Healthy Animals, Healthy Planet
(and Profits)!



A White Paper from BioResource International, Inc

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INTRODUCTION

Billions of people all over the world depend on animals for their food and livelihood. At times of crisis—during a flood, a pandemic, or a prolonged period of drought—it becomes clear just how closely linked animal health is to human welfare.

As this white paper will show you, animal health is important both in and of itself and because of its widespread effects on humans and the environment. Therefore, practices that promote and maximize animal health can significantly cut costs, boost profits, and help protect the world in which we live.

WHY SHOULD WE CARE ABOUT ANIMAL HEALTH?

Many human diseases, like Bird Flu, "Mad Cow" Disease, and salmonellosis are zoonotic, which means that they can be transmitted from animals to humans or vice versa. Eleven out of 12 of the major global disease outbreaks over the last decade were from zoonotic agents, according to the National Academies, in their 2005 report, Animal Health at the Crossroads: Preventing, Detecting, and Diagnosing Animal Diseases. As illustrated by the 2009 outbreak of the H1N1 "swine flu"—a strain of the influenza virus that contained genetic material from human, pig, and poultry viruses—animal diseases could very well lead to human pandemics.

Animal diseases have large economic implications as well. **In a 2005 report** published shortly after an outbreak of Bird Flu in Asia and Mad Cow Disease in North America, the Southern Regional Trade Research Committee noted that the resulting loss in trade could be as high as US$ 10 billion in lost revenue if import bans on meat and poultry continue.

At the time, approximately 100 million chickens had already died from the flu or had been culled to halt its spread. Export-dependent countries like Thailand were the hardest hit, but a shift in consumption patterns also undermined countries that were not directly affected. India for instance, saw a steep decline in the demand for chicken and eggs, as well as in chicken prices.

The economic threats posed by diseases contained in one or two farms may be less dramatic, but they still affect the livelihood of farmers, especially small family farms. It takes almost a year to grow a pig from weaning stage to market size. If a pig becomes too sick to harvest at any phase of growth, then a producer would lose a significant investment. And these diseases are rarely confined to just one or even a few animals.

Wonder Drugs No More

The better we can prevent and control animal diseases, the less chance there is for them to adversely affect trade and public health. And for a while, the solution seemed to lie in antibiotics.

Producers have been using antibiotics to treat infections in livestock for decades. Considered the "wonder drugs" of the 20th century, antibiotics such as penicillin and tetracycline initially allowed farmers to breed increasingly robust chickens, cattle, and pigs with no prescription and by doing little more than adding the drugs to water and feed.

By the 1970s, however, the overuse of antibiotics began to concern public health officials, who worried that it could lead to the emergence of drug-resistant "superbugs." These types of bacteria could endanger the lives of infected humans because they would not be able to be treated with routine antibiotic therapy. The European Union (EU) eventually banned the use of antibiotics in farm animals, but in the U.S., they are still widely used in conventional poultry and pig production. Eighty percent of antibiotics bought in the U.S. are actually used in animals, not humans.

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The jury is still out on whether feeding farm animals antibiotics does bring about the emergence of pathogens that are resistant to multiple drugs, but the U.S. has begun tightening its rules. In April 2012, the Food and Drug Administration **issued a new rule** that requires farmers and ranchers to seek a prescription from a veterinarian before giving antibiotics to animals.

New Animal Health Strategy

Fortunately, with proper nutrition and vaccines, many animal health problems can be controlled without the use of antibiotics.

Vaccines are an important part of any disease prevention and control program. In line with **the EU's new animal health strategy**, which is built on the maxim that "prevention is better than cure," the European Technology Platform for Global Animal Health is mobilizing public and private sectors in Europe to commit funds to research efforts designed to develop vaccines and diagnostic tests for controlling animal diseases.

Meanwhile, enzyme feed additives, such as the ones produced by BRI, can help improve animal health as well. Enzyme feed additives are natural alternatives that increase the protein digestibility of feed, which then results in bigger, healthier animals. They are not a direct replacement for antibiotics, but their use leads to healthier animals that are less susceptible to disease.

Aside from helping producers avoid the risk of emerging drug-resistant infections, feed additives help animals avoid sickness in the first place, which maximizes yield. Because even if a producer is able to successfully treat a sick animal, that animal needs to use a significant amount of energy to recuperate—energy that could have gone into increasing its muscle mass.

