# TRIAL SUMMARY

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# Clostridial vaccination of lambs with maternally-derived antibodies[1]

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## OBJECTIVE 1:

Determine if lambs with maternally derived antibodies (MDA) would respond to vaccination when injected with Multine® 5-in-1.

## OBJECTIVE 2:

Establish the non-inferiority of Multine compared to a reference vaccine (Ultravac® 5 in 1, Zoetis NZ Ltd) that had an existing claim for use in lambs at tailing.

## MATERIALS AND METHODS

### Design

The study was conducted on a commercial sheep farm in the North Island of NZ using a mob of 126 twin-bearing, Romney, 2-tooth ewes which had been previously vaccinated with a two-dose clostridial vaccination course, and their surviving twin lambs (n = 210).

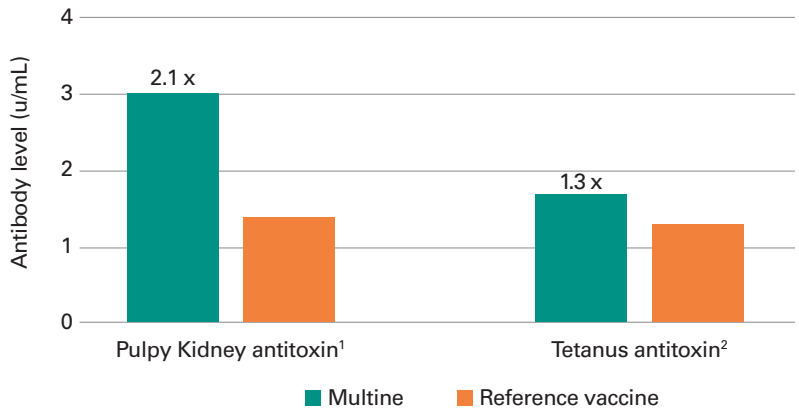
### Method

Prelamb, ewes were randomly allocated to the Multine (n = 63), or reference (n = 63) group and given a single injection of the appropriate vaccine. Lambs from 10 ewes, randomly chosen from each group, remained as non-vaccinated controls. The remaining twin lambs were randomly allocated, within pairs, to receive Multine or the reference vaccine. These lambs were vaccinated at tailing (V1, median age 36 days), and at weaning 49 days later (V2). Blood was sampled at V1 and V2 + 14 days.

## RESULTS

## MATERNALLY DERIVED ANTIBODIES

**Figure 1. Level of antibody transfer to lambs via colostrum from ewes vaccinated with Multine compared to reference vaccine.**




- Mean Pulpy Kidney antitoxin titre was **2.1 times** higher in lambs born to ewes vaccinated with Multine compared to those vaccinated with reference vaccine.
- Mean Tetanus antitoxin titre was **1.3 times** higher in lambs born to ewes vaccinated with Multine than lambs born to those vaccinated with reference vaccine.

[1] Pulpy Kidney (Geometric mean ratio = 2.1, P <0.0005)

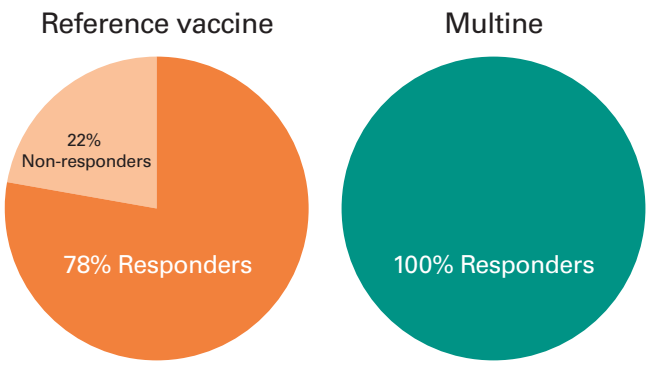
[2] Tetanus (Geometric mean ratio = 1.3, P <0.056)

This shows more antibodies were transferred into lambs via colostrum where pregnant ewes were vaccinated with Multine.

