Rationale For Probiotic Supplementation

Gastrointestinal Microbiology
All life exists in complex and essential relationships with other organisms and the environment. Vital environmental factors include food, water, and air, as well as less obvious influences such as sunlight, gravity, magnetism and the unseen microbial world. Recognizing and respecting these relationships is a key to health and well-being since it helps restore natural genetic context.

This realization has surfaced not so much from doing, but rather as a result of undoing. The pollution of air, water and earth, the fabrication of synthetic foods, and the misuse and/or overuse of various drugs and antimicrobials have disrupted important natural balances. We must reevaluate our dominionistic, somewhat marauding attitude toward our world.

Over time, man and microbe have reached an intricate state of co-existence through mutual adaptation. All warm-blooded animals are profoundly dependent on the microbial world. Despite the inclination to regard microorganisms as the enemy, the majority of these tiny life forms favor cohabitation and cooperation – not conflict. While some microorganisms are villains, others, termed probiotics, can and do play a very beneficial role in maintaining health. Such probiotic microorganisms mainly consist of lactobacilli, enterococci, lactococci, and bifidobacteria.

Intestinal probiotics, particularly bacteria, play an important role in determining the digestive mechanisms and general health of all animals, humans included. Disease may be related more to an organism’s inability to resist illness than to the actual presence of a microbe. Even tragic scourges have been shown to be ameliorated not because of antimicrobials, but rather as a result of the restoration of balances through hygiene and dietary improvements. The role of these symbiotic microorganisms in ruminants is well known and extensively studied, but their role in monogastrics (humans, dogs, cats, etc.) is less understood.

Our natural link to microorganisms is emphasized by evidence that basic cellular structure appears to be somewhat of a composite of once free-living microorganisms. Organelles, such as mitochondria, have been found to contain genetic material and other biochemical features suggesting a free-living microorganism origin. How it got from there to every cell in the body, I haven’t a clue... and “evolution” doesn’t conveniently solve it either. Nevertheless, it is persuasive of the idea that microorganisms have always been in intimate beneficial relationships with more complex life forms. Proper balance of friendly bacteria in the digestive tract is critical, not only after birth (inoculated through nursing), but also when humans and animals are under stress or being treated with antibiotics. Theoretically,
if beneficial organisms could be supported by, and/or introduced into the gastrointestinal tract, health could be enhanced and potential pathogens inhibited. The use of organisms for this purpose is termed probiosis, meaning “for life.” This is in contrast to antibiotics, represented primarily by antibiotics, which means “against life.” Because of their sometimes broad-spectrum antimicrobial activity, antibiotics often kill the normal desirable microflora of the intestinal tract. Potentially pathogenic bacteria may then fill this void.

The contents of the gastrointestinal tract are technically outside the body. Ingested materials are thus a part of an open ecosystem analogous to a stream with changing speeds, which can be interrupted by occasional eddies and rather stagnant pools. Each area in the gastrointestinal tract represents a unique habitat providing highly specialized niches of specific microbial populations (climax communities) consisting of both prokaryotic (cells with no nucleus) and eukaryotic (cells with a nucleus) organisms.

When it is considered that the microorganisms within the digestive tract of a human can exceed 100 billion cells per gram, over 100 trillion cells total, 10-fold the total number of eukaryotic cells, one can begin to understand their potential impact. Such an enormous population of microbiota interacts nutritionally and physiologically in profound ways. Studies have isolated and identified a host of autochthonous microorganisms (native inhabitants) in the gut and have further shown several of these to directly or indirectly affect health. There are over 40 generations that have been isolated from various climax communities of the human digestive tract. There are over 200 species of bacteria found in the digestive tract of dogs and cats. This is equivalent to 10 billion cells/gram or over 50% of total fecal weight. The nature and number of microorganisms differ greatly from one part of the GI tract to another, giving each section its own microbial personality.

