

# Beyond AGPs: Controlling necrotic enteritis through gut health optimization



Antibiotic growth promoters (AGPs) have routinely been used in intensive poultry production for improving birds' performance. However, in recent years, reducing the use of [antibiotics in animal production has become a top priority](#), due to concerns about the development of antibiotic-resistant bacteria and mounting consumer pressure. Multiple countries have introduced bans or severe restrictions on the non-

therapeutic use of antibiotics, including in the US, where the Food and Drug Administration has implemented measures to curb the use of antibiotics since 2017.

However, the removal of AGPs poses challenges for poultry performance, including reduced feed efficiency, decreased daily weight gain, as well as higher mortality. Moreover, the withdrawal of AGPs in feed is widely recognized as one of the predisposing factors for necrotic enteritis (NE). NE is one of the most common and economically important poultry diseases, with an [estimated global impact of US\\$ 5 to 6 billion per year](#). As a result of withdrawing AGPs, the usage of therapeutic antibiotics to treat NE has increased. To break out of this vicious cycle and to secure the efficiency of poultry production, alternatives are needed that combat NE where it starts: in the gut.

## Necrotic enteritis: a complex disease

NE is caused by pathogenic strains of *Clostridium perfringens* (CP): ubiquitous, gram-positive, spore-forming anaerobic bacteria. The spores of CP can be found in poultry litter, feces, soil, dust, and contaminated feed. Low levels of different CP strains are naturally present in the intestines of healthy birds, kept in check by a balanced microbiome. However, when gut health is compromised, [pathogenic strains can proliferate at the expense of unproblematic strains](#), resulting in clinical or sub-clinical NE.

Animals suffering from the clinical form show symptoms such as general depression, reluctance to move, and diarrhea, with mortality rates of up to 50%. Infected birds suffer from degenerated mucosa lesions in the small intestines. Even in its “mild”, subclinical form, which often goes unnoticed, the damage to the animals’ intestinal mucosa can result in permanently reduced performance and consequent economic losses for the producer.

Certain [predisposing factors](#) have been found to enable the proliferation of pathogenic strains in the gastrointestinal tract. Diet is a key example: the composition of the gut flora is directly linked to feed composition. High inclusion rates of cereals (barley, rye, oats, and wheat) that contain high levels of non-starch polysaccharides (NSPs), high levels of indigestible protein, and inclusion of proteins of animal origin (e.g. fishmeal) have been shown to predispose birds to NE.

A range of diseases (e.g. chicken infectious anemia, Gumboro, and Marek’s disease), but also other factors that have immunosuppressive effects, such as heat or cold stress, [mycotoxins](#), feed changes, or high stocking density, render birds more susceptible to intestinal infections. The single most prominent predisposing factor for the occurrence of NE is the [mucosal damage caused by coccidiosis](#).

## Gut health is key to combating necrotic enteritis

To control NE, a holistic approach to optimizing the intestinal health of poultry is needed. It should take into account not only parameters such as diet, hygiene, and stress, but should also make use of innovative tools.

Phytomolecules, also known as secondary plant compounds, are essentially plants’ defense mechanisms against pathogens such as moulds, yeasts, and bacteria. [Studies have demonstrated the antimicrobial effects](#) of certain phytomolecules, including against antibiotic-resistant pathogens. Phytomolecules have also been found to boost the production of digestive enzymes, to suppress pro-inflammatory prostaglandins and have antioxidant properties. These features make them a potent tool for optimizing gut health, potentially to the point of replacing AGPs.

## Can phytomolecules mitigate the impact of necrotic enteritis?

To study the impact of phytomolecules on the performance of broilers challenged with a NE-causing CP strain, a trial was conducted at a US-based research facility. In this 42-day study, 1050 male day-old Cobb 500 broiler chicks were divided into 3 groups, with 7 replicates of 50 chicks each.

On the first day, all animals were vaccinated against coccidiosis through a live oocyst spray vaccination. The experimental diets met or exceeded the National Research Council requirements, and were fed as crumbles/pellets. On days 19, 20, and 21, all pens, except the negative control group, were challenged with a broth culture of *C. perfringens*. A field isolate of CP known to cause NE (originating from a commercial broiler operation) was utilized as the challenge organism. On day 21, three birds from each pen were selected, sacrificed, group weighed, and examined for the degree of present NE lesions.

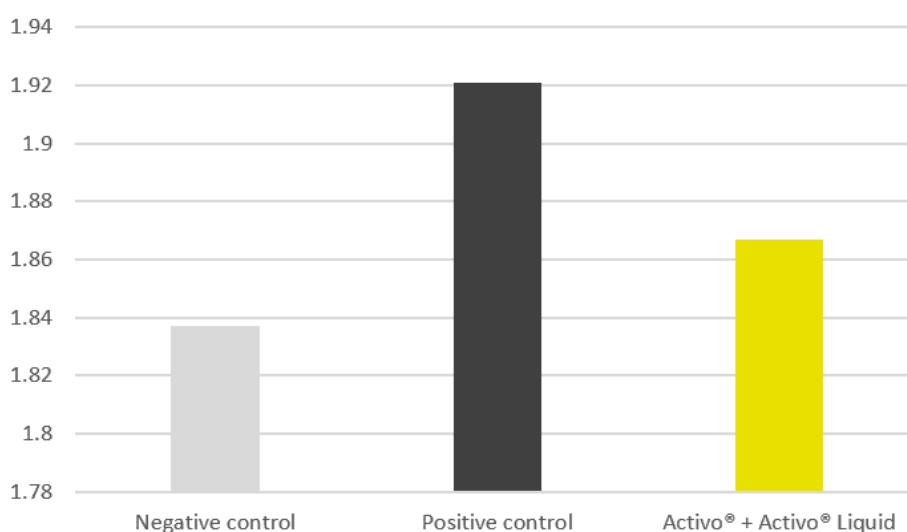
The positive control group received no supplements. The trial group received a synergistic combination of two phytogenic products containing standardized amounts of selected, microencapsulated phytomolecules: an in-feed phytogenic premix (Activo®, EW Nutrition GmbH) and a liquid complementary feed supplied via the drinking water (Activo® Liquid, EW Nutrition GmbH). The products were given at inclusion rates corresponding to the manufacturer's baseline antibiotic reduction program recommendations (Figure 1):

*Figure 1: Trial design*

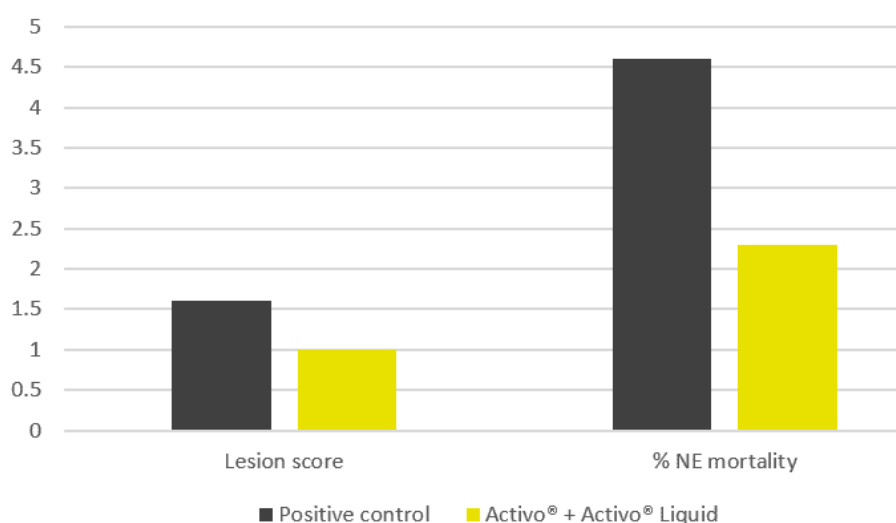
The trial results indicate that the addition of phytomolecules helps to mitigate the impact of NE on broilers' performance. The group receiving Activo® and Activo® Liquid showed a better feed conversion (Figure 2) compared to the positive control group (NE challenge, no supplement). Also, better lesion scores were noted for animals receiving phytomolecules (0.7 and 1) than for the positive control group (1.6).

