Leptospirosis in New Zealand dairy herds
1.0 Executive Summary

Given the zoonotic potential of leptospires it is vital that vaccines and vaccination programmes are robust and well understood.

This technical bulletin will increase your understanding of leptospiral protective antigens, leptospiral immunity and the influence of age and maternal interference on response to vaccination. Included is an extensive review of Leptospirosis literature, including existing New Zealand research, plus new information from recent Intervet/Schering-Plough studies.

Dairy herd vaccination, first implemented in 1971, has been highly successful in reducing the incidence of Leptospirosis. However, Leptospirosis is still the most common occupationally acquired infectious disease in New Zealand.

Vaccination should eliminate Hardjo from infected herds and prevent Hardjo, Pomona or Copenhageni infection in naïve animals. To achieve this, vaccination must prevent renal colonisation and urinary shedding. As there is significant regional genetic variation in leptospira, a vaccine's ability to prevent shedding should be proven in the country of use.

The scientific evidence for efficacy of vaccination in calves less than 3 months of age is scant and contradictory. Recent New Zealand research adds to the existing evidence that highlights the risk of vaccination of calves at a young age. It indicates a significantly reduced immune response in calves vaccinated at 1 compared with 3 months of age.

To avoid jeopardising the achievements gained from Leptospirosis control programmes, we must apply scientifically valid and proven vaccination programmes. This document provides the background understanding.
2.0 Background

Key Findings

- Leptospirosis is the most common occupationally acquired infectious disease in New Zealand, although its occurrence has dramatically reduced over 25 years.
- Infection with Hardjobovis, Pomona, Copenhageni, Ballum and Balcanica is recorded in NZ in dairy cattle and in humans.
- Leptospires localise in the kidneys and can be shed for extended periods in cattle, for example Hardjo shedding has been recorded for up to 19 months.
- There is significant genetic variation within each leptospiral serovar.

2.1 Classification

Pathogenic leptospires are classified using two independent systems. The most recent is genotypic. It divides the genus Leptospira into several (currently 17) species based on DNA relatedness. The older serological system, classifies isolates based on cross-agglutination of lipopolysaccharide (LPS) antibodies into more than 200 serovars. Antigenically related serovars are arranged into 24 serogroups (Bharti et al., 2003; Levett, 2001).

For practical reasons, both systems coexist. However, as neither serovar nor serogroup are indicative of pathogenicity, one serovar may belong to more than one species and members of the same genetic group do not necessarily belong to the same serogroup. For example the serovar Hardjo is found in 3 genospecies; i.e. L. interrogans, L. borgpetersenii, and L. meyeri (Levett, 2002). The L. interrogans genotype is often referred to as Hardjoprajitno, whereas L. borgpetersenii is named Hardjobovis. Even within a genotype there is variability between isolates. For example using Hardjobovis isolates from all over the globe, Zuemer and colleagues (1993) identified 14 genetic groups, including one unique to NZ.

2.2 New Zealand Leptospires and their Maintenance (or Reservoir) Hosts

Six serovars are recorded as being endemic (i.e. maintained) in NZ (Table 1). Two other serovars (Australis and Canicola) have been isolated, but are not endemic to NZ (Midwinter and Fairley, 1999).

Table 1: The maintenance and accidental host-serovar relationships of the six leptospiral serovars endemic in NZ

<table>
<thead>
<tr>
<th>Genospecies</th>
<th>Serogroup</th>
<th>Serovar</th>
<th>Maintenance host(s)</th>
<th>Accidental Hosts</th>
</tr>
</thead>
<tbody>
<tr>
<td>L. borgpetersenii</td>
<td>Sejroe</td>
<td>Hardjobovis*</td>
<td>Cattle, sheep, deer</td>
<td>Cattle, humans</td>
</tr>
<tr>
<td></td>
<td>Balcanica</td>
<td>Possum</td>
<td>Cattle, humans</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Copenhageni</td>
<td>Brown (Norway)</td>
<td>Ship rat, R. norvegicus, Cattle, dogs</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Copenhageni</td>
<td>Icterohaemorrhagiae</td>
<td>R. norvegicus, Cattle, dogs</td>
<td></td>
</tr>
<tr>
<td>L. interrogans</td>
<td>Pomona</td>
<td>Pomona*</td>
<td>Cattle, sheep, humans</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Tarassovi</td>
<td>Pigs</td>
<td>Cattle, humans, dogs</td>
<td></td>
</tr>
</tbody>
</table>