This complex sensitive microbial population containing, in one person, 20,000 times the organisms of the entire Earth’s human population, is affected by myriad allo- genic and autogenic factors. Allogenic factors include diet, temperature, pH, peristalsis, villus contraction, oxygen, redox potential, bile acids, epithelial turnover, mucus gel, antimicrobials, phagocytic cells, and antibodies. Autogenic factors include lactic acid, volatile fatty acids, hydrogen sulfide, bacteriocins, nutritional competition, and synergy. Alteration of any of these factors can create sweeping changes in microbial contents.

An improper intestinal microbial balance, or the selective killing off of normal flora, may precipitate serious disease. Therapeutic levels of antibiotics greatly disrupt autochthonous microflora and can result in rapid reinfection when withdrawn. Food animals have become the source of antimicrobial-resistant Salmonella infections in humans, with a direct link to antibiotic use on the farm. It is estimated that the purposeful digestive tract colonization with probiotics of 85% of food animals could eliminate 8.5 million cases of human food-borne illness at a savings of $850 million per year. The constant infusion of “friendly” organisms in the diet – as it happens for animals in the wild through contact with the mother’s milk and then from natural food sources – helps prevent the colonization of disease-producing bacteria such as Salmonella, E. coli, Shigella and others (see Figure 1). Probiotic bacteria implant on the mucus-coated walls of the intestine and prevent colonization of pathogenic or “unfriendly” microbes by competitive exclusion.

Normal gastrointestinal microflora play an indispensable role in combating potential pathogenic microorganisms. Certain species of probiotic bacteria are capable of rapid multiplication, competitive inhibition of disease-producing microorganisms, lowering of the intestinal pH by the production of lactic acid, and production of bacteriocins (natural antibiotics). The probiotic hypothesis suggests that if sufficient numbers of these bacteria are introduced into the intestinal tract at a time when the balance has swung in favor of pathogens (such as at birth, during periods of stress or disease, or following antibiotic therapy), then disease can be minimized or overcome. Further, lactic acid bacteria have many other mechanisms by which they are able to prevent the growth of potential anaerobic pathogenic bacteria.

Using neonatal pigs as a model, investigators have shown that feeding Lactobacillus bacteria significantly suppressed fecal coliform counts. This same study showed that there were no signs of diarrhea even 72 hours after a challenge dose of E. coli was given. In chickens, resistance to disease actually

<table>
<thead>
<tr>
<th>Probiotic Mechanisms of Action That Inhibit Pathogens in the Gut</th>
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<tbody>
<tr>
<td>1. Probiotics produce lactic acid and some fatty acids to help decrease intestinal pH.</td>
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<tr>
<td>2. Probiotics form hydrogen peroxide, a bactericide.</td>
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<td>3. Probiotics form antibiotics (bacteriocins) such as lactalin, acidophylin, acidolin, lactallin, and nisin.</td>
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<td>4. Probiotics decrease the production of toxic amines and ammonia.</td>
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<tr>
<td>5. Probiotic organisms displace harmful pathogens through competitive antagonism by colonization and adhesion to intestinal cells.</td>
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<tr>
<td>7. Probiotics produce digestive enzymes and B-vitamins, which aid in digestion and provide necessary nutrition.</td>
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<tr>
<td>8. Probiotics produce anti-enterotoxins.</td>
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Figure 1.
is decreased when increasing the “hygiene” of chicks by removing them from the mothers’ droppings. Resistance (to infective doses of 10^3-10^6 cells of *Salmonellae*, for example) can be increased by feeding the chicks these droppings. The droppings are the autochthonous probiotic inoculum (see Figure 2).

In another study of neonatal pigs, *Enterococcus faecium*, a probiotic culture found in several Wysong products, was fed for ten days after weaning, and total *E. coli* (a potential pathogen) counts were made of the feces. Counts in control pigs (not given probiotics) raised dramatically in the first five days and then came back down. The test group receiving the *Enterococcus faecium* maintained a low fecal *E. coli* count throughout the test period of ten days. The numbers of hemolytic *E. coli*, those thought to be pathogenic in baby pigs, were also measured, and the response similar. Of interest in these tests is the resurgence of *E. coli* after the *Enterococcus faecium* was discontinued, while there was no similar resurgence of the hemolytic bacteria. This suggests that *Enterococcus faecium* is particularly effective in controlling the pathogenic forms of *E. coli* bacteria.

