Nasalgen® 3-PMH TECH BULLETIN

MERCK Animal Health

Key Highlights

- Under conditions of this study, there were no adverse events attributed to administration of N3PMH.
- Results of this multi-site study demonstrated that N3PMH was safe when administered as a single IN, 2 mL-dose (given 1 mL per nostril).

Safety of Bovilis® Nasalgen® 3-PMH

Bovilis® Nasalgen® 3-PMH (N3PMH) is effective for vaccination of healthy cattle 1 week of age or older against Infectious Bovine Rhinotracheitis (IBR) virus, Bovine Respiratory Syncytial Virus (BRSV), Parainfluenza 3 (PI_3) virus, *Mannheimia haemolytica* (MH) and *Pasteurella multocida* (PM) that are pathogens implicated in the Bovine Respiratory Disease (BRD) complex. N3PMH is safe for use in pregnant cows and in calves nursing pregnant cows. Summarized here are results of a multi-site study of the safety of N3PMH under typical field conditions.

FIELD SAFETY

The objective of field safety trials (FST) is to assess the safety of the product in the target population of animals within the conditions of the intended use of the product. The goal of those studies is to detect the types and frequency of adverse events that might indicate the need for further investigation. Typically, FSTs are to be performed in three distinct regions of the United States with the species, type and age of the animal indicated on the label of the product, with the product administered according to the labeled instructions, and with protocols that include details for qualified investigators to observe, evaluate and report adverse events. An "adverse event" is defined as any observation, whether or not considered to be product-related, that is unfavorable and unintended and that occurs after the use of the vaccine.

The study with N3PMH used the same protocol at three geographically distinct study sites. A total of 998 calves (birth to 63 days old) were randomly assigned to be vaccinated with one of three treatments – Serial A or Serial B of N3PMH (contents as licensed for release) or a placebo – on the day of enrollment (Day 0) as a single IN, 2 mL-dose (given 1 mL per nostril).

Table 1. Description of calves enrolled at three sites for study of field safety.

	Number of calves in each group			Description of calves		
Study Site	N3PMH Serial A	N3PMH Serial B	Placebo	Total No. and (Sex)	Age (Days) on Day 0	Breeds
1	109	111	110	330 (165♂; 165♀)	1 to 63	Limousin cross; Wagyu cross
2	106	105	106	317 (157♂; 160♀)	Birth to 54	Holstein; Holstein-beef cross; Jersey
3	117	117	117	351 (171♂; 180♀)	2 to 28	Holstein; Holstein-beef cross; commercial dairy breeds
Total	332	333	333	998 (493♂; 505♀)	Birth to 63	Beef and dairy

Approximately one-third (346/998, 34.7%) of the calves were ≤ 7 days of age, and 37 were no more than 1 day old. Housing (hutches and pens) was consistent with commercial industry standards for calves and provided for their well-being. No surgical or medical intervention was administered during the week prior to enrollment. No treatment or processing procedure was administered until Day 0 of the study. Health care was provided by attending veterinarian(s) at the respective study sites.

The experimental unit was the individual calf. On Day 0 of the study, each clinically healthy calf was individually restrained with its head elevated slightly while the randomly assigned treatment was administered (1 mL per nostril). The attending veterinarian at the respective site observed the calves after vaccination on Day 0 and once daily for 14 days after vaccination.

Under the conditions of these studies, investigators determined that all observed adverse events were "unlikely" to have been caused by the administration of N3PMH or the placebo.

All investigators stated that N3PMH was "satisfactorily safe." Results of this multi-site study demonstrated that N3PMH was safe when administered as a single IN, 2 mL-dose (given 1 mL per nostril). Additionally, reversion to virulence studies demonstrated that none of the five components of N3PMH reverted back to virulent master seed organisms.

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