

Understanding and managing *Strep suis* in swine: The essentials



Strep suis causes vast losses in pig production and threatens human health, too. We still rely on antibiotics to control it - but we will have to change tactics to contain antimicrobial resistance.



Streptococcus suis is one of the most economically harmful pathogens for the global swine industry. When I started working in pig production 25 years ago, *S. suis* was already a problem on practically all the farms that I visited. Back then, our understanding of the pathogen and hence our control strategies were rudimentary: in farrowing rooms, we cut piglets' teeth, used gentian violet spray on their navels, and sometimes applied penicillin lyophilized with iron. For the nursery phase, we only had penicillin or phenoxymethylpenicillin at our disposal – until the first amoxicillin-based premixes arrived, which turned out to be highly effective.

To this day, we control *S. suis* mainly through oral beta-lactam antibiotics (in feed or water) or injectable solutions, administered to piglets at an early age. However, pig production has evolved dramatically over the past decades, and so has the scientific research on this complex pathogen. Crucially, we now know that the excessive use of [antibiotics contributes to the development of antimicrobial resistance](#).

Recent [Australian research](#) has discovered *S. suis* strains (both in humans and pigs) with a high degree of resistance to macrolides or tetracyclines, strains with intermediate sensitivity to Florfenicol, and others that are developing resistance to penicillin G. Additionally, we now know that *S. suis* is a zoonotic bacteria that affects not only at-risk farm or slaughterhouse personnel: *S. suis* is [among the leading causes of death from meningitis in countries such as Thailand, China or Vietnam](#). In light of these threats to human health, we in the swine industry more than ever have a duty to help control this pathogen.

This article first reviews our current state of knowledge about the epidemiology and pathogenesis of *Strep suis*; it then lays out virulence factors and the role of coinfections. The second part considers the dimensions of a holistic approach to *S. suis* prevention and control and highlights the central role of intestinal health management.

What we know about *S. suis* epidemiology and pathogenesis

Practically all farms worldwide have carrier animals, but the percentage of animals colonized “intra-farm” varies between 40 and 80%, depending on several factors such as environmental conditions, hygiene measures, and the virulence of the *S. suis* strains involved.

How *S. suis* strains are classified

S. suis strains were once classified into 35 serotypes, according to their different *capsular polysaccharides* (CPS), the outermost layer of the bacterial cell. Due to phylogenetic and genomic sequencing, some of the old serotypes (20, 22, 26, 32, 33, and 34) are now reclassified, either in other bacterial genera or in other *Streptococcus* species. This has reduced the total to 29 *S. suis* serotypes.

Globally, the prevalence of the disease varies between 3% and 30%. The main serotypes affecting pig population are type 2 (28%), 9 (20%), and 3 (16%); differences in the geographical distribution are shown in Figure 1.

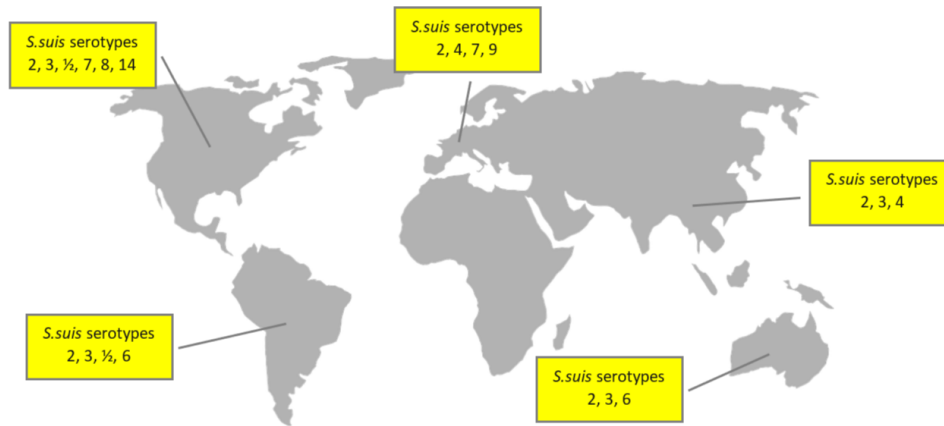


Figure 1: Global distribution of *S. suis* serotypes

Based on different sources, incl. [Goyette-Desjardins et al. \(2014\)](#), [Zimmermann et al. \(2019\)](#), and [Gebhart \(2019\)](#)

In addition to the serotype classification based on CPS antigens, *S. suis* has also been genetically differentiated into “sequence types” using the MLST (Multi Locus Sequence Typing) technique. The distribution of both porcine and human sequence types is detailed in Figure 2.

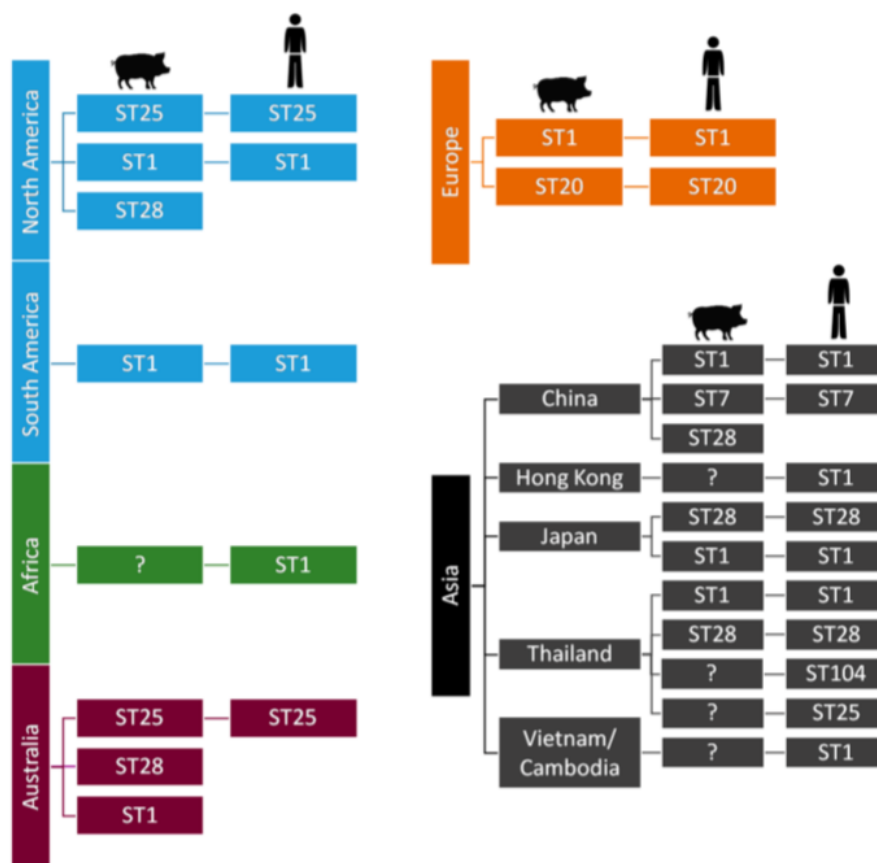


Figure 2: *S. suis* sequence types and their worldwide distribution

How *S. suis* is transmitted in swine

The main transmission routes are, firstly, the vertical sow-piglet route; the mucosa of the vagina is the first point of contamination. In the farrowing room, respiratory transmission from the sow to the piglets takes place. Horizontal transmission between piglets has also been proven to occur, especially during outbreaks

in the post-weaning phase. This form of transmission happens through [aerosols, feces, and saliva](#).