In addition to the inhibition of pathogens, probiotics are believed to exert a variety of subtle effects that can enhance overall health and disease resistance. In exchange for the nutrients and comfortable environment provided by the host (symbiosis), probiotics biosynthesize vitamins, essential amino acids, fatty acids, numerous enzymes and unidentified growth factors. Some probiotics also have the capability of inactivating carcinogenic intestinal beta-glucuronidase and nitroreductase. Probiotics also encourage appetite and facilitate the thorough breakdown and absorption of food substances.

**Prebiotic Oligosaccharides**

Short-chain carbohydrates, known as fructooligosaccharides (FOS) and mannanoligosaccharides (MOS), are components of yeast cultures, artichoke, garlic, and other plants. The IUB-IUPAC joint commission on biochemical nomenclature and the AOAC defines oligofructose as FOS containing 2 to 10 monosaccharide residues linked by glycosidic bonds, while MOS has a degree of polymerization (DP) of 3 to 9. Such prebiotics serve as a preferential food for probiotic organisms enhancing their growth, proliferation, and competitive exclusion of pathogens. Colonic bacteria ferment the undigested carbohydrate into hydrogen, carbon dioxide, and organic acids such as acetate, propionate, and butyrate which are then used as important fuel for the body’s enteroctyes that line the digestive tract. Prebiotics also act by binding lectin receptor sites on the pathogenic bacteria, thereby blocking implantation on cell membranes.

Digestive function is enhanced by increased digestibility of soluble fiber and fiber-like activity of non-digestible oligosaccharides. Stimulation of specific and non-specific immune responses, including cancer-preventing activity, is also a benefit. Studies in pigs and turkeys have shown that systemic IgG (Immunoglobulin G) and IgA concentrations increase significantly after consuming oligosaccharides, indicating enhanced immune response.

The functions of probiotics and prebiotics are just beginning to be revealed. Fermentive probiotic action can produce lactic, acetic, and propionic acids, vitamins (such as folic acid and B_12_), antibiotics, proteases, peptones, and unknown growth factors. They synthesize free amino acids such as lysine that are readily assimilated, and help to fill other essential amino acid requirements.

These capabilities help make monogastric organisms much less susceptible to dietary deficiencies, and may account for the amazing health of some animals fed diets which appear to be grossly deficient in a variety of “essentials.”

### Composition of the Autochthonous Intestinal Flora of Adult Humans

<table>
<thead>
<tr>
<th>Aerobes or Facultative Aerobes</th>
<th>Stomach</th>
<th>Jejunum</th>
<th>Ileum</th>
<th>Colon</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enterobacteria</td>
<td>0-10^2</td>
<td>0-10^3</td>
<td>10^2-10^7</td>
<td>10^4-10^10</td>
</tr>
<tr>
<td>Streptococci</td>
<td>0-10^3</td>
<td>10^2-10^4</td>
<td>10^2-10^6</td>
<td>10^2-10^10</td>
</tr>
<tr>
<td>Lactobacilli</td>
<td>0-10^3</td>
<td>10^2-10^4</td>
<td>10^2-10^6</td>
<td>10^2-10^10</td>
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<table>
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<tr>
<th>Anaerobes</th>
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<tbody>
<tr>
<td>Bifidobacteria</td>
<td>Rare</td>
<td>0-10^4</td>
<td>10^3-10^9</td>
</tr>
<tr>
<td>Streptococci</td>
<td>Rare</td>
<td>0-10^3</td>
<td>10^2-10^6</td>
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Figure 2.
that changes the natural, quiescent, homeostatic state can create stress, disrupting gastrointestinal flora. While the exact etiological mechanisms are still unknown, the untoward effects are certain. In agriculture, where ill health takes an economic toll, a proper enteric microorganism balance can mean the difference between loss and profit. This balance is accomplished through the use of supplemental probiotic cultures prepared under conditions that assure high concentrations and viability. Poor health resulting from microbial imbalance means unnecessary suffering and disease. Probiotics (pro-life), as opposed to antibiotics (anti-life), can enhance the immune system, inhibit pathogens, decrease disease recovery time, and create an overall improvement in health. Probiotics represent a safe and effective alternative to pharmaceutical methods, which introduce toxic chemicals foreign to biological experience. Probiotic usage is a rational, preventive approach to health care without contraindication.