The most significant effect was observed concerning mortality: the group receiving Activo® and Activo® Liquid showed a 50% lower mortality rate than the positive control group (Figure 3). These results clearly indicate that phytomolecules can play an important role in mitigating losses due to NE.

*Figure 1: Adjusted FCR*



*Figure 2: Lesion scores and mortality*



# Tackling necrotic enteritis in a sustainable way

In an age of AGP-free poultry production, a concerted focus on fostering animals' gut health is key to achieving optimal performance. This study strongly demonstrates that, thanks to their antimicrobial, digestive, anti-inflammatory and antioxidant properties, phytomolecules effectively support birds' intestinal health when challenged with NE. The inclusion of [Activo®](#) and Activo® Liquid, two phytogenic products designed to synergistically support birds during critical periods, resulted in improved feed conversion, better lesion scores, and 50% lower mortality.

In combination with good dietary, hygiene, and management practices, phytomolecules are therefore a potent tool for reducing the use of antibiotics: including Activo® and Activo® Liquid in their animals' diets allows poultry producers to reduce the incidence of NE, to mitigate its economic impact in case of outbreaks, and therefore to control NE in a sustainable way.

By A. Bhoyar, T. van Gerwe and S. Regragui Mazili

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## Challenging times for broilers? Phytomolecules, not antibiotics,



# are the answer



by **Ajay Bhoyar**, Global Technical Manager, EW Nutrition

Anyone working with today's fast-growing broiler chicken knows that it is a sensitive creature – and so is its gut health. Thanks to continuous improvements in terms of [genetics and breeding](#), nutrition and feeding, as well as general management strategies, broiler production has tremendously upped performance and efficiency over the past decades. It is estimated that, between 1957 and 2005, the [broiler growth rate increased by over 400%, while the feed conversion ratio dropped by 50%](#).

These impressive improvements, however, have come at the cost of intense pressure on the birds' digestive system, which needs to process large quantities of feed in little time. To achieve optimal growth, a broiler's [gastrointestinal tract \(GIT\)](#) needs to be in perfect health, all the time. Unsurprisingly, enteric diseases such as [necrotic enteritis](#), which severely damages the intestinal mucosa, hamper the intestines' capacity to absorb nutrients and induce an inflammatory immune response.

# The modern broiler's gut - a high-performing, but sensitive system

However, in a system as high performing as the modern broiler's GIT, much less can lead to problems. From when they are day-old chicks up to slaughter, broilers go through several challenging phases during which they are more likely to show impaired gut functionality, e.g. after vaccinations or feed changes. [Good management practices go a long way towards eliminating unnecessary stressors](#) for the animals, but some challenging periods are unavoidable.

The transition from starter to grower diets is a classic situation when nutrients are very likely to not be well digested and build up in the gut, fueling the proliferation of harmful microbes. Immunosuppressive stress in combination with an immature intestinal microflora results in disturbances to the bacterial microbiota. At "best", this entails temporarily reduce nutrient absorption, in the worst case the birds will suffer serious intestinal diseases.

## Phytomolecules - the intelligent alternative to antibiotics

To safeguard performance during stressful periods, poultry producers need to anticipate them and proactively provide effective gut health support. For many years, this support came in the form of antibiotic growth promoters (AGP): administered prophylactically, they were effective at keeping harmful enteric bacteria in check. However, due to grave concerns about the [development of antimicrobial resistance](#), non-therapeutic antibiotics use has been banned in many countries. Alternatives need to focus on improving feed digestibility and strengthening gut health, attacking the root causes of why the intestinal microflora would become unbalanced in the first place.

Phytomolecules are secondary metabolites active in the defense mechanisms of plants. Studies have found that certain phytomolecules [stimulate digestive enzyme activities](#) and stabilize the gut microflora, "leading to improved feed utilization and less exposure to growth-depressing disorders associated with digestion and metabolism" (Zhai et al., 2018). With other trials showing [positive effects on broilers' growth performance and feed conversion](#), the research indicates that phytomolecules might also specifically support chickens during challenging phases.

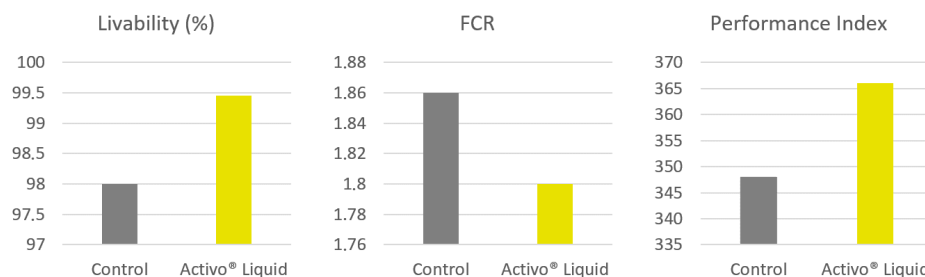
## The effect of phytomolecules on broilers during a challenging phase

A study was conducted over a period of 49 days on a commercial broiler farm of an AGP-free integration operation in Japan. The farm reported gut health challenges in the second and third week of the fattening period due to vaccinations and changes to the animals' diets. The trial included 15504 Ross 308 broilers, divided into two groups. The negative control group included a total of 7242 birds, kept in another house.

All the birds were fed the standard feed of the farm. The trial group (8262 birds) received Activo Liquid, which contains a synergistic combination of phytomolecules, administered directly through the drinking water. Activo Liquid was given at an inclusion rate of 200ml per 1000L of water (3.3 US fl oz per gallon of stock solution, diluted at 1:128), from day 8 until day 25, for 8 hours a day.

The results are summarized in Figure 1:

*Figure 1: Improved broiler performance for Activo Liquid group (day 49)*



The Activo Liquid group clearly showed performance improvements compared to the control group. Livability augmented by 1.5%, while the feed conversion rate improved by 3.2%. This resulted in a more than 5% higher score in terms of the performance index.

## Challenging times? Tackle them using phytomolecules

Poultry producers take great care to eliminate unnecessary sources of stress for their birds. Nonetheless, during their lifecycle, broiler chickens face challenging periods during which the balance of the intestinal microflora can easily become disturbed, with consequences ranging from decreased nutrient absorption to full-blown enteric disease.

The trial reviewed here showed that, after receiving Activo Liquid, broilers raised without AGPs showed encouraging performance improvements during a challenging phase of feed changes and vaccinations. Likely thanks to the activation of digestive enzymes and a stabilization of the gut flora, the broilers showed improved livability and feed conversion, thus delivering a much more robust performance during a critical phase of their lives. In times where the non-therapeutic use of antibiotics is no longer an option, phytomolecules allow poultry farmers to effectively support their animals during challenging times.