While in humans, the possibility of infection via the digestive tract has been confirmed, there are discussions about this route for swine. [De Greeff et al. \(2020\)](#) argue, based on *in vitro* and *in vivo* data, that infection through the digestive tract is associated with specific serotypes. Serotype 9, for example, would have a greater capacity for colonizing the [gastrointestinal tract](#), and from there, the bacteria's translocation takes place. The same authors point out that, in Western Europe, *S. suis* serotype 9 has become one of the most prevalent serotypes in recent years.

How *S. suis* colonization occurs

Although there are still unknown mechanisms in the pathogenesis of the disease, it can be schematically summarized how colonization occurs (Figure 3). From the different infection routes, the pathogen always passes through the mucosa. When *S. suis* enter the bloodstream, it can lead to a systemic infection, ending in septicemia, meningitis, endocarditis, or pneumonia, or a local infection at the joints level, causing arthritis.

According to Haas and Grenier (2018), [different pathogenicity factors](#) intervene in each of the processes. The CPS, for example, are relevant during colonization and the initial progression (indicated by black arrows). Microvesicles released by *S. suis* cell membranes are more involved in the passage to the bloodstream or, for example, the progression towards local or systemic infection (indicated by white arrows).

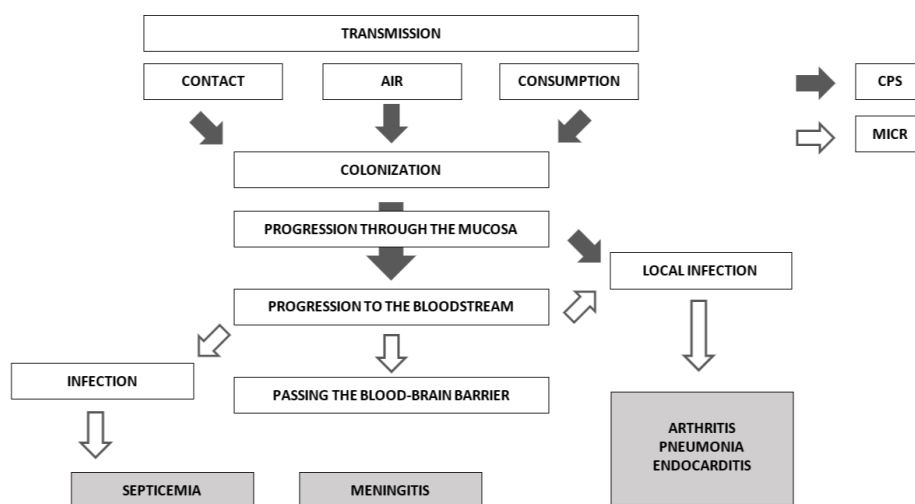


Figure 3: Pathogenesis of *S. suis* infection
Source: based on [Haas and Grenier \(2018\)](#)

Depending on the host and the immune response, the well-known clinical signs of the disease will occur. Although they may begin in the lactation phase, the highest prevalence of meningitis (the main clinical symptom) usually occurs between the 5th and the 10th week of life, that is, between two and three weeks after weaning.

How to diagnose *S. suis* infection

Diagnosing *S. suis* is relatively simple at a clinical level; however, we need to know how to differentiate it from *G. parasuis* in the case of animals with nervous symptoms. We also need to distinguish *S. suis* from other pathogens responsible for producing arthritis, such as *M. hyosynoviae* or the fibrin-producing agent *M. hyorhinis*.

Laboratory techniques are developing on two fronts. Among molecular techniques, multilocus sequence typing (MLST) is considered the gold standard for serotyping. It is still costly and not yet practicable for large samples at the farm level. In contrast, several types of polymerase chain reaction (PCR) show greater practical applicability. Quantitative PCRs (qPCR) are used for the evaluation of bacterial load, and some PCRs are based on the identification of specific virulence genes.

Due to the relevance of *S. suis* for human health, more complex techniques are also available, such as the complete sequencing of the bacterial genome. This type of method aims to develop epidemiological analyzes together with the differentiation between virulent and non-virulent *S. suis* strains. Research is also underway in serology, particularly on evaluating maternal immunity and its interference with the piglet, as well as autogenous vaccines monitoring.

Why *S. suis* sometimes causes disease: Virulence factors and coinfections

Streptococcus suis is a pathobiont, i.e., a microorganism that belongs to the commensal flora of animals but generates disease under certain conditions. In their daily work on farms, clinical veterinarians, for instance, find that *S. suis* often colonizes the upper respiratory tract, nasal cavity, and tonsils without causing disease. *S. suis* pathogenicity is associated with an astounding range of different circumstances or triggering factors; some sources list more than 100 virulence factors. Several factors are considered essential in the development of pathogenesis; others, however, are the subject of ongoing research (cf. [Xia et al., 2019](#), and [Segura et al., 2017](#)).

