WHITE PAPER

What Are The Concerns Of Doing Without Therapeutic Doses Of Zinc Oxide In Piglet Feeds?



Table of Contents

1. Zero zinc for an healthier gut microflora! A new paradigm for feeding piglets.

2. Commercial guidelines for successful zero-zinc oxide commercial piglet feeds

Ioannis Mavromichalis - Animal Nutritionist Consultant At Ariston Consulting

International......9

3. France: Zero-zinc ban at therapeutic dose is nothing new for the French feed industry.

David Guillou - Senior Researcher At Mixscience......15

4. Denmark: Looking for alternative to medicinal ZnO for weaning piglets.

Dorthe Carlson – Trial Manager At Testpig......18

5. Spain: The challenge of demedication.

Gilles Langeoire - Pig Nutritionist Consultant......23

6. Hizox® : A highly bioavailable source of Zinc.

ZERO ZINC FOR AN HEALTHIER GUT MICROFLORA!

A NEW PARADIGME FOR FEEDING PIGLETS

The author

Gilles Langeoire is a French pig nutritionist consultant with more than 30 years' experience in the pig industry.

General proposition: Mind feed intake by weaning at later stage + Improve protein digestibility + Increase acidification of the diet + take advantage of the dietary fiber's fermentation.

Alternative product solutions: inclusion of organic acids with low negative Acid Binding Capacity (ABC) + optimal level of dietary fibres + any feed additives that improve gut health and digestive processes (other forms of Zinc, pre and probiotics, phytogenic etc.)

Introduction

Since many years in Western Europe a general trend pushes the consumers demand toward a meat production clear from antibacterial residue. A ban of antibiotic as animal growth promoter started in 2006 followed by more and more reduction and regulation upon the use of antimicrobials during the animal breeding phase.

Developed in Denmark then in many other pig producing countries (UK, Germany, Spain...), the use of high level of zinc oxide (3kg/t) was considered as the solution to limit antibiotics and efficient against the post weaning diarrheas.

In France and in the Netherlands, very quickly the most negative consequence of the excreted zinc on the environment and later to the outbreak of antibiotic-resistant bacteria leaded to a ban of these therapeutic level of zinc oxide. Today it is estimated that more than 60% of the piglets produced in France are free from any antimicrobials. In June 2017 the EU commission, decided to ban the high level of zinc oxide in the piglet feed at weaning; the European pig producers had 5 years moratorium to apply that new regulation. Next June 2022, the European producers will have to change of paradigm: To wean piglets with limited antibiotics and zero zinc!

Definitely that new approach needs to be holistic, combining the piglet breeding management and the feed formulation.

From our experience, some points are of real importance:

- mind the feed intake: before and during weaning
- mprove the nutrients' digestibility: mainly protein
- increase the acidification of the diet: a low ph and a low ABC4
- take advantage of the dietary fibre's fermentation

1. The weaning issue:

For any pig farmer the prolificity of the sows is directly related to the economic performance of the herd. The weaning age of piglet is therefore crucial to improve the number of reproduction cycle/ sow/year. Early weaning (18-21 days) needs a specific attention to any breeding conditions (biosecurity, health care, sow management and feed intake...) and the risk of pathogenic trouble (PWD, oedema...) is increase.

To limit these consequences, weaning at a later stage (25-28d) can be beneficial: The milk consumption is reduced and the dry feed intake increases more naturally (especially with large litters). The piglets are heavier, the digestive tract is more mature and the nutrients' digestibility is better. The risk of digestive trouble is therefore limited.

2. A new feed formulation concept:

a. The Protein Issue:

The first concept developed to reduce the incidence of PWD is a reduction in the protein level of the diet. That reduction will slow down the indigestible protein fraction, which entering the hind gut, will induce proteolytic fermentations producing ammonia and others components (biogenic amins, indole, skatole...) mostly toxic for the young piglet. Reducing the indigestible protein through a reduction in the crude protein level is an easy and efficient way to reduce the diarrhoeas but in order to avoid any growth impaired it has to be balanced by synthetic amino acids, as much as the final protein level is low, which at the end can be costly and difficult to achieve.

