Production Best Practices (PBP) to Aid in the Control of Foodborne Pathogens in Groups of Cattle

Beef Industry Food Safety Council
Subcommittee on Pre-Harvest

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<u>1.0. The Scope of this Document</u>

This document is intended to serve as a guide and information resource that producers may use to keep abreast of and implement production best practices (PBP) to aid in the control of foodborne pathogens within groups of cattle. The document focuses on control of pathogenic Shiga-toxin-producing *E. coli* (STEC) and *Salmonella* in groups of cattle.

Beef producers are generally aware of *E. coli* O157:H7, an STEC associated with well-publicized outbreaks of disease. Some of these outbreaks have been linked to consumption of beef – typically non-intact beef such as ground beef – or exposure to cattle, or fomites, environmental sources or other foods that may be contaminated with cattle feces. In addition to *E. coli* O157:H7, the beef industry also is committed to controlling other pathogenic STEC collectively referred to as non-O157 STEC. Furthermore, the USDA/FSIS has implemented regulations whereby six additional STEC serogroups (i.e., O26, O111, O45, O145, O103, and O121) are considered adulterants in ground beef and components of ground beef. These six serogroups are sometimes referred to as the 'Big Six'.

In addition, this document includes information about *Salmonella* (specifically *Salmonella enterica* subspecies *enterica*). Just like *E. coli*, there are many ways to classify *Salmonella* and a commonly used approach is to assign names to indicate a specific serotype (i.e., serotype is a microbiological method to classify bacteria). For example, outbreaks of foodborne illness caused by the serotypes *Salmonella* Newport and *Salmonella* Typhimurium have been associated with beef products.

While important knowledge gaps remain about these foodborne pathogens (see section 7.0.), it is known that:

a) STEC and *Salmonella* are relatively common or even ubiquitous in cattle populations; and
b) Currently available control strategies will likely not eliminate these bacteria from groups of cattle but might, in specific instances, aid in their control in cattle.

Control of these foodborne pathogens should be viewed as a two-tiered approach. The ***first tier*** involves implementation of *pre-requisite programs*. These principle-based animal husbandry practices might not themselves reduce the burden of the foodborne pathogens but are "the right thing to do" and such practices are considered necessary for the success of the ***second tier*** of control (i.e., adoption of practices or technologies such as chemicals, probiotics [which are also known as direct fed microbials] or vaccines). Moreover, it is important to note that second-tier interventions are not replacements for first-tier, pre-requisite programs.

Furthermore, while producers may choose to implement a comprehensive approach to control foodborne pathogens, they are encouraged to work in partnership with those to whom they supply cattle.

2.0. Executive Summary

Following the 2003 *E. coli* Safety Summit, a Production Best Practices document was developed for the pre-harvest sector and ultimately published in 2004. At that time, most technologies to control *E. coli* O157 were in early evaluation aspects of their development although promising data were being generated. Because a) interest in controlling foodborne pathogens in the pre-harvest environment continues to grow; and b) additional data have been generated since the publication of the initial document, at the 2012 Beef Industry Safety Summit, a decision was collectively made to update the 2004 Production Best Practices document. Most knowledge about the ecology and potential avenues for control of foodborne pathogens concern *E. coli* O157:H7 although an expanding body of knowledge is shedding important light on non-O157 Shiga-toxin producing *E. coli* (STEC) and *Salmonella*. For effective control of foodborne pathogens, a two-tiered approach recommended. The first tier may be considered a *prerequisite program* and includes clean feed, clean water, appropriately drained and maintained environments, and relative freedom from pests, such as biting insects. While these first-tier practices might not reduce carriage of foodborne pathogens, it is believe they set the foundation for success of the second-tier practices. Two second-tier technologies that are supported by peer-reviewed reports are currently available to US producers and include a specific probiotic (also known as a direct-fed microbial) and a conditionally licensed vaccine. None of these second-tier technologies – currently available or in development – are 100% effective and it is unlikely that a *silver bullet* that completely controls foodborne pathogens will be identified. However, the desired public-health impact of best practices to control foodborne pathogens is a function of both the *efficacy* of the best practice and the *extent of its adoption*. Furthermore, a recent quantitative risk assessment indicated that even a poorly efficacious second-tier technology can have a meaningful public-health impact if it is broadly adopted across the industry. Needed, therefore, is consideration of those factors that foster adoption of production best practices that control foodborne pathogens in the pre-harvest production sector.