So why should we care about animal health? Because healthy animals translate to a healthy food supply. And as you can see, safeguarding animal health safeguards human health as well.

MAXIMIZE ANIMAL NUTRITION, MAXIMIZE ROI

Just like how it is with humans, animals that eat nutritious meals are more capable of fighting disease. Poor nutrition can also lead to disease. For instance, excess nutrients from poorly digested feed end up in the hindgut (similar to the large intestine in humans). As a result, a large number of opportunistic pathogens digest these nutrients and thrive, resulting in injury to the lining of the intestines and hampering the animals' ability to absorb nutrients through its gut.

Fortunately, we have come a long way in terms of understanding what components make up a nutritious meal. Again, just like with humans, animal feed is comprised of protein, carbohydrates, and fats. Protein typically comes from soybeans, carbohydrates from corn, and fats from vegetable oils or animal fat. Feeds are formulated as close as possible to the target animal's nutritional requirements to avoid excesses.

Decreasing Batch-to-Batch Variability

The livestock industry uses a process called "least-cost feed formulation" to meet animals' nutritional requirements at the lowest possible cost. There is a broad array of feed formulation programs, which rely on mathematical models and linear programming. It's like a recipe; substitutions can be made depending on available ingredients. If, for example, corn becomes less plentiful due to drought, producers can punch in commodity prices for rice, wheat, or barley, and then choose the least costly alternative.

However, least-cost feed formulas are based only on a general understanding of feed digestibility. Digestibility varies depending on an animal's genetics, as well as on factors such as how the crop was processed and what the weather was like when it was harvested. Corn and the soybean crops are widely grown and utilized and we have a fairly good handle on how to grow them, but there could still be batch-to-batch variation.

Natural feed enzymes promote animal nutrition by decreasing this variability and maximizing the performance of nutrients in feed. A protease-based natural enzyme feed additive distributed by BRI, for instance, increases the digestibility of protein and, more specifically, amino acids, which are the building blocks of protein. Trials have shown that adding it to lower protein diets increased feed efficiency (gain per kilogram of feed) to levels similar to that achieved by higher protein diets.

Sick animals drain profits. They often have to be culled, and even those that are successfully treated lose a significant amount of energy in the effort to get well. By maximizing the amount of nutrients animals can absorb, producers can help ensure that those animals reach full genetic potential in terms of weight, and thus maximize their return on investment.

ENZYMES AND THEIR USE IN ANIMAL FEED

Found in all living cells, enzymes catalyze chemical processes that convert nutrients into energy and new tissue. They do this by binding to substrates in the feed and breaking them down into smaller compounds.

Animal feed is the largest cost item in livestock and poultry production, accounting for 60-70% of total expenses. To save on costs, many producers supplement feed with enzyme additives, which enable them to produce more meat per animal or to produce the same amount of meat cheaper and faster.

Found in all living cells, enzymes catalyze chemical processes that convert nutrients into energy and new tissue. They do this by binding to substrates in the feed and breaking them down into smaller compounds. Enzymes can be classified by the types of substrates they work on. For instance, proteases break down proteins into amino acids, carbohydrases split carbohydrates into simple sugars, and lipases take apart lipids into fatty acids and glycerol.

Commercially available enzymes can be derived from plants and animals (e.g., actinidin from kiwi and rennet from calf stomachs) as well as microorganisms (e.g., amylase from Bacillus and lactase from Aspergillus). Aside from agriculture, other industries that use enzymes include the brewing, dairy, paper, biofuel, and rubber industries.

There are three types of enzymes that are typically considered for use in poultry feeds: **phytases, carbohydrases,** and **proteases.**

1. Phytases

Phytases break down phytate, a substrate that contains phosphorus. Phosphorus is a major nutrient that is essential for growth, maintenance, and cell and tissue repair. Corn, which is a major component of the typical poultry diet, contains significant amounts of phytate. Adding phytase to poultry feed allows the animal to absorb more of the phosphorus within the feed.

There is also an environmental advantage to maximizing the amount of phosphorus that an animal can absorb. Once excreted, undigested phosphorus seeps into the ground and ultimately makes its way to rivers, lakes, and the ocean. Given sufficient light, nutrients from the runoff fertilize algae and other aquatic plants. This produces huge algal blooms that deplete the water of oxygen. Laws that discourage phosphorus pollution in some states have contributed to the increased use of phytase over the years. Maryland, for example, mandates that phytase be used in poultry feed.