Another solution to reduce the indigestible protein troubles is to promote the use of more digestible source of protein, from milk and milk by product, potato protein, blood plasma, fish meal, and soy protein concentrate... Depending of the process to obtain soy protein concentrate, the digestibility can be more or less around 70% to 80%.

b. The diet acidification:

Acid binding capacity (ABC) and organic acids:

A better protein digestibility can be directly correlated to the diet acidity (estimated with the buffering capacity) and to the gut pH itself. For a weaned piglet the optimum pH for a maximum efficiency on pepsin (gastric enzyme able to predigest protein) is around 4. The inclusion of organic acid with a low negative ABC value (Formic, lactic, propionic acids...) will increase the diet acidity and the feed intake, improve the protein digestibility and limit the development of pathogens in the gut.

It is important to notice that high level of zinc oxide has an antagonist effect on ABC and most of the organic acid supplementation will be neutralised. A reduction in the zinc level will potentialized the acidification effect as antimicrobial and protein digestibility enhancer.

c. The fibre case:

The dietary fibre (DF) is the sum of Non-Starch Polysaccharides (NSP) plus lignin, where the main polysaccharide of NSP is cellulose and a large variety of non-cellulosic polysaccharides like β -glucan, arabinoxylans, xylan, pectin, gums...

NSP are resistant to digestion by endogenous enzymes in the small intestine thereby becoming the main substrate for bacterial fermentation, particularly in the large intestine. From that definition from KE Bach Knudsen, we can underline the digestibility and the fermentable potential of the dietary fibre.

Dietary fibre became the best solution to improve the morphological and physiological development of the piglet gut. For the very young piglet around weaning the use of fibre improves the gut functions:

- Its size: length of the intestine and volume of the stomach
- Enzymatic functions are increased: Slow gastric emptying, swelling capacity and motility.
- The dietary fibre will limit the proteolytic fermentations and ammonia production, improving well-being and gut health
- Physiologically, the dietary fibre fermentations induces the production of gas and volatile fatty acids (VFA) improving the acidification in the lower segment of the intestine increasing the microbial population and its diversity, limiting the development of the pathogenic bacteria (like E.Coli, Clostridium).

The dietary fibre shows many others important functions like the stimulation of the immune system (The gut is the second most important organ of immunity)

- Improving the gut defences and the mucus layer
- Improving the integrity of the epithelial tight junctions preventing pathogen and toxins penetration into the blood stream.

d. Using Feed additives

Many others feed additives can play an important role in the gut health and the digestive process around weaning.

- Other forms of zinc: more active at a low level of inclusion.
- Enzyme: hemicellulases, phytases, improving the digestibility of the dietary nutrients.
- Prebiotic (FOS, MOS, GOS...), Probiotic (Cell yeast, yeast extracts, lactobacillus...), acting as microflora regulator, limiting the gut dysbiosis.
- Phytogenic: a new era for plant extract with antimicrobial, anti-inflammatory, growth promoting effects.

Conclusion

It can be concluded that considering the general reduction of antimicrobials and the total ban of zinc oxide:

a highly digestible protein level can limit the risk of proteolytic fermentations and limit the risk of PWD.

a low ABC value will lead to a better organic acid efficiency, a better protein digestibility and a lower risk of digestive dysbiosis

an optimal level of dietary fibre will improve the gut morphology and through the NSP fermentations will improve the microbiota and the gut health status.

These recommendations will finally lead to better feed performance: Higher feed intake and better piglet growth by maintaining the eubiosis around weaning through the settlement of an optimal, stable and diversified microflora.



Commercial Guidelines For Successful Zero-zinc oxide Commercial Piglet Feeds

The author

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Based on more than 14 years experiences designing and feeding antibiotic and zinc oxide-free diets in piglets from the USA to SE Asia and beyond.

General proposition: higher level of feed-grade amino acids + maximal nutrient digestibility + ideal fiber profile + least possible feed antigens and ANF.

Alternative product solutions: other Zinc forms + Gut health additives (that eliminates bacteria and/or that promote beneficial bacteria and/or that enhance overall immunity) + Copper Sulphate.

Zinc oxide used at pharmacological doses of up to 3 000 ppm zinc will be banned in all EU states as of June 2022, although so e EU states have already implemented said ban, whereas others wait until the last moment. This ban follows a long history of partial restrictions and confusing regulations that aimed at reducing the use of zinc oxide in piglet feeds. Zinc is a heavy metal, and it is considered an environmental hazard (not only in the EU, but worldwide) as it can contribute to soil deterioration.

