



TECHNICAL UPDATE

NUPLURA™ PH provides advanced protection against *Mannheimia haemolytica*.

Fast-acting, technologically advanced protection in the battle against calf pneumonia, NUPLURA™ PH features:

- **Recombinant Leukotoxoid Technology**
- **Purified Antigen**
- **Consistent Leukotoxoid Levels**
- **10-Day Onset of Immunity**
- **High Degree of Safety**
- **Minimal Reactivity**



Introduction

NUPLURA™ PH is a new vaccine that provides immunity within 10 days after vaccination against bovine pneumonia caused by *Mannheimia (Pasteurella) haemolytica*.¹ The advanced molecular technology of NUPLURA PH speeds the onset of immunity to protect young calves prior to periods of stress or increased vulnerability to infectious disease.

Effective vaccination with NUPLURA PH can significantly reduce the incidence of bovine respiratory disease (BRD), a complex of diseases that includes pneumonia. NUPLURA PH differs from other vaccines because it is not a simple, inactivated whole-cell product like most other bacterins. It is the first and only cattle vaccine manufactured in the United States using advanced molecular technology and contains outer membrane proteins (OMP) that have been extracted and purified through a series of steps.

This proprietary process results in a reduction of cellular debris, allowing for a more focused immune response. NUPLURA PH also contains consistently pure and measurable levels of leukotoxoid in every dose to provide a strong immune response.

The manufacturing process assures that NUPLURA PH:

- Includes no whole cells and cellular debris
- Contains purified OMPs utilized as immunogens
- Features washed leukotoxoid in each dose
- Reduces safety concerns
- Decreases unnecessary and potentially toxic components of the bacteria
- Reduces level of endotoxins

In research trials, a single dose of NUPLURA PH demonstrated protective immunity as early as 10 days after administration. A booster dose can be administered prior to periods of stress or elevated risk of exposure. Safety has been demonstrated in calves 28 days of age and older.

The technical advantages of using NUPLURA PH mean livestock producers and veterinarians can experience peace of mind that calves have improved protection from the performance-robbing impact of *Mannheimia haemolytica* pneumonia.

NUPLURA PH EFFICACY AND ONSET OF IMMUNITY TRIALS ¹

Material and Methods

This study involved 30 Holstein calves between 75 and 83 days of age at vaccination. Calves were randomly assigned to one group of 20 and one group of 10. The group of 20 was vaccinated with 2 mL each of NUPLURA PH and challenged 10 days postvaccination to determine onset of immunity.

The remaining 10 calves formed the control group and were vaccinated with a placebo. All calves were challenged endoscopically with 80 mL of *Mannheimia haemolytica* challenge material.

Researchers observed animals for clinical signs of pneumonia, including body temperature, respiratory difficulties and depression. All 30 calves were examined postmortem for percent of lung tissue with pneumonic damage.

Results

The percent of lung lesions was significantly lower among the vaccinated calves compared to the control group. The mean percent of the lung with lesions was more than twice as high, 29.75%, among the control group compared to 12.28% among the vaccinates (see Table 1).

The effect of intervention expressed as mitigated fraction was .69 among the vaccinated calves (see Table 2).

Mitigated fraction is a statistical measure used to determine the relative probability that vaccinated animals will have less severe disease than nonvaccinated animals. Analysis of efficacy data demonstrated that with a mitigated fraction of .69, NUPLURA PH effectively aids in the prevention of pneumonic tissue damage caused by *Mannheimia haemolytica* (see Table 2).

Conclusion

- Research study supported a 10-day onset of immunity label claim for NUPLURA PH.
- Vaccination with NUPLURA PH:
 - Significantly reduces the disease severity of *Mannheimia haemolytica*.
 - Provides quick protection for calves when they are most stressed and vulnerable to respiratory disease.

TABLE 1. Impact of NUPLURA PH Vaccination on Pneumonic Tissue 10 Days After Vaccination*

Group	N	Mean	Std. Dev.	Minimum	Maximum	P value
Control	10	29.750%	18.713	4.610	57.750	—
Vaccinate 10-Day Onset	20	12.282%	10.641	0.970	41.3000	0.0024**

*Statistical analysis measured by ANOVA.