2. Carbohydrases

Carbohydrases improve the digestibility of carbohydrates in feed, thus increasing the amount of energy an animal can use to develop muscle and grow. Types of carbohydrases include amylase, which breaks down starch into fructose, maltose, glucose, and other simple sugars; and xylanase, which digests complex carbohydrates found in dietary fiber. Although chickens naturally produce enzymes that aid in the digestion of carbohydrates, they do not produce all the enzymes needed to break down fiber completely.

3. Proteases

Proteases break down complex proteins into shorter proteins, called peptides, and amino acids, which are the building blocks of protein. They are also capable of taking apart proteins that bind starch within feed ingredients, thus making more of the energy found in starch available to the animal.

BRI's natural enzyme feed additive, Versazyme, is a broad spectrum protease that degrades many protein substrates. A 2001 trial showed that chickens that were fed a 2% lower protein diet supplemented with Versazyme grew as large as birds that were fed a standard diet containing more protein.

While thousands of enzymes have been identified and several hundred are available commercially, only a fraction of these are produced on an industrial scale. In the next section of this white paper, we will discuss how biotechnology has enabled the mass production and application of enzymes in the agriculture industry.

BIOTECHNOLOGY AND ITS IMPACT ON AGRICULTURE

Biotechnology is broadly defined as the application of knowledge in the life sciences to create products or services that are beneficial to humans. Biotechnology is used in a variety of industries, from enhancing the quality and efficiency of food production to producing new medicines and vaccines.

Today, the majority of biotechnology research dollars funds the development of products that directly improve human health—vaccines, drugs, biologics, diagnostic tests, medical devices, laboratory services, and many others. But biotechnology also drives much innovation in the agricultural sciences. For example, scientists use biotechnology as a tool to develop crops that are resistant to pests and diseases, derive biofuels from various feed stocks, and produce enzymes that improve animal feed efficiency. In this case, we will explore the applications of biotechnology to enzyme development and production.

Optimizing Nutrition

Animal feed contains many ingredients that are poorly digested by livestock, such as phytate phosphorous and non-starch polysaccharides (e.g., fiber). Some, like soybean meal, also contain anti-nutritional factors that interfere with the absorption of protein. Producers use enzyme feed additives to remove anti-nutrients, increase the digestibility of nutrients and fiber, and supplement the enzymes that animals already produce.

As previously mentioned, enzymes catalyze biochemical processes that convert nutrients into energy and new tissue. They work by converting a specific set of reactants—or substrates—into specific products (e.g. amino acids and sugars) that fuel an animal's growth. For example, the enzyme phytase breaks down phytate so that more phosphorous can be absorbed by the animal, thereby lowering the amount of exogenous phosphorus supplementation required and decreasing phosphorus release into the environment.

Since the early 1980s, scientists have been using biotechnology to increase the production efficiency, quantity, and quality of enzymes.

Typically, producers ferment enzymes in large tanks with capacities of up to 150,000 liters. They adjust the temperature, nutrients, and air supply to ensure optimal development. When the process is complete, they take out a soupy mixture of enzymes, nutrients, and microbes and pass it through a series of filters to remove impurities and extract the enzymes. It's just like brewing beer!

Along with the standard operations of optimizing fermentation conditions, producers can also improve production efficiency and yield through biotechnology. For example, genetic engineering techniques can be used to increase enzyme activity and strain yield to meet their customers' demands.

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BRI's Experience

BRI's natural enzyme feed additive, Versazyme, is a broad spectrum protease that degrades many protein substrates. Dr. Jason Shih, professor at the North Carolina State University's Department of Poultry Science and co-founder of BRI, discovered it while developing a thermophilic poultry waste digester to generate power as part of his research on poultry waste management.

Dr. Shih noticed that poultry feathers shed in manure disappeared during the course of operation, and his curiosity and insightfulness eventually led him to identify the enzyme responsible for breaking down poultry feather protein. BRI further developed the enzyme and confirmed in a 2001 trial that chickens fed a low protein diet (21% protein) supplemented with Versazyme grew as large as birds that were fed a standard diet (23% protein).

versazyme®

Since then, BRI has used biotechnology to produce and deliver several thousand tons of feed enzymes through its partnership with Novus International, Inc. (sold under the Cibenza DP100 and IND900 brands). As a result, hundreds of poultry producers all over the world have reaped profits from the improved efficiency and profitability of their feed. All made possible through the power of biotechnology.

