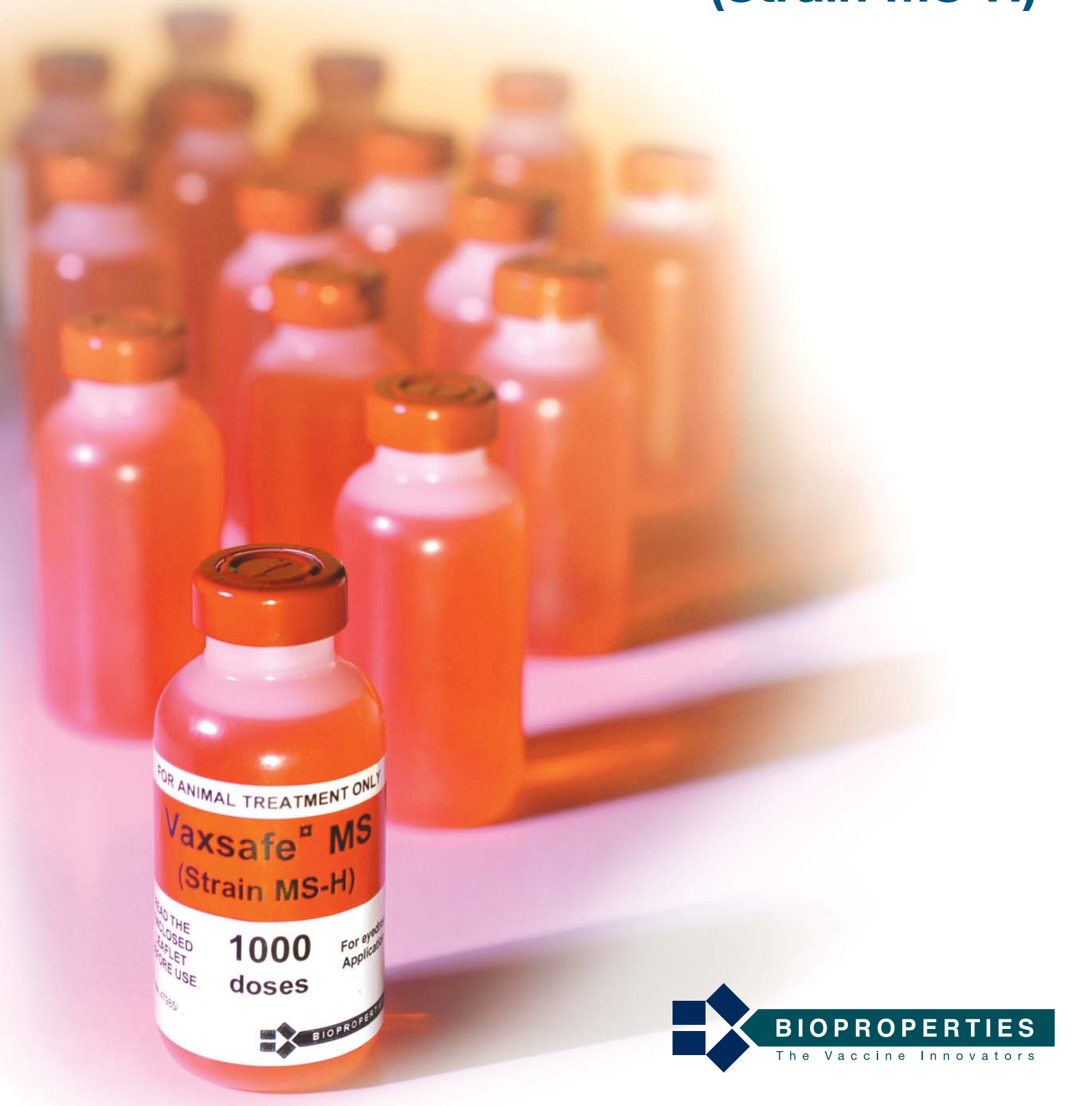
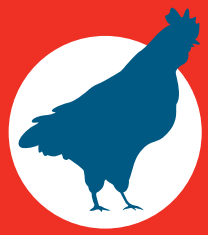
Vaxsafe® MS
(Strain MS-H)



BIOPROPERTIES
The Vaccine Innovators

Features of Vaxsafe® MS (Strain MS-H)

- Single dose for life-long protection
- Safe for poultry
- Protects against air sac infection
- Vaccine response can be monitored using RSA and ELISA serology
- Improves broiler, layer and breeder performance



Safety Studies

Pathogenicity

Vaxsafe® MS has been demonstrated to be apathogenic in chickens and turkeys. Vaccination of SPF chickens, either alone or in conjunction with exposure to infectious bronchitis virus (IBV), failed to induce gross lesions in the respiratory tract or synovial cavities. Likewise in mycoplasma-free turkeys, administration by eye-drop or coarse-spray did not induce gross lesions.