a. Hardjoprajitno has not been recorded in NZ (Collins-Emerson, 2005) or Australia (Biosecurity Australia, 2000).
b. A subtype of Pomona – Kennewicki – has been isolated from a foal in NZ (Midwinter and Fairley, 1999).
c. Strongly suspected but not definitively confirmed.

Transmission between maintenance hosts is generally high, but disease is unusual (e.g. Hardjobovis in cattle and Copenhageni in rats). “Spill-over” infection into accidental (or incidental) hosts often leads to clinical disease.

2.3 Infection, Transmission, and Disease in Cattle

Infection occurs directly with contact, ingestion or inhalation of urine from shedding hosts, or indirectly from exposure to urine contaminated matter, including water, soil, mud, effluent meat, hides or wool. Environmental survival of leptospires is variable (hours to days) depending on serovar (Pomona>>Hardjo), moisture, soil type, pH, and temperature. Transmission within a herd is enhanced by non-vaccination, wet weather, surface water, and contact between susceptible and shedding animals (Radositi et al., 2000).

Leptospires enter the circulation by penetrating abraded or inflamed skin, or intact mucous (in particular the conjunctival or nasal) membranes. Venereal infection is reported globally, but is of little, if any, significance in NZ. Following systemic spread, leptospires can localise in the kidneys and be shed for extended periods. As an example, Hardjo has being recorded as being shed for up to 19 months (Hellstrom, 1978; Mackintosh, 1981).

Infection with Hardjobovis, Pomona, Copenhageni, Ballum and Balcanica, is recorded in NZ dairy cattle. A brief summary of each follows:
Hardjo
Historically, Hardjobovis infection of dairy cattle was common (Hellstrom, 1978; Mackintosh, 1981). Although not formally surveyed, infection is now uncommon (Midwinter and Fairley, 1999; Pegram et al., 1998). This is primarily due to vaccination.

Globally, Hardjobovis strains vary genotypically and in their pathogenicity. For example, Hardjobovis is associated with abortions and agalactica in the United Kingdom (UK) and the United States (US) (Bolin, 2003; Dhaliwal et al., 1996a; Dhaliwal et al., 1996b; Ellis, 1994).

NZ isolates appear to be well adapted to their maintenance hosts. Infections are usually asymptomatic and are not considered a cause of herd sub-fertility (i.e., abortion and reduced conception rates) (Cordes et al., 1982; Hathaway, 1981). There is however insufficient research, and the current diagnostic tools are insensitive at detecting Hardjo in aborted foetuses, to draw final conclusions.

Pomona
Pomona infection was reasonably common. Now, due to reduced exposure to pig urine and vaccination, Pomona infection is uncommon.

Pomona causes abortion and agalactica in cattle, and haemoglobinuria and occasional deaths in young calves (Carter et al., 1982; Cordes et al., 1982; Hathaway, 1981).

Copenhageni
Calf infection with Copenhageni has been reported in the North Island, and in deer and dogs in both the North and South Islands (Firth et al., 1988; Inglis, 1984; Midwinter and Fairley, 1999). Maintenance of infection is dependent on the distribution of the Brown (Norway) rat. These rats are associated with human habitation, stock feeds, and the presence of water or sewage.

Dodd and Brakenridge (1960) reported disease outbreaks (acute nephritis and deaths) in young calves on 13 farms. Vaccination to protect against Copenhageni is important as rats are impossible to control and remain a source of infection for unvaccinated cattle.