## RESPONSE TO VACCINATION

**(defined antitoxin concentration at V2+14 increasing from MDA)**

**Figure 2. Flock-level response to vaccination of lambs at weaning with Multine compared to the reference vaccine (Pulpy Kidney).**

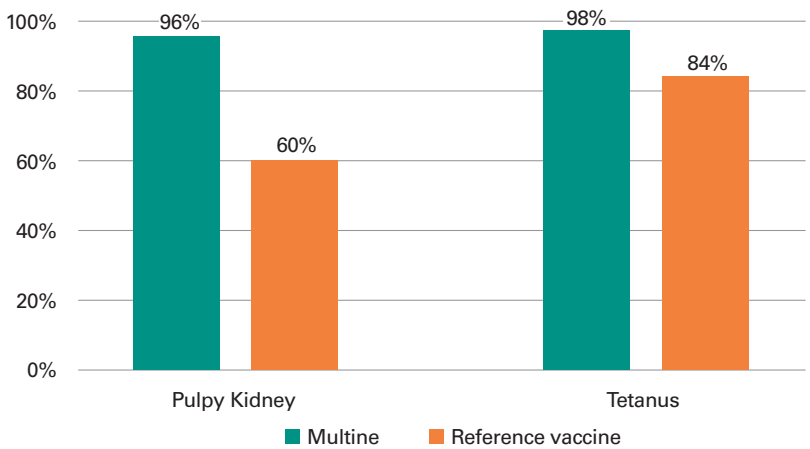



Responders = antitoxin concentration at V2+14 increased from MDA
Non-Responders = antitoxin concentration at V2+14 did not increase from MDA

Pulpy Kidney antitoxin concentration, 14 days after vaccination at weaning, increased above the MDA concentration in 68% of the non-vaccinated control lambs, 78% of the reference product vaccinated lambs and 100% of the Multine vaccinated lambs.

This indicates a mixture of natural exposure and response to vaccination.

**Figure 3. Percentage of lambs with antitoxin concentrations above the International (EP) vaccine standard.**



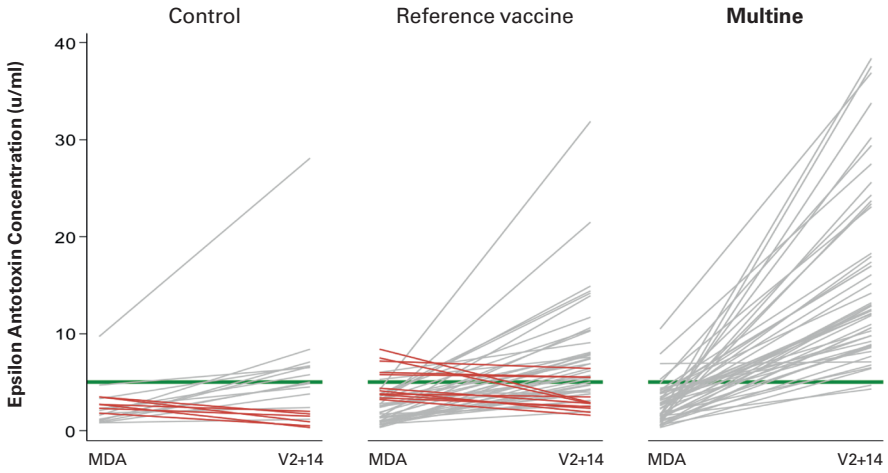

- Most (96%) lambs vaccinated with Multine had Pulpy Kidney antitoxin concentrations greater than the European Pharmacopoeial (EP) compendial standard (5 u/mL), compared with only 60% of lambs vaccinated with the reference vaccine.
- There was no evidence of natural exposure to *C. tetani*. Most lambs had tetanus antitoxin concentration greater than the EP standard (2.5u/mL); 98% of the Multine vaccinated lambs and 84% in the reference product vaccinated.

## Individual Lamb Responses

The following graphs show the responses of the lambs at an individual lamb level and how the lambs within the flock responded differently. This is important as maximising the number of lambs which respond to the vaccine is key to the overall level of protection provided.