Early piglet feeds (creep and pre-starters) will be particularly affected by this ban because supplementation with zinc oxide at high levels has been practiced from the late 80s on a global scale. The reason has been simple enough; zinc oxide exerts a beneficial effect on gut microbiota leading to reduced diarrhea problems and/or to enhanced growth performance. This effect is additional to that of in-feed antibiotics (also banned in the EU since 2006) and parallel to that of copper sulphate (another gut health agent).

The mode of action of zinc oxide remains unclear, despite the many theories and ideas that have been proposed and tested. It is more than likely zinc oxide has more than one mode of actions. Most authorities agree that zinc oxide controls and suppresses the growth of pathogenic bacteria in the gut, enabling the establishment of a healthier microbiota. To this end, any similar dietary intervention will help the transition to zinc-oxide free diets. Here, it is important to note that zinc from zinc oxide and other zinc sources will continue to be used at nutritional levels (up to 150 ppm) in piglet feeds. It is the pharmacological use of zinc that is being curtailed by the impeding ban.

Thus, to replace its pharmacological properties, the following are offered for consideration based on commercial and research experiences:





Balanced protein concentration

Feeds that contain excess protein invariably promote the proliferation of pathogenic microbiota. Escherichia coli bacteria, for example, thrive on protein, whereas in contrast, the beneficial lactobacteria require readily available fibers. But, reducing available protein is counterproductive because it reduces animal growth. In contrast, reducing crude protein concentration whilst using higher levels of feed-grade amino acids enables the formulation of a balanced diet that controls bacterial growth.



Maximal nutrient digestibility

It follows from the above that anything that reaches the large intestine will be used for feeding the microbiota living there. It is then up to the formulator to ensure that only desirable non-digestible ingredients reach the large intestine. To this end, using highly digestible ingredients will reduce the amount of non-digested nutrients. Equally important is the fact that digestibility drives feed intake, ensuring thus maximal enteric structural health. This prevents further damage and inflammation from starvation and lack of enteral nourishment.



Ideal fiber profile

Not all fibers behave the same, simply because not all fibers are the same. For example, hemicelluloses increase gut viscosity, reduce nutrient digestibility, and promote pathogenic bacteria growth. In contrast, lignocellulose has none of these problems and reduces upper gut leakage. Other, non-viscous prebiotic fibers can be used to promote healthy microbiota growth. The ideal balance between insoluble and fermentable fibers is currently the matter of investigation.

Thus, to replace its pharmacological properties, the following are offered for consideration based on commercial and research experiences:



Least possible feed antigens and ANF

Antigens and anti-nutritional factors invariably damage the gut and hinder its digestive process. A damaged gut is the ideal situation for opportunistic pathogenic bacteria to proliferate. Using ingredients that have the least amounts of antigens and anti-nutritional factors is one of the ways that can reduce this burden. Naturally, feed cost will be higher, but treating piglets for diarrhea is also a costly exercise.

Other zinc forms

Alternative zinc sources for piglet feeds include products such as potentiated zinc oxide, organic zinc, tetra-basic zinc chloride, encapsulated zinc oxide, nano-zinc oxide, and zinc sulphate. Not all of them work with the same efficacy, but at least some of the above offer a partial solution to replacing normal zinc oxide at lower levels. However, under EU conditions, their efficacy has been questionable at best.

Gut health additives

All the additives used in replacing in-feed antibiotics can be used also to replace zinc oxide. The list of such additives is quite long. Such products can be divided into three broad categories as follows:

- Additives that eliminate bacteria: examples include organic acids, phytogenics, medium-chain fatty acids, sources of immunoglobulins, copper sulphate, etc.
- · Additives that promote beneficial bacteria: examples include probiotics, prebiotics and functional fibres, nucleotides, dead yeasts, etc.
- · Additives that enhance overall immunity: examples include omega-3 fatty acids, beta-glucans, certain phytogenics, yeasts, antioxidants, etc.

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The least amount of research has been dedicated to the role of zinc oxide as an agent that promotes greater microbial diversity. It is well known that an animal will be overall healthier if its microbiota is not dominated by any single species of bacteria. Zinc oxide has been shown to do exactly that, but most research has focused on its potential to eliminate bacteria.

