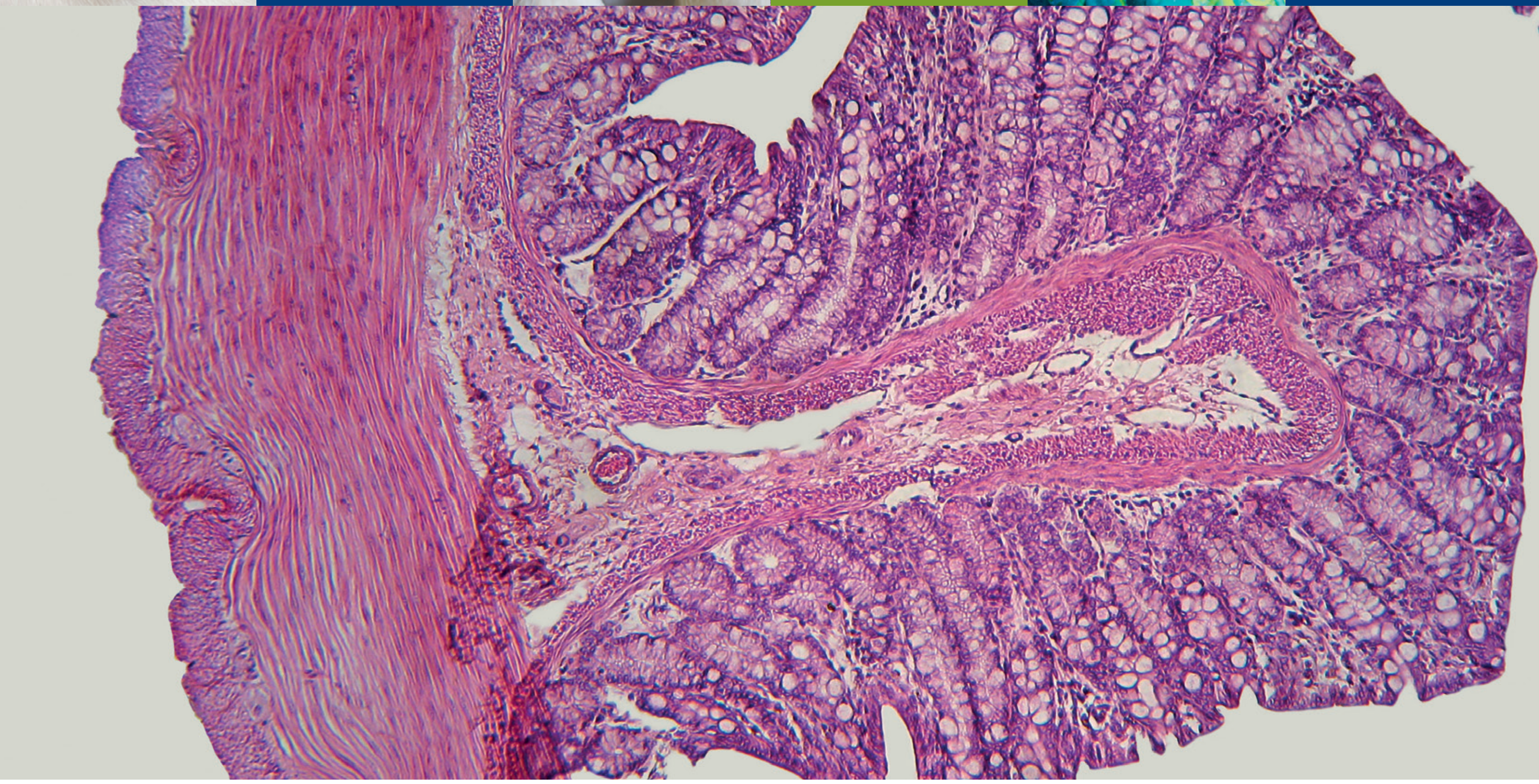


Lumance®

Intestinal health solution to lower medication and improve performance

innovad®
CREATE TRUST



How to keep
the performance
with less
medication?

Lumance®

Intestinal Health Solution to lower medication and better performance

Scientists and veterinarians agree that one single non-antibiotic molecule will have its limits in controlling the overall situation. However, an approach that combines the newest generation butyrate with various additives, appears to be very attractive.

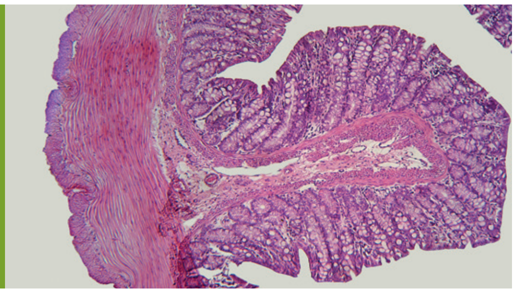
By controlling the microflora in the lumen and strengthening the intestinal epithelium integrity, **Lumance®** offers a comprehensive **GUT HEALTH MANAGEMENT** program that aims at reducing medication or cocktails of medication.

Lumance® is a complex structure, which contains the newest generation of butyrate, combining slow release and protection technologies, ensuring that acids, medium- chain fatty acids, essential oils, anti-inflammatory compounds and polyphenols are delivered in a gut active way for powerful and effective antibacterial control, high quality tight junctions, neutralisation of the produced ROS and tempering of the inflammatory cytokine production.

Lumance® is an effective and powerful tool to reduce inflammation, promote villi growth, tighten the intestinal junction and stabilise the microflora.

+ Active in the gut
+ Scientifically proven ROI & performance
+ Protects against ROS & inflammation

Available in liquid and dry form



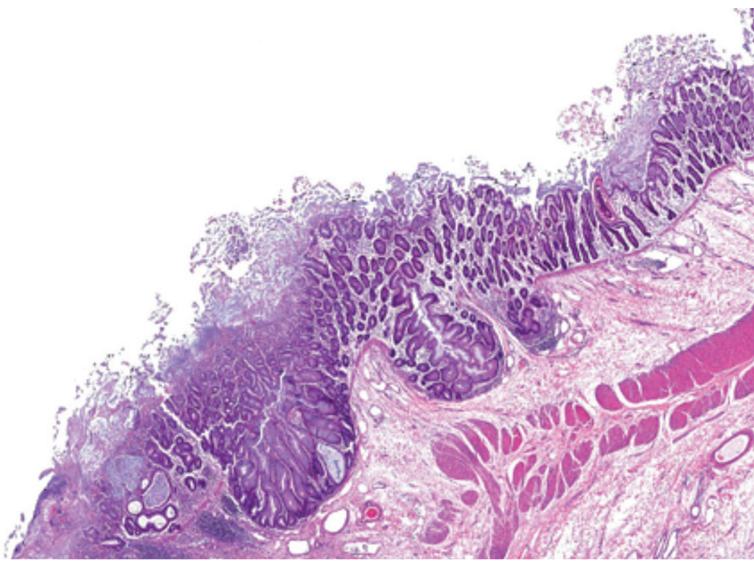
Intestinal Health

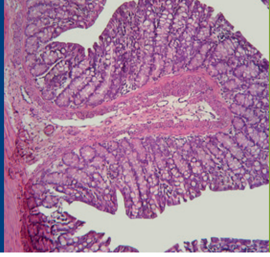
Intestinal health is the most determining factor for animal health in general, herd performance and eventually farm profitability. Harmful bacteria such as *E.coli* may colonise in the gastrointestinal tract, resulting in clinical and sub-clinical diseases. Reduced feed intake and daily gain, inactivity and decreased social interactions are all observed in animals with **bacterial infections.**

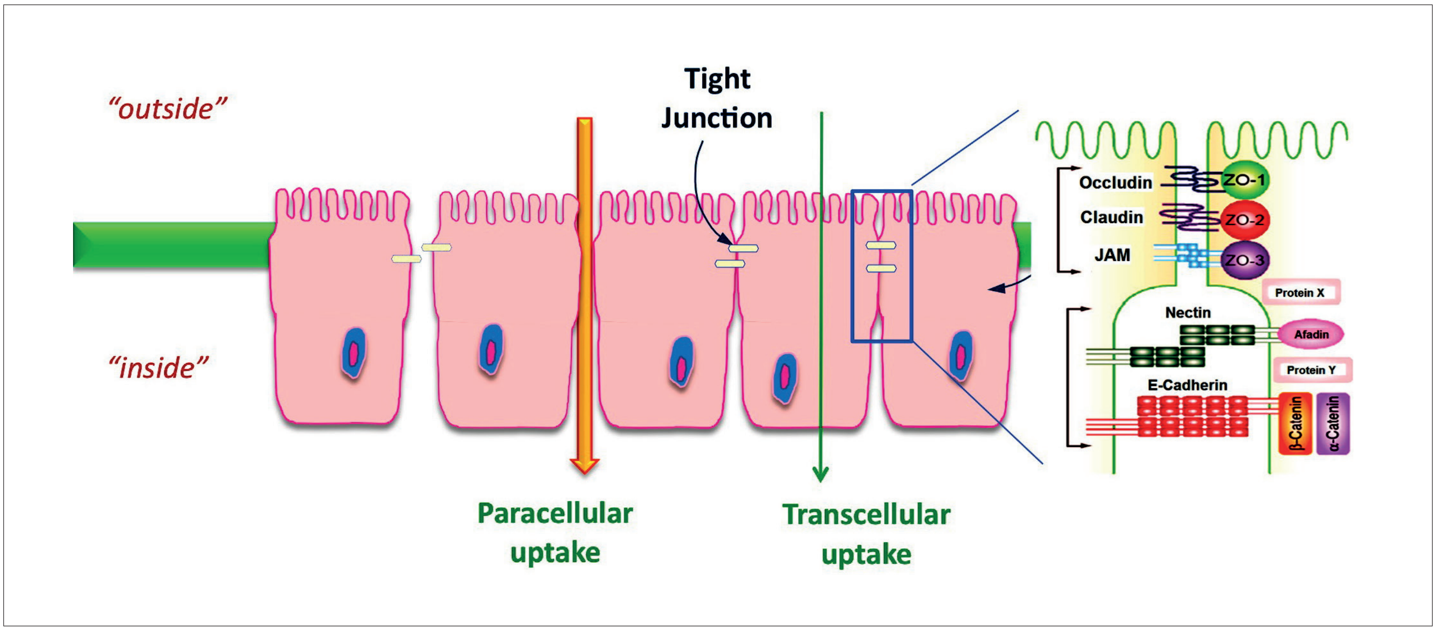
In an era of increasing volatility in raw material prices and availability, being able to secure sufficient raw materials of acceptable quality is becoming one of the main challenges for the livestock industry. In an effort to reduce feed costs and to obtain sufficient feed raw materials, livestock producers are often forced to make use of **unconventional protein and carbohydrate sources** or materials of lower quality. This means that animals need to be able to deal with continuously changing diet compositions and qualities, which means a risk factor for their health.

Stress plays such an important role in disturbing the gut environment, leading to **health challenges and intestinal disorders**. In pigs, the average litter size increased, with more lightweight and vulnerable piglets at weaning.

Regulation, food safety and animal welfare are setting up new trends towards limitations or restrictions of antibiotics, medicated feed, zinc oxide…







The space between epithelial cells is ‘sealed’ by tight junction proteins, a multi-functional complex which regulates the permeability of the intestinal barrier. Tight junctions are composed of trans-membrane components (proteins) that mediate adhesion and form the paracellular diffusion barrier.

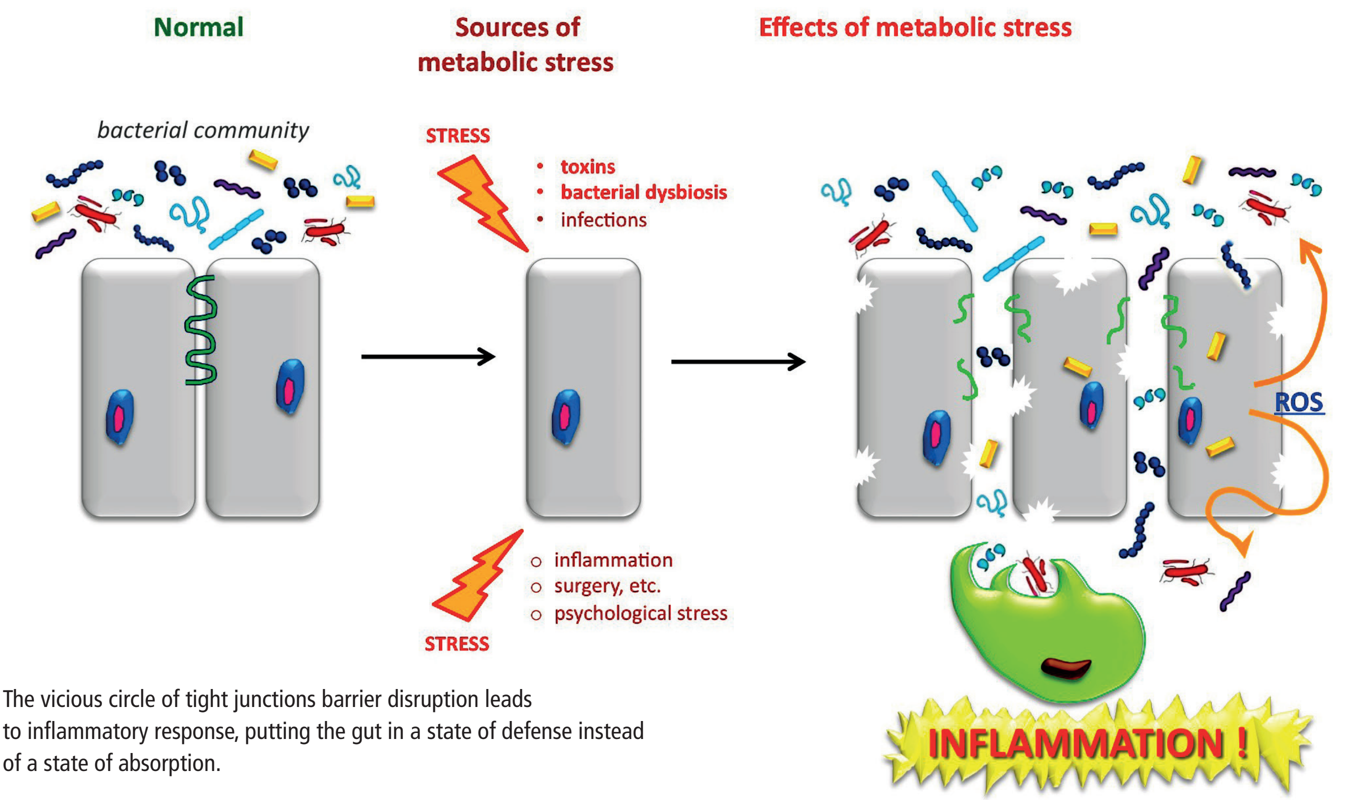
Inflammation




Several stress factors will have a negative impact on the quality of the tight junctions, leading to the 'leaking gut' syndrome, which enables big sized molecules such as toxins and aggressive radicals to pass in between, resulting in cell damage, production of 'Reactive Oxygen Species' (ROS) and activation of the immune system.

The latter is automatically paired with the production of **inflammatory cytokines**. The neutralisation of these inflammatory components will consume significant amounts of nutrients, which will lead to reduced growth and increased feed conversion rates.

Subclinical inflammation can cost up to 30% of the energy requirements. Although the mode of action of Antibiotic Growth Promoters (AGP) is not yet fully understood, there is evidence to believe that, besides regulation of the microflora, AGP also play an important role in reducing the level of inflammatory cytokines, which results in substantial energy saving and improved performance.



The vicious circle of tight junctions barrier disruption leads to inflammatory response, putting the gut in a state of defense instead of a state of absorption.

Leaky tight junctions with fluid from the host leaking into the lumen trigger inflammation, that translates into performance losses, wet litter situation in poultry, bacterial enteritis and diarrhea.



Host defence peptides (HDPs), also known as antimicrobial peptides, are present in virtually all species of life and constitute a critical component of the innate immunity. Defensins and cathelicidins represent two major families of HDPs in vertebrates. They are produced and secreted at the level of the intestinal epithelium.

These HDPs have a broad spectrum of antimicrobial activities against bacteria, protozoa, fungi and even viruses. Due to the complexity of the mode of action against microbes, there is a low chance of resistance, which makes them a number one candidate for alternatives to antibiotics.

As research is ongoing and it will take some more years before such molecules can be applied in feed or drinking water, there is currently an interesting approach to increase the synthesis of endogenous HDPs within the intestinal tract.

The intestinal microbiota is composed of more than 500 different species, which live in direct symbiosis with the host. They provide energy for the intestinal wall, prevent colonisation by pathogenic bacteria and help to maintain the intestinal immune system. It has often been demonstrated that the status of the immune system is (partly) defined by the presence and the type of microbiota in the intestine.

Based on the above, we can conclude that the basis for a high status of intestinal health is a balanced microflora, strong tight junctions, healthy long and slender villi, secretion of HDPs and low levels of ROS and inflammatory cytokines.

The role and importance of tight junctions

The intestine allows the absorption of nutrients, while also functioning as a **barrier which prevents antigens and pathogenic bacteria from entering the mucosal tissue** causing diseases.

- **Increased intestinal permeability** (= reduced barrier function) is implicated in autoimmune, inflammatory and atopic diseases.
- Chronic inflammatory diseases are characterized by a **leaky intestinal** barrier.
- Entry of unwanted antigens can lead to ***'systematic inflammatory response syndrome'***, characterised by a whole body inflammatory state and multiple organ failure.

Coccidiosis, necrotic and bacterial enteritis are an important concern globally because of production losses, increased mortality, increased veterinarian and medication costs, reduced welfare of birds and an increased chance of contamination of products for human consumption.

Although such diseases have a different pathology, they act synergistically since the development of enteritis is highly dependent on the intestinal damage caused by coccidiosis and also – more recently highlighted – by the presence of DON and Fumonisin toxins.

Challenges in poultry

Necrotic enteritis, bacterial enteritis

The causative agent of necrotic enteritis is *Clostridium Perfringens*, a gram positive spore forming anaerobe bacteria commonly found in soil, dust, faeces, feed, poultry litter and intestinal contents. Necrotic enteritis has long been controlled by the use of antibiotic growth promoters (AGP) in the feed, but with the recent ban or reduction in the use of antibiotics, bacterial enteritis has emerged worldwide as a common broiler disease.

Necrotic enteritis usually occurs 3-4 weeks after hatching (11). The necrotic lesions are mainly restricted to the small intestine and the infection can result in an acute clinical disease or can be present in a subclinical condition.

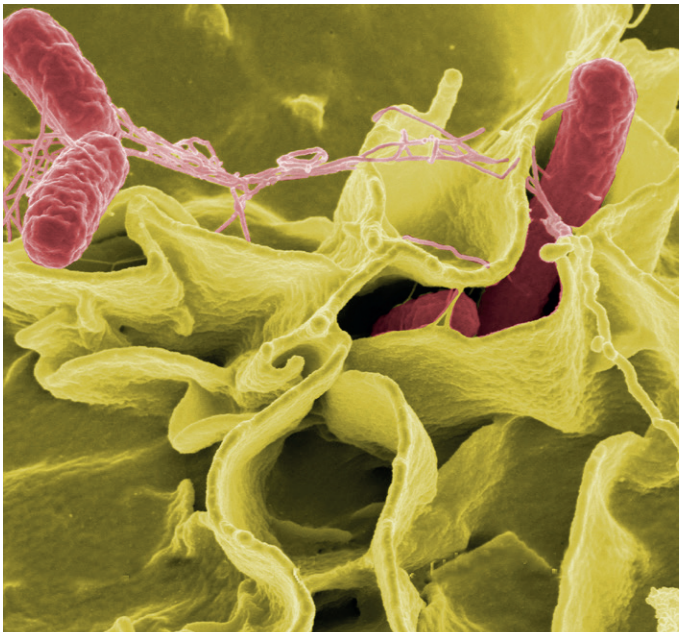
Although clinical outbreaks of necrotic enteritis may cause high levels of mortality, the subclinical form is economically more important as it often stays undetected in the broiler flock. Hampered growth and an increased number of condemnations at the slaughter line cause great economic losses to the poultry farmer.

The true economic impact of necrotic enteritis is not from birds that die from infection, but those who suffer from disease and survive the subclinical form. Bacterial enteritis is a multifactorial disorder that needs predisposing factors to develop. Strategies to control necrotic enteritis without the use of AGP and prophylactic or therapeutic treatment are challenging. To date, there is no single strategy against *C. perfringens* that can be associated with necrotic enteritis. The combination of good hygiene management of poultry houses, use of vaccination (against *C. perfringens* and coccidiosis) and dietary interventions can, to some extent, be an alternative for antibiotics to maintain production and to control necrotic enteritis. Low protein diets or the use of highly digestible protein sources in combination with enzymes to break down the undigestible structural components in the diet will reduce the opportunity of such bacterial growth.

Challenges in poultry

Assessing global trends in bacterial enteritis

A survey performed by a major pharmaceutical company (2015) revealed interesting findings from the field. Poultry professionals, including veterinarians, production managers, nutritionists, on farm managers, ... from the major poultry producing countries were interviewed.



Conclusions could be summarised in the following points:

- Bacterial enteritis continues to be very prevalent and affects productivity and profitability.
- Clostridial necrotic enteritis was seen most often (52.5%) but dysbacteriosis was nearly as common (51.9%).
- Bacterial enteritis continues to be a big concern, while consequences are the same or worse than 5 years ago.
- The effects of bacterial enteritis align directly with the economic concerns. Performance loss, impaired FCR (Feed Conversion Ratio)and reduced weight gain continue to be leading issues.
- The cost of bacterial enteritis is estimated at more than 0.5 USD per bird.
- Economic losses begin in the earliest stage, treatment should be initiated at the same period.
- End users (retailers, slaughterhouses, exporters) prefer a preventive approach to manage the disease.
- When it comes to prevention, water treatment or growth promoting non-antibiotic feed additives are considered most effective.



Achieving gut balance

"Balancing the Lumen"

The acquisition of a healthy microbiota in the first few days after hatching also has a profound effect on the overall health and performance of a broiler chick, and on the profitability of the entire flock.

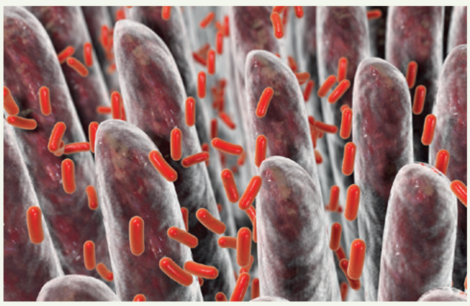
Immediately after hatching, the chick's gastrointestinal tract is populated by bacteria from the surrounding environment (for example from feed and litter).

The level of bacterial colonisation over these first couple of days quickly escalates. Intensive rearing conditions do not usually allow for the natural microbial succession that is required for the establishment of a positive microbiota and the sufficient development of a **mucosal immune system**.

Undigested nutrients flowing to the hindgut have not only shown to impact performance growth but also to directly contribute to undesirable shifts in the gut microbiota. This, in turn, impacts the dynamic balance of the mucus layer, epithelial cells and intestinal immune cells and negatively affects Feed Conversion Ratio (FCR) and chick health.

Antibiotic intervention on its own will not correct an unfavourable microbial ecology caused by diet related factors, particularly in young birds.

A balanced intestinal microflora is an important factor that contributes to intestinal health and consistent animal performance.



Modern pig production has been utilising antibiotics as a tool in keeping infectious diseases under control for decades. Bacteria naturally develop resistance to antibiotics. There is evidence that **global levels of resistance are increasing**. Potentially, any use of antibiotics can eventually affect the efficacy of health management. This can pose another challenge in health management of pigs. To help preserve the effectiveness of antibiotics, their use needs to be reduced.

Challenges in pigs

Post weaning challenge

Weaning time is a crucial period in the management of piglets. The risk of developing post-weaning diarrhea (PWD) is high and causes serious economic losses in pig herds. Piglet diarrhea is managed with systemic injection of antibiotics. However, both legislation and bacterial resistance discourage the use of antibiotics and antibiotic growth promoters.

During the first days after weaning, piglets suffer from post-weaning syndrome associated with inappetence and starvation, which is followed by ingestion of a volume of feed that increases the pH values and weakens the protective barrier function of the stomach against bacterial propagation in the gut.

Lumance® provides protection through its antibacterial action. It also contributes to the stabilisation of intestinal microflora due to its selective biocidal qualities and the ability to improve enzymatic digestion.

Growers

Time, inputs and quality are the main elements of pork production. Goals are to produce efficiently (optimal economic input) and to maximize the quality of pork.

Health and management interventions on the farm are always geared to these elements.

The need for safe and good pork. It is a challenge to keep up with consumer demand while optimising the productivity of the animal.

Health is the primary concern of the farm to optimise production. It is understood that reduction of health interventions such as antibiotics is feasible if productivity and welfare of animals are also taken care of.

Sow

A sow's gut microflora profile has a big influence on its piglet's gut health. At birth, piglets have a sterile GI tract and experience a very fast and diverse microbial community originating from the sow and its environment. By promoting the growth of beneficial bacteria in the sow's gut, we can produce a farrowing pen with a desirable microfloral environment ready for piglets.

