

A Study to Determine Interference of MLV IBR Vaccine on Titer Response to *Mannheimia haemolytica* Bacterin/Toxoid

Objective

To determine if calves vaccinated with a combination MLV (modified live virus) IBR and *Mannheimia haemolytica* bacterin/toxoid (**Express® 5-PHM**) would develop an immune response to *Mannheimia haemolytica*.

Key Points

- Response for *Mannheimia haemolytica* whole cell and leukotoxin antibody titers were significantly greater at days 14 and 28 versus day zero with or without MLV IBR, **Express® 5-PHM**, being administered concurrently.
- Whether calves were sero-negative or sero-positive to IBR prior to vaccination did not make a difference.
- It appeared that calves not receiving MLV IBR did have a greater titer response to *Mannheimia haemolytica* whole cell and leukotoxin, but due to insufficient group numbers this could not be shown statistically.

Study Background

Claims have been made that calves vaccinated concurrently with MLV IBR and *Mannheimia haemolytica* bacterin/toxoid, would not respond well to *Mannheimia haemolytica*.

In addition, it has been suggested that this interference of the MLV IBR vaccine is greater when the calves being vaccinated are sero-negative to IBR.

- The basis for these claims is a 1992 Canadian research paper that indicated this type of interference.
- In the Canadian study, a subunit *Mannheimia (Pasteurella)* vaccine was used that consisted of outer membrane protein from *Mannheimia haemolytica* and recombinant DNA produced attenuated leukotoxin.
- The test vaccine used in the Canadian study is not currently being marketed, so it is questionable if the interference that was experienced would be true for a whole cell and leukotoxin product that is currently licensed in the USA, **Pulmo-Guard™ PH-M**.
- Previous studies have shown no interference of the *Mannheimia haemolytica* bacterin/toxoid to any of the MLV in **Express® 5-PHM** (TB01-106).

Study Location and Design

Location: BIVI Research Farm, Cosby, MO

Study Time: Summer 2005

Study Design: 40 beef calves, approximately 6 months of age and sero-negative to IBR (<1:2) were randomly assigned into two treatment groups.

Group #1 - 20 calves were vaccinated with **Express 5-PHM** on days 0 and 14.

Group #2 - 20 calves were vaccinated with **Pulmo-Guard PHM** on days 0 and 14.

Group #3 - consisted of an additional 20 calves that were sero-positive to IBR (>1:8) and vaccinated with **Express 5-PHM** on days 0 and 14.

Serum was collected from each calf on days 0, 14 and 28.

Serum samples were analyzed in Dr. Tony Confer's laboratory at Oklahoma State University, College of Veterinary Medicine.

The lab measured anti-*Mannheimia haemolytica* whole cell antibody titers and anti-leukotoxin antibody titers.

Results

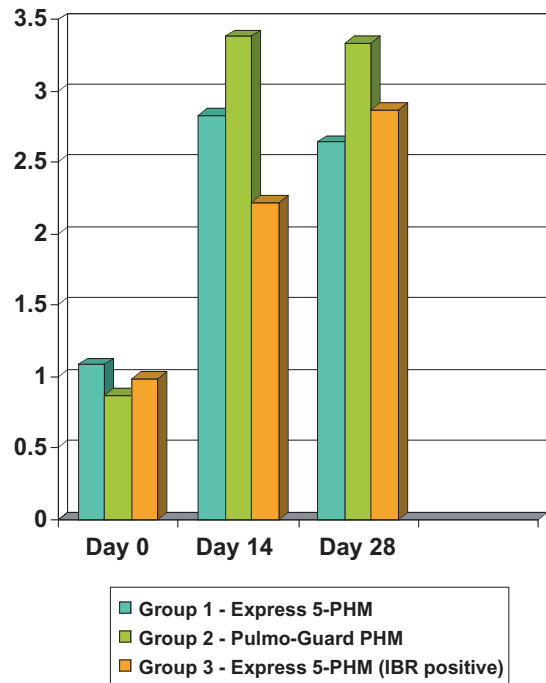
- Little is known as to what titer levels are necessary for protection, and protection is relative, based on degree of challenge versus degree of immunity.
- Some *Mannheimia* researchers have suggested that when vaccine induced immune response titers double compared to day zero, it is indicative of a significant immune response to the vaccine.
- That assumption was made in analyzing the data in this trial
- All titer results were converted to Log 2 base. A log₂ ratio was analyzed for each group, where ratio = day 14 log₂ titer (or day 28) / day 0 log₂ titer.
- It was determined that if the log₂ ratio for a given treatment approached 2 it would be considered a significant response based on prior assumption. Those ratios not approaching 2 would not be considered significant.
- Day 14 ratio responses of whole cell antibody for all three treatment groups varied from 2.27 to 3.51 with a P value ranging from <0.0001 to 0.0002, compared to day 0.
- Day 28 ratio responses for whole cell antibody also showed significant increases with P values for all three treatment groups at <0.0001, compared to day 0.
- Day 14 ratio responses of leukotoxin antibody for all three treatment groups varied from 2.27 to 3.62, with a P value of <0.0001 for all three groups compared to day 0.
- Day 28 ratio responses of leukotoxin antibody also showed significant increases with P values for all three treatment groups at <0.0001, compared to day 0.
- The following charts show actual GMT for the different treatment groups.

