THE CHALLENGE

THE PROBLEM IS IN THE GUT

Hundreds of millions of dollars are spent on interventions to manage intestinal disease in livestock, however, the indirect costs of intestinal diseases are more than producers once thought.

Consider the day-to-day life of your livestock. Every day, through their environment, your animals are exposed to a variety of pathogenic bacteria and viruses, including *Clostridia*, *Salmonella* and *Escherichia coli*.

Exposure to these pathogens can impact the microbiota of the gastrointestinal (GI) tract, which may have negative implications on GI function. These intestinal microbiotas contribute to several physiological functions, such as digestion and absorption, regulation of energy homeostasis, prevention of mucosal infections, and modulation of the immune system.1

As much as we want to keep the above pathogens at bay, exposure to harmful bacteria is inevitable. When cattle are co-mingled or exposed to a new pathogen, their risk of immune stimulation increases dramatically. In addition, parlor sanitation and pen cleanliness are factors which can have a tremendous impact on the proliferation of these harmful bacteria in the environment.

STRESS + PATHOGENIC BACTERIA = GUT HEALTH CHALLENGE

Just as exposure to pathogenic bacteria in the environment is inevitable, so are animal stress events. Under stress events, both the mucosal layer and the tight junctions are negatively impacted, often leading to inflammation and reduced integrity of the intestinal barrier. Reduced intestinal integrity indicates there is a breakdown in the tight junctions between the epithelial cell membranes, allowing for intestinal permeability. Without these tight junctions, pathogenic organisms like *Clostridia* are able to cross the intestinal barrier, resulting in an immune response which makes cattle more susceptible to diseases and reduces performance and profitability.

CATTLE STRESS FACTORS

- Heat or cold stress
- Diet changes
- Other diseases
- Handling
- Pre- and post-partum
- Changes of cattle in pen or adding cattle to herd
- Limited water supply or low water quality
- Mold mycotoxins
- Overall feed quality

TO OPTIMIZE ANIMAL HEALTH AND PERFORMANCE, YOU MUST OPTIMIZE INTESTINAL HEALTH.

IF PATHOGEN EXPOSURE AND STRESS ARE INEVITABLE, WHAT CAN YOU DO?

To optimize animal health, performance and profitability, you must optimize intestinal health. Active microbials are important tools in the fight against intestinal-compromising pathogenic bacteria. Active microbials are isolated and characterized bacteria shown to inhibit or eliminate harmful pathogens. Eliminating these potentially harmful pathogens is necessary to achieve a healthy, balanced microbiota.

BENEFITS OF ACTIVE MICROBIALS

- Positively impact intestinal bacterial populations
- Enhance resistance to disease
- Reduce shedding of pathogens
- Increase intestinal immunity
- Lessen disease symptoms
- Decrease *Clostridia* and other pathogenic bacteria
- Improve health

SELECTING THE RIGHT ACTIVE MICROBIAL

Not all probiotic products are active microbials, and not all active microbials are the same. When evaluating active microbial solutions to fight against intestinal-compromising pathogenic bacteria, four key criteria must be considered:

1. **MODE OF ACTION:** Does it have an understood and proven mode of action?
2. **PROVEN PATHOGEN INHIBITION AND EFFICACY:** Does in vitro and in vivo research prove efficacy against a broad spectrum of pathogens or just a few?
3. **STABILITY:** What is the product’s thermostability and GI tract stability?
4. **COMPATIBILITY:** Is the product compatible with common antibiotics and organic acids?

SELECTING THE RIGHT ACTIVE MICROBIAL

**BACILLUS SUBTILIS, PB6 MODE OF ACTION**

**THE ACTIVE MICROBIAL LEADER**

ClOSTAT™ contains a unique, patented, spore-forming strain of Bacillus subtilis, PB6, which was isolated from chickens who had survived a high exposure to Clostridium perfringens in the environment.

**MODE OF ACTION**

PB6 is a unique, naturally occurring, spore-forming microorganism. Once the PB6 spores are ingested by the animal, they will begin to germinate by low pH and bile salts. Vegetative cells of PB6 in the intestines produce secondary metabolites or lipopeptide surfactants. These surfactants then break into the bacterium’s cell wall, causing it to release its cytosol, resulting in death of the microorganism.³

**IN VITRO EFFICACY: PROVEN PATHOGEN INHIBITION**

A zone of inhibition test examines bacterial sensitivity and resistance to certain compounds. The size of the zone surrounding the common disk on the plate is an indication of microbial susceptibility to the compound.

