

## Frequently asked questions about TOXISORB® Classic and TOXISORB® Premium

### About trade names

Product	Also known in different markets as
Toxisorb® Classic	Bionit, Fixat, Fixat Classic
Toxisorb® Premium	Toxisorb, Fixat Premium

### About mycotoxins in animal feed

**Q. What are mycotoxins?**

A. Mycotoxins are compounds produced as secondary metabolites of toxigenic strains of several fungal genera and species, many of which have been strongly implicated as chemical progenitors of toxicity in man and animals. They are considered unavoidable contaminants in foods that agronomic technology has not yet advanced to the point where preharvest infection of susceptible crops can be completely eliminated (CAST, 2003; Diaz & Boermans, 1994).

**Q. What are the most common mycotoxins?**

A. The main mycotoxin classes include: aflatoxin B<sub>1</sub> (AFB<sub>1</sub>), trichothecenes, fumonisin B<sub>1</sub> (FB<sub>1</sub>), ochratoxin A (OTA), zearalenone (ZEN), and ergot alkaloids. They are produced mainly by three genera of fungi which include: *Aspergillus*, *Penicillium*, and *Fusarium*.

**Q. What are the permitted levels of mycotoxins in feed?**

A. Because the occurrence of mycotoxins in foods and feeds is not entirely avoidable, small amounts of these contaminants may be legally permitted, provided the amounts involved are not considered injurious to human and animal health. The worldwide occurrence of mycotoxins in foods and feeds has been recognized by the Food and Agricultural Organization (FAO) and the World Health Organization (WHO) for many years. Many countries worldwide have established food laws that impose limits on the concentrations of specific mycotoxins in foods. Analytical data obtained from food monitoring programs are coupled with available toxicological data and are used for making science-based risk assessment that can serve as a basis for establishing a particular regulatory level. Detailed information on worldwide mycotoxin regulation is available online: <ftp://ftp.fao.org/docrep/fao/007/y5499e/y5499e00.pdf>

**Q. How do I know that my feed is contaminated?**

A. The mycotoxin concentration of a bulk lot is usually estimated by measuring the concentration of relevant mycotoxins in a small portion of the lot or a sample taken from the lot. The mycotoxin concentration in the bulk lot is assumed to be the same as the measured mycotoxin in the sample. Mycotoxins are not distributed homogeneously. So it is very important to analyze a representative sample. The sampling procedure influences the result considerably. More information on sampling procedures can be found on CAST, 2003.

**Q. Is there an integral monitoring program to determine mycotoxins in feed?**

A. Yes, the United States Department of Agriculture (USDA) has developed a program called "Practical procedures for grain handlers". Detailed information is available under <http://archive.gipsa.usda.gov/pubs/primer.pdf>

**Q. How often should I monitor my grain/feed for mycotoxins?**

A. It is important to evaluate testing requirements and assess specific needs for testing. Each company's needs vary. Assess the kinds of test (specificity, sensitivity, ease of method, quantitative or screening, cost), the mycotoxins that need to be assessed, number of samples per day, and location where the test is to be done. In some cases, decisions need to be making whether to do in-house testing or use a contract laboratory.

**Q. How can I analyze mycotoxins?**

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- A. Mycotoxins can be detected with chromatographic (HPLC, LC-MS, GC-MS) and ELISA techniques. The chromatographic tests are more sensitive but also more sophisticated in equipment and carrying out. ELISA tests are easy to handle and deliver adequately exact results to judge the mycotoxin contamination of feeds.
- Q. Which ELISA kits should I use?**
- A. Both the United States Department of Agriculture (USDA) and the European Union (EU) have approved several commercially available immunological test kits and rapid methods (and specifications) for the analysis of mycotoxins. Key suppliers are:
- [Neogen](#)
  - [R-Biopharm](#)
  - [Romer Labs](#)
  - [Vicom](#)
- Q. Do you recommend the usage of mold inhibitors?**
- A. Yes. Although the mold inhibitor will not destroy the mycotoxins, it will stop the growth of mold producing them.
- Q. Can mycotoxins be destroyed by high temperature?**
- A. Only very high temperatures are able to destroy mycotoxins therefore they are usually considered as thermal stable. However, some nutrients are also destroyed at high temperatures.

