Development of an inactivated, iron-restricted vaccine for poultry to aid in the control of Salmonella Enteritidis and Salmonella Typhimurium, and the potential for broad spectrum protection against salmonellosis

H van den Bosch[1], F.A. Clifton-Hadley[2], S.W. Cooles[2], B Sheehan[1], S.B. Houghton[1] and M.J. Woodward[2]

1. Intervet, Walton Manor, Walton, Milton Keynes, Buckinghamshire, MK77AJ, United Kingdom 2. Department of Bacterial Diseases, Veterinary Laboratories Agency, Weybridge, New Haw, Addlestone, Surrey KT15 3NB, Uniited Kingdom.

Introduction

The incidence of Salmonella enterica serovar Enteritidis in poultry and poultry products, particularly eggs, and the concomitant risk associated with human infection has been a cause for concern throughout Europe for more than 10 years. We have previously shown that Salenvac, an inactivated vaccine produced under iron restriction, significantly reduces S. Enteritidis infection in commercial flocks. This was demonstrated in experimental studies, which showed decreased excretion, tissue infection and egg contamination. Vaccine efficacy was further confirmed in a large scale independent survey of the incidence of S. Enteritidis in eggs (Figure 1) following the introduction of Salenvac on the UK market in 1995. Vaccination of layers began on a significant scale in 1997 and the UK poultry industry subsequently adopted vaccination as part of the Lion Code, which describes standard practices designed to ensure product quality. The uptake of Salenvac was extensive and correlated with a substantial decrease in cases of human salmonellosis (Figure 2). During this period Salenvac was the only S. Enteritidis vaccine available in the UK.

Although reduction of S. Enteritidis was justifiably the primary concern, a multivalent Salmonella vaccine may further reduce the risk to human health of salmonellosis arising from poultry and poultry products. Of the other Salmonellas associated with poultry, and with human disease, Salmonella enterica serovar Typhimurium is the most significant. However, there are many other serovars of Salmonella that are implicated to a greater or lesser extent, primarily those belonging to Groups B and C.

Here we describe the development of an extension of Salenvac, Salenvac T. Salenvac T builds on the success achieved with Salenvac by providing protection against both S. Enteritidis and S. Typhimurium. We also report the results of studies designed to assess the efficacy of Salenvac T against other Group B and Group C Salmonellas.

Nobilis Salenvac - Effects on egg contamination

Field Studies*

	Number of eggs	SE incidence	Ratio
Vaccinated flocks	44750	0	0
Unvaccinated flocks	42642	6	1:1100

*Independant study performed on behalf of a major UK producer and retailer

Figure 1.
Efficacy of Nobilis Salenvac: Effect of vaccination on egg contamination with S. Enteritidis.
Results of an independent field study performed by a major egg producer and UK retailer.

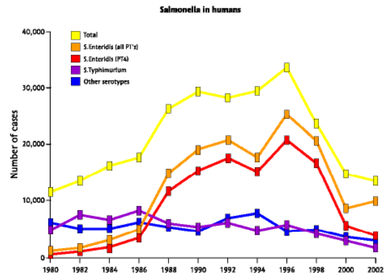

Figure 2.
Salmonella in humans: England and Wales, 1981-2002. Faecal & unknown reports excluding S. Typhi & S. Paratyphi for England and Wales, 1981-2002. Data supplied by Dr Linda Ward, Health Protection Agency (formerly PHLS).

Materials and Methods

Vaccine:

Nobilis Salenvac T

Description:

Bivalent formalin inactivated whole cell vaccine produced from cells grown under conditions of iron restriction.

Composition:

Active constituents (2 x 10^9 per ml each):

Salmonella enterica serovar Enteritidis PT4

Salmonella enterica serovar Typhimurium DT104

Excipients:

Adjuvant: Aluminium hydroxide gel

Preservative: Thiomersal

Vaccinations:

0.5 ml Nobilis Salenvac T administered intramuscularly at 4 & 6 weeks of age

Challenge model:

Efficacy was determined using either conventional, or specific pathogen free, chickens. All birds were challenged by the oral route at 8 weeks of age. The challenge was administered either (i) by direct instillation of the bacteria into the crop or (ii) indirectly, through the use of seeder birds previously infected with the challenge organism. In the case of (i) crop acid was neutralised immediately prior to challenge with two challenge volumes of 10% sodium bicarbonate. Details of the challenge organisms and the numbers of infecting bacteria are given in the legends to Figures 3-7.

To monitor excretion (shedding) of the challenge strain, cloacal swabs were taken at regular intervals up to 35 days post challenge (Figures 3-7) and cultured for the presence of the challenge organism. The growth of salmonellae on brilliant green agar or in selenite broths was recorded semi-quantitatively as heavy (>50 colonies), medium (1-50 colonies) or light (growth following enrichment in selenite broth only).

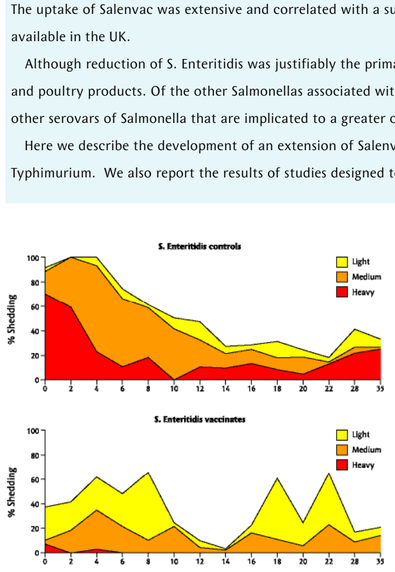

Figure 3.
Efficacy of Nobilis Salenvac T: S. Enteritidis challenge (Serogroup D). Specific pathogen free white leghorns were infected with S. Enteritidis strain 857 (1.3 x 109 cfu) by the oral route. Excretion of the challenge strain by unvaccinated birds is shown in (A); excretion by the Salenvac T-vaccinated cohort is shown in (B). Excretion was recorded semi-quantitatively as described in Materials and Methods.

