

Massey – NZVA Review

Best Practice use of Leptospirosis Vaccines

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Agenda

- Justification
- Purpose of vaccination
- Approval of ToC and objectives
- MDA: natural decay
- Age at first natural challenge in deer, sheep, cattle
- MDA interference with vaccine efficacy
- Vaccination in the face of challenge
- Age at first vaccination
- Format for Best practice recommendation by example of deer

Justification

- Uncertainties about
 - Age at first vaccination
 - Impact of dam vaccination
 - Effect of MDA
 - Age at first natural challenge
 - Seasonality of natural challenge
 - Open vs closed herds
 - Risk categories for dairy, beef, sheep, deer herds
 - *Bivalent vs trivalent vaccine ?*

Recent prevalence data NZ:

	Year	Farms	% H/P	Animals	% H/P
CATTLE					
Beef heifers 12-18 m old	2006	95	69%	1,265	39%
Mixed age beef cows	2009	116	97%	2,308	58%
Mixed age beef cows	2010	21	95%	338	55%
SHEEP					
Slaughter age lambs	2004	21	91%	619	19%
Slaughter age lambs	2005	74	31%	2,139	2.0%
Mixed age ewes	2009	161	97%	3,361	51%
DEER					
9-30m old non-vacc deer	2004	110	74%	2,016	64%
Mixed age deer	2009	98	76%	1,992	34%



Purpose of vaccination

- **Protect humans against exposure**
- **Reduce clinical disease**

Species	Farms with clinical disease	1-3 year incidence
Deer	11 / 233	4.7%
Sheep	14 / 1,193	1.2%
Beef cattle	22 / 1,061	2.1%

- **Reduce sub-clinical production loss**

e.g. DEER:

- -3.7kg to slaughter in sero-positive vs sero-negative growers (Ayanegui 2008)
- +16-26 g/d ADG in vaccinated vs control in 3/5 farms (Subharat et al. 2012)
- +6% weaning rates in vaccinated hinds (Subharat et al. 2012)

ToC Approval

1. Executive Summary; 2. Objectives; 3. Introduction

4. Host species and leptospira serovars

5. Prevalence in NZ livestock

6. Environmental effects

7. Farm management (AR, JW, SM, PK)

8. Production outcomes

9. History of vaccine use in NZ (dairy,pig)

10. Vaccine label claims and current recommendations

11. Vaccine efficacy

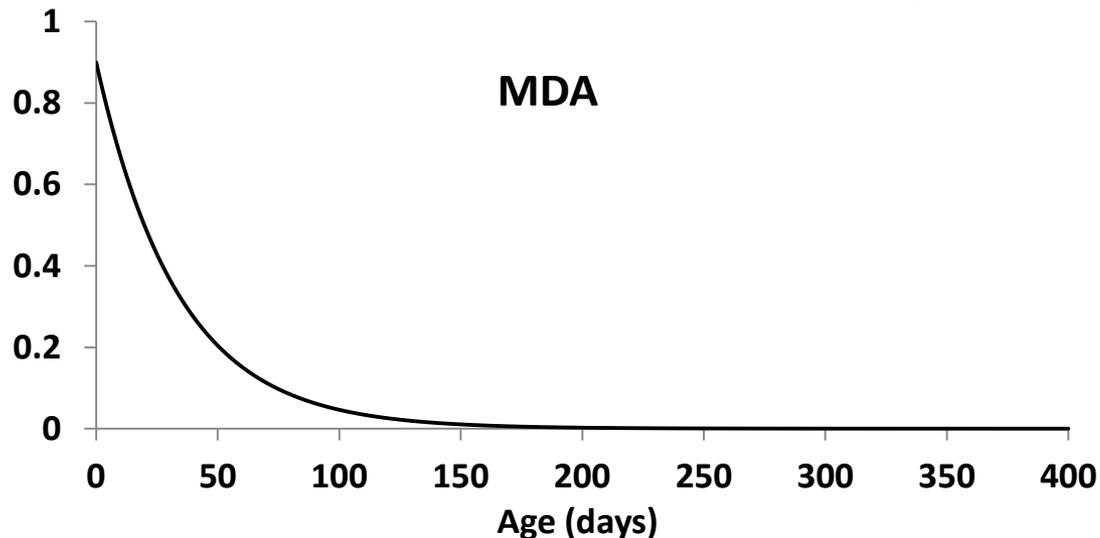
- **Immune response and duration of immunity**
- **Measuring vaccine efficacy**
- **Interference of maternally derived antibody (MDA) with vaccination**
- **Vaccination of dams for the protection of offspring**
- **Age of vaccination**