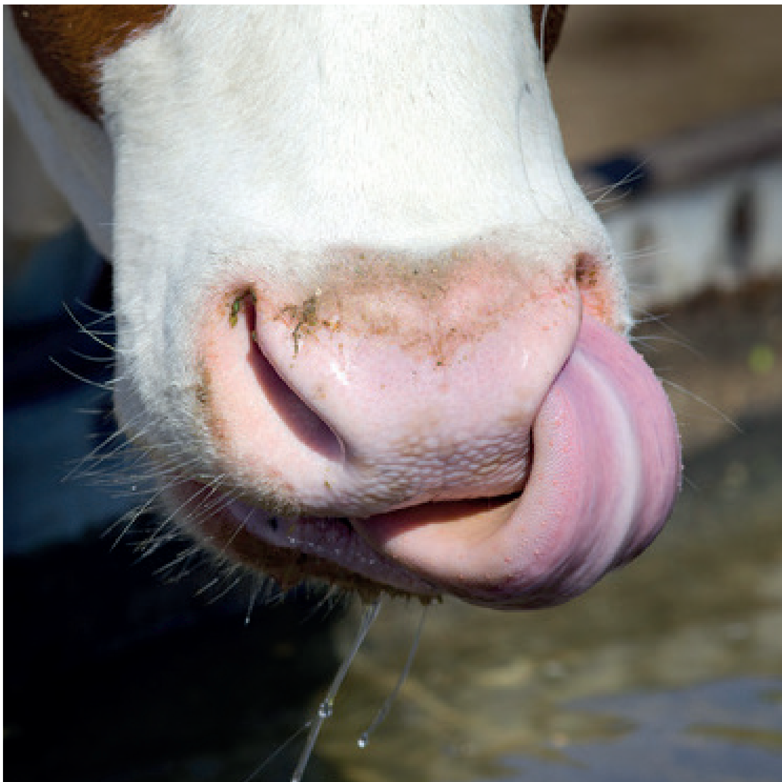
Sows are normally transferred a week – 5 days before farrowing. This will give a good chance to influence the microbial profile of sow faeces while waiting for the valued piglets. 48 hours after birth, the initial colonisation remains stable during suckling. Due to single substrate (milk), the dominant bacteria in this period are Bifidobacterium, Bacteroides and Clostridium.

When the intake of milk is affected there will be an imbalance with the microflora and early period diarrhea (0-7 days) is observed in weak piglets. Weak piglets are bullied and cannot compete for available teats.

Lumance® can encourage the good bacteria profile of the sow and therefore reduce the pathogenic microbial load of the farrowing pen. This will increase the chance for weaker piglets to survive in the most difficult time of their lives.

The immune system of calves at birth is developed but still very immature. Therefore morbidity and mortality can be very high at calf rearing or fattening stage. The best option to support calf health is adequate feeding of colostrum as it supplies immunoglobulin, leukocyte and cytokines. This enables the animal to fight bacteria and viruses.

The quality of the colostrum is affected by age, genes/genetic variation, feeding and husbandry of the cow, often leading to underfeeding of immune active components.



Challenges in calves

Depending on the supply of colostrum and the hygiene status of the calving and rearing pen, calves suffer strongly from bacterial and viral infections. The standard procedure is an antibiotic treatment, which is often not appropriate or too late or too short. Even if the antibiotic treatment is working well, the development of gut microflora will be impaired and thrown back by weeks or months.

Health issues in calves mainly manifest themselves in the respiratory and digestive system. Bacterial and/or viral infections are supported by husbandry issues (mainly respiratory diseases) and hygiene. As bacteria and viruses that cause diseases are omnipresent, basic health is key in prevention (together with proper hygiene and ventilation). Viruses cannot be attacked directly, but strengthening of gut and balancing of gut microflora will improve the overall abilities of calves to defend themselves.

Rearing calves

Financial loss due to mortality is often seen to be limited as male calves of dairy breeds are of less economic value. However, high losses indicate high morbidity (mainly respiratory issues and diarrhea) of all calves. Long lasting effects of calf health problems are often overseen, subsequently the performance of dairy heifers will be reduced, leading to higher age at first calving and reduced milk production.

The main causes for diarrhea within the initial weeks of life are *E. coli, Cl. Perfringens* and *Cryptosporidia*. Low colostrum quantity/quality and poor hygiene conditions will accelerate the problem. Accelerated feeding programs often induce a drop in growth when ad libitum feeding is reduced. The calves have difficulties in adapting to starter feed. The benefits of accelerated feeding schemes are even better when the health condition of the calf is improved.

Lumance® can reduce the pathogenic microbial load in the gut of calves and strengthen the gut wall. This will protect the animal from invasion of bacteria or toxins. Energy and nutrients can be directed to growth and do not have to be used for the immune system.

Veal calves

Veal production aims at producing healthy and palatable meat at a low cost. The most important part of reducing costs in production is to enable growth for optimum output. As for rearing calves, health is key in sustaining growth. Additionally, calves for fattening have to keep their growth rate to reach target weights in time. In veal production there is no time for compensatory growth.

Diarrhea occurs mainly in the initial weeks after arrival, later dysbacteriosis is seen repeatedly. At high rates of milk feeding some volume may flow back to the rumen or be strongly fermented by unwanted bacteria already present in the abomasum. Subsequent ruminal or abomasal bloat is threatening for the calf's life.

Lumance® can reduce the unwanted fermentation in rumen and abomasum by reducing and balancing the microflora. The digestive process is more stable. Furthermore, secretion of digestive fluids is improved and digestion of less valuable proteins (-> plant sources) is accelerated.

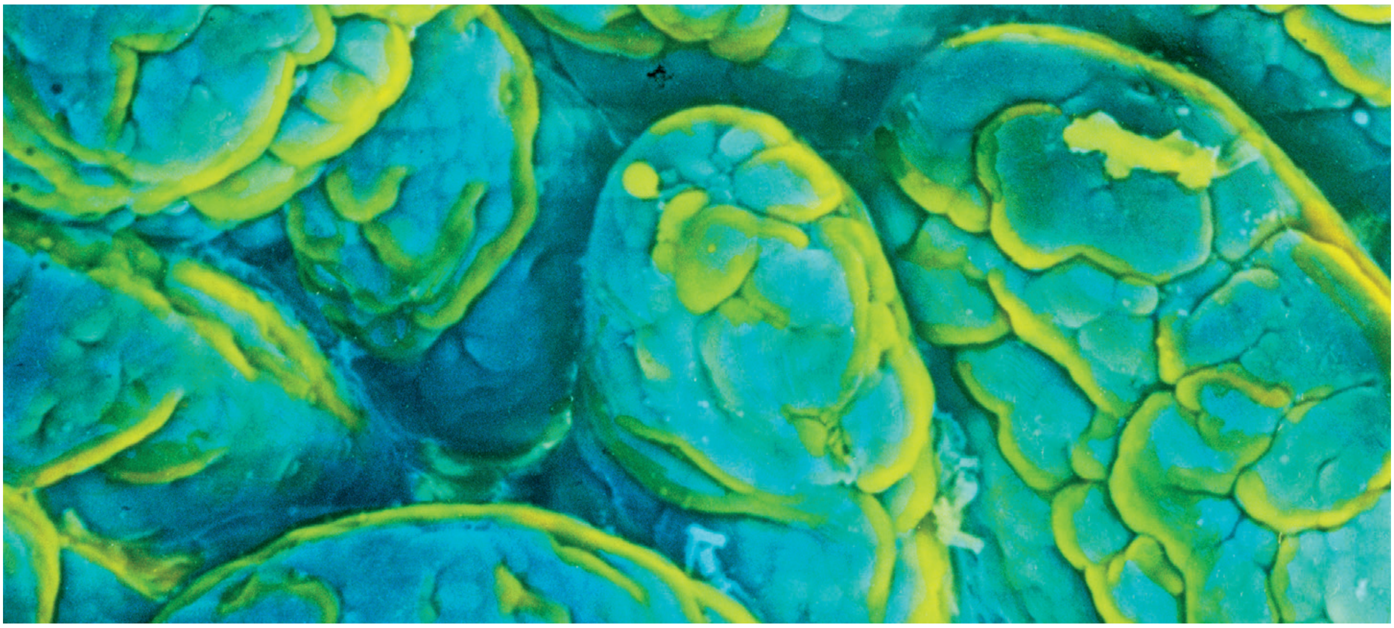
Lumance® application in calves:

Calf milk replacer:	2 - 8 kg/T
Calf starter feed:	2 - 4 kg/T
In standard hygiene and health conditions:	2-4 g/head per day
In difficult conditions, to support antibiotic treatment:	5-15 g/head per day

Lumance® Calf

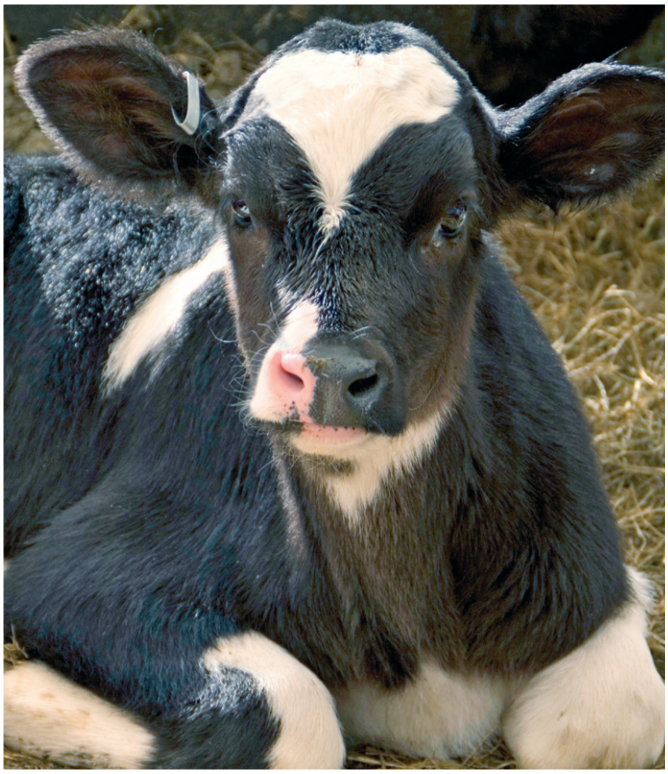
Calf gut conditioner

The profitability of dairy farms has been put under pressure due to volatile milk prices and increased feed costs. The main challenge with growing calves is the occurrence of diarrhea and its cost to the producer. The immune system of calves at birth is developed but still very immature. Therefore morbidity and mortality can be very high at calf rearing.



Challenge

Calves are born with limited immunity against diseases. They acquire resistance to diseases by timely and adequate intakes of high-quality colostrum. If not, morbidity and mortality of calves, mainly induced by diarrhoea, will be high. Calf diarrhoea can be caused by bacterial, viral, or protozoal infections.



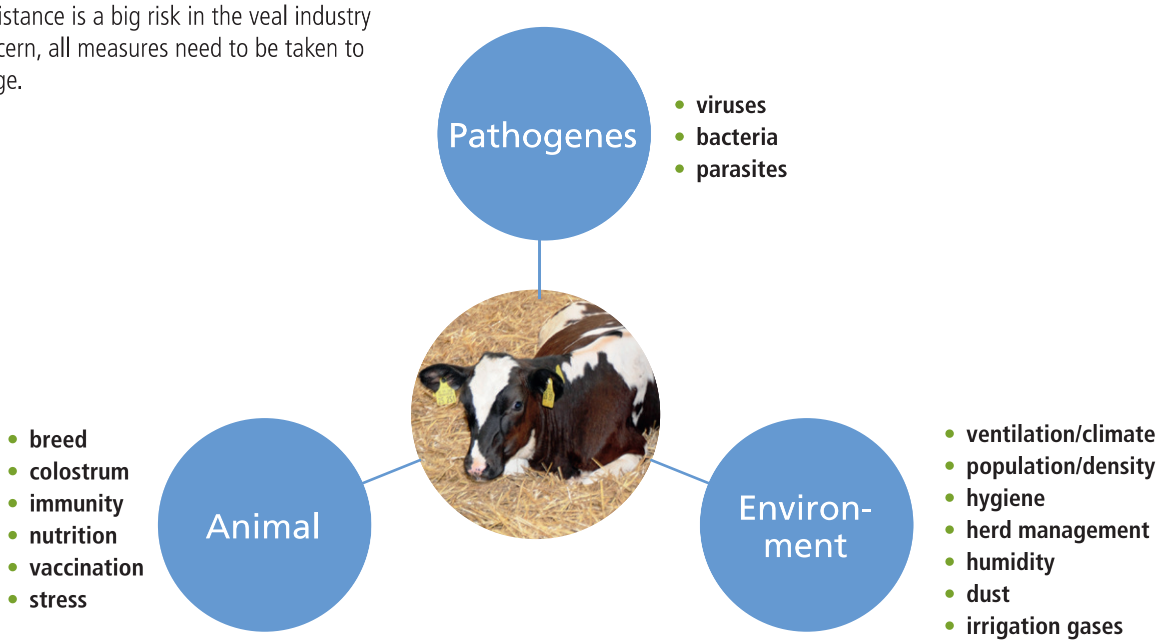
Collostrum feeding has to be given

- **early enough:** high absorption of immunoglobulins directly after birth and declines to zero after 24 hours;
- **in sufficient amount:** 2-4 kg recommended in first meal via teat-bucket;
- **at high quality:** >50 g/l immunglobulins in colostrum

Calves at highest risk are born at night or from heifers; the first because of unknown intake of colostrum and the second due to low collostrum quality.

The incidence of veal calf diseases differs between production systems and geographical locations and varies over time. Morbidity peaked in the first three weeks after arrival and gradually declined towards the end of the production cycle. The period of highest risk for mortality is the initial week after arrival. After about 30 days after arrival the incidence of health risks clearly reduces.

In general, treatment rate with antibiotics may reach 25% of calves. As multidrug resistance is a big risk in the veal industry and of great public concern, all measures need to be taken to minimize antibiotic usage.



Lumance® Calf
Calf gut conditioner

Lumance® Calf

Lumance® Calf has been developed as a gut conditioner to strengthen the barrier function, minimize the effect of scouring/ diarrhea, support faster recovery and enhance the innate immune system for a calf's long term development.

Its unique composition consists of a proprietary mixture of esterified butyrins and plant extracts which bring the following features and benefits:

- Help support the development of epithelial cells by providing a readily **available source of energy**
- Enhance enterocytes and intestinal villosity development by **stimulating villi growth**
- **Anti-microbial control**. Stimulate the ability of the animal to overcome bacterial infections
- Effect on the microbiota pattern and **balance**

Esterified butyrins are combined molecules composed of a glycerol structure and butyrate molecules. The final result of the esterification is a combination of mono-, di- and tri-butyrins which act as a source of butyrate molecules in the intestinal tract.

Based on the molecules origin, it is easy to understand that these "fat-type" structures can only be digested in the presence of the digestive enzyme lipase. By definition, this guarantees full stomach bypass properties at the level of the stomach while being activated after pancreatic lipase has been added.

Here is what the producer says about it:

(2,000 cow dairy in NY)

« **Lumance® Calf** has been an amazing addition to our calf rearing program.

While it has not eliminated scours completely, the calves that do scour never lose appetite – they continue to eat, drink and power through it… Our use of electrolytes has dropped. »

« We rarely have to tube calves anymore. Mortality of calves born alive is less than 1%. »

	ANIMAL GROUP	APPLICATION	DOSAGE	
Rearing calves	1-14 days of life	via milk or CMR	5-10 g/day	to strengthen health against risk of diarrhoea
	1st days of life till weaning		3 g/day	basic growth support
	Rearing calves	Via starter feed	3 g/kg	
Veal calves	1-30 days of life	via milk or CMR	5-10 g/day	to strengthen health against risk of diarrhoea
	Until slaughter		3 g/kg	basic growth support

How to apply ?

Lumance® Calf can be fed via milk (CMR) or starter feed until weaning at low dosage to improve well-being and growth.

At a higher dosage during the initial 14 days after birth the product will support calf health strongly at the most sensitive time of life.

- Freeflowing
- With NO SMELL
- Non-corrosive
- Heat & pelleting stable

Due to the balanced ester combination, **Lumance® Calf** combines butyrate supply (quantity) and strong antibacterial activities (quality).

Lumance®

Mode of action





Performance is linked to intestinal health, being vaguely defined in many literatures, but more and more clearly understood. Optimal gut health can only be achieved by optimising the gastro-intestinal integrity and the gastro-intestinal microflora and not to forget the relation between both. By controlling the microflora in the lumen and strengthening the intestinal epithelium integrity, **Lumance®** offers a comprehensive **GUT HEALTH MANAGEMENT program** that aims at reducing medication or cocktails of medication.

4 KEY MODES OF ACTIONS :

1. **Reinforce gut integrity**
2. **Reduce inflammatory response**
3. **Balance the lumen and its gastro intestinal microflora**
4. **Protects against ROS**

Gastro-intestinal integrity is defined by:

Villi health

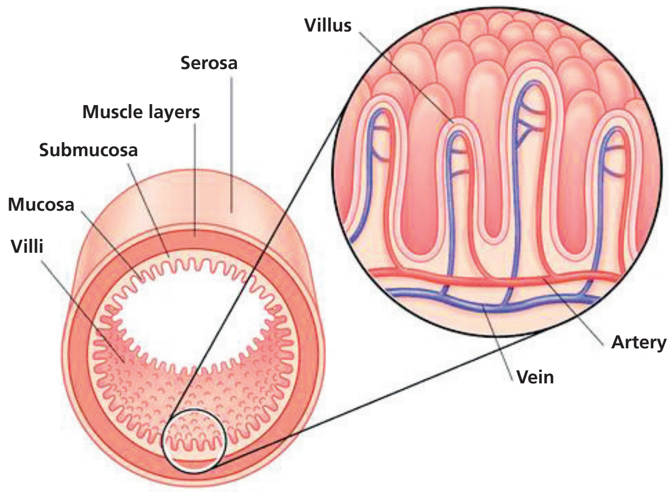
Cellular energy

Tight junction quality

Host defense peptides

Anti-inflammatory role

Intestinal coating



Mode of action

1. Reinforce gut integrity

As a starting point, the intestinal structure is of key importance. Achieving **long and slender villi** has been a priority for many years. They guarantee a high **absorption capacity** for the nutrients, which is not only important to obtain high performance and low FCR, but also to reduce the load of undigested/unabsorbed nutrients in the lower part of the digestive tract, which ensures a proper healthy fermentation. Many nutritional approaches have been tried, but one of the most effective ones became standard in many of today's feed formulations.

The area of the intestinal wall carries an important responsibility in selecting what can be absorbed and what should remain outside the body of the animal. To put this into the right perspective, it is important to realise that the surface of the intestinal tract is 300 times the size of the surface of the skin.

At the same time, it should give the similar level of protection against invaders, while being highly permeable in order to absorb nutrients.

Besides in poultry, the constant immunological challenge by *Eimeria* species concurrently with *C. perfringens*, makes the **barrier defense function** of the epithelial layer of great importance.

Tight junctions, a complex protein structure formed between epithelium cells, play a crucial role in protecting the insides of the animal from the challenges present in the lumen. Many molecules present in the digestive tract (free radicals, toxins,…) put these tight junctions under continuous stress, which increases the risk of passage of toxins and/or pathogenic bacteria through the intestinal wall, inside the animal's body.

Butyrate MODES OF ACTION

- Stimulating growth of **villi and number of micro-villi**
- **Balancing microflora** with selective control on pathogens and microorganisms
- **Reinforcing the intestinal defense by releasing HDP (host defense peptides)**
- **Directing antimicrobial effect on *C. Perfringens***
- Enhancing the intestinal barrier by facilitating **tight junction** assembly
- Protecting intestinal cells from **bacterial invasion and translocation**
- Acting as **signaling** molecule
- Protecting from oxidative stress, decreasing oxidative injury of tissues
- Potent **anti-inflammatory effect** and positively affecting the **immune system**
- Limiting the invasiveness of **salmonella**, reducing its colonisation
- **Reducing incidence** of necrotic enteritis
- **Preferred energy source** for the colonic cells (for epithelial cell proliferation and maintenance)
- **Reducing gene expression and salmonella invasiveness**

Butyrate has a strong capacity to enhance synthesis of endogenous antimicrobial Host Defense Peptides (HDP), which are critical components of the animal's innate immunity. HDP are important and efficient components of the innate immunity that have been counteracting the negative impact bacteria, protozoa, fungi and enveloped viruses, by means of complex modes of action, for so many centuries, that any type of resistance is unlikely to occur.

Health status of the animal, diet composition and environmental conditions influence the response of animals to butyrate supplementation.

2. Reduce inflammatory response

Inflammation of the intestinal tract is the result of an overactive immune response that is linked to an increased challenge of the intestinal immunity. As such, the production of inflammatory cytokines is a natural and positive response of the immune system, but the process is extremely energy demanding and will reflect almost instantly and significantly in the performance data of the farm.

Finally, the totality of the intestinal integrity can be protected by means of an intestinal coating. This protective layer can reduce the impact of invading mechanisms on the intestinal integrity itself.

Although the anti-inflammatory properties of butyric acid are present and beneficial, certain plant extracts rich in alkaloids can largely be counted that are responsible for the anti-inflammatory reactivity of Lumance®.

Their mode of action is well defined and understood, the results immediately show in gain and FCR figures.

The formation by complexation of tannin rich extracts with proteins present in the mucus layer will provide a protective intestinal coating

Mode of action

Butyrate Benefits

Improvements in growth performance observed in animals fed butyrate may be attributed to a **lower pro-inflammatory response** to nutritional, environmental and immune challenges, associated **with improved digestibility and absorption of dietary nutrients.** The latter can be explained by the modulating effects of butyrate on gut microbiota and perhaps by assumed effects of butyrate on gut endocrine regulation. Most of the mechanisms are likely to be affected by the delivery site of butyrate within the GIT.

Butyrate is a short chain fatty acid naturally produced in the digestive tract by the fermentation of fibers. The fatty acid is considered the most important energy source for intestinal cells and has multiple beneficial effects on vital intestinal functions.

Already in the small intestine butyrate favours the villi development, gut morphology and function. Further on in the digestive tract, butyrate represents the preferred energy source for the colonic cells and is a major precursor for lipid synthesis, used for incorporation into the cell membranes. By supporting the cell membrane structure, butyrate contributes to the maintenance of barrier and transporter functions in the gut.

In low concentrations butyrate reinforces the intestinal defense barriers by increasing the release of protective mucins in the mucus layer and the release of antimicrobial peptides. These peptides, also mentioned as **host defense peptides (HDP)** possess a broad spectrum antimicrobial activity against bacteria, protozoa, enveloped viruses and fungi.

HDP bind to the microbial membrane and cause membrane disruption, which results in microbial death. The research group of van Immerseel shows another antimicrobial efficacy of butyrate, whereby the fatty acid reduces the ability of pathogenic bacteria for adhesion to the gut cell wall.

Butyrate also plays a role as an anti-inflammatory agent. Tempering the inflammatory status of the chicken is a useful tool to overcome feed intake reduction and thereby reduce break down of muscle tissue during necrotic infection.

Uncoated butyrate will be directly absorbed in the first part of the small intestine and will not reach the lower parts of the digestive tract.



3. Balance the lumen and its gastrointestinal microflora

As important as intestinal integrity may be, proper attention should be given to **a balanced microflora**.

In this context, **Lumance®** does not strive to be an antibiotic complex, which eliminates all pathogens and beneficial bacteria. It is especially designed to **reduce the impact of the pathogenic bacteria**.

A moderate reduction of pathogenic bacteria will give more potential to the beneficial bacteria to obtain their required part of the microbiological balance in the intestine, allowing the animal to benefit completely from their symbiosis.

Organic acids have been used for over 15 years to positively influence the intestinal balance of microorganisms.

Gastro-intestinal integrity
Microbial Balance:

Selective
Reduction of pathogens
Stimulation of Bifidus bacteria
Multiple mode of action
Synergy
Target release

Capric, Caprylic and Lauric acid
are fat soluble components, with well-defined specific antibacterial properties, working complementary to the activity of butyric acid and its esters.

Besides short chain fatty acids, **medium chain fatty acids (MCFA's)** are also promising antibacterial compounds as they target pathogenic bacteria, which are less sensitive to SCFA.

Short chain fatty acids (SCFA) in general and butyric acid in particular, have demonstrated their selective antibacterial effect.

Specifically Salmonella and Campylobacter, butyric acid possess a specific and well defined pH independent inhibition mechanism, resulting in a reduced gene expression of HIL A, which finally significantly reduces the invasiveness of those bacteria strains.

The need for activity in the lower part of the digestive tract requires a target release source of organic acids.