In brief, there are plenty of products that can replace zinc oxide. It is important, however, to understand what function of zinc oxide we are replacing, because it has been shown that zinc oxide is an additive with many and diverse modes of actions.

Personal experiences

I have been designing piglet diets without antibiotics and no zinc oxide at pharmacological doses since 2012 – that is for the last 14 years. I use all the above principles, focusing on quality ingredients, and a small selection of feed additives. I must confess that copper sulphate is working extremely well – as it used to well before zinc oxide was introduced. Nevertheless, the best replacement for antibiotics and zinc oxide is a healthy environment upon which nutrition can further enhance animal performance.

France: Zero-zinc Ban at Therapeutic Dose is Nothing New For The French Feed Industry

The author

A french premix and service firm in France

General proposition: Prepare gut before weaning starting with sows feed and milk production + pay attention to gut inflammatory status.

Alternative product solutions: Fiber source + Probiotics + Phytogenics + Organic acids (Valopro Win)

In France, piglet pre-starter feeds have been designed for fast growth in the last three decades, at least. Cost and safety, defined as low incidence of scours, drive the market segmentation. Altogether, these diets can be defined as High Nutrient Density Diets, with more or less investment on feedstuffs and additives for digestive health control.

In the late 1980's, first reports on use of "pharmacological level" of zinc oxide (ZnO) crossed the Atlantic Ocean: 1500 to 3000 ppm ZnO added to the diet of piglets during one or two weeks postweaning were successful to control diarrhea and to promote growth. At the same time, national rules on maximum content of N, P and trace elements in pig feed were published, aiming to reduce the impact of pork production on the environment. Since the very start then, the French nutritionists were aware of the effect of ZnO on piglets, but it was forbidden to use in practice. It changed at the end of 2014, when a ZnO premix was registered in the EU as a vet prescription. This decision was rapidly challenged by political actions, resulting in the withdrawal of authorization for ZnO prescription voted in 2018, applicable early July 2022. From the start of 2015 to the end of 2020, high ZnO could be used in France. However, feeding practice had changed since the 1980's: feed volume with veterinary prescription in 2015 accounted for less than 40% of the total, compared to >95% in the 1990's. ZnO premix was exchanged for antibiotics, it did not boost the tonnage of prescription diets. Because of this, high ZnO inclusion has never been a main driver of piglet pre-starter feed design in our country. As a consequence, "Zero Zinc" era is nothing new for the local industry. Nevertheless, in a period of reduction of antibiotics usage, it is a major concern for the veterinarians, who miss a nice and cheap solution to help the pig farmers at controlling health issues at weaning.

For the nutritionist, weanling pig feed design remains driven by palatability, digestibility and cost. Ingredient selection is key. Accurate process monitoring is mandatory. Additives should be carefully evaluated in order to avoid to add costs to cost. Research made a lot of progress on describing the inflammatory response in piglets. Description of the gut microbiota with molecular techniques put emphasis on the role of strong bacterial ecosystem on piglet health. Gut barrier integrity remains an evolving research subject, but the results on nutritional effects can already be applied. Especially, gut should be prepared before weaning, starting with sows feed and milk production. Along with these modern concepts, emphasis has been put on: the role of fiber sources and probiotics to regulate appetite, digestion rate, gut transit and bacterial load and balance; the role of intermediate metabolites of plants (polyphenols, terpenoids, alkaloids) on microbiota metabolism and gut inflammation. Specific organic acids remain the gold standard for prevention of gut pathogen development.

Analysis of fecal total peroxidase activity

(TPO, expressed in myeloperoxidase -MPO- equivalent) has been implemented at Mixscience R&D laboratory since 2017 to quantify gut inflammatory status. Validation of the method was presented to the research community at the Digestive Physiology of Pigs meeting in 2018, and full methodology and preliminary results were shown at the ZERO ZINC congress in 2019. Based on this technique, a proprietary feed supplement based on fiber sources blend (Valopro Win) was developed in order to speed-up gut adaptation post-weaning and to reduce scours. This product is successfully implemented in the pre-starter diet range of the company. Ongoing research also resulted in designing phytogenic-based formula minimizing gut inflammation and reducing respiratory disease symptoms both.

