Issue 24 • Swine
A magazine of Biomin

Science & Solutions

The Latest in Mycotoxin Risk Management

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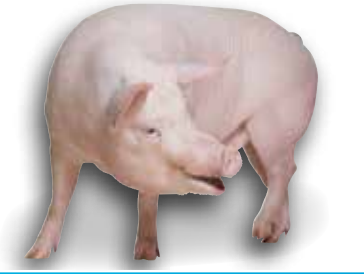

Liver protection for sows

Supporting healthy animals

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What's Wrong with My Pigs?

Part 3: Vomiting

Editorial

New Tool for a New Harvest

Mid-harvest time in Europe means looking forward for the initial test results for mycotoxins. Last year many countries across the globe had a very high mycotoxin contamination, mainly in corn (maize) and other key feedstuffs. Many of us had the misfortune witnessing the impacts of mycotoxin-contaminated feed on animals firsthand. Most cases saw a dramatic reduction in feed intake and lower growth performance, even with low amounts of corn in the diets.

Even low concentrations of mycotoxins can cause problems in animals which are under high pressure as sows are today. Higher performances place higher stress on sows' livers, making a healthy liver even more crucial for piglets' survival rate and profitability.

As many of our clients have been able to see for themselves through visits to the BIOMIN Research Center, at BIOMIN we invest significant capital into scientific research to help farmers deploy the most advanced mycotoxins deactivation strategies available. The fruits of these efforts has led us to announce the fifth generation of our leading mycotoxin deactivating product, Mycofix® 5.0, which combines leading scientific discoveries to deliver absolute protection.

With the help of robust mycotoxin risk management and the proper monitoring of raw materials using the right detection methods we can give farmers the tools needed to overcome critical periods as seen in last year. Maintaining high production while controlling costs depends on it.

André van LANKVELD
Swine Technical Manager

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Science & Solutions is a monthly publication of BIOMIN Holding GmbH, distributed free-of-charge to our customers and partners. Each issue of **Science & Solutions** presents topics on the most current scientific insights in animal nutrition and health with a focus on one species (aquaculture, poultry, swine or ruminant) per issue.
ISSN: 2309-5954

For a digital copy and details, visit: http://magazine.biomin.net
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The Latest in Mycotoxin Risk Management

By **Verena Starkl**, Product Manager, Mycotoxin Risk Management

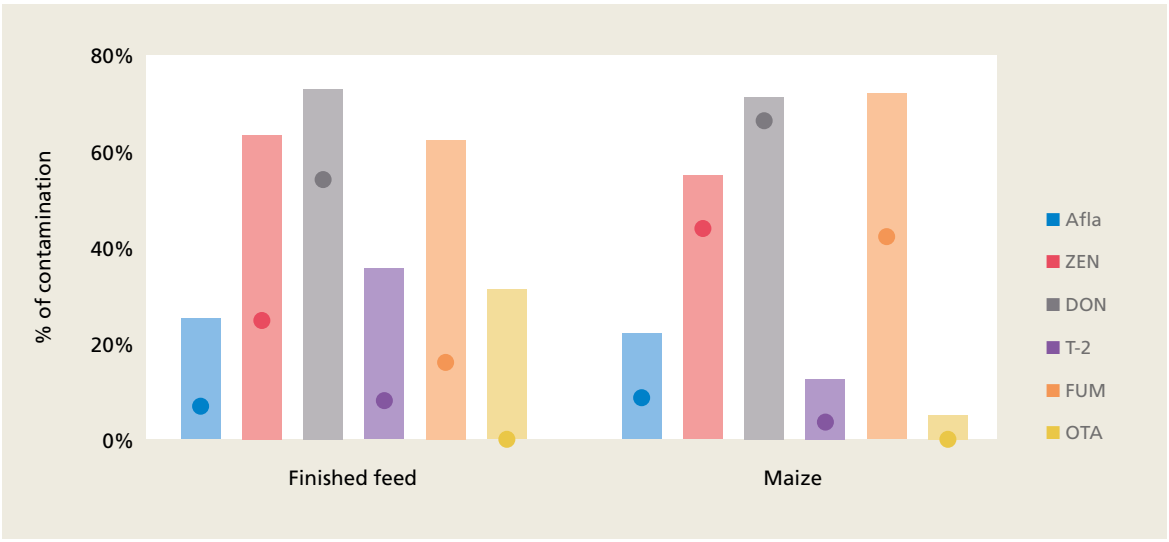
Given pigs' sensitivity to mycotoxins, damage caused by mycotoxin contamination costs the swine industry millions of dollars in losses globally each year. Recent advances have led to the most effective mycotoxin deactivating feed additive to date.