Critical virulence factors

- One of the most important proteins is the CPS that establishes serotypes. The CPS largely determines the bacteria's adhesion and colonization behavior. It can modify its thickness depending on the stage: it becomes thinner when adhering to the mucociliary apparatus and thicker when circulating through the bloodstream, protecting the bacteria against possible attacks by immune system cells.
- Likewise, *suis* has an adhesin known as Protection Factor H (FHB) that protects it from phagocytosis by macrophages and can also interfere with the complement activation pathways of the immune system.
- [Suilyisin](#) is one of the most critical *suis*' protein toxins. This toxin plays a fundamental role in the interaction with host cells (modulating them to facilitate invasion and replication within the host cells) as well as in the inflammatory response.
- *S. suis* is a mucosal pathogen and, hence, triggers a mucosal immunity response, mainly by immunoglobulins A (IgA). *S. suis* has developed proteases capable of destroying both IgA and IgG.
- Research is still in progress, but both *suis* serotype 2 and 9 encode the development of adhesion proteins that facilitate mucociliary colonization when salivary glycoproteins are present (these are called antigens 1 and 2).
- Other than Suilyisin, two of the bacteria's protein components that have been studied in-depth to develop subunit vaccines are the MRP (Muramidase Release Protein) and EF (Extracellular Factor) protein. Whether the expression of these proteins is associated with virulence depends on the serotype.
- Recent research indicates that greater biofilm production capacity is associated with the more virulent *suis* strains. The production of biofilm is closely related to the production of fibrinogen, which allows the bacteria to develop resistance to the action of antimicrobials, to colonize tissues, to evade the immune system, etc.

Concomitant factors for *S. suis* infection

Even though *S. suis* is a primary pathogen that can cause disease by itself, many factors can exert a direct or indirect influence on whether or not and to which extent disease develops.

Veterinarians and producers are well aware of the influence of environmental and management factors such as temperature variations, poor ventilation together with poor air quality, irritants for the respiratory tract, as well as correct densities for animals' welfare. Occasionally, depending on the geographical location, *S. suis* can be considered as a seasonal pathogen, showing a higher prevalence during the coldest months of the year when ventilation is lower or not well-controlled.

At the level of the individual animal, concomitant pathogens, environmental changes, diet changes, previous pathologies, piglet handling problems, etc., all come into play. Younger piglets tend to be more susceptible because of the decrease in maternal immunity or insufficient colostrum intake; diarrhea during the lactation phase also increases disease vulnerability.

Recently, researchers have started to explore the hypothesis that a change in the digestive tract microbiome balance may favor a pathogenic trajectory. [Some results](#) indicate that changes in the microbiota around the moment of weaning could indeed trigger disease. I will return to the vital topic of the digestive tract in *S. suis* pathogenesis below.

The role of coinfections

The virulence of *S. suis* can increase in the presence of other pathogens, both viral and bacterial. Among the main viruses, key interactants are the PRRS virus, the influenza virus (SIV), as well as Porcine Circovirus (PCV) and Porcine Respiratory Coronavirus (PRCV). At the bacterial level, *Bordetella bronchiseptica* and *Glaesserella parasuis* have the most direct interaction with *S. suis* ([Brockmeier, 2020](#)).

There are several mechanisms by which coinfections might increase *S. suis* virulence: some of them (i.e., *B. bronchiseptica* and SIV) alter the epithelial barrier, facilitating the translocation of *S. suis*. Moreover, viruses such as PRRS either cause an alteration in the response of the immune system or destroy relevant immune system cells.

[Valentin-Weigand et al. \(2020\)](#) posit that the influenza virus increases the pathogenic capacity of *S. suis* so that, for specific strains, the disease can develop even in the absence of the key virulence factor suilysin. This highlights the importance of controlling coinfections for successful *S. suis* management.

The five pillars of holistic *S. suis* management in swine

The challenge of managing this problematic pathogen with limited use of antibiotics prompts a review of all strategies within our reach. From birth to slaughterhouse, interventions must be coordinated and cannot work independently.

1. Biosecurity

The principles of biosecurity are easily understood. Yet, across different locations and production systems, farms struggle with consistently executing biosecurity protocols. For the moment, it appears unrealistic to avoid the introduction of new *S. suis* strains altogether. Also, complete eradication is not feasible with the currently available tools.

Genetic companies and research centers will likely continue to explore how to reduce bacterial colonization in animals, to produce piglets that have no or only minimal *S. suis* populations. Again, this option is not available for now.

At the farm level, the most promising and feasible approach is to reduce the risk of bacterial transmission, i.e., to optimize internal biosecurity. This extends to controlling both viral and bacterial coinfections. The two major viruses affecting the nursery stage are the PRRS virus and Swine Influenza virus. Bacteria that can contribute to the disintegration of the mucosa, both at the respiratory level and the digestive level, are

Atrophic Rhinitis (progressive or not) and digestive pathogens such as *E. coli*, Rotavirus and *Eimeria suis*. All possible measures to reduce the prevalence and spread of these co-infectants must be executed to help control *S. suis*.

2. The pre-weaning period

We need to consider several elements in the first hours after birth that influence the spread of the bacteria in the farrowing rooms:

- How is the colostrum distribution between the litters and the subsequent distribution of the piglets carried out?
- How is the “processing” of the piglets carried out after farrowing: iron administration, wound management, and tail docking?
- Are we taking any measure to prevent iatrogenic transmission of pathogens through needle exchange?

Until today, it is common practice to administer systemic (in-feed) or local (vaginally applied) antibiotics during the pre-weaning phase, albeit with partial or inconsistent successes in terms of reducing infection pressure. Notably, during the pre-weaning phase, the development of the piglet's microbiota begins to take shape, and the [systematic and prophylactic application of antibiotics in young animals can reduce bacterial diversity of the microbiome](#) (Correa-Fiz et al., 2019). This, in turn, leads to a proliferation of bacteria with a pathogenic profile that could detrimentally influence subsequent pathology.



S. suis is an ultra-early colonizer; piglets can get infected already at birth

3. The post-weaning period

The post-weaning period undoubtedly constitutes the most critical stage of the piglets' first weeks of life. In addition to social and nutritional stress, piglets are exposed to new pathogens. While maternal immunity is decreasing, piglets have not developed innate immunity yet; they are now most susceptible to the horizontal transmission of diseases. Hence, *S. suis* prevention during this phase center on measures that improve piglet quality. Key parameters include:

- Do we have a correct and homogeneous weight/age ratio at weaning?

- What is the level of anorexia in piglets? Do we practice suitable corrective measures to encourage the consumption of post-weaning feed?
- How are we feeding them? What medications do they routinely receive?
- How are housing facilities set up concerning density, environment, and hygiene?

Again, gut health is critical: Ferrando and Schultsz (2016) suggest that the [status of the piglet's weaning gastrointestinal tract](#) centrally influences the subsequent development of the disease. Their research supports the idea that some specific *S. suis* serotypes can develop their pathogenesis from the digestive tract, just as in human medicine. While in humans, this digestive route is associated with the consumption of raw or insufficiently processed pork, in swine, the most susceptible moments are sudden changes in diet. The transition from milk to solid feed, in particular, leads to an increase in alpha-glucans that favor bacteria proliferation. Likewise, an increase in susceptibility occurs when the integrity of the intestinal wall is lost, for example, due to viral and bacterial coinfections.

