SCIENTIFICALLY PROVEN

Protection against the most deadly diseases in cattle

Clostrivax B is the **ONLY 9 antigen multi-clostridial** formulation that protects against **BOTULISM** in cattle and *Mannheimia haemolytica* leukotoxin that causes bovine respiratory disease.

TARGET ANIMAL EFFICACY

Healthy Friesland cattle (n=30) were vaccinated and evaluated during a 35 day study:

- Local reactions for a period of 14 days after administration
- Systemic reactions after administration
- Serum antibody concentrations

RESULTS

Trial results are expressed in EU/ml using an indirect ELISA approach quantified against international reference sera.

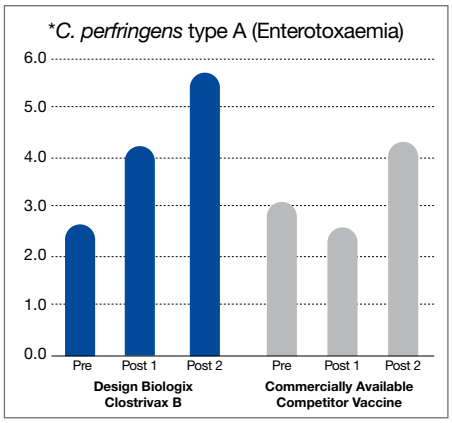

Figure E1.1 Antibody concentrations against *C. perfringens* type A phospholipase C antigen.

Clostrivax B: Mean serum antibody titres (EU/ml), where pre-samples were collected before vaccination on day 0, post 1 samples were collected before the booster vaccination at 28 days and post 2 samples collected at day 35. Following vaccination there was a significant rise in antibody titres. Final titre: 5.7 EU/ml. The in-house requirement is 1.0 EU/ml. There are no monographs available for *C. perfringens* type A. **Competitor:** The mean serum antibody titres (EU/ml) for **a commercially available competitor vaccine**, where pre-samples were collected before vaccination on day 0, post 1 samples collected before the booster vaccination at 28 days and post 2 samples were collected at day 35.

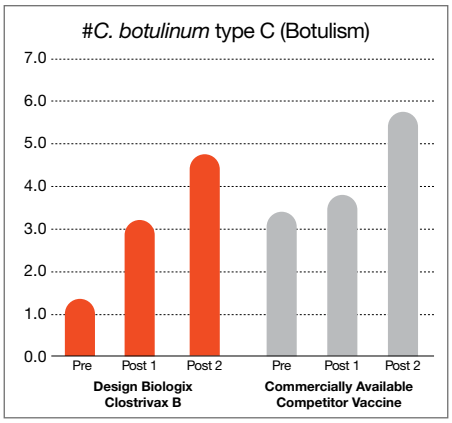

Figure E1.2 Antibody concentrations against *C. botulinum* type C toxoid.

Clostrivax B: Mean serum antibody titres (EU/ml), where pre-samples were collected before vaccination on day 0, post 1 samples were collected before the booster vaccination at 28 days and post 2 samples collected at day 35. Following vaccination there was a significant rise in antibody titres. Final titre: 4.8 EU/ml. The in-house requirement is 1.0 EU/ml. **Competitor:** The mean serum antibody titres (EU/ml) for **a commercially available competitor vaccine**, where pre-samples were collected before vaccination on day 0, post 1 samples collected before the booster vaccination at 28 days and post 2 samples were collected at day 35.

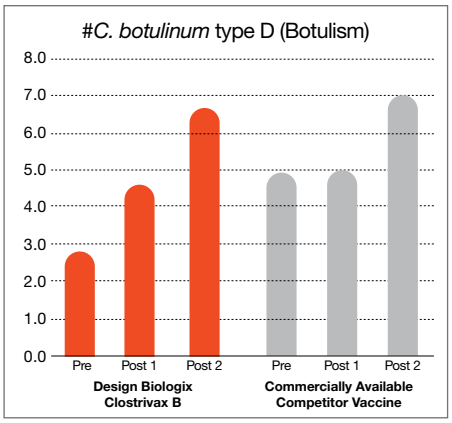

Figure E1.3 Antibody concentrations against *C. botulinum* type D toxoid.

Clostrivax B: Mean serum antibody titres (EU/ml) where pre-samples were collected before vaccination on day 0, post 1 samples were collected before the booster vaccination at 28 days and post 2 samples collected at day 35. Following vaccination there was a significant rise in antibody titres. Final titre of 66.5 EU/ml. The in-house requirement is 5.0 EU/ml. **Competitor:** The mean serum antibody titres (EU/ml) for **a commercially available competitor vaccine**, where pre-samples collected before vaccination on day 0, post 1 samples collected before the booster vaccination at 28 days and post 2 samples were collected at day 35.