5 FACTORS TO CONSIDER WHEN CHOOSING A PROTEASE FEED ENZYME

Poultry producers have been using commercial feed enzymes since the late 1980s to improve the digestibility of feed. Phytases were the first enzymes to gain commercial acceptance, and carbohydrases were introduced soon after. As described previously, when added to feed, phytase maximizes the available phosphorous essential for cell growth and repair, while carbohydrases increase the digestibility of starches and sugars, both key sources of energy in the diet.

In the past few years, a significant rise in the cost of protein feed ingredients have expanded the focus of commercial feed enzymes to include enzymes that can further break down animal and vegetable proteins in the feed, thus reducing the amount of protein required.

In the past few years, however, a significant rise in the cost of protein feed ingredients have expanded this focus to include enzymes that can further break down animal and vegetable proteins in the feed, thus reducing the amount of protein required. As a result, proteases are an emerging class of enzyme feed additives that are gaining interest and traction in the market.

Typically, broilers are only able to digest 80 to 90 percent of amino acids in feed. The rest make their way to the hindgut, where they serve as fodder for opportunistic pathogens that proliferate and cause inflammation, which in turn compromises the lining of the small intestine. Affected animals often have to be culled, and even those that recover lose a significant amount of weight in the effort to get well.

Since the introduction of protease feed additives in the market is fairly recent and customers have various commercial protease products from which to choose, we offer these five factors for poultry producers to consider when deciding which product will work best for their operations:

1. Is it a broad-spectrum protease?

The ideal enzyme additive breaks down a broad range of vegetable- and animal-based proteins, whether they are soluble, insoluble, highly digestible like soybean meal, or hard to digest like feather meal. BRI's protease feed additive, Versazyme, has been tested on a variety of vegetable and animal protein sources, including complex ones like keratin and elastin, and has been shown to degrade proteins better than other proteases tested.

2. Will it work optimally in the small intestine?

Nutrient absorption takes place in the small intestine, where pH levels range from neutral to alkaline. In chemistry, pH is a measure of a solution's acidity or basicity. Solutions with a pH less than 7 are acidic while those above 7 are alkaline. The pH level where the enzyme is most active is known as its optimum pH. An acidic protease will be most active in the stomach, while an alkaline protease will work best in the small intestine. BRI's alkaline protease has an optimal pH of approximately 7.5.

3. Is it stable throughout the feed production process and in the animal's gut?

All enzymes are complex biological structures. An enzyme's activity could be reduced or destroyed if its structure is altered, for example, by the high temperature conditions required for making pelleted feed, or by acidic pH conditions in the animal's gut. An ideal protease, therefore, should not be easily destroyed or altered by changes in temperature or pH. BRI's protease has demonstrated stability in the pelleting process for up to 90°C. A protease feed additive must also be able to withstand acidic conditions without losing its effectiveness as it makes its way from the stomach to the small intestine. BRI's protease shows pH stability both in the laboratory and in animal trials.

4. Does it work best in temperatures that match the temperature of poultry?

It is important for an enzyme to work optimally in temperatures that match the physiological temperature of most animals, including poultry. BRI's enzyme was discovered by BRI's founder, Dr. Jason Shih, in a thermophilic (heat-loving) poultry waste digester, so it can withstand high temperatures. It works best in temperatures of 35-55°C (95-131°F). The average body temperature of a chicken is 42°C (107°F).

5. Will it work well in a poultry farm environment?

Certain enzymes may work well in the laboratory but lose some of their effectiveness when deployed in the farm where most environmental factors cannot be controlled. BRI's feed enzyme was discovered and isolated in bacteria living in poultry waste. Thus, it is naturally well-adapted to living in the guts of chickens and around poultry farms. Not surprisingly, its effectiveness has been demonstrated not just in laboratory tests but in many commercial farm trials worldwide.

In summary, the chances that a protease feed enzyme will successfully make the transition from the laboratory to commercial poultry production are increased if it is a robust, heat-stable, broad-spectrum protease that works optimally in an animal's digestive system and is compatible with the poultry farm environment.

FROM CRISIS COMES OPPORTUNITY

How can enzymes help livestock producers overcome the cost challenges brought forth by the 2012 drought, which now ranks as the 10th worst drought in the United States since 1895?