Ballum & Balcanica
Ballum maintenance host infection is common (Hathaway, 1981). Infection of calves, is rare but can lead to hepatic photosensitisation and acute nephritis (Anonymous, 1976). Balcanica infection is very common in possums, but is uncommon in cattle. The only concern is cross-reactivity with Hardjo during microscopic agglutination testing (Hathaway et al., 1978; Hathaway, 1981).

2.4 Infection and Disease in Humans
Leptospirosis remains the most common occupationally acquired infectious disease in NZ. However, since the introduction of dairy herd vaccination, the annual incidence has declined markedly from a peak of 875 (20/100,000 population) cases in 1971 to an average of 87 (range 75 to 180) (3.5/100,000 population) laboratory confirmed cases in the last decade (Figure 1) (Thornley et al., 2002); of which 90% are considered occupationally acquired (Anonymous, 2001).

Serovar distribution has changed over the last 2 decades. A larger proportion of human infections are now caused by Tarassovi (pigs), Ballum (mice, rats, hedgehogs and possibly cattle) and Australis (contracted outside NZ). Hardjo (25 to 40%) and Pomona (15 to 25%) are responsible for about 50% of cases.

Historically, dairy farmers were at greatest risk (Philip, 1976); infection is now uncommon (Baker, 2004). Today, meat processing workers, with about 40 reported cases per annum, are at the greatest risk. Non-dairy farmers (30 cases/annum) have 3 times more cases than dairy farmers (Table 2). Hardjo and Pomona infection for meat workers and non-dairy farmers is associated with contact with sheep, beef cattle and deer (Brown, 2005; Dorjee et al., 2005; Houser and Davies, 2004). Human-to-human spread is rare and has never been recorded in NZ (Thornley et al., 2002).

The incubation period in humans is usually between 5–14 days, but ranges from 2–30 days. The clinical presentation ranges from sub-clinical to multiple organ failure and potentially death. The predominant early clinical features are sudden onset of headache, muscle pain and tenderness, fever, rigors, nausea, conjunctival suffusion, transient skin and mucosal rash, photophobia and other signs of meningism. Most cases (~90%) self-cure after a period of 3 or more months. In NZ, disease caused by Hardjo is usually mild; whereas Copenhageni or Australis are more commonly associated with severe disease (Anonymous, 2001).
3.0 Leptospiral Immunity

Key Findings

- Given the zoonotic consequences of Leptospirosis it is vital veterinarians understand the immune response, and be confident the prescribed vaccines and vaccine programmes are efficacious.
- Protection is mediated by opsonic, complement fixing, and probably agglutinating antibodies.
- Gamma interferon (IFN-\(\gamma\)) appears to be a useful indicator of vaccine efficacy.

3.1 Leptospiral Protective Antigens

Leptospires have a cylindrical body wound spirally around a modified flagellum. The body is surrounded by an external sheath made from two membranes. The outer membrane (i.e. bacterial surface) is mostly made from lipopolysaccharide (LPS) but also contains several lipoproteins (outer membrane proteins (OMP)). Interestingly, although similar in structure to typical LPS of gram-negative organisms, leptospiral LPS appears to be neither toxic nor pyrogenic (Shimizu et al quoted in Midwinter et al., 1994).

Leptospira are antigenically complex. Isolates even from the same serovar differ markedly in their outer membrane, periplasmic space, and flagella, as well as serovar-specific LPS (Bharti et al., 2003). In terms of protective immunity LPS is considered the major antigenic component (Ellis et al., 2000; Yan et al., 1999). However, it is evident that LPS is not the only antigen capable of eliciting protective immunity (Adler and Faine, 1982).

