



Vaxsafe® ND

(Strain V4)

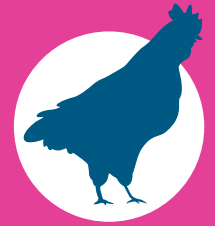


ANIMAL TREATMENT ONLY
Vaxsafe® ND
Strain V4: $\geq 10^{6.0}$ EID₅₀/mL
2000 doses
ACCOMPANYING LEAFLET
BIOPROPERTIES Pty Ltd
180029105

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Features of Vaxsafe® ND Vaccine (living)

- Produced from a low passage isolate of V4 held by CSIRO since isolation in 1966
- Seedlot development included bird-to-bird passages to ensure high bird infectivity
- Highly transmissible ensuring uniform flock protection
- Able to induce protection in the face of a low level of maternal antibody
- Compatible with other live viral vaccines including HVT, IB and IBD
- Proven safety and efficacy under field conditions



Product Development

Newcastle disease (ND) virus, strain V4 was first isolated at the Queensland Veterinary Research Institute in 1966. The strain was stored by CSIRO before supply to BIOPROPERTIES for vaccine development. BIOPROPERTIES undertook extensive testing in conjunction with Australian Animal Health Laboratory (AAHL), a division of CSIRO, to develop a seed lot that would provide a stable finished vaccine. BIOPROPERTIES then conducted the required regulatory testing of the vaccine under laboratory and field conditions. Vaxsafe® ND Vaccine (living) (Vaxsafe® ND) was registered in 2005 for vaccination of broiler chickens. The finished product consists of a freeze-dried suspension of live ND virus in SPF embryo allantoic fluid.

Biological and Molecular Characteristics of the Vaccine Seed

The precise identification of the seed lot used to produce Vaxsafe® ND was undertaken with AAHL. These studies confirmed that the master seed had biological and molecular characteristics consistent with those of reference and historical isolates of ND V4. In the region of the genome identified as the major virulence determinant, the fusion protein cleavage site, the master seed and finished product passage level were shown to have molecular characteristics consistent with other lentogenic ND strains.

Safety in Chickens

A number of experiments have been undertaken in chickens under laboratory and field conditions to prove the safety of the vaccine.

Pathogenicity testing in SPF chickens

Fourteen-day-old SPF chickens were vaccinated orally with a standard field dose, 10 times standard dose and 100 times standard dose of Vaxsafe® ND. Another group was vaccinated with 10 times standard dose on three occasions at 28 day intervals. No adverse reactions were detected in any of the groups up to 70 days of age (up to 84 days of age in the repeat vaccinated group). No pathological lesions were evident and the body weight of the chickens in all groups did not differ significantly from that of a group of unvaccinated chickens or from a group vaccinated with another registered live ND V4 vaccine.

Safety in broiler chickens

When 7, 12 and 17-day-old broiler chickens with maternal antibody to ND virus were vaccinated orally with Vaxsafe® ND, no adverse reactions were observed and there were no significant differences in body weight between the vaccinated and control groups. In addition, when Vaxsafe® ND was administered at 17 days of age to chickens previously vaccinated by coarse-spray with Vaxsafe® ND vaccine at 1-day-old, no adverse reactions were observed up to 42 days of age.

Comparative safety studies with another registered live ND V4 vaccine

In three comparative studies, Vaxsafe® ND showed safety characteristics equivalent to those of another registered live ND V4 vaccine. Both vaccines met the requirements of the Australian standard for safety.



In-contact transmission of Vaxsafe® ND

To assess the horizontal transmissibility of Vaxsafe® ND, vaccinated chickens were placed in close contact with unvaccinated chickens under laboratory conditions. The study was conducted using SPF and commercial broiler chickens. Evidence of rapid spread of vaccine virus to the in-contact birds was demonstrated by serological testing such that in-contact birds had a mean serum antibody level that was not significantly different from vaccinated birds at 14 days after vaccination. No adverse clinical reactions were observed and there was no significant difference in body weight between the vaccinated and the in-contact groups.