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Photo Source: [Aviagen](#)

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# Phytomolecules: Boosting Poultry Performance without Antibiotics



Antimicrobial resistance (AMR) is a major threat to global public health. It is largely caused by the overuse of antibiotics in human medicine and agriculture. In intensive poultry production most antibiotics are used as antimicrobial growth promoters and/or used as prophylactic and metaphylactic treatments to healthy animals. Reducing such antibiotic interventions is crucial to lowering the incidence of AMR. However, antibiotic reduction often results in undesirable performance losses. Hence alternative solutions are needed to boost poultry performance. Phytomolecules have antimicrobial, digestive, anti-inflammatory and antioxidant properties, which could make them key to closing the performance gap.



## Poultry performance depends on intestinal health

Poultry performance is to a large extent a function of intestinal health. The intestines process nutrients, electrolytes and water, produce mucin, secrete immunoglobulins and create a barrier against antigens and pathogens.

In addition, it is an important component of the body's immune defense system. The intestine has to identify pathogens and reject them, but also has to tolerate harmless and beneficial microorganisms. If the intestines do not function properly this can lead to food intolerance, dysbiosis, infections and diseases. All of these are detrimental to feed conversion and therefore also to animal performance.

Antibiotics reduce the number of microorganisms in the intestinal tract. From a performance point of view this has two benefits: first, the number of pathogens is reduced and therefore also the likelihood of diseases; second, bacteria are eliminated as competitors for the available nutrients. However, the overuse of antibiotics not only engenders AMR: antibiotics also eliminate probiotic bacteria, which negatively impacts the digestive tracts' microflora.

Products to boost poultry performance may be added to their feed or water. They range from pre- and probiotics to medium chain fatty acids and organic acids to plant extracts or phytomolecules. Especially the latter have the potential to substantially reduce the use of antibiotics in poultry farming.

## Phytomolecules are promising tools for antibiotic reduction

Plants produce phytomolecules to fend off pathogens such as moulds, yeasts and bacteria. Their antimicrobial effect is achieved through a variety of complex mechanisms. Terpenoids and phenols, for example, disturb or destroy the pathogens' cell wall. Other phytomolecules inhibit their growth by influencing their genetic material. Studies on broilers show that certain phytomolecules reduce the adhesion of pathogens such as to the wall of the intestine. Carvacrol and thymol were found to be effective against different species of *Salmonella* and *Clostridium perfringens*.

There is even evidence that secondary plant compounds also possess antimicrobial characteristics against antibiotic resistant pathogens. In-vitro trials with cinnamon oil, for example, showed antimicrobial effects against methicillin resistant *Staphylococcus aureus*, as well as against multiresistant *E. coli*, *Klebsiella pneumoniae* and *Candida albicans*.

Importantly, there are no known cases to date of bacteria developing resistances to phytomolecules. Moreover, phytomolecules increase the production and activity of digestive enzymes, they suppress the metabolism of pro-inflammatory prostaglandins and they act as antioxidants. Their properties thus make them a promising alternative to the non-therapeutic use of antibiotics.

## Study design and results

In order to evaluate the effect of phytomolecules on poultry performance, multiple feeding studies were conducted on broilers and laying hens. They were given a phytogenic premix ([Activo](#), EW Nutrition GmbH) that contains standardized amounts of selected phytomolecules.

To achieve thermal stability during the feed processing and a targeted release in the birds' [gastrointestinal tract](#), the product is microencapsulated. For each , the studies evaluated both the tolerance of the premix and the efficacy of different dosages.

### **Study I: Evaluation of the dose dependent efficacy and tolerance of Activo for broilers**

Animals: 400 broilers; age: 1-35 days of age

Feed: Basal starter and grower diets

Treatments:

- No supplement (negative control)
- 100 mg of Activo /kg of feed
- 1.000 mg of Activo /kg of feed
- 10.000 mg of Activo /kg of feed

Parameters: weight gain, feed intake, feed conversion ratio, health status, and blood parameters

**Results:** The trial group given the diet supplemented with 100 mg/kg [Activo](#) showed significant improvements in body weight gain during the starter period (+4%) compared to the control group.

Additional significant improvements in feed conversion ratio (FCR) in the growing period (+4%) resulted in an overall improvement in FCR of 3%. At a 1.000 mg/kg supplementation, a significant improvement in FCR of 6% was observed over the entire feeding period. Hematological parameters were within the reference range of healthy birds when feeding up to 10,000 Activo/ kg of feed.

### ***Study II: Evaluation of the dose depending efficacy and tolerance of Activo for laying hens***

Animals: 200 hens; age: 20 to 43 weeks

Feed: basal diet for laying hens

Treatments:

- No supplement (negative control)
- 100 mg of Activo/ kg of feed
- 250 mg of Activo/ kg of feed
- 500 mg of Activo/ kg of feed
- 5.000 mg of Activo/ kg of feed

Parameters: weight gain, feed intake, feed conversion ratio, health status, and blood parameters

**Results:** Inclusion levels from 100 mg/kg of Activo onwards improved laying performance, egg mass and egg weight and reduced FCR compared to the control group. Results recorded for hematological parameters were within the reference range of healthy birds when feeding up to 5.000 mg Activo/ kg of feed.

### ***Study III: Evaluation of the dose-dependent effects of Activo for coccidiosis vaccinated broilers***

Animals: 960 broiler chickens; age: 42 days

Feed: Standard starter and finisher feed

Treatments:

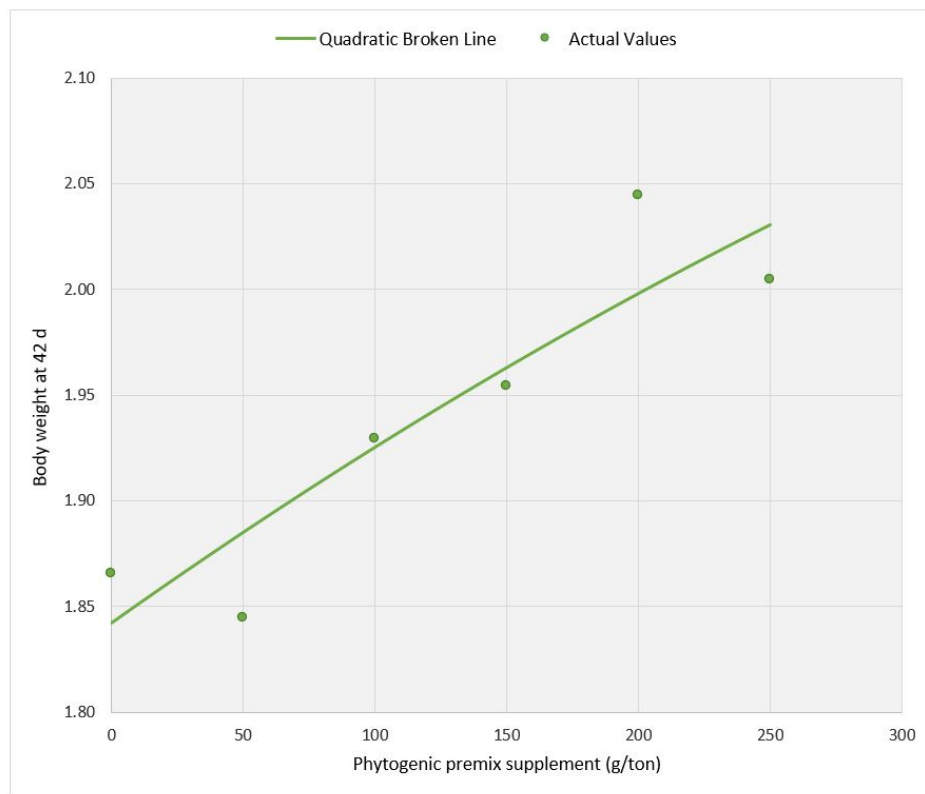
- No supplement (negative control)
- 50 g of Activo /US ton of feed
- 100 g of Activo /US ton of feed
- 150 g of Activo /US ton of feed
- 200 g of Activo /US ton of feed
- 250 g of Activo /US ton of feed
- Antibiotic growth promoter (AGP)(positive control)

