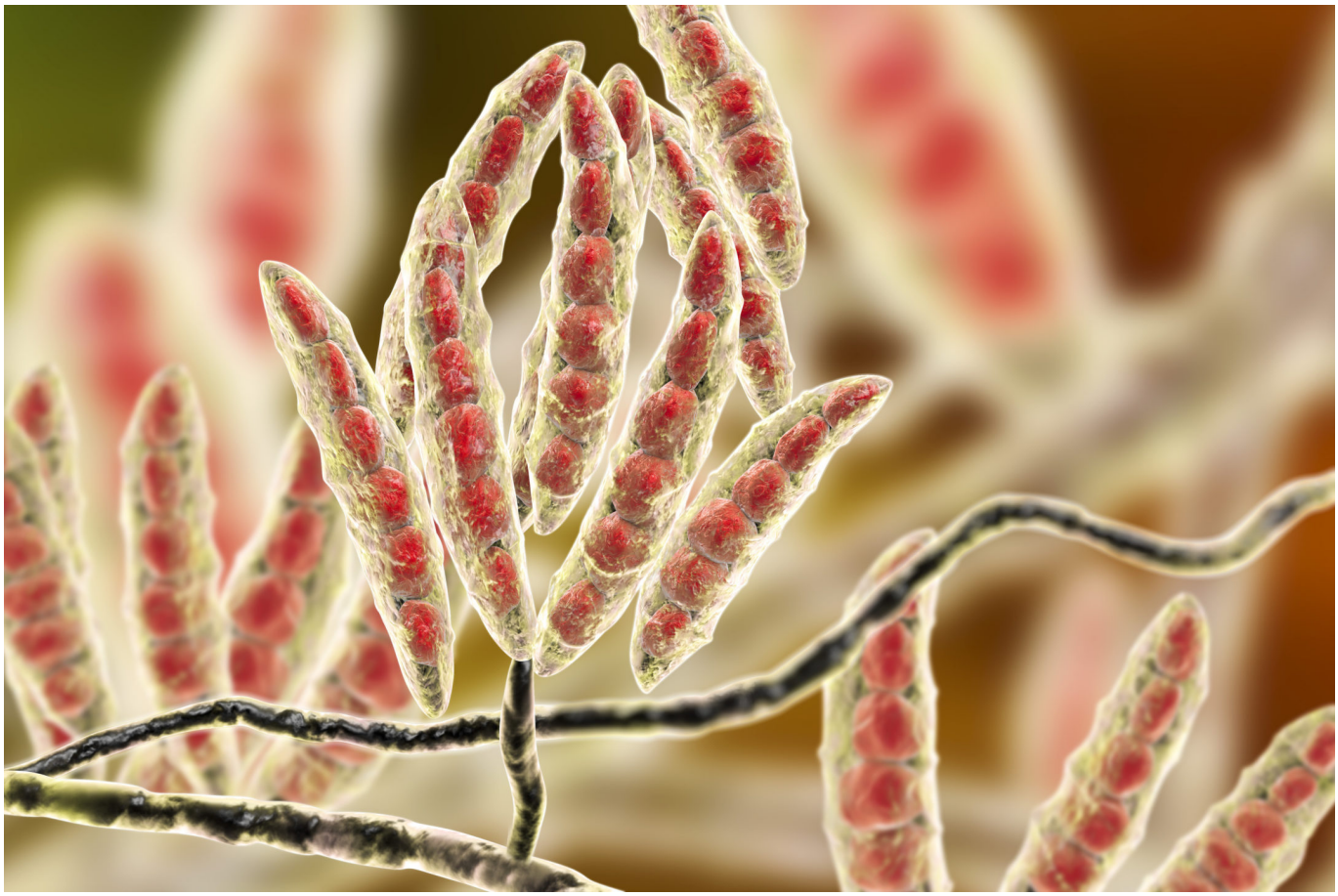
A complex battlefield: mycotoxins in the gastrointestinal tract



Most grains used as feed raw materials are susceptible to mycotoxin contamination. These toxic secondary metabolites are produced by fungi before or after harvest and cause severe economic losses all along agricultural value chains. For livestock, negative consequences include acute effects such as impaired liver and kidney function, vomiting, or anorexia, as well as chronic effects such as immunosuppression, growth retardation, and reproductive problems. Mycotoxin management is, therefore, of the utmost priority for animal producers worldwide.

But how is it that mycotoxins cause such damage in the first place? This article delves into the complex processes that take place when mycotoxins come into contact with the gastrointestinal tract (GIT). The intestinal epithelium is the first tissue to be exposed to mycotoxins, and often at higher concentrations than other tissues. A deeper understanding of how mycotoxins affect the GIT allows us to appreciate the cascading effects on animal health and performance, why such damage already occurs at contamination levels well below official safety thresholds – and what we can do about it.

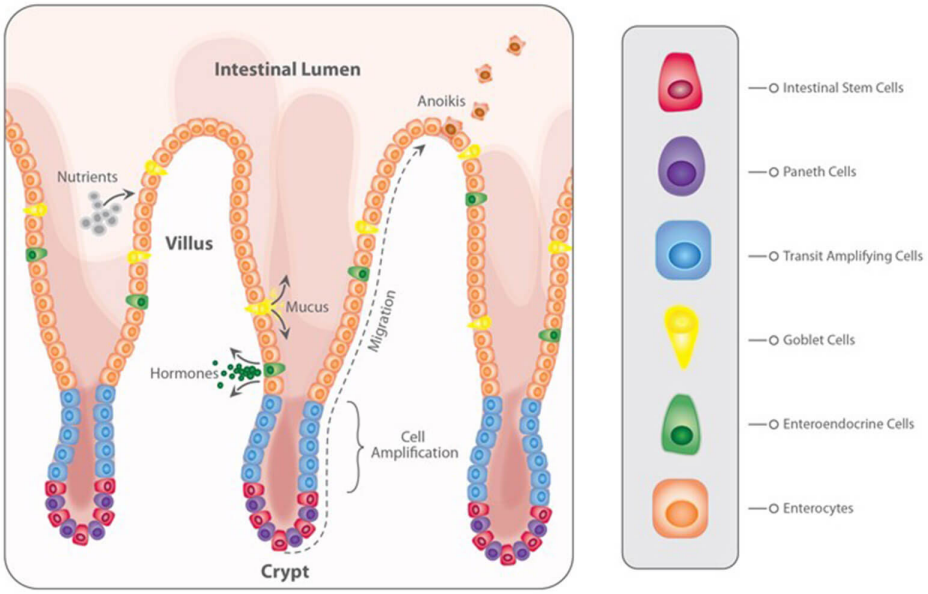
The intestinal epithelium: the busy triage site for nutrients and harmful substances

When mycotoxins are ingested, they encounter the GIT's intestinal epithelium (Figure 1). This single layer of cells lining the intestinal lumen serves two conflicting functions: firstly, it must be permeable enough to allow the absorption of nutrients. On the other hand, it constitutes the primary physiological barrier against harmful agents such as viruses, microorganisms, and toxins.

Within the intestinal epithelium, several types of highly specialized cells are involved in epithelial regeneration, nutrient absorption, innate defense, transport of immunoglobulins, and immune surveillance. The selective barrier function is maintained due to the formation of complex networks of proteins that link adjacent cells and seal the intercellular space. Besides, the intestinal epithelium is covered with mucus produced by goblet cells, which isolates its surface, preventing the adhesion of pathogens to the enterocytes (intestinal absorptive cells).

Due to its dual involvement in digestive and immune processes, the intestinal epithelium plays a pivotal role in the animal's overall health. Importantly, the epithelium is directly exposed to the entire load of ingested mycotoxins. Hence their effects can be problematic even at low concentrations.