### About mycotoxicosis in animals

- Q. How common are mycotoxins?**
- A. Mycotoxins are considered unavoidable contaminants in foods and feeds in that agronomic technology has not yet advanced to the point where preharvest infection of susceptible crops can be completely eliminated. The combined effects of the feed and food losses due to mycotoxins decrease the supply and raise the price of various farm commodities. The potential annual cost of mycotoxin contamination of crops was estimated to average US\$932 million in the US.
- Q. Are all species affected equally?**
- A. No. There are a multiplicity of factors affecting the toxic effects of a specific mycotoxin, which include:
- Breed;
  - Sex;
  - Age;
  - Environment;
  - Nutritional status, and
  - Other toxic entities that can affect the intoxication

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### Q. What are the clinical signs of the main mycotoxins affecting farm animals?

A. Fungal toxins produce a wide range of injurious effects in farm animals. Some of the clinical signs are presented in the table below:

Mycotoxin	Fungi	Clinical Signs
<b>Aflatoxin</b>	<i>Aspergillus (flavus and parasiticus)</i>	<ul style="list-style-type: none"> <li>• Carcinogenesis</li> <li>• Mutagenesis</li> <li>• Immunessupression</li> <li>• Teratogenesis</li> <li>• Hepatotoxicity</li> <li>• Impaired animal performance</li> </ul>
<b>Fumonisin</b>	<i>Fusarium moniliforme</i>	<ul style="list-style-type: none"> <li>• Equine leukoencephalomalacia</li> <li>• Porcine pulmonary edema</li> </ul>
<b>Trichothecenes</b>	<i>Fusarium</i>	<ul style="list-style-type: none"> <li>• Necrose and inflammation – oral cavity</li> <li>• Immunessupression</li> <li>• Vomits and diarrhea</li> </ul>
<b>Zearalenone</b>	<i>Fusarium roseum</i>	<ul style="list-style-type: none"> <li>• Hyperestrogenism:               <ul style="list-style-type: none"> <li>○ Vulvar edema</li> <li>○ Enlarged mammary glands</li> <li>○ Decreased litter size</li> </ul> </li> </ul>
<b>Ochratoxin</b>	<i>Aspergillus</i>	<ul style="list-style-type: none"> <li>• Nephotoxicity</li> <li>• Hepatotoxicity</li> <li>• Immunessupression</li> <li>• Impaired animal performance</li> </ul>

### Q. What are the effects of mycotoxins on the reproductive organs?

A. Several mycotoxins have shown to cause reproductive effects:

- **ZEARALENONE**: the major effects are estrogenic and primarily involve the urogenital system. Swine are the most commonly affected animals. Hyperstrogenism in female swine may be manifested as swelling of the vulva and enlargement of mammary glands, especially in prepubescent gilts.
- **ERGOT ALKALOIDS**: abortion may be observed after ergot ingestion, depending on species affected. In horses, the endophyte of tall fescue is the causative agent for reproductive abnormalities in pregnant mares. Increased gestational length, agalactia, foal and mare mortality, toughened and thickened placentas, weak and dysmature foals, and decreased serum prolactin and progesterone levels occur in mares consuming endophyte-infected tall fescue pastures.
- **AFLATOXIN B<sub>1</sub>**: has been associated with bovine abortions and may adversely affect nursing neonates through exposure to metabolites in milk.
- **T-2 TOXIN**: associated with decreased egg production. The T-2 toxin consumption by breeding sows has caused drastically decreased conception rates and weak piglets, with decreased litter sizes in those sows conceiving.

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### Q. Do mycotoxins affect people working in feed mills or farms?