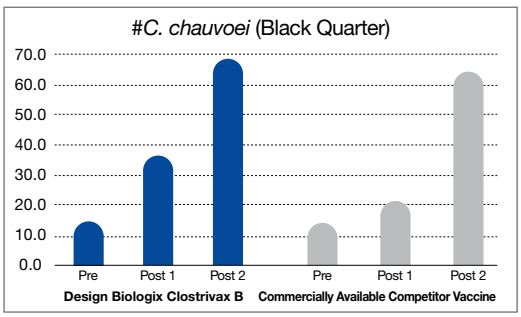

Figure E1.4 Antibody concentrations against *C. chauvoei* spores.

Figure E1.4:

Clostrivax B: Mean serum antibody titres (EU/ml) where pre-samples were collected before vaccination on day 0, post 1 samples were collected before the booster vaccination at 28 days and post 2 samples collected at day 35. Following vaccination there was a significant rise in antibody titres with a final titre of 68.0 EU/ml. The in-house requirement is 50.0 EU/ml.

Competitor: The mean serum antibody titres (EU/ml) for **a commercially available competitor vaccine**, where pre-samples were collected before vaccination on day 0, post 1 samples collected before the booster vaccination at 28 days and post 2 samples were collected at day 35.

Design Biologix

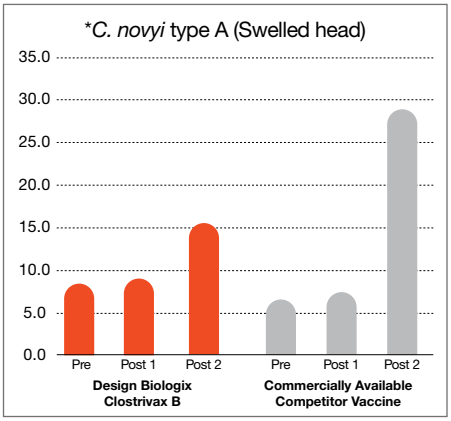

Figure E1.5 Antibody concentrations against *C. novyi* type A alpha toxoid.

Clostrivax B: Mean serum antibody titres (EU/ml) where pre-samples were collected before vaccination on day 0, post 1 samples were collected before the booster vaccination at 28 days and post 2 samples were collected at day 35. Following vaccination there was a significant rise in antibody titres with a final titre of 7.9 EU/ml. The in-house requirement is 3.5 EU/ml.

Competitor: The mean serum antibody titres (EU/ml) for **a commercially available competitor vaccine**, where pre-samples were collected before vaccination on day 0, post 1 samples collected before the booster vaccination at 28 days and post 2 samples collected at day 35.

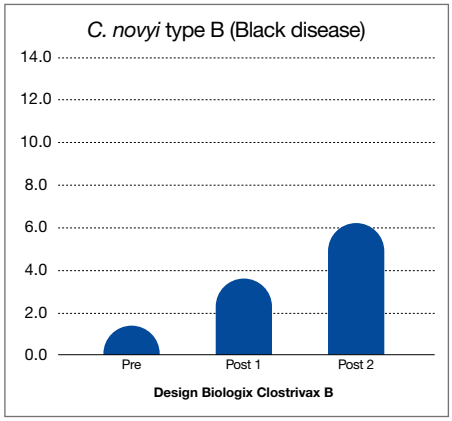

Figure E1.6 Antibody concentrations against *C. novyi* type B beta toxoid.

Clostrivax B: Mean serum antibody titres (EU/ml) where pre-samples were collected before vaccination on day 0, post 1 samples were collected before the booster vaccination at 28 days and post 2 samples were collected at day 35. Following vaccination there was a significant rise in antibody titres. Final titre of 12.5 EU/ml. The in-house requirement is 1.0 EU/ml. There is no monograph available for the beta toxin of *C. novyi* type B.

Competitor: No currently registered vaccine (control group) contains *C. novyi* type B in their formulations.

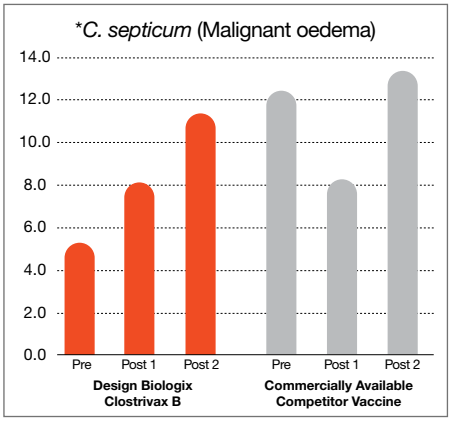

Figure E1.7 Antibody concentrations against *C. septicum* alpha toxoid.

