Brief summary from USDA CVB Public Meeting on pre-harvest vaccines against STEC O157

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STEC O157 is a worthy pre- and post-harvest opponent. While absolute victory over this zoonotic pathogen is not possible, there is good evidence that pre- and especially post-harvest interventions introduced over the past decade have lessened the public health food safety burden of this microbe. Effective vaccine utilization against this pathogen will almost certainly require strategic integration with these existing "multihurdle" technologies and management practices.

By biological analogy, STEC O157 is "**weed-like**". It can rapidly invade, inhabit, colonize and/or survive in many diverse primary and secondary habitats, ranging from soil and fresh produce, to cattle hides, the length of the bovine gastro-intestinal tract, to cattle carcasses, and fresh or frozen ground beef. It can even be detected in air samples. The agro-ecology of STEC O157 is complex and biologically noisy. Its occurrence can be accurately described as "**endemically unstable**" at the individual animal, pen, farm, ranch or processing plant levels environments. This biological variability hinders the evaluation of vaccine efficacy.

For food safety STEC O157 risk assessment and risk management, two factors are of pre-eminent importance: **hide status** and **season.** Contaminated hide is the immediate source of carcass contamination, while summer season is the dominant ecological driver (and best predictor) of STEC O157 live animal prevalence, post harvest meat contamination, and human disease incidence. Similarly, in Australia in the 1930s, season and hide were also eventually shown, after a huge research investment, to be the dominant drivers of economically devastating bacterial spoilage of beef carcasses during long overseas shipment to Britain. Thus, in some ways, history has repeated itself in the microbial ecology of beef.

A practical microbiological goal for the combined effects of pre- and post-harvest anti-STEC O157 interventions is to **"make summer cattle look like winter cattle"** when presented for slaughter. It appears that only a minority of cattle presented for slaughter are responsible for most of the STEC O157 microbiological risk, perhaps representing a variant of the 80:20 rule. Therefore, if high risk (ie high STEC O157 prevalence) pens of finished cattle can be identified and targeted with efficient pre-harvest interventions, the associated costs can be minimized and derived benefits maximized.

Regulatory assessment challenges and unmet needs for pre-harvest vaccines against STEC O157 include development of:

- evidence based, data driven designs to evaluate vaccine efficacy
- useful experimental challenge model systems, especially for vaccine pathogen load evaluation
- creative field trial designs ,especially for prevalence reduction-based vaccine evaluations
- sensitive microbiological techniques, especially for microbial load quantification

Additional challenges germane to pre-harvest vaccines against STEC O157 include:

- the preservation of pre-harvest microbiological benefits in the post-harvest period
- generating financial incentives for pre-harvest food safety investments which have
- benefits occurring post-harvest or later in the food chain

- the rational and justifiable definition of pre-harvest vaccine efficiency
- the integration of pre-harvest vaccines with other live animal chemical, biological, or
- immunological interventions possessing evidence-based efficacy (eg direct fed microbials).

An emerging phenomenon is STEC O157 strain heterogeneity in terms of capacity to both infect people given exposure, and in the severity of clinical disease given infection. In other words, **all STEC O157 strains are not created equal** in terms of human virulence potential. The impact of this virulence variability on pre-harvest vaccines is yet to be explored. However, it will be important to evaluate and ensure that pre-harvest vaccines have efficacy against the STEC O157 pathotypes with greatest human virulence potential in order to maximize their public health food safety benefits.