Mode of action

4. Protect against ROS

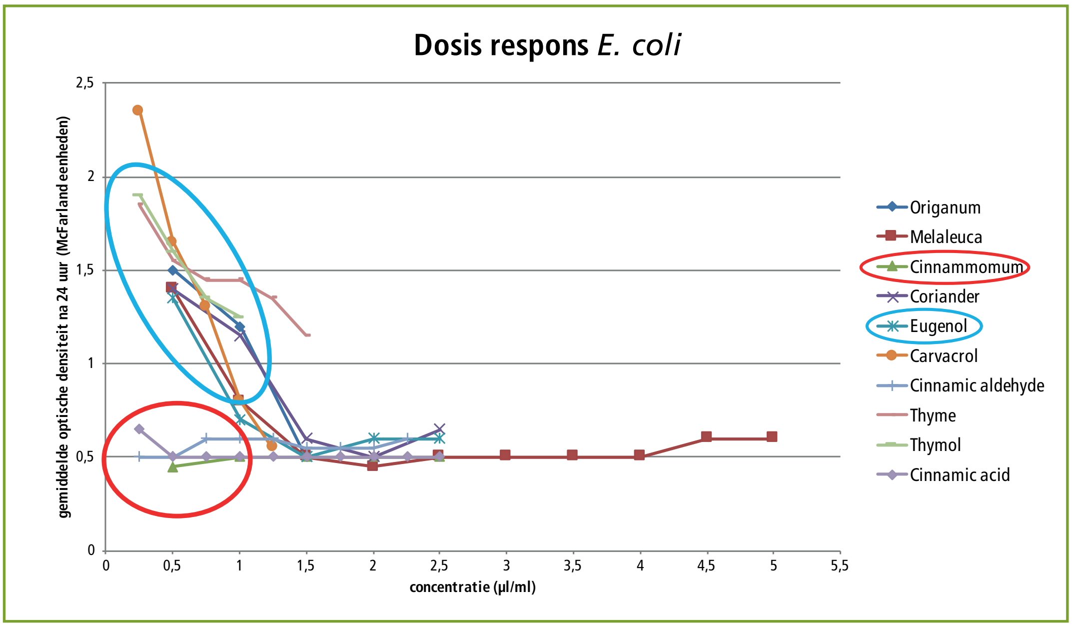
Essential oil and plant extracts are volatile aromatic components obtained from plant material through steam distillation.

They are chemically diverse and therefore, there are likely to be various mechanisms by which they exert their antimicrobial activity.

In general they are hydrophobic and likely to enter into cell membranes of microbes, which disturbs their normal functionalities.

Different essential oils are likely to have different molecular targets, which might explain the fact that combinations may be more effective than a single essential oil.

Botanicals enforce antibacterial activity



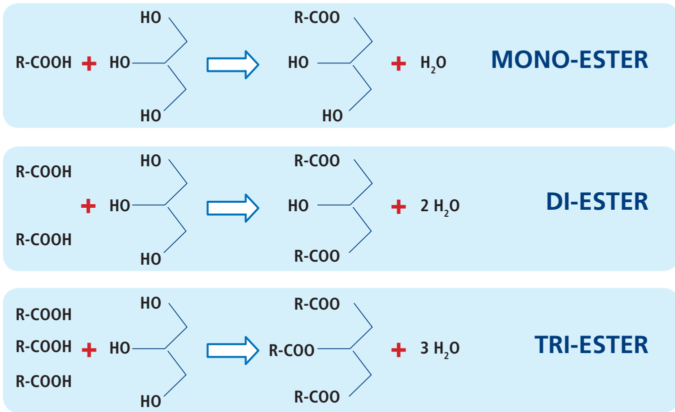
Eugenol and Cinnamic aldehydes interfere with the intracellular ATP (energy). They reduce the bacterial energy generation.

Esterified forms of butyric acid

Lumance® contains esterified forms of butyric acid. Mono-, di- and tri-esters of butyric acid are chemically produced and are composed of a glycerol molecule and respectively 1, 2 or 3 butyrate molecules.

Due to their similarity with triglycerides, they will automatically bypass the stomach during the digestive process, while the butyric acid molecules will be enzymatically released by lipase into the small intestine. Based on the origin of the molecules, it is easy to understand that these "fat type" structures can only be digested in the presence of the digestive enzyme lipase. By definition, this guarantees full stomach bypass properties at the level of the stomach while being activated after pancreatic lipase has been added.

Extremely important to guarantee the efficiency of the product are the types of esters provided, their stability and the know-how and the control of the esterification process. Free fatty acids, moisture and the typical smell of butyric acid can give a clear indication of whether the esterification process is complete and irreversible. During the esterification process, it is of utmost importance that the reaction is controlled carefully in order to guarantee the desired stability of the product. A correct catalyst, the right esterification speed and the final purification step need expertise and deep chemical knowledge, resulting in a highly concentrated, pure and clear product with a high stability in time and during pelleting process, guaranteed without the typical smell of butyric acid.



Key features and benefits of Mono-esters and Di-Tri esters

Different ester forms have different activities and benefits.
Esters are NOT pH dependent (like organic acids).
There is value in combining.

Mono-esters	Di-Tri esters
• pH stable (+ passes the stomach and crop) • Small molecule (+ easy uptake by bacteria leading to internal hydrolysis and effective anti-bacterial activity) • 1 side chain only (+ escape from endogenous lipase) • Uptake in the bloodstream (+ action within the whole metabolism) • Relative low supply of butyrate • Water soluble	• pH stable (+ passes the stomach and crop) • Bigger molecule (no bacterial uptake) • 2 or 3 side chains (hydrolysis by endogenous lipase) • High supply of butyrate (+)

Esterified forms of butyric acid

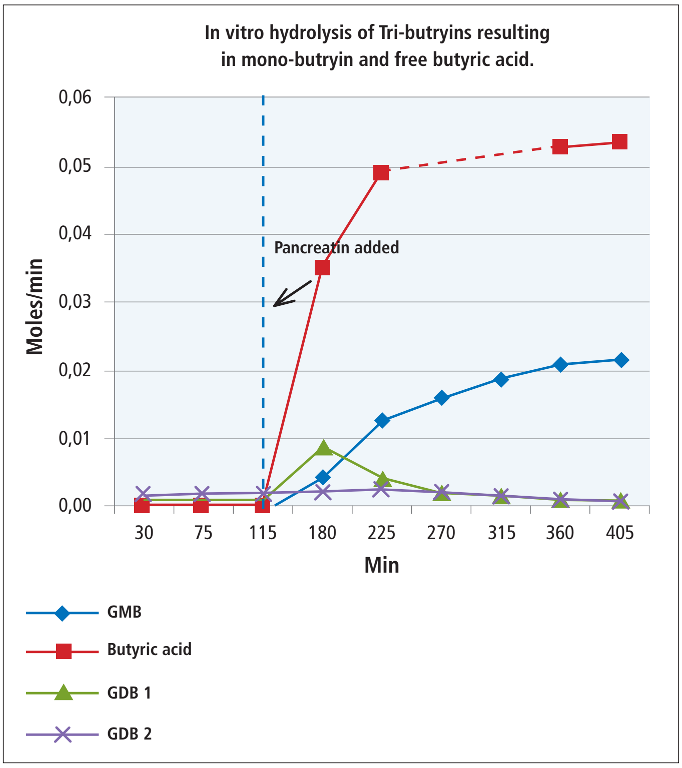
Esterified forms of butyric acid used in **Lumance®** are :

- Free-flowing
- Have no smell
- Non corrosive
- Heat stable
- Active in the gut

By carefully selecting the right combination and proportions of the different glycerides, **Lumance®** combines butyrate supply and sytrong antibacterial activities.

MIC	S. Typhimurium	E. Coli
Butyric acid	1:400	1:400
Mono-esterified butyrins	1:1600	1:800

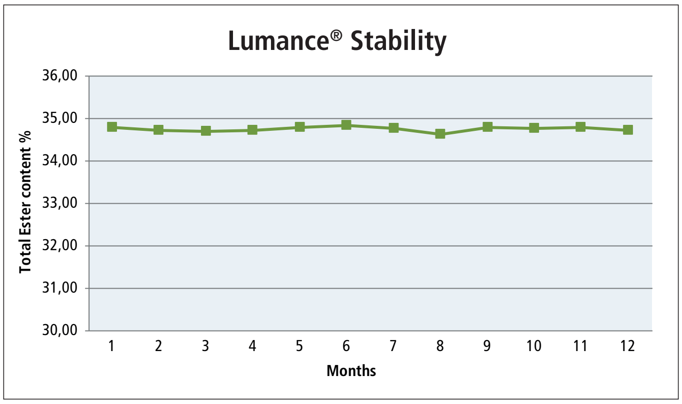
MIC concentrations for Mono-butyrin (Innovad 2012)



Innovad® Esterified Butyrins Target release properties

Esters are molecules that are similar to tri-glycerides and follow the same path of digestion. By definition this includes no significant digestion at stomach level. Once in the small intestine, addition of lipase will hydrolyse the triglycerides into mono-esters and free fatty acids. In the case of butyric acid esters, final product after hydrolysis are mono-butyrin, a strong antibacterial compound, and free butyric acid, which supports, as it is released in the intestinal tract, the intestinal integrity and the microbial balance.

Stability of esters is critical to explore their efficiency. It is the result of production process know-how, final purification and moisture elimination.

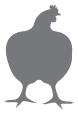


Trials & Scientific Experiments

Scientific *in vivo* experiment with broilers

Date: June – July 2012
Location: Department of Animal Production, Faculty of Agriculture, University of Jordan, Jordan

Species:
Broilers



Introduction:

- This study was conducted to determine the effect of dietary supplementation – esterified butyrins, propionic acid and sorbic acid with medium chain fatty acids and plant extracts – on the productive performance and mortality of growing broiler chickens.

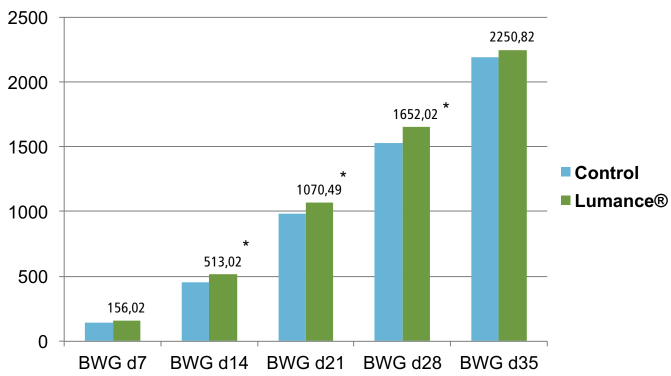
Protocol:

- 246 broilers of Ross 308 breed
- 2 treatments
  - **Control group:** corn/soya diet with multiple enzyme pack
  - **Trial group:** control diet + 1kg/T Lumance®
- Feeding regime:
  - **Starter** (1-11 days)
  - **Grower** (12-23 days)
  - **Finisher** (24-35 days)
- Parameters measured:
  growth performance parameters:
  - Initial + final body weight (BW)
  - Cumulative body weight gain (BWG)
  - Cumulative feed intake (FI)
  - Cumulative feed conversion ratio (FCR)
  - Feed efficiency based on the European efficiency index

European Efficiency Index = ADG (g) * Livebility (%)/(FCR*10)

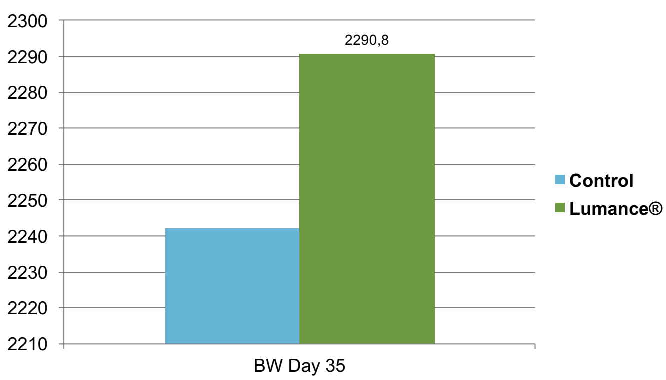
Results:

Cumulative Body Weight Gain (g)

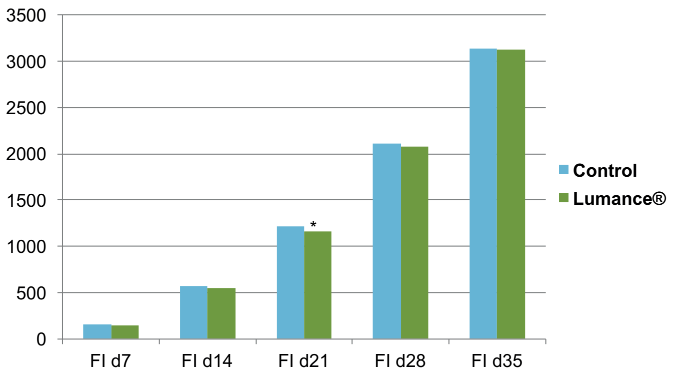


* *Significant difference (p<0,05)*

Final body weight (BW)

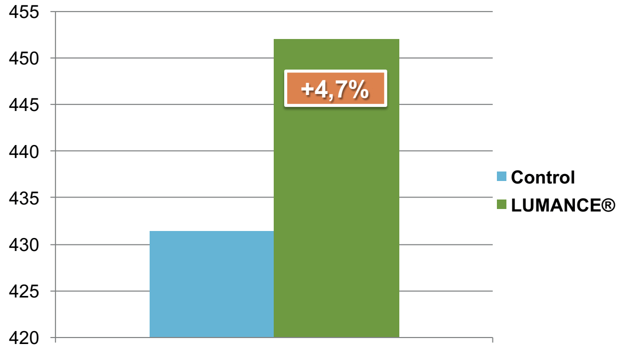


Cumulative feed intake (FI)



* *Significant different (p<0,05)*

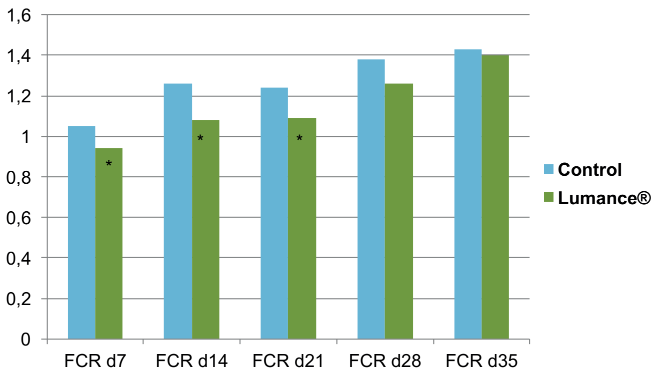
European efficiency index



*European Efficiency Index = ADG (g) * Livebility (%)/(FCR*10)*

5

Cumulative FCR



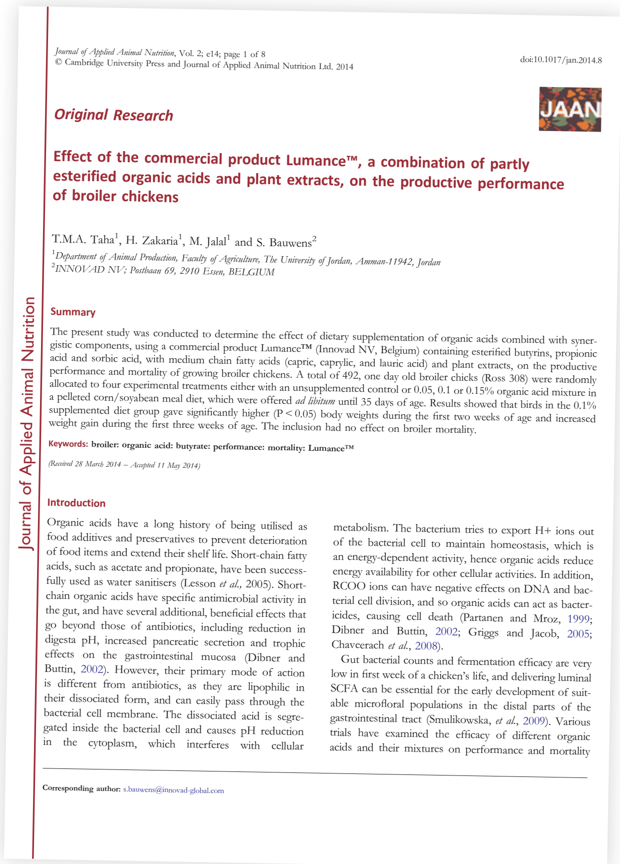
Conclusions:

In comparison with the control group, **Lumance®** significantly:

- Enhanced the BWG from day 14 until day 28 (p<0,05)
- Increased the FCR through the first three weeks (p<0,05)
- Improved feed efficiency with 4,7%.

No effects have been found on meat quality or serological parameters.

Published in Journal of Applied Animal Nutrition, Vol. 2; e14; page 1 of 8.



Journal of Applied Animal Nutrition, Vol. 2; e14; page 1 of 8

doi:10.1017/jan.2014.8

JAAN

Original Research

Effect of the commercial product Lumance™, a combination of partly esterified organic acids and plant extracts, on the productive performance of broiler chickens

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Summary

The present study was conducted to determine the effect of dietary supplementation of organic acids combined with synergistic components, using a commercial product Lumance™ (Innovad NV, Belgium) containing esterified butyrins, propionic acid and sorbic acid, with medium chain fatty acids (capric, caprylic, and lauric acid) and plant extracts, on the productive performance and mortality of growing broiler chickens. A total of 492, one day old broiler chicks (Ross 308) were randomly allocated to four experimental treatments either with an unsupplemented control or 0.05, 0.1 or 0.15% organic acid mixture in a pelleted corn/soyabean meal diet, which were offered *ad libitum* until 35 days of age. Results showed that birds in the 0.1% supplemented diet group gave significantly higher ($P < 0.05$) body weights during the first two weeks of age and increased weight gain during the first three weeks of age. The inclusion had no effect on broiler mortality.

Keywords: **broiler: organic acid: butyrate: performance: mortality: Lumance™**

(Received 28 March 2014 – Accepted 11 May 2014)

Introduction

Organic acids have a long history of being utilised as food additives and preservatives to prevent deterioration of food items and extend their shelf life. Short-chain fatty acids, such as acetate and propionate, have been successfully used as water sanitisers (Lesson *et al.,* 2005). Short-chain organic acids have specific antimicrobial activity in the gut, and have several additional, beneficial effects that go beyond those of antibiotics, including reduction in digesta pH, increased pancreatic secretion and trophic effects on the gastrointestinal mucosa (Dibner and Buttin, 2002). However, their primary mode of action is different from antibiotics, as they are lipophilic in their dissociated form, and can easily pass through the bacterial cell membrane. The dissociated acid is segregated inside the bacterial cell and causes pH reduction in the cytoplasm, which interferes with cellular metabolism. The bacterium tries to export H+ ions out of the bacterial cell to maintain homeostasis, which is an energy-dependent activity, hence organic acids reduce energy availability for other cellular activities. In addition, RCOO ions can have negative effects on DNA and bacterial cell division, and so organic acids can act as bactericides, causing cell death (Partanen and Mroz, 1999; Dibner and Buttin, 2002; Griggs and Jacob, 2005; Chaveerach *et al.*, 2008).

Gut bacterial counts and fermentation efficacy are very low in first week of a chicken's life, and delivering luminal SCFA can be essential for the early development of suitable microfloral populations in the distal parts of the gastrointestinal tract (Smulikowska, *et al.*, 2009). Various trials have examined the efficacy of different organic acids and their mixtures on performance and mortality

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Journal of Applied Animal Nutrition

In vivo experiment with broilers II

Date: June – July 2012
Location: Commercial broiler farm, Latvia

Species:
Broilers

Introduction:

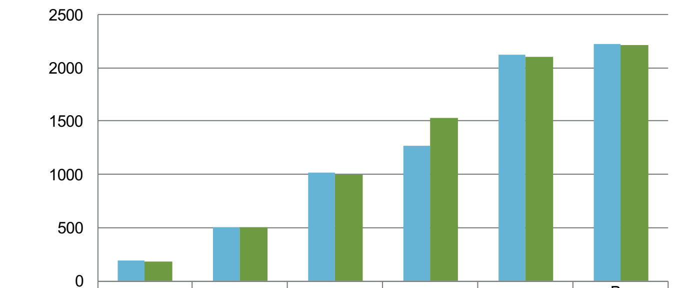
- This study was carried out to measure the benefit provided by **Lumance®** when supplemented to a lower quality and more economical diet compared to an enriched feed.

Protocol:

- 64.000 broilers
- 2 treatments
  - **Control group:** 32 000 birds fed a high quality feed enriched in medium chain fatty acids
  - **Trial group:** 32 000 birds fed a low priced standard feed which was known to result in enteritis problems with hypersecretion in duodenum and reduced performance + **Lumance®**
- Feeding regime trial group:
  - 0,5kg/T **Lumance®** in the first 10 days
  - 1 kg/T from day 11-25
  - 0,5 kg/T from day 26
- **Parameters measured:**
  growth performance parameters:
  - Initial + final body weight (BW)
  - Cumulative body weight gain (BWG)
  - Cumulative feed conversion ratio (FCR)
  - Feed efficiency based on the European efficiency index
  - Lesion score for enteritis at day 31 and 32

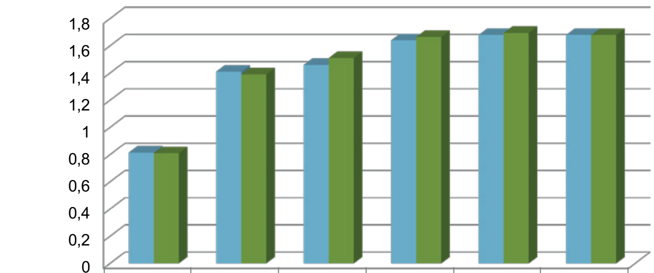
Results:

Body weight gr/chicken



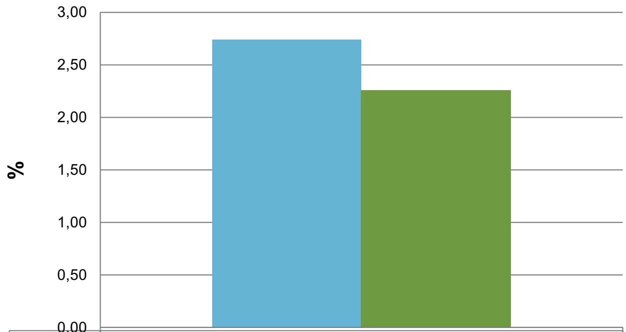
	1 week	2 week	3 week	4 week	5 week	By realization
Trial group	191	501	1018	1273	2121	2226
Control	184,5	505,5	993,5	1530	2106	2213

FCR

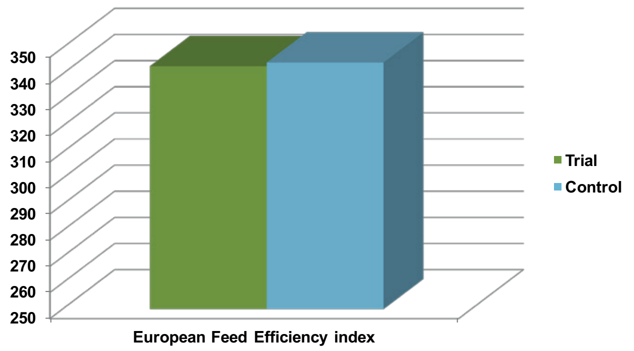


	1 week	2 week	3 week	4 week	5 week	By realization
Trial group	0,815	1,41	1,46	1,64	1,68	1,68
Control	0,81	1,39	1,51	1,665	1,695	1,68

Mortality



Trial group	2,74
Control	2,26



Conclusions:

The control group supplemented with **Lumance®** got an enteritis score of 5 and the control group a score of 10,5.

Overall conclusions state that supplementation of **Lumance®** to low quality feed lifts up performance to a similar level of high quality feed and resolves the problem of enteritis, in an undisputable way obtaining an enteritis scoring which is much better than the high quality feed.

Scientific *in vivo* experiment with broilers III

Date: April – May 2013
Location: University of Health Sciences, Lithuania

Species:
Broilers

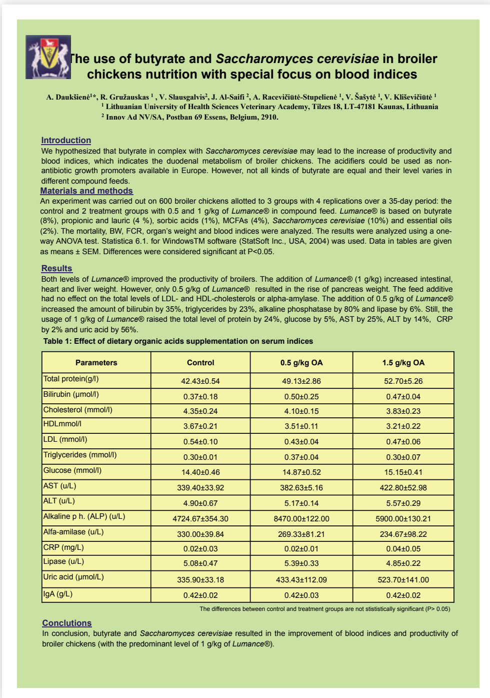
Introduction:

- This trial was conducted to investigate the influence of **Lumance®** on chicken productivity, digestive processes and the quality of meat.