The U.S. Department of Agriculture expects the drought to **increase the prices of milk, eggs, pork, beef, and poultry by 3-4%** in 2013. Corn accounts for most of the carbohydrates in animal feed, and soybean accounts for most of the protein. As prices for both soar in anticipation of dwindling supplies, farmers will have to pay more to feed their livestock—an expense that will ultimately trickle down to meat and dairy consumers.

But in the face of the challenges the agricultural industry must confront, new opportunities emerge, especially in the field of animal nutrition. To minimize the drought's impact on their businesses, farmers will have to find ways to produce the same amount of meat for significantly less cost. Since animal feed is the **highest input cost in livestock production**, improving feed digestibility and uptake in livestock animals is one of the most efficient ways to cut down expenses.

Feed enzymes boost the availability of nutrients in the feed, enabling farmers to do more with less. We detail below some examples of the ways enzymes help save feed costs:

1. Lower quantities of feed ingredients

The livestock industry uses a process called "least-cost feed formulation" to meet animals' nutritional requirements at the lowest possible cost. Based on the parameters of feed ingredient digestibility and the animals' nutritional requirements, the program calculates how much of which ingredients should be used.

Feed enzymes, by improving the digestibility of certain ingredients when added to the feed, enable the animal to absorb the same amount of carbohydrates, proteins, and/or fats from less feed. For instance, chickens that are fed a low protein diet supplemented with BRI's feed enzyme, Versazyme, can grow to be just as large as birds that are fed the standard diet. As long as the cost of the enzyme is less than the cost of the feed it replaces on a consistent basis, the farmer saves money.

2. Lower value ingredients

The value of a feed ingredient is directly proportional to its available nutritional content. Less digestible ingredients such as wheat, feather meal, and distillers dried grains with solubles (a by-product of ethanol production), have less available nutrients and are considered to be of lower value. For example, wheat is a good source of carbohydrates, but it has more hard-to-digest fiber than corn. Farmers improve the digestibility of wheat by adding xylanase, a feed enzyme that breaks down the complex carbohydrates found in dietary fiber.

In some cases, producers use feather meal to diversify their feed protein sources. However, the use of feather meal is limited due to its poor digestibility and unbalanced protein profile. BRI developed Valkerase specifically to break down keratin—the tough, tightly woven protein that makes up chicken feathers—and turn poorly digested feather meal into a more optimized source of digestible proteins and peptides.

The value of a feed ingredient is directly proportional to its available nutritional content. Less digestible ingredients such as wheat, feather meal, and distillers dried grains with solubles, have less available nutrients and are considered to be of lower value.

3. Non-traditional ingredients

Sorghum, a corn-like grain grown in South America, Africa, and some parts of Asia, is not traditionally used in animal feed. It contains anti-nutrients such as tannin and karfirin that interfere with how nutrients in the feed are digested by poultry.

Fortunately, enzyme feed additives not only increase the digestibility of nutrients and fiber; they also remove anti-nutrients. Dr. Edgar Oviedo-Rondon, a professor at North Carolina State University's

Department of Poultry Science, presented an abstract during the Poultry Science Association Annual Meeting in July 2012 describing how Versazyme (sold under the Cibenza DP100 brand) can improve the performance and energy utilization of chickens fed with high-tannin and high-karfirin sorghum.

In an environment where the supply of crops is diminishing just as the demand for food keeps escalating, growth opportunities for businesses that can help livestock producers boost feed performance, increase profits, and promote sustainability in animal production will continue to improve.

ENZYMES AND THE OPTIMIZATION OF LOWER VALUE FEED INGREDIENTS

As the price of feed ingredients continue to rise, poultry producers will need to increase the use of alternative, lower cost ingredients to mix into their feed. Some of these lower cost ingredients include the by-products of animal production, the use of which makes economic and environmental sense. Enzymes can assist in recovering the nutritional value of these by-products either as an enzyme feed additive, as described in the previous section, or in the industrial processing of lower value raw materials into higher value feed ingredients.

Feather meal is considered a low value ingredient in animal feed. Although it contains more valuable amino acids like lysine and arginine than other animal feed ingredients, much of that is bound up in the form of keratin, an insoluble, hard-to-digest protein. So while a pound of feathers has a higher protein content than a pound of soybean meal, animals aren't able to absorb as many nutrients from it.

