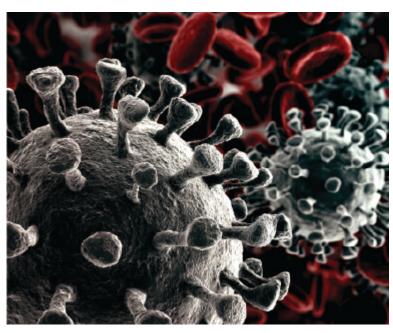
COVID-19: What we are doing and what you can do



Dear friends.

Over the past few weeks, we have all found ourselves facing a situation never before seen on this scale. How are we, at EW Nutrition, dealing with it? In a few words: with responsibility to customers, partners, and employees. To find out what we are doing as a company, but also to find out how COVID-19 might spread and what YOU can do to limit risks to yourselves and others, read more here.

What we are doing as a company

Recognizing the challenge posed by COVID-19 in our times, we at EW Nutrition remain on high alert, focused primarily on delivering solutions to our customers and security to our partners and employees.

No Coronavirus cases or known contact with such exist at present among our international teams, yet the EW Nutrition management is acting responsibly on three levels:

- Coordinating operations to ensure on-time and on-standard delivery to our customers
- Postponing/canceling all events that involve any relatively large group of customers and/or employees, regardless of the costs to the company, in order to ensure the health and safety of everyone involved (three events have been canceled/postponed so far: in Turkey, Germany, and Mexico)
- Coordinating with employees to ensure maximum levels of hygiene are observed, as well as best practices of social distancing and self-isolation in order to "flatten the curve". Where necessary and possible, remote work has been encouraged.

Moreover, to stay ahead of any potential disruptions and to keep on top of the news, the management team at EW Nutrition meets every morning for updates and sends out periodical communications to all concerned.

With the measures it has adopted and the positive code of conduct we are modeling, EW Nutrition is acting preemptively and responsibly to address any present and future challenges that the COVID-19 pandemic may raise. We are confident of our company's capacity to provide stability and value to our customers, partners, and employees.

How does the virus spread?

New <u>research</u> from the University of Austin, Texas, shows that more than 10% of the cases are transmitted by people without any observable symptoms – what is knows as "asymptomatic transmission". This type of transmission makes containment more difficult, warranting "extensive control measures including isolation, quarantine, school closures, travel restrictions and cancellation of mass gatherings."

Since this is a new virus, it is impossible to say with 100% certainty how it is spread. However, it is almost certain that one of the transmission pathways is through the cough or sneeze droplets from infected persons, even when these infected persons do not show very clear signs of the disease.

It is also possible that contact with objects on which such droplets reside may be a secondary pathway of transmission. So far, it is not known for certain how long COVID-19 can survive outside the body, but a related virus (MERS-CoV) was known to survive for up to 60 minutes in the air. Bear in mind, therefore, that objects in public spaces and confined spaces such as restrooms and elevators might also be sources of infection.

What can you do to reduce risks?

Social distancing

Keep a distance of at least a meter from other people: not just those who sneeze, cough or in any way appear to be ill, but generally from people you know have spent any time outside or with other people. This way you minimize the risk of being hit by droplets of saliva from people who may be already infected or carry the virus.

It is a radical practice, yet it is proven to be very effective. This is the solution that many countries that were hit by the SARS epidemic, for instance, adopted to curb the virus's explosive growth.

Wash your hands

Soap and water or an alcohol-based hand sanitizer are the best way to keep viruses away. Wash your hands thoroughly not just every two hours, but literally as often as you can, and especially after contact with other people or objects in public places.

Avoid public places

This includes bars, restaurants, theaters or any other places that may not already be closed. Since it is not yet clear how long coronavirus survives in the air or on objects, even places that may appear safe could potentially still harbor active viruses.

Assist the elderly - cautiously

The elderly and those with preexisting conditions are known to be at higher risk than the rest of the population. If you are an active member of the population outside these groups, it is important to minimize contact with those at risk. However, do assist them by ordering or delivering their shopping for them, or in any way that minimizes their exposure to potential sources of infection.