Protocol:

- 600 broilers
- 3 treatments
  - **Control group:** 200 birds fed a standard feed
  - **Trial group I:** 200 birds fed control diet + 0,5 kg/T **Lumance®**
  - **Trial group II:** 200 birds fed control diet + 1kg/T **Lumance®**
- **Parameters measured:**
  growth performance parameters:
  - Initial + final body weight (BW)
  - Cumulative body weight gain (BWG)
  - Cumulative feed conversion ratio (FCR)
  - Feed efficiency based on the European efficiency index

Presented at WPSA
(Word's Poultry Science Association)
Norway, June 2014.



The use of butyrate and *Saccharomyces cerevisiae* in broiler chickens nutrition with special focus on blood indices

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[1] Lithuanian University of Health Sciences Veterinary Academy, Tilzes 18, LT-47181 Kaunas, Lithuania
[2] Innov Ad NV/SA, Postban 69 Essens, Belgium, 2910.

Introduction
We hypothesized that butyrate in complex with *Saccharomyces cerevisiae* may lead to the increase of productivity and blood indices, which indicates the duodenal metabolism of broiler chickens. The acidifiers could be used as non-antibiotic growth promoters available in Europe. However, not all kinds of butyrate are equal and their level varies in different compound feeds.

Materials and methods
An experiment was carried out on 600 broiler chickens allotted to 3 groups with 4 replications over a 35-day period: the control and 2 treatment groups with 0.5 and 1 g/kg of *Lumance®* in compound feed. *Lumance®* is based on butyrate (8%), propionic and lauric (4 %), sorbic acids (1%), MCFAs (4%), *Saccharomyces cerevisiae* (10%) and essential oils (2%). The mortality, BW, FCR, organ's weight and blood indices were analyzed. The results were analyzed using a one-way ANOVA test. Statistica 6.1. for WindowsTM software (StatSoft Inc., USA, 2004) was used. Data in tables are given as means ± SEM. Differences were considered significant at $P<0.05$.

Results
Both levels of *Lumance®* improved the productivity of broilers. The addition of *Lumance®* (1 g/kg) increased intestinal, heart and liver weight. However, only 0.5 g/kg of *Lumance®* resulted in the rise of pancreas weight. The feed additive had no effect on the total levels of LDL- and HDL-cholesterols or alpha-amylase. The addition of 0.5 g/kg of *Lumance®* increased the amount of bilirubin by 35%, triglycerides by 23%, alkaline phosphatase by 80% and lipase by 6%. Still, the usage of 1 g/kg of *Lumance®* raised the total level of protein by 24%, glucose by 5%, AST by 25%, ALT by 14%, CRP by 2% and uric acid by 56%.

Table 1: Effect of dietary organic acids supplementation on serum indices

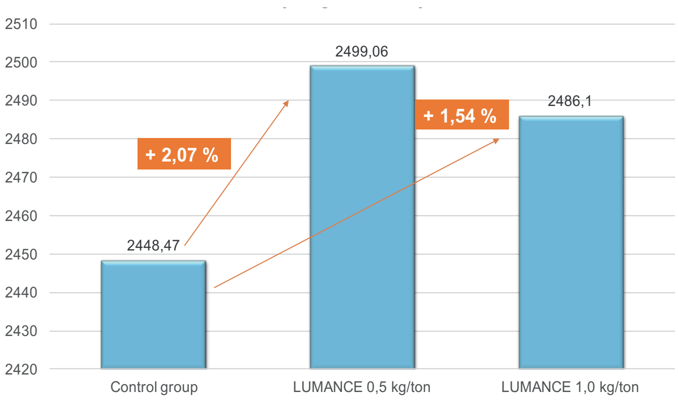
Parameters	Control	0.5 g/kg OA	1.5 g/kg OA
Total protein(g/l)	42.43±0.54	49.13±2.86	52.70±5.26
Bilirubin (μmol/l)	0.37±0.18	0.50±0.25	0.47±0.04
Cholesterol (mmol/l)	4.35±0.24	4.10±0.15	3.83±0.23
HDLmmol/l	3.67±0.21	3.51±0.11	3.21±0.22
LDL (mmol/l)	0.54±0.10	0.43±0.04	0.47±0.06
Triglycerides (mmol/l)	0.30±0.01	0.37±0.04	0.30±0.07
Glucose (mmol/l)	14.40±0.46	14.87±0.52	15.15±0.41
AST (u/L)	339.40±33.92	382.63±5.16	422.80±52.98
ALT (u/L)	4.90±0.67	5.17±0.14	5.57±0.29
Alkaline p h. (ALP) (u/L)	4724.67±354.30	8470.00±122.00	5900.00±130.21
Alfa-amilase (u/L)	330.00±39.84	269.33±81.21	234.67±98.22
CRP (mg/L)	0.02±0.03	0.02±0.01	0.04±0.05
Lipase (u/L)	5.08±0.47	5.39±0.33	4.85±0.22
Uric acid (μmol/L)	335.90±33.18	433.43±112.09	523.70±141.00
IgA (g/L)	0.42±0.02	0.42±0.03	0.42±0.02

The differences between control and treatment groups are not stististically significant ($P> 0.05$)

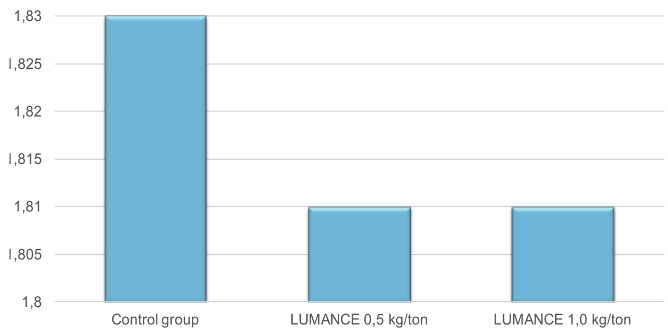
Conclutions
In conclusion, butyrate and *Saccharomyces cerevisiae* resulted in the improvement of blood indices and productivity of broiler chickens (with the predominant level of 1 g/kg of *Lumance®*).

Results:

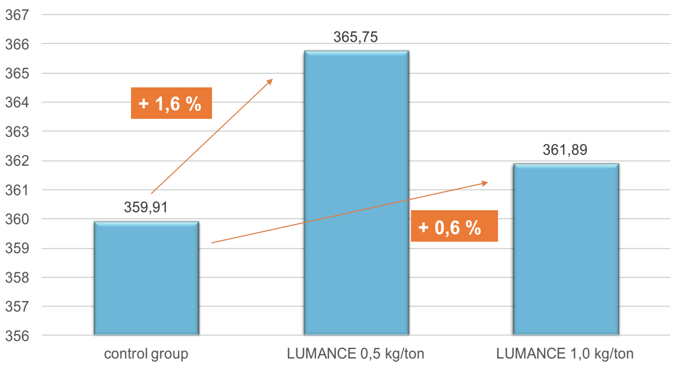
Body weight at 35 days



Feed convertion rate



European Efficiency Index



*European Efficiency Index = ADG (g) * Livebility (%) / (FCR*10)*

Conclusions:

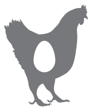
- Both trial groups increased body weight, improved FCR and efficiency index
- Growing curve: advised dosage during pre-starter and starter phase is 1kg/T and during grower and finisher 0,5 kg/T of **Lumance®**.

The dosages of 0,5 – 1 kg/T increased body weight and improved the FCR of broilers. The European efficiency index was improved for even both dosage levels. Based on full details of growing curve, 1 kg/T shall be advised during pre-starter and starter phase, where during grower and finisher 0,5 kg/T is most beneficial.

Scientific *in vivo* experiment with layers

Date: 2014
Location: Department of Animal Sciences, University of Health Sciences, Veterinary Academy, Lithuania

Species:
Layers



Introduction:

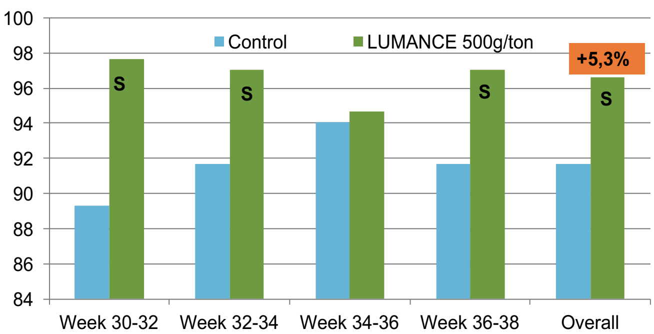
- The trial set up was to investigate the influence of multifunctional feed supplement **Lumance®** on productivity of egg production and quality of eggs.

Protocol:

- 60 layers of Hisex Brown breed
- Age of 30 weeks
- Duration of 56 days
- 2 treatments
  - **Control group:** standard feed
  - **Trial group:** control diet + 0,5kg/T **Lumance®**
- **Parameters measured:**
  - Growth performance parameters
  - Egg quality parameters

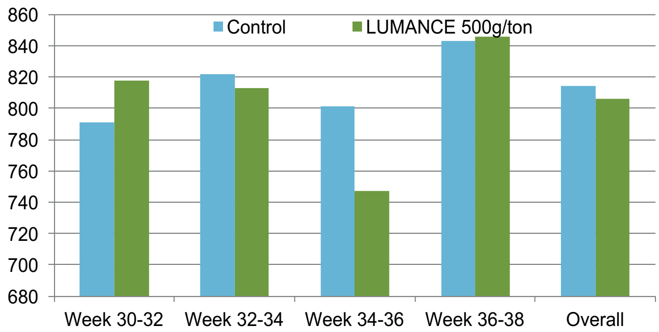
Results:

Laying



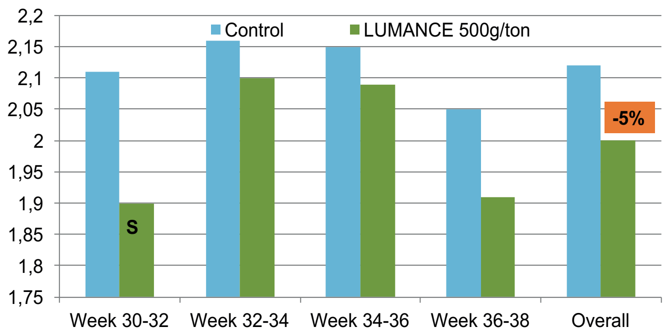
S: Significant difference (p>0,05)

Total egg weight (g)



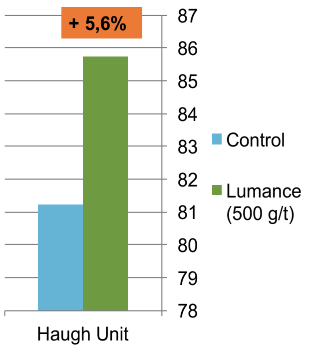
No significant difference in total egg weight or average egg weight.

FCR – Feed to obtain 1 kg of eggs



S: Significant difference (p>0,05)

Egg quality



Egg shell quality

	Control	Lumance® (500 g/ton)	% improvement
Egg shell hardness (kg/m²)	4,01	4,39	+ 9,4
Egg shell weight (g)	6,119	6,098	- 0,4
Thickness at point end (mm)	0,37	0,37	0
Thickness in middle (mm)	0,35	0,37	+5,7
Thickness at blunt end (mm)	0,36	0,37	+2,7
Thickness average (mm)	0,34	0,35	+2,9

Conclusions:

- Improved performance parameters
  – Significant differences in laying percentage, overall +5,3%
  – Significant differences in FCR (feed to obtain 1kg of eggs), overall -5%
- Improved egg shell quality
  – Hardness +9,4%
  – Average thickness +2,9%
- Improved egg quality
  – Haugh unit +5,6%
  – Oxidation rate
- No effects on palatability of yolk and albumen

General outcomes for the trial group were improved performance parameters including an increase of 5,3% in laying percentage and a decrease of the feed conversion ratio. Eggshells showed an improvement in hardness and thickness, meaning less broken eggs. Improved egg quality for certain parameters such as Haugh unit and oxidation rate was established.

Several blood parameters completed the trial. Uric acid level was measured as an indication of protein metabolism and C-reactive proteins as an inflammatory indication. Both parameters showed a numerical decrease due to the supplementation of **Lumance**®.

Presented at WPSA
(Word's Poultry Science Association) Beirut, 2014.
Presented at 12th Tagung zur Schweine- und Geflügelernährung, Martin Luther Universität, Halle Wittenberg, Germany.

Changes in eggs quality of laying hens fed with different amount of organic acids

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The study was conducted to investigate the impact of acids mixture (butyric, lauric and propionic) on the laying hens performance and quality of eggs. The study was performed on 36 Hisex Brown laying hens. The hens (30 wk of age) were assigned to three treatment groups (12 hens per each treatment group). For 8 weeks, the birds were fed compound feed 125 g per day. Hens of Control group were fed on compound feed; the feed of Experimental group I was supplemented with lauric and propionic acids mixture (0.5 kg/t); whereas the feed of Experimental group II contained 2.0 kg/t supplement. All laying hens were kept under the same conditions. Egg quality was determined using automatic egg quality analyzer „Egg Multi-Tester EMT-5200"; hardness of eggshell - the device „Egg Shell Force Gauge MODEL–II", and thickness of eggshell was evaluated with electronic micrometer „MITUTOYO". Draper and Hadley (1990) method (HPLC system) was used to determine content of MDA. During the test period (30-38 weeks) the minimum dosage (0.5 kg/t) of organic acids mixture had a tendency to increase egg quality parameters (except weight), i.e. eggshell hardness and thickness increased by 10% and 3%, respectively and the height of albumen and Haugh unit - by 4% and 6%, respectively compared with that of the Control group ($P<0.05$). In Experimental group II, the opposite was observed: 2.0 kg/t feed organic acids mixture had not effect on egg quality parameters. After storage for 28 days, MDA concentration in the egg yolk in Experimental group I decreased by 0.024 µmol/kg compared to that of the Control group ($P<0.05$). The results of the present study suggest that 0.5 kg/t supplementation of organic acids mixture tend to affect egg quality and MDA concentration, but don't affect eggs productivity and FCR of hens.

Keywords: organic acids; hens; egg quality

Introduction

Feed additives such a
alternative feeding strateg
Besides, they are utilized
(Guathier, 2005; Hernán
banned as a result of incr
Organic acids have been
feedstuffs (Giesen, 2005;
Organic acids includir
control harmful microorg
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The mode of action
accelerates the conversio
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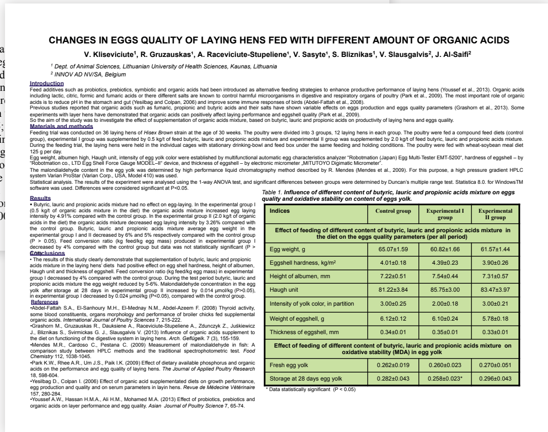

CHANGES IN EGGS QUALITY OF LAYING HENS FED WITH DIFFERENT AMOUNT OF ORGANIC ACIDS

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Introduction

Feed additives such as probiotics, prebiotics, symbiotic and organic acids had been introduced as alternative feeding strategies to enhance productive performance of laying hens (Youssef et al., 2013). Organic acids including lactic, citric, formic and fumaric acids or there different salts are known to control harmful microorganisms in digestive and respiratory organs of poultry (Park et al., 2009). The most important role of organic acids is to reduce pH in the stomach and gut (Yesilbag and Colpan, 2006) and improve some immune responses of birds (Abdel-Fattah et al., 2008).
Previous studies reported that organic acids such as fumaric, propionic and butyric acids and their salts have shown variable effects on eggs production and eggs quality parameters (Grashorn et al., 2013). Some experiments with layer hens have demonstrated that organic acids can positively affect laying performance and eggshell quality (Park et al., 2009).
So the aim of the study was to investigate the effect of supplementation of organic acids mixture, based on butyric, lauric and propionic acids on productivity of laying hens and eggs quality.

Materials and methods

Feeding trial was conducted on 36 laying hens of *Hisex Brown* strain at the age of 30 weeks. The poultry were divided into 3 groups, 12 laying hens in each group. The poultry were fed a compound feed diets (control group), experimental I group was supplemented by 0.5 kg/t of feed butyric, lauric and propionic acids mixture and experimental II group was supplemented by 2.0 kg/t of feed butyric, lauric and propionic acids mixture. During the feeding trial, the laying hens were held in the individual cages with stationary drinking-bowl and feed box under the same feeding and holding conditions. The poultry were fed with wheat-soybean meal diet 125 g per day.
Egg weight, albumen high, Haugh unit, intensity of egg yolk color were established by multifunctional automatic egg characteristics analyzer "Robotmation (Japan) Egg Multi-Tester EMT-5200", hardness of eggshell – by "Robotmation co., LTD Egg Shell Force Gauge MODEL–II" device, and thickness of eggshell – by electronic micrometer „MITUTOYO Digimatic Micrometer".
The malondialdehyde content in the egg yolk was determined by high performance liquid chromatography method described by R. Mendes (Mendes et al., 2009). For this purpose, a high pressure gradient HPLC system Varian ProStar (Varian Corp., USA, Model 410) was used.
Statistical analysis. The results of the experiment were analysed using the 1-way ANOVA test, and significant differences between groups were determined by Duncan's multiple range test. Statistica 8.0. for WindowsTM software was used. Differences were considered significant at $P<0.05$.

Results

• Butyric, lauric and propionic acids mixture had no effect on egg-laying. In the experimental group I (0.5 kg/t of organic acids mixture in the diet) the organic acids mixture increased egg laying intensity by 4.91% compared with the control group. In the experimental group II (2.0 kg/t of organic acids in the diet) the organic acids mixture decreased egg laying intensity by 3.26% compared with the control group. Butyric, lauric and propionic acids mixture average egg weight in the experimental group I and II decreased by 6% and 5% respectively compared with the control group ($P > 0.05$). Feed conversion ratio (kg feed/kg egg mass) produced in experimental group I decreased by 4% compared with the control group but data was not statistically significant ($P >$ 0.05).

Conclusions

• The results of this study clearly demonstrate that supplementation of butyric, lauric and propionic acids mixture in the laying hens' diets had positive effect on egg shell hardness, height of albumen, Haugh unit and thickness of eggshell. Feed conversion ratio (kg feed/kg egg mass) in experimental group I decreased by 4% compared with the control group. During the test period butyric, lauric and propionic acids mixture the egg weight reduced by 5-6%. Malondialdehyde concentration in the egg yolk after storage at 28 days in experimental group II increased by 0.014 µmol/kg ($P>0.05$), in experimental group I decreased by 0.024 µmol/kg ($P<0.05$), compared with the control group.

References

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•Mendes M.R., Cardoso C., Pestana C. (2009) Measurement of malondialdehyde in fish: A comparison study between HPLC methods and the traditional spectrophotometric test. *Food Chemistry* 112, 1038-1045.

Table 1. ***Influence of different content of butyric, lauric and propionic acids mixture on eggs quality and oxidative stability on content of eggs yolk.***

Indices	Control group	Experimental I group	Experimental II group
Effect of feeding of different content of butyric, lauric and propionic acids mixture in the diet on the eggs quality parameters (per all period)			
Egg weight, g	65.07±1.59	60.82±1.66	61.57±1.44
Eggshell hardness, kg/m²	4.01±0.18	4.39±0.23	3.90±0.26
Height of albumen, mm	7.22±0.51	7.54±0.44	7.31±0.57
Haugh unit	81.22±3.84	85.75±3.00	83.47±3.97
Intensity of yolk color, in partition	3.00±0.25	2.00±0.18	3.00±0.21
Weight of eggshell, g	6.12±0.12	6.10±0.24	5.78±0.18
Thickness of eggshell, mm	0.34±0.01	0.35±0.01	0.33±0.01
Effect of feeding of different content of butyric, lauric and propionic acids mixture on oxidative stability (MDA) in egg yolk			
Fresh egg yolk	0.262±0.019	0.260±0.023	0.270±0.051
Storage at 28 days egg yolk	0.282±0.043	0.258±0.023*	0.296±0.043

* Data statistically significant ($P < 0.05$)

Scientific in vitro experiment with broilers: pre-trial

Date: 2014
Location: Oklahoma State University Department of Animal Science, USA

Species:
Broilers

Introduction:

This trial took place with the objective to measure the influence of **Lumance®** on growth performance and host defense peptide gene-inducing activity in broiler chickens.

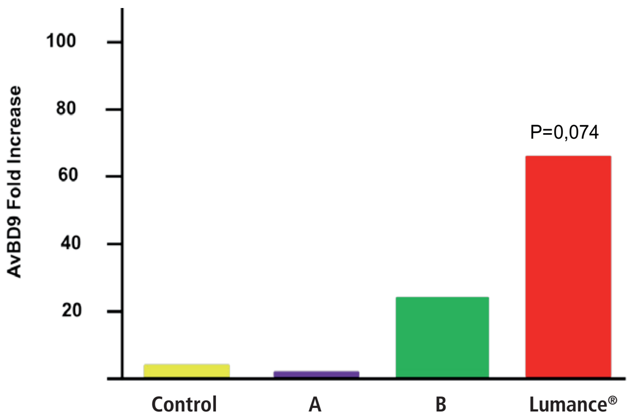
Host defense peptides (HDP), also known as antimicrobial peptides, are present in all species of life and constitute a critical component of the innate immunity. The innate immunity is a passive immunity, it is an important first line defense of the body. HDP possess a broad spectrum of activity against bacteria, protozoa, enveloped viruses and fungi. Therefore, HDP can be an alternative for antibiotics in many cases, however there is still not much known about the dosage, how to provide, etc. HDP have a strong capacity to activate various types of Leukocytes (= white blood cells).
It is a complex mechanism of physical interactions, so it is extremely difficult for pathogens to develop resistance to HDP. Two major families which represent HDP are defensis en cathelicidins.

Protocol:

- 450 day-of-hatch male broilers of Cobb 500 breed
- 5 treatments
  - Control group: antibiotic free corn-soybean basal mash diet
  - 4 Trial groups (T2-T5): control diet + supplementation
    - T4: control diet + 1,5kg/T **Lumance®**
- Setup:
  - 9 birds/pen, 10 pens/ treatment
  - Day 0 – Day 3 : Acclimatization period
  - Day 3 – Day 10: Antibiotic free basal diet + treatment
- Parameters measured:
  - Body weight at day 0 and 7
  - Feed intake on day 0-2-4 and 7
  - Feed conversion ratio (FCR) – calculated
  - HDP gene expression on day 2, 4 and 10 by PCR analysis on Beta-defensin 9 (AvBD9)

AvBD9 was chosen as a representative as it is most highly regulated by butyrate among all chickens HDP genes, situated in the crop of chickens. So a segment of the crop and jejunum was harvested from each bird and snap frozen in liquid nitrogen for RNA extraction and real-time PCR analysis.

Results:



Conclusions:

- Big increase of avBD9 expression in the crop on day 5 and 7
- Strong capacity to induce HDP expression
- Big impact on gut health (enteritis disorders) with long lasting effect

Further research in a more in-depth trial where measurements on intestinal integrity and micro-flora were also monitored (see next trial).

Scientific in vitro experiment with broilers

Date: 2014
Location: Oklahoma State University Department of Animal Science, USA

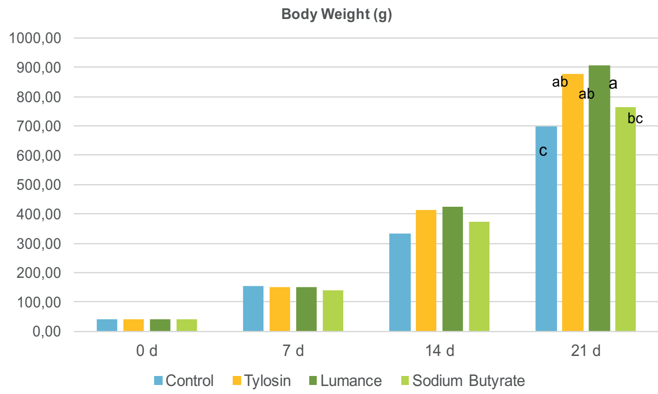
Species:
Broilers

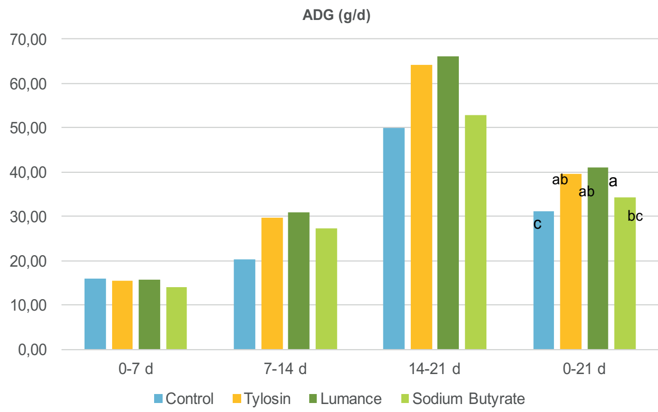
This trial followed from the pre-trial that was done earlier.