Since the poultry industry generates so many tons of feathers as a by-product of processing, adding feather meal to feed is a good way to utilize a natural resource and diversify an animal's protein sources. In order to increase the bioavailability of the nutrients in feathers, many large poultry processors "cook" and sterilize them in steam pressure cookers and then dry and grind them to produce feather meal. Others would send them to businesses (renderers) that specialize in producing feather meal.

Cooking feathers, however, can be a challenge. To break down the keratin and maximize the digestibility of the feather meal, producers subject the feathers to temperatures above 140ºC (284ºF). This may damage and/or overcook some of the proteins in the feather meal.

Lower Cooking Temperatures

We've talked about how natural feed enzymes enable animals to digest more of the nutrients in feed. Fortunately, these enzymes do not just work in the stomach and small intestine; they work in industrial cookers as well. In fact, BRI's first product, Valkerase, was discovered because of its ability to degrade feathers in a thermophilic poultry waste digester.

BRI's cofounder, Dr. Jason Shih, was developing the digester to generate power as part of his research on poultry waste management at North Carolina State University's Department of Poultry Science. While there, he noticed that poultry feathers mixed in with poultry manure were disappearing during operation.

A biochemist by training, Dr. Shih hypothesized that an enzyme in the manure was responsible for degrading the keratin. He eventually isolated the microbe that produced the enzyme and developed it into a commercial product.

The keratin-degrading effect of Valkerase now enables producers of feather meal and other low value ingredients such as meat-and-bone meal and poultry meal to achieve the same level of digestibility, but with lower cooking temperatures and less cooking time. Not only does this help decrease the risk of destroying vital nutrients, it also saves energy, both of which contribute to sustainable production of feed ingredients in the long term.

NATURAL FEED ENZYMES AND THE "LOW EMISSION CHICKEN"

Most chickens and pigs in the United States are raised in concentrated animal feeding operations (CAFOs). By congregating and feeding thousands of animals in a controlled area, CAFOs increase the efficiency of animal production. However, these operations also produce large amounts of waste that, if not properly managed, can have a detrimental impact on the air and water in the surrounding areas.

We've discussed in previous sections how natural feed enzymes boost profitability by increasing the availability of nutrients in feed, thus enabling farmers to do more with less. In this section, we will discuss how enzyme feed additives could also help lower the environmental impact of industrial farming.

Animals convert nutrients in the feed they consume into energy (calories), component minerals (phosphorus), and component protein building blocks (amino acids). However, digestion isn't always very efficient, especially in monogastric animals such as pigs and chickens, and undigested nutrients eventually get excreted in animal feces and urine.

Concentrated animal feeding operations (CAFOs) produce large amounts of waste that, if not properly managed, can have a detrimental impact on the air and water in the surrounding areas.

Preventing Oceanic "Dead Zones"

Undigested phosphorus and nitrogen in animal waste could seep into the ground and make their way into rivers, lakes, and ultimately the ocean. There, they fertilize algae and other aquatic plants, causing huge algal blooms. In estuaries and coastal oceans, nutrient-rich water layers over the denser salt water, creating a barrier that keeps oxygen in the atmosphere from reaching the bottom.

When the blooms die, they sink and decompose. Bacteria deplete the water of oxygen as they feed on dead algae. With no access to fresh oxygen, the area becomes a dead zone, and thus fish and other organisms that depend on oxygen in the ecosystem either avoid it or die.

Not surprisingly, poultry producers are feeling the pressure to reduce nutrients in animal waste. Laws that discourage phosphorus pollution in some states have already contributed to the increased use of phytase, a feed enzyme that breaks down phytate. Maryland, for example, **mandates that phytase be used in all poultry feed**.

The U.S. Environmental Protection Agency (EPA) has also for many years required all CAFOs to apply for a National Pollutant Discharge Elimination System (NPDES) permit from the state in which their farms are located and to develop and implement a Comprehensive Nutrient Management Plan (CNMP).

> When less protein is consumed, there's less waste, and consequently, less nitrogen emissions in the form of ammonia.

Reducing Ammonia Emissions

Meanwhile, as bacteria in the hindgut of all animals break down nitrogen in waste, ammonia is released into the atmosphere. Any surplus or poorly digested protein that is not metabolized by the animal is excreted in animal manure and can be converted into ammonia by bacteria in the animal's hindgut or by microorganisms in the environment.