Effect of Vaccine Overdosing

Vaxsafe® MS has been shown to be safe after administration of an overdose. SPF chickens were administered with up to 33 times the minimum recommended dose of Vaxsafe® MS (Table 1) without evidence of air sac or joint lesions, or any effect on body weight.

Table 1. Effect of an overdose of Vaxsafe® MS when administered by eye drop

Group (Vaccine batch #)	SPF chickens Male:Female ratio	Dose/bird (log_{10} Colour Changing Units)*	Mean body weight - 1 S.D. (g)		Air Sac lesion incidence	Median RSA Score^
			Initial	Post mortem		
NegativeControl	6:4	none	2.75.8 ± 21.9	645 ± 70	0/10	0 (0-0)
# 9501	6:4	7.54	245.4 ± 13.8	609 ± 63	0/10	0.5 (0-1)
# 9502	6:3	7.79	272.9 ± 29.7	629 ± 81	0/9	0.5 (0-1)
# 9503	7:3	7.92	269.5 ± 26.5	652 ± 67	0/10	0.5 (0-1)

* The doses administered were calculated to be 13.8, 24.5 and 33.1 times the proposed minimum end-of-shelf-life titre of Vaxsafe® MS of $10^{6.4}$ ccu/30L bird dose for each of the three batches, respectively.

^ RSA score 0 to 4+

Reversion to Virulence

SPF chickens, inoculated with Vaxsafe® MS, after rapid passage in chickens or mycoplasma medium did not develop clinical signs including respiratory disease or synovitis. This confirms that rapid passage in chickens or mycoplasma medium does not result in reversion to a virulent form of MS.

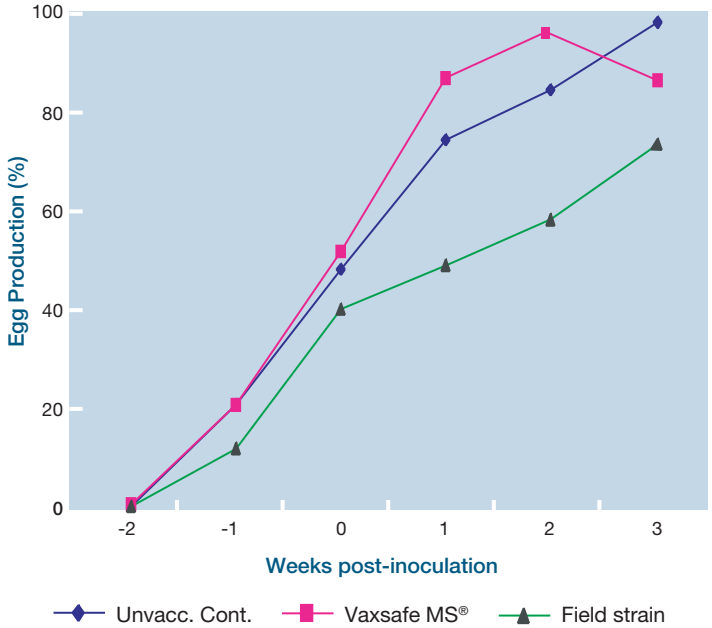
Bird to Bird Transmission of Vaccine Organism

Vaxsafe® MS will spread horizontally to chickens in close contact. However laboratory and field studies have demonstrated that Vaxsafe® MS is not transmitted vertically and does not colonise the oviduct. Although not recommended, Vaxsafe® MS has also been shown to be safe (no adverse effect on egg production) when administered to chickens in-lay (Figure 1).

Co-administration

Vaxsafe® MS is safe to administer with other respiratory vaccines such as Vaxsafe® MG (Strain ts-11), Infectious Bronchitis (VIC S) vaccine and ILT (Strain A20).

Figure 1. Hen-day egg production (%) for 18-week old pullets inoculated with Vaxsafe® MS, a field strain of *M. synoviae* (94011), or not vaccinated.