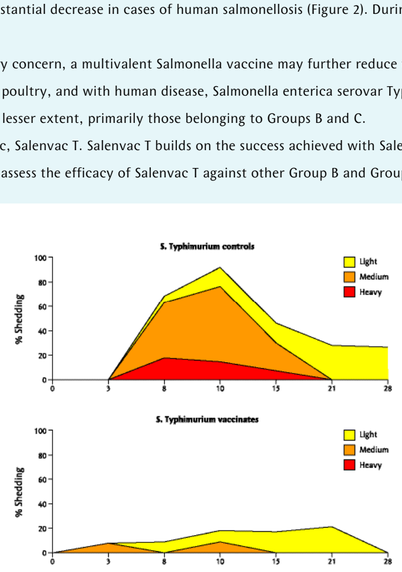

Figure 4.
Efficacy of Nobilis Salenvac T: S. Typhimurium challenge (Serogroup B). Conventional broiler breeders were infected with S. Typhimurium strain 2391 by housing them with 'seeder' birds previously infected with the challenge organism. Excretion of the challenge strain by unvaccinated birds is shown in (A), while excretion by the Salenvac T-vaccinated cohort is shown in (B). Excretion was recorded semi-quantitatively as described in Materials and Methods.

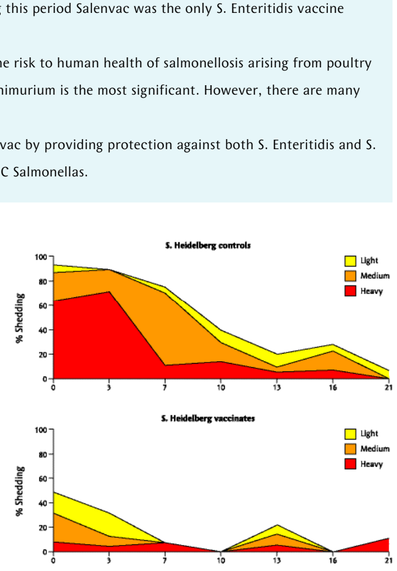

Figure 5.
Efficacy of Nobilis Salenvac T: S. Heidelberg challenge (Serogroup B). Specific pathogen free white leghorns were infected with a mixture of 5 virulent USA isolates of S. Heidelberg (1 x 109cfu total) by the oral route. Excretion of the challenge strain by unvaccinated birds is shown in (A); excretion by the Salenvac T-vaccinated cohort is shown in (B). Excretion was recorded semi-quantitatively as described in Materials and Methods. Similar results were obtained when birds were challenged with a virulent S. Heidelberg strain of UK origin (data not shown).

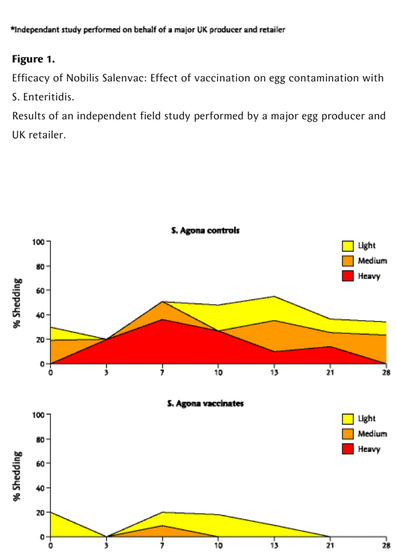

Figure 6.
Efficacy of Nobilis Salenvac T: S. Agona challenge (Serogroup B). Specific pathogen free white leghorns were infected with a mixture of 5 virulent UK isolates of S. Agona by housing them with 'seeder' birds previously infected with the challenge organisms. Excretion of the challenge strain by unvaccinated birds is shown in (A); excretion by the Salenvac T-vaccinated cohort is shown in (B). Excretion was recorded semi-quantitatively as described in Materials and Methods.

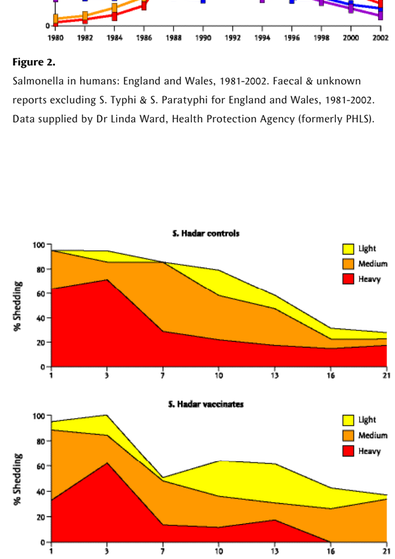

Figure 7.
Efficacy of Nobilis Salenvac T: S. Hadar challenge (Serogroup C). Specific pathogen free white leghorns were infected with a virulent S. Hadar isolate (2 x 109 cfu) by the oral route. Excretion of the challenge strain by unvaccinated birds is shown in (A); excretion by the Salenvac T-vaccinated cohort is shown in (B). Excretion was recorded semi-quantitatively as described in Materials and Methods.

Conclusions

- Salenvac T protects poultry against infection with S. Enteritidis and S. Typhimurium.
- Salenvac T does not protect against Salmonella enterica serovar Hadar (Group C).
- Significantly, Salenvac T does protect poultry against infection with other Group B Salmonellas, which may offer further benefits in extending the use of poultry vaccination to reduce human salmonellosis.

References

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