Much progress was achieved in nutrition. In order to transfer it to the field, the main difficulty lies today in piglet management around weaning: feed does not work alone, increased comfort is a key factor of success for good weaning outcome. However, cost pressure is high on pig farmers, promoting cheaper investment and simplified operating procedures. New feeder types, higher numbers of piglets per pen, new vaccination plans, new rules on animal welfare, etc... : all contribute to challenge the adaptation capacity to weaning, with consequence on the time dedicated by piglet to eat and drink. In France, even if the majority of pig farms ownership remains based on individuals, not companies, the increasing farm size requires qualified and trained workers. Like everywhere, qualified workforce is getting scarce: attracting and keeping the workers, as well as educating the future ones is highly important too, in order to contribute to this evolutive trend.

Denmark: Looking for Alternative to Medicinal ZnO for Weaning Piglets

The author

Dorthe Carlson, M.Sc., Ph.D. is trial manager at TestPig, a Danish Pig Advisory Center.

General proposition: Prepare the the piglet digestive system for the plant-based diet before weaning = improve management in farrowing and weaning units (hygiene +increase feed intake) + optimize weaning diets.

Alternative product solutions: Additives that improve digestibility + that reduce ph in the stomach + that enhances the immune system + that improves intestinal microbiota.

In the late nineties Denmark was among the first countries to ban the use of antibiotics for growth promotion in pig production. In the same period researchers discovered that high levels of zinc (from ZnO) in post weaning diets could reduce the incidence of post weaning diarrhea and improve piglet performance just after weaning. However, the allowance to control post weaning diarrhea with medicinal ZnO (max 2500 ppm Zn) in weaning diets was not given until 2004. Medicinal ZnO in weaning diets for the first two weeks after weaning has been widely used in Denmark since then. It has helped the piglets and the pig producers through the very sensitive period after weaning, where diarrhea often develops and hinders the pigs in thriving. However, from June 2022 this practice is not allowed anymore and consequently, during the last years scientists, feed companies, nutritionists, advisors, and pig producers have been busy trying to find alternative ways to obtain a successful weaning without increasing the use of antibiotics in Danish pig production.

Even though this "zinc-tool" has been widely used for almost two decades now it is striking that the exact mode of action is still very uncertain. Numerous studies have been made over the years showing how high levels of ZnO have a positive impact on performance in terms of increased feed intake, increased weight gain and improved feces score. Several studies have documented changes in biochemical and physiological parameters measured in blood, intestinal cells, and various other tissues from the animals evidencing that medicinal ZnO affects piglets' general health and immunity both locally in the gastrointestinal tract and more systemically (Bonetti, et al 2021, Carlson, 2003). In addition, to the physiological effects it has also been shown that medicinal ZnO has an antibiotic effect in the gastrointestinal tract. Yet, it seems not to be addressed against Coliforms and enterococci as these bacteria increased while lactic acid bacteria decreased in ZnO supplemented animals (Højberg et al., 2005).

Trying to understand the mechanisms behind the positive effect of medicinal ZnO it is important to remember that newly weaned piglets are in a very sensitive period of their life. They are moved abruptly from one environment to another. In addition, they are separated from the sow (and removed from sow milk) and from their littermates and mixed with unknown piglets from other litters. This is a very stressful situation for the young animals. Most piglets in Denmark are weaned at about 3-4 weeks of age. At this age they do not receive immunity from sow milk anymore and at the same time their own immunity is still not fully developed. In addition, to development of their immune system these piglets are in a transition period where their digestive system is starting to cope with a plant-based diet instead of a milk-based diet, and often also changing from wet- to dry feed. Due to all these stressors the feed intake is often very limited in the first week after weaning and the consequent low energy status results in weaned piglets that are susceptible for infections.

The abundance of physiological and antibiotic effects of medicinal ZnO indicates that the mode of action is multifactorial and therefore it is difficult to point out the exact mechanism that alternative products should imitate. Considering this it is also very unlikely to find one single ingredient that can perform the same impact on the animals as medicinal ZnO.

However, there seems to be no doubt that the weaning problems, that ZnO reduces, is a consequence of that we wean piglets that are not physiologically ready for weaning. In nature, weaning would include a gradually change from milk to plant-based diets and the load of pathogens would be much lower. In this situation the digestive system would slowly develop and become ready to cope with the plant-based diets.