Photo: Rawpixel Ltd

Most swine producers are familiar with the harm that mycotoxins cause and recognize the need for monitoring and mitigation as part of a complete mycotoxin risk management program. Results of the latest BIOMIN Mycotoxin Survey indicate that finished feed and maize (corn) frequently contain harmful mycotoxins at levels that pose a known threat to pig health and performance.

As *Figure 1* shows, deoxynivalenol (DON), fumonisins (FUM) and zearalenone (ZEN) were the most frequently occurring mycotoxins found in samples, followed by aflatoxins (Afla), T-2 toxin and ochratoxin A (OTA). Fumonisins were identified in three out of four corn samples tested, and in half of cases concentrations exceeded known risk thresholds. In finished feed, fumonisins were identified in 60% of samples, and in 30% of those cases the average concentrations exceeded the risk threshold.

Figure 1. Prevalence of mycotoxins in swine feed commodities.



Bars indicate percentage of samples testing positive for mycotoxin presence. Dots indicate percentage of samples registering concentrations known to impair animal health or performance.

Source: BIOMIN, 2015

> “Mycofix® 5.0 represents decades of scientific research on mycotoxin deactivation and combines the most cutting-edge

Find one, find many, find trouble

We know from decades of research on mycotoxins that they tend to occur in groups. This phenomenon, known as co-exposure, is not only common, but also more dangerous for animals. According to the 2014 BIOMIN Mycotoxin Survey, analyzed samples contained on average 30 different mycotoxins and metabolites per sample.

On the field this can cause greater overall harm to animals due to synergistic effects: when mycotoxins occur together the adverse consequences of each mycotoxin (separately, often in a lab) can be amplified.

Protecting pigs

In light of the variety of mycotoxins that can impair swine health and performance, a multi-pronged approach is needed to protect pigs.

In 2015 BIOMIN launches Mycofix® 5.0, an innovative, all-in-one feed additive that uses three modes of action – biotransformation, adsorption and bioprotection – to deliver absolute protection against mycotoxins.