Given the immunodominance of LPS, inactivated whole-cell leptospiral vaccines (bacterins) have been achieved in experimental animal models to date (Cullen et al., 2003). Following leptospiral infection, serum contains antibodies that recognise several protein antigens from the outer membrane, periplasmic space, and flagella, as well as serovar-specific LPS (Bharti et al., 2003). In terms of protective immunity LPS is considered the major antigenic component (Ellis et al., 2000; Yan et al., 1999). However, it is evident that LPS is not the only antigen capable of eliciting protective immunity (Adler and Faine, 1982).

3.2 Leptospiral Protective Immune Response

Innate immunity alone offers insufficient protection against Leptospirosis. Naturally or vaccine acquired immunity is therefore critical to host defence. Natural immunity is considered to be lifelong (Hathaway, 1981). There is strong evidence that this acquired immunity, regardless of serovar, is primarily mediated by immunoglobulins (Farrell et al., 1987; McGrath et al., 1984; Naiman et al., 2002; Tu et al., 1982; Wang et al., 1984; Yan et al., 1999).

More specifically, the importance of opsonising and complement fixing (primarily IgG2 in cattle) antibodies has been clearly demonstrated. Opsonic antibodies tag leptospires enabling phagocytic cells to ingest and destroy them. Complement fixing antibodies trigger leptospire destruction by complement proteins (McGrath et al., 1984; Tu et al., 1982; Wang et al., 1984; Yan et al., 1999).

B cells are induced to produce IgG2 in response to gamma interferon (IFN-\(\gamma\)). Importantly, production of Hardjo specific IFN-\(\gamma\) has been shown to be associated with vaccine induced protection from infection (Busk and Alt, 2001; Ellis et al., 2000; Naiman et al., 2002). IFN-\(\gamma\) has therefore become a useful surrogate measure of vaccine efficacy (Brown et al., 2003).

Several vaccines including Leptavoid H (the monovalent variant of Leptavoid 2), Leptavoid 3, and Spirovac (Developed by Biocore, USA) have been shown to result in significant and specific IFN-\(\gamma\) production following vaccination of cattle (Brown et al., 2003; Ellis et al., 2000; Naiman et al., 2001; Naiman et al., 2002, Moffat and Bruere, unpublished 2007).

IgM and IgG1 (i.e. agglutinating and complement fixing antibodies) are also produced in response to LPS (and other antigens) following challenge or vaccination (Naiman et al., 2002). However, their protective role has yet to be fully established; but as there is a leptospiraemiac stage following infection it would seem feasible that agglutinating antibodies play an important role in protective immunity.

Importantly, the microscopic agglutination test (MAT) measures IgM and IgG1 agglutinating antibody titres raised against LPS only (O’Keefe, 2002). There is some debate as to the significance of a MAT titre in terms of indicating protective immunity. Many studies have shown vaccinated cattle with no measurable MAT titres have resisted challenge. This observation is not new, and was first noted in the 1950s (Gibbs and Kenzey, 1958a; Hoag and Bell, 1955; McDonald and Rudge, 1957). Obviously, this does not indicate that agglutinating antibodies (as measured by the MAT) are non-protective, merely that circulating antibodies have waned. Bearing in mind that the aim of effective vaccination is the generation of memory cells, not antibodies per se, this observation should not be surprising.

Conversely, Bolin and colleagues (1989a, 1989b) induced leptospiuria following Hardjo challenge in vaccinated, MAT positive calves. Besides questioning the vaccine, they also suggested the MAT was not a good measure of protective immunity. Importantly, the vaccine used induced very low MAT titres. Some authors have suggested an association between the magnitude of post-vaccination titres and protection (Gibbs and Kenzey, 1958a). In support of this, there are no reports of effective challenge in the face of high MAT titres. Furthermore, in an interesting Hardjo challenge study, Yan and others (1999) demonstrated the only protective monoclonal antibodies, of the large number tested, were those that induced a positive MAT titre. Given the evidence, post-vaccination MAT titre cannot be ruled out as a measure of protective immunity. Regardless, the MAT remains a very useful tool in determining past or even present infection.