12. Required information (future research)

- **Annexes: BP Dairy, Beef, Sheep, Deer**

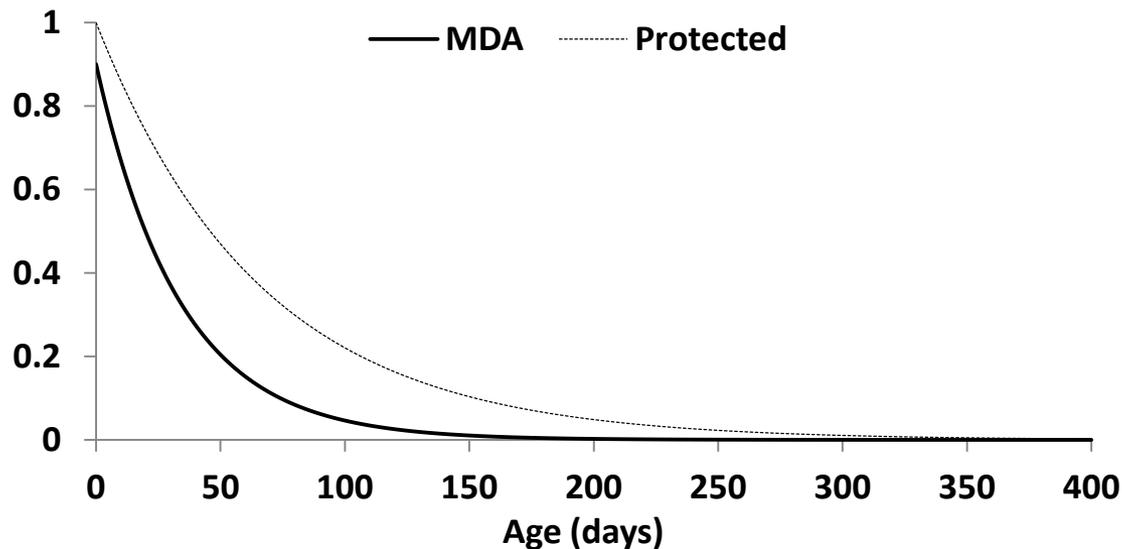
MDA decay

- AB = primary immune response
- Peak MAT titres 11h after birth (single colostrum intake)
- Half life 16-20 days, IgG1 (Hellstrom 1978, Nielsen 1978)
- Protection waned off by 6 months of age (Hellstrom 1978)