4. Treatments and vaccination

Since weaning is such a difficult phase for the life of the piglet, it is a common practice on farms across the world to include one or several antibiotics in the post-weaning phase. Sometimes, when the legal framework allows, producers use a systematic antibiotic (i.e., beta-lactams or tetracyclines) and another one with a digestive profile (e.g., pharmacological doses of ZnO, trimethoprim, sulfa drugs and derivatives).

While antibiotics, for the most part, effectively prevent infection in the post-weaning phase, they can have adverse effects on the digestive tract. According to [Zeineldin, Aldrige, and Lowe \(2019\)](#), continued antibiotics use:

- might increase the susceptibility to other infections because of the imbalance of the microbiome,
- the immune system might be weakened, together with an alteration in metabolism,
- and it fosters a greater accumulation of bacteria that are resistant to antibiotics.

The effectiveness of curative antibiotics treatments varies considerably. In any case, early detection is critical; affected animals need to be isolated and provided with a comfortable environment. Therapeutic parenteral antibiotics are best combined with high-dose corticosteroids. Some sick animals are unable to stand or walk. As a complementary measure, it is recommended, where possible, to help them ingest some feed and water.

Much research attention is focused on finding suitable vaccines to control the disease. This is a challenging task: *S. suis* shows high genetic diversity, making the identification of common proteins difficult, and is protected against antibody binding by a sugar-based envelope. The research group around Mariela Segura and Marcelo Gottschalk, for example, is [working on a subunit vaccine strategy](#) that addresses both dimensions. Recently, Arenas et al. (2019) identified [infection-site specific patterns of *S. suis* gene expression](#), which could serve as a target for future vaccines.

The arrival of a universal, affordable *S. suis* vaccine is still a distant hope, though. Inactivated vaccines generally offer low levels of antibodies at the mucosal level and would need some adjuvant to increase them. A multiple injection protocol will not work from a commercial and practical point of view. On the other hand, live attenuated vaccines risk re-developing virulence with potentially drastic effects on human health. To complicate the topic of vaccination further, there is a controversy regarding the time of application and what animals we should vaccinate – sows, piglets, both?

Today, though with variable results, the alternative to scarce commercial vaccines is autogenous vaccines. These are based on the suspected serotype(s) present on a particular farm. This strategy hinges on the difficult procedure of isolating the strain from the meninges, spleen, or joints of the animals. If this step is successful, a laboratory can then develop the autogenous vaccine. Immunization occurs mainly in piglets, but occasionally some sows are vaccinated during the lactation period.

5. Hygiene

Just as for any other pathogen, hygiene management is critical. The infection pressure can be lowered through simple steps, such as washing the breeders before they enter the farrowing room. It is, or it should be, standard practice to maximize hygiene in the processing of piglets, avoiding injuries or pinching of the gums during teeth cutting, as well as disinfecting the umbilical area.

We know that *S. suis* is usually very sensitive to most disinfectants, but that it can form a biofilm that allows it to withstand hostile conditions. Physical or chemical methods to eliminate biofilm-formation are thus vital for combatting *S. suis* effectively.

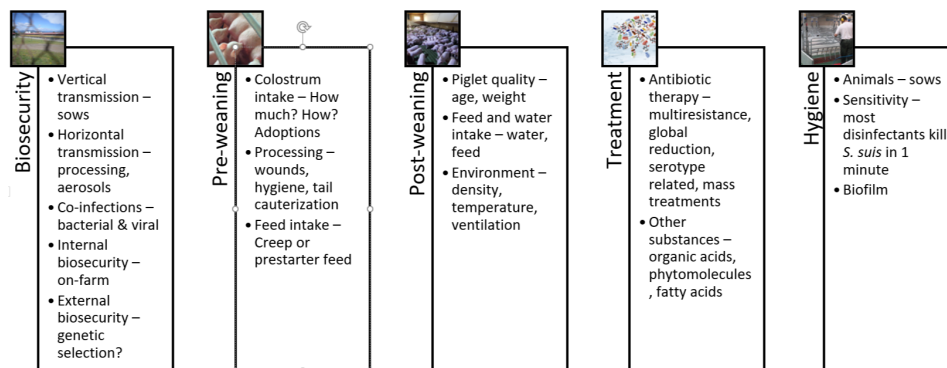


Figure 4: The 5 pillars of *S. suis* control and prevention

S. suis control and prevention: The future lies in the gut

There is no ideal solution for totally controlling *S. suis* yet: autogenous vaccines are only partially effective, and since we cannot continue to administer antibiotics systematically, it is necessary to look for alternatives. Pending the arrival of a universal vaccine, the most promising efforts focus on the [gastrointestinal tract](#).

Microbiome balance to keep *S. suis* in check

The gastrointestinal tract is not only the site where nutrient absorption takes place. The gut is the largest immune system organ in the body and most exposed to different antigens; therefore, what happens at the digestive level has a considerable influence on the immune system, locally and systemically.

The microbiome can be defined as the set of autochthonous bacteria that reside in the digestive system of animals. This group of bacteria is continually evolving and changes at critical moments in the life of animals. Simply put, a healthy microbiome is one that has a high bacterial diversity in the digestive tract (alpha diversity). The diversity between animals, on the other hand, should be low (beta diversity). A healthy microbiota implies the absence of dysbiosis and pathogens. Finally, one wants to promote the presence of bacteria that can produce substances with a bactericidal effect, such as short-chain fatty acids or bacteriocins.

Can we influence the microbiome to have fewer *S. suis* problems? Research by [Wells, Aragon, and Bessems \(2019\) compared](#) microbiota samples of the palatine tonsils from healthy and infected animals. They found that animals that would later develop the disease showed less diversity and, in particular, a diminished presence of the genus *Moxarella*. Importantly, they found that these differences in the microbiome's composition of animals that later developed the disease were noticeable *before* weaning and at least two weeks before the outbreak occurred.

The same authors investigated in more depth, which bacteria in the microbiome were able to maintain homeostasis at the digestive level, finding that this was mostly the case for the genera *Actinobacillus*, *Streptococcus*, and *Moraxella*. Moreover, they found that *Prevotellaceae* and *Rhotia* produce antibacterial substances against *S. suis*.

Nutrition can impact the microbiome through targeted ingredients

We have to think about the microbiome of locations other than the digestive system as well. As we previously saw, the bacteria are transmitted through the mucosal route in the vagina, through the respiratory route, and there are recent studies that consider [saliva as a leading source of infection in oral transmission](#).