1. Complement is a complex biochemical system that results in the binding of proteins to the surface of microbes. These proteins destroy invading organisms. Binding of complement proteins is triggered either by antibodies on the surface of a microbe (The classical pathway) or directly by carbohydrate structures on the microbe’s surface (The alternative pathway). The complement system thus bridges the innate system based on the recognition of foreign carbohydrates, and the induced system based on antibody formation.

2. A North American registered 5-serovar mineral oil (i.e. Al NZ are aluminium adjuvanted bacteria. Note: not only were the post-vaccination MAT titres much lower than those of vaccines it was compared with, it did not induce production of IFN-\(\gamma\).
4.0 Vaccine Efficacy

Key Findings

► Vaccination should eliminate Hardjo from infected herds and prevent infection in Hardjo, Pomona or Copenhageni free animals.

► To achieve this, vaccination must prevent renal colonisation and urinary shedding.

► Evidence for leptospiral vaccine efficacy in calves vaccinated before 3 months of age is scant and contradictory and does not support routine vaccination of this age group.

► For annual vaccination to be effective, 12 months protection against urinary shedding must be provided. There is no published data supporting 12 months protection if used in calves earlier than 6 months.

► Vaccine efficacy in one country does not necessarily mean protection of animals exposed to other strains in another country.

Leptospira are antigenically complex. Within a serovar, isolates differ markedly in their genotypic and phenotypic characteristics. This is particularly evident when isolates from different geographic regions are compared (Zuaznaren et al., 1993). Efficacy of a serovar in one country therefore does not necessarily imply protection of animals exposed to other strains in another country. Hence vaccine strain selection, vaccine manufacture and choice of isolate used in challenge studies is very important (Bolin et al., 1994; OE, 2005).

Leptospiral vaccination has 3 aims:

1. Reduce and eventually eliminate Hardjo infection from infected herds.

2. Prevent the establishment of infection in Hardjo free animals.

3. Prevent sporadic infection and disease due to Hardjo, Pomona or Copenhageni. These aims are primarily achieved by prevention of renal colonisation and urinary shedding.

4.1 Prevention of Renal Colonisation and Urinary Shedding

The critical evidence of vaccine efficacy is prevention of renal colonisation and urinary shedding following Hardjo challenge. To permit confidence in annual vaccination, this challenge must occur at least 12 months after vaccination.

Leptavoid® 2 and Leptavoid® 3 are whole cell, aluminium adjuvanted bacterins, grown in serum-free media.

Table 3: Published (peer and non-peer reviewed) challenge studies in calves vaccinated for the first time after 3 months of age.