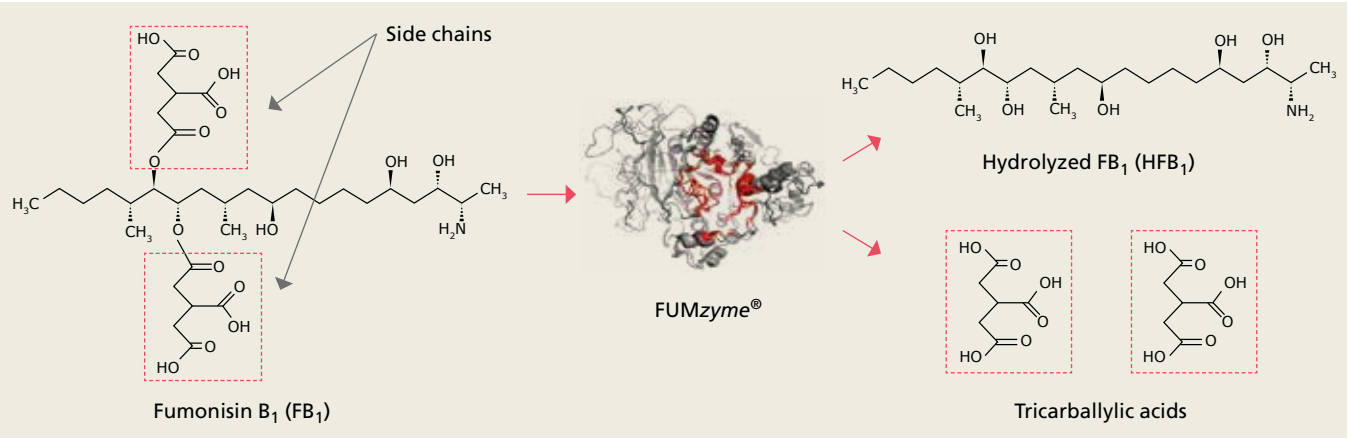
What´s new

“Mycofix® 5.0 represents decades of scientific research on mycotoxin deactivation and combines the most cutting-edge mycotoxin mitigation strategies available anywhere,” according to Ursula Hofstetter, Director Competence Center Mycotoxins. This fifth incarnation introduces five new features.

1. Broader spectrum of mycotoxins

Various components act according to one of three complimentary modes of action so that Mycofix® 5.0 acts against the broadest range of mycotoxins found. A number of these components work in ways that are both specific (target a single mycotoxin) and irreversible (cannot be undone) through biotransformation. In addition to components in Mycofix® 5.0 that deactivate trichothecenes, zearalenone, ochratoxin A and aflatoxins, FUM*zyme*® is a patented purified enzyme that specifically cleaves off the two tricarballylic acid side chains of the fumonisin molecules. This hydrolysation renders fumonisins non-toxic, protecting pigs from fumonisin-related respiratory problems such as porcine pulmonary edema and liver damage and weakened immune systems.

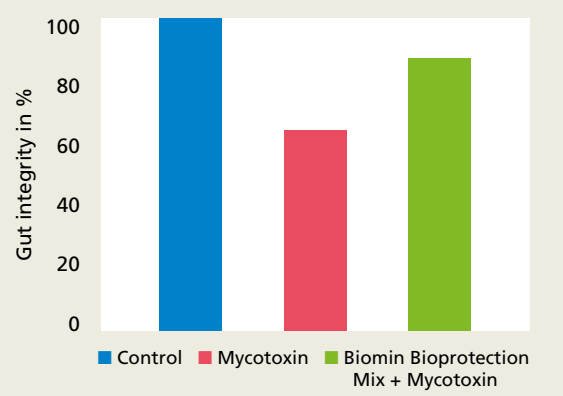
Figure 2. FUM*zyme*® detoxifies fumonisin molecules by cleaving the two tricarballylic acid side chains.



Verena Starkl
Product Manager, Mycotoxin Risk Management

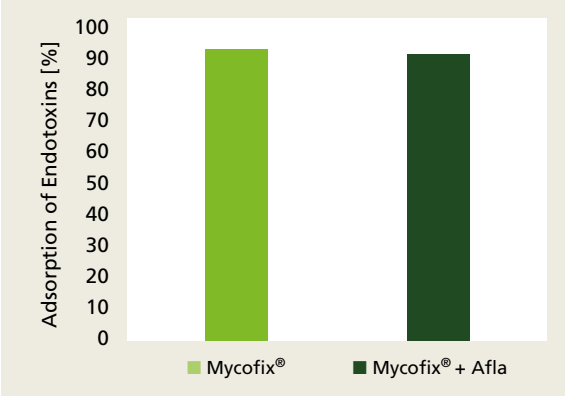
mycotoxin mitigation strategies available anywhere.”

Figure 3. Mycofix® 5.0 supports the intestinal cell layer and immune system.