**Synbiotics**

The term synbiotic is used to describe the synergistic combination of probiotics and prebiotics. This term is reserved for products in which prebiotic compounds selectively favor certain probiotic organisms, such as the combination of FOS with a bifidobacterial strain or lactitol in conjunction with lactobacilli. It is with this understanding that Probiosyn™ has been formulated by Wysong scientists to match the right dosage of FOS targeted particularly to foster *L. Bifidus & L. Plantarum*. As an example of just one benefit, when bifido bacteria feed on FOS, they convert it to propionic acid - a short chain fatty acid (SCFA) that is used by the liver to decrease serum triglycerides and cholesterol.

**Specific Wysong Probiotics**

*(Technical Facts)*

*Lactobacillus species*

*Lactobacillus* cultures have been used for hundreds of years to produce a variety of fermented food products.
including yogurt, cheese, sweet acidophilus milk, and soy sauce. In fact, the long life span of the Balkans and Asians is believed to be attributable in part to the ingestion of fermented milk.

Lactobacillus casei decreases intestinal disturbance, balances intestinal bacteria (inhibiting pathogens), lowers fecal enzymes, and impedes superficial bladder cancer. Strains of L. casei reportedly utilize xylitol to produce organic acids such as lactic and acetic acids. These organic acids may in turn have beneficial effects on human glucose and lipid metabolism. Particularly the reduction of serum acetate can reduce the concentration of serum fatty acids, which are an important factor in lowering glucose use by tissues and insulin resistance.

Beyond this commercial role, Lactobacilli are important health-enhancing residents of the gastrointestinal tract. Ideal pH conditions of approximately 5.0 to 7.0 will allow Lactobacilli bacteria to vigorously compete with pathogenic microbes for essential nutrients and attachment sites. Along with numerous mechanisms of actions that are part of probiotics’ ability to inhibit pathogens, Lactobacilli bacteria actively secrete lactic acid, making the environment about them more suitable for their growth and the exclusion of pathogens.

Lactobacilli cultures inhibit the growth of over 25 enteropathogenic organisms and have a direct nutrition-enhancing effect (see Figure 3). Lactobacilli also inactivate carcinogenic intestinal beta-glucuronidase and nitroreductase. Lactobacillus fermentation products will increase resistance to stress and resultant disease, food palatability and appetite, feed efficiency, and weight gain.

The presence of Lactobacillus species in mammary milk is now believed to be nearly as important as colostrum. Lactobacilli quickly implant in the young’s digestive tract and exert a protective and beneficial role. Conversely, animals deprived of their mother’s milk are very susceptible to intestinal pathogens. Lactobacillus implantation in young chicks has been shown to be beneficial in preventing Salmonella infections, which are often passed on to humans. In the mass production of chicks in hatcheries, production is carried out under such sanitary conditions that the autochthonous microflora is never introduced. Therefore, only a single cell of Salmonella may infect newly hatched chicks. Efforts have been made to replace this natural inoculation through the introduction of intestinal flora of adult birds using suspensions of fecal droppings, fecal material, or anaerobic cultures.

There are three main strains of Lactobacillus species involved in maintaining “normal” intestinal flora and preventing growth of undesirable bacteria. These include Lactobacillus bulgaricus, Lactobacillus acidophilus, and Lactobacillus bifidus. While all three of these organisms are able to tolerate an acidity within a pH range of 4.0 to 8.0, L. bulgaricus is not able to withstand the low surface tension created by bile. Therefore, only L. acidophilus and L. bifidus are able to reach the large intestine.