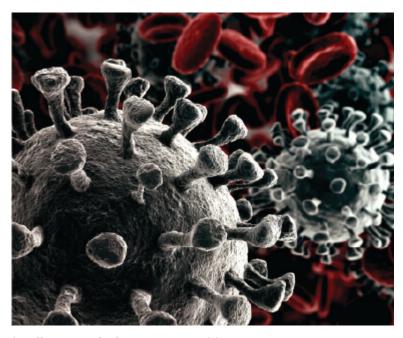
Avoid touching your face

Your mouth, nose, and eyes are easy pathways for the virus to transfer from your hands to inside your body. Even between sessions of hand-washing, it is important to remember not to touch your face. You may be unaware of certain gestures, either when touching objects or when touching your face, so this is a type of learned behavior that we all need to pay attention to.

Do not rush to the ER

If you do feel unwell, it is important to not rush out to a clinic or hospital. Please call the emergency services and follow their instructions. Rushing out in case of infection can be detrimental to your health and the health of other people you will be exposing. Bear in mind that, in most cases, the symptoms of COVID-19 are mild (fever and coughing being the most common) and there is no cause to panic.

8 ways COVID-19 might impact your business



by Ilinca Anghelescu, EW Nutrition

By now there is no doubt the economic impact of COVID-19 will be massive. The question is, how exactly will the pandemic impact your business – and what can you do to mitigate or prevent what's coming?

Since January, the international community has been aware of the seriousness and ease of contagion of COVID-19. Despite that, internet searches for "coronavirus" only exploded over the past couple of weeks. Worldwide, as a population, we were more interested in Harry Styles, home loan rates and Gal Gadot than in the impending crisis.

In other words, we individually, as well as markets, were slow to understand and accept the long-term

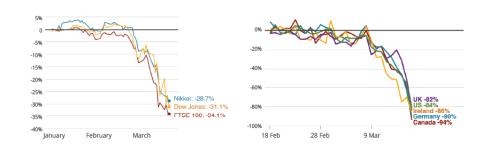
implications of the pandemic.

Google searches for "Coronavirus" since December and which countries did it most



Now that the seriousness of the pandemic has hit home, there are known losses in some industries: airlines worldwide are expected to lose \$29BN, with some smaller players being forced out of business by reduced demand. Other low-margin industries, like restaurants or the travel industry, are likewise already sustaining major losses.

Figure 1 - Visualization of COVID-19 impact on markets / Restaurant reservations



And while we are seeing the world slowly understanding and adapting to a new reality, you, like everyone else, have to prepare for the impact of COVID-19 on your business. *Quick note:* though it may appear so at first, not all the ways the pandemic affects businesses are negative!

Labor shortage

As workers are affected by the pandemic, many will either choose to stay home or will be forced to. In some countries, self-isolation measures are elective. In other regions that are more severely affected, the government may require workers in non-essential industries to not break isolation measures. This may affect your company at all levels, from processing feed or feeding animals to delivering goods across quarantined regions.

What you can do:

- Identify proximity workers you can rely on
- Preemptively create crisis scenarios for a reduced workforce
- Create a waiting list of short-term labor resources



Supply shortages

Lockdowns in China, Italy or Spain already provide examples of what happens when regions go into full isolation. Consider how massive shortages in the antibiotic supply from China or shipment delays across the world, for instance, are already affecting the animal production industry.

What you can do:

- Overstock now
- Contact alternative suppliers to create an improved supply chain
- Check expiration dates for your existing supply and consume early dates first
- Choose alternatives for products with an uncertain supply chain



Demand shortages

Depending on the industry and the market, you may be faced with reduced demand. Simply consider the fact that reduced demand for restaurants will lower, in turn, demand for supplies for the restaurant: less meat, butter, milk consumed in restaurants is less meat ordered.

What you can do:

- Prepare for basic production only
- Prepare to stock raw materials long-term if possible
- Discuss with suppliers to cut or minimize deliveries

Government policies

The Food and Drug Administration, the United States' highest authority in food and medicine safety, announced it would suspend inspections of foreign food manufacturers. The impact of this decision could be felt in the quality of foreign feed or raw materials quality. Other governments are already – or might soon be – limiting imports, restricting non-essential activities, offering financial packages for at-risk businesses,

What you can do:

- Review government policy updates on a daily basis and tailor production and operations to ensure compliance
- Give early feedback to government measures
- Apply early for relief measures, even if not severely impacted yet

Lower biosecurity standards

Even now, biosecurity is implemented more in theory than in practice. Routinely there are small infringements – and we can expect their numbers to grow massively in times of crisis. People are less likely to go through the motions if personnel is reduced, supervision is less strict, and the financial pressure of the pandemic is high. This will trigger severe risks for the animal and feed production industries, as well as for product packaging. Workers who hide symptoms to be able to sustain wages; workers attempting to speed up work because of reduced personnel; reduced or looser inspections and monitoring – all these

could perpetrate risks to your operations and to the population at large.