This research contributes insights into how we might approach *S. suis* management through nutritional strategies. The question for nutritionists is, can you formulate feed that reduces the availability of *S. suis*' favorite nutrients? *S. suis* appears to develop best when the feed contains [large quantities of carbohydrates or starches](#). Other nutritional factors include the feed's buffering capacity and the stomach pH of the piglets.



*In times of antimicrobial resistance, additives are crucial for *S. suis* control and prevention*

Gut health and nutrition approaches come together in the area of additives: targeted gut health-enhancing additives to feed or water will become a cornerstone of *S. suis* control. What we want to see in such products are molecules or substances that are capable of limiting, inhibiting, or slowing down the growth of *S. suis* by altering the membrane or interfering with the energy mechanisms of the bacteria.

There are already several products on the market with different active ingredients, such as

phytomolecules, medium-chain fatty acids, organic acids, prebiotics, probiotics, etc. Soon, those products or combinations of them will be a part of our strategy for controlling this pathogen of such importance to our industry.

By Technical Team, EW Nutrition

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Do we have the tools to reduce antibiotics in swine production?



The global swine industry is going through unprecedented challenges. On the one hand, the threat of the African Swine Fever virus is global, despite the fact it hasn't arrived in all markets. The virus is today alive among the wild boars in the Polish and Belgian forests. Every day it keeps gaining a few more meters to the border, threatening the German swine industry, one of the largest in the European Union.

If this happens, we might be seeing important changes to the pork supply chain on the meat market worldwide – in Europe in addition to current issues in the USA meat plants. The profitability of swine businesses depends in many ways on the export capacity of large corporations based in Germany, Spain, Denmark, etc.

On the other hand, the presence of COVID-19 in most countries is changing human behavior, meat consumption at home, and the way we look at the future. Perhaps a virus overload via the news, some “fake news” conveying wrong messages on what's coming, and suddenly we feel the future will never be the same.

The future of the swine industry

At least for the swine industry, the future will indeed never be exactly the same. We will be facing different challenges. Some of these will be structural, such as the issue of decreased manpower and how to substitute manpower by machines, through the implementation of Precision Livestock Farming, for instance.

We are also facing important health challenges to our animals: not just ASF, but also new and more aggressive PRRS strains, among other pathogens. Our sows' production capacity is increasing annually, yet in some cases 25% of the new-born piglets are lost from birth to market. Increasingly, we may start to see increased levels of mortality not only in the nursery but in fattening pigs and sows as well.

It is becoming clearer all the time: the future of the global swine industry lies in producing more pigs with reduced antibiotics. To stay the course, we need to take further action and implement corrective measures.

Why we should remove antibiotics in pig production

Pressure from stakeholders and regulators

There is, and there will be, increasing pressure from many stakeholders worldwide to work toward pig production with reduced or no antibiotics. Meat suppliers, slaughterhouses and processors, governments at different levels, and, of course, the European Union – all are demanding reductions in the level of antibiotics in livestock production.

There is also an increasing awareness at the global societal level regarding [antimicrobial resistance](#) related to antibiotic usage in farming production. Consumer pressure will grow exponentially as the terrible COVID-19 experience will be “digested” by the global population.

Pressure to accede to the pork market

There is yet another important reason to start working in that direction: the global swine meat market. Today, China’s pork meat shortage is opening the market. Now any producer could potentially sell meat, either to China or to any other country. We are starting to see moves from companies in the USA or Brazil banning the use of Ractopamine in their operations because they want to get access to the ractopamine-free market (Europe & Asia, over 70% of the global population).

According to M. Pierdon (AASV 2020 Proceedings), there will be two types of markets: the “Niche ABFree” and the “Commodity ABFree”. Companies will have to analyse what their future is on the meat market. Not all the producers may be willing to enter this new phase, but for sure many will try.

Strategies for antibiotic reduction

In Europe, the time has arrived. Zinc oxide will be banned in June 2021 and there is now more than a trend in production with less or no antibiotic use. In some cases, there is a need; in others, this is simply profitable.

Challenges to antibiotic reduction

Producing pigs completely without antibiotics is not easy, and not affordable for all. Initially we may have to give up some performance parameters in order to achieve the balance between what we want and what we can achieve in animal performance. But the time will arrive when these two objectives will converge; there is no alternative.

To that end, we will have to include in our pig production strategy all the available tools and technologies: genetic selection, immunization against some key pathogens, environmental control (mandatory but often forgotten), early detection of diseases, etc.

In this new era we are entering, nutrition and feed additives will play a key role. It will be crucial to find solutions targeting the microbiome’s stabilization and diversification, creating and maintaining healthy farms and achieving all the performance parameters.

Do we have the tools for antibiotic reduction?

Even today there are companies able to produce completely antibiotic-free pigs – proof that **yes, the tools are already in place.**

Nevertheless, for most producers, the answer to – **Can we produce without antibiotics?** is most likely “probably not”. This will require a holistic approach, given the specific case of piglets.

