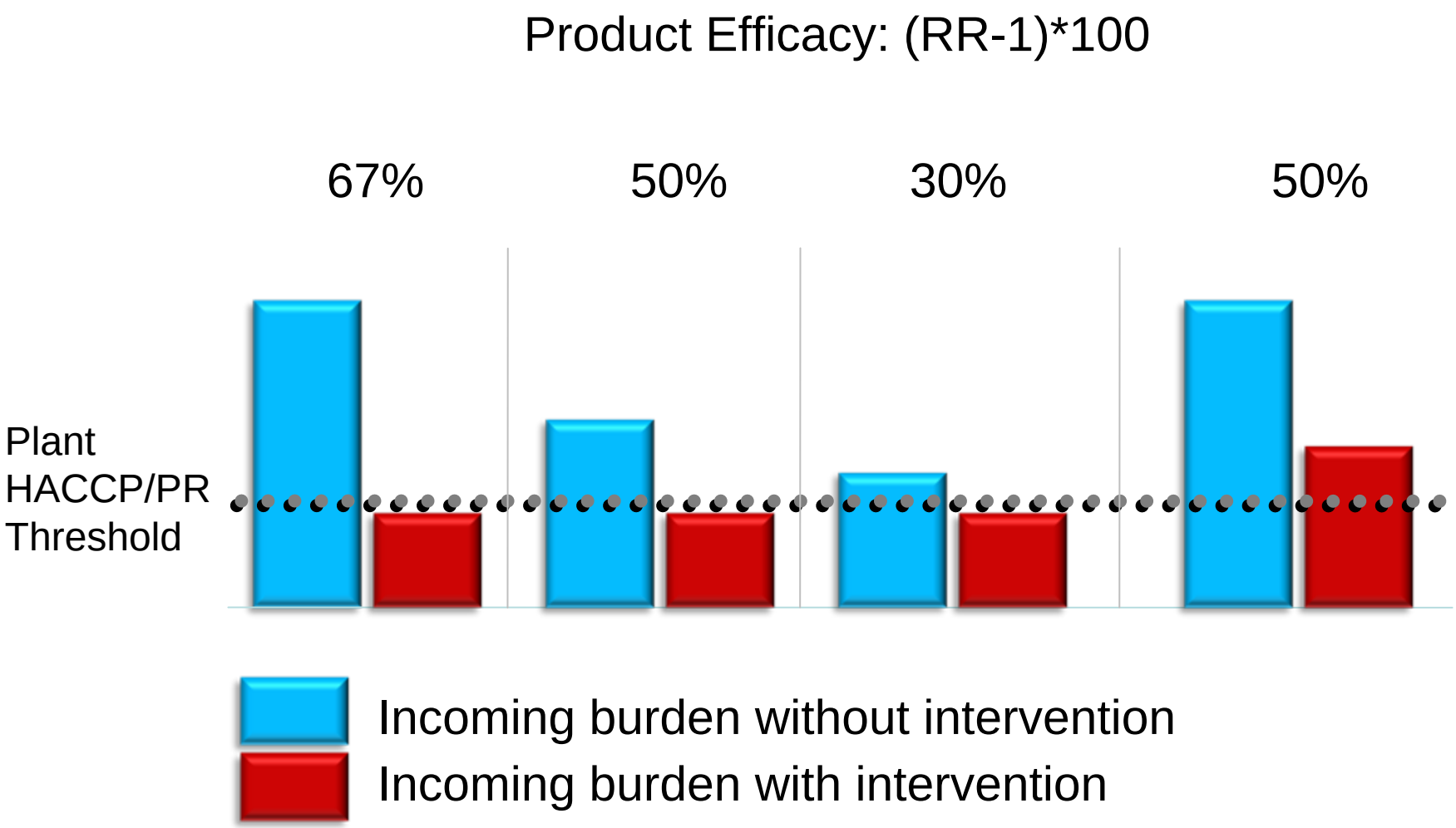


Not a fail-safe system
In-coming load can overwhelm the system

Purpose of a Pre-Harvest Intervention?

- Purpose not simply to reduce burden
- Purpose is to ensure burden of *E. coli* O157 on cattle presented for harvest is within acceptable
  - The in-plant series of HACCP/PR interventions effectively mitigate the burden on incoming cattle
- In this scenario, intervention efficacy need not be (or even approach) 100%
- Will be part of a multi-hurdle system within the production continuum
  - Should not be evaluated in isolation
- Desired efficacy depends on the burden within groups of cattle *and* on the pathogen-mitigation capacity of the plant

Purpose of a Pre-Harvest Intervention?