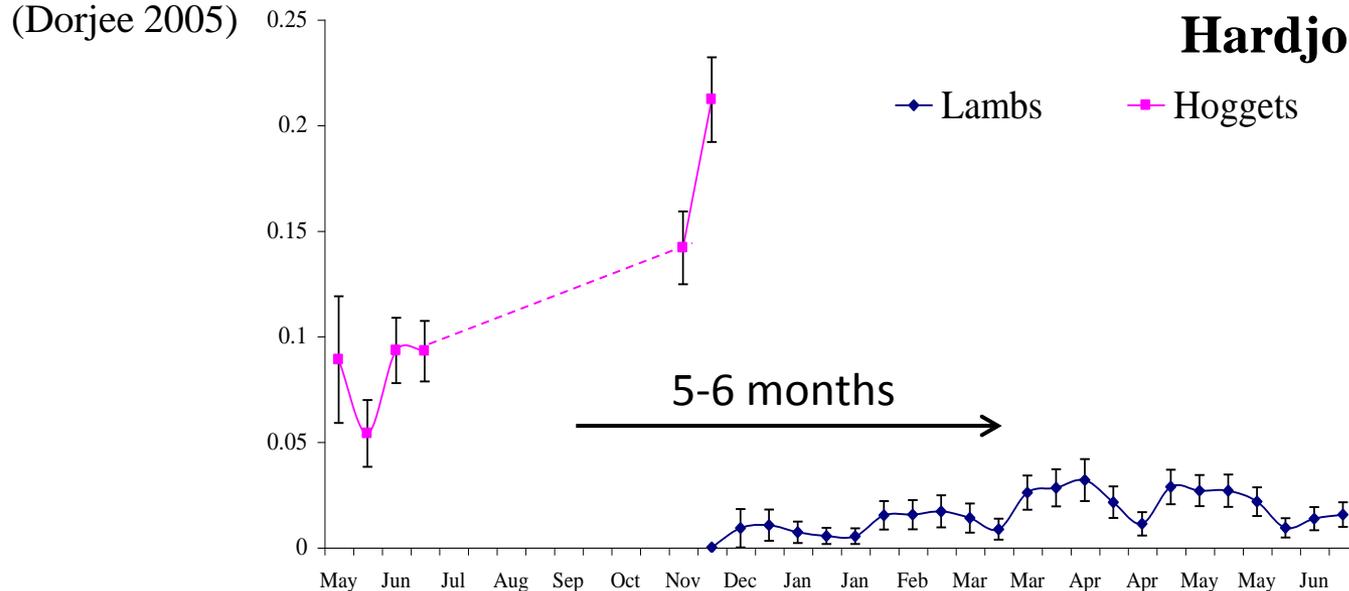
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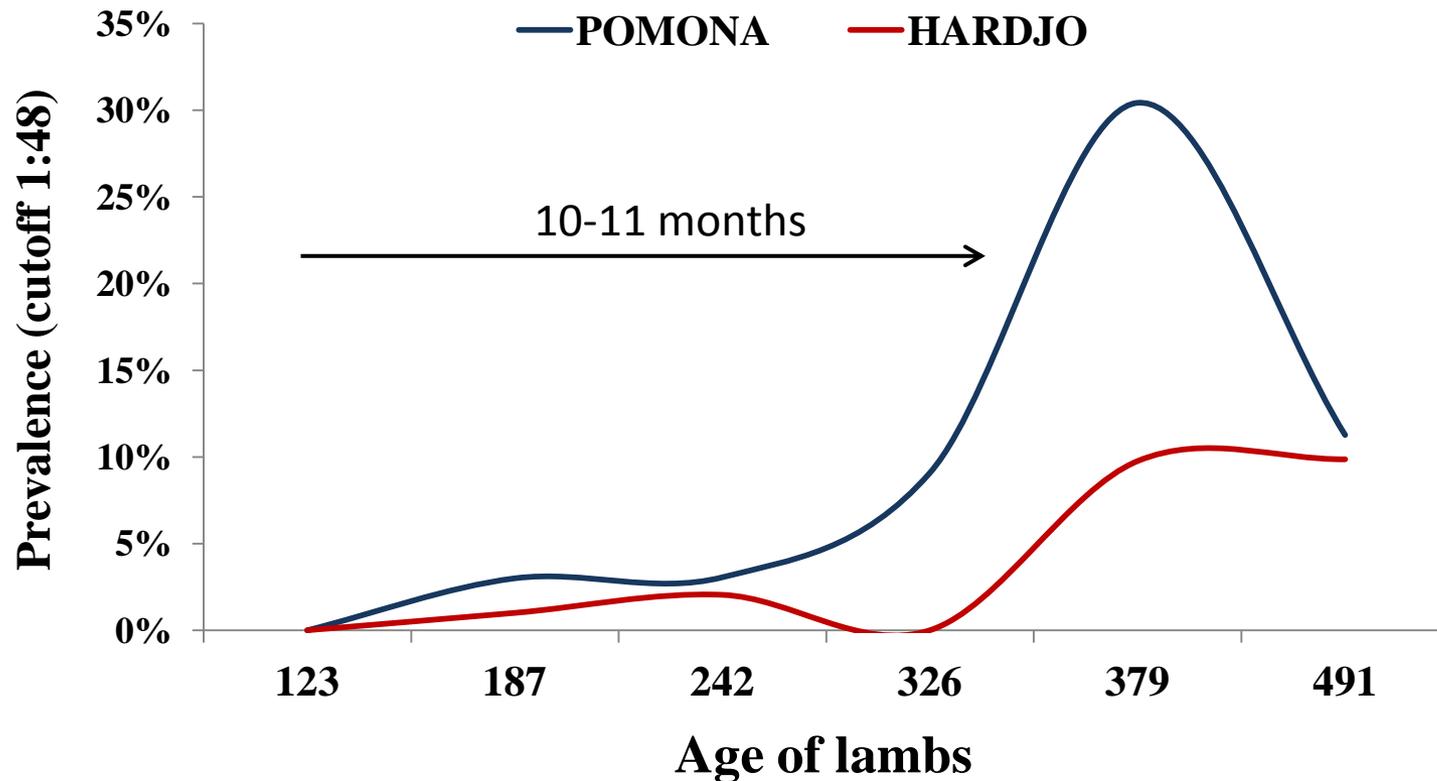