Source: BIOMIN, 2015

Figure 4. Adsorption of endotoxins by the 5th generation of Mycofix® even in the presence of 4000 ppb aflatoxin.



Source: BIOMIN, 2015

2. Proven safety and effectiveness backed by three EU authorizations

Mycofix® 5.0 contains the only three EU authorized feed additives proven to adsorb harmful mycotoxins or to biotransform mycotoxins into nontoxic metabolites (Regulation No 1060/2013, No 1016/2013 and No 1115/2014). Each Mycofix® 5.0 ingredient was evaluated in scientific and practical relevant field trials to assure safety and effectiveness.

3. Enhanced bioprotection

Mycotoxins affect immune cells, damage the liver and also negatively affect the intestinal barrier function. The bioprotection mix in the fifth generation of Mycofix® not only supports liver and immune system but also improves the integrity of the intestinal barrier function. The effectiveness of this scientifically proven blend of carefully selected plant and algae extracts can be seen in results from a TEER (trans-epithelial electrical resistance) test.

This test measures the integrity of cell layers of porcine intestinal epithelial cells. Mycotoxins reduce the electrical resistance in these cells by opening up the cell layer, making them more “leaky” –allowing pathogens to enter the bloodstream more easily. Mycofix® 5.0 reduces leakage, supporting the cell layer and the pig’s intestinal barrier function (*Figure 3*).

Not all authorizations are equal

European Commission Regulation (EC) No 1831/2003 established the rules governing EU authorization of additives for use in animal nutrition.

Additives fall into various categories and functional groups. “Substances for reduction of the contamination of feed by mycotoxins” are functional group (m) of the category “technological feed additives” (1).

Other functional groups of technological additives include anticaking agents, binders, preservatives, etc. Only those authorized by the EU in category/functional group “1m” have the legal basis for official claims regarding mycotoxin deactivation and were subject to scrutiny by the European Food Safety Authority with regards to product safety and effectiveness.

4. Protection against endotoxins

Endotoxins, also known as lipopolysaccharides (LPS), are part of the outer membrane of the cell wall of all Gram-negative bacteria (e.g. *E. coli*, *Salmonella*,

Table 1. Trial set-up.

			Control	Mycofix® Plus
		Number of piglets	30	30
Phase 1 (days 1-14)	Mycotoxin contamination	DON (ppb)	3800	3800
		ZEN (ppb)	200	200
		FUM (ppb)	2500	2500
	Mycofix® Plus (kg/ton of feed)		--	1
Phase 2 (days 15-56)	Mycotoxin contamination	DON (ppb)	2200	2200
		ZEN (ppb)	100	100
		FUM (ppb)	2600	2600
	Mycofix® Plus (kg/ton of feed)		--	1

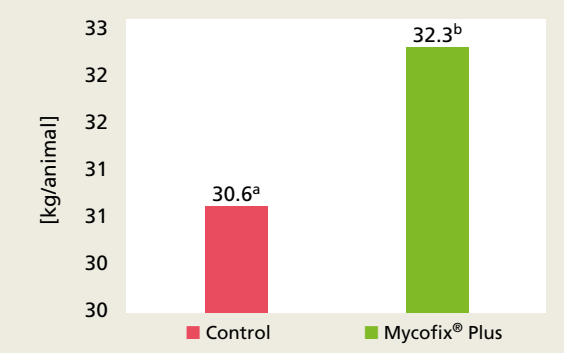
Shigella, *Pseudomonas*) that can elicit strong immune responses, weakening animals' immune systems and impairing performance.

Results show that 0.05% of the fifth generation of Mycofix® adsorbs more than 90% of 500 Endotoxin Units per milliliter. What's more, the interlayer sheet structure of the bentonite contains enough binding sites to achieve a similar level of binding capacity in the presence of 4000 parts per billion (ppb) of aflatoxin B_1 (*Figure 4*). The bioprotection strategy provides further support.