Parameters: weight gain, feed efficiency

Specific: In order to represent field conditions, the birds were challenged with used, homogenized litter.

**Results:** A clear dose response for both body weight gain and feed efficiency was observed (see Figure 1): the more phytogenic premix given, the better the birds' performance. The group with 200g of Activo /US ton of feed showed similar performance levels than the positive control group supplemented with AGP.

*Figure 1: Dose-dependent effects of for coccidiosis vaccinated broilers*



#### **Study IV: Evaluation of the dose-dependent effects of Activo for laying hens**

Animals: 40 hens; age: week 20 to 43

Feed: basal diet for laying hens

Treatments:

- No supplement (negative control)
- 100 mg of Activo/ kg of feed
- 250 mg of Activo/ kg of feed
- 500 mg of Activo/ kg of feed
- 5.000 mg of Activo/ kg of feed

Parameters: weight gain, feed intake, egg production, feed conversion ratio, health status

Duration: 168 days of feeding period

**Results:** The laying hens showed a higher laying rate when fed with a higher concentration of phytomolecules (Figure 2). Similarly improved results were observed for the feed efficiency. The more phytogetic premix added to their diet the better feed efficiency (Figure 3).

*Figure 2: Dose-dependent effects of Activo on laying rate in laying hens*

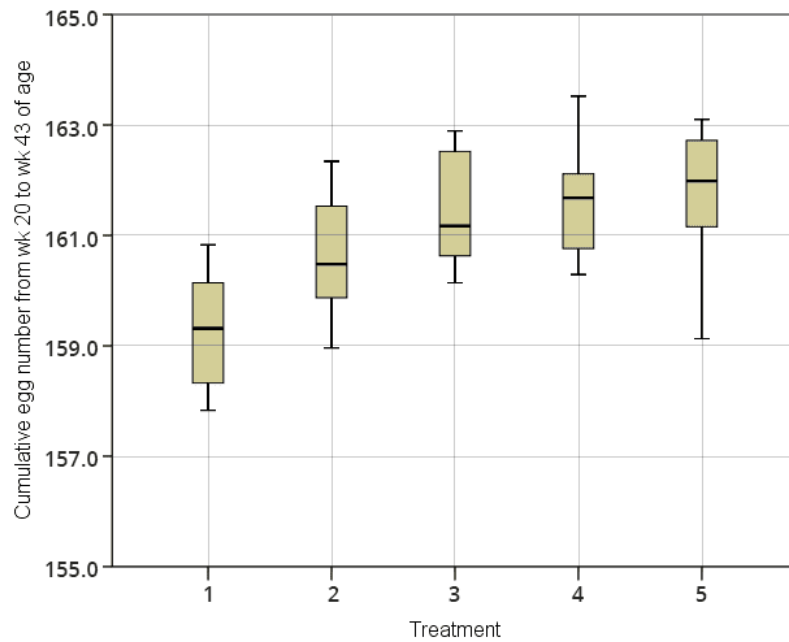
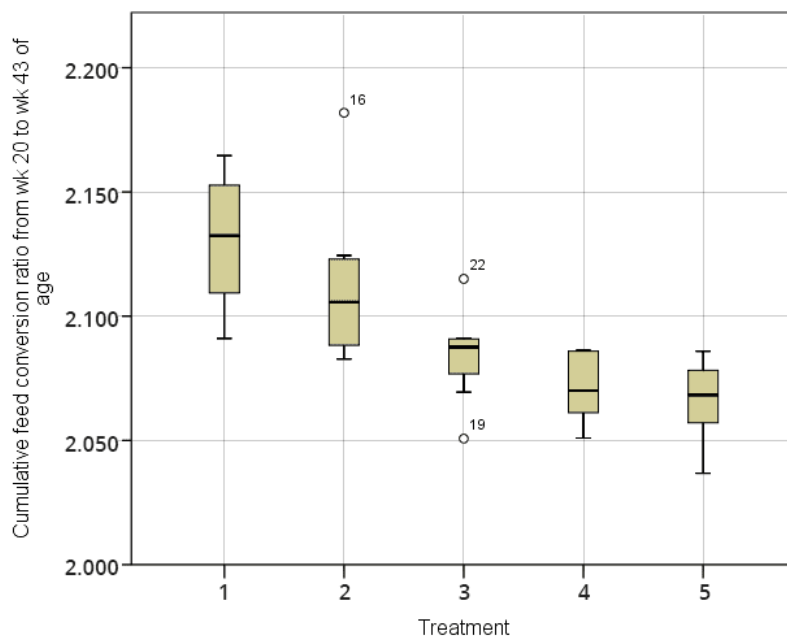


Figure 3: Dose-dependent effects of Activo on feed efficiency in laying hens



In conclusion, all four studies indicate that the inclusion of phytomolecules in broilers' and laying hens' diet improves their performance. Increasing levels of a phytogenic premix (Activo) significantly increased the production parameters for both groups. These improvements might bring performance in antibiotic-free [poultry production](#) on par with previous performance figures achieved with antimicrobial growth promoters.

The studies also showed that microencapsulated phytogenic premixes are safe when used in dose ranges recommended by the suppliers. No negative effects on animal health could be observed even at a 100 fold / 50 fold of the recommended inclusion rate in diets for broiler or laying hens, respectively. Thanks to their positive influence on intestinal health, phytomolecules thus boost poultry performance in a safe and effective way.

By Technical Team, EW Nutrition



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# EW Nutrition USA - Increased profitability in poultry production



### **Increased profitability in poultry production: EW Nutrition presents new comprehensive programs for the American market at Midwest Poultry Federation (MPF)**

To support customers with effective solutions in animal production, EW Nutrition introduces the programs for [Antibiotic Reduction](#) and [Toxin Risk Management](#) in poultry. These programs contribute to solving the problem of antibiotic resistance by minimizing the input of antibiotics. In addition to innovative products the programs include customized consultancy services in the fields of animal nutrition, management and biosecurity.

At MPF, EW Nutrition will present new programs to reduce antibiotic use in broiler, broiler breeder and turkeys. A program to manage the toxin risk in poultry will also be introduced. One part of the programs is innovative products supporting gut and liver health and mitigating the impact of myco- and bacterial toxins. The other part is formed by consultancy services tailored to the particular needs of the customers.

The goals of the poultry programs are:

- stabilization of performance throughout the whole cycle
- constant high numbers of high quality chicks
- a reduced variety between flocks
- improved weight gain and feed conversion.