Therefore, to obtain successful weaning without medicinal ZnO (and without antibiotics) the goal seems to be preparing the piglet digestive system for the plant-based diet before weaning and to use feed stuffs and feed additives that results in a higher feed intake and a higher digestibility in the young un-developed digestive system. Furthermore, it is important that the environment is as clean as possible to reduce the load of pathogenic bacteria and hence reduce the challenge on the piglet's immune system.

Accordingly, the alternative to medicinal ZnO for piglets seems to be a good weaning combination between improved management and optimizing weaning diets for the digestive system of the weaning piglets and there seems to be consensus within the Danish pig industry that this is the answer. Hence good management in the farrowing unit as well as the weaning unit is more important than ever. Good management includes various aspect, but in this context, there is increasing focus on hygiene and increased feed intake before and after weaning.

To optimize weaning diets for the piglet digestive system focus should be on feed stuffs, additives and/or feed ingredients that improves digestibility, reduces pH in the stomach, enhances the immune system and/or improves the intestinal microbiota. In 2021, the nutritionists at The Danish Pig Advisory Center composed a diet (SR-Elite 1.0) that was optimized in all these aspects. We tested the diet on our test farm and the results showed that this diet was fully comparable with a standard diet containing medicinal ZnO. In fact, the SR-Elite 1.0 diet resulted in a higher numerically daily weight gain and significantly better Feed Conversion Rate compared with the control diet (Carlson et. al., 2021).

Numerous promising ingredients are available on the market and several others are to be developed. As the number of ingredients on the market increases it becomes more and more important the feed industry provides scientific that documentation made by an impartial part under Danish pig production conditions. At TestPig we provide this service and we have already been so privileged to test several products on newly weaned piglets and we are ready to test more. You can find reports from some of the trials here: https:// danishpigadvisory.com/testpig/test-results/. The coming years will show which solutions there will be most effective and mostly used in practice.

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Gilles Langeoire is a French pig nutritionist consultant with more than 30 years' experience in the pig industry.

General proposition: Improve piglet management + better digestibility of raw materials in Feed formulation +use of feed additives + improve housing conditions (density, heating, ventilation...) + higher level of biosecurity.

Alternative product solutions: Copper sulphate + Acidifiers + double dose of Phytase + antioxidant + Anti-inflammatories ingredients.

June 2017 the EU commission, under the pressure of France and the Netherlands' governments, decided to ban high level of zinc oxide in the piglet feed at weaning, the European pig producers will have 5 years moratorium to apply that new regulation.

June 2022, included into the PRAN*: National plan to reduce antibiotics, the maximum legal rate of inclusion of zinc will dropped to 150 mg/kg (including zinc from the raw materials). For the Spanish farmers after a first ban attempt in 2005, having being postpone and finally dropped due to economical and sanitary reasons, this time no loophole! most of them think that they will have to accept it and change of paradigm. And they have to come a long way:

A study made in 2012 (Moreno), shown that 57% of the piglets received high level of zinc before weaning and 73% during their growing phase (27-75 days).

The first word in that matter for the Spanish leaders of the pig production was education with very few successes and awareness during the years 2018,2019. At the end of 2020 and more during 2021 many meetings, symposiums, news conferences took places with more and more attendees, from the feed industry, the Animal health companies and the farmer organizations.

The main point in these meetings was the emphasize and the understanding of the risks of zinc issues:

- in the environment: accumulation and antimicrobial activities in the soil,
- and the induction of antibiotic resistance of pathogen bacteria.

A second important point was to plan the impact of the demedication at a production level:

A recent calculation (from Miguel Angel Higuera, ANPROGAPORC, Asociación Nacional de Productores de Ganado Porcino) made with some accurate hypothesis, gives an important risk of economic losses: $-3.35 \notin$ / piglet, $-77 \notin$ / Sow / year, meaning at least 125 million euros for the whole Spanish production!!! For him the biggest challenge is the great heterogeneity of the Spanish pig farms in their technical and economical performances. The impact of the ban of zinc oxide would therefore be split into different point of view:

- Optimistic: With a correct transition to no zinc oxide, no post weaning diarrhoeas. No increase in antibiotics use and no negative impact on the pig production economy.
- Pessimistic: Impossible to stop the curative zinc oxide, with a huge risk of health problems and a high mortality rate of piglets. An increase of the antibiotic's treatment and important economic losses ...