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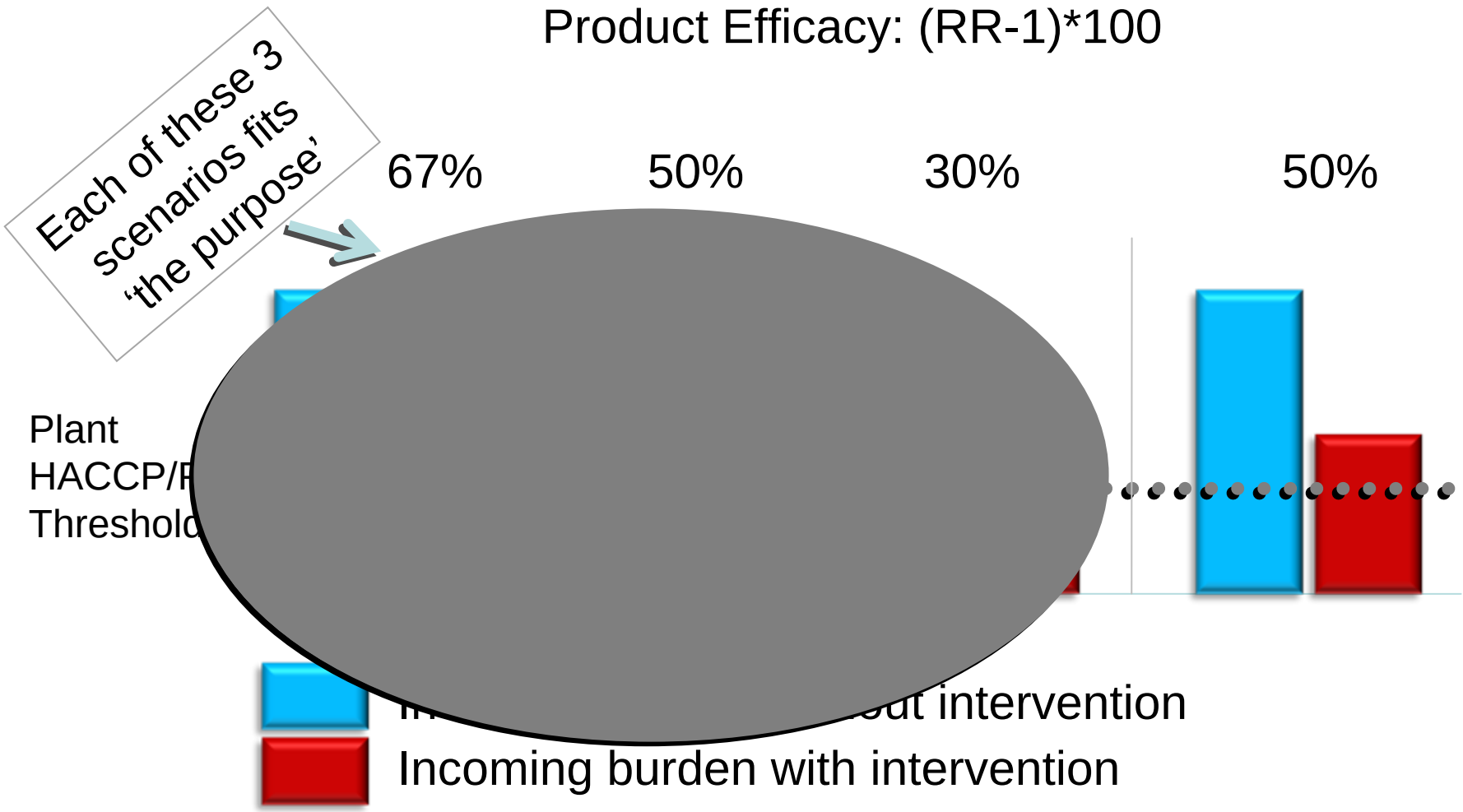
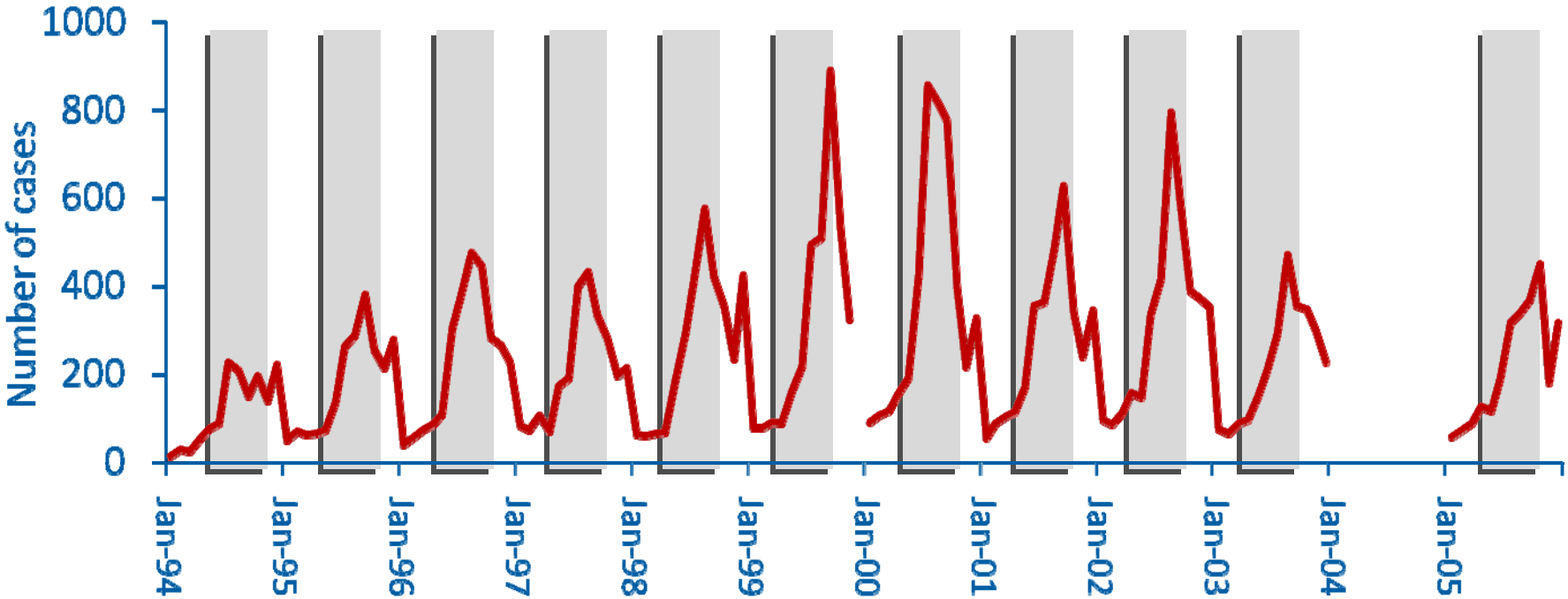