Interaction with other vaccines

Vaxsafe® ND was administered to broiler chickens in a large-scale field trial at 10 days of age following the use of Herpesvirus of turkeys (HVT) vaccine *in ovo* and Infectious bronchitis (IB) vaccine at day-old. No adverse reactions were reported. In addition, Vaxsafe® ND has been given to SPF chickens at three weeks after the administration of Vaxsafe® IBD without any adverse effects or reduction in ability to stimulate production of ND Haemagglutination Inhibition (HI) antibody.

Efficacy of Vaxsafe® ND

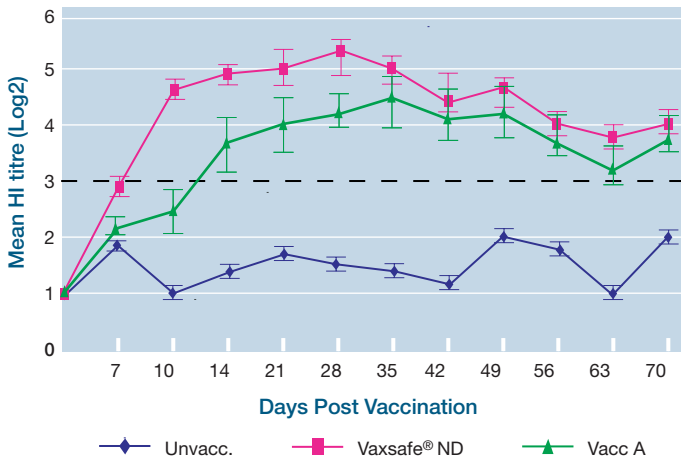
As there is a high correlation between ND HI antibody response and protection against virulent ND virus challenge, all studies on the efficacy of Vaxsafe® ND were undertaken without challenge with virulent ND virus.

Laboratory efficacy studies

Four laboratory efficacy studies were undertaken using both SPF White Leghorn chickens and commercial broiler chickens. In SPF chickens, and in ND maternal antibody negative commercial broilers, Vaxsafe® ND, with a titre equivalent to the minimum allowable at the end of its shelf life, induced HI antibody responses well in excess of those required for protection against virulent challenge (Figures 1 & 2 respectively).

It was also found that in a dose response study involving SPF chickens, Vaxsafe® ND had a wide dosage margin. This wide margin gives confidence that other external factors such as ND maternal antibody or poor storage conditions will have less of an effect on the performance of the vaccine. When required, it was found that a further vaccination with Vaxsafe® ND, 4 weeks later could further boost HI antibody levels.

Figure 1. Serum antibody response after oral vaccination of 14-day-old SPF chickens with Vaxsafe® ND to 10 weeks post vaccination.

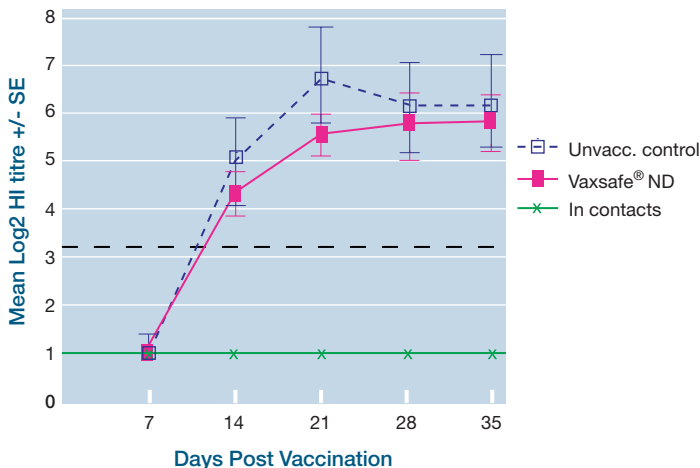


Notes: Vaxsafe® ND administered orally to SPF chickens at 14 days of age. Dotted line indicates minimum mean HI titre to comply with national ND vaccination SOPs. Vacc A is an existing registered V4 vaccine.