Figure 1: The intestinal epithelium



Problematic effects of mycotoxins on the intestinal epithelium

Most mycotoxins are absorbed in the proximal part of the gastrointestinal tract (Table 1). This absorption can be high, as in the case of aflatoxins (~90%), but also very limited, as in the case of fumonisins (<1%); moreover, it depends on the species. Importantly, a significant portion of unabsorbed toxins remains within the lumen of the gastrointestinal tract.

Some of the mycotoxins that enter the intestinal lumen can be bio-transformed into less toxic compounds by the action of certain bacteria. This action, however, predominantly happens in the large intestine – therefore, no detoxification takes place before absorption in the upper parts of the GIT. Part of the absorbed mycotoxins can also re-enter the intestine, reaching the cells from the basolateral side via the bloodstream. Furthermore, they re-enter through enterohepatic circulation (the circulation of substances between the liver and small intestine). Both actions increase the gastrointestinal tract's overall exposure to the toxins.

Table 1: Rate and absorption sites of different mycotoxins

Mycotoxin	Primary absorption sites	Absorption rate in poultry	Absorption rate in swine	Observations
Aflatoxin	Duodenum / Jejunum	~90%	~80%	Subject to enterohepatic circulation
DON	Duodenum / Jejunum	Up to 20%	Up to 60%	Subject to enterohepatic circulation and to biotransformation in the large intestine
Fumonisin	Duodenum / Jejunum	Less than 1%	Less than 5%	Subject to enterohepatic circulation
Ochratoxin	Jejunum	~40%	~60%	Subject to enterohepatic circulation and to biotransformation in the large intestine
Zearalenone	Small & large intestine	~10%	~80%	Subject to enterohepatic circulation

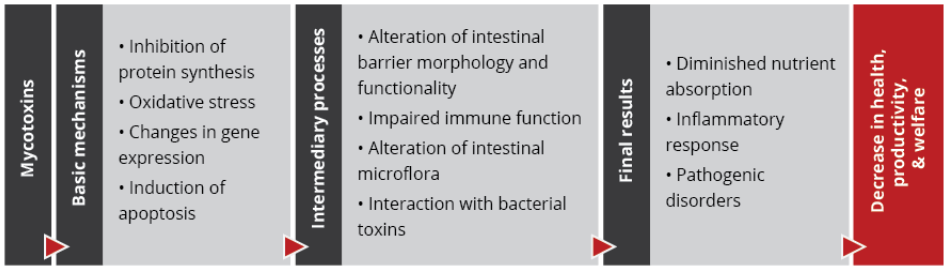
Adapted from: Biehl et al., 1993; Bouhet & Oswald, 2007; Devreese et al., 2015; Ringot et al., 2006

The damaging impact of mycotoxins on the intestinal epithelium initially occurs through:

- A decrease in protein synthesis, which reduces barrier and immune function (Van de Walle et al., 2010)
- Increased oxidative stress at the cellular level, which leads to lipid peroxidation, affecting cell membranes (Da Silva et al., 2018)
- Changes in gene expression and the production of chemical messengers (cytokines), with effects on the immune system and cellular growth and differentiation (Ghareeb et al., 2015)
- The induction of programmed cell death (apoptosis), affecting the reposition of immune and absorptive cells (Obremski & Poniatowska-Broniek, 2015)

Importantly, studies based on realistic mycotoxin challenges (e.g., Burel et al., 2013) show that the mycotoxin levels necessary to trigger these processes are lower than the levels reported as safe by EFSA, the Food Safety Agency of the European Union. The ultimate consequences range from diminished nutrient absorption to inflammatory responses and pathogenic disorders in the animal (Figure 2).

Figure 2: Mycotoxins' impact on the GIT and consequences for monogastric animals



1. Alteration of the intestinal barrier's morphology and functionality

The mycotoxins DON, fumonisin, and T2 induce a reduction in the rate of epithelial cell proliferation and differentiation. This causes a decrease in the height and the surface of the intestinal villi, which in turn leads to a reduction in nutrient absorption. Additionally, some nutrient transporters are inhibited by the action of mycotoxins such as DON and T2, for example, negatively affecting the transport of glucose.

Several studies indicate that mycotoxins such as aflatoxin B1, DON, fumonisin B1, ochratoxin A, and T2, can increase the permeability of the intestinal epithelium of poultry and swine (e.g. Pinton & Oswald, 2014). This is mostly a consequence of the inhibition of protein synthesis. As a result, there is an increase

in the passage of antigens into the bloodstream (e.g., bacteria, viruses, and toxins). This increases the animal's susceptibility to infectious enteric diseases. Moreover, the damage that mycotoxins cause to the intestinal barrier entails that they are also being absorbed at a higher rate.

2. Impaired immune function in the intestine

The intestine is a very active immune site, where several immuno-regulatory mechanisms simultaneously defend the body from harmful agents. Immune cells are affected by mycotoxins through the initiation of apoptosis, the inhibition or stimulation of cytokines, and the induction of oxidative stress. Studies demonstrate that aflatoxin, DON, fumonisin, T2, and zearalenone interact with the intestinal immune system in such a manner that the animal's susceptibility to viral and bacterial infections increases (e.g., Burel et al., 2013). Moreover, by increasing their fecal elimination, the horizontal transmission of pathogens is extended.

For poultry production, one of the most severe enteric problems of bacterial origin is necrotic enteritis, which is caused by *Clostridium perfringens* toxins. Any agent capable of disrupting the gastrointestinal epithelium – e.g. mycotoxins such as DON, T2, and ochratoxin – promotes the development of necrotic enteritis. The inhibition of the intestinal immune system caused by mycotoxins such as aflatoxin, DON, and T2 also collaborates with the development of this disease.

3. Alteration of the intestinal microflora

The gastrointestinal tract is home to a diverse community of bacteria, fungi, protozoa, and viruses, which lines the walls of the distal part of the intestine. This microbiota prevents the growth of pathogenic bacteria through competitive exclusion and the secretion of natural antimicrobial compounds, volatile fatty acids, and organic acids.

Recent studies on the effect of various mycotoxins on the intestinal microbiota show that DON and other trichothecenes favor the colonization of coliform bacteria in pigs. DON and ochratoxin A also induce a greater invasion of *Salmonella* and their translocation to the bloodstream and vital organs in birds and pigs – even at non-cytotoxic concentrations. It is known that fumonisin B1 may induce changes in the balance of sphingolipids at the cellular level, including for gastrointestinal cells. This facilitates the adhesion of pathogenic bacteria, increases in their populations, and prolongs infections, as has been shown for the case of *E. coli*.

From the perspective of human health, the colonization of the intestine of food-producing animals by pathogenic strains of *E. coli* and *Salmonella* is of particular concern. Mycotoxin exposure may well increase the transmission of these pathogens, posing a risk for human health.

4. Interaction with bacterial toxins

When mycotoxins induce changes in the intestinal microbiota, this can lead to an increase in the endotoxin concentration in the intestinal lumen. Endotoxins or lipopolysaccharides (LPS) are fragments of Gram-negative bacteria's cell walls. They are released during bacterial cell death, growth, and division. Hence endotoxins are always present in the intestine, even in healthy animals. Endotoxins promote the release of several cytokines that induce an enhanced immune response, causing inflammation, thus reducing feed consumption and animal performance, damage to vital organs, sepsis, and death of the animals in some cases.

The synergy between mycotoxins and endotoxins can result in an overstimulation of the immune system. The interaction between endotoxins and estrogenic agents such as zearalenone, for example, generates chronic inflammation and autoimmune disorders because immune cells have estrogen receptors, which are stimulated by the mycotoxin. The combination of DON at low concentrations and endotoxins in the intestine, on the other hand, has been shown to engender a decrease in transepithelial resistance and to alter the balance of the microbiota.