3.0. Beef Industry Commitment to Food Safety

The Beef Industry Food Safety Council (BIFSCo) is an organization representing all segments of the beef industry from pre-harvest production to food-service and retail. This organization aims to develop industry-wide, science-based strategies to solve the problem of *E. coli* O157:H7 and other foodborne pathogens in beef. BIFSCo enjoys strong and active participation and organizational support from the National Cattlemen's Beef Association, the oldest and largest national trade association representing cattlemen and women in the United States.

Each year since 2003, BIFSCo, with Beef Checkoff support, has held the Beef Industry Safety Summit. At the first Safety Summit, in excess of 200 participants who spanned the farm to fork continuum vowed to work cooperatively to reduce and eventually eliminate *E. coli* O157:H7 in the beef supply. Attendees further agreed that food safety should not be a platform for competition because a foodborne illness outbreak has consequences to all – not just the company (or companies) that produced the product.

Since that initial meeting, the beef industry has made meaningful strides in its efforts to control *E. coli* O157:H7 in beef. The proportion of ground beef samples from which the USDA/FSIS is able to recover *E. coli* O157:H7 has decreased approximately 90% during the last decade from 0.87% in 2001 to 0.015% in 2012. Moreover, the Centers for Disease Control and Prevention (CDC) reported that the human incidence of *E. coli* O157:H7 has decreased 44%. Most efforts to control *E. coli* O157:H7 in raw beef products have occurred within slaughter operations. Despite the success of this largely single-sector approach, the beef industry recognizes that opportunities exist to achieve further improvements, particularly within the pre-harvest production sector where many foodborne pathogens originate.

At the 10th anniversary Beef Industry Safety Summit in 2012, participants further pledged 'As leaders in the beef industry, representing each link in the beef production chain, we reaffirm our commitment to further reduce the risks associated with foodborne pathogens by utilizing scientifically proven production practices and technologies. Our united goal is to produce, deliver and serve wholesome and safe beef for each and every family'.

4.0. Role of the Pre-harvest Production Sector in Food Safety

Most available U.S.-relevant literature focuses on *E. coli* O157:H7 and *Salmonella*. Recently, more information has become available about non-O157 STEC and the collective body of literature will increase quite rapidly in the coming years. Clearly important knowledge gaps exist; yet despite some deficiencies in our scientific understanding of these pathogens, it is generally well accepted that:

1. STEC are endemic in cattle populations – that is, they can be found in all types of cattle populations across the country, in every state and in every type of farm production environment. There is some evidence of regional differences in the prevalence of *Salmonella* in cattle populations in that in some regions (e.g., the south), *Salmonella* is widely prevalent yet in other regions, it is rarely detected.
2. STEC and, with some exceptions, most of the *Salmonella* serotypes do not seem to cause detectable disease within cattle. Some of the notable exceptions include *Salmonella* serotypes Dublin, Newport, and Typhimurium, which can cause severe disease in cattle.
3. Seasonal differences in the frequency with which cattle excrete these pathogenic bacteria in their feces, called "shedding", have been noted. Shedding peaks in summer and early fall, and is lowest in winter and early spring.
4. In one of the most confusing findings, groups or pens of cattle housed in a single operation may show very different amounts (prevalence and concentration) of shedding.
5. The extent of shedding of these bacteria within groups of cattle varies greatly over time and it may appear as if infections come and go (that is, cattle sometimes shed at detectable concentrations and at other times, they either do not shed the organism or they do so at levels below the limit of detection of the sampling

scheme and microbiological assay used in the study). Furthermore, infection does not necessarily result in protective immunity against subsequent infection.

For the foodborne pathogens covered within the scope of this document, most literature has examined a potential relationship between the burden of *E. coli* O157 in cattle presented for harvest with subsequent food safety metrics. Only recently have quantitative models been developed that provide estimates of the magnitude of the relationship between pre-harvest pathogen burden and subsequent, post-harvest metrics such as the extent of contamination of carcasses or ground beef, or various measures of human illnesses. It is important to note that all of these models, regardless of the level of scientific sophistication used to construct them, rely on various assumptions and ultimately provide a *reasoned* and *mathematical estimate* based on available data. As such, the quality of the data upon which the models are built and the assumptions about those data can substantively affect the accuracy and precision of the estimates.

Given uncertainties and assumptions associated with the various models, one can conclude from the published work that as the burden of *E. coli* O157:H7 increases in groups of cattle, then the extent of beef contamination and resultant human illnesses also increases. Some models also provide estimates of the extent of reduction in beef contamination or human illnesses resulting from reductions of pathogens in cattle populations. These models can be used, therefore, to help determine if adoption of a specific intervention will likely produce a meaningful reduction in beef contamination and improvement in public health.

