

CLOSTAT®

BACILLUS SUBTILIS PB6
AN ACTIVE MICROBIAL FOR BEEF CATTLE

A TARGETED APPROACH TO IMPROVING CATTLE HEALTH



KEMIN
INTESTINAL
HEALTH

CLOSTAT® from Kemin is a unique, patented strain of *Bacillus subtilis* PB6, a gram positive, spore-forming *Bacillus* that populates the lower intestinal tract. It effectively targets and disrupts *Clostridium perfringens*, *Salmonella* and *Escherichia coli*, resulting in better overall intestinal health in beef cattle. Extensive research within large commercial feedyards and with universities demonstrates a consistent animal response and significant return on investment. CLOSTAT is the direct-fed microbial of choice for improved animal health.

THREE MODES OF ACTION

B. subtilis PB6, found in CLOSTAT, uses three modes of action^{1,2} — **pathogen inhibition, reduction in intestinal inflammation and quorum quenching effects** — to support intestinal health, which supports the immune system and ultimately improves animal health. Extensively researching CLOSTAT's modes of action allows Kemin to more accurately predict a consistent and repeatable animal response.

MODE OF ACTION 1: PATHOGEN INHIBITION

B. subtilis PB6 secretes multiple biocidal proteins that inhibit certain strains of pathogenic bacteria.^{1,2} Its active metabolites have a cyclic structure comprised of seven amino acids, collectively known as surfactins.

Surfactin molecules can form pores on the cell walls of the bacteria, which provides the mode of action.³ These proteins disrupt the bacteria membrane, causing the cell contents to leak, ultimately killing the pathogenic bacteria without harming the beneficial gut microflora (Figure 1).

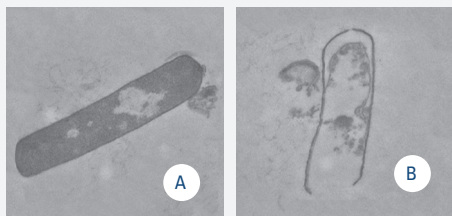


Figure 1: The effect of *B. subtilis* PB6 on *C. perfringens* at 37° C. (a) Disruption of the cell wall and loss of cytoplasmic contents into the exterior after one hour. (b) Rupture and death of cell after 4 hours.³ (Transmission electron micrograph magnification: 29,000X)

MODE OF ACTION 2: REDUCED INTESTINAL INFLAMMATION

Intestinal inflammation can occur if the intestinal lining becomes damaged and allows molecules such as bacteria and pathogens and their toxins to pass between epithelial cells, known as Leaky Gut Syndrome (Figure 2). This triggers an immune response to destroy and remove these invasive organisms, resulting in an inflammatory process that pulls energy from other key performance functions.⁴

B. subtilis PB6 secretes cyclic lipopeptide surfactins through normal metabolism to reduce inflammation.



Figure 2: Gut inflammation

MODE OF ACTION 3: QUORUM QUENCHING

Quorum sensing facilitates the initiation of infection, colonization and disease progression in the intestine where diffusible signaling molecules are produced, secreted and detected by the bacterial cells in the intestine.⁵⁻⁸ **Quorum quenching** is the mode of action that can disrupt the quorum sensing system through degradation of quorum sensing signaling molecules, the inhibition of signal biosynthesis and the inhibition of signal detection.⁹ Quorum quenching also aids in the prevention of toxin production and formation of biofilm.³ *B. subtilis* PB6 can prevent quorum sensing of *C. perfringens*.



Figure 3: *Clostridium*



WHY DOES INTESTINAL HEALTH MATTER IN BEEF CATTLE?

More than 70% of the immune system resides in the gastrointestinal (GI) tract, which is regularly exposed to 10 trillion microorganisms.¹⁰ The GI tract digests and absorbs nutrients, maintains a balanced microbiome, prevents harmful compounds from entering the host, and defends against harmful pathogens. Maintaining optimal intestinal health thus supports the immune system.

IMPACT OF PATHOGENS

Bovine respiratory disease (BRD) affects 16.2% of all cattle placed in feedlots, resulting in economic losses exceeding \$2 billion per year,¹¹ of which BRD treatment costs contribute \$75 million.^{12,13} Viral pathogens weaken the animal's immune system and physically damage the epithelial mucosa of the upper respiratory tract, resulting in bacterial pathogen proliferation.¹⁴ As a multifaceted disease, BRD is potentiated by stressors such as shipping, receiving, commingling and inclement weather, resulting in cattle often succumbing to bacterial pneumonia. Producers incur significant costs associated with BRD including metaphalaxis, vaccination, increased labor and treatment.

CLOSTAT IS THE SOLUTION

CLOSTAT, through its pathogen inhibition, reduction in intestinal inflammation and quorum quenching effects, has been shown to support intestinal health, which supports the immune system and ultimately improves animal health. **CLOSTAT has shown improvements in BRD incidence and associated antimicrobial treatment costs, and has an ROI of 6:1.**¹⁵⁻²⁰



INTESTINAL HEALTH



IMMUNE HEALTH



ANIMAL HEALTH



CLOSTAT®

Dive deeper into the research-backed direct-fed microbial of choice at kemin.com/clostat-beef.



See CLOSTAT in action.

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