Elevated levels of ammonia in animal facilities can stunt the growth of broilers or reduce egg production in laying hens. It can also trigger respiratory and cardiovascular problems in the people who work on those farms.

Ammonia emissions from animal agriculture are not directly regulated. However, in 1997, the U.S. EPA issued National Ambient Air Quality Standards (NAAQS) for particulate matter (PM) with a diameter of 2.5 microns or less. Since a large fraction of PM 2.5 is derived from ammonia, any regulation aimed at reducing its concentration will likely require reductions in ammonia emissions from livestock operations in the future.

Strategies for reducing ammonia levels include improving the ventilation inside animal facilities and decreasing the amount of moisture in manure. Of course, another way is to boost the efficiency with which animals digest protein, so there's less excess nitrogen in waste. Animal trials have shown that BRI's protease feed enzyme Versazyme can reduce the amount of nitrogen in the manure of laying hens.

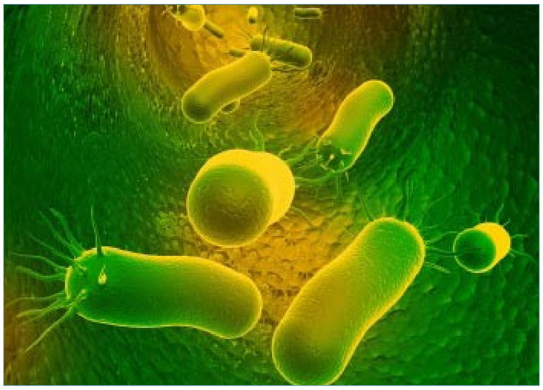
Protease enzymes also allow poultry producers to formulate lower protein diets without compromising the health and weight of their animals. When there's less protein consumed, there's less waste, and consequently, less nitrogen emissions in the form of ammonia.

WHAT'S IN YOUR MICROBIOME? AND WHY YOU SHOULD CARE…

You have probably had someone say to you that "you are what you eat." But has anyone told you that you are largely a product of the microbes that live in you and on you? In fact, all living things have an ecosystem of bacteria that live symbiotically with their human or animal hosts. That ecosystem is known as a "microbiome" and is an active area of research. In fact a 2012 article in The Economist featured a cover story on the human microbiome. It describes people not as lone individuals, but as ecosystems where the human host lives among—and has a mutually beneficial relationship with—trillions of bacteria.

The article drew much of its exposition from **the Human Microbiome Project (HMP)**, a five-year federal initiative that sequenced genetic material from bacteria in nearly 250 healthy people. The human microbiome comprises approximately three million genes from several hundred species of bacteria that live in and around us, which makes the human genome seem tiny with a mere 23,000 genes.

The Chicken Microbiome



Just like people, animals are also part of a dynamic microbial ecosystem. There is a cat microbiome, a dog microbiome, and an alligator microbiome. And just this summer, researchers at North Carolina State University's Department of Poultry Science received a grant from the U.S. Department of Agriculture to study the chicken microbiome. Their first project will look into whether bacteria in the chickens' digestive system play a role in their ability to resist and/or fight Salmonella infections.

In a healthy ecosystem, the interests of host and bacteria align with each other. Animals provide bacteria with raw material and shelter, while bacteria offer up protection and nutrients. We typically associate bacteria with disease, and rightly so, as certain types, like E.coli and Salmonella, can wreak havoc on the host's health and well-being. Trillions of bacteria, however, are essential for life to continue. As anyone who has eaten a cup of yogurt can appreciate, both humans and animals need "good" bacteria to digest food, synthesize vitamins, and protect against the disease-causing bad bacteria.

Many of these beneficial bacteria live in the digestive tract. These bacteria are able to utilize nutrients that the host animal is unable to digest. After the bacteria have digested these nutrients, the waste products produced by the bacteria can often be used by the host animal as a source of nutrition. In addition to the nutritional benefits of microbial digestion, beneficial bacteria tend to create an acidic environment in the gut by producing compounds such as lactic acid. Many disease-causing bacteria prefer environments that are more basic in nature and will not thrive in the acidic environment.