Age at first natural challenge in deer, sheep, cattle

- Calves found infected at 6m (Pegram et al 1998)
- Deer found infected at 3m or 9m (Ayanegui-Alcerreca 2006)
- SHEEP: slaughter lambs found infected at 5-6m (Dorjee 2005)

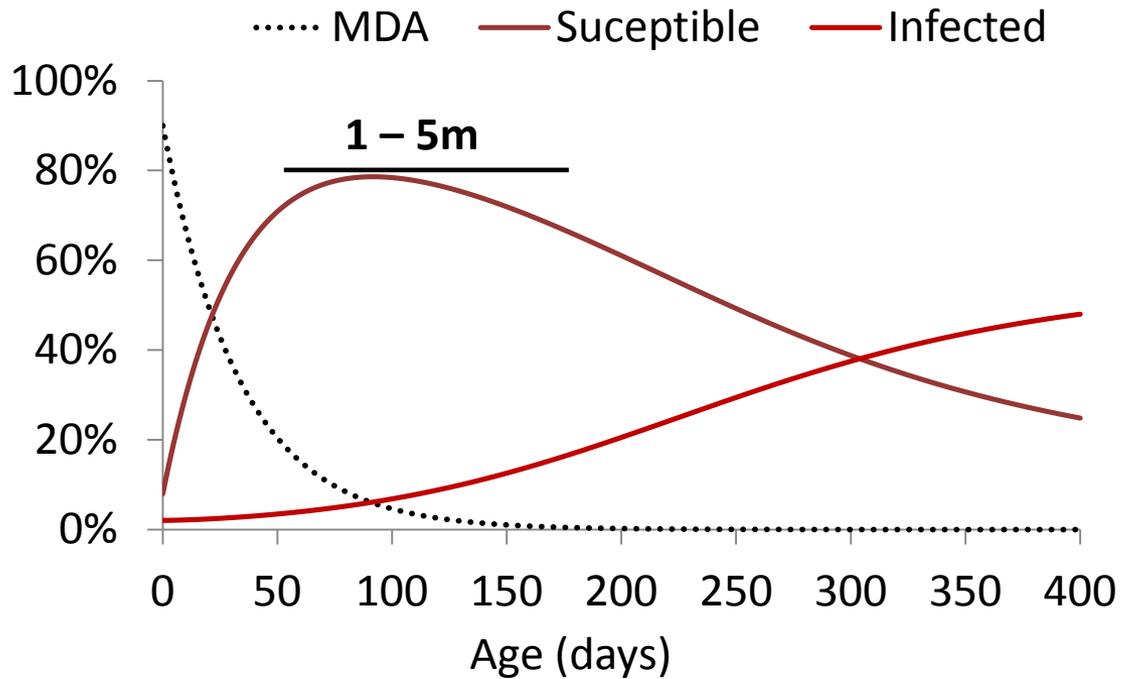


SHEEP: Cohort of 100 hoggets MAT-tested from Dec04 – Dec05 one year after a clinical leptospirosis-outbreak in 2004 (Heuer, West 2005)