### **MARK RICHARDS, President of EW Nutrition USA**

“Keeping performance high by simultaneously reducing the use of antibiotics is a balance act in animal production. We are convinced that the reduction of antibiotic use is the best way to reduce antibiotic resistance. With our comprehensive programs we support integrators, farmers and animals in coping with challenges occurring in animal production while increasing customers’ profitability.”

### **EW Nutrition:**

The customer-oriented company focusses on solving critical issues in animal nutrition by offering holistic and tailored programs for antibiotic reduction, toxin risk management and young animal nutrition. For this purpose EW Nutrition introduced innovative products and services resulting from solid R&D and business development. A global network of local commercial and technical support by experts guarantees the closeness to the customer. The reliable family-owned company is situated in Germany and has own R&D,



production and application facilities in different parts of the world.

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# Diarrhoea? Egg powder to the rescue



**Another tool to reduce the use of antibiotics is the use of immunoglobulins from eggs. Trials showed that this product is effective to support a calf's start in life and also to offer support when challenged by various forms of diarrhoea.**

The main cause for calf losses during the first two weeks of life is diarrhoea. In general diarrhoea is characterised by more liquid being secreted than that being resorbed. However, diarrhoea is not a disease, but actually only a symptom. Having diarrhoea has a protective function for the animal, because the higher liquid volume in the gut increases motility and pathogens and toxins are excreted faster. Diarrhoea can occur for several reasons. It can be caused by incorrect nutrition, but also by pathogens such as bacteria, viruses and protozoa.

**Bacteria in the gut**

*E. coli* belong to the normal gut flora of humans and animals and can be mainly found in the colon. Only a

fraction of the serotypes causes diseases. The pathogenicity of *E.coli* is linked to virulence factors. Decisive virulence factors are for example the fimbria used for the attachment to the gut wall and the bacteria's ability to produce toxins.

*Salmonella* in general plays a secondary role in calf diarrhoea, however, salmonellosis in cattle is a notifiable disease. Disease due to *Clostridia* is amongst the most expensive one in cattle farming globally. In herbivores, clostridia are part of the normal gastro-intestinal flora, only a few types can cause serious disease. In calves, *Clostridium perfringens* occurs with the different types A, C, and D. *Rotaviruses* are the most common viral pathogens causing diarrhoea in calves and lambs. They are mainly found at the age of 5 to 14 days. *Coronaviruses* normally attack calves at the age of 5 to 21 days. *Cryptosporidium parvum* is a protozoa and presumed to be the most common pathogen causing diarrhoea (prevalence up to more than 60 %) in calves.

### Undigested feed and incorrect use of antibiotics

Plant raw materials (mainly soy products) are partly used in milk replacers as protein sources. These products contain carbohydrates, that cannot be digested by calves which can lead to diarrhoea. The transition from milk to milk replacer can also be a reason.

An early application of tetracyclines and neomycin to young calves can lead to a change in the villi, malabsorption and therefore to slight diarrhoea. Longer therapies using high dosages of antibiotics can also lead to a bacterial superinfection of the gut. The problem is that in a disease situation, antibiotics are often used incorrectly. The use of antibiotics only makes sense when there is a bacterial diarrhoea and not due to viruses, protozoa or poor feed management. To keep the use of antibiotics as low as possible, alternatives need to be considered.

### Egg powder to add immunoglobulins

In order to achieve optimal results in calf rearing two approaches are possible. Firstly, the prophylaxis approach. This is the method of choice as diarrhoea can mostly be prevented. Therefore, it is necessary to supply the calf with the best possible equipment. As antibodies are one crucial but limiting factor in the colostrum of the "modern" cow, this gap needs to be minimised. A study conducted in Germany in 2015 demonstrated that more than 50% of the new-born calves had a deficiency of immunoglobulins in the blood. Only 41% of the calves showed an adequate concentration of antibodies in the blood (>10 mg IgG/ml blood serum). Immunoglobulins contained in hen eggs (IgY) can partly compensate for poor colostrum quality and serve as a care package for young animals. A trial was conducted with an egg powder product\* on a dairy farm (800 cows) in Brandenburg, Germany. In total 39 new-born calves were observed until weaning (65<sup>th</sup> day of life). Before birth, the calves were already divided into control and trial group according to the lactation number of their mother cow. All calves were fed the same and received four litres of colostrum with  $\geq 50$  mg IgG /ml on the first day of life.

Control (n=20): no additional supplementation  
 Trial group (n=19): day 1 - 5: 100 g of the egg powder product per animal per day mixed into the colostrum or milk.

It was shown that the calves in the trial group showed a significantly higher (13%) weaning weight (105.74 kg compared to 93.45 kg in the control group) and 18% higher average daily gain (999 g compared to 848 g in the control group) (Figure 1 and Figure 2).

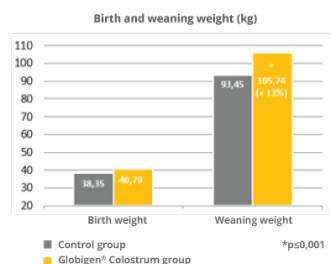


Figure 1: Effect of an egg powder product on weaning weight (kg)

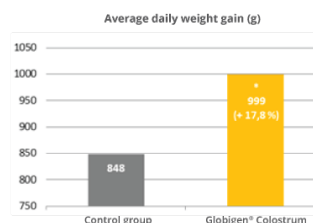


Figure 2: Effect of an egg powder product on ADG (g)

### Support during acute diarrhoea

When diarrhoea occurs, the calf has to be treated. So the second approach is to find the best and quickest solution. It is not always necessary to use antibiotics, as they do not work against virus or protozoa. Egg



antibodies can be an answer when combined with electrolytes as the following trial shows. On a dairy farm (550 cows) in Germany a feeding trial with a product based on egg powder and electrolytes\*\* was conducted from December 2017 to May 2018. Two groups of calves were used. Before birth the animals were allocated into the two groups according to the calving plan and were examined from day one until weaning (77<sup>th</sup> day of life). All calves suffering from diarrhoea (38 in total, 17 in the control and 21 in the trial group) were treated as follows:

Control (n=17):            Application of electrolytes

Trial group (n=21):      50 g of the egg powder and electrolytes product twice daily, stirred into the milk replacer until diarrhoea stopped.

If the diarrhoea did not stop or even got worse, the animals were treated with antibiotics. It was shown that in the control group the antibiotic treatment necessary was nearly twice as long as needed in the trial group (Figure 3). This means also that nearly twice the amount of antibiotics were used. This leads to the conclusion that calves in the trial group had an improved health status compared to calves in the control group. A further result from the improved health status was an increase in performance in the trial group (Figure 4).

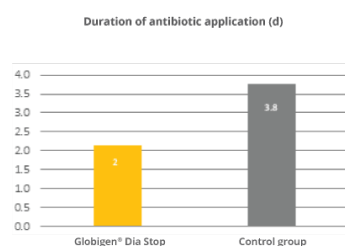


Figure 3: Duration of antibiotic application (d)

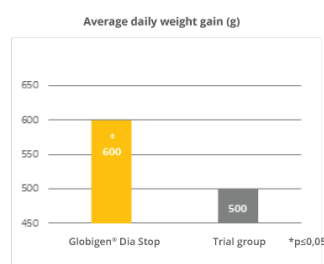


Figure 4: Effect on average daily weight gain (g)

The average daily weight gain of the trial group was 20% higher than in the control (600 vs. 500 g per day) leading to a significantly higher weaning weight (87.8 kg) than in the control (80.7 kg).