**NOT ALL BACILLUS SUBTILIS ARE THE SAME**

Figure 3: PB6 surfactants impact on Clostridium perfringens cell wall structure.

**PROVIDING BROAD SPECTRUM CONTROL**

With more than 15 years of research in livestock and poultry across the globe, PB6 has proven inhibition efficacy against Clostridia and other pathogenic species.³

**Figure 4: Characteristics of Bacillus subtilis, PB6 on A) Clostridium perfringens ATCC 13124, B) Escherichia CVCC 1555, C) Salmonella typhimurium ATCC 14028.**

**Figure 2: Effect of PB6 against Clostridium difficile.**

**Figure 1: Antagonistic assay between Bacillus subtilis, PB6, Bacillus subtilis ATCC 6633 and Clostridium perfringens ATCC 13124.**
OPTIMIZE ANIMAL HEALTH, PERFORMANCE AND PROFITABILITY

REDUCING THE NEGATIVE IMPACT OF PATHOGENIC SALMONELLA TYPHIMURIUM IN WEANELED HOLSTEIN STEERS

A research trial conducted with the United States Department of Agriculture (USDA) at the Livestock Issues Research Unit in Lubbock, Texas, evaluated the potential for CLOSTAT to reduce the severity of salmonellosis in weaned Holstein steers challenged with Salmonella typhimurium. Calves were fed either control diets (no CLOSTAT) or 13 g/h/d CLOSTAT in a starter ration for 35 days. Calves were then assigned to one of four treatments, consisting of CLOSTAT or no CLOSTAT and Salmonella (1.6 x 10⁷ Salmonella typhimurium) or no Salmonella. The CLOSTAT calves displayed decreased rectal temperatures (P < 0.001) after the study, compared to the control calves challenged with Salmonella. Mounting an immune response to a pathogen challenge requires a significant amount of energy. It has been estimated that an increase in core body temperature by 1.8°F (1°C) requires an increase of 10-13 percent in an animal’s metabolic rate. Mediating this change in body temperature would potentially spare glucose, allowing energy to be put towards other productive functions.

STABILITY AND COMPATIBILITY

Processing, packaging and blending of feeds, as well as normal pelleting conditions, can all have an impact on the long-term efficacy of an active microbial. When evaluating an active microbial solution, stability of the product needs to be considered.

In addition to thermal stability, stability of the active microbial in the harsh environment of the GI tract is also an important factor. When considering both factors, PB6 proves to be stable under both conditions.

EFFECTS OF FEEDING BACILLUS SUBTILIS, PB6 ACTIVE MICROBIAL ON CLINICAL HEALTH, PERFORMANCE AND CARCASS CHARACTERISTICS OF FEEDLOT STEERS

Newly received cattle in a feedlot setting face a host of stressors, including transportation, weaning, environmental changes and co-mingling. A research trial conducted at the Willard Sparks Beef Research Center in Stillwater, Oklahoma, evaluated Bacillus subtilis, PB6 on its ability to improve health and performance of feedlot calves. The control treatment was a top-dressed supplement which contained ground corn and wheat middlings fed at a rate of 0.5 lb/h/d. PB6 was also a top-dressed supplement fed at 0.5 lb/h/d and designed to provide 9,500,000 CFU/g of PB6.

Table 2: Effects of feeding PB6 active microbial on finishing feedlot steer performance

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Item</th>
<th>Control</th>
<th>PB6</th>
<th>SEM</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BW1, lb 0-60</td>
<td>753</td>
<td>752</td>
<td>14.1</td>
<td>0.97</td>
<td></td>
</tr>
<tr>
<td>BW1, lb 0-230</td>
<td>1319</td>
<td>1327</td>
<td>15.5</td>
<td>0.40</td>
<td></td>
</tr>
<tr>
<td>ADG, lb 0-230</td>
<td>3.53</td>
<td>3.58</td>
<td>0.10</td>
<td>0.74</td>
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<tr>
<td>ADG, lb 60-230</td>
<td>3.33</td>
<td>3.38</td>
<td>0.03</td>
<td>0.25</td>
<td></td>
</tr>
<tr>
<td>ADG, lb 0-230</td>
<td>3.32</td>
<td>3.35</td>
<td>0.03</td>
<td>0.33</td>
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<tr>
<td>DMI, lb 0-230</td>
<td>26.2</td>
<td>25.7</td>
<td>0.30</td>
<td>0.15</td>
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<tr>
<td>DMI, lb 0-230</td>
<td>23.8</td>
<td>23.6</td>
<td>0.29</td>
<td>0.46</td>
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<tr>
<td>HCW, lb</td>
<td>6.69</td>
<td>6.58</td>
<td>0.06</td>
<td>0.36</td>
<td></td>
</tr>
<tr>
<td>HCW, lb</td>
<td>7.15</td>
<td>7.00</td>
<td>0.07</td>
<td>0.07</td>
<td></td>
</tr>
<tr>
<td>F:G 0-230</td>
<td>7.06</td>
<td>7.24</td>
<td>0.21</td>
<td>0.36</td>
<td></td>
</tr>
<tr>
<td>F:G 0-230</td>
<td>6.69</td>
<td>6.58</td>
<td>0.06</td>
<td>0.36</td>
<td></td>
</tr>
<tr>
<td>Item</td>
<td>SEM</td>
<td>Treatment</td>
<td></td>
<td></td>
<td></td>
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<td>------</td>
<td>------</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.52</td>
<td>Control</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.48</td>
<td>PB6</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.78</td>
<td>SEM</td>
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<td></td>
</tr>
<tr>
<td>1.81</td>
<td>P-value</td>
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</tbody>
</table>