What you can do:

- Tighten biosecurity measures and controls
- Supplement lower government monitoring with additional on-location measures
- If you operate with a reduced workforce, periodically check how downscaling affects biosecurity implementation

Immediate economic downturn

At this point, almost all industries have a global component: your raw materials may be imported; the ingredients in the antibiotics or vaccines you use may come from anywhere around the world; your packaging may be produced in China; your software solutions may come from the Indian subcontinent; your quality controls may be managed by a consultancy from a distant European country – and so on. However much we may try to avoid it, there may be immediate repercussions on your business. Either because your goods may be inaccessible for part of the world, because of lower demand on the consumer side, or because of diminished production capacities, you may feel the impact of the pandemic sooner rather than later.

What you can do:

- Cut costs for non-essentials
- If you are in feed production, consider stocking on toxin binders, search for alternative suppliers, and assess your supply levels
- If you are in livestock production, employ solutions for animal health and welfare to lower disease risk
- Apply for government bailout early
- Assess your export strategy and prepare to zoom in on domestic
- Assess long-term payroll capacities during diminished business demand

Changing consumption trends

It turns out that, after all, the impact could be positive for some industries. The meat industry seems to be doing relatively well, despite the challenges. While in China, severely affected by ASF on the animal side and now by COVID-19 on the human side, meat production was dramatically affected, in other regions demand for – and supply of – animal protein is stable. Consider the new opportunities for frozen or prepackaged food products: as less fresh meat is consumed in restaurants or bought because of infrequent store visits, consumption of these meat products and by-products is not expected to go down – in fact, it may well increase.

The market might, however, first have to be taught to embrace these prepackaged or frozen products.

What you can do:

- Prepare for less fresh meat demand by upping prepackaged meat production
- Teach your end-users about the benefits of frozen products, from meat to egg whites, for instance



Negative impact for others, positive impact for you

While the negative effects are real, there are ways you can balance the COVID-19 impact by taking advantage of some of the positives. Consider that, to give just one example, the energy market is likely going to take a hit. This, in turn, may lead to lower fuel costs for farmers.

Reduced travel means more savings for your company, and while working from home (WFH) may lead in some cases to somewhat reduced productivity, taking an early stand and instructing your team on how to structure WFH days will help preserve productivity while cutting down on energy, fuel and other travel costs, cleaning, in-office equipment depreciation, and other such expenses.

What you can do:

- Check your balance sheets regularly
- Transfer savings from quick benefits into investments into long-term strategy
- Most importantly never panic!

Ongoing research into treating COVID-19 already shows great promise. While we do not yet know how long these unusual circumstances will last, you can make provisions for the near future and think long-term of how to protect your businesses from this pandemic or any future such challenges.

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.

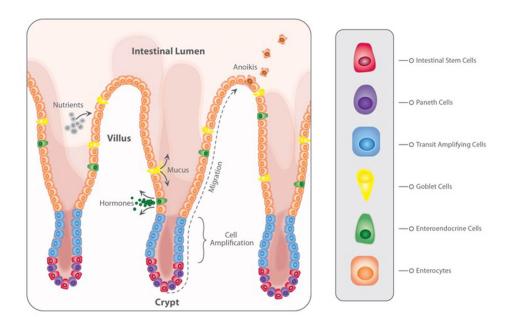


Figure 1: The intestinal epithelium

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 (\sim 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

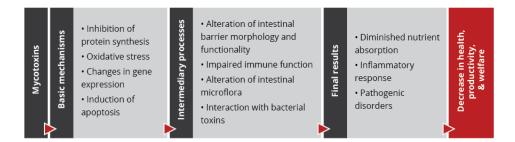
Adapted from: Biehl et al., 1993; Bouhet & Oswald, 2007; Devreese et al., 2015; Ringot et al., 2006