And finally,

• More realistic: A combination of both situations: With few motivations to stop using high level of zinc before the very last moment, little interest in new alternatives to zinc oxide and moderate to heterogenous economic losses...

From Gonzalo Gonzales Matteo's presentation made last year during an Elanco Working Group, a review of all the practical technical tools is able to counter balance and even provide better results on the pig productivity if the use of antibiotics and zinc oxide at a high level are drastically reduced. But for him most of the feed additives could not be as efficient as any antibiotics. It is of no use to wait for a miracle solution. But if we had to compare the efficiency of antibiotics versus Feed additives, we can observe that the antibiotics will reduce the growth of many pathogens, but in the same time, will reduce the microbiota diversity and increase the risk of antibiotic resistance. On the contrary, the feed additives are less efficient to control the pathogen contamination, but they can increase the bio diversity of the gut microflora, then will improve the response to the antibiotic's treatments. Feed additives in anyway are to be preferred on a long-term efficiency.

Overall, for him, accurate nutrition and feed formulation will be the key for implementing the productivity performances, if and only if genetic and animal management are complete.

	Post weaning 1	Post weaning 1	Post weaning 2
	Antibiotics + ZnO	No AB – No ZnO	
Weaning Age, d	21-24	> 25	
BW at weaning, kg	5.5 – 6.0	> 6.5	
NE, Kcal/kg	2.500	< 2.450	2.450
CP %	19.0	< 17.0	< 16.0
Lys SID, %	1.4	1.1	1.02
Thr SID, % Lys	65	67	67
NDF,%	NDF,%	8.0	8.5
Calcium,%	0.65	0.6	0.66
Dig P, %	0.45	0.40	0.35
Phytase	+	++	++

Professor G.Gonzalez Matteo recommendations for piglet feed:

• Plus, other feed additives

Considering the use of feed additives, he ranges Copper sulphate as the most efficient growth promoter, followed by the anti-bacterial activities of acidifiers, then a double doses of phytase, the use of antioxidant and anti-inflammatories...

In conclusion, even if many pig producers are still waiting to the very last moment to take their decision and many others are expecting a miracle powder, most of the key players feed mills, integrators... are on line with the main admitted recommendations regarding:

- the piglet management, as the weaning age and body weight
- the feed formulation: digestibility and gut health control
- the use of feed additives: acidifiers, enzymes, pre and probiotics...
- the housing conditions: density, heating and ventilation...
- and High level of biosecurity

But still today, many opinion leaders are warning about banning zinc oxide and most of antibiotics will be solely a feed formulation concern! That position would reflect the difficulties the pig farmers will face in investing in a more efficient means of production without being confident in a possible compensation of the loss of performances due to the ban of zinc oxide....

"For the PRAN, the use of medicated feeds containing antimicrobials for preventive use is prohibited, the aim is to avoid routine prophylactic and metaphylactic use of antibiotics and to limit the use in animals of antimicrobials that are of crucial importance to prevent or treat life-threatening human infections"

Hizox®: A Highly Bioavailable Source of Zinc. Animine Company

The author

With more than 15 years of experience, Animine is a global supplier of trace elements for animal nutrition.

The problem: risk/benefit

Pharmacological zinc oxide in piglet diets is highly effective on growth promotion and/or diarrhea prevention BUT there are 6 negative consequences:

1	Contamination by heavy metals Impurities in commercial zinc oxide are hazardous for animal and human health when product quality is not strictly controlled.	Cadmium
2	 Nutritional interactions Impaired iron status of weaned piglets. Negative effect on phytase activity. Antagonistic effect with feed acidifiers. 	
3	Zinc toxicity High doses of zinc oxide may affect piglet health if used for a long period.	Ro 103
4	Reduced palatability Palatability is key in stimulating the piglets appetite. High levels of zinc oxide may degrade feed intake.	
5	Environmental concerns High levels of zinc oxide supplementation after weaning increases by almost 30 percent the total quantity of zinc excreted in the pig's growing life.	
6	Zinc and microbial resistance Intensive usage of zinc in animal diets used in combination with antibiotics favor the development of bacterial resistance.	