The majority of humans become lactase (the enzyme necessary for milk lactose digestion) deficient during the first 10-20 years of life. The inability to digest lactose causes a decrease in milk product consumption, eliminating a high quality source of protein and calcium. L. acidophilus and L. bifidus participate in the hydrolytic digestion of ingested lactose. Therefore, ingestion of milk products with live Lactobacillus is better tolerated and may actually alleviate malabsorption in lactose intolerant people. In order for this lactase activity to be increased, however, cultures must be fully active and added after pasteurization. Probiotics in yogurt also potentiate the production and release of gamma interferon by immuno-competent cells, and may thereby increase immune response.

Small intestine digestion of lactose is markedly impaired in the premature

<table>
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<tr>
<th>Beneficial Effects of Enterococcus faecium:</th>
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<tr>
<td>1. Fermentation of carbohydrate to lactic acid, thus lowering gastrointestinal pH and discouraging pathogenic growth.</td>
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<tr>
<td>2. An increase in palatability of the food it is found in and growth stimulation.</td>
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<tr>
<td>3. Production of antitoxins, which help to neutralize enterotoxins from E. coli.</td>
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<tr>
<td>4. Production of hydrogen peroxide, which has a bactericidal effect on anaerobic microorganisms.</td>
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<tr>
<td>5. Production of a metabolite that has specific activity against E. coli.</td>
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<tr>
<td>6. Production of antibiotics and bacteriocins, such as acidophylin, acidolin, lactalin, and nisin. These act against a variety of pathogenic species such as S. proteus, P. aeruginosa, B. subtilus, Salmonella, Shigella, and Clostridium.</td>
</tr>
<tr>
<td>7. Change in the re-dox (oxidation-reduction) potential, thus creating an unsuitable environment for the aerobic pathogenic microorganism.</td>
</tr>
<tr>
<td>8. Crowding out of the other microorganisms by implanting on the mucous surfaces and villi, thus decreasing the coliform count.</td>
</tr>
<tr>
<td>9. A low sensitivity to most common antibiotics. May be used safely in combination with: Aureomycin, Oxytetracycline, Bacitracin, Lincomycin, A SP-250, Furacin, Carbadox (Mecadox), and Virginiamycin. Proven to be sensitive to: Ampicillin, Tetracycline.</td>
</tr>
<tr>
<td>10. Inhibition of bacteria that degrade intestinal protein to non-utilizable forms.</td>
</tr>
</tbody>
</table>

Figure 5.

Probiotics 5
infant, since fetal lactase does not reach its maximum activity until 36-40 weeks of gestation. However, by measured breath hydrogen, there was minimal non-digested carbohydrate-derived energy in premature infants fed formulas of either 50% or 100% lactose as the carbohydrate source. This leads to the conclusion that lactose reaching the colon is virtually completely fermented by autochthonous organisms with efficient absorption of the short chain (volatile) fatty acid by-products. This colonic bacterial fermentation may also prevent accumulation of sugars in the colon, which are the principal osmotic stimuli for diarrhea from carbohydrate malabsorption. The quality and quantity of colonic bacterial metabolism may be a crucial determination of whether diarrhea develops in infants.

**Enterococcus faecium**

*Enterococcus faecium* is a gram positive, non-pathogenic, non-hemolytic, and non-proteolytic bacterium, isolated from the healthy gastrointestinal tracts of infants. It is a fast growing (divides every 18 minutes), ciliated organism, which makes implantation and colonization extremely successful. The rapid rate at which *Enterococcus faecium* will grow and multiply enables this probiotic culture to act as an aggressive agent in blocking the growth of pathogenic, toxin-producing microbes. Known as a lactic acid secreting bacteria, *Enterococcus faecium* is both a prophylactic and therapeutic aid for intestinal disorders. It has been used for many years throughout the world in farm animal production (see Figure 5).

The development of a wide variety of pathogenic agents can be partially or entirely inhibited by *E. faecium* (see Figure 6). These cumulatively beneficial properties of *E. faecium* have resulted in a 15% increase in feed efficiency and a 20% improvement in daily weight gain in various species. Its use as a prophylactic against intestinal disorders has resulted in a decline in the mortality of a wide range of animals.