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

- A decrease in protein synthesis, which reduces barrier and immune function (<u>Van de Walle et al.,</u> 2010)
- Increased oxidative stress at the cellular level, which leads to lipid peroxidation, affecting cell membranes (<u>Da Silva et al., 2018</u>)
- Changes in gene expression and the production of chemical messengers (cytokines), with effects on the immune system and cellular growth and differentiation (<u>Ghareeb et al., 2015</u>)
- 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., <u>Burel et al., 2013</u>) show that the mycotoxin levels necessary to trigger these processes are lower than the <u>levels reported as safe</u> 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 <u>a reduction in the rate of epithelial cell proliferation and differentiation</u>. 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 <u>nutrient transporters</u> 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 <u>necrotic enteritis</u>, 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 <u>the development of necrotic enteritis</u>. 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 <u>DON and other trichothecenes favor the colonization of coliform bacteria in pigs</u>. DON and ochratoxin A also induce a <u>greater invasion of Salmonella</u> 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, <u>as has been shown for the case of *E. coli*.</u>

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 Gramnegative 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%.

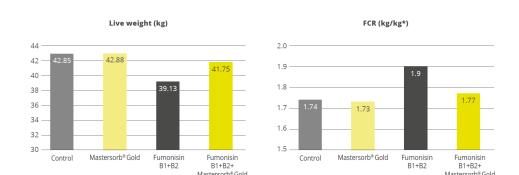


Figure 3: Mastersorb Gold boosts performance for pigs fed a fumonisin-contaminated diet

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.

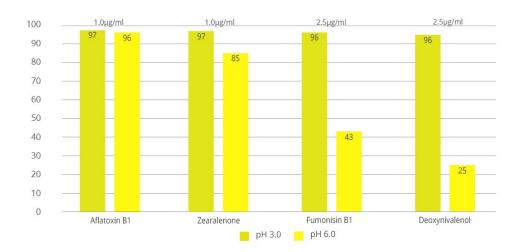


Figure 4: Mastersorb Gold binding capacity against different mycotoxins (%)

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 <u>register of feed additives</u>, 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 <u>150ppm is the legal limit</u> 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

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 <u>issue of antimicrobial resistance</u>. This time, <u>they were successful</u>.

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 <u>german</u>, dutch and <u>spanish</u>.

Poultry health and welfare: Phytomolecules for poultry diets



The large majority of poultry specialists in Europe consider phytomolecules as one of the key elements in diets for broilers, broiler breeders, and layers when birds are raised without antibiotics. A quick glance at the market will reveal more commercial products than can possibly be imagined. There are three basic elements you should bear in mind when making your choice:

- 1. **Most phytomolecules are volatile**. As such, unprotected products will soon evaporate if left exposed to the open air as it happens, for instance, with feed prepared in commercial farms. Microencapsulation is therefore essential.
- 2. **There are countless phytomolecules.** Consequently, finding the right mix for the task required is essential, as not all mixtures will get you the desired result. When designing a phytomolecule mix, the manufacturer must have the necessary knowledge and experience to achieve the desired result.
- 3. **Phytomolecules are powerful.** This is to say that you cannot just keep adding higher quantities to achieve a better result. Finding the exact inclusion rates for the right purpose is a difficult balancing exercise.

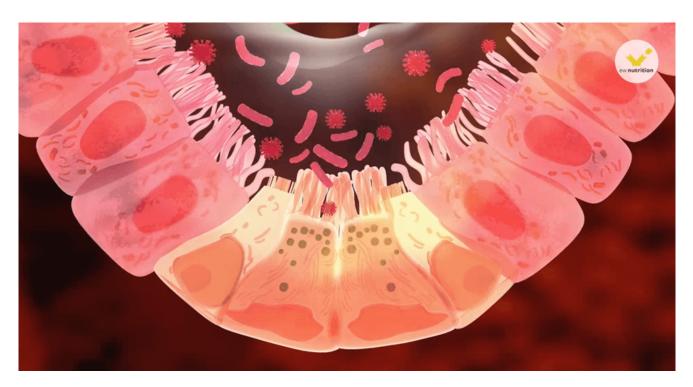
In fact, the right protection, the right mix and the right inclusion rates must be combined to ensure that the animals do not refuse the feed (worst case scenario) or just fail to benefit from the inclusion of phytomolecules.