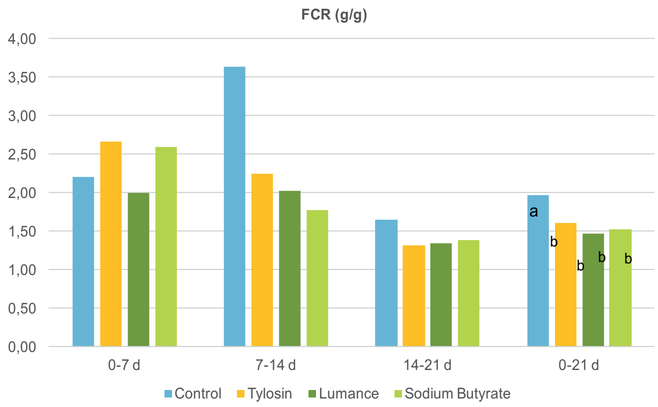
Protocol:

- 350 day-of-hatch male broilers of Cobb 500 breed
- 5 treatments
  - Control group: antibiotic free basal diet
  - 4 trial groups (T2-T5): control diet + supplementation
- T3: control diet + 1 kg/T **Lumance®**
- T5: control diet + 20mg/kg Tylosin (an in-feed antibiotic)
- Setup:
  - 7 birds/pen, 10 pens/ treatment under standard management
  - From day 0 until day 21 of age
- Parameters measured:
- Average body weight (BW)
- Average daily gain (ADG)
- Average daily feed intake (ADFI)
- Feed conversion ratio (FCR) – calculated
- HDP and TJP expression in a segment of the distal jejunum on day 7
- Morphometric measurements in a segment of the proximal ileum on day 21

Results:







Conclusions:

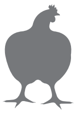
- BW increased significantly by 29,7%
- FCR reduced significantly by 25,4%
- Height of villi enhanced significantly ($p<0,001$)

Lumance® strongly promoted animal growth performance and intestinal health with a similar efficiency to Tylosin, a commonly used in-feed antibiotic, by enhancing the intestinal development and nutrient absorption. **Lumance®** therefore has the potential to be used as an effective alternative to antibiotics.

Scientific *in vivo* experiment with broilers

Date: September – November 2015
Location: Independent Research Center, Czech Republic

Species:
Broilers



Introduction:

The objective was to evaluate the effects of supplementation of chosen feed additives on performance of chicken broilers from 1st to 35th day of age.

Protocol:

- 1.440 one-day male broilers of ROSS 308 breed
- 6 treatments
  – Control group: commercial mash feed mixture without any feed additive
  – 5 trial groups (T2-T6): control diet + chosen feed additives
- T4: control diet + **Lumance®**
- Feeding regime of **Lumance®**:
  – Starter (14 days) 1 kg/T
  – Grower (15-28 days) 0,5 kg/T
  – Finisher (29-35 days) 0,25 kg/T
- Setup: 48 boxes with 30 birds each, 8 repetitions/treatment
- Parameters measured: growth performance parameters:
  – Body weight (BW)
  – Average daily feed intake
  – Average daily body weight gain (BWG)
  – Feed conversion ratio (FCR)
  – Mortality

Results:

Lumance® improved growth parameters of broilers following 35 days of supplementation *(See Figures 1 and 2)* as compared to the control group. ADG, ADFI and ALW were significantly increased on birds with **Lumance®** throughout the experiment. FCR were improved by 3 points with supplemented group. This improvement is due to improved ADG while ADFI is similar to control, which indicates efficiency in digestion and utilisation of nutrients. In addition to efficiency, ALW were significantly increased at the end of trial.

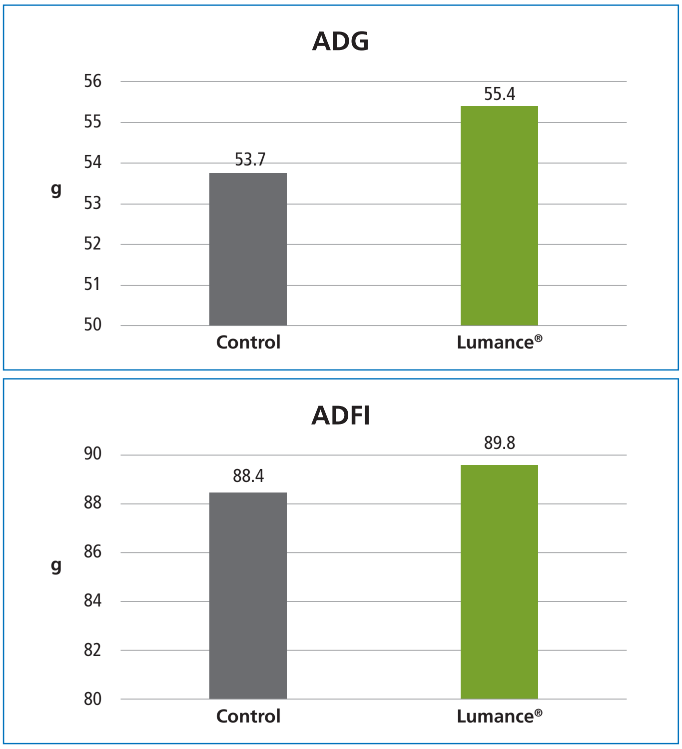


Figure 1. Average daily gain (ADG) and Average feed intake (ADFI) of birds at 35 days growing.

Criteria of performance		Control	Lumance®
Body weight	kg/bird	**1.943**	**1.980**
	SD	0.049	0.046
	Diff. to Control (%)	x	+1.91
	P-value	x	0,590
Feed intake	g/bird/day	**88.36**	**89.80**
	SD	2.883	1.822
	Diff. to Control (%)	x	+1.63
	P-value	x	0,708
Weight gain	g/bird/day	**53.73**	**55.35**
	SD	1.175	1.217
	Diff. to Control (%)	x	+3.01
	P-value	x	0,185
Feed conversion	kg/kg weight gain	**1.645**	**1.623**
	SD	0.017	0.015
	Diff. to Control (%)	x	-1.34
	P-value	x	0,172
Mortality	%	2.083	0.83
	SD	2.857	2.205
	Diff. to Control (%)	x	-1.25
	P-value	x	0,919

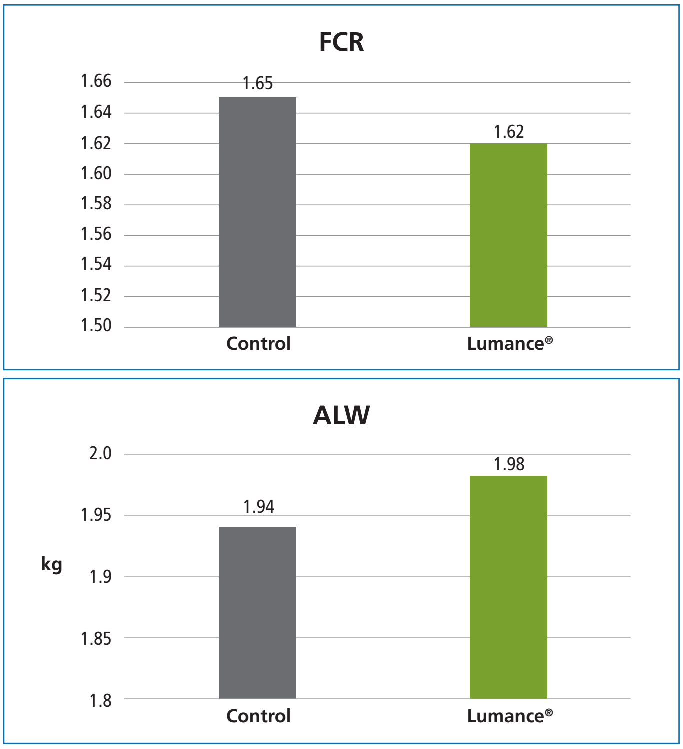


Figure 2. Feed conversion ratio (FCR) and Average live weight (ALW) of birds at 35 days growing.

Conclusions of Lumance® over the whole trial period:

- Numerically higher intensity of growth
- Statistically significant best feed conversion ratio (p<0,05)

Lumance® improved growth parameters of broilers following 35 days of supplementation *(See Figures 1 and 2)* as compared to the control group. ADG, ADFI and ALW were significantly increased on birds with **Lumance®** throughout the experiment. FCR were improved by 3 points with supplemented group. This improvement is due to improved ADG while ADFI is similar to control, which indicates efficiency in digestion and utilization of nutrients. In addition to efficiency, ALW were significantly increased at the end of trial.

Scientific *in vivo* experiment with broilers

Date: 2018 (on going trial)
Location: Applied Animal Research Center, Mexico

Species:
Broilers

Introduction:

This trial shows effectiveness of **Lumance®** for secure protection against necrotic enteritis in broilers, replacing antibiotics and anti-coccidials.

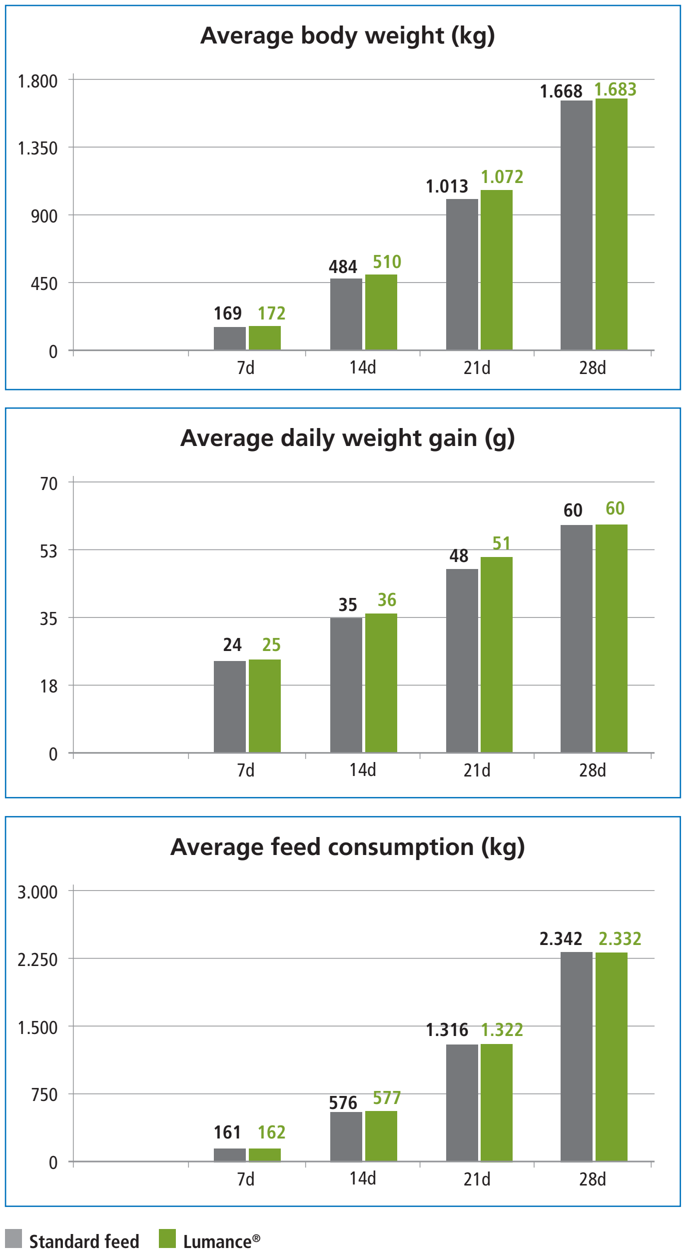
Protocol:

- 496 birds in each group
- **Lumance®** vs standard feed

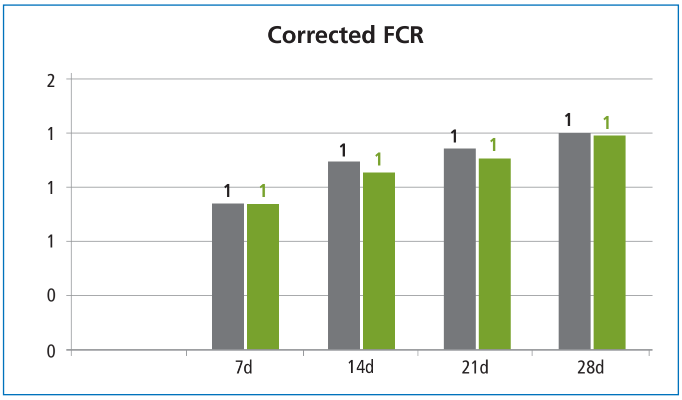
- Standard feed:
  D0 - D21 Nicarbazine (125 ppm)
  D0 - D42 BMD (55 ppm)
  D22 - D28 Salinomycin (66 ppm)
  D29 - D42 Salinomycin (60 ppm)

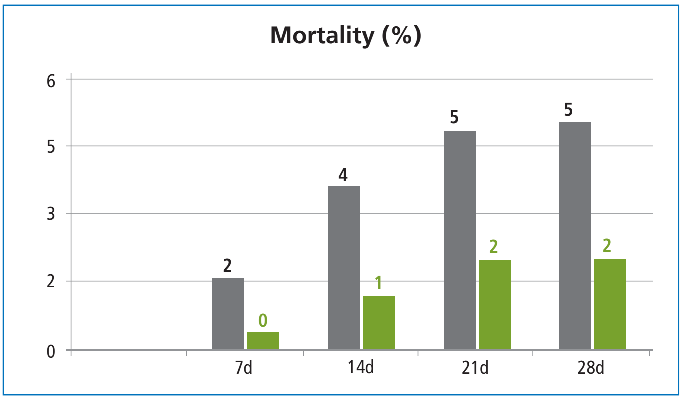
- **Lumance®**
  D0 - D21 : 1.5 kg/T
  D21 - D42 : 1 kg/T
  NO antibiotic growth promoter, NO anti-coccidials

Preliminary Results:



Standard feed Lumance®





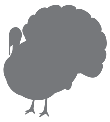
At 28 days of age the group treated with Lumance® shows:

– Better body weigh
– Better average daily weigh gain
– Similar feed consumption
– Better feed conversion
– Significantly lower mortality

Scientific *in vivo* experiment with turkeys

Date: 2017
Location: Field trial, UK

Species:
Turkeys



Introduction:

This trial shows effectiveness of **Lumance®** on performance of turkeys in comparison with regular program of antibiotic growth promoters and anti-coccidals.

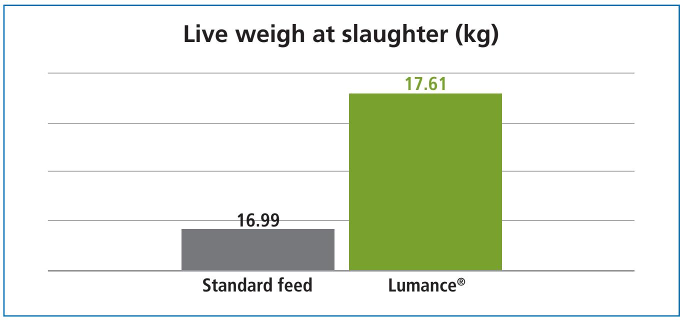
Protocol:

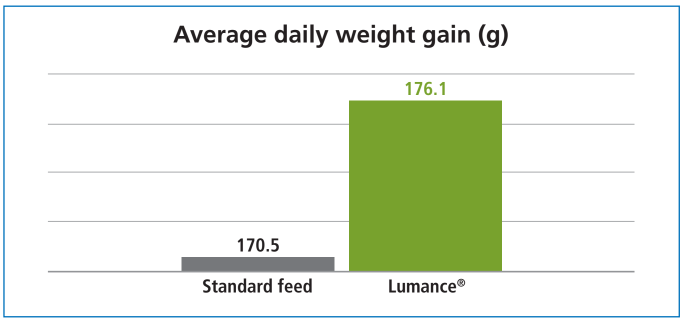
- **Lumance®** vs standard feed
- Control: 19 488 birds (3 houses)
- Trial: 10 250 birds (2 houses)

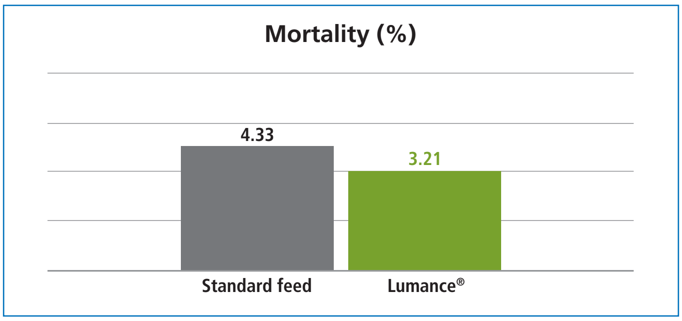
- Standard feed: Regular feeding program

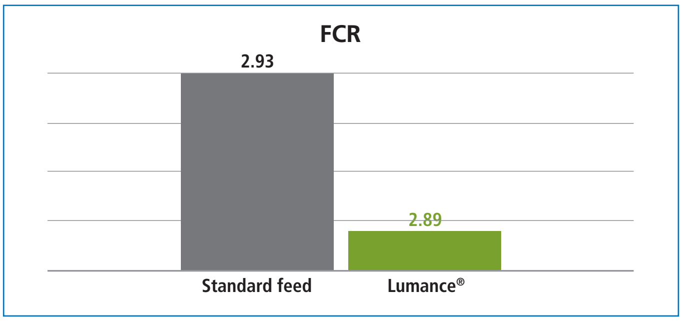
- Trial feed: **Lumance®**

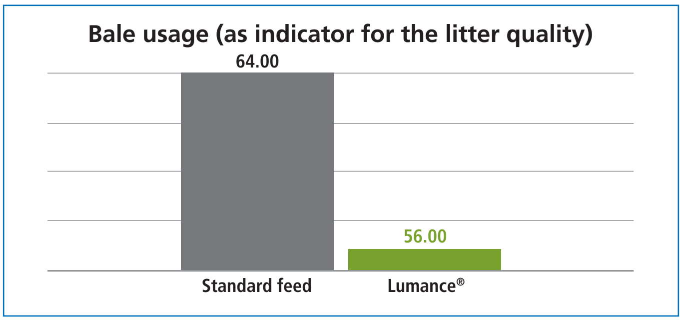
Results:











Turkeys with Lumance® :

– Grow faster
– Are heavier at slaughter
– Have better feed conversion
– Have less mortality

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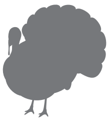
Scientific *in vivo* experiment with turkeys

Date: 2016
Location: Industrial research farm, USA

Species:
Turkeys



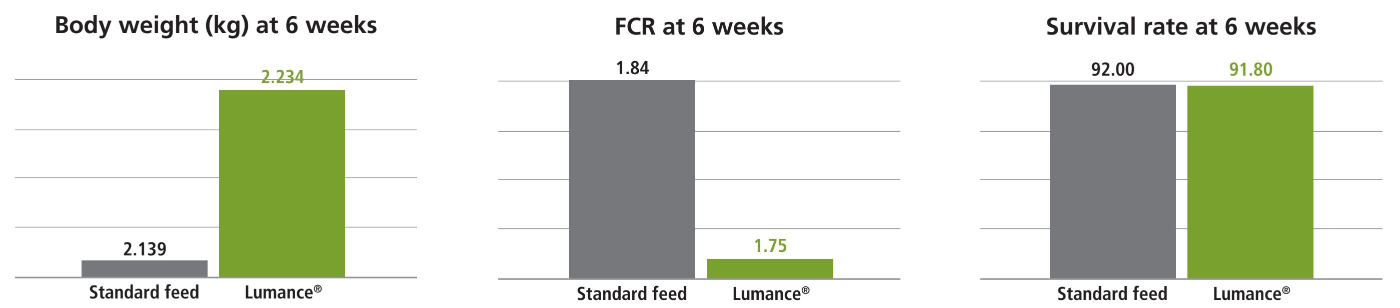
Introduction:

This trial shows effectiveness of **Lumance®** on performance of turkeys in comparison with regular program of antibiotic growth promoters and anti-coccidials.

Protocol:

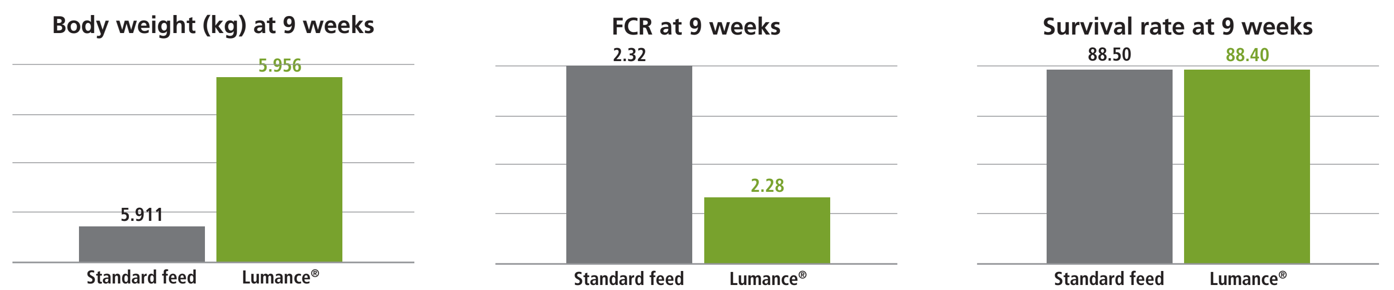
- 100 birds (4 pens x 25 birds in each) in each treatment
- **Lumance®** vs Standard feed
- Standard feed: Regular feeding program with growth promoter and anti-coccidials
- Trial feed: **Lumance®** 2 lb/T (~1 kg/T) for 6 weeks. No growth promoter and no anti-coccidials

Results at 6 weeks:



Significant improvement in average weight gain (respectively body weight) at 6 weeks in Lumance® group ($p<0.07$). Clear difference started from week 2. Improved feed conversion in Lumance® group. Similar liveability in both groups.

Results at 9 weeks:

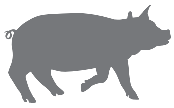


Significantly better average weight gain (respectively body weight) at 9 weeks in Lumance® group ($p<0.466$). Improved feed conversion in Lumance® group ($p<0.104$). Similar liveability in both groups.

Commercial pig trial

Date: 2017
Location: Farm 1600 sows, farrow to finish, Bulgaria

Species:
Pigs



Introduction:

This trial shows effectiveness of **Lumance®** against clinical symptoms of post weaning diarrhoea and improving of the growth performance of pigs weaned without regular use of colistin.

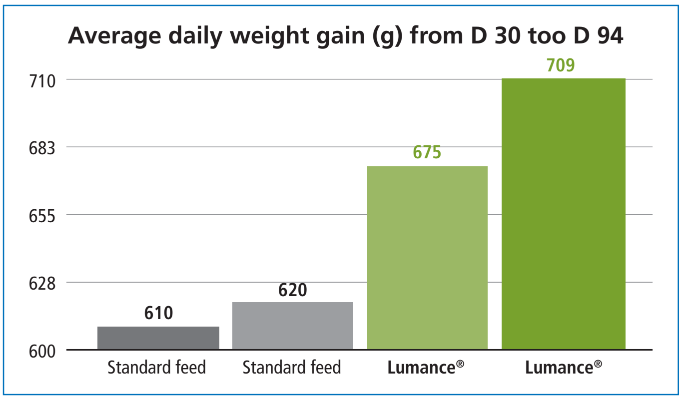
Protocol:

- 400 pigs per each treatment, 2 repeats,
- **Lumance®** vs Standard feed
- From 21 to 94 days of age
- Weaning age - 30 days
- Average weaning weight - 8.5 kg

- **Standard feed:** Colistin 12% 2000 ppm, ZnO 3000 ppm

- Trial feed:
  Lumance® 1.5 kg/T, ZnO 3000 ppm
  Lumance® 1 kg/T, ZnO 2500 ppm

Results:

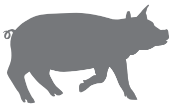


No clinical symptoms of post weaning diarrhoea. 7 days faster to slaughter of pigs treated at weaning with Lumance®.

Commercial pig trial

Date: 2017
Location: Integrator, 33 000 sows, Spain

Species:
Pigs



Introduction:

This trial shows effectiveness of **Lumance®** against clinical symptoms of post weaning diarrhoea and mortality and keeping and improving of the growth performance of pigs weaned without regular use of neomycin and ZnO.