**Bifidobacterium bifidum**

Like *Lactobacilli* bacteria, *Bifidobacterium bifidum* is lactic acid producing, as well as formic acid and acetic acid producing. Additionally, *Bifidobacterium bifidum* secretes a number of important enzymes including urease and glycosidases as well as various enzymes responsible for cellular repair. *Bifidobacterium* is one of the predominant microflora found in infants that are breastfed, and has been shown to assist in the prevention of diarrhea and enteritis in the infant. In fact, non-breastfed infants given supplemental *Bifidobacterium* had fewer incidences of diarrhea than those non-breastfed infants who did not receive the supplement. *Bifidobacterium* is thought to prevent enteritis and diarrhea by preventing the onset and shedding of rotavirus, the main cause of such problems in infants.

Wysong probiotic-enhanced foods and supplements are beneficial additions to the diet of both humans and companion animals. Wysong Probiosyn™ and Cheezyme™ are excellent sources of probiotics for humans. Wysong Feline and Canine Dry Diets™ are enrobed with beneficial probiotics. Pet Inoculant™ (canine/feline), AddLife™ (canine/feline), F-Biotic™ (feline), C-biotic™ (canine), Call of the Wild™ (canine/feline), and PDG™ (canine/feline) provide additional probiotics to companion animal diets.

In summary, whole food sources, careful processing, natural stabilization, and an increase in probiotics are key to digestive health.

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*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.*
Companion Animal Probiotic Supplements

Pet Inoculant™ (canine/feline) – An orally-dosed concentration of probiotic cultures and immunoglobulins.
Each cc (which equals 1 pump squeeze) contains 200 million CFU (CFU=colony forming units) of four bacterial species:

- **Bifidobacterium bifidum** 50 million CFU
- **Lactobacillus acidophilus** 50 million CFU
- **Lactobacillus lactis** 50 million CFU
- **Enterococcus faecium** 50 million CFU

*Ingredients: Cold Pressed High Oleic Safflower Oil, Cold Pressed Flax Seed Oil, Dried Whey Product, Dried Lactobacillus lactis Fermentation Product, Dried Lactobacillus acidophilus Fermentation Product, Dried Bifidobacterium bifidum Fermentation Product, Dried Enterococcus faecium, Lactobacillus acidophilus, Lactobacillus bifidus, Lactobacillus plantarum.*

Cheezyme™ – A natural seasoning from cheese, food enzymes, digestive cultures, antioxidants, and over 74 trace minerals. Wonderful sprinkled on popcorn and salads.

*Ingredients: White Cheddar Cheese, Monterey Jack Cheese, Swiss Cheese, Wysong Whole Salt™, Protease, Amylase, Lipase, Cellulase, Enterococcus faecium, Lactobacillus acidophilus, Lactobacillus bifidus, Lactobacillus plantarum.*

Companion Animal Enzyme Supplements

AddLife™ – designed for cats and dogs to enhance and augment the nutritional value of processed foods.


C-Biotic™ (Canine) and F-Biotic™ (Feline) – designed to enhance and augment the nutritional value of processed foods.


Relevant Wysong Products

**Companion Animal (Continued)**

**Biotic pH+™ (canine/feline)** – designed for animals needing assistance generating and maintaining an alkaline urine to help prevent oxalate, cystine, or urate crystal formation.


**Biotic pH-™ (canine/feline)** – designed for animals needing assistance generating and maintaining an acidic urine to help prevent struvite crystal formation. Sprinkle onto foods.


**Call Of The Wild™ (canine/feline)** – designed to balance fresh meat meals. Helps achieve archetypal feeding habits by providing organ meat, fats, connective tissue proteoglycans, minerals, vitamins, enzymes, probiotics, herbs and innumerable other micronutrients in the levels and proportions found in natural prey. Sprinkle onto foods.


**PDG™ (canine/feline)** – provides natural archetypal nourishment including vitamins, minerals, enzymes, and probiotic cultures to animals that are anorectic, undernourished, or otherwise debilitated. Can be used to boost nutrition of pet foods or made into a gruel or paste to administer when animal stops eating, or sprinkle onto foods.


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