Among the feed additives, phytomolecules (or secondary plant compounds) stand out as a class of active ingredients that may help to improve gut health and thereby reduce the use of antibiotics. Synthesized by

plants as a defense mechanism against pathogens, phytomolecules promote the digestion of feed ingredients (Zhai et al. 2018), prevent loss of gut integrity during enteric challenges (Liu et al. 2018), and have antimicrobial properties that hinder the growth of potential pathogens (Chowdhury, 2018). Phytomolecules can prevent the overgrowth of opportunistic pathogens, thereby reducing the frequency of occurrence of diseases such as necrotic enteritis and dysbacteriosis and thus improve performance data such as daily weight gain and feed efficiency.

Beyond the <u>phytomolecules' proven effects</u>, what works best in supporting the health and welfare of your animals is, in fact, a holistic program (such as those offered by EW Nutrition) that consists of an effective combination of innovative products and consultancy services in the fields of gut health, nutrition, AMR monitoring, and biosecurity management.

*This article is available in Dutch.



New distribution partnership with Russian key player in poultry feed additives





Moscow – September 18, 2019 – VITOMEK and EW Nutrition are pleased to announce that they have signed a distribution partnership agreement, combining the accumulated knowledge, experience, and effective solutions in the field of animal nutrition at VitOmek with a portfolio of comprehensive programs, innovative products, and services from EW Nutrition.

Dmitry Chudakov, General Director, VitOmek: "The partnership agreement with EW Nutrition has become an important event for us and another milestone on the road to success. We are pleased that our new partner is a company with many years of experience in the animal nutrition industry. We are confident that our scientific and technical potential, in conjunction with the valuable experience of the partner, will bring rich benefits in the form of joint development, creation of unique products and services, and the implementation of even more ambitious projects. Our philosophy: "Focus on high results. Give shape to courageous ideas in the final product."

VitOmek is one of the largest Russian producers of agricultural feed and feed additives, offering comprehensive, effective solutions for agricultural holdings and small enterprises in the poultry and livestock sector. The company's range of services includes technological, veterinary and engineering support of farms, audit and consulting on microclimate and animal welfare.

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Pavel Vladimirovich Bogatkin, General Director, EW Nutrition Russia: "We are very pleased to cooperate with VitOmek. Years of experience in the market, as well as great resources and coverage, making them an excellent ally in our common efforts. In addition to a similar market development philosophy, we see for ourselves a similar mission: mitigating the effects of antimicrobial resistance by providing comprehensive solutions in the field of animal feeding, toxin risk management, and young animal nutrition. Achieving these goals ultimately helps to increase the effectiveness of human healthcare."

EW Nutrition researches, develops, manufactures, markets, and services its products and programs around the world. Headquartered in Germany, EW Nutrition's manufacturing facilities are located on 4 continents. Innovation is carried out by our own research laboratories in Germany, with development centers in 5 major animal nutrition markets. EW Nutrition is active worldwide, with its own staff in 27 countries. Our slogan, "Functional Innovations Backed by Science," is being implemented through technical support at the local, regional, and global level.

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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. <u>Modern pig diets thus include zinc supplementation</u> to meet the animals' requirements. The European Food Safety Authority (EFSA) currently suggests that <u>a total level of 150ppm</u> 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 <u>all EU member states will thus have to withdraw marketing authorizations</u> for veterinary medicinal products containing zinc oxide that are administered orally to food-producing species.

In its <u>decision</u>, 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 <u>increase the proportion of multidrug-resistant *E. coli* and <u>Salmonella</u>, two of the most important pathogens in pig production.</u>

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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High-performance swine production with reduced use of antibiotics: 2nd workshop by EW Nutrition and OPP Group



High-performance swine production with reduced use of

antibiotics: Second workshop by EW Nutrition and OPP Group

From 4 to 7 November, in Lleida, Spain, OPP Group and EW Nutrition are hosting their second workshop on animal health and welfare with reduced antibiotic use.

The two-day event offers swine producers and other stakeholders essential, actionable information on developing profitable swine operations while reducing the use of antibiotics. "This is a very useful opportunity to learn from the experts, as well as from each other," says Michael Gerrits, Managing Director, EW Nutrition.

For this second workshop, OPP Group, highly experienced in integral swine production advisory, is partnering with EW Nutrition, an expert in animal nutrition solutions to mitigate antibiotic resistance. "Participants will learn a lot about reducing antibiotic use while keeping performance high," says Joan Sanmartín Suñer, CEO of OPP Spain. "Everyone will leave the workshop with new ideas and solutions – and new friends."