5. Brand new, optimized formulation

The fifth generation of Mycofix® is a fully revamped formulation of the Mycofix® product line. It has been optimized in order to boost effectiveness in the field. A trial under field conditions was performed with 60 weaned piglets receiving a diet naturally contaminated with mycotoxins over 56 days (*Table 1*). At the end of the trial, piglets supplied with Mycofix® Plus had a final weight of 32.3 kg versus 30.6 kg for the control group (*Figure 5*). An economic calculation based on the weight difference between the two groups clearly showed the overall benefit of the optimized Mycofix® with an ROI of 7.42 based on feed and piglet live weight prices based on average European price for June 2015.

Figure 5. Final average weight per piglet at day 56.



Note: [a,b] indicate significant difference (p<0.05)

Source: BIOMIN, 2015

Conclusion

The risks that mycotoxins pose to swine are well-known and represent significant economic losses to producers. Mycofix® 5.0 represents a genuine innovation in the combat against mycotoxins in five ways. First, it acts against a broader range of toxins. Second, it contains the only three EU authorized feed additives proven to deactivate mycotoxins. Third, it offers enhanced bioprotection. Fourth, it provides endotoxin protection. Finally, field trial results demonstrate its effectiveness and ability to generate meaningful return on investment.

The Importance of Liver Protection for Sows

By **André Van Lankveld**, Swine Technical Manager and **Karin Nährer**, Mycotoxin Risk Management Product Manager

A sow's liver is commonly under stress. A number of actions can help protect the liver and support healthy animals.

With the higher demand for energy around farrowing and milk production increases, the liver plays a crucial role (*Figure 1*). This greater need for energy causes an increase in body fat and protein mobilization that can result in metabolic disorders. The liver is often under stress due to problems such as fatty liver syndrome and poor nutrient utilization. This is often shown in weak born piglets, lower birth weights, more splayed legs and a lack of milk production. It is important to keep the liver as healthy as possible and to avoid additional stress from toxins, e.g. mycotoxins, endotoxins, antibiotics, diseases such as Porcine Circovirus 2 (PCV2) infection and feed with high concentrations of fat or protein.

Recent data from the BIOMIN Mycotoxin Survey shows that 80% of all tested samples were found to contain at least one mycotoxin. Mycotoxicoses are caused by oral uptake of mycotoxin-contaminated foods and feeds by animals. Specific mycotoxins affect various organs and tissues like the liver, kidneys, brain as well as mucous membranes of the gastrointestinal, respiratory and genital systems. The course of mycotoxicoses can be acute, subacute or chronic, depending on several factors like the presence of other toxic substances and farm management practices.

Acute outbreaks of mycotoxicoses are infrequent in modern animal production. Animals are often exposed to other interacting factors in the field. The impact of mycotoxins are therefore often subclinical and affect, for instance, the immune system (antibody titre after vaccination, phagocytic activity, immunoglobulins, lymphocytes), antioxidant systems (uric acid, antioxidant enzymes, vitamins) and

Figure 1. Higher demands placed on a sow's liver functions.