Care and Feeding of the Microbiome

However, even good bacteria can act as opportunistic pathogens in animals with low or compromised immunity. Good nutrition is critical to maintaining a healthy balance of bacteria. Animals that cannot absorb adequate nutrients from food are more susceptible to a misalignment of interests between host and the microbial ecosystem. Thus, feeding animals a nutritious diet and maximizing their ability to absorb nutrients from feed are among the best ways to ensure that the host-bacteria relationship remains mutually beneficial.

Good nutrition is critical to maintaining a healthy balance of bacteria. Animals that cannot absorb adequate nutrients from food are more susceptible to a misalignment of interests between host and the microbial ecosystem.

As described in a previous section, one way to boost the ability of chickens to digest nutrients is to supplement their food with natural feed enzymes. In fact, many of the commercially available feed enzymes were derived from microbes that were resident in the animal's gut environment. For example, BRI's protease enzyme Versazyme was derived from a microorganism that lived in and around chickens, and had become well-adapted for its environment.

It's easy to see how good nutrition fosters an environment where beneficial bacteria can grow and flourish, while bad nutrition tips the scale in favor of disease-causing bacteria. Thus, not only does optimizing the amount of digested nutrients boost profitability and reduce the environmental impact of animal production, it also helps animals become less susceptible to disease.

AN INDUSTRY RIFE WITH CHALLENGES DRIVES INNOVATION AND OPPORTUNITY

We covered a lot of ground in this white paper, beginning with a discussion of the economic and public health implications of animal health. We talked about the big impact of zoonotic diseases such as the "Bird flu", and how, despite their initial promise, the continued reliance on antibiotics in animal production may not be sustainable.

This flowed naturally to a discussion of how maximizing animal nutrition supports animal health, thus preventing disease-causing pathogens from wreaking havoc in the first place. At the same time, we saw how difficult it is for livestock producers to achieve optimal nutrition in their feeds, because with "least-cost feed formulations", even the best estimates can result in batch-to-batch variation.

When Enzymes Add Value

Subsequent sections showed how animal producers are addressing this problem by using natural feed enzymes. We described the three types of enzymes that are typically used in poultry feed–phytases, carbohydrases, and proteases–and then explored further the features of high quality protease enzymes, an emerging class of feed enzymes that is steadily gaining market traction.

We then talked about how enzymes increase the value of feed ingredients, not just of traditional feed ingredients but also of lower value and nontraditional ingredients. As prices of corn and soybeans continue to skyrocket in response to the 2012 drought, producers around the world must seize the opportunity to use non-traditional ingredients to decrease their feed costs without compromising the performance of their animals when using enzymes.

And while we dedicated several sections to the discussion of how enzymes can increase the digestibility of feed, we also delved into a lesser known but highly beneficial application of enzymes in the livestock industry—rendering, or assisting in the recovery of nutritional value from byproducts such as feathers, bone, and other parts of the animal that would otherwise just end up in a landfill.

Complexity Begets Opportunity

We also covered topics that do not squarely fall under the category of animal health but have a significant effect on how it is promoted and maintained. For instance, we looked into how biotechnology, broadly defined as the application of knowledge in the life sciences to create products and services that are beneficial to humans, has made it possible to scale the production of commercially available enzymes, such as by increasing enzyme activity and strain yield.

> An industry rife with challenges drives the development of innovative solutions that are just waiting to be identified, refined, and implemented.

On the flip side, we considered how poor animal health nutrition can damage the world we live in. It is no secret that by congregating and feeding thousands of animals in a controlled area, concentrated animal feeding operations (CAFOs) generate large amounts of waste. However, by reducing the amount of undigested phosphorus and nitrogen in animal feces, natural feed enzymes allow producers to raise "low emission chickens," which helps lower the environmental impact of industrial farming.

For those who are not yet familiar with it, we also introduced the "chicken microbiome," referring to the collection of microorganisms that live in and on chickens that make them part of a dynamic microbial ecosystem, as opposed to just individual creatures. We learned how feeding the microbiome with adequate nutrients makes chickens less vulnerable to the possibility that a symbiotic relationship would turn into an opportunistic one.

Taken all together, these discussions illustrate just how much animal health and nutrition are influenced by multiple factors that producers have to navigate. There are various factors to consider and many decisions to be made, yet it is precisely this complexity that gives rise to new growth opportunities. An industry rife with challenges drives the development of innovative solutions that are just waiting to be identified, refined, and implemented. We at BRI look forward to working with our partners, customers, and scientists on the challenges and opportunities that lie ahead.

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