



RESEARCH REPORT

REASONABLE EXPECTATION OF EFFICACY DEMONSTRATED BY KILLED BACULOVIRUS VECTOR VACCINE FOR VIRAL PAPILLOMAS (WARTS)

Cambridge Technologies has completed a pair of studies that show a reasonable expectation of efficacy (REE) for our Wart Vaccine, Killed Baculovirus Vector.

STUDY ONE: VACCINATION AND SEROLOGY

The first study used a pseudovirus serum neutralization (pSN) assay to demonstrate the production of neutralizing antibodies in calves vaccinated with a baculovirus-expressed L1 of bovine papillomavirus 1 (BPV1), formally classified as *deltapapillomavirus 4* (DPV4). Sixteen angus-cross, healthy colostrum-deprived calves confirmed to be DPV4 negative were randomly assigned to one of two test groups, with eleven calves receiving a dose of vaccine every two weeks for a total of three administrations and five calves receiving a placebo at the same times.

Serum was collected from each calf upon arrival, at time of first vaccination, day of third vaccination, and two weeks post-final vaccination. Calves were approximately 14 weeks old at the onset of the study, and 14, 16, and 18 weeks of age at each respective vaccination. All calves were comingled at Cambridge Technologies' research farm and observed daily.

The pSN assay was performed on all collected serum. In this study, 11/11 vaccinated calves seroconverted (pSN titer ≥ 20) after two doses of the test vaccine. Titers continued to increase following administration of the third dose. All placebo-vaccinated calves remained negative (pSN < 20) to DPV4 by the pSN assay.

This study demonstrated the production of pSN neutralizing antibodies in all vaccinated calves, while all unvaccinated placebo calves remained seronegative. No papillomas were detected at any time on any enrolled animal, and no systemic adverse reactions to vaccine administration nor any injection site reactions were noted in any calves.

Calf ID	pSN post 3 rd VX	Group
352	1280	Vaccinate
354	1280	Vaccinate
355	2560	Vaccinate
356	≤ 20	Control
357	640	Vaccinate
358	≤ 20	Control
359	≤ 20	Control
360	1280	Vaccinate
361	≤ 20	Control
362	2560	Vaccinate
363	1280	Vaccinate
364	1280	Vaccinate
365	≤ 20	Control
366	2560	Vaccinate
367	1280	Vaccinate
368	2560	Vaccinate

TABLE I. pSN titers post-third vaccination with Cambridge Technologies' Wart Vaccine, Killed Baculovirus Vector

STUDY TWO: CHALLENGE OF VACCINATED ANIMALS

Following the conclusion of the first study, the same calves were used to establish a reasonable expectation of efficacy for baculovirus-expressed DPV4 L1 in bovines by demonstrating that the seroconversion observed in the first study was adequate to protect those calves from a prototypic papilloma-inducing challenge.

At the time of this second study, all calves were approximately 7.5 months of age and were co-mingled at a challenge facility.

One-hundred and six days following the final vaccination being administered in study #1, each calf was intradermally challenged with each of two prototypic challenge preparations (two sites per strain): one being a wart homogenate from a 2022 field case (BPV2), and the other being BPV material obtained from ATCC (BPV1). Calves were observed daily and challenge sites palpated multiple times throughout the duration of the study. On the final day, all calves were bled for pSN testing, and any calf who showed a palpable anomaly at the challenge site had a sample taken for sequencing to confirm challenge.

The presence of warts was first observed on three animals on day 38 post-challenge. When examined on day 60 by a blinded veterinarian, five animals had developed warts. All excised tissue from the challenge sited yielded sequencing results consistent with the presence of papillomavirus in the sample.

Calf ID	Study 1 Group	Papilloma + sites	DPV sequence detected
352	Vaccinate	0	NA
354	Vaccinate	0	NA
355	Vaccinate	0	NA
356	Control	2	BPV1+
357	Vaccinate	0	NA
358	Control	4	BPV1+ BPV2+
359	Control	4	BPV1+ BPV2+
360	Vaccinate	0	NA
361	Control	2	BPV2+
362	Vaccinate	0	NA
363	Vaccinate	0	NA
364	Vaccinate	0	NA
365	Control	4	BPV1+ BPV2+
366	Vaccinate	0	NA
367	Vaccinate	0	NA
368	Vaccinate	0	NA

All five animals that developed papillomas were in the original placebo-vaccinated control group. No DPV4-vaccinated animals developed papillomas.

This study confirmed a reasonable expectation of efficacy for Cambridge Technologies' Wart Vaccine, Killed Baculovirus Vector, when used to vaccinate cattle against warts (papillomas).

TABLE 2. Number of papillomas and sequence type of papillomas detected post-challenge

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