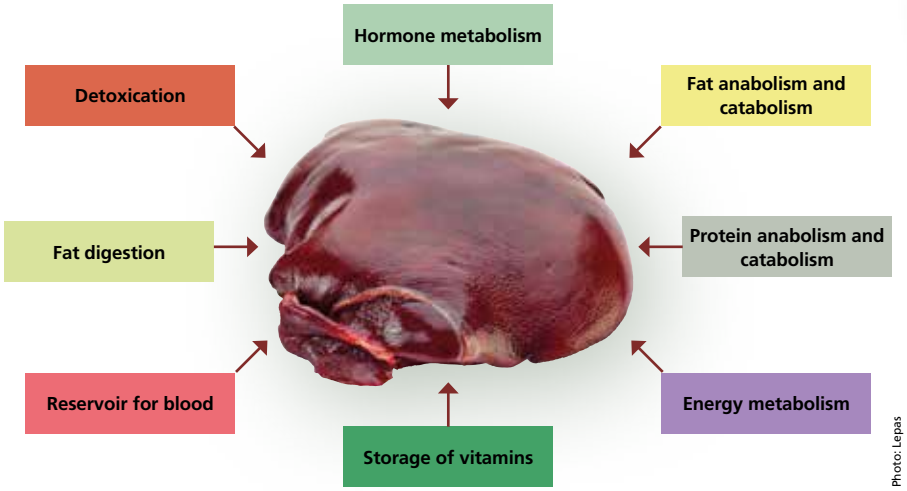


Photo: Lepas

Recent data from the BIOMIN Mycotoxin Survey shows that 80% of all tested samples were found to contain at least one mycotoxin.

Table 1. Selected mycotoxins primarily affecting the liver and their basic symptoms.

Mycotoxins	Possible effects
Aflatoxins	Liver diseases (hepatotoxic, hepatocarcinogenic); carcinogenic and teratogenic effects; hemorrhages (intestinal tract, kidneys); reduced growth rate; diminution of performance; immune suppression
Ochratoxins	Nephrotoxicity; carcinogenic effects; mild liver damage; enteritis; teratogenic effects; poor feed conversion; reduced growth rate; immune suppression
Fumonisins	Pulmonary edema; nephrotoxicity; hepatotoxicity; immune suppression

blood chemistry (liver enzymes, total proteins, albumin/globulin ratio).

Mycotoxins affect the liver

Major mycotoxins such as aflatoxins, ochratoxin A and fumonisins and lesser known ones such as sporidesmin, rubratoxins and phomopsins are known to cause significant liver damage in swine. *Table 1* provides an overview of the negative impacts of the major (more well-known) mycotoxins in swine. Among them, aflatoxins are the most potent liver toxins and animals exposed to these toxins show signs of liver disease ranging from acute to chronic. Acute aflatoxin toxicity causes significant biochemical alterations in the liver resulting in hemorrhage or parenchymal cell necrosis.

Aflatoxins are rapidly transformed in the liver into various metabolites. The metabolism of AfB_1 has been extensively reviewed (IARC, 1993; IARC, 2002 and Eaton *et al.*, 2010). AfB_1 in liver and other tissues is metabolized by P450 cytochromes enzymes to aflatoxin P_1, aflatoxin M_1, or aflatoxin Q1 and AfB_1-8,9-epoxide (Riley and Voss, 2011).

Mode of action

Aflatoxins enter the cell and are either metabolized via monooxygenases in the endoplasmic reticulum to hydroxylated metabolites. They are then metabolized to glucuronide and sulfate conjugates or oxidized to the reactive epoxide which go through hydrolysis to the AFB_1-8,9-dihydrodiol and bind to proteins resulting in cytotoxicity. The epoxide can react with DNA or protein, or be detoxified by an inducible glutathione S-transferase to the glutathione-conjugate.

Mycotoxin residues in liver

Several cases of aflatoxin carry-over in swine have been reported with residues found in porcine liver and muscle tissues. OTA tends to accumulate in the kidneys, liver and muscle tissue, but also in blood serum and, therefore, represents a potential hazard in the human food chain (Battacone *et al.*, 2010). Similar results were also reported for fumonisins. Fumonisin carry-over in sow milk and pork meat may only occur after a high level of exposure over a longer period, accumulating in the liver and kidneys (Völkel *et al.*, 2011; Meyer *et a*l., 2003).

Synergistic effects

In many cases it is seen that sows in an overly fat condition have more problems coping with even low levels of toxins. Sows with already fatty livers have less capacity to detoxify and transport the different toxins out of the body. It is therefore crucial to keep sows in the right condition and avoid the compound stress of liver problems and toxins.