What to do? Proactive toxin risk management

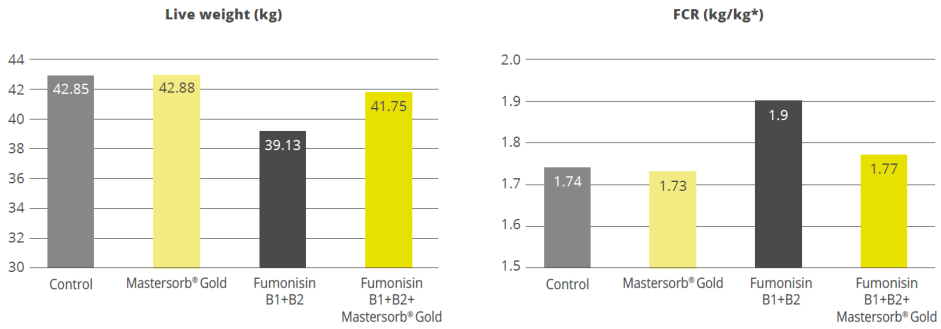
To prevent the detrimental consequences of mycotoxins on animal health and performance, proactive solutions are needed that support the intestinal epithelium's digestive and immune functionality and help maintain a balanced microbiome in the GIT. Moreover, it is crucial for any anti-mycotoxin product to feature both anti-mycotoxin and anti-bacterial toxin properties and that it supports the organs most targeted by mycotoxins, e.g., the liver. EW Nutrition's Mastersorb Gold premix is based on the synergistic combination of natural clay minerals, yeast cell walls, and phytomolecules. Its efficacy has been extensively tested, including as a means for dealing with *E. coli* endotoxins.

Mastersorb Gold: anti-mycotoxin activity stabilizes performance and strengthens liver health

A field trial conducted in Germany on male Ross 308 broilers showed that for broilers receiving a diet contaminated with DON and zearalenone, adding 1kg of Mastersorb Gold per ton of feed to their diet led to significant performance enhancements. Not only did they recuperate the mycotoxin-induced weight loss (6% increase relative to the group receiving only the challenge), but they gained weight relative to the control group (which received neither the challenge nor Mastersorb Gold). Feed conversion also improved by 3% relative to the group challenged with mycotoxins.

A scientific study of crossbred female pigs showed that Mastersorb Gold significantly reduced the deleterious effects of fumonisin contamination in the feed. The decrease in weight gain and the decline of feed conversion could be mitigated by 6.7% and 13 FCR points, respectively (Figure 3). Also, the sphinganine/sphingosine (Sa/So) ratio, a biomarker for fumonisin presence in the blood serum, could be decreased by 22.5%.

Figure 3: Mastersorb Gold boosts performance for pigs fed a fumonisin-contaminated diet

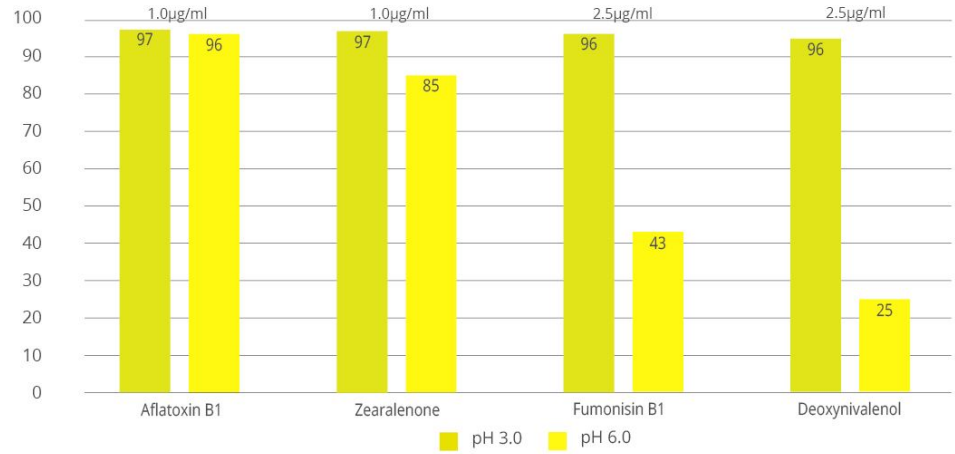


Another study of crossbred female piglets, carried out at a German university, investigated whether Mastersorb Gold could support performance as well as liver health under a naturally occurring challenge of ZEA (~ 370ppb) and DON (~ 5000ppb). Mastersorb Gold significantly improved weight gain and feed conversion in piglets receiving the mycotoxin-contaminated diet: daily body weight gain was 75g higher than that of a group receiving only the challenge, and the FCR improved by 24% (1.7 vs. 2.25 for the group without Mastersorb Gold). Moreover, Mastersorb Gold significantly improved the liver weight (total and relative) and the piglets' AST levels (aspartate aminotransferase, an enzyme indicating liver damage). A tendency to improve spleen weight and GGT levels (gamma-glutamyl transferase, another enzyme indicative of liver issues) was also evident, all of which indicate that Mastersorb Gold effectively counteracts the harmful impact of mycotoxin contamination on liver functionality.

In-vitro studies demonstrate Mastersorb Gold's effectiveness against mycotoxins as well as bacterial toxins

Animal feed is often contaminated with two or more mycotoxins, making it important for an anti-mycotoxin agent to be effective against a wide range of different mycotoxins. Besides, to prevent mycotoxins damaging the GIT, an effective product should ideally adsorb most mycotoxins in the first part of the animal's intestine (under acidic conditions). In-vitro experiments at an independent research facility in Brazil showed that an application of 0.2% Mastersorb Gold binds all tested mycotoxins at rates from 95 to 97% at a pH level of 3, using realistic challenges of 1000ppb (Aflatoxin B1 and ZEA) and 2500ppb (Fumonisin B1 and DON). The binding results achieved for Fumonisin and DON, which are often considered outright "nonbinding," under challenging close to neutral conditions (pH 6), are particularly encouraging.

Figure 4: Mastersorb Gold binding capacity against different mycotoxins (%)



Concerning its efficacy against endotoxins, an *in vitro* study conducted at Utrecht University, among other studies, has shown Mastersorb Gold to be a strong tool against the LPS released by *E. coli.* For the test, four premium mycotoxin binders were suspended in a phosphate buffer solution to concentrations of 0.25% and 1%. *E. coli* LPS were suspended to a final concentration in each sample of 50ng/ml. Against this particularly high challenge, Mastersorb Gold achieved a binding rate of 75% at an inclusion rate of 1%: clearly outperforming competing products, which at best showed a binding rate of 10%.

