BGs AS VETERINARY VACCINES

Bacterial Ghosts (BGs) are empty, non-living bacterial particles generated from Gram-negative bacteria such as *E. coli*, Actinobacillus, Salmonella and many other important veterinary pathogens through a proprietary, genetically induced inactivation process. Bacteria leading to BGs can also be genetically engineered in various ways to enrich them in their envelope with target antigens of other infectious diseases creating combination vaccine.

The major goals of veterinary vaccines are to improve the health and welfare of companion animals, to increase production of livestock and aquaculture in a cost effective manner and to prevent animal-to-human transmission from both domestic animals and wildlife population.

Veterinary vaccines in general can be classified into two major domains: live attenuated vs inactivated vaccines.

BGs belong to the group of inactivated vaccines with no need to add adjuvants

Competitive Advantages of BG Vaccines

- Retention of natural surface components and full immunogenic potential of living bacteria
- A conservation of immunogenicity of recombinant antigens introduced into BGs
- No need to add adjuvants to elicit strong humoral and cellular immune responses
- High stability and immunogenicity of freeze-dried product for several years at ambient temperature
- Stable in liquid formulation stored at +4°C for minimum of 1 year

BGs represent an innovative vaccination approach with technological and cost advantages over existing veterinary vaccines

BIRD-C's commercial model is to develop veterinary vaccines against major microbial livestock infections and to license the vaccine(s) to veterinary pharmaceutical companies.

A list of *in vivo* proof of concept studies for the induction of immune responses in Fish, Pigs, Cattle, Chickens, Dogs and Possums are given on back side of this leaflet.

Overview of immune responses against BGs for Veterinary applications			
Animal	**Disease caused**	**BG carrier**	**Immune response/conferred protection**
Fish	Edwardsiellosis	*Edwardsiella tarda*	• Fish immunized with *E. tarda* BGs showed higher protection than fish immunized with formalin killed *E. tarda* vaccine. • Significant systemic and mucosal Ag-specific humoral immune response; significant increase of total T helper and cytotoxic T cell populations; significant rates of protection (86,7%) compared to negative control (33%) after challenge.
	Hemorrhagic septicemia	*Aeromonas hydrophila*	• Ag-specific humoral immune response; increased rates of protection after challenge compared to negative control. • Oral immunization with *A. hydrophila* BGs elicits systemic and mucosal immune responses and has higher potential to induce protective adaptive immunity than formalin-killed vaccine.
		Escherichia coli	• Ag-specific immune response; protection after challenge (> 80%).
	Columnaris disease	*Flavobacterium columnare*	• Ag-specific immune response; grass carp (*Ctenopharyngodon idellus*) immunized with *F. columnare* BGs showed significantly higher serum agglutination titers and bactericidal activity than control group.
	Streptococcosis	*Streptococcus iniae*	• Tilapia (*Oreochromis niloticus*) immunized with *S. iniae* BGs showed better protection and higher bactericidal activity as compared to formalin killed vaccines.
Pig	Porcine pleuropneumonia	*Actinobacillus pleuropneumoniae*	• Ag-specific humoral immune response; increased T helper cytotoxic T cell ratio; complete protection against challenge infection. • Full protection against clinical disease and lung lesions; prevented colonization of the respiratory tract.
	Mastitis/septicemia	*Klebsiella pneumoniae*	• Antibody titers were comparable to titers obtained after infection with virulent bacteria; cross reactivity to related subspecies
	Glässer's disease	*Heamophilus parasuis*	• Piglets immunized with *H. parasuis* BGs exhibited higher levels of T helper cells relevant for protection
	E. coli colibacillosis	*Salmonella typhimurium (ETEC)*	• Oral Immunization of piglets with *S. typhimurium* BGs expressing enterotoxigenic *E. coli* (ETEC) fimbriae provides protection to *E. coli* colibacillosis.
Cattle	Bovine respiratory disease	*Pasteurella multocida, Mannheimia haemolytica*	• Protective immunity against homologous challenge; cross-reactivity to various *Pasteurella* serotypes. • Ag-specific humoral immune response
	EHEC carrier status Diarrhea	*Escherichia coli 0157:H7*	• Induction of EHEC specific antibodies, significant reduction of both duration and total shedding of EHEC offer oral challenge.
Chicken	Salmonellosis/ Enteritis and systemic disease	*Salmonella enteritidis*	• BG-vaccinated specific pathogen free chicks showed higher levels of antibodies, IFNγ and IL-4. • Significant increase in T helper and cytotoxic T cells; the latter is linked to the clearance of intracellular Salmonella. • Double immunized chickens showed protection against intestinal, liver, splenic and ovarian colonization of *S. enteritidis*; Ag specific lymphocyte proliferative response in immunized chickens. • Significant Ag-specific plasma IgG and intestinal secretory IgA response; increased levels of splenic T helper and cytotoxic T cells. • Chicks from hens vaccinated with *S. enteritidis* BGs had 80% survival rate as compared to un-vaccinated control (30%).
	Fowl typhoid	*Salmonella gallinarium*	• Significant Ag-specific systemic IgG response; increased mRNA level of Th1 cytokines (IFNγ and IL-2).
Dog	Kennel cough	*Bordetella bronchiseptica*	• *Bb*BG vaccine showed equivalent results when compared to the positive control vaccine (Bronchicine CAe®) in terms of safety and efficacy.
Possum	Fertility control	*Escherichia coli*	• BGs carrying possum zona pellucida protein-2 helped reduce possum fertility when delivered mucosally.

Ag: Antigen; *Bb*BG: *Bordetella bronchiseptica* Bacterial Ghosts; BGs: Bacterial Ghosts; EHEC: Enterohaemorrhagic *E.coli*; ETEC: enterotoxigenic *E. coli*; IFNγ: interferon gamma; IgA: Immunoglobulin A; IgG: Immunoglobulin G; IL-2: interleukin 2; IL-4: interleukin 4; Th1: T helper cell type 1;