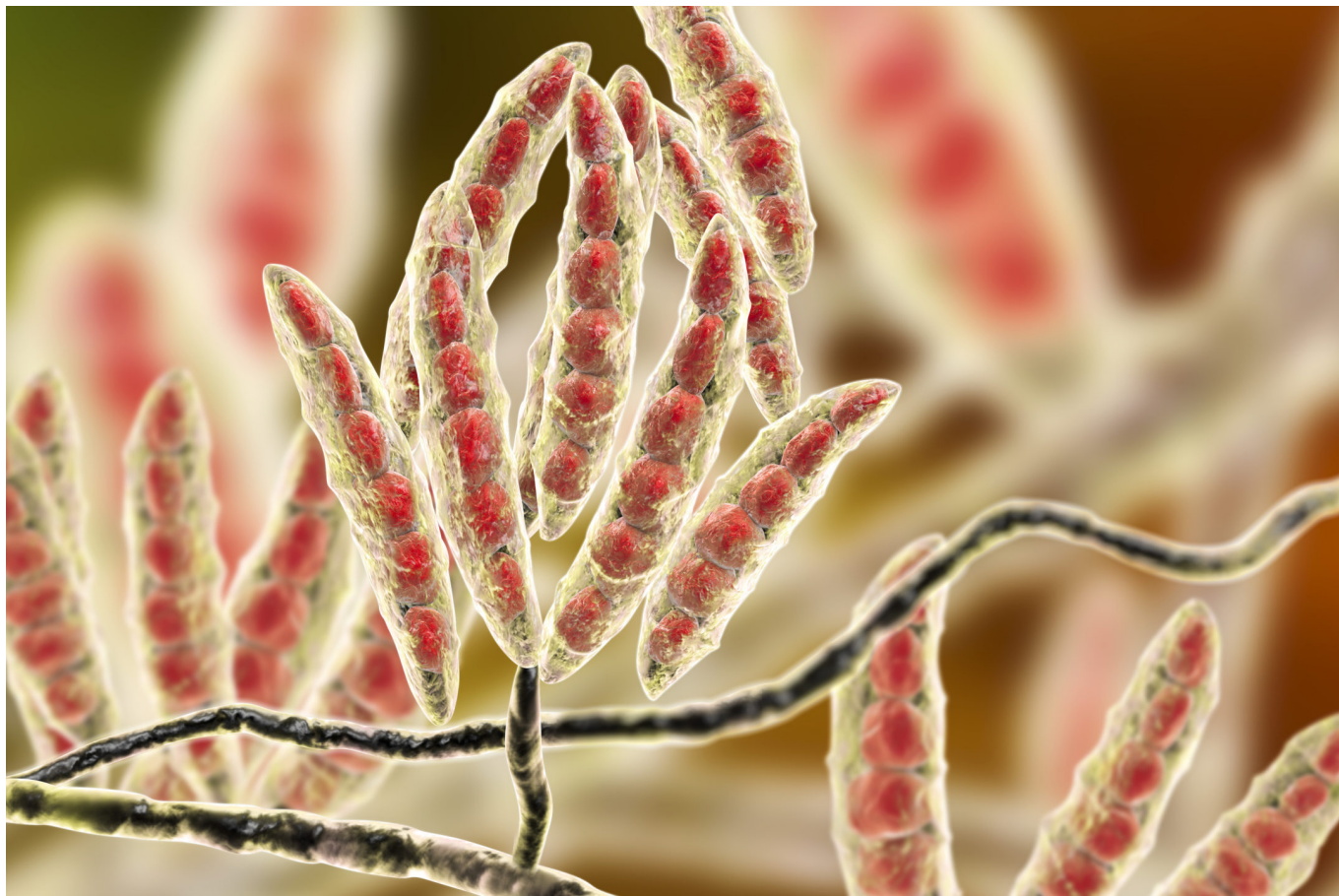
The microbiome of the piglet is strongly influenced by birth and the subsequent weeks. What, then, are the elements that will be part of this new game that comprises a new approach?

- The colostrum intake & the management of the piglets
- Antibiotic usage and its influence on the gut
- The piglets’ microbiome and its evolution during the periweaning period
- The weaning process, appetite, and water intake
- Zinc oxide removal and its influence on the microbiome
- The immune system and the relationship with the GIT status
- Inflammation and its modulation at the gut level
- The health status and the effect on the concomitant infections: which ones are key and which ones are secondary pathogens
- The all-important biosecurity, management, and hygiene

To summarize: there is no one tool, but rather a **holistic approach** to face this new challenge that the swine industry is facing nowadays. The answer is not a silver bullet, but a journey that we all must undertake.

Available in Spanish [here](#).

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

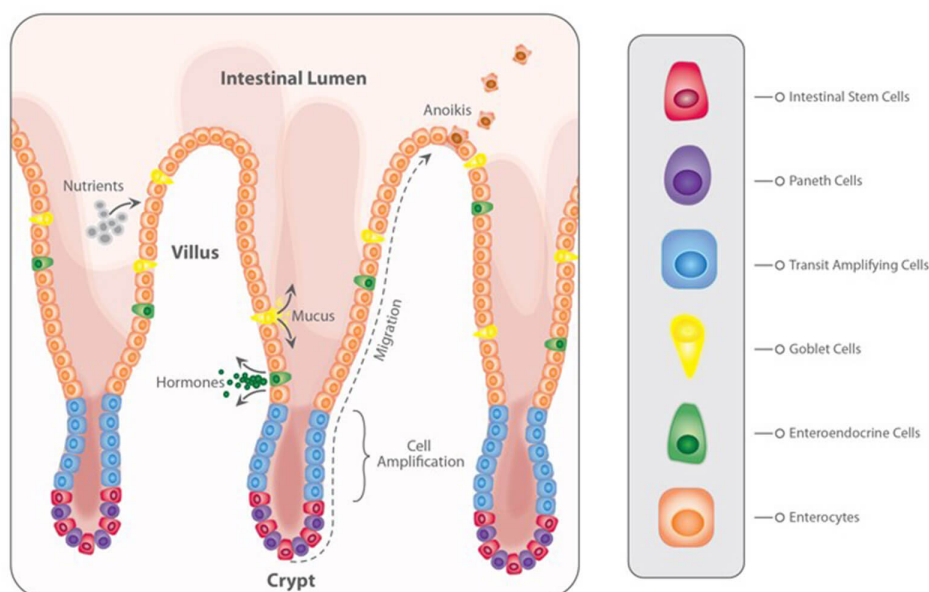
When mycotoxins are ingested, they encounter the GIT's intestinal epithelium (Figure 1). This single layer of cells lining the intestinal lumen serves two conflicting functions: firstly, it must be permeable enough to allow the absorption of nutrients. On the other hand, it constitutes the primary physiological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

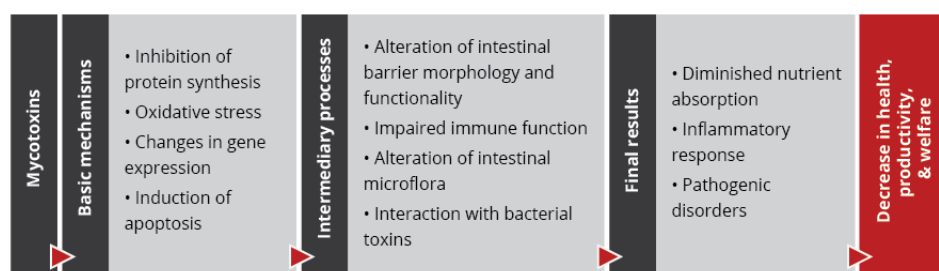
Adapted from: [Biehl et al., 1993](#); [Bouhet & Oswald, 2007](#); [Devreese et al., 2015](#); [Ringot et al., 2006](#)