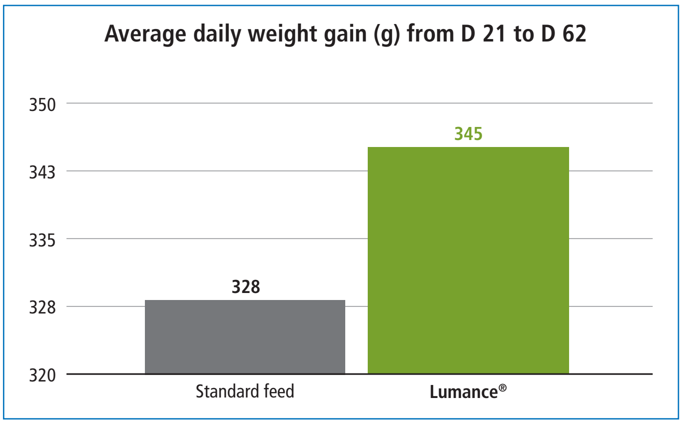
Protocol:

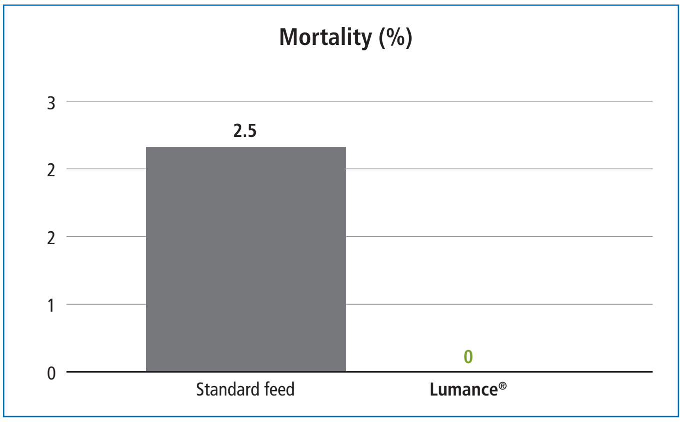
- 40 pigs per each treatment, 2 repeats
- **Lumance®** vs standard feed
- From 21 to 60 days of age
- Weaning age - 21 days
- Average weaning weight - 6 kg

- Standard feed:
  Pre-Starer: Neomycin, ZnO 2500 ppm
  Starter: Neomycin, ZnO 1500 ppm

- Trial feed:
  Lumance® 3 kg/T

Results:





FCR

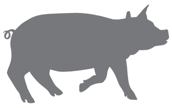
Standard diet	Lumance®
1.45	1.39

No clinical symptoms of post weaning diarrhoea.

Commercial pig trial

Date: 2017
Location: Farm, Spain

Species:
Pigs



Introduction:

This trial shows effectiveness of **Lumance®** against clinical symptoms of post weaning diarrhoea, and keeping and improving of the growth performance of pigs weaned without regular use of ZnO.

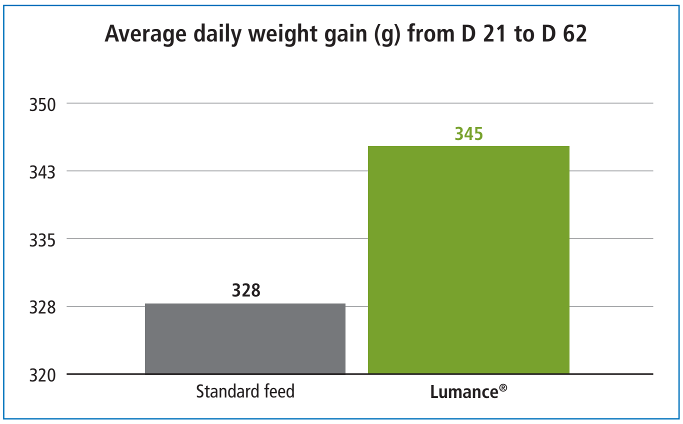
Protocol:

- 100 pigs per each treatment, 3 repeats,
- **Lumance®** vs Standard feed
- From 21 to 54 days of age
- Weaning age - 21 days
- Average weaning weight - 5.2 kg

- Standard feed:
  Pre-Starer: Neomycin, ZnO 2500 ppm
  Starter: Neomycin, ZnO 1500 ppm

- Trial feed:
  Lumance® 3 kg/T

Results:



FCR

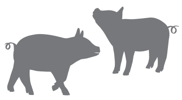
Standard feed	Lumance®
1.35	1.27

No clinical symptoms of post weaning diarrhoea. Better average daily gain and feed conversion in pigs treated with Lumance®.

Commercial Farm Trial in piglets

Date: September – October 2012
Location: 5,000 SL farm in Italy

Species:
Piglets



Introduction:

Antibiotic use is still widely practiced to manage the health and performance of pigs. This trial demonstrates that **Lumance®** can be used to reduce antibiotic while keeping the expected performance of the animal.

Protocol:

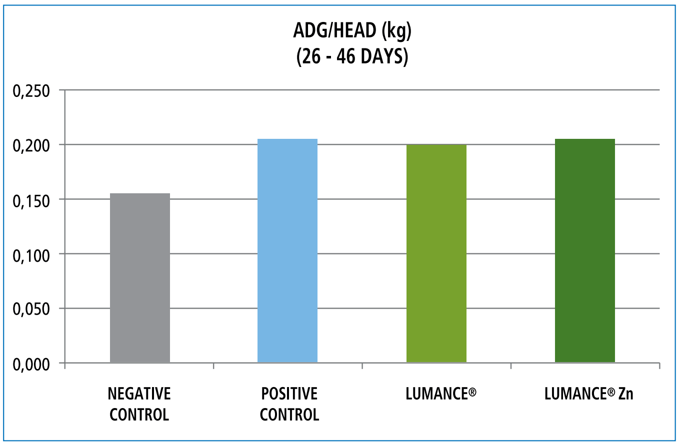
- 320 piglets at weaning (26/27 days old), 2 repetitions
- 4 treatments, 2 pens/treatment, 20 piglets/pen
- Treatments schedule below:

Feed	Treatment	Extra cost compared to Negative Control (€/ton)
Negative Control	500 ppm amoxicillin	—
Positive Control	500 ppm amoxicillin 120 ppm Colistin 3000 ppm Zinc Oxide	16,5
Lumance®	500 ppm amoxicillin 1 kg/ton **Lumance®**	5,5
Lumance® Zn	500 ppm amoxicillin 1,125 kg/ton **Lumance® Zn**	10

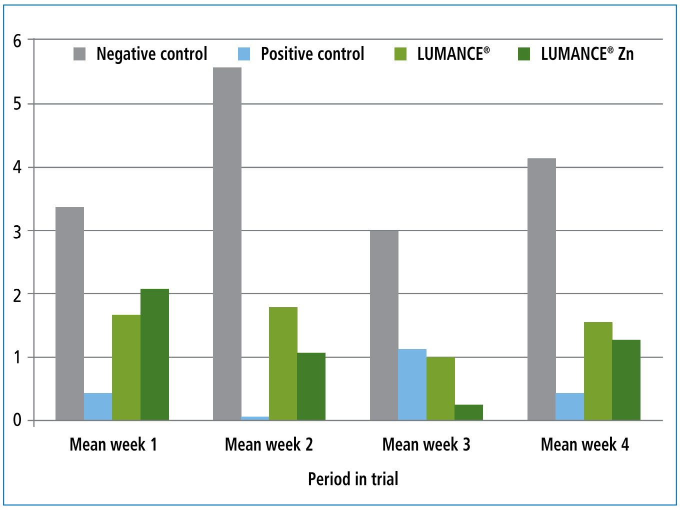
- Parameters Measured: growth performance.
  – Average daily gain
- Medication treatments
  (number of piglets in treatment/day)
- Average fecal scoring

Results:

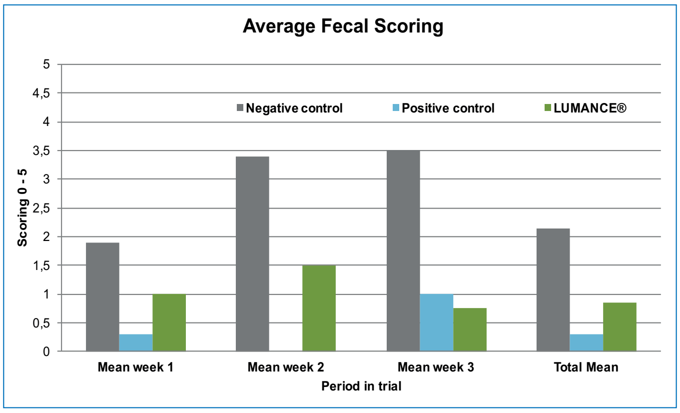
Average daily gain



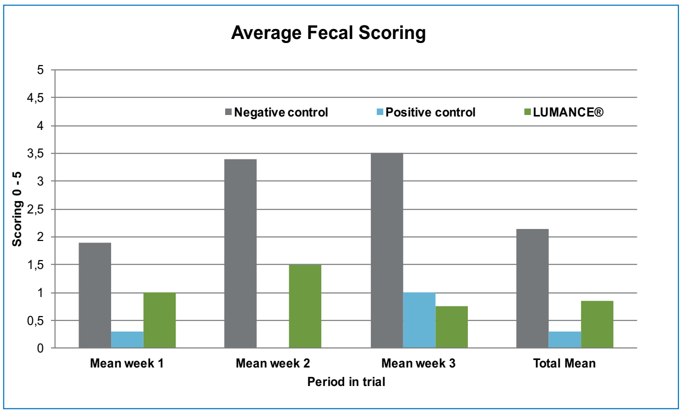
Average number of piglets in treatment/day*

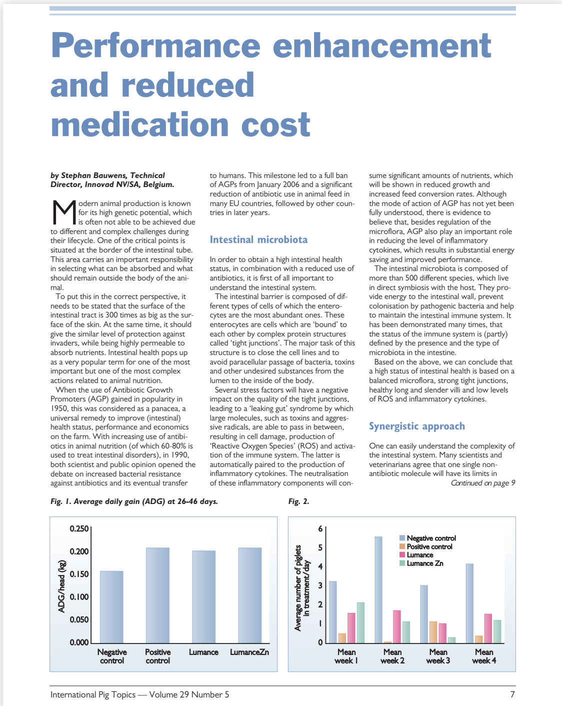


Average daily gain



Average Fecal Scoring





Performance enhancement and reduced medication cost

by Stephan Bauwens, Technical Director, Innovad NV/SA, Belgium.

Modern animal production is known for its high genetic potential, which is often not able to be achieved due to different and complex challenges during their lifecycle. One of the critical points is situated at the border of the intestinal tube. This area carries an important responsibility in selecting what can be absorbed and what should remain outside the body of the animal.

To put this in the correct perspective, it needs to be stated that the surface of the intestinal tract is 300 times as big as the surface of the skin. At the same time, it should give the similar level of protection against invaders, while being highly permeable to absorb nutrients. Intestinal health pops up as a very popular term for one of the most important but one of the most complex actions related to animal nutrition.

When the use of Antibiotic Growth Promoters (AGP) gained in popularity in 1950, this was considered as a panacea, a universal remedy to improve (intestinal) health status, performance and economics on the farm. With increasing use of antibiotics in animal nutrition (of which 60-80% is used to treat intestinal disorders), in 1990, both scientist and public opinion opened the debate on increased bacterial resistance against antibiotics and its eventual transfer to humans. This milestone led to a full ban of AGPs from January 2006 and a significant reduction of antibiotic use in animal feed in many EU countries, followed by other countries in later years.

Intestinal microbiota

In order to obtain a high intestinal health status, in combination with a reduced use of antibiotics, it is first of all important to understand the intestinal system.

The intestinal barrier is composed of different types of cells of which the enterocytes are the most abundant ones. These enterocytes are cells which are 'bound' to each other by complex protein structures called 'tight junctions'. The major task of this structure is to close the cell lines and to avoid paracellular passage of bacteria, toxins and other undesired substances from the lumen to the inside of the body.

Several stress factors will have a negative impact on the quality of the tight junctions, leading to a 'leaking gut' syndrome by which large molecules, such as toxins and aggressive radicals, are able to pass in between, resulting in cell damage, production of 'Reactive Oxygen Species' (ROS) and activation of the immune system. The latter is automatically paired to the production of inflammatory cytokines. The neutralisation of these inflammatory components will consume significant amounts of nutrients, which will be shown in reduced growth and increased feed conversion rates. Although the mode of action of AGP has not yet been fully understood, there is evidence to believe that, besides regulation of the microflora, AGP also play an important role in reducing the level of inflammatory cytokines, which results in substantial energy saving and improved performance.

The intestinal microbiota is composed of more than 500 different species, which live in direct symbiosis with the host. They provide energy to the intestinal wall, prevent colonisation by pathogenic bacteria and help to maintain the intestinal immune system. It has been demonstrated many times, that the status of the immune system is (partly) defined by the presence and the type of microbiota in the intestine.

Based on the above, we can conclude that a high status of intestinal health is based on a balanced microflora, strong tight junctions, healthy long and slender villi and low levels of ROS and inflammatory cytokines.

Synergistic approach

One can easily understand the complexity of the intestinal system. Many scientists and veterinarians agree that one single non-antibiotic molecule will have its limits in

Continued on page 9

Fig. 1. Average daily gain (ADG) at 26-46 days.

Fig. 2.

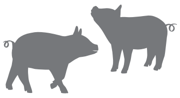
Conclusions:

- Reduction of antibiotics in the feed clearly impacts the performance negatively.
- **Lumance®** and **Lumance® Zn** were able to demonstrate an increase in performance that is comparable with positive control.

Scientific *in vivo* experiment with piglets

Date:
Location: Independent Research Center, Lithuania

Species:
Piglets



Introduction:

The experiment investigated the effect of **Lumance®** on the productive performance of piglets and intestinal disorder. **Lumance®** can be seen as effective additive to improve performance for piglets with challenged health status.

Protocol:

- 2 x 100 piglets (Pietrain x Large White)
- From 30 to 60 days old
- Control vs **Lumance®** (1.5 kg/ton inclusion)
- Parameters measured:
  - BW
  - ADG
  - Number of cases of intestinal disorder

Results:

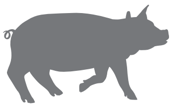
Performance improvement and a reduction in gastro-intestinal disorders with Lumance®				
Piglet	5BW (kg) at Start	BW (kg) at end	ADG	Diagnosed cases of intestinal disorder
Control	10,4 ± 1,35	18,4 ± 0,86	266	18
Lumance®	10,5 ± 1,58	19,2 ± 0,97	290	6

Naturally healthy piglets at optimum performance with Lumance®.

Commercial pig trial

Date: December 2012
Location: Pig Farm JUBILEJNYJ, 33 000 pigs, Belarus

Species:
Pigs



Introduction:

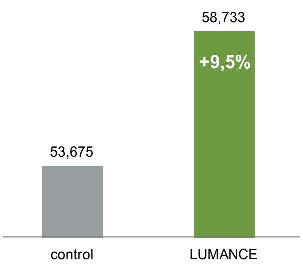
This trial shows improvement of growing pigs using **Lumance®** vs standard feed at the farm. Economic benefits on the farm can be shown in the increased ADG and reduced mortality of the growing pigs.

Protocol:

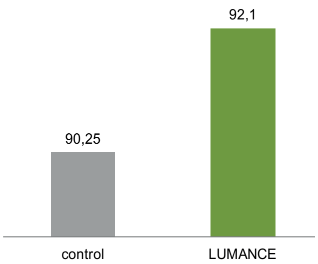
- 500 pigs per treatments, 3 repetition, **Lumance®** vs standard feed
- Feeding: pelleted feed with standard acidifier and toxin binder
- Medication for Control (Olaquindox)
- Growers: 60 to 105 days old
- Starting weight: 9.7 kg for both control and **Lumance®**.

Results:

Average of weight at 105 days old, kg



Total grown pigs at 105 days old (%)



Conclusions:

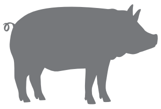
Veterinarian and service staff noticed an improvement of health status of animal under **Lumance®**.

- Less diarrhea and rectal prolapse. Lower medical cost.
- Better feed consumption seen.

Scientific *in vivo* experiment

Date: October 2014
Location: Lithuanian University of Health Science, Veterinary Academy research center, Lithuania

Species:
Pigs



Introduction:

This experiment shows the effect of **Lumance®** on morbidity of diseases and mortality on the farm. Productive performance was also shown to improve.

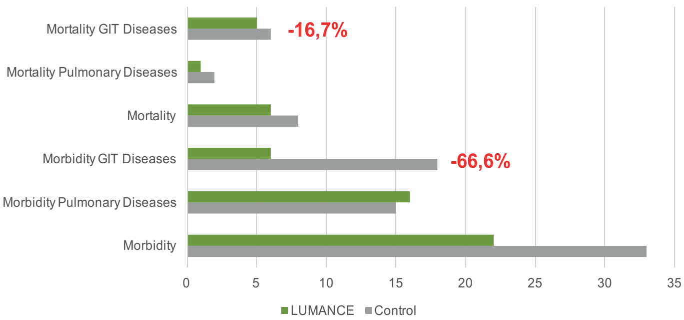
Protocol:

- 150 pigs, 2 repetition (Pietrain x Large White)
- From 70kg to slaughter
- Control vs **Lumance®** (1.5kg/ton inclusion)

Results:

Performance improvement with Lumance®			
Growers	BW (kg) at Start	BW (kg) at end	ADG
Control	70,9 ± 4,89	116,3 ± 6,35	857
Lumance®	71,7 ± 5,23	120,8 ± 4,26	926

**Mortality and morbidity (%)
when using Lumance® vs control**



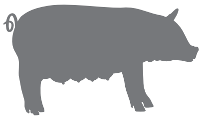
Conclusions:

- Improved growth performance (+8%)
- Lower morbidity (-66%) and mortality (-16%)

Field *in vivo* experiment

Date: March 2016
Location: Swine farm "Brashlen". Danbred farm (2700 sows), Bulgaria.

Species:
Pigs



Introduction:

Following the stricter regulations and recommendations on limiting or eliminating the use of medicated feed and specific antibiotics*, this well run, high performance progressive Danbred pig farm evaluated the use of **Lumance®** in its weaning and pre-starter diets.

- Decision was issued from CVMP (Committee for Medicinal Products for Veterinary Use) concerning vet medicinal products containing colistin in combination with other antimicrobial substances to be administered orally to food producing species. Due to concerns related to antimicrobial resistance and the need to ensure responsible use of the substance in protecting animal health and limiting the possibility of future risk to public health, the CVMP recommended the withdrawal of MA for the products (referral Art 35).

Protocol:

- 2 piglet batches (Danbred breed) fed their weaning/ pre-starter diet (fed before and up to 2 weeks after weaning)
- **Lumance®** : 1kg/Ton inclusion

Results:

Colistin is used constantly in the piglet prestarter and sometimes starter diet. They removed Colistin and replaced it with **Lumance®**.

The comments from the swine manager on farm :
*"**Lumance®** gives us the possibility to replace the antimicrobials in regular use around weaning of the pigs and with that we are already a step closer to reducing antibiotic treatment in our farm"* said Dr. Hristo Stoykov – General Manager of swine farm "Brashlen", one of the best farms of DanBred genetics in the world.

No oedema disease.
No gastrointestinal disorder.
No diarrhea.
Good looking roundish bellies.

Conclusions:

- Very impressed with the pigs' response.

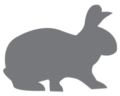
  A step ahead in reducing their antibiotic usage.

  Are now considering continuing with **Lumance®** in their starter feed at 500 g/T.

Scientific *in vivo* experiment with rabbits

Date: 2014 – 2015
Location: Veterinary Academy of Lithuanian University of Health Sciences.

Species:
Rabbits



Introduction:

The trial was conducted to investigate the effect of **Lumance®** on the productivity and digestion process of rabbits.

Protocol:

- 14 Californian rabbits – individually housed
- 2 treatments:
  - – Control
  - – Control + **Lumance®** (2 kg/MT)
- Trial Period: 28 days – 77 days of life
- Parameters measured:
  - – Technical performance (weight, daily weight gain, growth rate, FCR)
  - – Intestinal health parameters (intestinal tract pH, digesta DM content, villi / crypt depth.

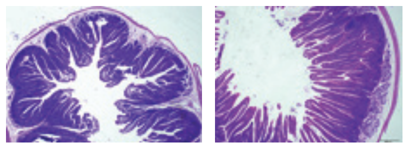
Results:

Performance			
	Control	Lumance®	Relative to control
Live weight at 28 days (g)	483,33	482,97	
Live weight at 77 days (g)	1296,60	1403,30	+8,23%
ADG (g) (28-77 days)	16,60	18,78	+13,1%
Growht rate [1] (28-77 days)	1,68	1,91[a]	+13,6%
Feed consumption (g/day) (28-77 days)	78,25	82,24	+5,09%
FCR (28-77 days)	4,71	4,38	-7,01%

1) Growth Rate = (GS-PS) / PS; where GS - final weight; PS - initial weight (Handa et al., 1995)
a) Differences are statistically different (p<0.05)

Performance		
	Control	Lumance®
Crypt depth (µm)	234.60±8.66	246.14±8.30
Villi height (µm)	571.59±18.43	853.10±25.27*
Villi height/ crypt depth	2.44±0.21	3.47±0.42

* – The data differences are statistically reliable p<0.05



Other parameters:

- Histomorphology of the ileum follows the same trend as the results in the duodenum.
- **Lumance®** shows a significant pH reduction in the lower part of the digestive tract (Colon / Caecum)
- **Lumance®** tends to increase the dry matter content of the digesta in the caecum.

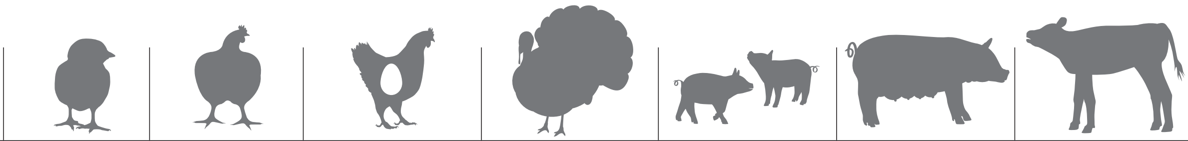
Conclusions:

Lumance® added at 2 kg/MT of rabbit feed had a significant effect on performance (ADG, FCR and growth rate).

This performance improvement is most likely related to a more optimal and healthy gut environment based on the data obtained from histomorphological investigation. Other intestinal health parameters also tend to improve as a result of the addition of the feed additive.

Lumance® application

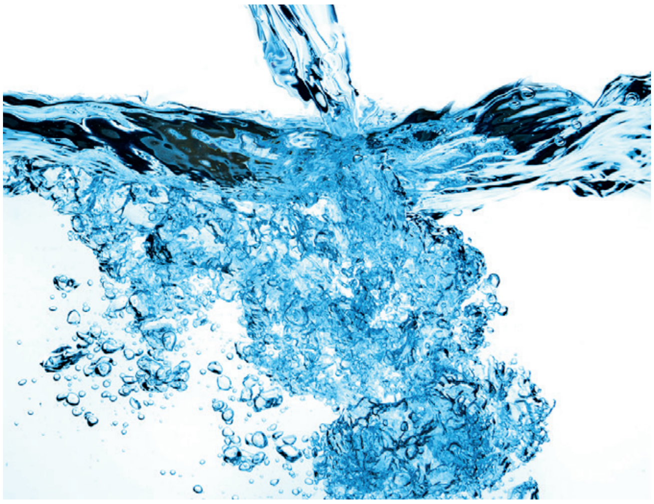
Dosis



Gr/Ton of feed	Chicks	Broilers	layers	turkey	Piglets	Sow	calves
Avg gr/ton of feed	1000	250-1000	500	500-1000	750-1500	500-1000	1000-2000
starter		1000		1000	500		1500
Grower		500	250				
Finisher		250					
Pullets			1000				
Laying			350				
Starter 2				500			
Weaning - Prestarter					1500		
Gestation						500	
Lactation						750	

Packaging

Available in Liquid and dry form



Articles

Weaning piglets without antibiotics

60-80% of antibiotics are used for digestive problems. The period after weaning is known for its regular antibiotic application and could be a perfect target for an important step in antibiotic reduction.

BY MILENA SEVASTIYANOVA, TECHNICAL & COMMERCIAL MANAGER CENTRAL EUROPE AND STEPHAN BAUWENS, TECHNICAL DIRECTOR, INNOVAD

PHOTO: RONALD HISSINK

Restrictive use of antibiotics is no longer an exception, but a global target. Besides the EU, also the US and Asia, started to implement changes. To restrict antibiotic usage (and ZnO in EU) without compromising animal health, welfare and economic viability, it is crucial to understand the complex mechanism that maintains intestinal health and to support and optimise this mechanism with non-antibiotic solutions. Because of the complexity of the intestinal system, scientists and veterinarians agree that one single non-antibiotic molecule has its limits in controlling the overall situation especially with weaning stress, which involves interactions between many factors.

Stable microbiome and pathogen bacteria

A stable intestinal microbiota has important protective and metabolic functions and a major role in the immune system and development of the epithelium and natural defence mechanisms against pathogens. This vast array of intestinal bacteria responds to stress but is also subject to antibiotic induced disturbances.