Q4: How Much Intervention is Enough?

Seasonal Occurrence of Human Illnesses

- Repeatable overrepresentation of cases during May-October
  - 70% of reported cases in 6 months of the year



- In winter, prevalence in cattle, percentage ground beef samples positive, and human cases are all substantially lower compared to summer
  - Target winter-time burdens. Supported by data.

Q4: How Much Intervention is Enough?

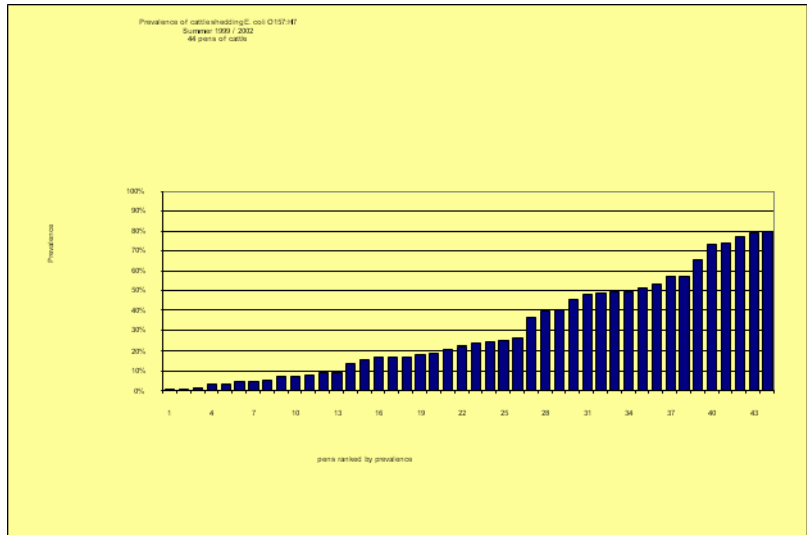
Smith DR, et al. 2001.
J Food Prot 64 (12) 1899-1903