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## Understanding the dangers of mycotoxins for breeder hens



**Breeding hens are a valuable asset for the poultry industry, as they produce the hatching eggs and day-old chicks. It is therefore important to manage contamination as well as possible. Mycotoxin management is part of that.**

As the producers of hatching eggs and day-old chicks, breeding hens are the backbone of the poultry industry. Hence it is common practice to pay particular attention to this valuable asset's feed, selecting raw materials of high nutritional quality and safety. However, in any feed formulated for animals in production and reproduction, [studies show](#) that it is almost inevitable to find a certain level of mycotoxin contamination.

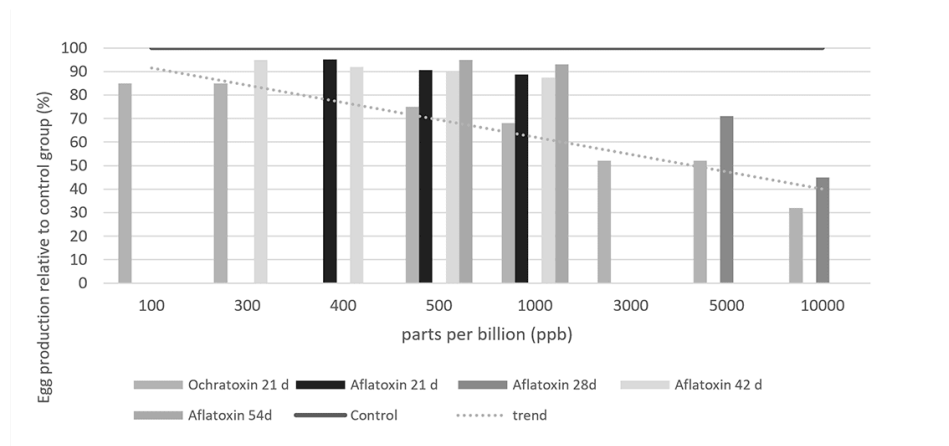
Mycotoxins exert toxic effects mainly on the gastrointestinal tract, liver, and kidneys and can accumulate in some tissues but also in the eggs. Mycotoxin contamination in breeding birds rations does not always lead to visible symptoms, such as when [trichothecenes cause oral lesions](#). However, it may influence productivity, egg quality, hatchery performance, as well as chick quality and immunity. Mycotoxin risk management is thus an essential part of managing breeder hens.

## **Type of mycotoxin and exposure time determine effect on egg production**

[Mycotoxicosis in hens can cause reduced egg production](#), most likely because it causes a decrease in protein synthesis. A lower synthesis of albumin results from a degeneration of the liver tissue due to aflatoxin, ochratoxin, T2 and DON exposure. The liver then may look pale, friable and occasionally shows superficial haemorrhages.

The contamination levels at which these effects can be observed are as low as 100ppb in feed, for example during a 21 day exposure to ochratoxin (*Figure 1*). With increasing levels of the toxin, production further decreases. A similar effect is observed when breeder hens are exposed to aflatoxins.

*Figure 1 – Effect of mycotoxins on egg production, compared to non-contaminated control (=100 %).*



Egg production, however, is not the only parameter that is affected when breeding hens are exposed to mycotoxins. Earlier on in the reproductive cycle they already impact on embryonic mortality and hatchability. These effects are potentially more severe and may even occur without any noticeable change in the number of eggs produced.

## Mycotoxins' insidious consequences for eggshell quality and embryonic mortality

The eggshell is important to protect the progeny: thin and fragile shells can increase embryonic mortality, lower embryonic weight gain and decrease hatchability. Egg shell quality is a function of the hen's calcium and vitamin D3 metabolism. The bioavailability of calcium and of vitamin D3 depends on intestinal integrity and on the production of enzymes and transporters that aid in feed metabolism. These processes can be adversely affected by aflatoxins, DON, T2, and Fumonisin.

The gastrointestinal tract is not the only site of mycotoxin action, however. Mycotoxins such as aflatoxins and ochratoxins have nephrotoxic effects, affecting calcium metabolism and increasing its excretion via the urine, while lowering its levels in blood serum.

Moreover, mycotoxins damage the liver, which plays a central role in egg production, being responsible for vitamin D3 metabolism and the synthesis of the lipids that make up the yolk. Moreover, the synthesis of transporters for lipids, calcium and carotenoids – important components of the egg– also takes place in liver. When liver function is impaired, the internal and external quality of the egg declines, which, in the end, affects the production of day-old chicks.

*Figure 2 – Effects of mycotoxins on eggshell quality and embryonic mortality.*

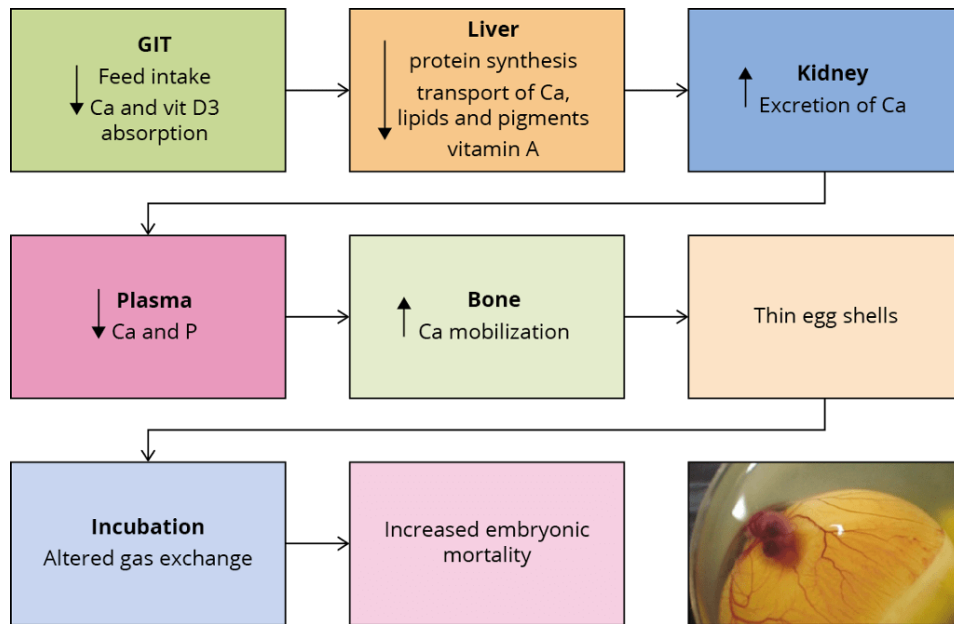


Figure 2 summarises the possible ways in which mycotoxins can negatively affect eggshell quality and, as a consequence, increase embryonic mortality. If a hen's intestinal integrity is compromised, the utilisation of nutrients decreases. Liver and kidney damage leads to a diminished availability of calcium and other nutrients necessary for egg formation. The birds' calcium (and phosphorus) levels in the plasma are then lower and may lead to a [greater mobilisation of calcium from the bones](#). However, this response cannot be maintained and the eggs get a thinner shell.