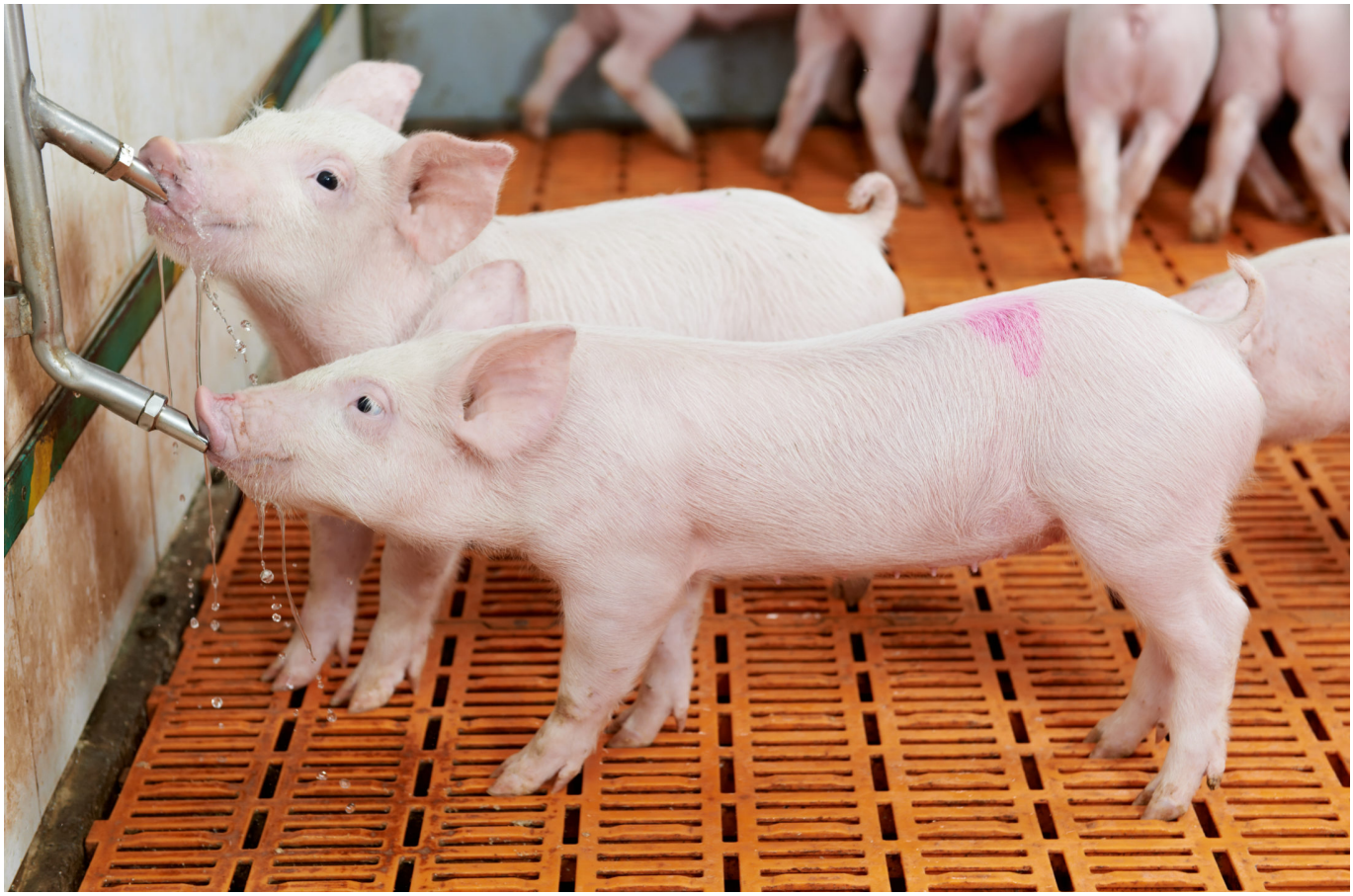
Conclusion

A healthy gastrointestinal tract is crucial to animals' overall health: it ensures that nutrients are optimally absorbed, it provides effective protection against pathogens through its immune function, and it is key to maintaining a well-balanced microflora. Even at levels considered safe by the European Union, mycotoxins can compromise different intestinal functions such as absorption, permeability, immunity, and microbiota balance, resulting in lower productivity and susceptibility to disease.

To safeguard animal performance, it is important to continually strive for low levels of contamination in feed raw materials – and to stop the unavoidable mycotoxin loads from damaging the intestinal epithelium through the use of an effective anti-mycotoxin agent, which also supports animals against endotoxins and boosts liver function. Research shows that Mastersorb Gold is a powerful tool for proactive producers seeking stronger animal health, welfare, and productivity.

By Technical Team, EW Nutrition

5 key facts pig producers need to know about the EU’s ZnO ban



We all know the headlines, “European Commission adopts ZnO ban” or “Zinc oxide to be phased out at EU level by 2022”. Clearly, EU legislation has far-reaching consequences for European pig producers – but in the jungle of acronyms and legalistic jargon, it’s not always clear which institution gets to decide what and why. Here are five key facts that help pig producers make sense of the EU’s zinc oxide ban.

1. Zinc oxide can only be used as a feed additive (low dosage)

Pigs require zinc to maintain various metabolic functions, hence it is included in their diet as a feed additive. This use will not be banned: ZnO is included as a source of zinc in the so-called register of feed additives, which applies to the whole EU. The European Commission decides which products are included in the register based on the opinions of the European Food Safety Authority (EFSA), which also advises the Commission on topics like animal welfare and African swine fever. The EFSA currently suggests that a total level of 150ppm meets the animals’ physiological needs for zinc. The European Commission has turned this recommendation into law, hence 150ppm is the legal limit for zinc supplementation for piglets.

2. The EU sets common rules for veterinary medicinal products

ZnO-based products to treat post-weaning diarrhea in piglets, on the other hand, contain pharmacological doses of zinc oxide. A commonly administered dosage is 100mg per kg body weight per day for 14 consecutive days, amounting to 2500ppm zinc in the feed. These products are classified as veterinary medicinal products (VMPs) and are thus covered by Directive 2001/82/EC on medicinal products for veterinary use and by Regulation (EC) No 726/2004. These pieces of legislation set out the EU's rules for the production, distribution, and authorizations of VMPs, and they establish the European Medicines Agency (EMA). Just as the EFSA advises the European Commission on feed additives, they turn to the EMA regarding VMPs.

What is the difference between a "regulation" and a "directive"?

Regulations automatically apply to all EU countries, without needing to be transposed into national law. A directive requires EU members to achieve certain objectives – and to transpose them into national law – but lets them to choose how to do so, as long as they meet a set deadline.

Zinc oxide – two different uses, two different situations

	ZnO as a feed additive	ZnO as a veterinary medicinal product (VMP)
EU agency	European Food Safety Authority (EFSA)	European Medicines Agency (EMA)
Legislation	Regulation (EC) No 1831/2003 on additives for use in animal nutrition	Directive 2001/82/EC on veterinary medicinal products + Regulation (EC) No 726/2004 Note: by 2022 these two will be replaced by the new Regulation (EU) 2019/6
Levels	Max. total 150ppm of zinc (from ZnO and other sources)	Normal dosage ca. 2500ppm
Ban?	No! There is no indication at the moment that zinc oxide will be banned as a feed additive.	**Yes!** Marketing authorizations for VMPs containing zinc oxide will be withdrawn the across EU by June 2022.

3. ZnO products licenses are a national topic – but subject to EU scrutiny

One of EMA's key topics are marketing authorizations: VMPs can only be sold and traded in the EU if they have received a marketing authorization, which is basically a license. Depending on the type of VMP and on when it was first released, the marketing authorization is either issued by the EMA or by national authorities. Veterinary medicines containing zinc oxide are (or rather were) within the remit of national authorization procedures. However, national authorities are supposed to turn to the EMA's Committee for

Medicinal Products for Veterinary Use (CVMP) if they have any issues with an application that is submitted to them. This is what happened in the case of zinc oxide.

4. France and the Netherlands initiated the review of zinc oxide

A European company in the feed industry had applied for marketing authorization for its ZnO-based medicated feeding stuff for piglets in the United Kingdom, hoping for a so-called decentralized authorization procedure to take place. This procedure would mean that the marketing authorization issued in the UK would also be valid in other EU countries. However, France and the Netherlands objected to this on the grounds of environmental concerns. Initially, the CVMP ruled that the marketing authorization could be granted, but France and the Netherlands persisted. In a second round, they raised doubts about the efficacy of risk mitigation measures and the added issue of antimicrobial resistance. This time, they were successful.

5. Bottom line: ZnO products will no longer get a marketing authorization

In March 2017, the CVMP concluded that zinc oxide's benefits of preventing diarrhea do not outweigh the risks to the environment. Therefore the panel recommended that national authorities withdraw existing marketing authorizations for zinc oxide-based VMPs and that they no longer grant new authorizations. Shortly after that, on 26 June 2017, the European Commission adopted the CVMP's recommendation, which means that all EU countries have to implement it. This decision also says that countries may defer withdrawing the marketing authorizations if they think that the lack of available alternatives and necessary changes in farming practices put too much pressure on their pig sectors. They can only defer for five years though; hence, the decision must be implemented no later than 26 June 2022.