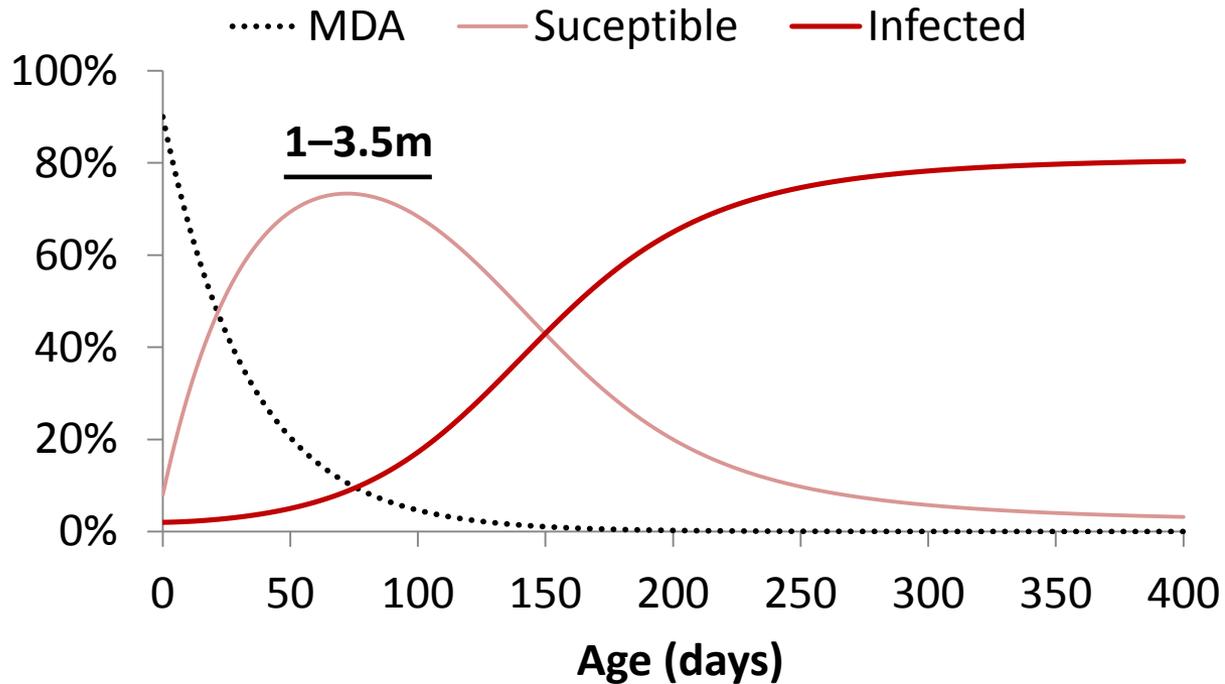
Age at first natural challenge in deer, sheep, cattle

Model: MDA to 100d assuming full protection and strong natural challenge: *worst case scenario*



Age at first natural challenge in deer, sheep, cattle

Model: MDA to 100d assuming full protection and strong natural challenge: *worst case scenario*



MDA interference with vaccine efficacy

- If MDA are absent: vaccines are effective at 28d vaccination (Gallo et al 2006 = 3 Pfizer studies? Details?)
 - Gillespie 1958: vaccine (pom) failure
- If MDA are present
 - Palit study 1991: low MAT(+) calves vacc at 28d effective
 - AHSC study 2000: highly MAT++ calves vacc at 21-28d
- CMI present in calves?
 - Would not reduce vaccine efficacy

Conclusion: MDA may/may not interfere, conflicting evidence

Studies specifically examining effect of MDA on vaccine efficacy

1. Palit (AVJ, 1991) concluded that ‘calves as young as 4 weeks old, vaccinated in presence of MDA, can be fully protected against homologous virulent challenge. However also noted that post-vaccination rise in MAT titre was inversely proportional to pre-vaccination titre
2. Ankenbauer-Perkins (Internal report, 2000) found ‘vaccinating calves as young as 3 weeks of age...did not prevent urinary shedding of *Leptospira* after challenge

Differences in the studies

- **Route of infection:** Palit I/P, Ankenbauer conjunctival/intranasal
- **Time to challenge:** Palit 24 weeks after 2nd dose, Ankenbauer 12 weeks
- **MDA titres:** Palit 4-64, Ankenbauer up to 1:1,536 as calves were specifically selected to have high (>1000mg/Dl) IgG levels,
- **Leptospirosis:** Palit 0/3 while Ankenbauer 4/10
- **Success of challenge :** 7/7 Palit controls leptospiruric, Ankenbauer 4/10

Vaccination before/after natural challenge

- Pre-challenge vaccination: 80-100% efficacy
 - Mackintosh (1984): 9/10 controls vs 2/10 vaccinates shedding
 - Short duration of shedding in 2 vaccinates
 - Most published experiments rendered vaccines highly protective against shedding, all had low numbers (3-10/grp)
- Post-challenge vaccination
- Ayanegui-Alcerreca (2006): deer study, natural challenge
 - Infected herd: 37 – 44% reduction in shedding due to vaccination
- Hancock (1984): natural challenge
 - shedding rates before and after vaccination were similar in controls and vaccinates, but low numbers

