Klebsiella Vetovax™ SRP®

KLEBSIELLA PNEUMONIAE BACTERIAL EXTRACT VACCINE

What is *Klebsiella*?

- Gram negative fecal coliform bacteria
- Found on almost all dairy farms
- Significant environmental mastitis pathogen, especially in large herds
- Hard to diagnose on culture as bacteria dies quickly
- Upon death, bacteria releases a difficult to treat endotoxin causing devastating disease in dairy cattle
- Significant pathogen in human medicine as well
- Two major pathogens: *Klebsiella pneumoniae* and *Klebsiella oxytoca*

Sources of *Klebsiella*?

- Feces, bedding, feed
- Milking equipment
- Drinking water
- Cow hide and mucosa
- Extended survival in environment

The importance of iron

- All animals and most bacteria require iron, an essential element for cellular metabolic functions
- Ferric iron (Fe^{+3}) is poorly soluble in biological environments, therefore animals and bacteria have special protein systems to bind, transport, and store iron in fluids and secretions
- To survive inside a host, a bacterial pathogen MUST competitively acquire protein-bound iron from the host (bound by host transferrin, lactoferrin, heme, and intracellular proteins)

Bacterial iron acquisition

- When bacteria encounter a low iron environment, such as inside an animal host, they secrete small proteins called SIDEROPHORES which take iron away from the host binding proteins
- At the same time, bacteria express pore-like SIDEROPHORE RECEPTORS in their outer membrane. These specialized proteins recognize siderophore-iron complexes, transporting them through the cell wall
- Siderophore receptors belong to a family of proteins called "PORINS"

What is **SRP® Technology**?

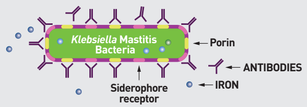
- **SRP** > **S**iderophore **R**eceptor and **P**orin technology
- **Porins** > protein pores in the cell wall that allow essential nutrients to enter the cell
- **Siderophore receptors** > specialized porin proteins that transport iron-siderophore complexes through the cell wall during times of iron deprivation
- **SRP® technology** > siderophore receptor and porin proteins, extracted from the bacterial cell wall and used as vaccine antigens

How does it work

- Gram negative coliforms require iron for growth
- Vaccine creates antibodies to block transfer of iron
- Gram negative bacteria share similar SRP proteins
- Vaccination is a good tool to be used as part of a whole herd solution with dairy farm management

The mode of action of SRP® vaccines is different from that of whole-cell autogenous or core antigen vaccines. The **SRP® vaccine-induced antibodies binds and blocks transfer of iron** and nutrients through bacterial cell wall pores, **starving bacteria of needed nutrients**. Since it is designed from siderophore receptors and porins, specialized proteins on the outer membrane of the bacteria, the **SRP® vaccine provides greater overall immunity**.

SRP® vaccine technology



Pr Klebsiella Vetovax™ SRP®

KLEBSIELLA PNEUMONIAE BACTERIAL EXTRACT
Siderophore receptors and porins
Veterinary use only VLN365/PCN 2879.00

new

Indication
This product has been shown to be effective for vaccination of healthy cattle 22 months or older against mastitis caused by *Klebsiella pneumoniae*. The duration of immunity is unknown. For more information regarding efficacy and safety data, see productdata.aphis.usda.gov under Klebsiella Pneumoniae Bacterial Extract.

Dosage and administration
Shake well before use. Administer 2 mL (1 dose) subcutaneously. Revaccinate in 2 to 4 weeks. Heifers should receive their first dose 30 days after calving. Dry cows should be vaccinated twice before calving. Whole-herd vaccination may be done at any stage of lactation. The need for annual booster vaccination has not been established for this product; consultation with a veterinarian is recommended.

Cautions
Store at 2 °C to 8 °C (35 °F to 46 °F). **DO NOT FREEZE**. Use entire contents when first opened. Do not vaccinate within 60 days of slaughter. Transient swelling at the injection site (>5 cm) may occur. Heifers less than 22 months of age should not receive this product until 30 days after calving. In case of allergic response, administer flunixin meglumine and/or epinephrine. Contains formaldehyde and polymyxin-B as preservatives. Do not mix with other products.

Warning
In case of human exposure, contact a physician.

Patent information
www.epitopix.com/patents

Technical inquiries
1 800 363-1700

Manufactured by:
Epitopix, Willmar, MN, USA 56201

Distributed by:
Vetoquinol N.-A. inc.,
2000, chemin Georges, Lavaltrie (Québec) Canada J5T 3S5

REFERENCES

1 RUEGG, P.L. 2003. Investigation of mastitis problems on farms. *Vet.Clin. North Am. Food Anim. Pract.* 19:47–73.

2 OLIVEIRA, L. RUEGG, P.L. 2014. Treatments of clinical mastitis occurring in cows on 51 large dairy herds in Wisconsin. *J. Dairy Sci.*, 97:9, p. 5426-5436.

