ZOETIS INC.
333 PORTAGE STREET, KALAMAZOO, MI, 49007
Telephone: 269-359-4414
Customer Service: 888-963-8471
Website: www.zoetis.com

PROTIVITY™

Zoetis

See productdata.aphis.usda.gov for a summary of the studies approved by the USDA for licensing this product. The package insert also contains additional information developed by the licensee.

Mycoplasma Bovis Vaccine

Avirulent Live Culture

For use by, or under the supervision, of a veterinarian on premises having a history of *M. bovis* disease.

This product has been shown to be effective for the vaccination of healthy cattle 1 week of age or older against respiratory disease caused by *Mycoplasma bovis*. Duration of immunity has not been established. For more information regarding efficacy and safety data, see productdata.aphis.usda.gov.

Safety:

A field safety study was conducted to demonstrate the safety of Protivity in dairy and beef calves of varying sources, including those raised in high population densities, high stress situations and intensive calf raising facilities. Only antimicrobials that had no activity against *M. bovis* were allowed. In this study, a total of 1069 calves (355 unvaccinated controls and 714 vaccinated with Protivity) were enrolled at three distinct geographical locations. The age range of the calves enrolled were between 8 days of age and younger and approximately 30 days of age. The calves were administered Protivity (n = 714) by subcutaneous route on Day 0 and 21. The frequency of adverse events (mainly neonatal diarrhea and respiratory infections which are common in these age of calves) in the control and vaccinated groups were similar. One out of 714 (0.14%) vaccinated calves developed arthritis. The vaccine strain was isolated from the affected joint.

Number (n) of calves in the field safety study		**Calves with no AE* (%)**	**Calves with AE* (%)**
Enrolled	1069		
Controls	355	264 (74.4%)	91 (25.6%)
Vaccinated	714	551 (77.2%)	163 (22.8%)

*AE= Adverse Events

An extended duration of safety evaluation (120 days) was also completed in 4 to 7-day old calves. A total of 148 calves were enrolled, and 97 were administered Protivity by subcutaneous route on Day 0 and 21. Deep nasal swabs for *M. bovis* culture were evaluated and no *M. bovis* was ever isolated. Over the 120-day period, there was no major difference in adverse events between control and treatment group calves.

Number (n) of calves in the field safety study		**Calves with no AE* (%)**	**Calves with AE* (%)**
Enrolled	148		
Controls	51	43/51** (84.3%)	8/51** (15.7%)
Vaccinated	97	79/97 (81.4%)	18/97 (18.6%)

*AE= Adverse Events (mainly diarrhea and respiratory events)

** One control calf was humanely euthanized for overeating/bloat on day 107.

An organ dissemination study was completed using a total of 20 colostrum deprived calves, 5 to 7 days of age. Five calves were untreated controls, and 15 calves were inoculated both subcutaneously and intramuscularly, concurrently, with equivalent to an 8x overdose as measured by total Colony Forming Units (CFU) administered. Health observations were performed daily, and 5 inoculated calves and 1 to 3 untreated controls were randomly selected for necropsy on days 10, 20 and 29. Calves were evaluated for the presence of *M. bovis* in whole blood, urine, swabs (nasal, nasopharyngeal, middle ear, conjunctival, tracheal, injection site, testes) and various tissues (lung, synovial fluid, tonsil, kidney, liver, uterus). Transient nasal shedding did occur in one out of 15 inoculated calves on day 3, 6 and 9. This calf did not display any adverse clinical signs. At the time of necropsy, the vaccine strain was found to have disseminated in 5 out of 15 vaccinated calves. Dissemination was identified on day 10 and

20 at necropsy in the following tissue samples: conjunctiva (n=1), tonsil (n=1), lung (n=1), synovial joint fluid (n=1), and lymph nodes (n=1). The vaccine strain was present in 2 of 5 calves necropsied on day 29 (middle ear & lung n=1; synovial fluid n=1). Although lameness was observed in equal numbers in both vaccinates and controls, all calves were normal for the duration of the study for respiratory effort, nasal discharge, cough, and head tilt/dropped ear.

A Shed & Spread study was completed using a total of 16 calves, 6 to 7 days of age, where 8 calves were vaccinated with a 5x overdose as measured by CFU administered, and then comingled with 8 control calves. Calves were evaluated daily for the presence of *M. bovis* in nasal and nasopharyngeal swabs through day 28. No calves developed pyrexia or were scored with abnormal attitude, nasal discharge, respiratory effort, cough, and head tilt/ear drop for the duration of the study. Lameness was observed in equal numbers in both vaccinates and controls, and *M. bovis* vaccine strain was never isolated from any joint. No vaccinated calves or control calves were ever positive for *M. bovis* in nasal or nasopharyngeal swabs, thus no shed or spread of the vaccine strain was observed.

Efficacy:

An efficacy study was completed using a total of 83 calves, 7 to 12 days of age. Calves were split into three treatment groups including 39 Protivity vaccinated calves, 39 saline vaccinated controls, and 5 non-vaccinated and non-challenged controls. All calves were seronegative to *M. bovis* prior to vaccine administration, given as two doses subcutaneously, 21 days apart. Calves were challenged with a virulent strain of *M. bovis*, and lungs were examined at 28 days post-challenge. The Protivity vaccinated calves had a median percent of total lung lesions of 4.3% compared to the controls with total percent of lung lesions of 16.5%.

Five Number Summary of Percent of Total Lung with Lesions

Treatment	n	Minimum	1st Quartile	Median	3rd Quartile	Maximum
Control Group	39	0.1	9.1	16.5	31.5	71.2
Vaccinated Group	39	0.0	0.8	4.3	10.2	39.5

Directions:

General Directions: Aseptically rehydrate the freeze-dried vaccine with the sterile diluent provided, mix well and administer 2 mL subcutaneously.

Primary Vaccination: Healthy cattle should receive two doses administered 21 days apart.

Revaccination: The need for annual booster vaccination has not been established for this product; consultation with a veterinarian or the manufacturer is recommended.

Precautions:

This modified live *M. bovis* strain may disseminate into joint synovial fluid and may cause arthritis.

This product may cause transient injection site swellings that resolve within 21 days of vaccination.

This product has not been tested in pregnant or lactating animals.

Store at 2°-8°C. Prolonged exposure to higher temperatures and/or direct sunlight may adversely affect potency. Do not freeze.

Use entire contents when first opened.

Sterilized syringes and needles should be used to administer this vaccine. Do not sterilize with chemicals because traces of disinfectant may inactivate the vaccine.

Inactivate unused contents before disposal.

Do not vaccinate within 21 days before slaughter.

As with many vaccines, anaphylaxis may occur after use. Initial antidote of epinephrine is recommended and should be followed with appropriate supportive therapy.

Do not mix with other products, except as specified on the label.

In case of human exposure, contact a physician.

Technical inquiries should be directed to Zoetis Inc. Veterinary Services, (888) 963-8471.

This product has been shown to be efficacious in healthy animals. A protective immune response may not be elicited if animals are incubating an infectious disease, are malnourished or parasitized, are stressed due to shipment or environmental conditions, are otherwise immunocompromised, or the vaccine is not administered in accordance with label directions.

VLN 190/PCN 1750.00

Zoetis Inc., Kalamazoo, MI 49007, USA

51379600

Presentation: 10 and 50 doses.

CPN: 3690594.0