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

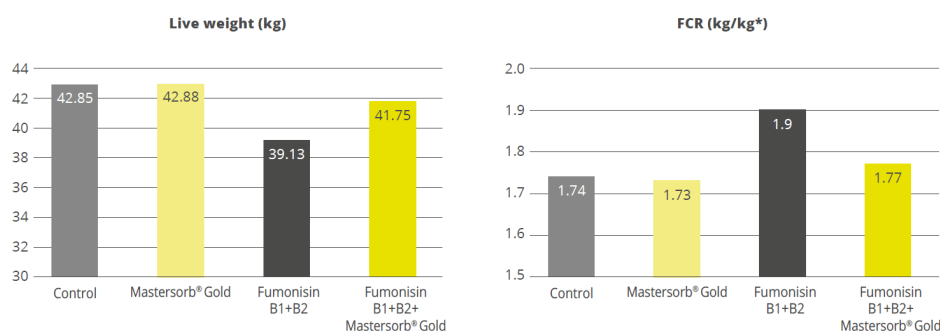
To prevent the detrimental consequences of mycotoxins on animal health and performance, proactive solutions are needed that support the intestinal epithelium's digestive and immune functionality and help maintain a balanced microbiome in the GIT. Moreover, it is crucial for any anti-mycotoxin product 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

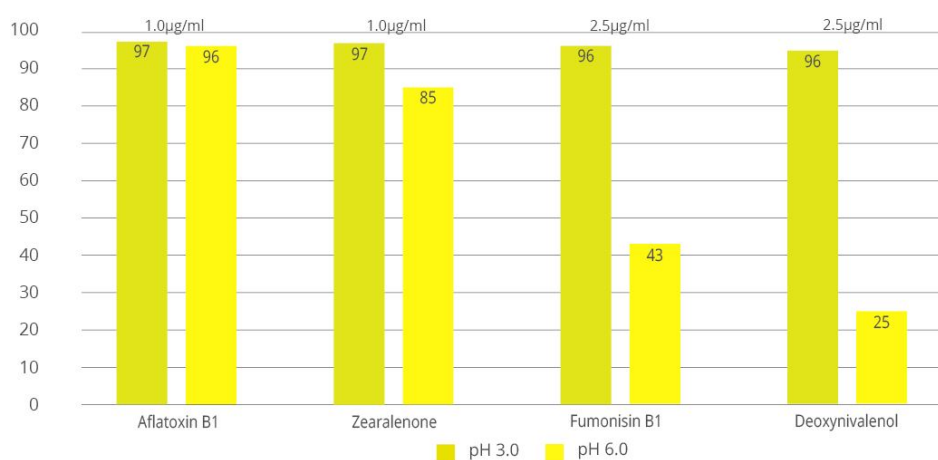


Another study of crossbred female piglets, carried out at a German university, investigated whether Mastersorb Gold could support performance as well as liver health under a naturally occurring challenge of ZEA (~ 370ppb) and DON (~ 5000ppb). Mastersorb Gold significantly improved weight gain and feed 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](#).

Egg immunoglobulins as a plasma replacer



Animal plasma has been widely used in piglet feeding, not only as a protein source, but also as a tool to reduce gastrointestinal disorders after weaning. Drs FELLIPE BARBOSA and INGE HEINZL consider a safe alternative in order to keep animals healthy and*

to avoid loss of performance.

The recent developments surrounding the health risks associated with using animal plasma as a piglet feed ingredient is growing serious concerns in China. After the reported cases of African swine fever (ASF) commencing in August 2018, the Chinese government decided to ban the use of pig blood (and its by-products) in animal feed for some time.

The reason for the temporary ban of pig blood ingredients: African swine fever.

ASF is a viral disease of pigs and wild boars. The virus causes a lethal hemorrhagic disease in pigs. In some cases, the death of infected animals can occur during one week after the infection. There are no vaccines against the ASF Virus. When it hits the herd it is virtually impossible to stop its spread contaminating all animals.

Spreading of the virus occurs as follows:

- contact with contagious pigs from infected areas,
- contact with contaminated materials, being fed with kitchen waste and
- non-trusted animal origin feed ingredients.

Table 1: Performance of pigs weaned at 19 days of age fed for 15 days post-weaning a diet containing different plasma or fractions.

	Casein	Plasma	Albumin	IgG*	LMW**
Weight gain (g/day)	19 ^a	134 ^b	78 ^{ab}	158 ^c	50 ^a
Feed intake (g/day)	181 ^a	262 ^b	244 ^{ab}	273 ^b	191 ^a

Gatnau et al., 1995

*Immunoglobulins; **Low molecular weight

rows with different superscripts are significantly different $p < 0.05$

There is a risk of pig blood carrying different types of viruses like ASF virus. Therefore, from time to time the use of ingredients based on blood is questioned by pig producers. To minimise this risk, the use of ingredients derived from pig slaughterhouses (including animal plasma) in pig feed is no longer allowed in China. This measure will cause not only a protein deficit in piglet feeds but also reduced protection of weaned piglets when intestinal disorders are concerned.

Immunoglobulins from animal plasma and its benefits on reducing post-weaning diarrhea (PWD)

The use of animal plasma has a positive effect on post-weaning performance of piglets. It is generally known that as a palatable ingredient, animal plasma stimulates feed intake. This results in better growth and a higher post-weaning performance in piglets. However, a closer inspection on the mode of action of spray dried plasma reveals its properties as an immune-ingredient and shows its supporting effect on the overall health status of the animals. Scientific publications showed that the positive influence on growth when feeding plasma to piglets is mainly due to its “immunoglobulin fraction”. This assigns to plasma a specific role in nutrition of weaned pigs to prevent PWD and to reduce the need for antibiotics.

Egg immunoglobulins: a natural way of protecting weaned piglets

[Globigen® Jump Start](#) (EW Nutrition GmbH) is a functional and standardized product based on whole egg powder. It contains natural immunoglobulins (IgY – “immunoglobulins from yolk”) mixed with a carrier. IgY are cells of the immune system from birds similar to the IgG in mammals. They have the main function of identifying and neutralizing harmful substances in the body. IgYs are obtained through a non-invasive process and are natural ingredients from eggs. There is no connection with blood and slaughter by-products and therefore no risk of carrying animal diseases.

Globigen® Jump Start is used to support piglets during critical stages of life, as long as their natural immunity is not completely developed. Scientific data confirmed that the IgY present in egg powder are capable of supporting intestinal health and growth performance of newly weaned piglets. More recently, also the possibility of using immunoglobulins as alternatives to zinc oxide (ZnO) and in-feed antibiotics (Hedegaard et al., 2017; Li et al. 2015) were evaluated with promising results.

Table 2: Effect of IgY against diarrhea caused by bacterial pathogens in piglets.