Various studies confirm a stimulating effect of butyric acid (BA) and medium chain fatty acids (MCFA) on beneficial microflora in pigs while decreasing the number of coliforms (*E. coli*). To guarantee the presence of BA in the intestine, recent attention goes to esterified forms of BA. Similar to triglycerides, they automatically bypass the stomach and the butyric acid molecules are enzymatically released (mainly from di- and tributyrins) by lipase into the small intestine. Polar mono-butyrins pass the hydrophilic membrane of pathogenic bacteria (*E. coli, Salmonella, Clostridium perfringens*), disturbing their metabolism and inactivating them. Mono-glycerides work immediately and are much more antibacterially active compared to the original acid (*Table 1*), which is important when the microbiome is stressed during the weaning process. The effect of MCFA and essential oils, both strong in selective antimicrobial activity, is well documented.

Barrier function and tight junctions

Beyond the compromised digestive and absorptive capacity, the intestinal barrier function and tight junctions' quality are also deteriorated at weaning. BA induces the production of host defence peptides and repair of the intestinal tract architecture through an increased cell proliferation, tight junction assembly and immune cell regulation. At weaning, the activation of the intestinal immune system and up-regulation of genes of pro-inflammatory cytokines lead to a significant inflammatory reaction, resulting in intestinal mucosal injury and dysfunction. The energy needs for an activated immune system increases (>20%). The anti-inflammatory properties of BA and alkaloid rich plant extracts can largely temper the inflammatory reaction, which contributes to an energy saving and growth promoting effect.

Table 1 – MIC (*in vitro*): acid vs mono-esters.

MIC	*S. Typhimurium*	*E. coli*
Butyric acid	1:400	1:400
Mono-esterified butyrins	1:1600	1:800

Innovad 2012

Weaning stress is also related to increased reactive oxygen species (ROS). Glutathione, positively influenced by BA, plays a critical role in many biological processes as major redox-buffer in mammalian cells. An intensive renewal process of the intestinal cells (2-7 days) requires adequate energy supply. SCFA and MCFA stimulate mitosis, maturation and differentiation of intestinal mucosal cells and inhibit their apoptosis.

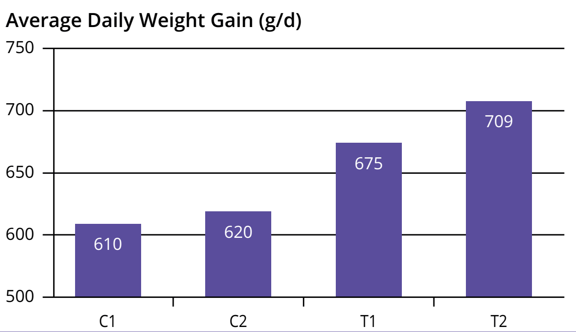
Results from the field

Three trials set out to illustrate the effectiveness of Lumance, a precise and synergistic combination of SCFA and MCFA, plant extracts and essential oils, in a real farm situation on clinical symptoms of post weaning diarrhoea (PWD) and performance of the pigs without antibiotics (for PWD) and in more difficult situations without both – antibiotics and ZnO.

Trial 1: Non-antibiotic for PWD

A group of 1600 piglets (400 piglets per group, 2 repetitions) was set up in a field trial at an integrator farm in Bulgaria. Piglets in the trial groups T1 and T2 were treated with the product in the feed from weaning (D30, 8 kg BW) for 20 days onwards (respectively 1.5 kg/T and 1 kg/T) and ZnO (respectively 3000 ppm and 2000 ppm). Control groups C1 and C2 received, in the feed from weaning, respectively, Colistin (2 kg/T) for 10 days & ZnO (3000 ppm) for 20 days. Clinical symptoms of PWD and average daily weight gain (ADWG) from D30 till D94 were monitored. No symptoms of PWD or increased mortality were observed in treatment or control groups. The results (*Figure 1*) show increased ADWG in T1 with 65 g and T2 with 89 g respectively. Additionally, pigs of T1 and T2 achieved slaughter weight (107 kg) seven days earlier (at 150 days).

Figure 1 - Average daily weight gain (g/d) for the antibiotic control groups (C1 & C2) and the Lumance groups (T1 &T2).



Trial 2: Non-antibiotic and ZnO-free feed for PWD

In a field trial (Spain) 40 piglets in the trial group received the product at 3 kg/T in the feed (D21- D62), starting from the day of weaning (21 days, 6 kg). The control group (40 piglets) was on a regular treatment with Neomycin 150 ppm (D21- D42) and ZnO (2500 ppm from D21-D42 and 1500 ppm from D42-D62). Live weight (*Figure 2*), FCR, mortality and PWD-symptoms were monitored from D21 till D62.
ADWG was similar for both treatments. FCR: Control = 1.45; Lumance =1.39. Mortality: Control = 2.5%; Lumance = 0%. PWD symptoms were observed in 1 box of the control group.

Trial 3: Non-antibiotic and ZnO-free feed for PWD vs with or reduced antibiotic and ZnO-feed – preliminary results

In a large field trial (Spain) 2423 piglets/four treatments/four repetitions per treatment: T1 (576 pigs) – only Lumance (3kg), T2 (608 pigs) – Lumance (3kg) + ZnO 1500 ppm, T3 (616 pigs) – Lumance (3kg) + Apramycin, C1 (623 pigs)- regular treatment with ZnO + Apramycin). All treatments started from day of weaning (21d, 5.8 kg). PWD and ADWG from D21 till D48 were monitored. No differences in ADWG or quality of the pigs were observed between groups at the end of the period. The difference in ADWG between the best performing group and the weakest group is only 14 g per piglet. (*Figure 3*). In terms of general results (based on the preliminary data) the results are comparable between the different scenarios.
The Lumance concept supports the mechanisms of intestinal health: strong tight junctions, long and healthy villi, balanced microflora, low levels of ROS and inflammatory cytokines. It prevents PWD similarly to standard antibiotics, but in addition it has the potential to improve animal performance and even effectively prevent PWD and keep performance in the most difficult scenarios without antibiotics and ZnO.

References available on request

Figure 2 - Performance data (kg LW) of control versus Lumance.

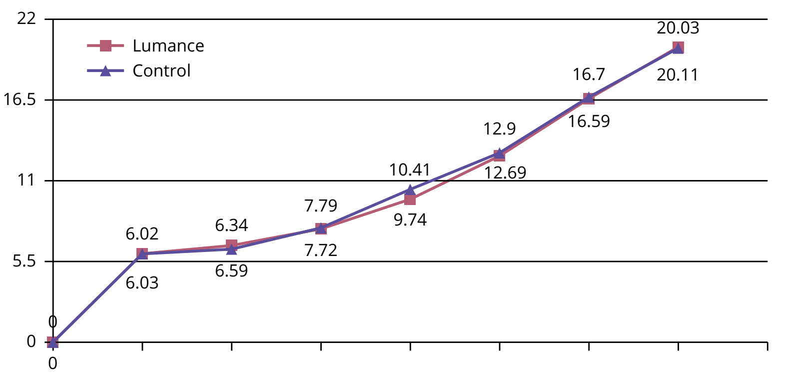
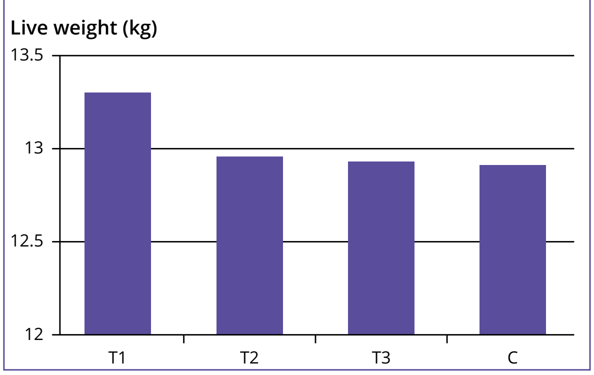


Figure 3 - Live weight (kg) of the piglets at the end of the trial (D48).



Gut integrity, intestinal microbiota and intestinal barrier or the strategy for enhanced performance and reduced medication and ZnO

By Dr. Milena Sevastiyanova

Abstract

The gut carries an important responsibility in selecting what can be absorbed and what should remain outside the body. To put this in the right perspective, it is important to note that the surface of the intestinal tract is 300 times the size of the surface of the skin.

Post-weaning diarrhoea (PWD) causes mortality and morbidity in pig production and is a reason for regular antibiotic treatment. Two concerns are related with PWD:

- Lost profit due to mortality, lower average daily weight gain (ADWG), additional medication costs.
- Recommendation of European Medicines Agency for reducing the usage of Colistin related to the risk of antimicrobial resistance.

To reduce (stop) antibiotics for PWD and to enhance performance is crucial to understand and to support the complex mechanism that maintains the gut health. This trial investigated the effectiveness of in feed combination of short and medium chain fatty acids, plant extracts and essential oils (**Lumance®**, Innovad®, Belgium) on PWD and ADWG in a commercial farm in Bulgaria.

Introduction

The gut integrity and microbiota appear to be the key for a mechanism that maintains the gut health. Supporting the intestinal barrier to decrease the risk of infectious and inflammation is crucial. Tight junctions have a major task to avoid paracellular passage of undesired substances from the lumen to the inside of the body. Different factors could have a negative impact on the tight junctions, leading to "leaking gut" which resulting further in cell damage, production of "Reactive Oxygen Species" (ROS) and activation of the immune system. This automatically unlocks the production of inflammatory cytokines. Their neutralisation will consume significant amounts of nutrients, leading to reduced growth and increased FCR. It is documented that butyrate enhances the intestinal barrier by facilitating tight junction assembly and regulating of immune cells function (1,2). Butyric acid contributed with plant extracts rich alkaloids show strong anti-inflammatory action, improved gain and FCR. Butyrate stimulates epithelial cell proliferation ensuring larger absorptive surface and improved feed utilisation. It preserves

Lumance® suppresses inflammatory response in LPS-stimulated macrophages through inhibition of nitric oxide synthase, suitable as antibiotic replacement

Alireza Khadem[1,2], Jamal Al-Saifi[2], Ben Letor[2], Stephan Bauwens[2], Francis Combes[3] and Niek Sanders[3]

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3 Laboratory of Gene therapy, Faculty of Veterinary Medicine, Ghent University, Merelbeke, Belgium

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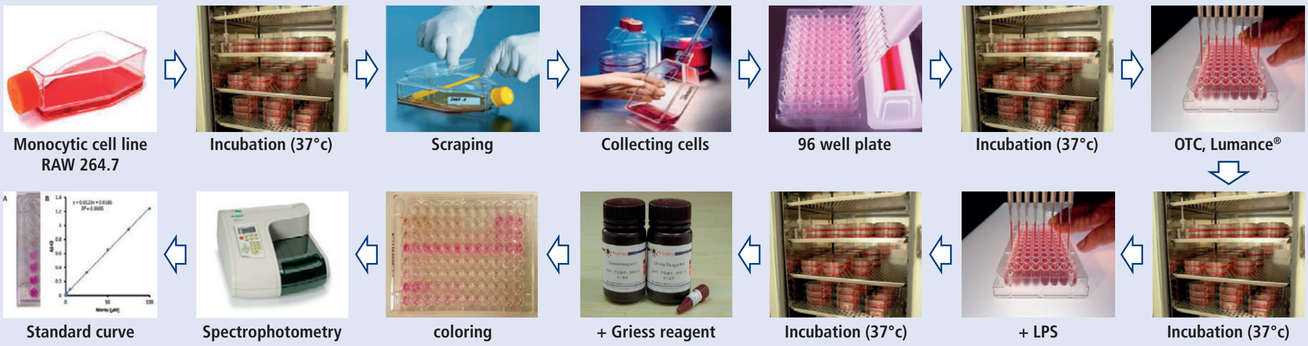
Introduction

- Inflammation resulting from either feed or disease is inversely related to growth and health.
- Earlier, the beneficial effects of antimicrobial growth promoters (AGP) were attributed to their antibiotic character.
  This is unlikely for a variety of reasons:
  - i) Sub-therapeutic concentrations used
  - ii) The absence of a relationship between antibiotic activity and spectrum
  - iii) AGP still appeared to work in the presence of widespread antibiotic resistance
- It has therefore been proposed that AGP such as oxytetracycline (OTC) work rather by direct inhibition of the (intestinal) inflammatory response (Niewold., 2007).
- Consequently, alternatives to AGP should be anti-inflammatory rather than antibiotic.
- Among the proposed anti-inflammatory alternatives to antibiotics is **Lumance**® (Mixture of SCFA, MCFA, essential oil and plant extract) with anti-inflammatory activities (Innovad® NV/SA, Berchem, Belgium).

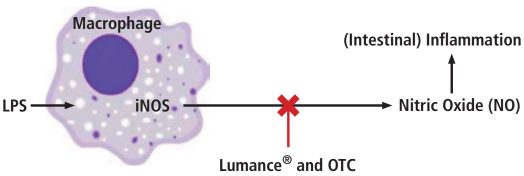
Materials and Methods

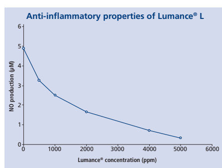
- Anti-inflammatory activity of **Lumance**® and OTC was tested using the RAW 264.7 assay, as described by Wu et al (2003).



Results

- **Lumance**® and OTC had a strong anti-inflammatory effect *in vitro* and inhibited LPS-induced Nitric Oxide production by macrophages.
- **Lumance**® is an effective alternative for AGPs (OTC) which have direct anti-inflammatory effects on the animals gastrointestinal track.





Discussion

- **The non-antibiotic anti-inflammatory theory of antimicrobial growth promoters (AGP) predicts that effective alternatives can be selected by specific *in vitro* tests.**
- **Effective growth promoters must be inhibitors of inflammatory responses, including metabolic inflammation.**
- **Innovad®'s technology with Lumance® confirms the ability to successfully replace the anti-inflammatory and antibacterial effect of antibiotics geared towards digestive problems.**

Reference: *Niewold et al. (2007); Wu et al (2003).*

Performance enhancement and reduced medication cost

by Stephan Bauwens, Technical Director, Innovad NV/SA, Belgium.

Modern animal production is known for its high genetic potential, which is often not able to be achieved due to different and complex challenges during their lifecycle. One of the critical points is situated at the border of the intestinal tube. This area carries an important responsibility in selecting what can be absorbed and what should remain outside the body of the animal.

To put this in the correct perspective, it needs to be stated that the surface of the intestinal tract is 300 times as big as the surface of the skin. At the same time, it should give the similar level of protection against invaders, while being highly permeable to absorb nutrients. Intestinal health pops up as a very popular term for one of the most important but one of the most complex actions related to animal nutrition.

When the use of Antibiotic Growth Promoters (AGP) gained in popularity in 1950, this was considered as a panacea, a universal remedy to improve (intestinal) health status, performance and economics on the farm. With increasing use of antibiotics in animal nutrition (of which 60-80% is used to treat intestinal disorders), in 1990, both scientist and public opinion opened the debate on increased bacterial resistance against antibiotics and its eventual transfer to humans. This milestone led to a full ban of AGPs from January 2006 and a significant reduction of antibiotic use in animal feed in many EU countries, followed by other countries in later years.

Intestinal microbiota

In order to obtain a high intestinal health status, in combination with a reduced use of antibiotics, it is first of all important to understand the intestinal system.

The intestinal barrier is composed of different types of cells of which the enterocytes are the most abundant ones. These enterocytes are cells which are 'bound' to each other by complex protein structures called 'tight junctions'. The major task of this structure is to close the cell lines and to avoid paracellular passage of bacteria, toxins and other undesired substances from the lumen to the inside of the body.

Several stress factors will have a negative impact on the quality of the tight junctions, leading to a 'leaking gut' syndrome by which large molecules, such as toxins and aggressive radicals, are able to pass in between, resulting in cell damage, production of 'Reactive Oxygen Species' (ROS) and activation of the immune system. The latter is automatically paired to the production of inflammatory cytokines. The neutralisation of these inflammatory components will consume significant amounts of nutrients, which will be shown in reduced growth and increased feed conversion rates. Although the mode of action of AGP has not yet been fully understood, there is evidence to believe that, besides regulation of the microflora, AGP also play an important role in reducing the level of inflammatory cytokines, which results in substantial energy saving and improved performance.

The intestinal microbiota is composed of more than 500 different species, which live in direct symbiosis with the host. They provide energy to the intestinal wall, prevent colonisation by pathogenic bacteria and help to maintain the intestinal immune system. It has been demonstrated many times, that the status of the immune system is (partly) defined by the presence and the type of microbiota in the intestine.

Based on the above, we can conclude that a high status of intestinal health is based on a balanced microflora, strong tight junctions, healthy long and slender villi and low levels of ROS and inflammatory cytokines.

Synergistic approach

One can easily understand the complexity of the intestinal system. Many scientists and veterinarians agree that one single non-antibiotic molecule will have its limits in

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Fig. 1. Average daily gain (ADG) at 26-46 days.

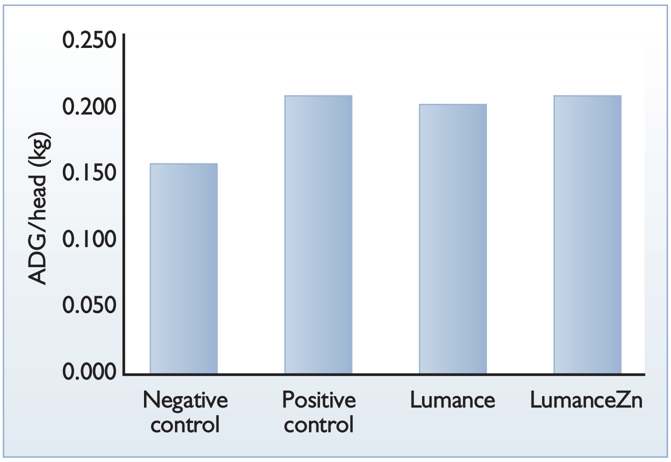
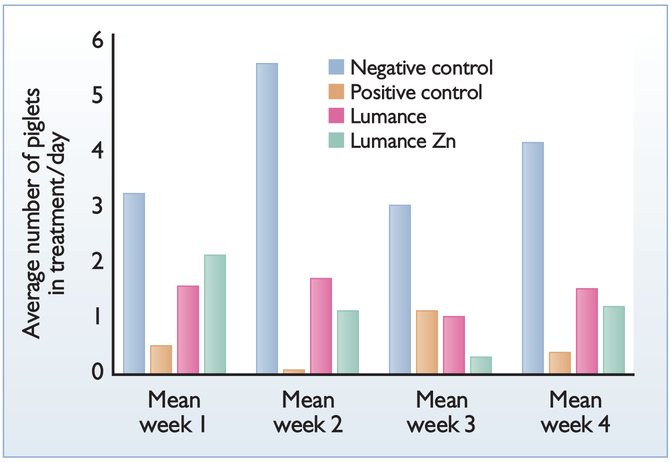


Fig. 2.



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order to control the overall situation. Therefore Lumance proposes a concept and a synergistic approach to ensure a high intestinal health status. Lumance is a complex combining slow release and protection technologies ensuring that acids, medium chain fatty acids, butyrate, essential oils, anti-inflammatory compounds and polyphenols are delivered in a gut active way for a powerful and effective antibacterial control, high quality tight junctions, neutralisation of the produced ROS and tempering of the inflammatory cytokine production.

In an Italian pig trial, a positive control (500ppm amoxicillin, 120ppm colistin and 3000ppm zinc oxide) was compared with a negative control (500ppm amoxicillin) and two treatments (500ppm amoxicillin + 1kg Lumance and 500ppm amoxicillin + 1kg Lumance Zn).

Both treatments were more economical compared to the positive control. The negative control clearly demonstrated the challenge on the farm by reduced performance, high medication use and negative faecal scoring. Both Lumance and Lumance Zn were able to totally compensate for the loss in performance up to the same level as the positive control.

Antibiotic treatment was strongly reduced and faecal scoring was significantly improved compared to the negative control, for which Lumance Zn showed a slight advantage.

Piglets	BW (kg) at start	BW (kg) at end	ADG (g)	Diagnosed cases of intestinal disorders
Control	10.4±1.35	18.4±0.86	266	18
Trial	10.5±1.58	19.2±0.97	290	6

Table 1. Piglet trial results.

Pigs	BW (kg) at start	BW (kg) at end	ADG (g)	Diagnosed cases of intestinal disorders
Control	70.9±4.89	116.3±6.35	857	16
Trial	71.7±5.23	120.8±4.,26	926	6

Table 2. Pig trial results

On a university experimental farm in Lithuania, two groups of 200 piglets (Pietrain x Large White) were divided into two groups (Table 1). A control diet was compared to a treatment with 1.5kg/ton of Lumance from 30 to 60 days of age.

In a second trial, 300 finishing pigs (Pietrain x Large White) were divided into two groups following the same treatment from 70kg of live weight up to slaughter (Table 2).

In both the piglet and pig trial performance was improved in favour of the Lumance treatment, while a clear reduction was observed in gastro-intestinal disorders.

The high genetic potential of today's production animals, combined with a clear and inevitable tendency to reduce the use of antibiotics, resulting in an increased risk of enteric problems, is a complex situation to manage.

Obviously, a one single molecule approach is not dealing with all aspects of intestinal health management and will never be able to compete with conventional use of antibiotics. Lumance, being a synergistic concept, has been shown to be a valid alternative for reduced use of antibiotics. In addition, Lumance has proven to be a valid performance enhancer, even in the absence of an intestinal challenging situation. ■

Butyrate: A tool to improve gut health

The goal to further reduce antibiotic use in animal production is a serious challenge. Adding unprotected sodium butyrate to the diet, have shown promise in promoting growth and productivity, and can therefore be used as effective alternatives to antibiotics.

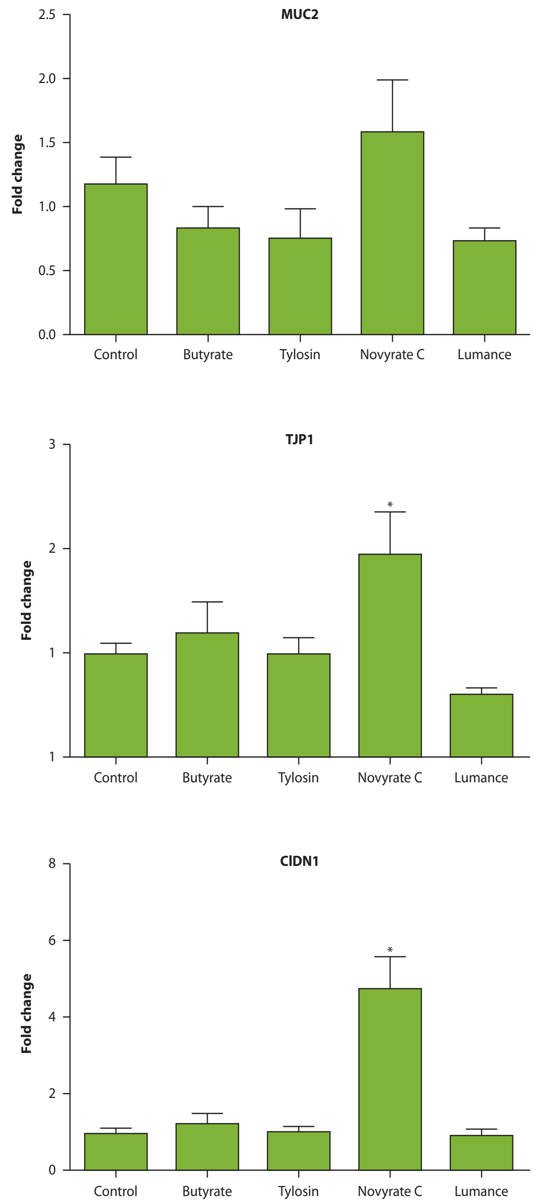
By Stephan Bauwens, technical director Innovad, Belgium

The ban on antibiotic growth promotors in the EU was the first step in the strategy to dealing with antibiotic use and the antibiotic resistance issue. At the same time, today's high performing animal production systems challenge the health and well-being of the animal in general and the intestinal health in particular. Intestinal health comes up as a very popular term for one of the most important yet one of the most complex actions related to animal nutrition. A high status of intestinal health is based on a balanced microflora, an optimal intestinal tract and all interactions between both.

Desirable effects on gut health

Organic acids have been used as an alternative for antibiotic use in feed for decades. Mainly short chain fatty acids have shown many desirable effects on gut health by enhancing cell growth and proliferation and intestinal barrier function, while reducing inflammation and oxidative stress. However, because of rapid absorption and metabolism, free unprotected SCFA generally showed a marginal effect in disease control. Alternative forms of butyrate, encapsulated or esterified are more desirable as the release of the active ingredient is programmed to be further down in the intestinal tract. Besides many desirable effects that have been described for SCFA in literature, a new immune boosting function has been revealed. SCFA, butyrate in particular, have a strong capacity to enhance synthesis of endogenous antimicrobial host defense peptides, which are critical components of the animal's innate immunity. Botanical components are commonly used as additional/synergistic active and antimicrobial feed additives. But the world of flora is much richer than only antimicrobial compounds. Strong anti-inflammatory components and anti-diarrhoeal extracts can be selected, which fit very well in the concept of antibiotic replacement.