Efficacy Studies

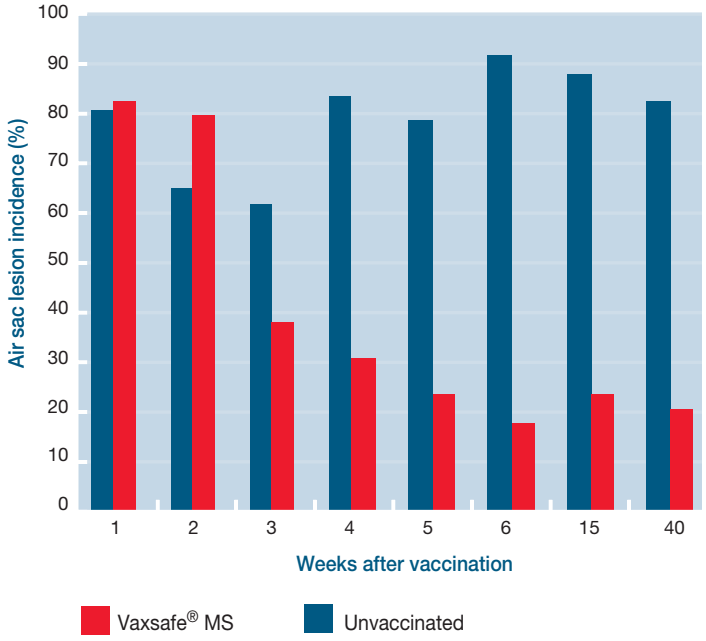
Local Immunity

Vaxsafe® MS has been demonstrated to induce superior protection to that of an inactivated *mycoplasma synoviae* (MS) vaccine. Vaxsafe® MS stimulates local immunity, rather than humoral antibody immunity, in the respiratory tract during its persistence on the mucosal surface.

Efficacy

Vaxsafe® MS is highly efficacious. Laboratory challenge studies were undertaken using a virulent wild-type MS combined with IB virus. A significant reduction in the number and severity of air sac lesions was observed in Vaxsafe® MS vaccinated chickens (Figure 2). Vaxsafe® MS has also been found to be efficacious in turkeys when administered by eye-drop.

Figure 2. Air sac lesion incidence after vaccination of 5-week old SPF chickens with Vaxsafe® MS and challenge 3 weeks later with wild-type *M. synoviae*.



Duration of Immunity

Vaxsafe® MS provides a high level of protection after a single vaccination for at least 40 weeks. Vaxsafe® MS persists on the mucosal surfaces of the upper respiratory tract of the bird, where it continues to provide antigenic stimulation for induction of local and systemic immunity.

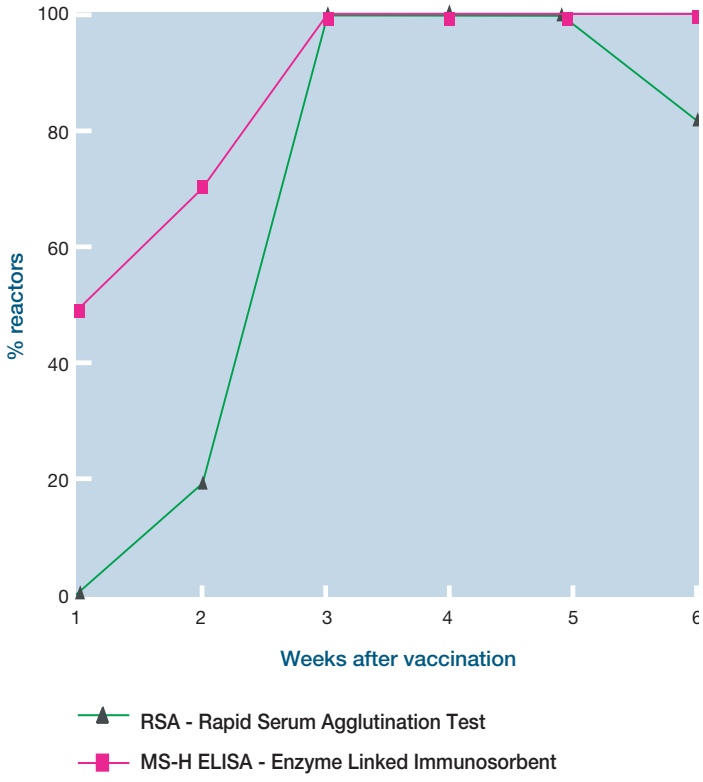
Onset of Immunity

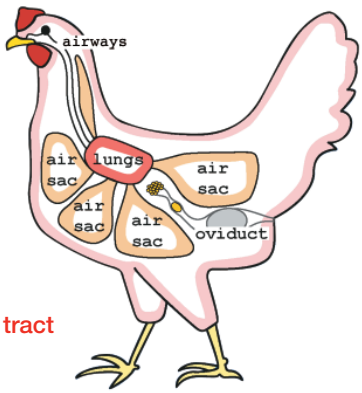
Vaccination of chickens with Vaxsafe® MS results in a rapid onset of immunity with maximum levels of protection being achieved by three weeks after vaccination.