<table>
<thead>
<tr>
<th>Country</th>
<th>Vaccine</th>
<th>Age at 1st vac. (mths)</th>
<th>MAT at 1st vac.</th>
<th>Interval to challenge from 2nd vac.</th>
<th>Challenge method</th>
<th>Challenge serovar</th>
<th>No. with leptospiruria</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>NZ</td>
<td>Leptavoid 2</td>
<td>3 to 4</td>
<td>Neg. (&lt;24)</td>
<td>7 to 11 mths</td>
<td>Hardjo</td>
<td>natural</td>
<td>0/8</td>
<td>10/10</td>
</tr>
<tr>
<td>NZ</td>
<td>Leptavoid 3</td>
<td>4 to 6</td>
<td>Neg. (&lt;30)</td>
<td>14 days</td>
<td>Hardjo</td>
<td>natural</td>
<td>1/10</td>
<td>7/10</td>
</tr>
<tr>
<td>NZ</td>
<td>Leptavoid 2</td>
<td>6</td>
<td>Neg. (&lt;30)</td>
<td>½ at 6 &amp; ½ at 12 mths</td>
<td>Hardjo</td>
<td>conjunctival &amp; natural</td>
<td>0/10</td>
<td>10/10</td>
</tr>
<tr>
<td>NZ</td>
<td>Leptavoid 2</td>
<td>10</td>
<td>Neg. (&lt;24)</td>
<td>6 to 56 wks</td>
<td>Hardjo</td>
<td>natural</td>
<td>0/8</td>
<td>9/10</td>
</tr>
<tr>
<td>NZ</td>
<td>Leptavoid 2</td>
<td>6</td>
<td>Neg. (&lt;30)</td>
<td>19 days</td>
<td>Pomona</td>
<td>subcutaneous</td>
<td>0/11</td>
<td>8/11</td>
</tr>
<tr>
<td>NZ</td>
<td>Exp. Pomona</td>
<td>9</td>
<td>Neg. (&lt;25)</td>
<td>11 mths</td>
<td>Pomona</td>
<td>i.m.</td>
<td>0/4</td>
<td>4/4</td>
</tr>
<tr>
<td>Ausl</td>
<td>Ultravac®</td>
<td>4 to 5</td>
<td>Neg.</td>
<td>48 wks</td>
<td>Hardjo</td>
<td>i.p.</td>
<td>2/8</td>
<td>9/8</td>
</tr>
<tr>
<td>Ausl</td>
<td>Exp. Hardjo/ Pomona</td>
<td>8 to 12</td>
<td>Neg.</td>
<td>8 weeks</td>
<td>Hardjo</td>
<td>i.p.</td>
<td>0/10</td>
<td>6/6</td>
</tr>
<tr>
<td>US</td>
<td>Sprinovac®</td>
<td>8 to 12</td>
<td>Neg. (&lt;12)</td>
<td>16 wks</td>
<td>Hardjo</td>
<td>conjunctival</td>
<td>0/9</td>
<td>4/9</td>
</tr>
<tr>
<td>UK</td>
<td>Leptavoid H</td>
<td>7</td>
<td>3000g</td>
<td>Neg.</td>
<td>6 mths</td>
<td>Hardjo</td>
<td>conjunctival</td>
<td>0/8</td>
</tr>
<tr>
<td>UK</td>
<td>Exp. Pomona</td>
<td>0 to 6</td>
<td>Neg.</td>
<td>11 mths</td>
<td>Pomona</td>
<td>conjunctival</td>
<td>1/12</td>
<td>5/5</td>
</tr>
</tbody>
</table>

Notes

1. The challenge was heavy, as after 8 weeks all unvaccinated controls had positive titres.

2. These studies form the basis of the 12 month non-shedding claim for Leptavoid vaccines.

3. Challenge was heavy and included instillation into the nose and eyes on three consecutive days, plus natural challenge from unvaccinated controls that shed.

4. The Hardjo MAT titres in the Leptavoid vaccinated calves were significantly (P<0.05) higher compared with the other vaccine.

5. Monovalent Hardjo variant of Leptavoid 2 showed protection from renal colonisation and urinary shedding when challenged with a different (Het.) heterologous species of Hardjo.

*Registered trademark of Pfizer Animal Health. #Developed in the US by Biocare. †Precursor to Leptavoid.
Elimination of Hardjo Infection
Another important role of an effective vaccination programme is the elimination of herd infection, as this reduces the zoonotic risk. Leptospires have a high reproductive index. Therefore if leptospires are to be maintained in a population, they require a high percentage of susceptible animals. If not, infection will not be maintained, and will be eliminated (Thursfield, 2004).

Indirect evidence of the use of Leptavoid to eliminate Hardjo infection comes from the sharp decline in human infections following the introduction of vaccination. For example, Marshall and Chereskii (1962) noted “the dramatic fall in the number of notified cases [677 in 1979 to 325 in 1983 and to about 100 in 1998] of Leptospirosis in humans” with the introduction of Leptavoid 2. Furthermore, Ryan et al (1994) in a study involving about 460 herds and 1350 people on the Hauraki Plains showed of the 21 milkers infected with Pomona or Hardjo, 19 were associated with non-vaccinated herds, and in the 2 cases associated with the vaccinated herds, both had exposure to non-vaccinated stock.