- A. Yes. Reports on human mycotoxicosis have been mostly associated with oral ingestion of the toxin. However, inhalation was recognized as another important route of entry. Thus mycotoxins have a potential to affect people working in feed mills or farms. The airborne nature of either ochratoxin or particles laden with this mycotoxin is now considered a potential risk for human exposure (Richard *et al.*, 1999). Stachybotryotoxicoses is another illness associated with toxin inhalation. Hay dust *Stachybotrys*-contaminated is inhaled and it causes inflammation of the nose, fever, chest pain, and leucopenia.

### About product efficiency

### Q. What is the difference between TOXISORB® Classic and TOXISORB® Premium?

- A. The main difference between TOXISORB® Classic and TOXISORB® Premium is the organophilic activation TOXISORB® Premium goes through. This process allows it to become more lipophilic, which increases its ability to bind non polar mycotoxins, such as zearalenone, ochratoxin, deoxynivalenol, and fumonisin.

### Q. Is there a difference in dosage depending on species and stage? What is the recommended dosage for TOXISORB® Classic and TOXISORB® Premium?

- A. Yes. The recommended concentration of TOXISORB® Classic and TOXISORB® Premium depends on several factors, such as:
- Species;
  - Mycotoxin(s);
  - Contaminated level(s).

The recommended concentration in low contamination and/or preventive use is 1 to 2kg/ ton feed; in medium contamination levels and feed containing mixed mycotoxins it is recommended 2 to 3kg/ton feed; and in high contamination with critical mix of mycotoxins the concentration that should be used is 3 to 4kg/ ton feed.

### Q. Are TOXISORB® Classic and TOXISORB® Premium used preventively or therapeutically?

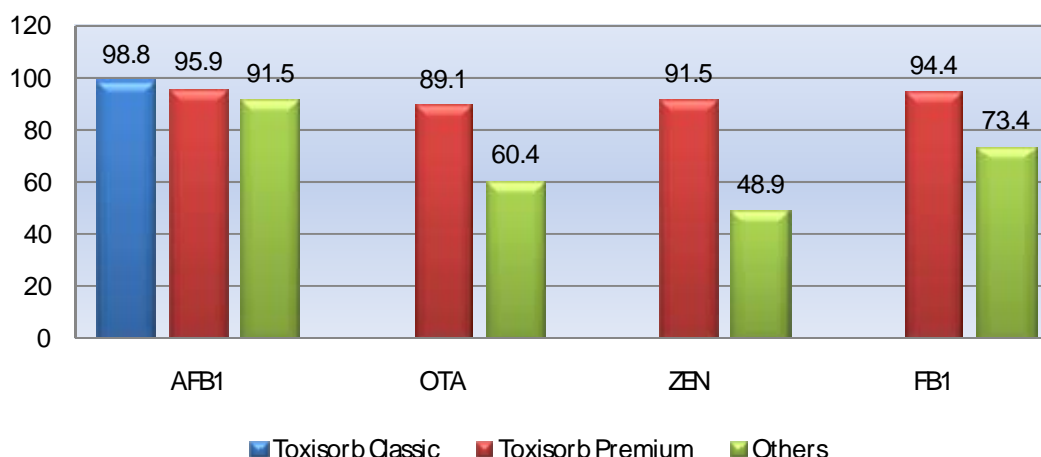
- A. TOXISORB® Classic and TOXISORB® Premium act by binding the mycotoxins efficiently in the gastro-intestinal tract more in a prophylactic rather than in a therapeutic manner, avoiding the toxic effects for livestock and carryover of the toxins to animal products.

### Q. How do TOXISORB® Classic and TOXISORB® Premium compare against competitors?

- A. TOXISORB® Premium and TOXISORB® Classic were tested *in vitro* and compared to the main mycotoxin binders available in the Brazilian, Mexican, and Peruvian markets. Adsorption analyses for different mycotoxins were performed by recognized laboratories, including: Laboratório de Análises Micotoxicológicas da Universidade Federal de Santa Maria (LAMIC – UFSC) in Brazil, and TRILOGY Analytical Laboratory Inc., in the USA. Some tests were also performed in our R & D units in Germany. TOXISORB® Classic and TOXISORB® Premium adsorption efficiency are shown in the Figure below, and they were compared to some mycotoxin binders' competitors. TOXISORB® Classic and TOXISORB® Premium over performed competitors.