None of the predictive models capture the impact of potential cross-contamination of *E. coli* O157:H7 between groups of animals, e.g., during transportation or lairage at the slaughter establishment. Some evidence suggests cross-contamination is common between groups of cattle while on trucks or during lairage. Because current models do not account for this, it is not presently possible to evaluate to what extent potential cross-contamination impacts the efficacy of pre-harvest interventions.

To date, no models have been published that explore the quantitative relationship between pathogenic non-O157 STEC or *Salmonella* and important outcome metrics related to consumer exposure or public health. Indeed, recent data indicate the need for more sophisticated models of *Salmonella* that capture and quantify the various routes by which it may contaminate beef products and ultimately infect consumers.

5.0. Prerequisite Programs

Since the beginning of livestock production, animal husbandry has involved caring for animals in the way best for the animal and the producer. The first step in efficient and wholesome production of any animal-based food is to make sure production areas are well-maintained, clean, appropriately drained and free from vermin and pests. While cleanliness of production areas is not currently proven to directly affect the burden of pathogenic STEC or *Salmonella,* principle-based animal husbandry lays a good and necessary foundation for optimum animal health and welfare.

Today's principle-based animal husbandry must also incorporate best practices to achieve beef producers' mission of feeding an enormous number of people worldwide by providing safe and wholesome beef. Therefore, principle-based animal husbandry should be included in every producer's PBP involving live animals. Basic principles of cattle management should include:

1. Clean feed (free from fecal contamination);
2. Clean water (free from fecal contamination);
3. Appropriately drained and maintained environments; and
4. Relative freedom from pests, such as biting insects.

These practices are fundamental to any livestock operation, and should be incorporated as the first tier (i.e., a foundation) upon which the likelihood of success of the second tier of targeted practices or technologies designed to reduce the burden of pathogenic STEC or *Salmonella* depends. Additionally, these first tier pre-requisites are practices grounded in good animal husbandry. Second-tier interventions, including practices or technologies, are not a replacement for principle-based animal husbandry. In other words, interventions will likely fail without implementation of appropriate principle-based animal husbandry practices. For example, an intervention might not appear to work if animals are constantly re-inoculated with *E. coli* O157 from contaminated feed or water. In other words, the extent of exposure may overwhelm the protective effect of the intervention. Hence, a broader assessment of how animals might be exposed to foodborne pathogens from their environment is necessary.

6.0. Pre-harvest Interventions to Aid in Pathogen Control

A variety of management practices and technologies have been evaluated for control against STEC or *Salmonella* in groups of cattle and might serve as second-tier interventions. It is beyond the scope of this document to provide a comprehensive review and we refer the reader to other relevant sources (Callaway et al. 2013. Shiga Toxin-Producing *Escherichia coli* (STEC) ecology in cattle and management based options for reducing fecal shedding. *Agric. Food Anal. Bacteriol.* 3:39-69.)

The majority of information about interventions to control STEC or *Salmonella* is specific to *E. coli* O157:H7; however, some data are available for non-O157 STEC and *Salmonella*.

Interventions can be broadly categorized as*:

Management Practices	Most efforts to apply management practices to control *E. coli* O157:H7 appear wholly unsuccessful. This is likely because *E. coli* O157:H7 has co-evolved with cattle and is well-adapted to life within the ruminant gut regardless of the production system or management practice. That said, first-tier, pre-requisite programs are part of principle-based animal husbandry and need to be

	implemented to ensure the success of second-tier controls. There is some data pertinent to dairy operations in which sand bedding may reduce pathogen shedding. In feedlot settings, prevalence of *E. coli* O157 was elevated in pens that were excessively dry and dusty, and in pens that were excessively wet and muddy (i.e., the extremes of dry and wet relative to the ideal situation).
Isolation of infected animals	In some instances of disease in cattle caused by *Salmonella*, preventing exposure of susceptible animals to the virulent strains of *Salmonella* is warranted. In such instances, it is recommended that producers consult with their veterinarians to develop appropriate control programs.
Abrupt Changes in Diet Composition	Many abrupt diet modifications, such as replacing starch with roughage (e.g., replacing corn with hay), have been proposed but the effect is inconsistent and in some cases, may actually result in undesirable outcomes. Fasting of cattle just prior to slaughter reduces gut fill, but has been associated with increased populations of *E. coli* O157 in the intestinal tract of cattle.
Diet components	Some dietary components have been shown to affect STEC populations in cattle. Barley and distillers grains have been shown to increase shedding of *E. coli* O157. Also Steam-flaked corn fed cattle shed more *E. coli* O157 than did those fed dry-rolled corn. Other diet modifications, such as replacing starch with roughage (e.g., replacing corn with hay), have been proposed but the effect is inconsistent and, in some cases, may actually result in undesirable outcomes. Moreover, lack of alternative feed commodities means that diets are not readily modifiable and not, therefore, suited as an intervention.
Feed Additives	
Chemical additives	Sodium chlorate administered in prepared water and feed, significantly reduced *E. coli* O157:H7 and *Salmonella* concentrations compared to controls. Sodium chlorate is awaiting FDA approval for this use and may not be used in cattle intended for slaughter for human food.
Probiotics (also referred to as direct-fed microbials [DFM])	A commercially available probiotic product, BOVAMINE® DEFEND, has been widely documented to reduce the prevalence (with some evidence of reduced concentration) of *E. coli* O157:H7 in feedlot cattle. This product includes a