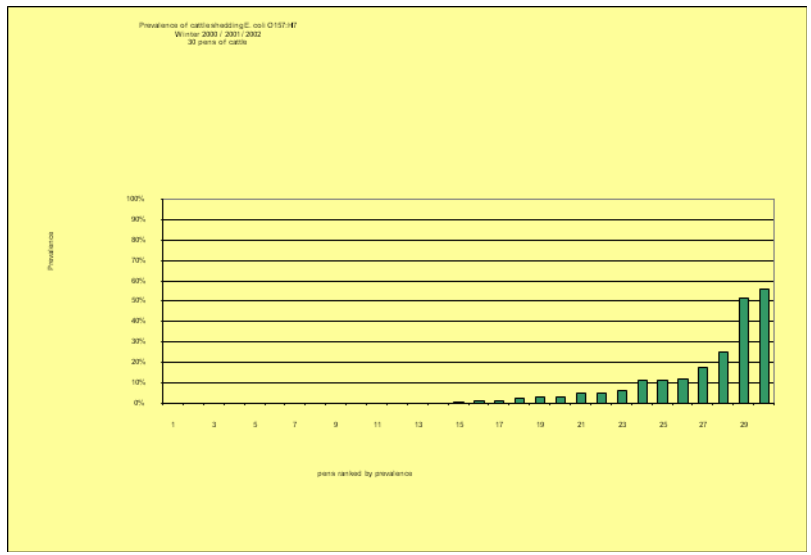
USDA NAMHS Feedlot '99 Study

- 73 feedlots visited twice
  - 3 pens per visit, 10,415 samples
- Summer (Apr-Sep) 15.8% of samples
- Winter (Dec-Mar) 5.6% of samples
- 64.5% lower during winter

Dave Smith, *J Food Prot* 2001;64:1899

- Summer 4,952 cattle, 44 pens
  - 30% of samples (1-80%)
  - EVERY pen (100%)
- Winter 2,941 cattle, 30 pens
  - 6.1% of samples (0-56% within pens)
  - 16/30 pens (53%)
- 79.7% lower during winter
- Distribution also critically important