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### Adsorption Efficiency (%)



\* Others = average results of the main mycotoxin binders available in the Brazilian, Mexican, and Peruvian markets. It was not included values lower than 50%.

A mycotoxin adsorbent available on the Asian market was tested *in vivo* in comparison to TOXISORB® Premium. The adsorbents were used in the dosage recommended by the producer. In South East Asia, weaned piglets were divided into 4 treatments as shown in Table 1. Mycotoxin levels of the feeds are shown in Table 2.

**Table 1. Dietary treatments.**

Treatment	Mycotoxin-contaminated corn	Adsorbent
T1	-	-
T2	+	-
T3	+	1.5kg TOXISORB® Premium/ton
T4	+	1.0kg mycotoxin binder A/ton

**Table 2. Mycotoxin levels in feed.**

Treatment	Aflatoxin B <sub>1</sub> (ppb)	Zearalenone (ppb)	T-2 toxin (ppb)	Fumonisin B <sub>1</sub> (ppm)
T1	17.1	70.6	0.0	1.0
T2	30.8	151.1	48.7	1.8
T3	13.6	168.8	53.5	1.5
T4	17.4	156.3	48.9	1.8

Piglets were given experimental diets *ad libitum* with free access to tap water for 28 days. A commercial mycotoxin binder was compared to TOXISORB® Premium. Growth performance parameters were evaluated and they are shown in Table 3.

**Table 3. Growth performance of piglets fed experimental diets for 28 days.**

Treatment	T1	T2	T3 (TOXISORB® Premium)	T4
Ave daily FI (kg/d)	1.33±0.32	1.42±0.76	1.77±0.33	1.97±0.12
Ave daily BWG (kg/d)	0.76±0.36	0.61±0.45	<b>1.01±0.32</b>	0.91±0.06
Feed conversion (g : g)	1.74±0.46	2.33±1.92	<b>1.75±0.26</b>	2.16±0.16

It was concluded that mycotoxin-contaminated corn in feed adversely affected growth performance of weaned piglets. Piglets fed diets supplemented with TOXISORB® Premium

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showed better daily weight gain compared to piglets fed control diets. Feed conversion of animals fed diets supplemented with TOXISORB® Premium was not different than animals fed control diets.

It was also observed that piglets fed diets supplemented with TOXISORB® Premium presented better values of growth performance parameters when compared to animals supplemented with the commercial mycotoxin binder.

### Q. What is adsorption efficiency? How do you measure the adsorption efficiency?

- A. *In vitro* tests are done trying to simulate most of the physiological conditions of the animal GI tract. Then, when conducting such a test, the first measurement that is made is the adsorption under acid pH (simulating stomach environment). The second measurement is the desorption under neutral or basic pH (simulating intestinal environment). Finally, adsorption efficiency is calculated by subtracting the desorption measurement from the adsorption value:

$$\% \text{ adsorption efficiency} = \% \text{ adsorption} - \% \text{ desorption}$$

### Q. Do TOXISORB® Classic and TOXISORB® Premium work on any type of feed?

- A. TOXISORB® Classic and TOXISORB® Premium do work on any type of feed. Feed formulation and different ingredients will not interfere with TOXISORB® Classic and TOXISORB® Premium mode of action.

### Q. Do TOXISORB® Classic and TOXISORB® Premium adsorb the mycotoxins from the grain or in the digestive system?

- A. TOXISORB® Classic and TOXISORB® Premium act by binding the mycotoxins efficiently in the gastro-intestinal tract, avoiding the toxic effects for livestock and carryover of the toxins to animal products.

### Q. How long does the adsorbent stay active?

- A. An adsorbent will keep its activity as long as binding sites are still available. Then, saturation of these sites will limit the binding capacity of an adsorbent.

### Q. Can TOXISORB® Classic and TOXISORB® Premium be used in aquaculture?

- A. Yes, however studies evaluating the efficiency of clays in aquaculture are still limited.