Direct evidence was generated in the UK by Broughton et al (1984) where, after 4 years of vaccination with the monovalent variant of Leptavoid 2 in an endemically infected (50% sero-positive) 600 cow herd, they could not isolate Hardjo (0/406 urine samples).

Hardjo Shedding Prevention Studies in Other Species
As part of a comprehensive prevention programme, risk should be managed in other farmed species a herd comes into contact with. The ability in NZ of Leptavoid vaccines to reduce shedding has been assessed in sheep (Ayanegui-Alcerreca et al., 2005) and deer (Palikanen and Aalto, 1997).

4.2 Concurrent Vaccination
Veterinarians often prescribe the concurrent use of Leptospirosis vaccines with other (e.g. clostridial) vaccines. Antibody “overload” is however suggested as an issue when numerous antigens are given concurrently. This dogma was evaluated in a recent NZ field trial.

The serological responses (i.e. MAT titres) of sero-negative 7-8 month old dairy calves (n = 240) to vaccination with Covexin™10 and Leptavoid 3 given concurrently (i.e. group 1: same animal different sides of the neck) was compared to the same vaccine injected individually (i.e. groups 2 and 3: different animals given single vaccine); and with two positive controls (Group 4: Ultravac® 7in1 – Pfizer; Group 5: experimental Cattlevax - SPAH). Unvaccinated controls (Group 6) were maintained as sentinals of natural infection.

The results showed:

- **Pomona** antibody response: there was no significant difference between the Covexin 10 + Leptavoid 3, the Leptavoid 3, the Ultravac 7in1, and the exp. Cattlevax vaccinated calves.
- **Copenhageni** antibody response: there was no significant difference between the Covexin 10 + Leptavoid 3, and the Leptavoid 3 vaccinated calves.
- **Hardjo** antibody response: there was a significant difference (p <0.05) between groups. The Ultravac 7in1 and exp. Cattlevax vaccinated calves had titres that were significantly lower than the Covexin 10 + Leptavoid 3, and Leptavoid 3 vaccinated calves.

Leptavoid 3 and Covexin 10 can therefore be given concurrently without risk of a detrimental immune response. Leptavoid 3 also produced, significantly higher Hardjo antibody response compared to Ultravac 7in1 and exp. Cattlevax.

(See trial sheet for more information)
In summary, calves vaccinated at less than 3 months of age, the data shows a lack of efficacy against Pomona (Gillespie and Kenzey, 1958a) or Hardjo challenge (SPAH, 2000- unpublished), and there is no Copenhageni challenge data. The evidence supporting Hardjo efficacy has weaknesses. In the 2 trials (Goddard et al., 1986; Palit et al., 1991) calves had negative (or at best extremely low) maternal antibodies, non-NZ Hardjo challenge strains were used, and the challenge methods were sub-standard (i.e. the i.v. or i.p. route did not mimic a natural route of infection) (Bohn, 2003).

Furthermore, there is no challenge data using combination leptospiral clostridial vaccines in young calves. The only published study (McCull and Pailt, 1994) conducted in Australia with 4 to 5 month old cattle speculated “…that the presence of the clostridial component may have lead to a lessening of the peak serological response…”, as following Lp. challenge 2/8 vaccinated calves were infected. This reduced serological Hardjo response in cattle vaccinated with combined clostridial and leptospiral vaccines has also been observed in 2 subsequent NZ studies (Bryan and Moffat, 2006; Moffat and Bruere, 2007 unpublished).

The inefficacy seen in young calves is not related to the vaccine, as the vaccines have been shown to be efficacious in older animals (See table 3). The likely reason is a combination of age related immune system immaturity and the level of passive immunity.

Without repeat vaccination of calves vaccinated under 3 months of age, a herd may contain animals that have not had an effective primary vaccination. These animals may remain susceptible to infection and disease, and transmit leptospires to humans. This is supported by the ACVM who state: “We are particularly concerned that a tendency towards earlier vaccination of calves without booster vaccination at 6 to 8 months will place in jeopardy the success of the leptospirosis control programme in New Zealand.” (Deaux, 1991).