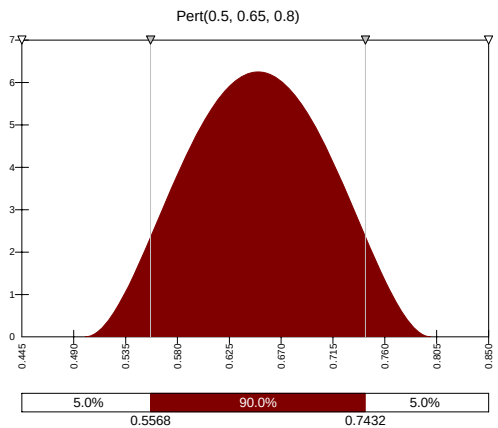


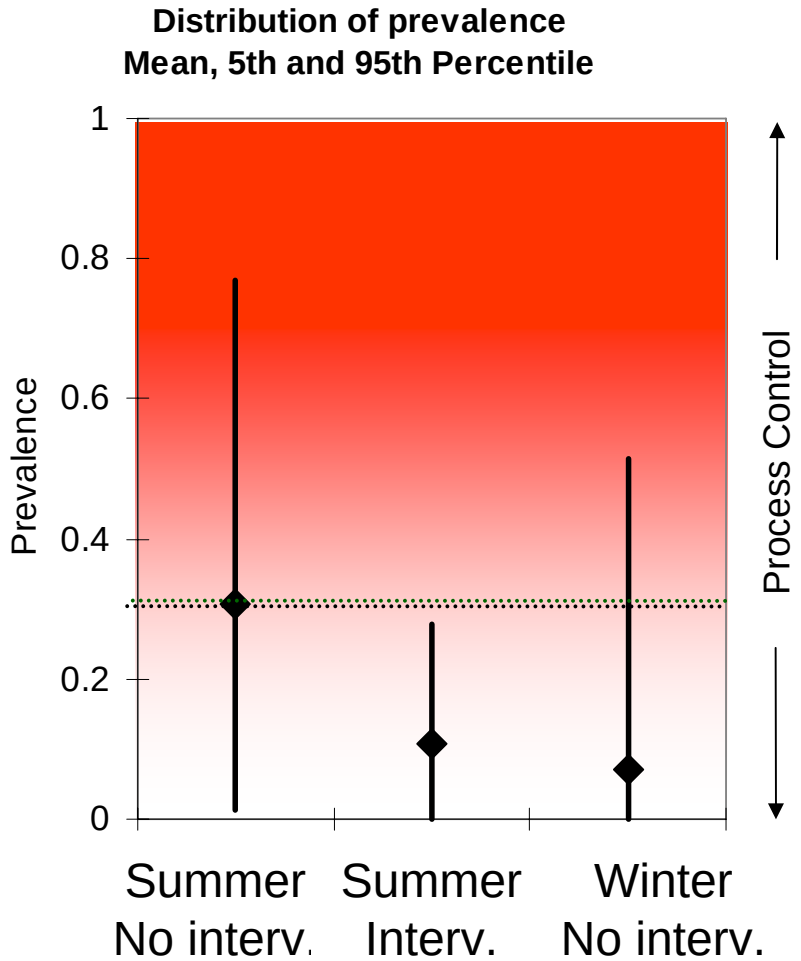
Dr. Smith's project was supported by the National Research Initiative of the USDA Cooperative State Research, Education and Extension Service, grant number #0002501.

Model to Compare Prevalence of Cattle During Summer, Winter, and with intervention (Summer) Data-driven Simulation. Source, Dave Smith, UNL

- Stochastic simulation model of the prevalence of *E. coli* O157:H7 in live cattle with vaccination (@risk 4.5)
- 5,000 pen simulations

  (500,000+ cattle)
  - Intervention: Summer (vaccine)
  - No intervention: Summer
  - No intervention: Winter
- Intervention efficacy 65%
  - Pert(50, 65, 80)





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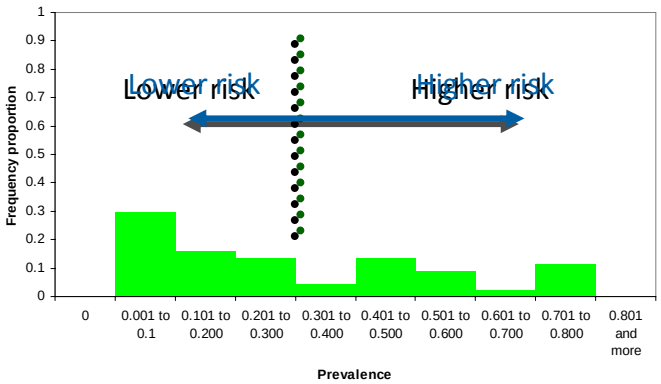
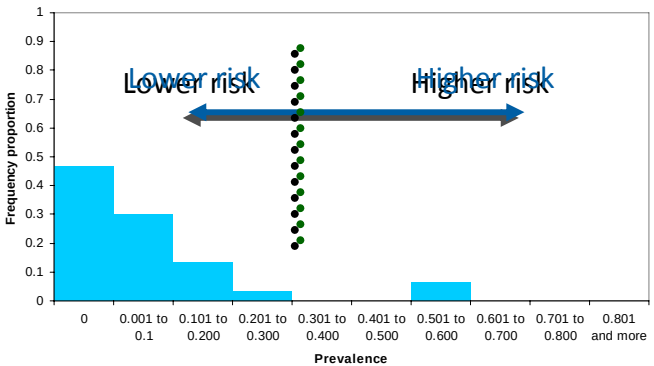
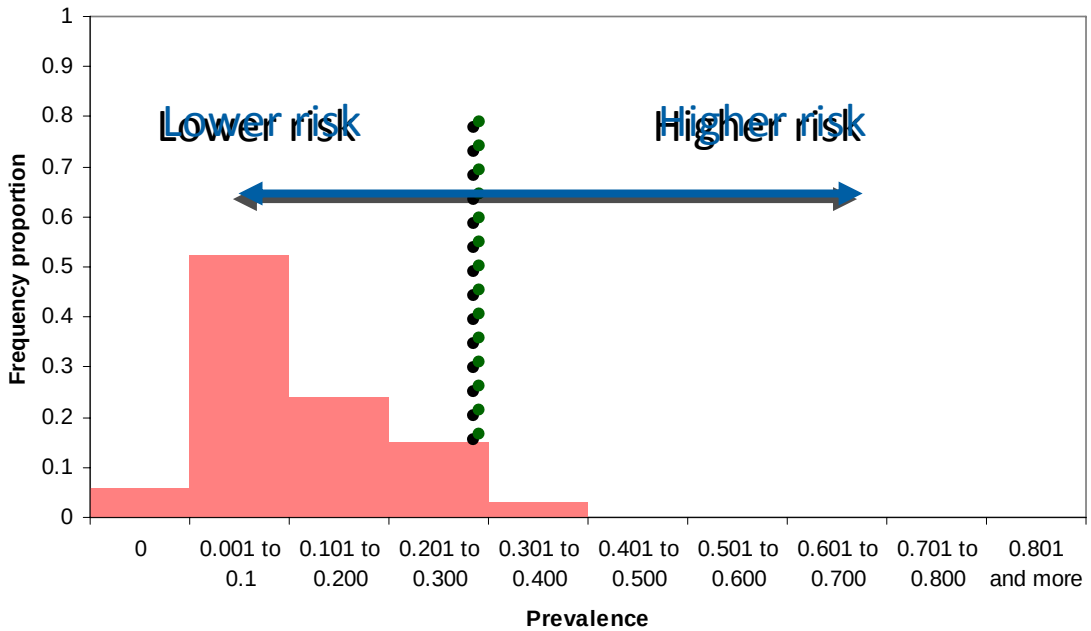
Summer, no intervention