The event will take place at the OPP headquarters in Lleida and will bring together international speakers with stellar research and technical backgrounds.

About the hosts

EW Nutrition is an animal nutrition company that offers integrators, feed producers, and self-mixing farmers holistic solutions for gut health management and antibiotic reduction, young animal nutrition, toxin risk management, and more. **OPP GROUP** is a leading company providing integral swine production consulting and advisory around the world. It is present in the animal health, farming turnkey projects, and R&D business lines. OPP is working to improve animal welfare and the quality of management practices employed on farms.

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EW Nutrition Opens New Production Plant in China



Press Release

EW Nutrition Opens New Production Plant in China

On 29 October, German-based company EW Nutrition will officially open its new production plant in China. The new plant is the next step in the successful development of EWN Biotechnology Shanghai.

By offering holistic, science-backed solutions, EW Nutrition supports the Chinese industry in its effort to reduce antibiotic use. "With this latest investment," says Craige Allen, General Manager, EWN Biotechnology Shanghai, "we are offering a twofold benefit to our Chinese customers: bringing our high-value products closer to the end-user, while implementing our policy of <u>supporting antibiotic-free production in China."</u>

The new facility in Haimen will produce the three leading product lines in the company's portfolio. They represent EW Nutrition's answer to gut and <u>respiratory health issues</u>, as well as toxin risk management. "We are pleased to bring our programs closer to our customers, further increasing service levels," says Michael Gerrits, Managing Director, EW Nutrition. "But we are even more pleased and honored to bring here our mission of mitigating the impact of antimicrobial resistance by providing comprehensive animal nutrition solutions."

The virtual opening will take place at the Melia Hotel in Shanghai, to be followed by a one and a half-day symposium on "Reducing Antibiotic Use and Mitigating the AMR Risk – 2020 Vision". Speakers include Prof. Chen Junshi, Prof. Jia Yanxiong, Prof. Suwit Chotinun, as well as other prestigious national and international guests.

About EW Nutrition

EWN Biotechnology Ltd. is the Chinese arm of EW Nutrition, an international animal nutrition company that offers integrators, feed producers, and self-mixing farmers comprehensive animal nutrition solutions for antibiotic reduction, young animal nutrition, toxin risk management and more.

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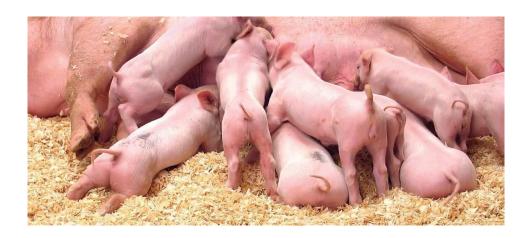
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Egg antibody technology for nursery pig application



Pigs at birth having insufficient immunity are simply not able to cope with the stress situations they face early in life. They of course become susceptible to the many pathogens common in the farrowing house. The resulting negative effects are added medical costs for treating the pigs and often an increased mortality. Strengthening the immune system by applying egg antibodies (IgY) during the first days of piglet's life is a proven viable option.



Immunity in pigs

Humans and animals are protected against diseases by specific antibodies (AB). Newborns receive the antibodies maternally (**passive immunity**) and they produce them after contact with pathogens (**active immunity**). But unlike humans, who receive maternal AB within the womb, sows possess a multi-layered placenta which prevents the transfer of AB during gestation. Therefore, an early intake of AB from colostrum is essential. This intake should begin immediately after birth as absorption decreases with every hour. But, the maternal antibodies are only a "starter immune kit". The young pigs immediately must begin to develop their own "active immunity".

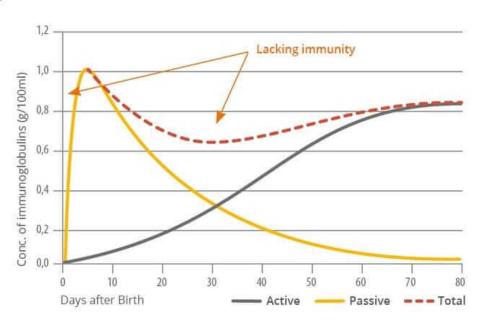
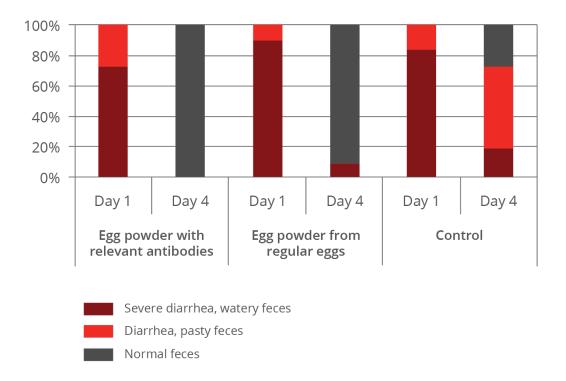


