Vaxsafe® ST
(Strain STM-1)
Features of Vaxsafe® ST (Strain STM-1)

- Live bacterial cells, freeze-dried and suspended in a buffered sucrose solution
- Reduction in the incidence and carriage of Salmonella typhimurium infection in chickens
- For administration to chickens

Background

The Problem of Salmonella

Salmonellae are a problem in all sectors of the food industry. Some Salmonella appear to be particularly well adapted to poultry production systems and specific control measures are needed to decrease the risk poultry products pose to consumers.

Salmonella typhimurium is one such Salmonella which can chronically infect poultry and be vertically transmitted to the next generation. Horizontal transmission within flocks reared on the floor is particularly efficient and rapid. Young birds are at high risk from establishing infection after challenge before they develop mature intestinal microflora. Consequently Salmonella control strategies need to focus on brooding and rearing of poultry. Colonisation of poultry flocks by S. typhimurium with subsequent contamination of meat and eggs can be a source of Salmonella infection in man and can be detrimental to the health of the bird. S. typhimurium is probably the most important Salmonella currently existing in poultry in the Australian egg and poultry meat industries.

Salmonella control in layers and breeders begins with sourcing stock from Salmonella-free breeding stock. Biosecurity with an emphasis in effectively disinfected premises, rodent control and prevention of contact with other sources of infection is important. Control of Salmonella in feed is a particularly difficult area. The risk feeds pose can be minimised by the quality control of raw materials with special attention to animal proteins and feed mill hygiene. Processes like pelleting and feed additives like organic acids can further decrease the risk but it is very difficult to eliminate infection with these processes alone (although laboratory testing of these feeds may be consistently negative, this is no guarantee of total elimination of the Salmonella) (Figure 1).

Figure 1: Simple epidemiological model of the potential sources of Salmonella contamination for poultry flocks.

<table>
<thead>
<tr>
<th>Year</th>
<th>1981</th>
<th>1983</th>
<th>1985</th>
<th>1987</th>
<th>1989</th>
<th>1991</th>
<th>1993</th>
<th>1995</th>
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<th>1999</th>
<th>2001</th>
<th>2003</th>
<th>2005</th>
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<tbody>
<tr>
<td>S. typhimurium</td>
<td>25000</td>
<td>5000</td>
<td>10000</td>
<td>15000</td>
<td>20000</td>
<td>0</td>
<td>0</td>
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<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>S. Enteritidis</td>
<td>25000</td>
<td>5000</td>
<td>10000</td>
<td>15000</td>
<td>20000</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Other serotypes</td>
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<td>5000</td>
<td>10000</td>
<td>15000</td>
<td>20000</td>
<td>0</td>
<td>0</td>
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</tbody>
</table>

Control measures have to be implemented at each potential portal of entry. In addition, increasing the resistance of the chickens to infection may also help.

Until now the Australian poultry industries have struggled to control Salmonella. Overseas vaccination of poultry with both live and killed vaccines has helped control infections especially at the broiler breeder, layer and broiler levels. Certainly there is evidence in the UK that human infection rates with the poultry associated Salmonella Enteritidis have decreased as control measures including vaccination were introduced (Figure 2).

Figure 2: Human infections with Salmonella (especially Salmonella Enteritidis) in England and Wales from 1982 - 2000 (PHLS)

The increase in Salmonella Enteritidis cases from 1986 associated with increased infection in the National Poultry flock. The decrease after 1997 was associated with the impact of better biosecurity and the introduction of vaccination of the poultry layer flock.
Product Development

STM-1

Strain STM-1 (the basis of Vaxsafe® ST) was developed in Australia from a naturally occurring Australian wild strain of S. typhimurium PT44 isolated from chickens which has been attenuated by deletion of part of the aroA gene (Figure 3). This rendered the organism both dependent on vitamins and other organic molecules being supplied by the growth media in the laboratory (aromatic amines) and non-virulent, without impairing the ability of the strain to induce a protective immune response in the bird.

Figure 3: Aromatic Biosynthetic Pathway

Many bacteria have the ability to synthesise organic compounds considered vitamins or essential amino acids in animals. The removal of the aroA gene in STM-1 makes this organism totally dependent on supply of the aromatic amine metabolites from media to grow.

The attenuation process has not introduced any foreign DNA into the STM-1 vaccine strain and it is not considered by Australian authorities to be a Genetically Modified Organism (GMO). The deletion provides total protection from reversion to virulence as the aroA gene has been extensively disrupted. This makes the STM-1 vaccine strain totally dependent on the media it is grown in supplying some vitamins and amino acids that previously the wild strain readily synthesised. The STM-1 vaccine strain can not obtain sufficient quantities of these now essential nutrients from the environment or the host so STM-1 fails to grow outside the laboratory. This intrinsic limitation on growth does not require the host to be immunocompetent making the vaccine very safe. The initial infection with Vaxsafe® ST mimics the wild-type infection and the attenuation has not altered the vaccine’s antigenic properties.

Safety

For registration trials, birds were given x10 maximum release titre (maxRT). No clinical effects, lesions or negative effect on growth (Figure 4) were observed.

Figure 4: Comparison of body weight of STM-1 vaccinated (x10 maxRT) and unvaccinated birds at weekly time intervals during trial.

No significant difference in growth between vaccinated and unvaccinated birds was observed.

Efficacy

Vaxsafe® ST is given orally and is an aid in the reduction of colonisation in chickens by S. typhimurium. Vaxsafe® ST has been shown to reduce the excretion of virulent S. typhimurium (Figure 5) and provide chickens with protection against challenge by this strain.

Figure 5: Reduction in colonisation and shedding at various times after wild-type S. typhimurium challenge by vaccination with Vaxsafe® ST.

Mechanism of Action

Mucosal Immunity

Mucosal immunity is typically short lived and the effect of maternal antibody may be minimal. There is some evidence overseas that the protection afforded by live Salmonella vaccines is broader than that generated by killed Salmonella vaccines, which appear to be limited to only the homologous serotype (Cookson & Fan, 2002).
Identification of STM-1 in the Laboratory

STM-1 will grow on most laboratory media that contain yeast extract but is readily differentiated from wild type Salmonella by not producing H₂S. On biochemical grounds during initial characterisation it would appear to be a Citrobacter or H₂S negative Salmonella. It can only be detected in chickens for less than 14 days after vaccination but in most cases the infection is rapidly terminated.

References & Further Reading

- Bioproperties internal trial, (2007), A study to assess the safety and efficacy of Vaxsafe® ST Vaccine (living) when given to SPF chickens at one-day of age.

Note that Vaxsafe® ST was previously marketed in Australia as Salvax.