Winter, no intervention



Predicted intervention distribution (summer)



Current Interventions

- Several interventions evaluated in field settings
  - Some interventions work (e.g., vaccine, LAB NP51)
  - Some interventions don't work (Tasco, water chlorination, cleaning pens)
- Other interventions in development and appear to have promise

Summary of UNL vaccine studies 2002-2006

Bioniche product; Source of data: Dave Smith, UNL

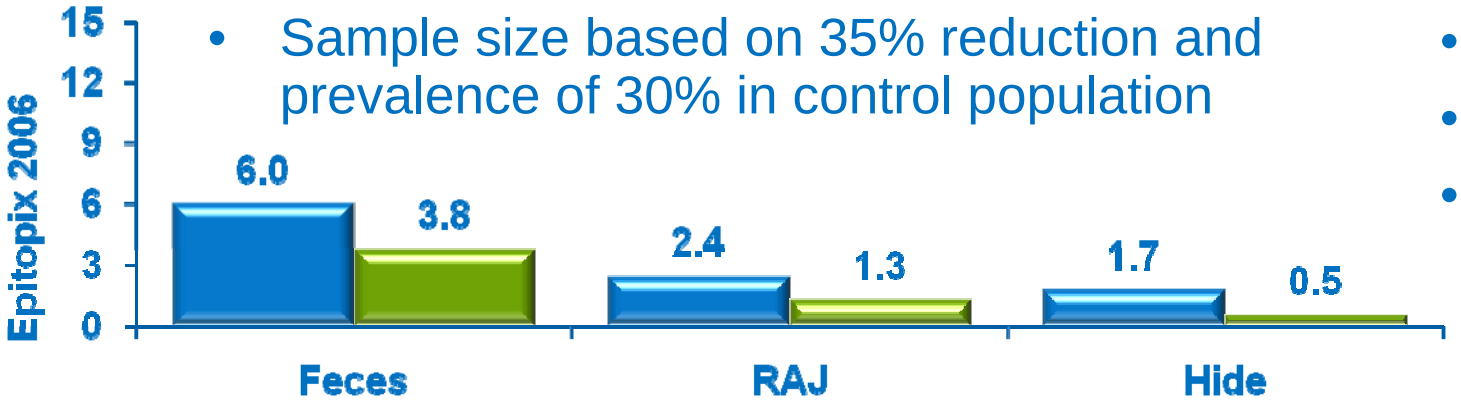
Year	# of cattle	Regimen	Outcome	Odds ratio	Vaccine efficacy	*P*-value	Comments
2002	192	3-dose	Feces	0.36	59%	0.04	"bench-top" vaccine
2003	608	1-dose	Feces	0.25	68%	0.0001	
		2-dose	Feces	0.26	67%	0.0001	
		3-dose	Feces	0.20	73%	0.0001	
		0-dose	Feces	0.36	59%	0.0003	herd immunity?
2003	1003	3-dose	TRM	0.67	NS	>0.10	ranch vaccination, low prevalence
			Feces	0.81	NS	>0.10	
2004	288	3-dose	TRM	0.014	98%	0.0001	
			Feces	0.81	NS	0.56	low prevalence
2004	718	2-dose	TRM	0.07	83%	0.0008	
	20,556		ROPES	0.59	27%	0.004	19 NE feedlots
2005a	504	2-dose	Feces	0.35	62%	0.002	Between pens
			TRM	0.71	NS	0.65	
			Hides	0.45	54%	0.005	
2005b	168	2-dose	Feces	0.40	58%	0.005	Within pens
			TRM	0.73	NS	0.48	
			Hides	0.70	28%	0.06	
2006	480	2-dose	Feces	0.66	33%	0.09	Dose effect
		3-dose	Feces	0.34	65%	0.002	