How do you say "ZnO ban" in EU terms?

The withdrawal of marketing authorizations for veterinary medicinal products containing zinc oxide to be administered orally to food-producing species.

Today we stand at the half-way point before the ban of VMP ZnO as a veterinary medicinal product kicks in across the EU. Hence the search is on for effective strategies to control post-weaning diarrhea: without zinc but through continuous improvements in management and feed practices, as well as the support of targeted, functional feed additives.

By Technical Team, EW Nutrition
Article available in german, dutch and spanish.

Why we need to replace zinc oxide in tackling post-weaning diarrhea

Piglets experience significant stress when they are weaned from the sow and change diet, making them susceptible to gastrointestinal disorders. Primarily during the first two weeks after weaning, they are likely to suffer from post-weaning diarrhea (PWD). PWD is a significant problem for pig producers worldwide: it leads to severe dehydration, stunted growth and mortality rates of up to 20-30%. Treatment and additional labor costs further squeeze farm profitability and necessitate unwanted antibiotic interventions.

Zinc oxide: an effective but highly problematic tool

Since the early 1990s zinc oxide (ZnO) has been used to control post-weaning diarrhea and promote growth in piglets, mainly at pharmacological dosages of 2500 to 3000ppm. Its mode of action is still not entirely understood; effects on immune or metabolic processes, altered microbiota, or post-absorptive metabolism are likely to play a role. What is clear is that the use of ZnO in European pig production has strongly increased since the EU banned the use of antibiotic growth promoters such as colistin in 2006 to curb the development of antimicrobial resistance.

Pigs depend on a continuous supply of zinc. Among other roles, this trace element constitutes a functional component of around 300 biochemical enzymes, making it pivotal to most metabolic processes, and by extension to optimal health, production and reproduction. Modern pig diets thus include zinc supplementation to meet the animals' requirements. The European Food Safety Authority (EFSA) currently suggests that a total level of 150ppm of zinc in feed matches the animals' physiological need for zinc. The EFSAs concerns are solely connected to the environmental concerns arising from pharmacological high dosages of ZnO.

These concerns are grave indeed: zinc is a heavy metal after all. Too much zinc is toxic for the animal, hence its physiology ensures that excessive zinc intake is excreted. The bioavailability and absorption of zinc from zinc oxide is particularly low. Therefore most of the zinc given to piglets in this way accumulates in their manure – which is widely used as an organic fertilizer for agricultural soils.

The continual application of manure gradually increases topsoil zinc concentrations; leaching and run-off then lead to contamination of groundwater, surface waters, and sediment. As zinc is non-volatile and non-degradable, it is only a matter of time before concentrations lead to ecotoxic effects, including food crops, aquatic life, and drinking water. Classic mitigation measures such as diluting the manure or keeping certain minimum distances between application areas and surface waters can only slow down the environmental accumulation of zinc, not prevent it.

EU ban: ZnO to be phased out by 2022

In 2017, the European Medicines Agency (EMA) – the EU agency responsible for the scientific evaluation, supervision and safety monitoring of medicines, including veterinary medicinal products – conducted an overall risk-benefit analysis for ZnO. It concluded that the benefits of preventing diarrhea in pigs did not outweigh the significant environmental risks caused by zinc pollution. By June 2022 all EU member states will thus have to withdraw marketing authorizations for veterinary medicinal products containing zinc oxide that are administered orally to food-producing species.

In its decision, the EMA's Committee for Medicinal Products for Veterinary Use also points out the risk that, due to co-resistance, the use of zinc oxide might promote the development of antimicrobial resistance. High doses of zinc supplementation have been shown to increase the proportion of multidrug-resistant *E. coli* and *Salmonella*, two of the most important pathogens in pig production.

What is more, studies show that excessive zinc can accumulate in the liver, the pancreas, and blood serum, and that it permanently reduces the *lactobacilli* population of the gut flora. With what consequences for performance in the fattening phase? Hence, there are plenty of reasons why getting rid of zinc oxide is a good thing and will ultimately result in even better, more sustainable pig production – but, of course, only if effective replacement strategies to control PWD and boost piglet performance are in place.

Towards zero ZnO: smart feed additives optimize gut health

The search for ZnO alternatives takes us right back to the start, to the piglets' challenged gastrointestinal tract. During their first three months of life, pigs' gastrointestinal system undergoes a complex maturation process of its epithelial, immune, and enteric nervous systems. Only once all of these systems are fully developed is the gut capable of delivering its normal functions (digestion, nutrient absorption, immunity, etc.), while also providing an effective barrier against the pathogens, antigens, and toxins in the lumen.

Unlike in nature, where weaning occurs around the time when GIT functions have matured, weaning in commercial pig production takes place during this vulnerable developmental period. Post-weaning diarrhea is ultimately a consequence of intestinal dysbiosis, a state of imbalance in the intestinal microbiome which in turn is induced by the dietary, behavioral, and environmental stressors of the weaning phase (such as separation from the sow, vaccinations, transport, introduction of solid feed).

PWD control thus starts with managing these stressors, which includes ensuring sufficient colostrum intake, gradual feed changes, and meticulous nursery hygiene. Critically, the weaning diet needs to optimally support gut health. Intelligent feed additive solutions are able to

- reduce the pathogenic load in the piglet's GIT,
- strengthen the piglet's maturing gut barrier functionality, and
- selectively induce the development of beneficial microorganisms within the microbiome.

A synergistic combination of phytomolecules, medium-chain fatty acids, glycerides of butyric acid, and prebiotics achieves these objectives in a reliable and cost-effective manner. Thanks to their antimicrobial, anti-inflammatory, and digestive properties these selected ingredients effectively support piglets during this critical phase of their postnatal gut development, while also boosting their feed intake.

In the past decade, the European pig sector has successfully adapted to the 2006 ban on antibiotic growth

promoters through significant improvements in management and feed practices. Cutting out zinc oxide is an ambitious challenge – but with the support of targeted, functional feed additives, producers will be able to set their piglets up for a strong, sustainable, zero ZnO health and growth performance.

*You can find this article in polish and italian.

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Mind the immunity gap: egg immunoglobulins bolster piglets' immune system

In contrast to humans, piglets do not receive any maternal immunoglobulins via the placenta. It is therefore of vital importance for these young animals to receive maternal antibodies via the colostrum as soon as possible after birth. Otherwise, they are more vulnerable to illnesses in their early stages of life.

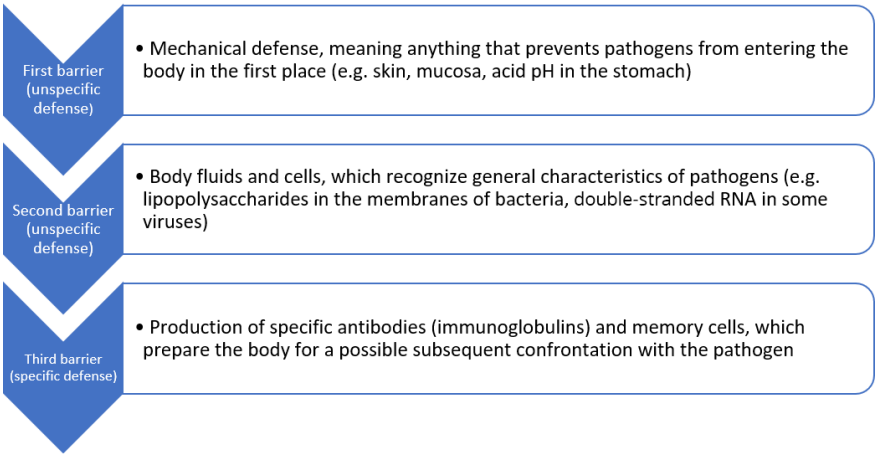
In this article, we look in-depth at how the immune system works and which role antibodies play in it. We then consider why immunoglobulins from the egg (IgY) might potentially be a powerful tool for supporting young animals immunologically, allowing producers to maintain young animals' health and to promote their performance.