Required knowledge

- Serovars and prevalence of dairy heifers and cows
- Duration of vaccine induced immunity >>12m?
 - Relevant for aligning timing of vacc of calves to adults
 - QU: longer than 12m, i.e. 15 – 18m?
 - Zuerner: CMI 18-40w, then waning off(?)
 - Virbac tec-review: 1 pom-infection 15-18m p.v. (no M&M detail)
 - Mackintosh 1980: 56 weeks p.1st vacc.
 - Hamel (1997): 52 weeks p. 1st vacc.
 - No information after 56 weeks p.v.
- Vets and farmers !! Sources of infection
 - Human Ethics approved (LS)
 - NZVA – June: sampling and data-entry venues/facilities

Required knowledge + design

- Role of MDA and efficacy when vaccinating dams and/or offspring
 - Suggest 2 x 3 designed clinical trials for cattle, sheep, deer:
 - (1) Dam-vacc x (2) Dam-control x
 - (1) Offspring-vacc at 1m
 - (2) Offspring vacc at 3m
 - (3) Offspring-control
 - Serology and shedding at vaccination and during 18m follow-up (natural exposure)

Best Practice format

- Production systems x species
 - Dairy:
 - Closed vs. open herds
 - Home reared vs. off-farm grazing of replacement calves
 - Beef:
 - Breeding/finishing: open vs closed
 - Mixed species:
 - Sheep:
 - Breeding/finishing
 - Finishing
 - Deer:
 - Closed vs open
 - Single vs multispecies
 - Velveting and breeding stags

Best Practice format

- Age at first vaccination (x2) and booster
 - Dairy:
 - 3m old calves in Dec
 - booster June + annual
 - Beef :
 - calves when weaned or yarded for the first time (Mar/Apr)
 - booster annually in May/June
 - Sheep:
 - Year1: 3m old lambs at weaning (Dec), booster Jun/Jul, +annually
 - Year2 lambs + 2T (Jun/Jul)
 - Year3 lambs + 2T + adult (Jun/Jul)
 - Deer:
 - calves when weaned or yarded for the first time (3-4m, Mar)
 - Booster Oct, than annually

Best Practice format

Wilson PR, Heuer C, Subharat S, Ayanegui-Alcerreca AM, Collins-Emerson JM.
Leptospirosis od deer farms: to vaccinate or not? In: A Deer Course for Veterinarians.
Proc. Deer Branch NZVA No26.89-94. 2009

DEER:

- Closed herd – deer only
 - Replacement hinds: 1st vacc at 100d of age (Feb/Mar), 2nd after 4-6w
 - 1st booster at 15m
 - Replacements: annual booster late Oct (3-4w a.p.)
 - Velveting+breeding stags: start any time
- Open herd – deer only
 - Purchased deer (if not vacc'ed prior):
 - Vacc prior to transfer with certificate, or
 - Quarantine, vaccinate and integrate 4w after booster, or
 - Treat with streptomycin
- Closed herd – deer and other stock
 - Vaccinate other stock if in contact with deer as for closed herds/flocks
- Open herd – deer and other stock
 - Vaccinate other stock if in contact with deer as for open herds/flocks

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Beef year 1

- Calves: vacc x2 by weaning before transfer out
 - 1st vacc when youngest calf is 4w old (at marking)
 - Cows fully vaccinated (low risk): vacc at 3m
 - Else, high risk: 1st vacc at 4-6w + 3rd vacc at 6m (Pfizer-plan)
- MA cows: annually <2m pre-calving (2nd vacc 2-8w a.p.)
 - Previously unvaccinated heifers&cows: 2x same time
 - Timing: 1st vacc 2-3m a.p., 2nd vacc 1-2m a.p.
 - Within humoral ab-duration of 3-6m
 - Or at TB- or pregnancy testing, whatever is the last yarding a.p.
- Male stock remaining on property: annually

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Beef year 2

- Calves
 - Low risk: 1st vacc at 3m, 2nd vacc at weaning
 - High risk: as in year 1