Summary of KSU Vaccine Studies

- Epitopix vaccine; Dan Thomson et al., KSU

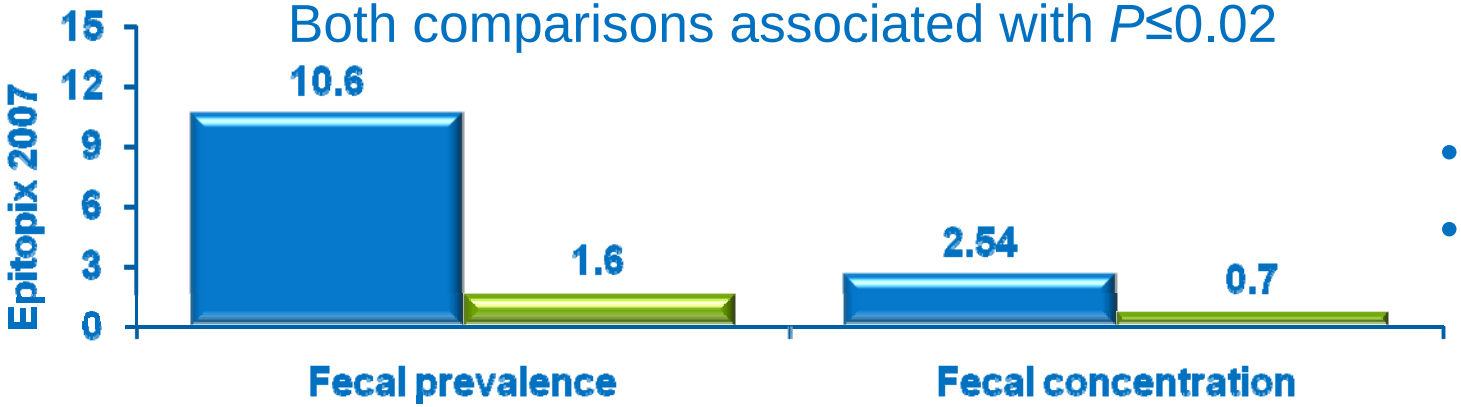
No comparisons were associated with $P<0.05$