5.0 Control and Vaccination Programme

Key Findings

- Vaccination of the herd is the key component in prevention of infection with most leptospiral serovars.
- Additional management strategies are required to minimise the risk of leptospiral infection.
- Do not routinely begin vaccination until calves are older than 3 months, vaccination prior to this requires a repeat of the primer and booster injection.
- Booster vaccinate calves after 6 months of age to ensure 12 month protection until the annual herd vaccination.
- The implementation of scientifically valid and proven vaccination programmes by veterinarians and farmers has been “spectacularly successful” in the NZ dairy industry.

Given the serovars that infect cattle (Table 1), numerous strategies are required to minimise the risk of leptospiral infection. General approaches include rodent control, drainage of wet pasture, prevention of access to free standing water, and farm biosecurity. While management factors are important, vaccination of the herd is the key component in prevention of infection with most leptospiral serovars. Importantly, the leptospiral status and contact risk with non-vaccinated cattle, sheep, pigs or deer must be assessed and an appropriate plan formulated.

Recommendations for Leptovaid vaccination

Vaccine programmes that are not supported by solid scientific evidence risk leptospirosis control in New Zealand. These scientifically proven recommendations are based on the epidemiology of infection, protection derived by maternal antibodies, the risk of vaccine failure due to age related immune system immaturity or maternal antibody interference (Fulton et al., 2004; Gillespie and Kenzey, 1959; Heilbronn, 1979; Schollum and Marshall, 1986).

The promotion and implementation of this programme by NZ veterinarians has been “spectacularly successful” (Marshall et al., 1996) in reducing the incidence of leptospirosis infection in herds and in dairy farmers (Marshall, 1987; Marshall and Choreshsky, 1996; Ryan et al., 1982; Ryan et al., 1982 Baker, 2004).

Use vaccines proven in New Zealand

- There is significant genetic variation within each leptospiral serovar. Efficacy in one country therefore does not necessarily mean protection of animals exposed to other strains in another country.
- Advocate farm biosecurity
  - Ensure no animals of unknown infection or vaccination status come into contact with the herd. Control rodents.

Advocate farm biosecurity

- Ensure no animals of unknown infection or vaccination status come into contact with the herd. Control rodents.
### Primary Vaccination
- Vaccinate calves from 3 months of age with a sensitizer followed by a booster 4-6 weeks later.
- If first vaccinated between 3 to 6 months of age, a booster is required after 6 months of age. This repeat vaccination ensures calves remain protected for at least 12 months until their annual herd vaccination.
- Do not routinely begin vaccination until calves are older than 3 months of age.
- The evidence for vaccine efficacy in calves younger than 3 months is scant and contradictory. If vaccination is performed in young calves (i.e. due to increased risk due to off-farm contact with non-vaccinated stock) some calves will not respond to vaccination and require repeat vaccination.

### Annual booster
- Vaccinate the herd annually 1-2 months prior to calving and ensure colostral transfer.
- This maximises the colostral protection of calves against leptospires, and provides other factors essential for calf health.

### Vaccination Timing Options

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### Replacement and Herd Vaccination Programme Options

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### References
Adler, B., Fair, S., 1982. Evidence that leptospiral lipopolysaccharide is not an important protective antigen. Journal of Medical Microbiology 13, 259-262.
Dodd, D., Brakenridge, D., 1960, Leptospira icterohaemorrhagiae infection in calves. New Zealand Veterinary Journal 8, 71-76.
Leptavoid®: the only leptospirosis vaccine developed and researched to work in New Zealand conditions*. www.intervet.co.nz

Disclaimer: While every attempt was made to ensure information in this publication is accurate and up to date, omissions or errors are possible and advances in knowledge occur. ISPAH assumes no responsibility or makes no warranty for results obtained based on the contents of this publication.


*Refers to published data.