Bottom Line

- Responses to *Mannheimia haemolytica* after vaccinating with **Express 5-PHM** or **Pulmo-Guard PHM** alone were statistically significant (P< 0.05) at days 14 and 28 when compared to day 0.
- While there may have been some interference from the MLV vaccine, it did not appear to interfere with the immune response to the two antigenic fractions measured.
- Whether calves were sero-positive or sero-negative to IBR did not affect results.

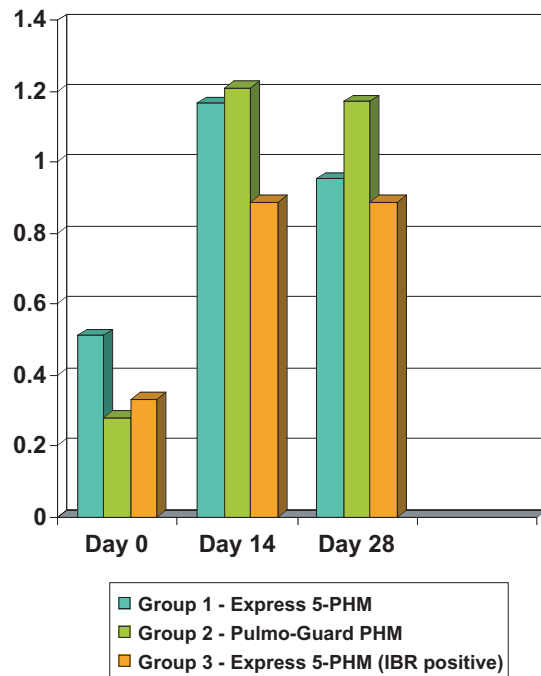
Geometric Mean Titers

Whole Cell Antibody to *Mannheimia haemolytica*



Geometric Mean Titers

Mannheimia haemolytica Leukotoxin Antibodies



Express® 5-PHM Vaccine Efficacy and Interference Study

Evaluating the antibody response induced by **Express® 5** vaccine with a diluent of *Pasteurella haemolytica* and *multocida* bacterin-toxoid is the objective of this efficacy and interference study.

Study Design

Thirty-five 4 to 12 month old calves were randomly assigned to three test groups. The Express 5 group received Express 5 rehydrated with sterile water. Controls were administered sterile water. **Express 5-PHM** group received Express 5 rehydrated with PHM bacterin-toxoid.

On Days 0 and 28, each calf was subcutaneously administered a 2 mL dose of assigned vaccine in the neck.

Results

IBR, BVD Types 1 & 2, PI₃, and BRSV serology titers were analyzed following the first dose of vaccine; BRSV serology titers were analyzed following the second dose of vaccine.

IBR Serology*			
Days	0	14	28
Control	<2	<2	<2
Express 5	<2	19.3	18.3
Express 5-PHM	<2	48.4	68
PI₃ Serology*			
Control	<2	<2	<2
Express 5	<2	1.5	5.5
Express 5-PHM	<2	2.5	15.1

BVD Type 2 Serology*			
Days	0	14	28
Control	<2	<2	<2
Express 5	<2	<2	29.1
Express 5-PHM	<2	<2	30.9
BVD Type 1 Serology*			
Control	<2	<2	<2
Express 5	<2	19	2476
Express 5-PHM	<2	7.08** 16.2***	2205** 2450***

Includes a calf with no response to BVD Type 1; *Excludes a calf with no response to BVD Type 1

BRSV Serology*					
Days	0	14	28	42	49
Control	31.0	16.3	9.7	18.3	13.2
Express® 5	21.0	275.7	68.4	296.1	153.1
Express® 5-PHM	28.6	119.7	52.3	272.1	86.0

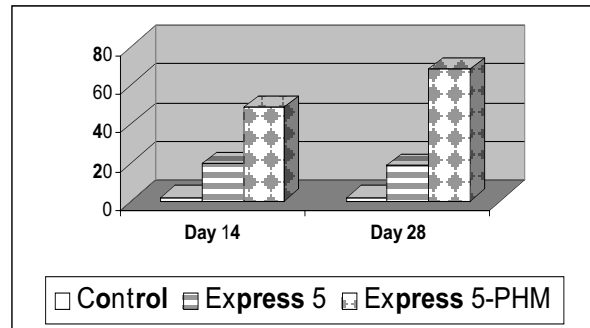
*Geometric Mean Titers

Calves with BRSV titers ≤ 64 on Day 0 of the trial were included in the study; calves seroconverting prior to Day 0 were excluded.

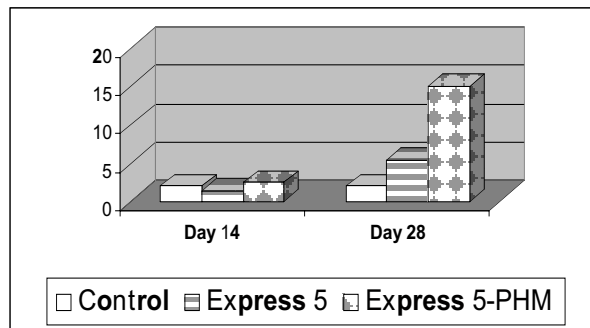
Conclusion

Using a *Pasteurella haemolytica and multocida* bacterin-toxoid as a diluent for **Express 5** causes no interference in serological response to IBR, BVD Types 1 & 2, PI₃, or BRSV.

PHM bacterin-toxoid appears to have an adjuvanting effect on the IBR and PI₃ components in **Express 5**. There is nearly a four-fold increase in IBR and PI₃ titers.



IBR Serology



PI₃ Serology