3 HERTL, J. A., Y. H. SCHUKKEN, D. BAR, G. J. BENNET, R. N. GONZALEZ, B. J. RAUCH, F. L. WELCOME, L. W. TAUER, and Y. T. GRÖHN. 2011. The effect of recurrent episodes of clinical mastitis caused by gram-positive and gram-negative bacteria and other organisms on mortality and culling in Holstein dairy cows. *J. Dairy Sci.* 94:4863-4877.

4 GORDEN, P., KLEINHENZ, M.D., YDSTIE, J.A., BRICK, T.A., SLINDEN, L.M., PETERSON, M.P., STRAUB, D.E., BURKHARDT, D.T. 2018. Efficacy of vaccination with a *Klebsiella pneumoniae* siderophore receptor protein vaccine for reduction of *Klebsiella* mastitis in lactating cattle. *J. Dairy Sci.*, 101:11, p. 10399.

5 PINZÓN-SANCHÉZ, C., CABRERA, V.E., RUEGG, P.L. 2011. Decision tree analysis of treatment strategies for mild and moderate cases of clinical mastitis occurring in early lactation. *J. Dairy Sci.*, 94:1873-1892.

6 GORDEN, P. *et al.*, Efficacy of vaccination with a *Klebsiella pneumoniae* siderophore receptor..., *op. cit.*, p. 10399.

Product	VTQ	CDMV	VP	WDDC	AVP
Klebsiella Vetovax® SRP® (*Klebsiella pneumoniae* bacterial extract)	458807	xxxxxx	xxxxxxx	xxxxxx	xxxxxxx

vetoquinol.ca

vetoquinol ACHIEVE MORE TOGETHER

VETOQUINOL.YOUR PARTNER
IN THE PREVENTION AND TREATMENT OF CLINICAL MASTITIS

Pr Klebsiella Vetovax™ SRP®

KLEBSIELLA PNEUMONIAE BACTERIAL EXTRACT VACCINE

vetoquinol.ca

vetoquinol ACHIEVE MORE TOGETHER

Klebsiella Vetovax™ SRP®: ironclad solution against clinical mastitis. Keep your cows in the herd longer.

***Klebsiella* Vetovax™ SRP® is a vaccine that uses the new siderophore receptor and porin (SRP) technology and it is made from *Klebsiella pneumoniae* bacterial extract** that has been shown to be effective for vaccination of healthy cattle 22 months or older against mastitis caused by *Klebsiella pneumoniae*.

Dairy farmers are justified in seeing mastitis as the utterly devastating disease that it is. According to Pamela Ruegg, "mastitis is the most common and costly health concern for dairy producers"[1] and "results in around 65-85% of the industry's overall use of antibiotics."[2] Mastitis is most frequently caused by bacteria. Cows become exposed through many sources (feces, bedding, milking equipment, water, other animals, etc.). Identifying the correct pathogen is crucial in determining prevention and treatment.

Not all sources of mastitis are alike...

Bacteria that cause mastitis come from two sources: contagious pathogens (such as *Streptococcus agalactiae* and *Staphylococcus aureus*) and environmental pathogens such as coliform bacteria and environmental *Streptococci* (other than *Strep. agalactiae*). Methods of control differ by pathogen, which is why it is important to identify the different bacteria causing a herd issue and address them accordingly. This document focuses on a specific and innovative new vaccine against coliform mastitis caused by *Klebsiella pneumoniae* bacteria.

Since "Gram-negative clinical mastitis (CM) is more severe than Gram-positive mastitis due to its effect on milk yield, discarded milk, treatment costs, death, and culling[3], the lack of effective treatments historically made *Klebsiella* CM especially troublesome. ***Klebsiella* Vetovax™ SRP®** — a new vaccine using the innovative SRP® technology against mastitis caused by the coliform bacteria *Klebsiella pneumoniae* — is now available from Vetoquinol.

Key features of *Klebsiella* mastitis

- Environmental coliform mastitis
- Very prolific in organic bedding (sawdust)
- Bacteria often causes a rapid infection
- Very frequently undetected by the farmer/robot before disease starts
- Causes a local and systemic toxemia
- Infection almost always destroys the quarter
- Infection often kills the animal
- >50% of cows with *Klebsiella* CM exit the herd[4]

Why vaccinate?

- Difficult to prevent and treat
- Costly disease: average milk loss of 700 to 1,400 kg/case[5]
- Vaccines can help save on treatment costs
- Vaccination reduces the need for antibiotics in treating disease

Choosing the right vaccine is highly recommended. "Whereas core antigen (J5) vaccines are available, coliform mastitis, especially *Klebsiella* mastitis, continues to cause problems for dairy producers."[6] ***Klebsiella* Vetovax™ SRP®** is a new technology high-quality vaccine that addresses coliform clinical mastitis directly by going beyond traditional bacterins to help you keep cows in the herd longer.