Prevention and mitigation strategies

Some nutrients and feed additives can support the liver supporting the citric acid cycle with some B-vitamins, choline chloride, L-carnitin and plant extracts. Depending on the situation, these can be added in the lactation, transition or even in the gestation diets. Proper mycotoxin risk management combining multiple strategies that offer proven protection against the major agriculturally-relevant mycotoxins (aflatoxins, trichothecenes, zearalenone, fumonisins, ochratoxin A and ergot alkaloids) is essential. Moreover, it should include a blend of scientifically studied and carefully selected plant and algae extracts that counteract the negative effects caused by mycotoxins by supporting the immune system, reducing the risk of inflammation and protecting against liver damage.

Sows with already fatty livers have less capacity to detoxify and transport the different toxins out of the body. It is therefore crucial to keep sows in the right condition and avoid the compound stress of liver problems and toxins.

Cut & Keep Checklist

What's wrong with my pigs?

Part 3: Vomiting

Vomiting should not be confused with regurgitation. Vomiting is the ejection of stomach contents through the mouth. Regurgitation is swallowed food that does not reach the stomach, and is ejected through the mouth. If there is any confusion of whether vomiting or regurgitation is occurring, it may be settled by measuring the pH of the ejected material. Vomitus has an acid pH and regurgitated material is alkaline. Pig vomiting is a symptom of several swine diseases.

Pathogenic causes of pig vomiting. Vomiting is a prominent clinical sign of Hemagglutinating encephalomyelitis (HEV), Porcine epidemic diarrhea (PED), Transmissible gastroenteritis (TGE). It is also a clinical symptom of African swine fever (ASF), Classical swine fever (CSF), and Aujesky's disease. Younger piglets are more susceptible to viral infection, as are older piglets. To do differential diagnosis, check major symptoms and organ systems affected by pathogens, then start disease control.

Toxigenic causes of pig vomiting. Deoxynivalenol (DON), also known as vomitoxin, and in rare cases T-2 toxin can be a cause of pig vomiting. Vomitoxin is a trichothecene mycotoxin isolated and characterized in 1973 as a major emetic and feed refusal factor for swine. It can be found in corn and cereal grains contaminated in the field mainly by *Fusarium graminearum*.

Nutritional causes of pig vomiting. Clinical sign and subclinical deficiency symptoms for several nutrients are a wide variation in the amount of time that elapses before symptoms of nutrient deficiency begin to appear. Certain nutritional deficiencies are more common and have greater consequences than others today in swine. For example, some vitamins as niacin, riboflavin, thiamine (vitamin B_1), pyridoxine (vitamin B_6), vitamin D, and zinc deficiencies can be a cause of pig vomiting. On the other hand, too much vitamin D and B_1 can sometimes cause vomiting.

	Potential cause	Checklist	Corrective action
MYCOTOXINS	• Deoxynivalenol, T-2 toxin	☐ Positive raw materials (ELISA) or feed (HPLC) ☐ Origin of raw materials historically contaminated	☐ Prevent molds, purchase clean raw materials ☐ Use Mycofix® at suitable inclusion rate
PATHOGENS	***Virus:*** • TGE, PED, Aujesky's disease, ASF, CSF, HEV ***Parasites:*** • *Strongyloides* spp., *Ascaris suum*	☐ Epidemiology ☐ Virus isolation ☐ Necropsy ☐ Histopathology ☐ PCR, RT-PCR ☐ ELISA ☐ IHC	☐ Biosecurity ☐ Vaccination ☐ Good sanitation procedures ☐ Anthelmintic
OTHERS	• Foreign body • Vitamin deficiency (Niacin, B_1, B6, D) • Excess of vitamin D • Toxicity of microelements (arsenic, fluorine, selenium, etc.) • Zinc deficiency	☐ Analyze feed samples	☐ Remove foreign body ☐ Check nutrient requirement ☐ Adjust diet formulation

References are available on request

For more information, visit **www.mycotoxins.info**