- Sample size based on 35% reduction and prevalence of 30% in control population



- Feces – 39%
- RAJ – 48%
- Hides – 70%

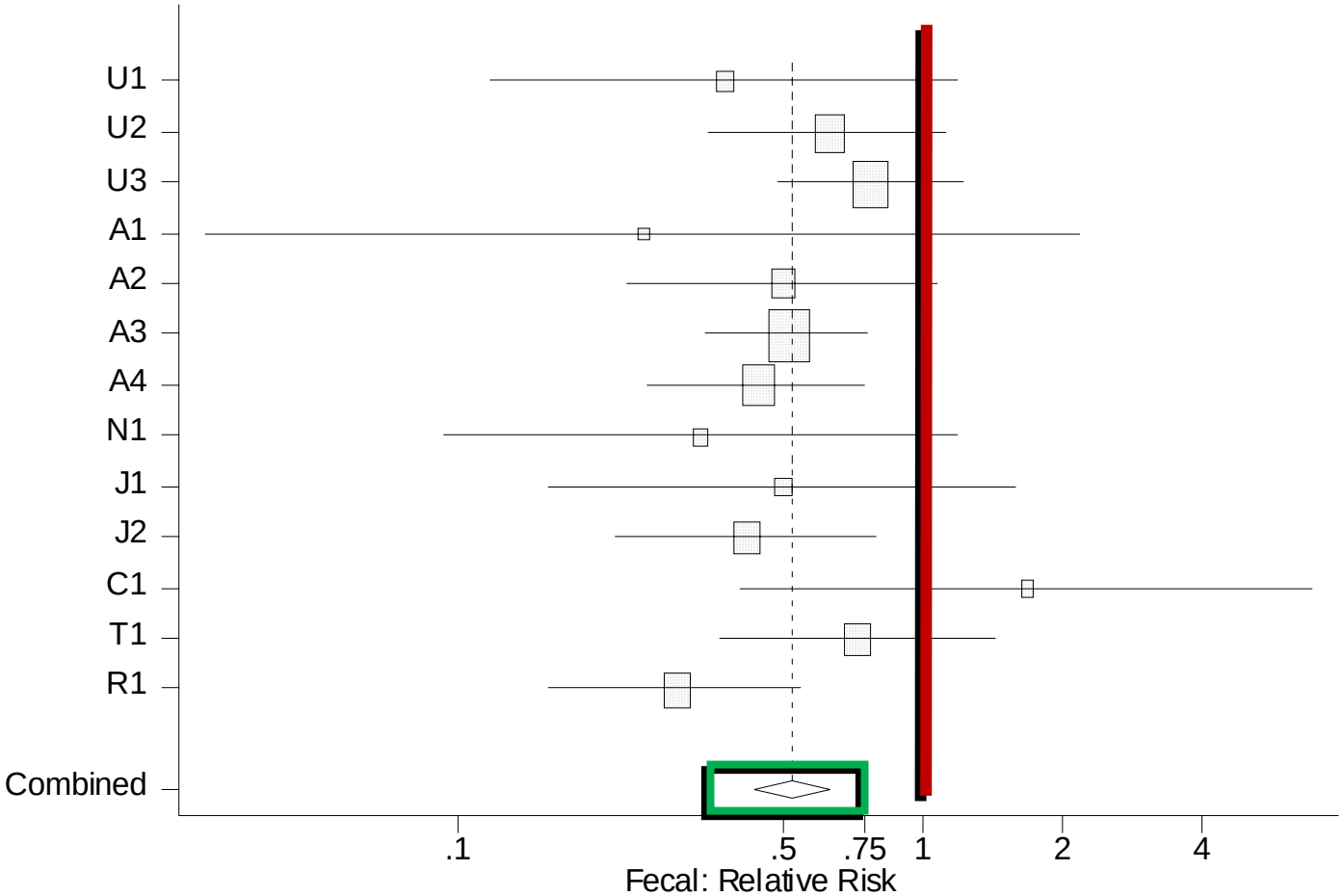
Both comparisons associated with $P\leq0.02$



- VE – 86%
- Conc – 98%

Summary of *LAB* NP51 studies 2001-2006

Multiple sites, multiple investigators



RR Feces	Product Efficacy	Lower 95% CL	Upper 95% CL	*P* value
0.60	40%	0.49	0.75	<0.01

Other Interventions

- Variety of other interventions in development, evaluation, and/or licensing/approval
  - Sodium chlorate
  - Bacteriophage
    - In feed
    - Hide wash
  - Probiotics/CE (other than LAB)
- Some may suit certain production systems more than others

Summary: Pre-harvest Control of *E. coli* O157:H7

- Much speculation about what, if anything, happened during 2007
- Pre-harvest control of *E. coli* O157 is possible
- No intervention will be 100% effective
  - BUT no need to be 100% to help reduce beef contam.
  - Adds hurdle in a multi-hurdle approach across segments
- Preliminary models and empirical data indicate pre-harvest interventions are both effective and ultimately should reduce consumer exposure to *E. coli* O157
  - *LAB* NP 51 available; vaccines closest to a labeled claim
- Challenges exist in development, licensing/approval, and implementation but are by no means insurmountable

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