Overview of the study conducted by Iowa State University

- 429 cows
- 378 milking
- Free stall barn houses all lactating cows with manger headlocks
- Currently bedded with manure solids (not heat treated)
  - ~30% dry matter coming off the separator.
  - Stalls are re-bedded 3x/week.
- J5 Vaccination
  - 4 x/lactation (-45, -28, 25, & 90 DIM)

It is important to note that the herd had an ongoing *Klebsiella* mastitis issue even with frequent J5 vaccination.

General conclusion of the study conducted by Iowa State University

The prevalence and incidence of *Klebsiella* mastitis was significantly reduced in Kleb-SRP vaccinated cows compared to placebo vaccinated controls. Prevalence, the portion of individuals that tested positive during the study, was reduced by 71% in vaccinates compared to controls. Milk Production increased in Kleb-SRP vaccinated cows by 2.0 pounds per cow per day compared to placebo cows. In conclusion, vaccination with a *Klebsiella pneumoniae* vaccine based on the SRP® technology provided statistically significant protection from *Klebsiella* mastitis.

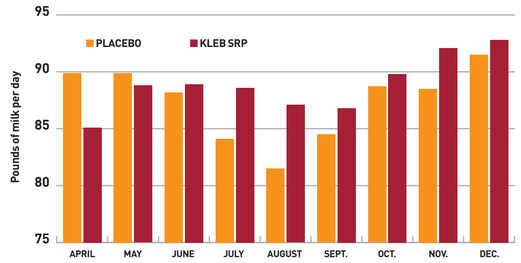
Source for the data provided here

GORDEN[1], P., KLEINHENZ[1], M., YDSTIE[1], J., SLINDEN[2], L., STRAUB[2], D., PETERSON[2], M., BURKHARDT[2], D. (2017), Application of Siderophore Receptor Proteins and Porins (SRP®) Technology for Controlling *Klebsiella* Mastitis in a Commercial Dairy Herd, *NMC Annual Meeting Prodeedings*, 169-170. [1] Iowa State University, Field Services, Ames, Iowa, USA; [2] Epitopix, LLC, Willmar, Minnesota, USA.

Klebsiella Vetovax™ SRP®

KLEBSIELLA PNEUMONIAE BACTERIAL EXTRACT VACCINE

Average daily milk production per cow
from cows vaccinated with *Klebsiella* SRP vaccine versus placebo



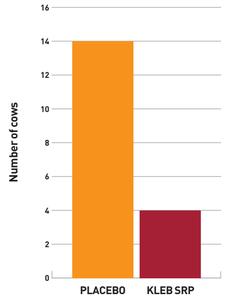
INCREASED MILK PRODUCTION PER COW, PER DAY

Overall 2.002 pound of milk advantage in *Klebsiella*-SRP Vaccinates per cow per day. P=0.0000

REDUCED PREVALENCE OF *KLEBSIELLA* MASTITIS

71%

Prevalence of *Klebsiella* mastitis
in cows vaccinated with *Klebsiella* SRP vaccine versus placebo

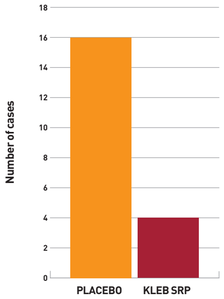


Prevented Fraction 0.7143; 95% CI: 0.1453 to 0.9045 P=0.0171

REDUCED INCIDENCE OF *KLEBSIELLA* MASTITIS

76%

Incidence of *Klebsiella* mastitis
in cows vaccinated with *Klebsiella* SRP vaccine versus placebo

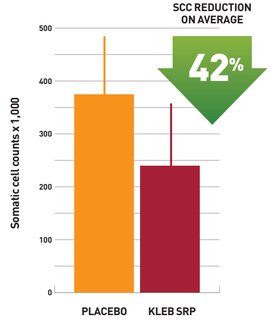


Prevented Fraction 0.7594; 95% CI: 0.2804 to 0.9195. P=0.0056

SCC REDUCTION ON AVERAGE

42%

Effect of *Klebsiella* SRP vaccine
on somatic cell counts (SCC)

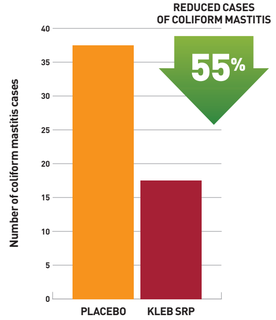


Error bars show 95% CI. Controlling for other variables, vaccination with *Klebsiella*-SRP reduces SCC on average 42%. P <0.001.

REDUCED CASES OF COLIFORM MASTITIS

55%

Cumulative cases of coliform mastitis
from cows vaccinated with *Klebsiella* SRP vaccine versus placebo



Over a ten-month period
Prevented Fraction 0.5478; 95% CI: 0.1953 to 0.7459. P=0.0057