The thickness of the eggshell influences the egg's moisture loss and exchange with the environment during the incubation period. An eggshell of optimal quality does not allow the loss of nutrients and prevents bacterial contamination. Thinner eggshells are less able to fulfil these functions, leading to higher embryo mortality.

Figure 3 – Effects of mycotoxins on embryonic mortality

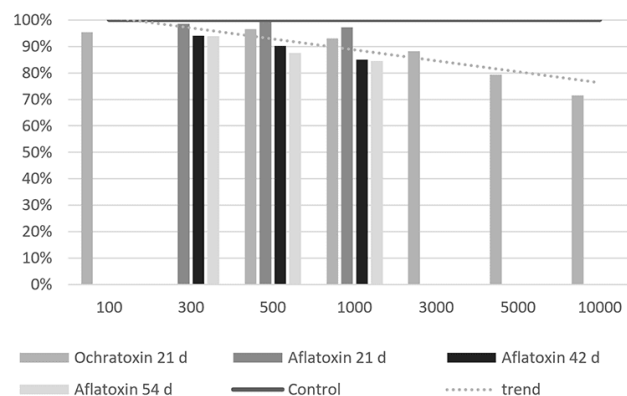


Figure 3 shows the effect of different mycotoxins on embryonic mortality. Incremental levels of ochratoxin or aflatoxin heighten embryonic mortality in a range from 1.5 to 7.5 times the embryonic mortality of the control group. In some cases, embryos are affected even when the hens received feed contaminated with mycotoxin levels that are within the guidelines suggested by the [EFSA](#).

For example, an exposure to 4900ppb of DON for ten weeks increases the number of embryos with abnormalities. The causes are not entirely clear, as only traces of DON can be found in the egg. However, we do know that this mycotoxin can affect the protein synthesis at the level of the hen's liver and therefore compromise the deposition of nutrients into the egg.



# Mycotoxins' effects on the progeny may cause long-term damage

Ochratoxin and aflatoxin can be transferred into the egg, where they exert toxicity on the embryos. This does not necessarily result in mortality. However, the [chicks can suffer from a compromised immune function](#) due to two reasons: lower transmission of antibodies from the hen and lower viability of the chickens' immune cells, accompanied by a lower relative weight of the bursa of Fabricio and the thymus.

When both aflatoxin and ochratoxin are present in the feed, [the effect on these parameters is synergistic](#). As a consequence of mycotoxin contamination, the animals' immune response is impaired, which makes them more susceptible to infection. The final result could be an increased early chick mortality due to a higher incidence of bacterial and viral infections.

The transmission of other mycotoxins into the egg is minimal. While this means that a direct effect on the progeny is unlikely to occur, mycotoxin contamination still has a snowball effect: we have to consider the indirect effect of a lower deposition of nutrients on chick quality.

## Prevention is key: mycotoxin risk management for breeder hens

The best approach to manage mycotoxin risk is to implement an integrated strategy that includes good crop and grain storing practices, regular raw material sampling and mycotoxin evaluation and analysis. Management tools (such as [MasterRisk](#)) can help to evaluate mycotoxin interactions and to choose the best strategy for dealing with specific mycotoxin challenges.

The results of mycotoxin analyses can be used to take decisions regarding the inclusion levels of raw materials and in choosing [feed additives](#) that counteract mycotoxins. Products based on plant extracts, yeast cell walls and clay minerals can help to stabilise a digestive system challenged by mycotoxins. They support the barrier function in the intestine, preventing the passage of mycotoxins into the bloodstream.

[Phytomolecules](#) are another piece of the puzzle: thanks to their antimicrobial, anti-inflammatory and antioxidant properties, they support liver function. This is particularly important for long-living animals prone to accumulating mycotoxins in their body tissues.

For a long time the “deleterious effects” of mycotoxins on breeder hens and “their repercussions on progeny health status and performance have not received from a scientific point of view as much attention” ([Calini and Sirri, 2007](#)) as they ought to have. However, now that the dangers of mycotoxins for breeder hens' welfare, health and performance are better understood, it is clear that mycotoxin risk evaluation and management is central to successful poultry production.

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Read Mycotoxins: Their effect in breeder hens, [the full article](#)

*ALL ABOUT FEED, Mycotoxins, Background, 31.October.2018*

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# Fewer pathogens with egg immunoglobulins



**For newborn pigs there are often a host of different challenges - think of crushing or contamination of the farrowing pen. For the last problem, solutions exist. A dietary approach can help to relieve pathogenic pressure through sow manure.**

The main objective of a piglet producer is to maximise the number of healthy weaned piglets per animal per year. Nowadays, it is not difficult to find production systems delivering more than 30 piglets weaned/sow/year. Combining strategies on management, feeding, and health of both piglets and sows, is crucial for increasing sow's productivity. A unique environment that can determine the success of a piglet farm is the farrowing unit. It is important to reduce as much as possible losses during this period. Pre-weaning mortality must always be monitored and targets must be set. In European conditions, it ranges between 8-10%.

One important driver in reducing pre-weaning mortality is understanding the fragility of newborn piglets. At birth, the resources of a piglet are very scarce: low energy reserves and practically no immune defence against existing pathogens in their new environment. Problems are prone to happen and will be mostly caused by pathogens present in the environment, in the feed, in the water and most important, in the faeces of the sow. The main contamination source for newborn piglets is their mother's manure. And this first contamination can be quite severe causing diarrhoea and increasing piglet mortality.

Together with crushing, diarrhoea definitely causes a high percentage of total losses during the first days of life. In most of the cases, the disease is caused not only by one agent but by a combination of enteric infections from different pathogens or at least different strains of a pathogenic species. *E. coli* and clostridia are two of the most important diarrhoea causing pathogens during the first weeks after birth.

### Pathogens during the first days

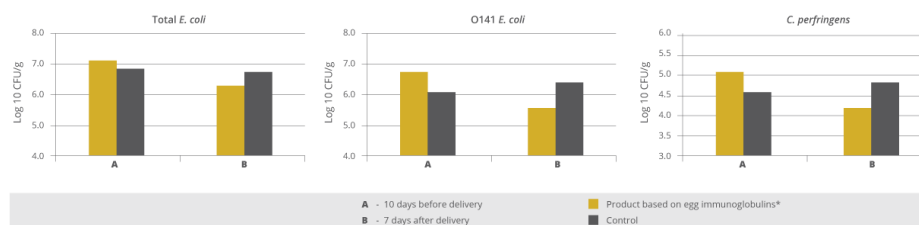
*E. coli* is well known as one of the main responsible pathogens for pre-weaning diarrhoea. And although it belongs to the normal intestinal flora of pigs, part of the different *E. coli* strains are pathogenic. *E. coli* cause about 80% of diarrhoeas in piglets and 50% of losses in piglet production. The factors making *E. coli* pathogenic, the so-called virulence factors include e.g. fimbria to attach to the intestinal wall and the capacity to produce toxins.

The *Clostridium* species are another important pathogen class. During the suckling phase, piglets are quite susceptible to *Clostridium perfringens* type C. This bacteria causes necrotic enteritis in piglets and the clinical symptoms appear during the first days of life. This disease provokes serious disturbances in the organism with a mortality up to 100%. It causes significant decrease in daily gain and in weaning weight.