Antibody Response

Antibodies against MS-H develop quickly and reach peak titres in the blood of SPF chickens within 3 weeks of vaccination with Vaxsafe® MS. This allows assessment of the vaccine 'take' and the development of the humoral antibody response (Figure 3).

Figure 3. Antibody response following administration of Vaxsafe® MS to SPF chickens at 5 weeks of age.





Anatomy of avian respiratory tract

Vaxsafe® MS (Strain MS-H)

Product Development

Vaxsafe® MS is a live attenuated (temperature sensitive) vaccine for the control of disease caused by MS in chickens. The technology was developed at the University of Melbourne and licensed to BIOPROPERTIES Pty Ltd.

The original MS field isolate was attenuated by chemical mutation, grown at a low temperature (33°C) and selected for a temperature sensitive (ts+) phenotype. The temperature sensitive clone selected for vaccine development was identified as Strain MS-H. A seed lot system was developed to ensure uniformity of production batches and following proof of safety and efficacy, the product was registered in Australia in 1996.

The finished product, containing a suspension of live MS Strain MS-H organisms in mycoplasma medium, is presented in plastic bottles each containing 1,000 doses. A dropper teat is supplied for vaccine administration. Safety and efficacy have been confirmed by a number of laboratory scale and field use studies.

Productivity Benefits

Vaxsafe® MS vaccination confers major productivity benefits when vaccinated flocks are compared with unvaccinated flocks exposed to MS field strains. Meat breeder and broiler performance has been monitored in Australia and Mexico. Vaccination with Vaxsafe® MS has been found to consistently improve egg production and reduce leg weakness from synovitis and respiratory disease. Mexican field experience (Soto, *et al* 2002) estimates these improvements to be equivalent to an increase in egg production of between 4.5 and 13 eggs per hen production cycle.

Field trials, and experience, in Australia have demonstrated that Vaxsafe® MS may:

- Increase egg production by 2 to 8 eggs per hen cycle in breeders.
- Improve chicken quality, FCR and body weights in broiler progeny.
- Reduce antibiotic usage.

Vaccine Use

A full description of the storage, handling and method of administration of Vaxsafe® MS is described in the product leaflet that accompanies the vaccine.

Vaccine Presentation

Vaxsafe® MS is supplied in a plastic peel-top 30mL eyedropper bottle with a rubber stopper and aluminium seal. Each bottle is supplied with a dropper teat and contains 1,000 doses.

Vaccine Administration

Thaw each bottle in a 35°C water bath. Remove the aluminium seal and stopper and insert the dropper teat. A full eye drop dose should be administered to each bird. A blue dye can be added to the vaccine to check the accuracy of administration. Use within two hours of thawing.

Vaccine Storage

Vaxsafe® MS is supplied frozen (on dry-ice) and should be held at –70°C or lower if the full shelf-life of four years is to be achieved. The vaccine will, however, maintain its potency for up to 4 weeks if held in a freezer at –20°C.

Vaccination Program

Birds should be vaccinated with Vaxsafe® MS once between 3 and 6 weeks of age. Birds should not be moved into an MS infected area until at least three weeks after vaccination. Vaccination of flocks in which antibiotics are being used (especially those with anti-mycoplasma activity) must be avoided. Where antibiotics have been used, allow for a period of drug withdrawal as prescribed for the antibiotic before vaccinating with Vaxsafe® MS. Vaxsafe® MS can be co-administered with other live respiratory vaccines, including Vaxsafe® MG.

References and Further Reading

- Morrow, *et al.,* (1998). Production of temperature-sensitive clones of *Mycoplasma synoviae* for evaluation as live vaccines. Avian Dis. 42:667-670
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- Markham, *et al*., (1998). Field evaluation of the safety and efficacy of a temperature-sensitive *Mycoplasma synoviae* live vaccine. Avian Dis. 42:682-689
- Soto, *et al*., (2002). Experiences with MS-H in Mexico. Mycoplasma symposium held in conjunction with the 51st Western Poultry Disease Conference, Puerto Vellarta, Mexico. pp1-6.

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