** Indicates statistical significance at $P \leq 0.01$.

TABLE 2. NUPLURA PH Mitigated Fraction and Associated Confidence Limits

Group	Mitigated Fraction	Lower Confidence Limit	Upper Confidence Limit
Vaccinate 10-Day Onset	.69	36.33	100.00

NUPLURA PH FIELD SAFETY STUDY²

Material and Methods

The purpose of the study was to evaluate the safety of NUPLURA PH when administered under field conditions.

The study involved 626 calves at locations in Iowa, Texas and Utah. The Iowa location included Holstein and Guernsey-cross calves 4 – 12 months of age. The Texas location included beef calves 11 – 13 months of age while the Utah site had Holstein calves 5 – 28 days of age to evaluate the safety of the vaccine for very young cattle.

- All calves received 2 mL of NUPLURA PH injected subcutaneously in the neck. There was no control group.
- Calves were monitored for adverse effects of the vaccine, including vaccine hypersensitivity/anaphylaxis and morbidity.
- Monitoring for palpable swelling at the injection site was done on the day of vaccination, day 2, day 7 and day 21. Calves with injection site swelling greater than a walnut on day 21 were monitored again on day 35.
- Researchers divided the animals into four groups based on the degree of injection site swelling, ranging from no swelling to swelling greater than the size of a walnut.

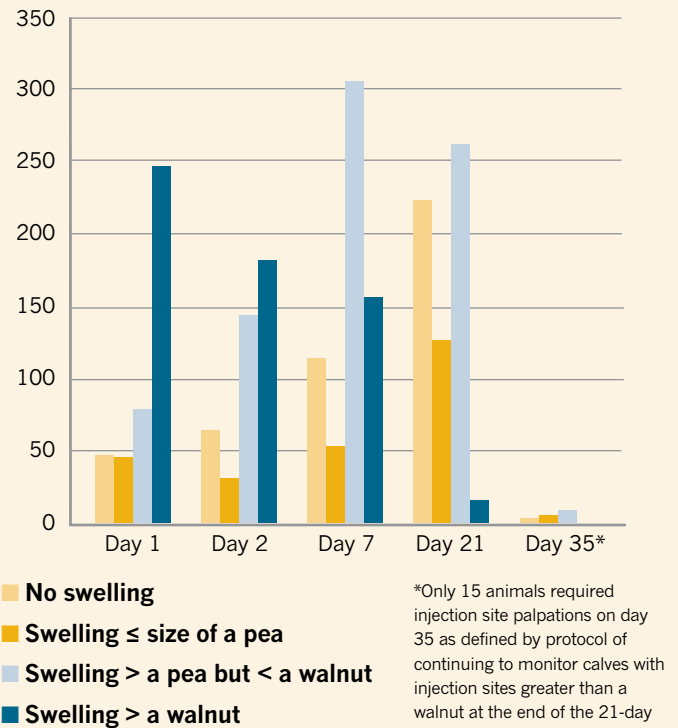
Results

With the exception of transient swelling at injection sites, no adverse safety effects were observed during the trial. All injection sites resolved upon completion of the study (see Figure 1.)

Conclusion

- The research demonstrated that NUPLURA PH is safe for use in calves 28 days of age and older.
- Following proper administration guidelines, there should be no effect on the meat of the carcass at slaughter due to injection site reactions.

FIGURE 1. Summary of Palpations Recorded for Entire Study





Summary

NUPLURA PH is the fastest-acting and most technologically advanced protection available to livestock producers and veterinarians in the battle against calf pneumonia.

NUPLURA PH is:

- **First.** Newest advancement in cattle pneumonia protection in the past decade.
- **Fast.** The only *Mannheimia haemolytica* vaccine demonstrated to deliver immunity in as soon as 10 days.
- **Strong.** Consistent leukotoxoid levels to provide superior protection and a strong immune response.
- **Pure.** Purified outer membrane proteins result in reduction of cellular debris and endotoxins.
- **Safe.** Demonstrated to be safe for calves as young as 28 days.
- **Economic.** Recombinant leukotoxoid technology provides a more efficacious vaccine at less cost.

For more information about NUPLURA PH and how it can help you, contact your local Novartis Animal Health representative or visit www.livestock.novartis.com.

1 Data on file, Novartis Animal Health US, Inc.
2 Data on file, Novartis Animal Health US, Inc.