How the immune system defends the

body: three barriers

The immune system aims to prevent pathogens such as viruses, bacteria, and fungi from entering the body or to eliminate them when they have already entered. Furthermore, it seeks to prepare the body for quicker reactions, in case of subsequent infections, by building an immunological memory. Generally, in case of an attack by pathogens, there are three barriers against the “enemy” (Figure 1).

Figure 1: The three barriers of the immune response



First barrier: the immediate, physical defense upon contact with pathogens

The animal body has several anatomical features that prevent pathogens from entering in the first place, such as cilia and mucus. Skin, intestines and nose lining are colonized by a community of beneficial micro-organisms that form a physical barrier against pathogens. Other barriers include the urinary system, the acid pH of the stomach, as well as tears and saliva, which contain antibacterial lysozymes.

Second barrier: the unspecific, native defense that does most of the work

If the mechanical mechanisms of defense were not successful, the unspecific, innate immune defense enters into play (Murphy and Weaver, 2018, 47ff.). At this stage, the body needs to differentiate between “known” and “alien” agents, and between “potentially harmful” and “harmless” ones.

To identify alien, potentially harmful agents, the unspecific defense looks for so-called PAMPs (pathogen associated molecular patterns). These are general characteristics often displayed by pathogens, such as lipopolysaccharides in the bacterial membrane or double-stranded RNA in viruses. Everything that shows PAMPs is heavily targeted.

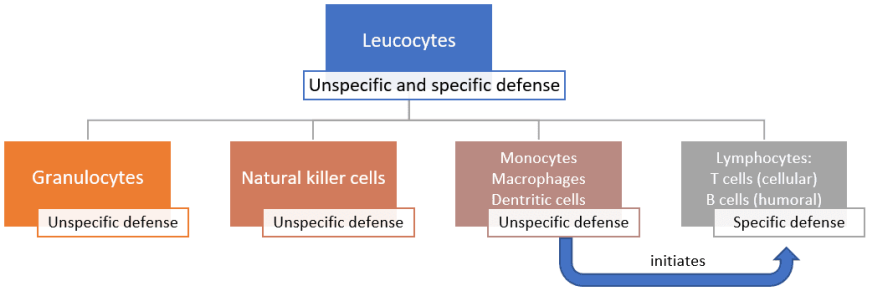
The unspecific defense can be further divided into the humoral and the cellular defense. **The humoral defense** consists of substances dissolved in the body fluids, such as enzymes, reactive oxygen compounds, signal molecules and a whole cascade of proteins. Some of these substances kill pathogens directly; others “mark” the pathogens and “call for” the help of leucocytes.

The **cellular defense** consists of different leucocytes, also known as white blood cells (because they do not contain any red hemoglobin). The main task of leucocytes is the defense of the body against pathogens, hence many leucocytes are capable of phagocytosis (the ingestion of other cells). To prevent phagocytes from accidentally ingesting the body’s own cells, these own cells are marked with the so-called major histocompatibility complex (MHC). This acts as a red flag, saying “I belong to the body!”.

The cellular defense consists of:

- Neutrophil granulocytes (60-70% of the leucocytes), which mainly act against bacteria
- Eosinophil and basophil granulocytes (1.5% of the leucocytes), which mainly act against parasites
- Natural killer cells, which mainly act against viruses
- Monocytes (3-8% of the leucocytes; they differentiate into macrophages and dendritic cells)

Figure 1: The three barriers of the immune response



The monocytes, as well as their macrophage and dendritic cell "offspring", are the bridge to the next step, the specific defense. When these phagocytes digest pathogens, minuscule protein structures (antigens) of the pathogens remain. These antigens are unique to each pathogen. During a process called antigen presentation, the antigens are tied to the cell's MHC and transported to the cell surface. This triggers the production of specific antibodies, the immune system's third barrier.

Third barrier: the specific immune defense that creates antibodies and immunological memory

The specific (also called adaptive or acquired) immune response kicks in a few days after contact with specific pathogens and is mostly carried out by lymphocytes called T and B cells (Murphy and Weaver, 2018, 177ff.). They are active at the cellular and the humoral level, respectively.

T cells possess receptors on their surface through which they can recognize the antigens presented to them by phagocytes. What they do subsequently depends on the subtype of the T cell:

- Cytotoxic T cells (CD8+) directly destroy the antigen-phagocyte-combination
- T helper cells (CD4+) attract other cells that can destroy the pathogens (e.g. macrophages) and stimulate B cells to produce antibodies against them

B cells also possess receptors through which they can recognize antigens. Once they spot an antigen (and T helper cells "confirm" that an immune response is required), they divide and mature into so-called plasma cells. Plasma cells, in turn, secrete plenty of antibodies (or immunoglobulins) into the bloodstream and the lymphatic system. Antibodies are protein structures that lock onto and neutralize antigens through different mechanisms.

The chemical reaction between antibodies and antigens is the body's most powerful immune response through which it can protect itself from pathogens and their toxins. Antibody production continues for several days to remove the antigens, and antibodies usually remain in circulation for a few months.

Moreover, certain T and B cells memorize the first attack of a pathogen and turn into memory cells. The T memory cells CD4+CD8+, for instance, match the antigens from certain past, latent, and particularly persistent viral infections. This immunological memory, created by acquired immunity, can be thought of as a library of antibodies that the body adds to whenever it deals with a new pathogen or receives a vaccine. In case of a subsequent contact with the pathogen, the right antibody "model" already exists and mass production can start up very quickly.

Why young animals' immune defense is so vulnerable – and what IgY can do about that

Building one's immunological memory takes time. A lot of new-born animals are in a vulnerable position: they have not had time yet to acquire immunity of their own, but they are also particularly fragile and susceptible to being attacked by commonly occurring pathogens such as corona and rotaviruses, *E. coli*

and *clostridia*. The toxins that *E. coli* and *clostridia*, for instance, release, may cause diarrhea, edema, endotoxic shock, and even death.

To be protected during the first critical days of their lives, new-born animals thus need to receive a foundational stock of antibodies (passive immunity) from their mother. Humans receive maternal immunoglobulins via the placenta. Piglets, because a sow's placenta is constructed differently, are dependent on receiving them through the colostrum after birth. If this is not the case – due to inadequate quantity or quality of the colostrum – they need to receive immune support in a different way.

Egg-yolk antibodies have been proposed as a powerful tool for supporting young animals during the critical period after birth. These special proteins support the colostrum supply and guarantee that every animal in the herd has some degree of protection. This protection mostly takes place in the gut. The IgY recognize and tie up pathogens and render them ineffective.

Trial: can egg immunoglobulins support piglet immunity?

In 2009, research at the National Veterinary Research Institute in Pulawy, Poland, was conducted to probe this hypothesis. The objective of the trial was to evaluate whether an oral application of egg immunoglobulins would have a quantifiable, positive influence on the immune system of the piglets. Different immunological parameters were measured, including different types of leucocytes.

Trial design

The test consists of 6 litters with 67 piglets in total divided into two groups. The control group (n=32) received the prophylaxis customary on the farm; the trial group (n=35) additionally received a product based on egg powder (EP)[1], applied at the inclusion rate recommended by the producer. Blood samples were taken on days 0 (before application of the product), 7, 14, and 28. They were analyzed with respect to the percentages of different types of lymphocytes.

Trial results

For the group receiving egg powder, the number of leucocytes in peripheral blood was significantly elevated compared to the control group on the 7th day of life (table 1). The amounts of lymphocytes and monocytes – indicators for the specific immunological defense – were also significantly increased on day 7, whereas the total amount of granulocytes – indicator for the innate, unspecific immune defense – remained constant. Hence, already during the first days, the piglets supplied with EP disposed of a higher level of adaptive (specific) immune defense, compared to the animals in the control group. In addition, there was a significant increase in the number of CD4-positive (CD4+) and CD4-CD8-double positive (CD4+CD8+) T cells in the EP group, compared to the control animals, indicating an active stimulation of the immune system.