### Strategy to protect the piglets

In order to maximise the sow's performance – measured in piglets weaned per year – it is crucial to provide the best possible conditions to the piglets. Therefore the reduction of the pathogenic pressure in the farrowing unit ranks first. Cleaning of the pen is a way to get rid of germs like *E. coli* and *Clostridium* species, the most important pathogens during the first days. This should be completed by an effective gut health management in sow and piglets. For this purpose natural ingredients can be used. Supplying natural and active immune cells, the so called antibodies, has been proven to be quite efficient in supporting gut health. Applied to piglets, immunoglobulins from the egg bind to pathogens within the intestinal tract. They show efficiency in supporting piglets' performance, decreasing the incidence of diarrhoea, mortality and increasing daily gain.

The idea was to check if these immunoglobulins from the egg could also bind pathogens in the sow's gut and generate harmless complexes. That way pathogenic pressure for the piglets could be reduced. Thus a trial was conducted in Japan to check this thesis.



### \*Globigen Sow

#### Trial

In the trial two groups contained eight sows each. The sows of the control group received standard lactation feed, the trial group was also fed standard feed with a supplement containing egg immunoglobulins (Globigen Sow, EW Nutrition, at a dosage of 5 g/sow twice daily) on top during the last ten days before and the first seven days after delivery. The faeces of the sows were obtained by rectal stimulation (in order to get no contamination from the environment) on day 10 before and day 7 after delivery. The amount of colony forming units (CFU) of total *E. coli*, *E. coli* O141 and *Clostridium perfringens* were determined.

Results are shown in Figure 1. At the beginning of the trial, before the application of the immunoglobulin supplement, both groups showed nearly the same level of the evaluated pathogens with a slight disadvantage for the supplement group. After 17 days of applying the product based on egg immunoglobulins, a reduction of the colony forming units of total *E. coli*, *E. coli* O141 and of *Clostridium perfringens* could be seen. The sows of the supplement-fed group showed a lower level of pathogens in their excrements than the sows of the control group.

#### Conclusion

It is important for swine producers to understand what adversely influences the results on the farm. One



consideration is to improve farrowing unit conditions of the piglets, aiming to [reduce pre-weaning mortality](#). The results of the trial showed that a supplement based on egg immunoglobulins supplied on top of standard sow diets substantially reduced the amount of pathogenic colonies in sow manure. The reduction on pathogenic pressure and therefore the incidence of diarrhoea may be an alternative for increasing the profitability of piglet producers by increasing the number of healthier piglets weaned/sow/year.

*\*References are available on request.*

*By Dr Inge Heinzl.*

*Published on PigProgress | 20th July, 2018.*

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## **Mycotoxin interactions: An obstacle to risk assessment**



**In animal feed, multi-mycotoxin contamination is found quite frequently and seems to be the rule rather than the exception in practical diets. Here is a quick overview of the known interactions.**



# What are the most common mycotoxins in feed?

Mycotoxins represent an exceptional challenge for feed and animal producers: they are produced by common molds, occur in a great variety and number, are sporadic or heterogeneous in their distribution, and their effects on farm animals are seldom recognized as mycotoxicosis. Among hundreds of known mycotoxins, aflatoxins, mainly produced by *Aspergillus* species, ochratoxin A, produced by *Aspergillus* and *Penicillium* species, as well as fumonisins, trichothecenes (especially DON and T-2 toxin) and zearalenone, primarily produced by many *Fusarium* species stand out as the most common contaminants.

## Consequences of mycotoxin contamination

Ingestion of these mycotoxins may cause an acute toxicity or chronic disorders, depending on the concentration and duration of exposure. In farm animals, this might manifest as decreased performance, feed refusal, poor feed conversion, reduced body weight gain, immune suppression, reproductive disorders, and residues in animal food products.

Due to their frequent occurrence and their severe toxic properties, many countries appointed legal regulations or guidance for the major mycotoxins to protect animals and human consumers. The current regulations are typically very specific in terms of animal species and even for the production stage considering that mycotoxins affect for example poultry in a different way than cattle and broilers in a different way than breeders or laying hens. The threshold and/or guidance values for each species, however, were determined based on toxicological data from studies investigating a monoexposure leaving out the possibility of any combined effects of mycotoxins.

## Multi-contamination: the rule, not the exception

If we were able to ensure that the animals were exposed to only one mycotoxin at a time, following the regulatory guidelines would allow us to protect our animals in most of the cases. Several worldwide surveys show, however, that mycotoxin multicontamination of animal feed is found very frequently\* and seems to be the rule rather than the exception in practical diets. The concurrent appearance of mycotoxins in feed can be explained as follows: each mold species has the capacity to produce a number of mycotoxins simultaneously. Each species, in turn, may infest several raw materials leaving behind one or more toxic residue. In the end, a complete diet is made up of various raw materials with individual mycotoxin loads resulting in a multitude of toxic challenges for the animals.

Several researchers showed that the effects observed during multiple mycotoxin exposure can differ greatly from the effects observed in animals exposed to a single mycotoxin, indicating that the simultaneous presence of mycotoxins may be more toxic than predicted from the mycotoxins alone. This is because mycotoxins interact with each other. The interactions can be classified into three main different categories: *antagonistic*, *additive*, and *synergistic*.

## Types of mycotoxin interactions

**Additivity** occurs when the effect of the combination equals the expected sum of the individual effects of the two toxins (*Figure 1a*).

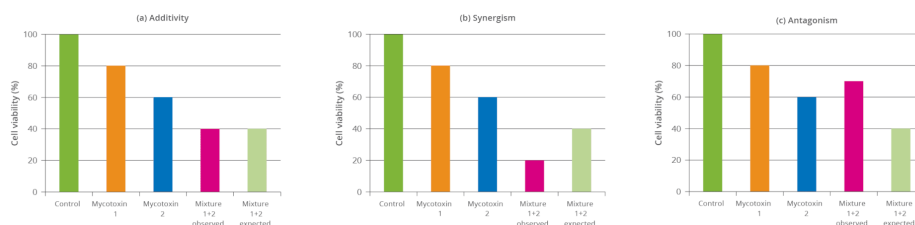
**Synergistic** interactions of two mycotoxins lead to a greater effect of the mycotoxin combination than would be expected from the sum of their individual effects (*Figure 1b*). A special form of synergy, sometimes called potentiation, occurs when one or both of the mycotoxins do not induce effects whereas the combination induces a significant effect.

When the effect of the mycotoxin combination is lower than expected from the sum of their individual effects, **antagonism** can be observed (*Figure 1c*). In general, most of the mycotoxin mixtures lead to additive or synergistic effects, highlighting a significant threat to animal health and being the major reason that impedes risk assessment. Synergistic actions may occur when the single mycotoxins of a mixture act at different stages of the same mechanism, e.g. T-2 increases ROS production while AFB1 decreases its clearance when the presence of one mycotoxin increases the absorption of another or decreases its metabolic degradation.

## Be aware of contaminations

Given their complex interactions, the toxicity of [combinations of mycotoxins](#) cannot merely be predicted based upon their individual toxicities. Knowing that even low levels of mycotoxin combinations can harm animal productivity, health, and welfare, it is useful for feed and animal producers to be aware of present contaminations, to be able to [link them to the risk they pose](#) for the animal and consequently take actions before the problems appear in the field.

Figure 1 - Characterisation of the interaction between mycotoxins (Smith et al., 2016).



\*References are available on request.

**By Technical Team, EW Nutrition**  
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