Clostrivax B: Mean serum antibody titres (EU/ml) where pre-samples were collected before vaccination on day 0, post 1 samples were collected before the booster vaccination at 28 days and post 2 samples were collected at day 35. Following vaccination there was a significant rise in antibody titres. Final titre of 11.3 EU/ml. The in-house requirement is 2.5 EU/ml.

Competitor: The mean serum antibody titres (EU/ml) for **a commercially available competitor vaccine**, where pre-samples were collected before vaccination on day 0, post 1 samples collected before the booster vaccination at 28 days and post 2 samples collected at day 35.

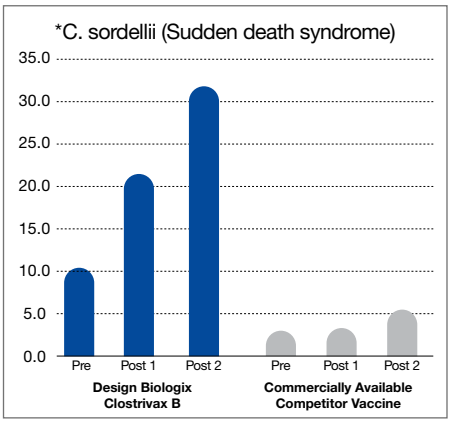

Figure E1.8 Antibody concentrations against C. *sordellii* lethal toxoid.

Clostrivax B: Mean serum antibody titres (EU/ml) where pre-samples were collected before vaccination on day 0, post 1 samples were collected before the booster vaccination at 28 days and post 2 samples were collected at day 35. Following vaccination there was a significant rise in antibody titres. Final titre of 16.2 EU/ml. The in-house requirement is 1.0 EU/ml.

Competitor: The mean serum antibody titres (EU/ml) for a **commercially available competitor vaccine**, where pre-samples were collected before vaccination on day 0, post 1 samples were collected before the booster vaccination at 28 days and post 2 samples were collected at day 35.

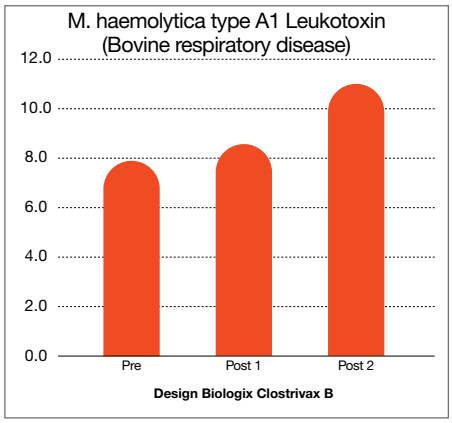

Figure E1.9 Antibody concentrations against M. *haemolytica* type A1 leukotoxin.

Figure E1.9:

Clostrivax B: Mean serum antibody titres (EU/ml) where pre-samples were collected before vaccination on day 0, post 1 samples were collected before the booster vaccination at 28 days and post 2 samples were collected at day 35. Following vaccination there was a significant rise in antibody titres. Final titre of 11.0 EU/ml. There is no monograph available for *M. haemolytica* type A1 leukotoxin.

Competitor: The commercially available competitor vaccine did not have *M. haemolytica* type A1 leukotoxin in the formulation.

CONCLUSION

Clostrivax B was evaluated for its ability to elicit a humoral immune response in cattle. All antigens involved in the formulation of **Clostrivax B** showed good immunogenicity in the target animal.

Clostrivax B is safe to use in cattle during any trimester of pregnancy. Primary vaccinations in previously un-vaccinated calves are recommended at a minimum age of 2 months with an annual re-vaccination period.

Clostrivax B is an adjuvanted multi-component vaccine for the active immunisation of cattle against diseases caused by *Clostridium perfringens* type A (enterotoxaemia), *C. botulinum* types C and D (botulism), *C. novyi* type A (swollen head), *C. novyi* type B (black disease), *C. chauvoei* (black quarter), *C. sordellii* (sudden death syndrome), *C. septicum* (malignant oedema) and *Mannheimia haemolytica* type A1 (bovine respiratory disease).

Clostrivax B for cattle. Reg. Nr. G4483 (Wet 36/1947)

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