Figure 1: Immune status of the young pig (Sieverding, 2000)

Figure 1 shows gaps of low immunity shortly after birth and about six weeks after, as the level of passive immunity begins to drop and the active immunity starts to build up. The strength of the passive immune protection depends on quantity and quality of the colostrum consumed by the nursery pig. The quality is determined by the pathogens the sows have been confronted with during their life. Young gilts and sows with only short adaptation time into the herd often do not have the farm-specific antibodies needed to pass to their nursing pigs.

Birth Weaning How can egg antibodies serve as a tool? E. coli K88 Young pigs are challenged by different pathogens (see figure E. coli K99 2). From studies made by the German internist Felix Klemperer (Klemperer, 1893) we know that hens which come in contact *E. coli* 987F with pathogens (in his studies with tetanus bacillus) produce antibodies against these pathogens. The antibodies are transferred to the egg yolk and are intended for being a starter protection kit for the chicks. Technology allows us today to produce a highly valuable TGE Virus product based on egg powder. It contains significant amounts of natural egg immunoglobulins (IgY - immunoglobulins from Cryptosporidium the **y**olk). These egg antibodies mainly act in the gut. There they recognize and tie up pathogens and in this way render Rotavirus them ineffective. Figure 2: Commonly occurring pathogens causing diarrhea in pigs as they age

Not all egg powders are equal



Early work done by Kellner et al. (1994) showed the effectiveness of egg powder containing relevant antibodies against diarrhea causing pathogens in nursery pigs. In the trial they evaluated three groups receiving egg powder with relevant antibodies, egg powder from regular eggs or no additive (negative control).

Results:

(Figure 3: Effects of egg powder with relevant antibodies and egg powder from regular eggs in comparison to a negative control):

- The group that received egg powder containing relevant antibodies completely recovered from diarrhea on day 4.
- In the group fed normal egg powder on day 4 still 9 % suffered from severe diarrhea.
- In the control more than 70 % showed either severe or light diarrhea.

The results show that the effectiveness of egg powder depends on its content of antibodies.

Reducing mortality by oral administration of egg antibodies

The effectiveness of egg antibodies in pigs was demonstrated also in other studies (Erhard et al., 1996, Yokoyama et al., 1992, Nguyen et al., 2005, Yokoyama et al., 1997). One trial conducted in Germany showed promising results concerning reduction of mortality in the farrowing unit. For the trial 96 sows and their litters were divided evenly into three groups (32 sows each) and the pigs were treated as follows:

Group	Number of pigs	Treatment
Negative Control	530	no treatment
Group EP - 1+3	494	egg powder-based product Globigen Pig Doser, 4 ml on day 1, 2 ml on day 3
Group EP - 1, 2, 3	527	egg powder-based product Globigen Pig Doser, 4 ml on day 1, 2 ml on day 2 and 3

*EP = Egg powder-based product

Results:

Figure 4 shows regardless of the frequency of oral application dosage given to pigs both were very supportive and significantly reduced mortality compared to the control. This resulted in a higher number of weaned pigs than in the control.

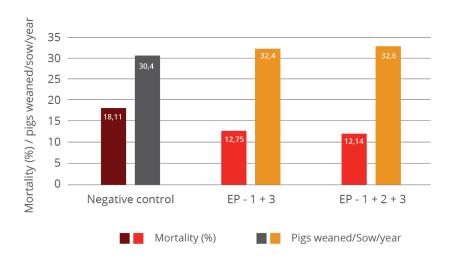


Figure 4: Mortality and resulting number of pigs weaned per sow and year

Conclusion

Using egg antibodies in pig nutrition is an effective tool to <u>reduce mortality</u> in young pigs. They can be applied individually by doser (newly weaned pigs) or via powder in the feed. Both practices have proven effectively in commercial operations.

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