### Q. Do TOXISORB® Classic and TOXISORB® Premium work in granulated feed?

- A. Yes. Feed manufacturing processes such as pelletizing do not interfere with TOXISORB® Classic and TOXISORB® Premium mode of action.

### Q. Can TOXISORB® Classic or TOXISORB® Premium control molds?

- A. No. TOXISORB® Classic and TOXISORB® Premium are mycotoxin binders. They adsorb mycotoxins efficiently in the GI tract, avoiding the toxic effects for livestock and carryover of the toxins to animal products. However, TOXISORB® Classic and TOXISORB® Premium can indirectly control mold growth. TOXISORB® Classic and TOXISORB® Premium reduce water activity, and this condition limits growth for certain mold species.

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- Q. Would you recommend the usage of TOXISORB® Classic and TOXISORB® Premium without having determined the levels of mycotoxins?**
- A. Yes. TOXISORB® Classic and TOXISORB® Premium are also recommended for preventive usage, and the concentration indicated in this case should be 1 to 2kg/ ton feed.
- Q. How long should a treatment last?**
- A. Animals should be fed TOXISORB® Classic or TOXISORB® Premium as long as contaminated or suspicious feed is being fed. There is no need to withdraw TOXISORB® Classic or TOXISORB® Premium from the feed days before the slaughter. Then, TOXISORB® Classic and TOXISORB® Premium can be added to animal feed from day 1 to slaughter day.
- Q. At what age can you start adding TOXISORB® Classic and TOXISORB® Premium?**
- A. From day 1 or since animal starts being fed dry feed.
- Q. TOXISORB® Premium is known as an organoclay. What is the meaning of organophilic activation?**
- A. TOXISORB® Premium is a type of clay that goes through an organophilic activation process. This process is intended to increase its ability to attract and bind non polar mycotoxins, such as zearalenone, fumonisin, and ochratoxins.
- Q. Süd-Chemie has many mines all over the world. Are the raw materials designed to TOXISORB® Premium originated from all these mines?**
- A. Süd-Chemie does have more than 30 mining sites from where our raw materials are obtained. After analyzing the clay source and evaluating some important characteristics, different products can be manufactured, depending on the activation process it goes through. Due to some characteristics found sometimes in the raw materials not all sources are exactly suitable for mycotoxin adsorption. Therefore, one of the main steps in developing our products is the selection of the most suitable raw material for mycotoxin adsorption. Other than selection of raw material, TOXISORB® Premium undergoes an activation process. For this reason, it is only produced in Germany, Mexico, and Brazil so far.
- Q. Independently on the source of raw material, is the quality of products guaranteed, i.e. will TOXISORB® Premium always present the same composition?**
- A. Yes. In the different markets Süd-Chemie does guarantee the quality of its products which are manufactured with local raw materials. Products that are manufactured and shipped to the Asian market are produced exclusively in Germany. For Mexico and Central America they are produced in Mexico; and to supply Brazilian market, they are produced in our plant in Brazil.
- Q. How can TOXISORB® Premium activation process be characterized?**
- A. Depending on the source of raw material the clays go through different activation processes:
- Acid activation: process intended for selective creating pores;
  - Alkaline activation: process intended for optimizing surfaces in aqueous solutions;
  - Organophilic activation: process intended for conferring lipophilic properties.

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**Q. What is the difference among the mycotoxin binders available in the market?**

- A. In general, mycotoxin binders can be classified as:
- Products based on Hydrated calcium and sodium aluminosilicate (HSCAS), which can be unmodified HSCAS or organically modified HSCAS;
  - Products based on HSCAS combined with manonoligossacharides (MOS);
  - Products based on HSCAS combined with enzymes;
  - Products based only on MOS.

**Q. The minimum CEC (cation exchange capacity) value required by our customer for clay based toxin binders is 50mEq. What happens if CEC value is different than 50mEq?**

- A. It has been demonstrated that a variety of functional properties of clay are critical for the immobilization of diverse ligands. Then, the binding capacity of clay is determined by a combination of factors, not only one single characteristic. The variety of functional properties affecting the binding capacity of a ligand includes:
- Cation exchange capacity (CEC);
  - Surface area;
  - pH value;
  - Porosities;
  - Predominant exchangeable cation;
  - Ligand specificities;
  - Ligand capacity; and
  - Temperature of adsorption.

