EU Registration
A worldwide quality benchmark

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The need for biomarkers

Apart from the laborious and costly experiments required to confirm the safety of a product, companies face the further challenge of developing and accomplishing biomarker studies that can directly prove the deactivation of mycotoxins in vivo (Box 2).

Most studies for mycotoxin deactivation products are performance studies trying to prove the mitigation of the harmful effects of mycotoxins but not the claimed deactivation of the toxin itself. To date, Biomin is the only company that has successfully proven the deactivation of mycotoxins with biomarkers.

Biomarker studies are quite difficult to accomplish. Most laboratories already fail to establish a validated analytical detection of mycotoxins in blood, urine or feces, where very sensitive and precise methods are needed. Conducting representative feeding trials and evaluating biomarkers requires advanced scientific expertise.

Bacteria and bentonite

The final authorization of Mycofix® Secure, Biomin® BBSH 797 and FUMzyme® is issued by the EU as non-holder specific authorization. ‘Non-holder specific’ means that a product, fulfilling the criteria of the regulation, is allowed to claim the capability to deActivate a specific mycotoxin, independent of the company that submitted the dossier.

No other company can legitimately sell the unique trichothecene-detoxifying bacteria Biomin® BBSH 797, as Biomin is the sole patent holder. Only Biomin is allowed to use the claim ‘deoxynivalenol biotransformation’, unless another company files its own dossier and receives authorization with its own strain supporting this claim (Box 3). The same applies to FUMzyme®.

It is different in the case of bentonite: The EU regulation legalizing bentonite for aflatoxin deactivation is based on the dossier submitted by Biomin on its specific bentonite solely included in the Mycofix® product line. Any company selling bentonite fulfilling the criteria is now allowed to sell the product “registered for mycotoxin deactivation (1m)” without submitting its own dossier.

Aflatoxin-binding claim

In the case of any non-Biomin bentonite, no evaluation is required by the European Feed Safety Authority (EFSA) with regard to the identity, safety and efficacy of the product before it can be placed on the market. The claim “aflatoxin-binding” is allowed only for products that fulfill the main criteria.

The majority of products currently in the market do not meet the criteria. Aflatoxin-binding claims made without the right data in place are considered illegal in the EU, and offending parties may face legal action.

EU Registration

A worldwide

The EU registration for mycotoxin deactivation products is not only the legal basis for official mycotoxin claims. It is also a detailed and safety of a product. To date, FUMzyme®, Mycofix® Secure are the only products to have undergone the complete EFSA procedure with all experiments and trials for identity, safety and efficacy and succeeded in a final authorization.

Until 2009, there was no legislation in place recognizing feed additives with mycotoxin counteracting properties. As a result, more than 100 mycotoxin deactivation products available in the market were sold under non-mycotoxin specific claims, such as anti-caking agents. In 2010, after the EU introduced a new functional group of feed additives to recognize mycotoxin deactivation capabilities in products, Biomin submitted the first dossier.

Submitting a dossier for mycotoxin deactivation products requires a comprehensive number of in vitro and in vivo experiments.

Not all bentonites are equal

Bentonite is a natural clay and differs largely depending on the origin. Only the specific bentonite sold exclusively in the Mycofix® product line has undergone the complete EFSA procedure with all experiments and trials for identity, safety and efficacy and succeeded in a final authorization.

Biomin is responsible for legalizing the aflatoxin-binding claim of bentonites and the biotransformation of trichothecenes by Biomin® BBSH 797 in the European market.

Till now, Biomin is the only company to have received the authorization of the dossiers submitted for mycotoxin deactivation products. This authorization, which comes with strict and rigid requirements in the EU, helps customers to comprehensively compare products and make informed decisions with the scientific assurance of quality.
The EU registration for mycotoxin deactivation products is not only the legal basis for official mycotoxin claims. It is also a detailed evaluation with high standards for the efficacy and safety of a product. To date, FUMzyme®, Biomin® BBSH 797 and the specific bentonite Mycofix® Secure are the only products to have undergone the complete registration procedure and succeeded in a final authorization. Why does this make a difference?

(Box 1). The stringent guidelines effectively discouraged many manufacturers from having their anti-mycotoxin additives legally authorized. This is where Biomin differs. Because of its long-standing focus on mycotoxin research, Biomin was able to provide all the trials and experiments needed for the successful authorization of Mycofix® Secure for pigs, poultry and ruminants, FUMzyme® and Biomin® BBSH 797 for pigs. For more than two decades, Biomin has had its own research center working on creative and targeted solutions for mycotoxin deactivation and developing strong relationships with the mycotoxin research community globally.

1 Stringent EFSA guidelines for dossiers

- **Mycotoxin specificity**: Target mycotoxin(s) for the product must be declared.
- **Species specificity**: Data from a minimum of three *in vivo* studies performed in at least two different locations showing statistically significant effects must be provided to demonstrate efficacy at the lowest recommended dosage in a specific species.
- **Biomarkers**: Demonstration of product efficacy must be provided in the form of scientifically recognized relevant biomarkers.
- **Safety**: Data ruling out the possibilities of interaction with other feed components such as vitamins should be presented for mycotoxin binders such as clays. For mycotoxin deactivators that modify the chemical structure of mycotoxins, the effects of the deactivating substance as well as the resulting metabolite(s) on the safety of target animals, the consumer and the environment must be presented.

2 Why do we need biomarkers?

According to EFSA “In general, mycotoxin/metabolites excretion in feces/urine, concentration in blood/plasma/serum, tissues or products (milk or eggs) or other relevant biomarkers should be taken as end-points for demonstration of efficacy of substances for reduction of the contamination of feed by mycotoxins.”

Significant effects must be proven by relevant biomarkers in different studies, with sufficient number of animals and replicates for statistical analysis of data.

- Scientifically relevant biomarkers are, for example, the reduction of aflatoxin M1 in milk, the reduction of deoxynivalenol in serum or the reduction of the sphinganine/sphingosine ratio caused by fumonisins in blood.
- Improved animal performance may be due to an indirect effect of the additive, e.g. compensation of toxic effects by antioxidants, immune stimulators, and pharmacological substances.
- Therefore *in vivo* data and performance studies proving the efficacy of mycotoxin deactivating products are not enough to qualify an EU dossier for authorization.

3 Facts about Biomin® BBSH 797

- From the 1990s, Biomin started to invest heavily in the research and development of biotransformation products. The scientific community at that time had already acknowledged that binder products were ineffective in the adsorption of certain mycotoxins e.g. trichothecenes. Biomin® BBSH 797 isolated from rumen fluid produces specific enzymes which are able to detoxify trichothecenes in the intestinal tract of animals.
- In 2000, Elisabeth Fuchs and her co-workers first published the characterization of metabolites derived from the degradation of A- and B-trichothecenes by Biomin® BBSH 797.
- According to recent taxonomic studies, Biomin® BBSH 797 can now be assigned to a new genus in the family of *Coriobacteriaceae, Gen. nov.: (formerly Eubacterium), sp. nov.*