Numerous tendencies for F:G existed in the experiment, indicating that PB6 fed steers were more efficient during the finishing period and overall (receiving and finishing). The results of this experiment suggest that the supplementation of PB6 to provide 9,500,000 CFU/g improves feed efficiency in feedlot cattle.

Table 1: Effects of feeding PB6 active microbial on receiving feedlot steer performance

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Item</th>
<th>Control</th>
<th>PB6</th>
<th>SEM</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BW1, lb 0-60</td>
<td>556</td>
<td>556</td>
<td>13.1</td>
<td>0.78</td>
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</tr>
<tr>
<td>BW1, lb 0-60</td>
<td>753</td>
<td>752</td>
<td>14.1</td>
<td>0.87</td>
<td></td>
</tr>
<tr>
<td>ADG, lb 0-60</td>
<td>3.27</td>
<td>3.28</td>
<td>0.06</td>
<td>0.91</td>
<td></td>
</tr>
<tr>
<td>ADG, lb 0-60</td>
<td>18.0</td>
<td>18.0</td>
<td>0.31</td>
<td>0.77</td>
<td></td>
</tr>
<tr>
<td>ADG, lb 0-60</td>
<td>5.52</td>
<td>5.48</td>
<td>0.09</td>
<td>0.78</td>
<td></td>
</tr>
</tbody>
</table>

1. All body weights were adjusted by %.
2. Data are presented as means ± standard errors. For the feed intake data, animals were removed on calculated maintenance intake.
3. Data were presented as means ± standard errors. For the feed intake data, animals were removed on per average intake by treatment.
4. A beta agonist (Optaflexx®; Elanco Animal Health, Greenfield, IN) was fed during this period at a calculated 300 mg/hd/d.
5. For all body weights, animals were removed by %.
6. Data from all calves (A, B, C, and D) for Group 1 (trucks 1 and 2), Group 2 (trucks 3 and 4), and Group 3 (truck 5).
7. For all body weights, animals were removed by %.
8. A beta agonist (Optaflexx®; Elanco Animal Health, Greenfield, IN) was fed during this period at a calculated 300 mg/hd/d.


4. Final receiving BW was recorded on d 61 for Group 1 (trucks 1 and 2), d 60 for Group 2 (trucks 3 and 4), and Group 3 (truck 5).

3. d 0 of finishing was d 61 for Group 1 (trucks 1 and 2), d 60 for Group 2 (trucks 3 and 4), and d 57 for Group 3 (truck 5).

2. Fed a supplement at 0.5 lb/hd/d containing corn and wheat middlings (control) or the control with added PB6 to provide 9,500,000 CFU/g.

1. Fed a supplement at 0.5 lb/hd/d containing corn and wheat middlings (control) or the control with added PB6 to provide 9,500,000 CFU/g.
KNOCK OUT PATHOGENS.
24 HOURS A DAY. 365 DAYS A YEAR.

Twenty-four hours a day, 365 days a year, your livestock are exposed to harmful environmental pathogens. These pathogens, coupled with the intestinal impact of stress events, result in a daily fight to maintain gut integrity and animal performance. Feed CLOSTAT active microbial daily to KNOCK OUT harmful bacteria and encourage beneficial bacteria while promoting a healthy GI tract.

Help each animal reach its full production potential. Establish the intestinal integrity and protection your livestock need by using a platform of solutions through our Gut Health Triple Check.

Kemin.com/CLOSTAT-US
Kemin.com/GutHealth
1-800-752-2864