Elanco

NUPLURA® PH+™

Research Brief 2

# NUPLURA® PH+ Safety Demonstration

## KEY FINDINGS

- **NUPLURA PH+ is safe for calves as young as 28 days of age**
- **Most calves experienced either no adverse events or transient injection site swelling only. The swelling was typically less than 5 $cm^2$ and when administered as recommended did not affect meat of the carcass at slaughter due to injection site reactions.**
- **Injection site swelling typically resolved by day 14 to 21. All injection site reactions were minor and similar to those observed with similar vaccines containing the same type of adjuvants.**
- **The deaths of the eight calves were not considered to be related to the vaccines. The incidence rates noted in this study were quite low.**

## STUDY OVERVIEW[1]

A study was conducted to demonstrate the safety of using a NUPLURA PH+* vaccination designed to protect against both *Mannheimia haemolytica* and viral causes of BRD in 627 calves ranging from 18 to 29 days of age housed in three field locations across the United States. This study followed the calves for a minimum of 42 days post-vaccination and evaluated the vaccine for its safety when administered to calves 28 days or older.

This study demonstrated that NUPLURA PH+ is safe for calves 28 days or older. This study supported the licensing of NUPLURA PH+3 (IBR, BVD Types 1 and 2) and NUPLURA PH+BVD.

## TRIAL DESIGN

- **Calves at three field locations were vaccinated with NUPLURA PH+. The three field locations varied by region:**
  - Wisconsin
  - Idaho
  - Texas

## MATERIALS AND METHODS

Study population—627 calves, 18 to 29 days of age at time of vaccination, individually housed in a calf hutch. Calves were randomly selected in three field locations, vaccinated on the left side of the neck with NUPLURA PH+ on study day 0, and vaccinated on the right side of the neck with a monovalent modified-live BRSV booster on study day 14, and visually observed daily by a veterinarian or trained professional. All calves were monitored for approximately 2 hours after vaccination for clinical signs of hypersensitivity or anaphylaxis.

- **Animals were observed at least once daily by the site investigator on study days 0, 1, 2, 7, 14, 21, 28, 35 and 42; all other daily observations were completed by the herdsman**
- **All adverse events were observed and documented until study day 42 in Wisconsin and Idaho and study day 50 in Texas**

* The combination of NUPLURA PH + Titanium® 5 was assessed in this safety study and supported the licensing of the following vaccines: NUPLURA PH+3 (IBR+BVD) and NUPLURA PH+BVD. NUPLURA PH + Titanium 5 is not licensed as a combination.

Of the 627 vaccinated calves, 329 did not exhibit an adverse event following vaccination. Injection site reactions were observed in 260 of the 627 calves. Other adverse reactions are typical fall and winter health issues observed on calf ranches during this time of year.

Table 1 shows the compiled number of calves with injection site reactions recorded at both injection sites at all three field locations on each of the observation days.

Table 2 lists the Veterinary Dictionary for Drug Regulatory Activities (VeDRRA) category and the total number and percentage of calves exhibiting the condition at all three field locations.

TABLE 1. **NUMBER OF INJECTION SITE REACTIONS BY FIELD LOCATION**

| Location | Number of Animals | Vaccination | Study Day | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | 1 | 2 | 7 | 14 | 21 | 28 | 35 | 42 | 50‡ |
| WISCONSIN | 207 | FIRST | 1 | 0 | 3 | 3 | 1 | 0 | 0 | 0 | n/a |
| | | SECOND | n/a | n/a | n/a | n/a | 0 | 0 | 0 | 0 | n/a |
| IDAHO | 210 | FIRST | 57 | 65 | 53 | 82 | 32 | 10 | 1 | 0 | n/a |
| | | SECOND | n/a | n/a | n/a | n/a | 23 | 4 | 0 | 0 | n/a |
| TEXAS | 210 | FIRST | 79 | 82 | 69 | 71 | 46 | 17 | 16 | 10 | 6 |
| | | SECOND | n/a | n/a | n/a | n/a | 0 | 0 | 0 | 0 | 0 |
| TOTAL | 627 | FIRST | 137 | 147 | 125 | 156 | 79 | 27 | 17 | 10 | 6 |
| | | SECOND | n/a | n/a | n/a | n/a | 23 | 4 | 0 | 0 | 0 |

‡ An additional observation day was added for the field location in Texas because injection site reactions were still present on study day 42.

TABLE 2. **ADVERSE EVENTS AT ALL THREE FIELD LOCATIONS**

| VeDRRA Term | Number of Calves | Percent of all Calves |
|---|---|---|
| NO ADVERSE EVENTS | 329 | 52.47 |
| INJECTION SITE SWELLING | 260 | 41.47 |
| INCREASED RESPIRATORY RATE | 39 | 6.22 |
| DEATH† | 8 | 1.28 |
| ANOREXIA | 4 | 0.64 |
| FEVER | 13 | 2.07 |
| HYPOTHERMIA | 3 | 0.48 |
| ARTHRITIS | 1 | 0.16 |
| CONJUNCTIVITIS | 1 | 0.16 |
| DIARRHEA | 14 | 2.23 |

| VeDRRA Term | Number of Calves | Percent of all Calves |
|---|---|---|
| LABORED BREATHING | 1 | 0.16 |
| COUGH PRODUCTIVE | 1 | 0.16 |
| RESPIRATORY DISTRESS | 5 | 0.80 |
| LAMENESS | 2 | 0.32 |
| PINKEYE | 11 | 1.75 |
| BLOATED | 1 | 0.16 |
| LETHARGY | 2 | 0.32 |

† Necropsies confirmed death was not related to the vaccination. Deaths were the result of pneumonia, low caloric intake and bloating—common issues found on most calf ranches.

***To learn more about NUPLURA® PH+, contact your herd health veterinarian, Elanco sales representative, technical consultant or visit NUPLURA.COM***

**The label contains complete use information, including cautions and warnings.**
**Always read, understand and follow the label and use directions.**

[1]Elanco Animal Health. Data on File.