## Pulpy Kidney

**Figure 4. Individual lamb responses to Pulpy Kidney vaccination.**




Pulpy Kidney antitoxin concentration, 14 days after booster vaccination at weaning, increased (grey lines in Fig. 4) above the MDA concentration in:

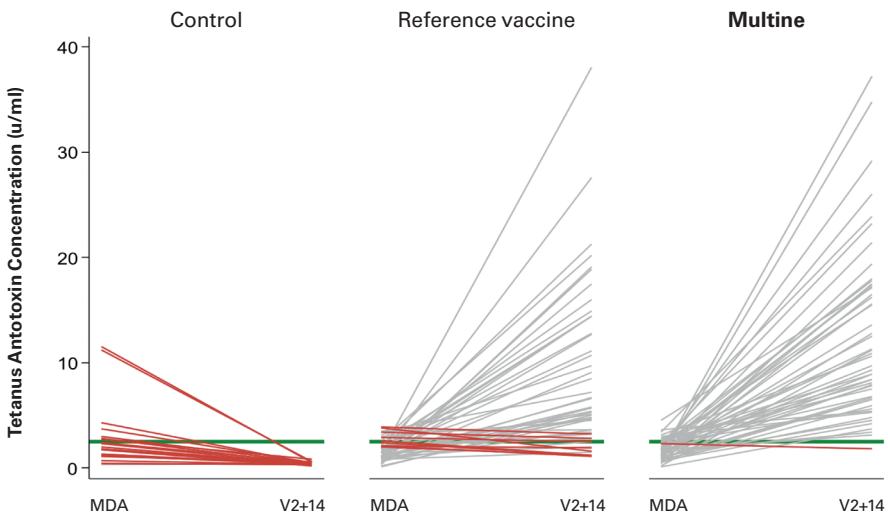
- 13 of 19 (68%) of the non-vaccinated control lambs
- 39 of 50 (78%) of the reference vaccine vaccinated lambs
- 49 of 49 (100%) of the Multine vaccinated lambs.

*Grey lines indicate increase in concentration, red lines indicate decrease in concentration. The green line indicates the international standard for vaccine potency release of 5u/mL. This differs from documented protective concentrations of 0.1 to 0.2.*

Increased antitoxin concentration in the control group indicates individual lamb responses across the three groups may be caused by a combination of natural exposure and/or response to vaccination.

## Tetanus

**Figure 5. Individual lambs response to Tetanus vaccination.**




Tetanus antitoxin concentration, 14 days after booster vaccination at weaning, was greater than the EP standard (2.5u/mL) in:

- 0 of 19 (0%) of the non-vaccinated control lambs
- 42 of 50 (84%) of the reference vaccine vaccinated lambs
- 49 of 50 (98%) of the Multine vaccinated lambs

There was no evidence of natural exposure to Tetanus as shown by decreasing tetanus antitoxin concentration in 100% of the non-vaccinated control lambs.

*Grey lines indicate increase in concentration, red lines indicate decrease in concentration. The green line indicates the international standard for vaccine potency release of 2.5u/mL. This differs from documented protective concentration of circa 0.1.*

In the reference vaccine group, the decline in Pulpy Kidney and Tetanus antitoxin (red lines in Pulpy Kidney and Tetanus individual lamb response graphs) was significantly ($P < 0.05$) negatively associated with the MDA concentration. In other words, in the reference vaccine group if lambs had higher MDA levels they were less likely to respond to the vaccination. This contrasts with the Multine group which demonstrated higher MDA levels overall, yet no negative association with Pulpy Kidney or Tetanus antitoxin concentrations in lambs.

## CONCLUSIONS

1. Vaccination of 4-5 week-old lambs with Multine induced individual immune responses superior to EP cutoffs in the face of MDA.
2. Lambs born to Multine vaccinated ewes obtained **more than double** the mean level of antibodies to Pulpy Kidney and **30%** more antibodies to Tetanus than lambs in the reference vaccinated group.
3. **100% of lambs in the Multine vaccinated group** showed an increase in Pulpy Kidney antibodies between tailing and weaning (sensitiser and booster vaccinations), compared to 78% of lambs in the reference vaccinated group.
4. **98% of lambs in the Multine vaccinated group** showed an increase in Tetanus antibodies between tailing and weaning (sensitiser and booster vaccinations), compared to 82% of the lambs in the reference vaccinated group.
5. Lambs in the Multine vaccinated group had higher overall MDA levels, yet in contrast to the reference group this had no negative association with response to vaccination.


## MULTINE.® New Zealand's leading 5-in-1 clostridial vaccine[2].

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1. MSD data on file. Review and assessment by ACVM not finalised at time of publication.
   ACVM No: A3585 Ultravac is a registered trademark of Zoetis New Zealand Ltd.
2. Baron Audit Data 2021



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