Efficacy in broiler chickens without ND maternal antibody

When maternal antibody negative broiler chickens were vaccinated with Vaxsafe® ND at 7 days of age, all birds were considered positive (HI titre $\geq 2^3$) at 14 days post vaccination (Figure 2). Unvaccinated hatch mates developed an antibody response that was not significantly different from vaccinated birds, with all birds positive within 14 days after contact with vaccinated birds, indicating a high level of transmission.

Figure 2. Serum antibody response after oral vaccination of 7-day-old maternal antibody free broiler chickens with Vaxsafe® ND to 5 weeks post vaccination.

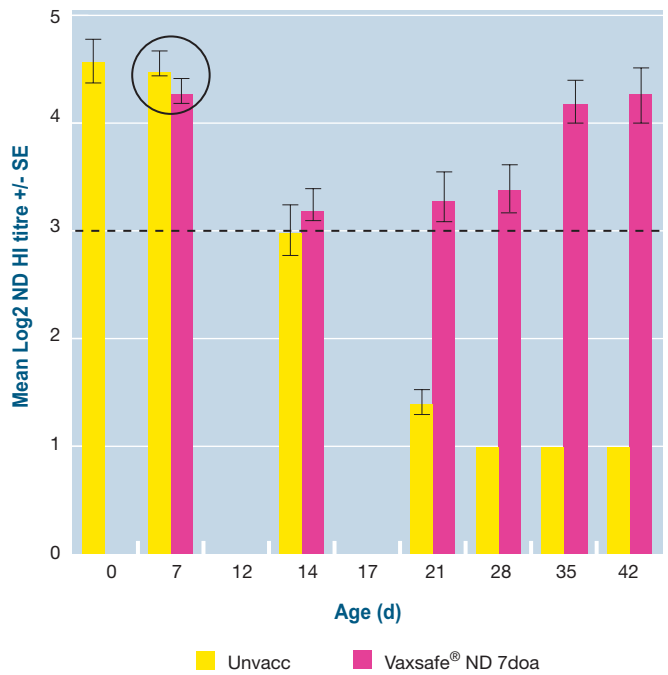


Notes: Solid pink line indicates antibody response in vaccinates; purple dotted line indicates antibody response in unvaccinated, in contact hatch mates. Black dotted line at 2^3 HI units indicates minimum mean HI titre to comply with national ND vaccination SOPs.

Efficacy in broiler chickens with ND maternal antibody

When 7, 12 and 17-day-old broiler chickens with high to low levels of ND maternal antibody to ND virus, respectively were vaccinated orally with Vaxsafe® ND, all age groups produced protective levels of ND HI antibody. However, the broiler chickens vaccinated at 7 days of age had the most consistent protective levels of antibody (Figure 3). Vaxsafe® ND induced an active antibody response significantly earlier than another registered live ND V4 vaccine. When Vaxsafe® ND was administered at 17 days of age to chickens previously coarse-spray vaccinated with ND V4 vaccine at 1-day-old, it did not induce antibody levels as high as a single dose given at 17 days of age when passive antibody levels had fallen. However, both vaccination programs induced HI antibody responses well in excess of the minimum standards required under the current Australian Government ND control program.

Figure 3. Comparison of mean ND HI titres to 42 days of age in maternal antibody positive commercial broilers vaccinated with Vaxsafe® ND at 7 days of age and similar unvaccinated chickens.



Notes: Vaxsafe® ND administered (oral) to commercial maternal antibody positive broiler chickens at 7 days of age. Dotted line indicates minimum mean HI titre to comply with national ND vaccination SOPs. Circle indicates age of vaccination.

Onset and duration of protection

In SPF chickens, a protective antibody response was achieved as early as 7 days after oral vaccination with Vaxsafe® ND. However, in the presence of maternal antibody in broiler chickens, protective levels were delayed until 10-11 days post vaccination. As indicated above, Vaxsafe® ND induced superior efficacy characteristics in terms of earlier onset of immunity, higher protective titre and a longer duration of immunity. Overall, the duration of protection induced by Vaxsafe® ND would adequately cover chickens to the age at which the majority of broiler chickens are slaughtered.