Contamination by heavy metals

The presence of heavy metals, such as: arsenic, cadmium and lead, in ZnO represent a risk not only to the animal, but also for human health, as they accumulate in organs that are used for human consumption. Indeed, kidney and liver are organs often included in human diet and are the main sites of accumulation of these heavy metals.

Zinc oxide (ZnO) is an element with a vast application in many industry segments. Its application in animal feeding is rather limited and therefore little attention is paid to the consequences of feed safety.

Nutritional interactions

Although pharmacological levels of ZnO is an efficient solution to reduce post-weaning diarrhea in piglets, such high inclusion also brings negative effects and mask/inhibit the effects of other feed components, such as (1) the buffer capacity reducing the effectiveness of organic acids, (2) interactions with phytate, reducing the performance of phytase, (3) interactions with other minerals, compromising their absorption such as iron and copper.

Zinc toxicity

The usage of Zinc at levels up to 20 times their nutritional requirements can lead to toxicity if used during prolonged feeding period.

Reduced palatability

Feed intake, a key parameter in the after weaning period, can be compromised due to the reduced palatability of feed containing high levels of ZnO, especially when piglets get older.

Antimicrobial resistance

Intensive usage of Zn in animals combined with antibiotics favor the development of bacterial resistance.

Environmental concerns

Even given for a limited time, pharmacological levels of ZnO can significantly increase the total quantity of Zn excreted in the environment. 3 kg/T ZnO in the post weaning period increases by almost 30% the total quantity of Zn excreted in the pig's growing life, as shown by INRAe balance model: https://animine.eu/simmin/

Actually, 3g zinc in 1 kg of complete feed is not minor: it is as much as in the whole body of an adult pig !

Source : Animine

Prevention measures against postweaning diarrhoea In order to reduce the risks of diarrhoea at weaning, pig nutritionists, veterinarians and pig producers have a tool box which include dietary and non-dietary solutions. Genetic susceptibility to E.coli, biosecurity program, animal management, vaccination options are variables which interfere with feed and water quality. These conditions will influence the efficacy of pharmacological dosage of zinc oxide in piglet diets.

Decisions from regulators:

- History of Zn regulation in EU countries : feed regulation vs
 veterinay regulations
- Experience from countries which almost never used medicated ZnO (France, NL)
- 2022 : EU ban of medicated ZnO
- Examples of other countries which want to reduce Zn supplementation levels (China, Canada...)

Modes of action of supra-nutritional zinc oxide

For three decades, scientists tried to understand the mechanism of ZnO, but without definite consensus. Researchers hypothesised some modes of actions, but still, nobody is able to hierarchize them. This is probably due to the roles of zinc as a nutrient in many body functions and of zinc oxide on gut function. Both roles are intertwined and contribute to its efficacy.

Animine solutions

EU ban encourages pig nutritionists to pay more attention to the zinc source, choosing a source that first provide a highly bioavailable source of Zn, to ensure a proper supply even under the weaning conditions where feed intake is low and a source that is efficient in modulating the microbiota at low inclusion levels, such as HiZox®.

HiZox is the most documented zinc oxide source for piglet feeds. The efficacy of this potentiated source of zinc oxide has been presented at many international conferences and shown in peer-reviewed publications (Journ. Anim. Sci, 2012a, 2012b; Anim. Sci. Journ, 2015; Journ. Anim. Sci, 2016; Philipp. J. Vet. Anim. Sci, 2017; Journ. Anim. Phys. Anim. Nut, 2018; Chin. Journ. Anim. Nut, 2018; Anim. Sci. Journ, 2019).

zinc0supp Research Program

Animine has initiated the largest research program with a focus on zinc oxide in piglet feeds: zincOsupp. With the goal of better understanding the ZnO mode of action, zincOsupp is an ambitious scientific program that involves several renowned Universities in Europe and addresses the SUPPression of pharmacological levels of ZnO, while studying the proper SUPPlementation of a potentiated zinc source, HiZox®.

Objectives of the research program are shown at https://animine.eu/zincosupp/

zincOsupp Guide

In February 2022, Animine launched zincOsupp Guide for supplementation, a practical tool in order to fine tune recommendations for HiZox® supplementation, according to farm conditions. zincOsupp Guide is available from all Animine network.