	combination of bacteria (i.e., *L. acidophilus* NP51 and *P. freudenreichii* NP24). A dose response has been observed in that approximately 10^9 colony forming units (cfu) of NP51 per animal per day provided greater reductions than a dose of approximately 10^7 cfu of NP51 per day. The former is marketed as BOVAMINE® DEFEND and the later as BOVAMINE®. This product has no FDA-approved label claim against any foodborne pathogens.
Other	Feedstuffs such as orange peel contain essential oils that are toxic to bacteria. Feeding of fresh orange peels along with orange pulp pellets reduced intestinal populations of *Salmonella* and *E. coli* O157:H7 in sheep used as a model. At this time, however, orange peel feeding has not been sufficiently proven to recommend its use. Tannins and other phenolic compounds found in feedstuffs show promise for reducing *Salmonella* and *E. coli* O157:H7 populations but may be hampered by deleterious anti-nutritional aspects of their use. Numerous other products have also been evaluated, such as a seaweed extract known as TASCO 14, and the data are insufficient to recommend their use.
Vaccines	The USDA/APHIS/VS/CVB conditionally licensed a vaccine as an aid in the control of *E. coli* O157 in groups of cattle. The vaccine, *Escherichia coli* Bacterial Extract vaccine with SRP® Technology, is designed to produce a targeted immunity to reduce the bacterium's ability to acquire iron, an essential nutrient. An increasing body of evidence supports the efficacy of this vaccine to reduce the prevalence (and with some evidence of reduced concentration) of *E. coli* O157:H7 in the feces of feedlot cattle. This vaccine is conditionally licensed with a 3-dose regimen. Published data demonstrates that with 2 doses, this vaccine is associated with a significant reduction in prevalence of *E. coli* O157:H7 as well as a reduction in the prevalence of so-called super shedders. Various definitions are used for super shedders but in general, this class of animals sheds substantial quantities of the pathogen at the time of sample collection and often exceeds 10^4 cfu/g feces. A similar product with antigens harvested from *Salmonella* Newport is conditionally licensed as *Salmonella* Newport

	Bacterial Extract vaccine with SRP® Technology. Most data are derived from dairy studies and support this product as an aid in the control of *Salmonella* in herds of cattle. Interestingly, this product has been associated with increased milk yields, which may help explain its broad adoption within the dairy industry. An *E. coli* O157:H7 vaccine, ECONICHE™, is fully licensed in Canada but has yet to be licensed – conditionally or fully – in the U.S. This product reduces the bacterium's ability to adhere to the gut wall and a compelling body of evidence supports the efficacy of this vaccine as an aid in the control of *E. coli* O157:H7 in groups of cattle.
Bacteriophage	A commercially available bacteriophage cocktail, FINALYSE®, is available for application to the hides of cattle after unloading at the slaughter establishment. While widely used by the beef industry, few published data are available about the efficacy of this product. Other studies have shown that phage administered orally to ruminants can reduce populations of *E. coli* O157:H7. However, no commercially available product is available in the U.S.
Other approaches	Some evidence exists indicating that exposure to short-chain fatty acids might be an effective approach to control. However, this approach is prohibitively expensive to engineer the short-chain fatty acids such that they bypass rumen fermentation and are delivered in an active form to the small intestine.

* see Callaway et al. 2013. Shiga Toxin-Producing *Escherichia coli* (STEC) ecology in cattle and management based options for reducing fecal shedding. *Agric. Food Anal. Bacteriol.* 3:39-6 and Pre-harvest Management Controls and Intervention Options for Reducing *Escherichia coli* O157:H7 Shedding in Cattle. Available at: www.beefresearch.org/CMDocs/BeefResearch/Safety_Fact_Sheets/Pre_Harvest_Control_of%20E_coli.pdf

7.0. Key Knowledge Gaps and Needs:

1. Most knowledge about pre-harvest control of foodborne pathogens is about *E. coli* O157:H7, though it is assumed that non-O157 STEC may behave in a similar fashion. A variety of interventions have been developed and evaluated in field settings. The body of literature provides compelling evidence that it is possible to reduce the burden of *E. coli* O157 in groups of cattle yet the efficacy is always less than 100%. A recurrent question is then, therefore, will this predictable yet less than absolute reduction result in

meaningful improvements in downstream metrics such as reduced beef contamination or improved public health.