Except for CD4+CD8+ T cells (which remained elevated in the EP group), on day 14, the differences in cellular immune response were no longer significant. This is most probably the case because by that time the immune system of the control group had activated its own protective response. The EP product therefore supported the young animals precisely when it was necessary, during the critical first days of life.

Table 1: Hematological parameters measured in piglets after prophylactic application of an egg powder based product (EP1)

Parameter evaluated	Unit	Average values± SD				
		Day 0	7th day of life		14th day of life	
			EP	Control	EP	Control
Erythrocytes	10^{12}/L	4.77 ±0.77	4.90 ± 1.61	4.56 ± 0.18	5.94 ± 0.45	5.78 ± 1.16
Hemoglobin	mmol/L	9.15 ± 1.57	9.47 ± 2.71	9.55 ± 1.63	12.03 ± 0.67	11.30 ± 2.04
Leucocytes	10^9/L	7.97 ± 3.41	**11.73[2)] ± 2.08**	**7.05[2)] ± 0.64**	10.98 ± 3.26	9.45 ± 2.58
Lymphocytes	10^9/L	2.62 ± 0.73	**7.03[2)] ± 1.97**	**3.1[2)] ± 0.57**	5.35 ± 1.76	4.88 ± 1.68
	%	36 ± 6.00	**60[2)] ± 5.77**	**45[2)] ± 4.24**	50 ± 5.74	52 ± 7.53
Monocytes	10^9/L	0.85 ± 0.24	**1.63[2)] ± 0.15**	**0.95[2)] ± 0.21**	1.25 ± 0.41	1.03 ± 0.29
	%	10.75 ± 2	13 ± 1.57	13 ± 1.44	11 ± 0.82	10 ± 0.82
Granulocytes	10^9/L	4.5 ± 2.52	3.07 ± 0.21	3.00 ± 0.14	4.38 ± 1.35	3.53 ± 1.01
	%	53.25 ± 8	26[2)] ± 4.73	42[2)] ± 5.66	40 ± 5.45	38 ± 8.17
CD4+	%	12.47 ± 6.14	**18.00[3)] ± 5.22**	**12.82[3)] ± 4.94**	21.52 ± 5.86	22.20 ± 3.77
CD8+	%	24.83 ± 1.77	32.45[3)] ± 3.65	35.08[3)] ± 2.57	33.88 ± 5.13	33.65 ± 3.71
CD4+CD8+	%*	6.27 ± 4.35	**12.98[3)] ± 5.67**	**8.55[3)] ± 4.10**	**15.85[1)] ± 2.95**	**9.62[1)] ± 3.62**
** in percent of the lymphocytes* *Statistical significance: 1) α ≤ 0.01; 2) α ≤ 0.05; 3) α ≤ 0.1*						

[1]Ig-PRO P (EW Nutrition)

The improvement of immune status, as indicated by the presence of the specific immune cells, was confirmed by the results for the incidence of diarrhea and mortality (table 2). The animals of the control group showed a nearly 1.5 times higher incidence of diarrhea and a 1.6 times higher rate of mortality. Another explanation of these results could be the mode of action of egg immunoglobulins: by neutralizing the pathogens directly in the gut, they prevent them from causing diarrhea in the first place.

Table 2: Incidence of diarrhea and mortality

		Piglets showing diarrhea symptoms		Piglets dead due to diarrhea	
	N/litter, ø	N/litter, ø	%	N/litter, ø	%
EP group	10.97	1.95	18.76	0.37	3.37
Control group	10.94	2.94	27.21	0.59	5.39

In conclusion, this trial demonstrates that immunoglobulins from eggs (IgY) effectively support the immune system of piglets during the critical period of the first days of life.
Thanks to the stimulation of the young animals' specific immune defense and the direct neutralization of pathogens in the gut, the incidence of diarrhea – one of the main causes of losses during the first weeks of life – decreases. Hence, mind the immunity gap: providing piglets with a suitable egg powder based product sets them up for long-term health, growth, and performance.

By I. Heinzl, Editor, EW Nutrition

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Optimal conditions in the farrowing unit put piglets in pole position

The most important parameters for a pig producer are the number of healthy pigs weaned/sow/year and their weaning weight. Due to improved genetics, it is possible today to find production systems that deliver more than 30 pigs weaned/sow/year. Strategies to increase sow productivity need to take into account the management, feeding, and health of both the piglets and the sows.

Pigs' start in life – limited energy reserves and practically no immune protection

It is generally known that pigs are born physiologically immature. Their energy reserves are limited. They only possess 1-2 % fat, the main part of which is subcutaneous or structural fat protecting organs, joints and skin. Thus, the young pigs depend on the glucose of the glycogen deposits in the liver as main source of energy. This energy supply only meets their requirements for the first few hours.
Besides that, pigs cannot count on maternal antibodies. Unlike in humans, a sow's placenta is not built to enable the transfer of these protective cells within the womb. At birth, the amount of protective cells in a pig's intestine, the main site of pathogenic contamination, is therefore virtually zero. As they are born without any immune protection, new-born pigs rely on an early supply of antibodies from the maternal colostrum. During the first 24-36 hours after birth, antibodies are absorbed in the intestine and pass directly to the bloodstream. The intestinal barrier then closes. Importantly, the content of antibodies in the colostrum decreases with every hour after birth.

Prevention – the best way to protect the progeny!

Given this difficult situation in the early stages of life, it is clear that the farrowing unit should be as comfortable as possible for the young animals:

- It should be warm, as low temperatures contribute to hypoglycemia. The search for body heat at the sow additionally increases the risk of crushing, one of the main causes of pig losses. The problem arising here is that sows and the new-born pigs have different temperature requirements. One good solution is a heat lamp, installed specifically for the piglets.
- It should be clean, and pathogenic pressure should be as low as possible. Due to their poor immune status, young pigs are susceptible to diarrhea-causing pathogens like E. coli and Clostridium perfringens during their first days of life. In order to meet hygiene requirements, the first step is a careful cleaning and disinfection of the farrowing unit prior to placing the sows/gilts.

Sows' manure – the first source of contamination

Cleaning both the farrowing unit and also the sows/gilts before placing them is helpful. Producers, however, have to understand that a sow is continuously shedding pathogens through her feces and that her young come into contact with them. In fact, sow manure is the first source of contamination for new-born pigs.
There are several methods to decrease pathogens within the sow's gut. Feeding them natural substances such as probiotics or phytomolecules (also known as secondary plant compounds) in order to improve gut health is one possibility: beneficial microbes such as lactobacilli or bifidobacteria compete with pathogens such as E. coli or clostridia for nutrients and prevent their proliferation. Phytomolecules such as carvacrol and cinnamaldehyde, on the other hand, were found to have antimicrobial properties.
Could feeding them egg immunoglobulins be another possibility?

Egg immunoglobulins – the key to reduce pathogenic pressure?

Yokoyama et al. (1992 and 1997) already showed that immunoglobulins from eggs applied to piglets bind to pathogens within their intestinal tract. If they also bind pathogens in the sow's gut – generating

harmless complexes – this could be the key to reduce pathogenic pressure in the farrowing unit.

Trial

Method
To evaluate this possibility a trial was conducted in Japan. Two groups of eight sows were used. The sows of the control group received standard lactation feed. The trial group was also fed standard feed, but additionally received a supplement containing egg powder product (EPP) with immunoglobulins* at a dosage of 5g/sow twice daily during the last ten days before and the first seven days after delivery. The feces of the sows were obtained by rectal stimulation (in order to rule out 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 was determined.