Figure 1- Impact of different treatments on expression level of tight junction proteins and mucin proteins.



Poultry trial with butyrate

In order to verify the efficacy of different sources of butyrate, whether or not in combination with botanical extracts, a research trial was set up in broilers. Different groups received different diets: Diet A was the control group. Second group received 1 g/kg powdered Sodium Butyrate (unprotected) (SB) (diet B), third group received 20 mg/kg Tylosin (diet C). Diet D was an antibiotic-free basal diet supplemented with or without 2 g/kg of a butyric acid*. Diet E was 1 g/kg of a a complex combining slow release and protection technologies**. Diet E was the control group. The diets were fed for 21 days. It was shown that diets C, E and D all had a strong tendency to improve growth performance of broilers following three weeks of supplementation (*Table 1*).

Compared to the control group, diet C and D significantly increased the BW, ADG, and FCR of chickens ($P < 0.05$) without affecting the ADFI over a period of three weeks. Overall, diet D and E were comparable to, if not better than, diet C. Chickens in diet group D had significantly higher BW and ADG in the first week than all other groups ($P<0.05$), whereas group C and E did not show an enhancement of BW and ADG until the second week.

At the end of the third week, as compared to the control group, the BW of the group C, D and E increased significantly by 25.5%, 29.7%, and 25.6%, respectively. Because of largely no significant differences in ADFI among these four groups throughout the entire three weeks, the FCR in the group C, D and E reduced significantly by 28.9%, 25.4%, and 18.3%, respectively, relative to the control group. Such differences began to show up from the second week.

Overall, the results clearly indicated that supplementation of 2 g/kg of the diet D and 1 g/kg of diet E strongly promoted animal growth performance with a similar efficiency to a commonly used feed antibiotic.

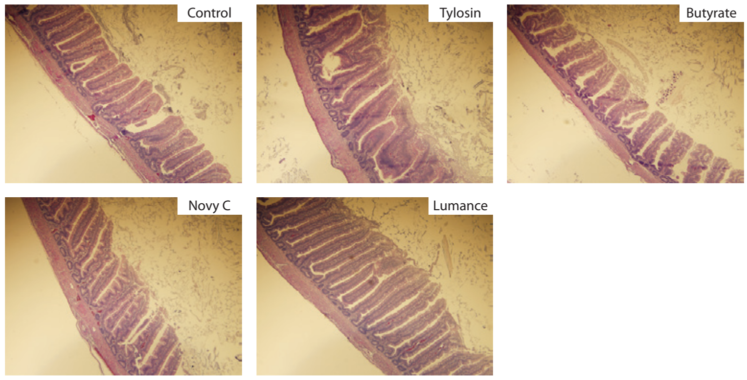
Effect of target release

It is also worth mentioning that feed supplementation with 1 g/kg of diet B showed a numerical, but statistically insignificant increase ($P>0.05$) in the BW at the end of the second and third week, relative to the control group. However, because of a trend ($P>0.05$) in reducing the feed intake, the birds fed unprotected butyrate showed a significant improvement ($P<0.05$) in the FCR over the control group and were comparable to those of the other groups.

However, group B showed an obvious but insignificant reduction in BW and ADG as compared with the diet group D or E, both of which contain target released sodium butyrate, suggesting that butyrate microencapsulation or esterification enhances feed intake and growth performance of birds.

Consistent with the role of butyrate in barrier protection, diet A significantly increased the expression levels of several major tight junction proteins including claudin-1 (CLDN1) and TJ-protein-1 (TJP1 or ZO1) ($P < 0.05$) (*Figure 1*). It is noted that unprotected butyrate lost its ability to induce CLDN1 and TJP1 gene expression, presumably due to its quick metabolism and degradation in the GI tract, reinforcing the positive effect of butyrate coating and protection.

Figure 2- Impact of different treatments on villus height.



Diet D also had a tendency to increase the expression of mucin-2 (MUC2), the most abundant intestinal mucin protein present in the mucus.

Effect on villus height

The effect of diets on the ileal morphology of chickens after three weeks of supplementation was further evaluated (*Figure 2*). Clear morphological improvements can be observed between the control and the different diets tested, of which diet E significantly enhanced the height of villi ($P<0.001$), relative to the control group.

Overall, diet D and E appear to be superior to unprotected sodium butyrate and are comparable to Tylosin in promoting growth and productivity of broilers, and can therefore be used as effective alternatives to antibiotics.

*Novyrate®C, **Lumance®

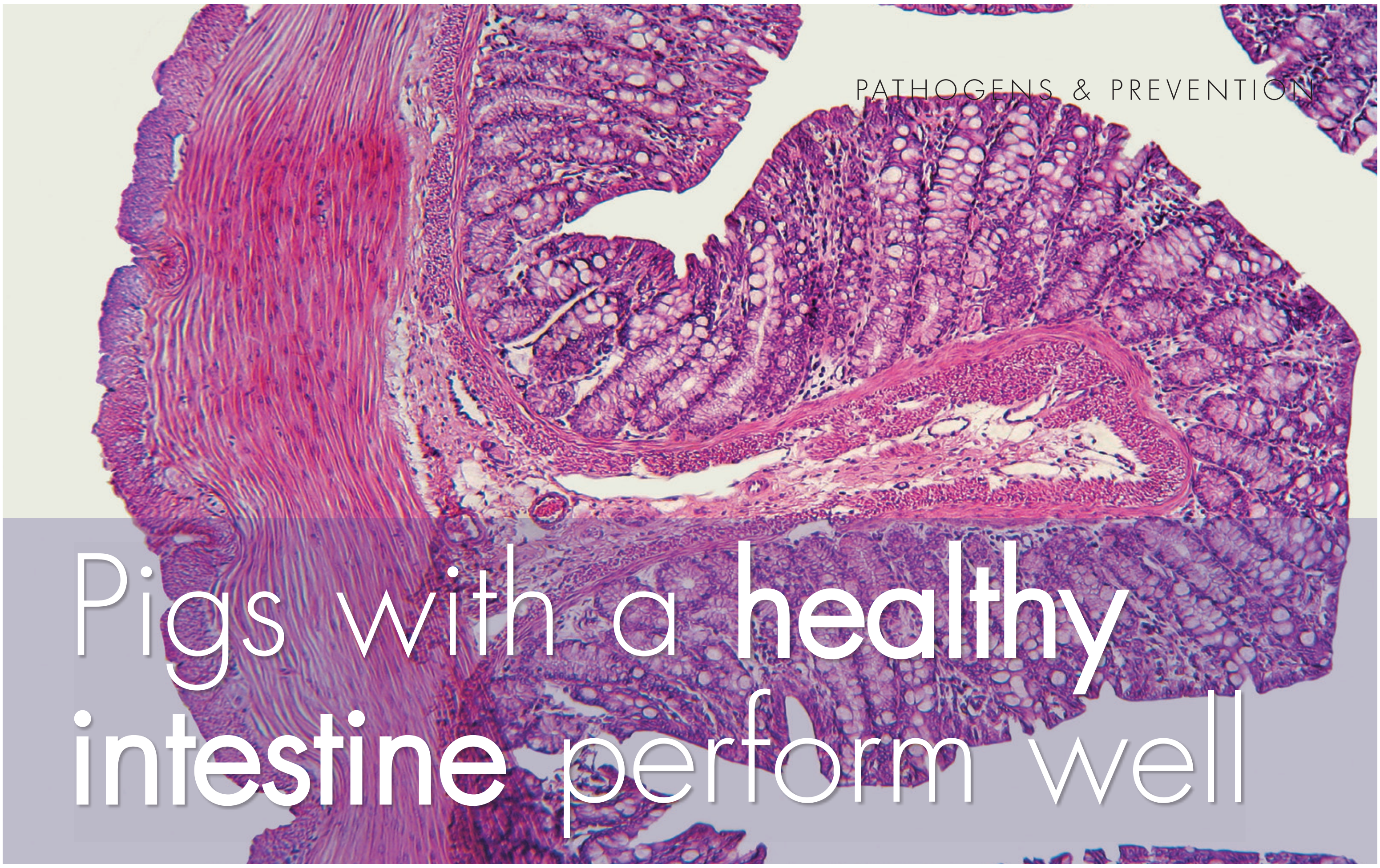
Table 1 - The effect of different diets on the growth performance of the chickens.

Items[1]	Treatments [2,3]					SEM	*P*-value
	Control (diet A)	Diet B	Diet C	Diet D	Diet E		
BW, g							
0 d	41.68	41.86	41.79	41.89	42.10	1.30	0.965
21 d	697.53^{c}	764.22^{bc}	875.88^{ab}	875.33^{ab}	905.23^{a}	117.02	<0.001
ADG, g/d							
0-21 d	31.23^{c}	34.40^{bc}	39.72^{ab}	39.69^{ab}	41.10^{a}	5.57	<0.001
ADFI, g/d							
0-21 d	58.47^{ab}	52.31^{b}	63.67^{a}	55.54^{ab}	60.22^{ab}	7.31	0.014
FCR, g/g							
0-21 d	1.97^{a}	1.53^{b}	1.61^{b}	1.40^{b}	1.47^{b}	0.49	<0.0001

[1] *BW = average body weight; ADG = average daily gain; ADFI = average daily feed intake; FCR = feed conversion ratio (ADFI/ADG).*

[2] *Data are means of 10 replications of 4-7 birds/pen.*

[3] *Means in the same row with no common superscript letters differ significantly ($P < 0.05$).*



Pigs with a **healthy** **intestine** perform well

Scientists and veterinarians agree that one single non-antibiotic molecule will have its limits in controlling the overall situation. An approach which combines the newest generation butyrate with various additives, however, appears very attractive.

By Stephan Bauwens, technical director, Innovad, Belgium

Intestinal health is the most determining factor for health in general, herd performance and eventually farm profitability. Harmful bacteria like E. coli may colonise the gastrointestinal tract, resulting in clinical and sub-clinical diseases. Reduced feed intake and daily gain, inactivity and decreased social interactions are all observed in animals with bacterial infections.

Intestinal health pops up as one of the most important and one of the most complex actions related to animal nutrition. Intestinal health is the sum of intestinal tract functionality and integrity, the established micro-flora and its symbiosis with the host, which is far more important than what nutritionists ever believed.

Surface of intestinal tract

The surface of the intestinal tract is 300 times the size of the surface of the skin. At the same time, it should give a similar level of protection against invaders, while being highly permeable to absorb nutrients. Tight junctions have the major task of closing the cell lines and avoiding paracellular passage of bacteria, toxins and other undesired substances from the lumen to the inside of the body. Several stress factors will have a negative impact on the quality of the tight junctions, leading to the 'leaky gut' syndrome by which big sized molecules such as toxins and aggressive radicals are able to pass in between, resulting in cell damage, production of 'Reactive Oxygen Species' (ROS) and activation of the immune system. The latter is automatically paired to the production of inflammatory cytokines. The neutralisation of these inflammatory components will consume significant amounts of nutrients, which will be shown in reduced growth and increased feed conversion rates. Although the mode of action of Antibiotic Growth Promoters (AGPs) has not yet been fully understood, there is evidence to believe that, besides regulation of the microflora, AGPs also play an important role in reducing the level of inflammatory cytokines, which results in substantial energy saving and improved performance.

The intestinal microbiome is composed of 10^{14} microbes originating from more than 500 different species. They supply energy and substrate to the gut wall, prevent colonisation by harmful bacteria and regulate the intestinal immune system.

Usage of AGPs

When the usage of AGPs gained popularity in 1950, this was con-

Table 1 - Performance improvement and a reduction in gastro-intestinal disorders with new-generation butyrate*.

Piglets	BW (kg) at start	BW (kg) at end	ADG (g)
Control	10.4 ± 1.35	18.4 ± 0.86	266
Trial	10.5 ± 1.58	19.2 ± 0.97	290

* Lumance, Innovad

Figure 1 - Results of an Italian pig trial, comparing a positive control, a negative control and a reduced antibiotic treatment.

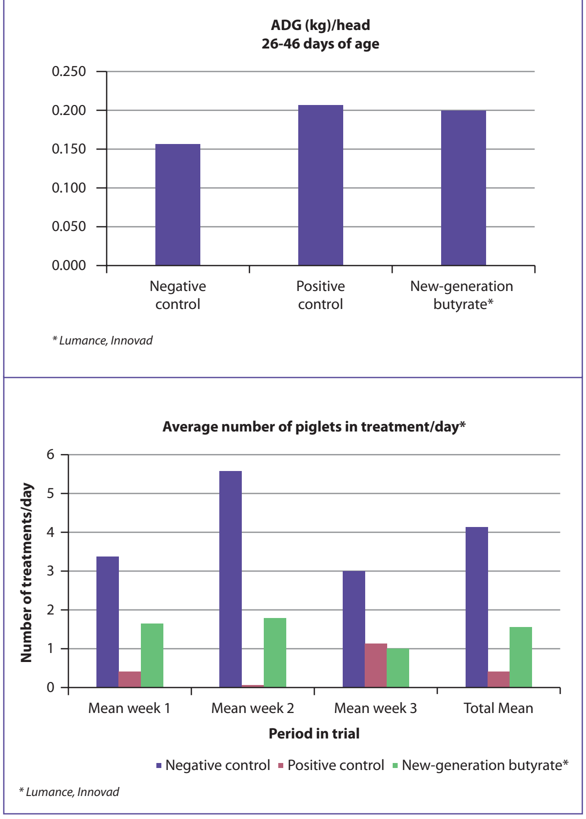
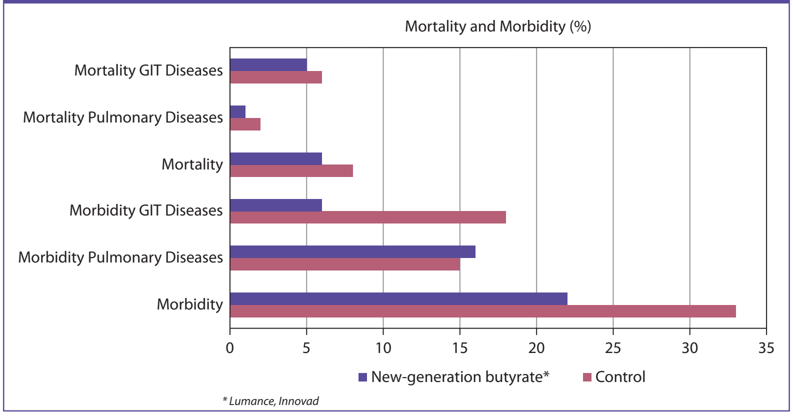


Figure 2 – Mortality and morbidity (%) when using new-generation butyrate*.



sidered a panacea, a universal remedy to improve (intestinal) health status, performance and economics on the farm. With an increasing use of antibiotics in animal nutrition (of which 60-80% is used to treat intestinal disorders), in 1990 both scientist and public opinion opened the debate on increased bacterial resistance against antibiotics and its eventual transfer to humans. This milestone led to a full ban of AGPs since January 2006 and a significant reduction of antibiotic use in animal feed in many countries of the European Union (EU). Different countries set their targets to reduce antibiotic use in animal feed by 50-70% in the next two to five years. Management and nutrition will certainly have their role to play to achieve these goals. One can easily understand the complexity of the intestinal system. Many scientists and veterinarians agree that one single non-antibiotic molecule will have its limits in controlling the overall situation. Lumance, developed three years ago by Innovad's R&D department, offers a concept and a synergistic approach that ensures a high intestinal health status. The product is a complex structure, containing the newest generation of butyrate, combining slow release and protection technologies, ensuring that acids, medium-chain fatty acids, essential oils, anti-inflammatory compounds and polyphenols are delivered in a gut active way for a powerful and effective antibacterial control, high quality tight junctions and tempering of the inflammatory cytokine production.

Italian trial

In an Italian pig trial, a positive control (500 ppm Amoxicillin, 120 ppm Celestine and 3000 ppm Zinc Oxide) was compared with a negative control (500 ppm Amoxicillin) and a reduced antibiotic treatment (500 ppm Amoxicillin + 1 kg new-generation butyrate). The application turned out to be more economical compared to the positive control. The negative control clearly demonstrates the challenge on the farm by reduced performance, high individual medication treatment and low faecal scoring. The new generation butyrate was able to compensate totally the loss in performance up to the same level as the positive control. Individual antibiotic application was strongly reduced by adding the additive to the diet and faecal scoring was significantly improved compared to the negative control, see *Figure 1*.

Table 1 shows the results of an academic experimental farm in Lithuania (Lithuanian University of health Science, Veterinary Academy, 2014), 400 piglets (Piétrain x Large White) were divided into two groups. A control diet was compared to a treatment with 1.5 kg/tonne of butyrate from 30 days of age till 60 days of age. Performance was improved in favour of the additive treatment while a clear reduction was observed in gastro-intestinal disorders, see *Figure 2*.

Maintaining health and performance

The decision to reduce the use of antibiotics in feed, maintaining healthy and well performing animals is not an easy situation to manage. Both management and nutrition should go hand in hand in order to compete with the conventional use of antibiotics. Lumance, being a synergistic concept, has shown to outperform single component feed additives and be a valid alternative for reduced use of antibiotics or single feed additive based performance enhancers, even in the absence of an intestinal challenging situation.

Strategy for enhanced performance and reduced medication

by Stephan Bauwens, Innovad SA/NV, Belgium.

Modern animal production is known for its high genetic potential, which is often not able to be achieved due to different and complex challenges during their lifecycle. One of the major challenges is situated at the border of the intestinal tube. This area carries an important responsibility in selecting what can be absorbed and what should remain outside the body of the animal. To put this in a right perspective, it needs to be stated that the surface of the intestinal tract is 300 times as big as the surface of the skin. At the same time, it should give the similar level of protection against invaders, while being highly permeable to absorb nutrients. Intestinal health pops up as a very popular term for one of the most important but one of the most complex actions related to animal nutrition.

When the use of Antibiotic Growth Promoters (AGP) gained in popularity in 1950, this was considered as a panacea, a universal remedy to improve (intestinal) health status, performance and economics on the farm.

With increasing use of antibiotics in animal nutrition (of which 60-80% is used to treat intestinal disorders), in 1990, both scientists and public opinion opened the debate on increased bacterial resistance against antibiotics and its eventual transfer to humans. This milestone lead to a full ban of AGP since January 2006 and a significant reduction of antibiotic use in animal feed in many countries of EU, now being followed by many other countries.

Intestinal microbiota

In order to obtain a high intestinal health status, eventually in combination with a reduced use of antibiotics, it is first of all important to understand the intestinal system.

The intestinal barrier is composed of different types of cells of which the enterocytes are the most abundant ones. These enterocytes are cells which are 'bound' to one another by complex protein structures, called 'tight junctions'. This structure has a major task to close the cell lines and to avoid paracellular passage of bacteria, toxins and other undesired substances from the lumen to the inside of the body.

Several stress factors will have a negative impact on the quality of the tight junctions, leading to the syndrome 'leaking gut' by which big sized molecules such as toxins and aggressive radicals are able to pass in between, resulting in cell damage, production of 'Reactive Oxygen Species' (ROS) and activation of the immune system.

The latter is automatically paired to the production of inflammatory cytokines. The neutralisation of these inflammatory components will consume significant amounts of nutrients, which will lead to reduced growth and increased feed conversion rates.

Subclinical inflammation can cost up to 30% of the energy requirements. Although the mode of action of AGP has not yet been fully understood, there is evidence to believe that, besides regulation of the microflora, AGP also play an important role in reducing the level of inflammatory cytokines, which results in substantial energy saving and improved performance.

Host defence peptides (HDPs), also known as antimicrobial peptides, are present in virtually all species of life and constitute a critical component of the innate immunity. Defensins and cathelicidins represent two major families of HDPs in vertebrates. They are produced and secreted at the level of the intestinal epithelium.

These HDPs have a broad spectrum of antimicrobial activity against bacteria, protozoa, fungi and even viruses. Due to the complexity of the mode of action against microbes, there is a low chance of resistance, which makes them a number one candidate for alternatives to antibiotics.

As research is ongoing and will take some more years before such molecule can be applied in feed or drinking water, there is currently an interesting approach to increase the synthesis of endogenous HDPs within the intestinal tract.

The intestinal microbiota is composed of more than 500 different species, which live in direct symbiosis with the host. They provide energy to the intestinal wall, prevent colonisation by pathogenic bacteria and help to maintain the intestinal immune system. It is demonstrated many times, that the status of the immune system is (partly) defined by the presence and the type of microbiota in the intestine.

Based on the above, we can conclude that a high status of intestinal health is based on a balanced microflora, strong tight junctions, healthy long and slender villi, secretion of HDPs and low levels of ROS and inflammatory cytokines.

A single molecule has its limits

One can easily understand the complexity of the intestinal system. Many scientists and veterinarians agree that one single non-antibiotic molecule will have its limits in order to control the overall situation.

Therefore a concept and a synergistic approach to ensure a high intestinal health status should be recommended. Such strategy lies in combining active ingredients, slow release effects and precision technologies.

This know-how ensures that acids, medium chain fatty acids, butyrate, essential oils, anti-inflammatory compounds and polyphenols are delivered in a 'gut-active way' for a powerful and effective antibacterial control and enteric support and protection.

The high genetic potential of todays' production animals, combined with a clear and inevitable tendency to reduce the use of antibiotics, resulting in an increased risk of enteric problems, is a complex situation to manage.

Obviously, a one single molecule approach is not dealing with all aspects of intestinal health management and will never be able to compete with conventional use of antibiotics.

A well balanced synergistic concept has shown to be a valid alternative for reduced use of antibiotics. Besides, both in layer and broiler diets, such combination has proven to be a valid performance enhancer, even in the absence of an intestinal challenging situation. ■

Gut Health
A continuously challenged eco-system

Stephan Bauwens, Technical Director, INNOVAD® NV/SA, Belgium (s.bauwens@innovad-global.com)

1. Introduction

- The widespread use of antimicrobial agents in human and veterinary medicine has favoured the spread of resistance.
- In view of the transmission risk of highly antibiotic-resistant strains between animals and humans, controlling resistance is essential to safeguard the future efficacy of antimicrobial agents in veterinary as well as in human medicine.
- Today many countries in the EU, but also outside the EU-borders, are taking initiatives to reduce medication use in general and in animal feed in particular.
- The aim of this trial was to evaluate the performance a synergistic blend of target released butyric acid source in combination with medium chain fatty acids (MCFA) and plant extracts* as a possible alternative to in-feed used antibiotics.

2. Materials and Methods

FARM CHARACTERISTICS

5000 sow farm (Italy)
26 - 27 weaned piglets / sow / year

Health status :
PRRS pos., mycoplasma pos., streptococcus suis pos.,
PCV2 + and Aujeszky neg animals.
E.Coli diarrhea after weaning common without in-feed antibiotics.

TRIAL DESIGN

240 piglets – 2 repetitions – 3 treatments – 2 pens/treatment – 20 piglets/pen
Weaning at 24 - 26 days of age
Trial period: 26 - 46 days of age

Positive control (PC)	Negative control (NC)	Treatment (T)
– 500 ppm Amoxicillin – 120 ppm Colistin – 3000 ppm Zinc Oxide	– 500 ppm Amoxicillin	– 500 ppm Amoxicillin – 1 kg/MT esterified butyrins combined with MCFA and plant extracts*

In case of diarrhea, individual animals are treated with Enrofloxacin

3. Results

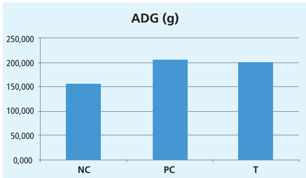


Fig. 1: Average daily gain (g/day) from 26-46 days of age.

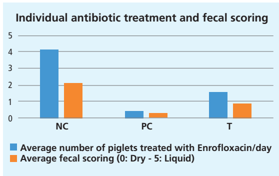


Fig. 2: Individual antibiotic treatments and fecal scoring (average from 26-46 days of age).

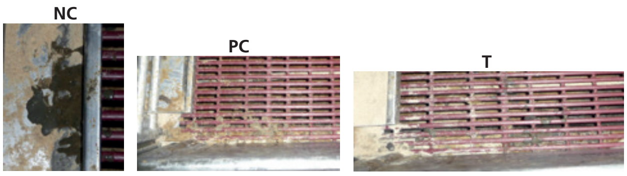


Fig. 3: Visual fecal scoring of different treatments.

- The performance data clearly demonstrated the positive effect of the antibiotic cocktail as the PC-group performed better compared to the NC-group (ADG of 206 g/day vs 156 g/day respectively). **(Fig. 1)**
- The trial group T performed equally with an average daily gain of 200 g/day. **(Fig. 1)**
- The average number of individual antibiotic treatments/trial day was 4,14 for the negative control. A significant improvement was noticed for the trial group (T) (1,55) and 0,45 for the positive control (PC). **(Fig. 2)**
- The fecal scoring followed the same trend. **(Fig.2 and 3)**

4. Conclusions

Well selected active ingredients like butyric acid, MCFA and well-chosen botanical extracts*, combined in an optimal blend, have a clear potential to improve intestinal health, reduce intestinal disorders and eventually allow reduction of antibiotic growth promoters and in-feed antibiotics, while maintaining or even improving performance data.

* ***Lumance®*** *(INNOVAD® NV/SA, Belgium)*

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