A recent outcomes-based risk assessment attempted to quantify this relationship. A salient outcome of this model is that *impact* – e.g., improvements in public health – is a function of both of the *efficacy* of an intervention and the *extent of its adoption* across the industry. For example, a poorly efficacious intervention might have a meaningful public-health impact if broadly adopted. In another model that explored various scenarios, the savings in costs associated with *E. coli* O157 illnesses was exceeded the cost of implementing an intervention program to control *E. coli* O157 in cattle. Yet even while there was a net economic benefit given the assumptions of the model, all the costs of implementation were at the live-animal, production stage and all the benefits were elsewhere.

Needed, therefore, are two events. Firstly, the farm to fork continuum, including its various stakeholders such as consumers and regulators, need to ask the fundamental question of *whether or not it is warranted to adopt these imperfectly efficacious interventions*. If so, the industry might then design approaches that equitably share the costs and benefits in order to foster broad adoption of these technologies.

2. While it has been shown that cattle can shed non-O157 STEC, relatively little is known about the ecology and epidemiology of pathogenic STEC in groups of cattle. Many assumptions about non-O157 STEC have been based on the similarity to *E. coli* O157:H7, however, the non-O157 STEC population is a collection of hundreds of different serotypes. As such there is tremendous diversity in the number and type of virulence factors carried by these bacteria. The spectrum of pathogenicity, from potentially avirulent to highly virulent appears to be much greater for the non-O157 STEC collective than that observed within *E. coli* O157:H7. That spectrum of strains will run the gamut from avirulent or highly virulent, or somewhere in between. While recent publications indicate a larger proportion of non-O157 STEC found in cattle are avirulent as opposed to highly virulent, the details of the population structure are not yet understood.

For the most part, non-O157 STEC research has been hindered by the lack of accurate and reliable detection methods for these pathogens. This has led to deficiencies in data collection. Of particular concern is a lack of any form of quantitative (or even qualitative) risk assessment or estimates of food attribution for the non-O157 STEC. Consequently, if it were possible to intervene pre-harvest, there is no informed, science-based understanding of the extent of the improvements, if any, in meaningful public-health metrics. Moreover, very little information is available to assess the efficacy of pre-harvest interventions against non-O157 STEC in general or against the pathogenic STEC in particular.

These fundamental knowledge gaps need to be filled with reliable data. The USDA/NIFA recently funded a large Coordinate Agricultural Project award (contract # 2012-68003-30155) to a collaboration of institutions and it is anticipated many of these data gaps will be addressed in the years ahead. In addition, there are various other projects funded by the USDA/NIFA, the Beef Checkoff and other institutions in which investigators are exploring the ecology of non-O157 STEC in cattle populations.

3. Innovation and development of technologies that control foodborne pathogens in the pre-harvest environment will require a clear, consistent, and predictable pathway from discovery to application. A fundamentally important step in this pathway that can serve to encourage or discourage innovation is the regulatory approval process. It must be understood that these technologies will not eliminate the pathogens from animals but are designed to serve as aids in their control. As such, pre-harvest interventions will not exist in isolation but, rather, will serve as an additional hurdle to those effective practices already implemented within packing plants. Expeditious approval or licensing of imperfectly efficacious products will serve to encourage further innovation of new products or improvements to existing ones. Needed, therefore, is a clear, achievable, and expeditious regulatory process by which interventions can be approved or licensed.

4. From the perspective of *impact* (e.g., public health benefits), the *extent of adoption* across the industry is just as important as *efficacy*. Adoption of a practice or a technology represents a behavior change for producers. While economics is an overt driver of behavior, there are many other reasons beyond economics why producers choose to adopt or to not adopt a technology. For instance, vaccines may require additional animal movement and restraint which might increase the risk of animal or human injury. As another example, diets that incorporate recently steam-flaked corn may be of such temperature that probiotics may be inhibited.

Consequently, changing behavior from the *status quo* is not always a straightforward process. Because broad producer adoption of technologies will be critical to achieve a desired public-health impact, research grounded in the social sciences (e.g., economics, political science, and behavioral science) is needed to discover, design and test approaches that foster adoption of technologies. Furthermore, ease of implementation, real or perceived, of interventions needs to be considered in their design.