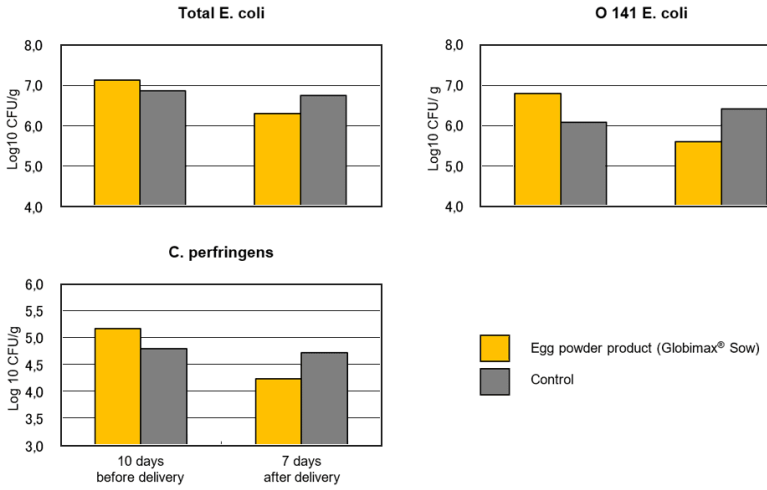
Results
The results are shown in figure 1. At the beginning of the trial, before the application of the EPP, both groups showed nearly the same level of the pathogens evaluated, with a slight disadvantage for the EPP group. After 17 days of using the EPP, the sows of the EPP group showed lower levels of pathogens in their excrements than the sows of the control group. A reduction in the colony-forming units of total Escherichia coli (from 107.12 to 106.3), Escherichia coli O141 (from 106.8 to 105.6) and of Clostridium perfringens (from 105.17 to 104.24) could be seen.

*The product used in this trial was Globimax® Sow, EW Nutrition.

Egg immunoglobulins – a tool to optimize conditions in the farrowing unit

It is important for pig producers to understand how they can combat adverse influences on their animals' performance. The results of this trial showed that supplementing the standard sows' diets with the EPP substantially reduced the amount of pathogenic colonies in sow's manure. Reducing pathogenic pressure in the farrowing unit is central to reducing the incidence of diarrhea and pre-weaning mortality. Giving young pigs the best possible start in life sets them up for delivering the best possible performance – and more healthy and heavy pigs weaned/sow/year means a more profitable farm.

Figure 1: Amounts of total E. coli, O 141 E. coli and Clostridium perfringens in the feces of sows 10 days before delivery (before the first application of EPP) and 7 days after delivery (after the last application of EPP)



By Inge Heinzl, Editor, EW Nutrition

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Diarrhea? 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 diarrhea. 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. Diarrhea 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 diarrhea, 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 diarrhea. 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 diarrhea 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 (65th 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 ≥ 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).*

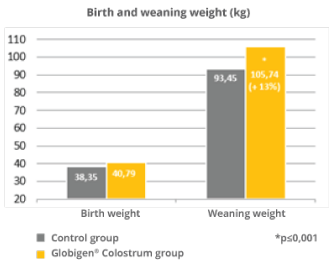

Figure 1: Effect of an egg powder product on weaning weight (kg)

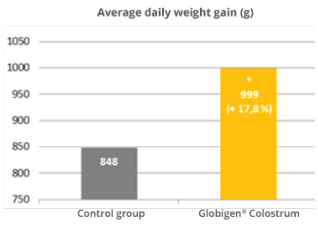

Figure 2: Effect of an egg powder product on ADG (g)

Support during acute diarrhea

When diarrhea 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 (77th day of life). All calves suffering from diarrhea (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 diarrhea stopped.

If the diarrhea 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).

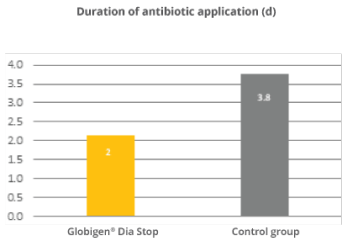

Figure 3: Duration of antibiotic application (d)

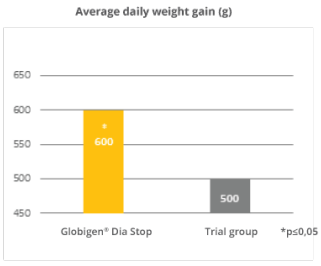

Figure 4: Effect on average daily weight gain (g)

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).

By Dr. Inge Heinzl, Editor EW Nutrition
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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.
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Using egg immunoglobulins to enhance piglet survival

The number of healthy piglets weaned is the most important factor for the calculation of profit in piglet production.

Losses in the farrowing unit normally occur during the first seven days of life as piglets are born with very little protection in the form of immunity. The intake of immunoglobulins from colostrum is therefore of vital importance. Besides cleanliness and special feeding, piglets can be additionally supported by two

strategies that mimick the effect of colostrum:
– a direct one, meaning the feeding of immunoglobulins (IgY from eggs) to piglets that would support the immune system in the gut or
– an indirect one, meaning a supply of IgY to the sow to keep the pathogenic pressure in the farrowing unit as low as possible.

Piglets are born with no immune protection and very low energy reserves
It is well known that piglets are physiologically immature at birth. Their energy reserves are very low with only 1 – 2% body fat comprising mainly of structural and subcutaneous fat. Therefore, in the first hours of life they rely on the glucose supply from glycogen from the liver as their main energy source. However, this will only cover their needs for a few hours.
Due to the construction of the sow's placenta, a transfer of immunoglobulins (antibodies) within the uterus is not possible. This means that piglets are born with practically no immune protection and depend on the immediate intake of immunoglobulins from colostrum. The immunoglobulins can be absorbed in the gastrointestinal tract and immediately transferred into the bloodstream – but also only for a short time. The absorption ability of the piglets starts to decrease soon after birth and ends after 24 to 36 hours.

Strategy 1: Making the farrowing unit as safe as possible
The piglets' environment should be warm to prevent hypoglycaemia. Piglets looking for heat close to the sow can also get crushed. Since the temperature needs of the sow and piglets are different, a piglet nest with a special heat lamp is recommended. Furthermore, the farrowing unit should be clean. Due to their low immune status, piglets are susceptible to common pathogens such as *E. coli, Clostridium perfringens*, and rotavirus that can all lead to diarrhoea.

Most pathogens can be traced to those found in the sow's faeces. To keep this amount as low as possible, different measures can be taken:
– A vaccination increases the immune defences of the sow. The antibodies fight against the pathogens so that less "functioning" pathogens are excreted.
– Feeding of probiotics increases the number of good bacteria like Lactobacilli and Bifidobacteria competing with the pathogens for binding sites and nutrients.
– Administration of egg immunoglobulins, which bind to the pathogens within the gastrointestinal tract and make them harmless. These pathogen-immunoglobulin-complexes can be ingested by the piglets without any danger.

Strategy 2: Supporting the piglets with immunoglobulins
The aim here is to strengthen the local immunity in the gastrointestinal tract by increasing the amount of immunoglobulins (Ig). As already mentioned, the intake of sow colostrum is of vital importance. With the vaccination of the sow, the content of antibodies in the colostrum can even be enhanced.
An additional measure would be to orally supply the piglets with egg immunoglobulins (IgY). Both classes of immunoglobulins (IgG from mammals, and IgY from birds) can bind to pathogens in the gut, preventing them from binding to the intestinal wall and reducing the incidence of diarrhoea. The difference is in the degree of effectiveness and specificity.

Conclusion
To maximize the number of piglets weaned, it is necessary to support their immune system during the first days of life. Besides good hygiene management, the administration of egg antibodies to the sow will also help reduce the amount of shed pathogens keeping the pathogenic pressure low. The application of egg antibodies directly to the piglets supports their immune system by binding the pathogens in the gut, minimizing the risk of diarrhoea.