The CEC of 50mEq not necessarily determine the mycotoxin binding capacity of clay, but the sum of the above listed factors.

**Q. Which cation is prevalent in TOXISORB® Premium: sodium or calcium? What is the difference regarding toxin binding capacity among sodium bentonite and calcium bentonite?**

- A. TOXISORB® Premium is based on a modified calcium bentonite. Both sodium and calcium bentonite have similar surface areas, which means similar amounts of mycotoxins can homogeneously be distributed on both bentonite molecules. Sodium bentonites have higher CEC and higher swelling capacity compared to calcium bentonites, leading to greater chemical activity. Therefore, it will potentially enhance interactions with nutrients from the diet. So sodium bentonites has a higher probability to adversely affect animal performance.

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### About product safety

**Q. Do TOXISORB® Classic or TOXISORB® Premium adsorb vitamins or other nutrients?**

A. Studies on the interaction of TOXISORB® Premium with serum vitamins and minerals showed that they are not adsorbed by this mycotoxin binder. The results of this study are presented below in a tabular form:

Mineral	Control (without TOXISORB® Premium)	Group A (0.4% TOXISORB® Premium)	Group B (0.6% TOXISORB® Premium)
Calcium (mmol/L)	2.62	2.56	2.5
Magnesium (mmol/L)	1.75	1.39	1.67
Iron (µg/dL)	149	150	127
Copper (µg/dL)	183	194	168
Zinc (µg/L)	1119	811	1059
<b>Vitamin</b>			
Vitamin A (mg/L)	0.29	0.27	0.35
Vitamin E (mg/L)	0.7	1.4	1.2

**Q. Are TOXISORB® Classic and TOXISORB® Premium free of dioxins and heavy metals?**

A. TOXISORB® Classic and TOXISORB® Premium are safe for use in animal feed. They fulfill the strict EU requirements to dioxins and heavy metals.

**Q. Is there maximum permitted dosage for TOXISORB® Classic and TOXISORB® Premium?**

A. Natural sorbents are generally recognized as safe (GRAS) for animal feed at levels of 2% (20 kg/ton) or less by the United States Food and Drug Administration (FDA).

**Q. What is the LD<sub>50</sub> of TOXISORB® Classic and TOXISORB® Premium?**

A. LD<sub>50</sub> Rat > 5000mg/kg.

**Q. Are TOXISORB® Classic and TOXISORB® Premium manufactured under EU regulation?**

A. TOXISORB® Classic and TOXISORB® Premium are produced in Germany under regulation EC 1831/2003. They are both registered as E558 (Bentonite – Montmorillonite).

**Q. Are Süd-Chemie's plants GMP certified?**

A. Süd-Chemie does not have HACCP and FAMI/QS. However, HACCP will be implemented by the end of 2007. As the most of the FAMI/QS requirements are included in HACCP, Süd-Chemie will apply for FAMI/QS after getting the HACCP certificates.

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### About product handling

**Q. How should I store TOXISORB® Classic and TOXISORB® Premium?**

A. To maintain the high performance, both TOXISORB® Classic and TOXISORB® Premium need to be stored in closed and low humidity areas. They must not be stored next to chemicals that give strong odor or evaporate easily, since it can absorb fumes to a high degree. They can be stored in silos and conveyed with compressed air (dry and oil free).

**Q. What is the shelf life of TOXISORB® Classic and TOXISORB® Premium?**

A. Under above mentioned storage conditions, the shelf life of TOXISORB® Classic and TOXISORB® Premium is typically 3 years after packing.

**Q. What happens if the material gets wet?**

A. If TOXISORB® Classic or TOXISORB® Premium get wet, they will generally build clumps that will make the product's handling complicated. The clumps should be disintegrated before using the product to make sure that the product can be mixed into the feed homogeneously. Nevertheless, its mycotoxin adsorption efficiency is not affected by this.

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### Literature

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