Items			%		Outcome measured considered mortality (M) or diarrhea (D)
Prophylactic effect			Intervention	Control	
Reference	Pathogens	Piglet age			
Imberechts <i>et al.</i>	F18 + ETEC	Weaned (21-28d old)	33	66	D
			25	75	D
			0	25	M
Marquardt <i>et al.</i>	K88 + ETEC	Neonatal (3d old)	12.5	62.5	M
		Weaned (21-28 d old)	0	30	M
		Weaning (14-18 d old)	1.9	3.9	D

Adapted from Li *et al.*, 2015

Better results than plasma IgG: understanding the antigens causing post-weaning diarrhea

Animal plasma is a by-product of the meat industry. The animals slaughtered were possibly exposed to various diseases over their whole life. It cannot be considered as a standardized product in terms of immunoglobulins (either quantity nor quality). The Ig contained could be useful but also totally useless, depending on the pathogens the animals have been confronted with. As a source of immunoglobulins Globigen Jump Start is a costefficient and effective alternative to replace plasma in piglets' diets. Its IgY content will have the same protection effect in the gut as IgG, but the nutritionist will have the possibility of choosing different protein sources in the market, either because of price or availability of raw materials. Our recommendation is that 40kg of plasma can be replaced by 2kg of Globigen Jump Start supplied with different high digestible protein sources.

A piglet trial was conducted with the objective of evaluate the efficacy of [egg immunoglobulins](#) on performance parameters of weaned piglets and to evaluate it as a substitute for animal plasma. Piglets were challenged with F4 and F18 enterotoxigenic E. coli (ETEC) strains and feed either 2kg of [Globigen Jump Start](#) (GJS) or 40kg of spray dried plasma (SDP) in the weaner diet. The comparison was also done to a negative group (NG - microbiological challenge and no protection in the diet); and a positive group (PG - no microbiological challenge and antibiotics + ZnO in the diet).

Piglets from NG had lower feed intake, weight gain, and feed efficiency than animals from PG. The same was observed for piglets from GJS and SDP group. However, the impact of bacterial challenge on weight gain was lower for GJS piglets than for SDP (-14% and -52% when compared to PG); whereas feed intake was similar for both groups (-13% and -14% when compared to PG). The results showed that piglets receiving GJS were more efficient on converting feed into growth even when challenged when compared to SDP animals.

Table 3: Effect of IgY compared to plasma on performance of challenged piglets.

Parameters	1 to 7 days after adaption period								
	NG	GJS	SDP	PG	NG ↔ PG	NG ↔ GJS	SDP ↔ GJS	SDP ↔ GJS	SDP ↔ PG
Feed intake (kg)	1.46 ^a	2.16 ^{ab}	1.93 ^{ab}	2.47 ^b	-41%	-32%	-13%	-11%	-14%
Weight gain (kg)	0.78 ^a	1.88 ^{bc}	1.04 ^{ab}	2.19 ^c	-64%	-58%	-14%	-44%	-52%
Feed efficiency (kg weight gain / kg of feed)	0.39 ^a	0.80 ^{ab}	0.45 ^{ab}	0.89 ^b	-56%	-52%	-10%	-44%	-49%

different superscripts within the row are significantly different p<0.05

Trial conclusion

In this trial, the product based on egg immunoglobulins showed better influence on the performance of piglets than blood plasma. This may be due to the fact that the quality of the plasma depends on the animals slaughtered and on their contact with diseases, determining how much and which antibodies are available in this feed.

Additionally, blood plasma includes the danger of infectious diseases.

Safe and standard: free of swine related diseases and ruminant material

EW Nutrition clearly understands the importance of maintaining standardisation. It is a key factor for the customers to have a product that they can depend on every day.

Therefore, through specific steps during the production of Globigen products, EW Nutrition ensures product quality. During production, all eggs are pasteurised and dried to a whole egg powder. In between steps include microbiological analysis, Salmonella, and avian disease controls to ensure the final product is free of the mentioned threats. Furthermore, as Globigen products are originated from laying hen farms there is no risk of contamination with any swine disease, like the devastating ASF. Finally, [Globigen](#) products do not contain any raw materials produced from, or substances derived from ruminants nor do the products come in contact with risk materials during the whole process (not be at risk for carrying transmissible spongiform encephalopathy or bovine spongiform encephalopathy – BSE).

ASIAN FEED MAGAZINE – February/March 2019

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*).

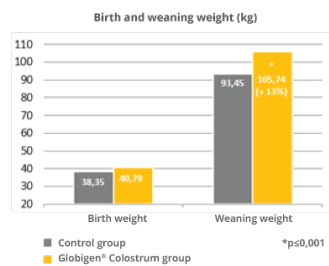


Figure 1: Effect of an egg powder product on weaning weight (kg)

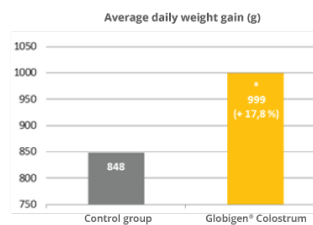


Figure 2: Effect of an egg powder product on ADG (g)

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).

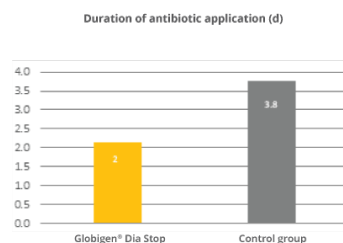


Figure 3: Duration of antibiotic application (d)

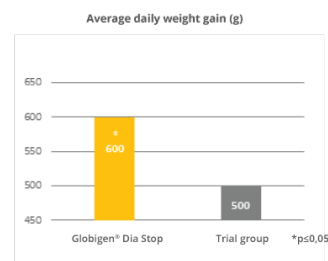


Figure 4: Effect on average daily weight gain (g)

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

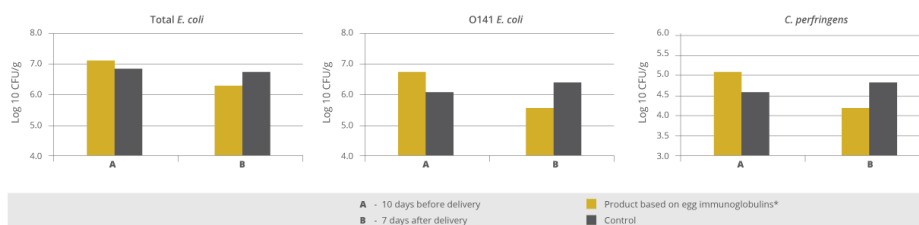
E. coli is well known as one of the main responsible pathogens for pre-weaning diarrhoea. And although it belongs to the normal intestinal flora of pigs, part of the different *E. coli* strains are pathogenic. *E. coli* cause about 80% of diarrhoeas in piglets and 50% of losses in piglet production. 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.