Mycotoxin Risk Management:
A 30-year Journey of Triumphs and Milestones

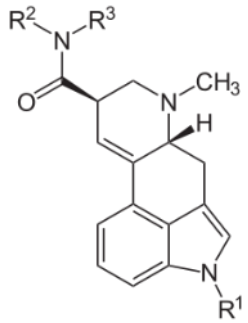
Dian Schatzmayr

Conference hosted by Bulgarian Feed Manufacturers Association,
October, 2025

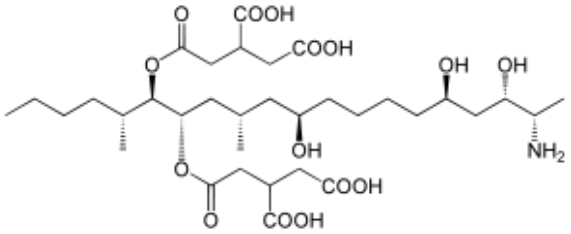
dsm-firmenich

What makes Mycofix® UNIQUE?

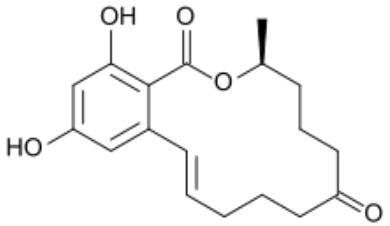
Mycotoxin Research



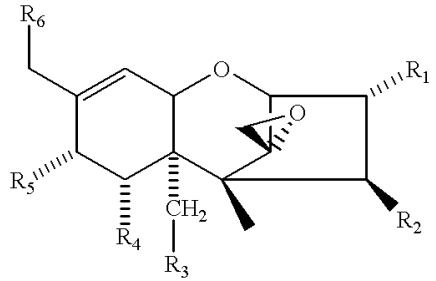
Ergot alkaloids



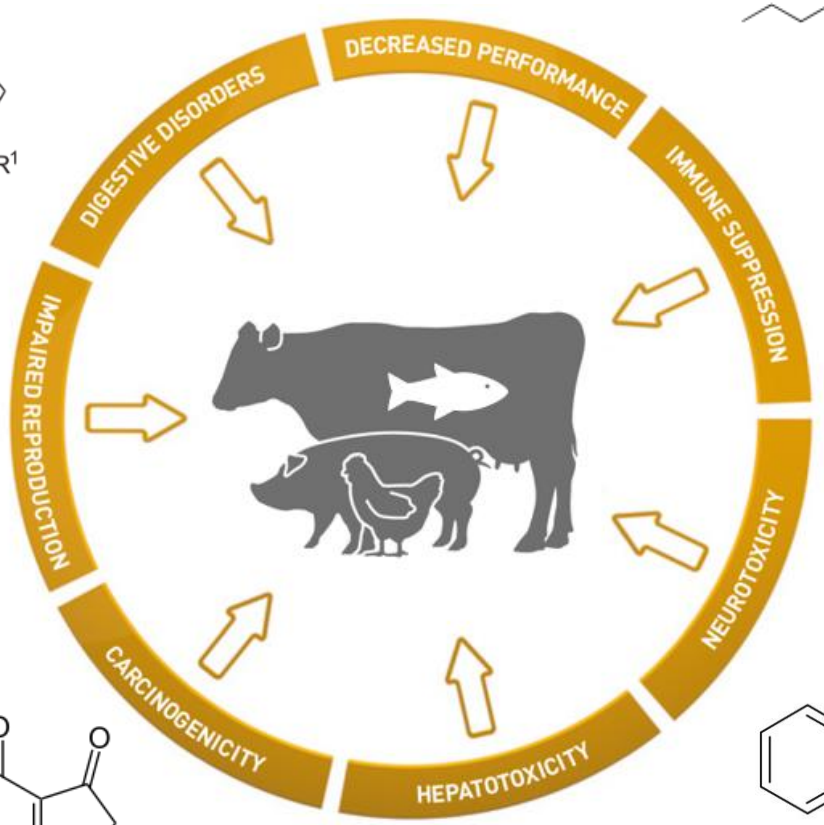
Fumonisins

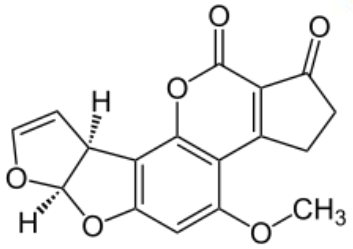


Zearalenone

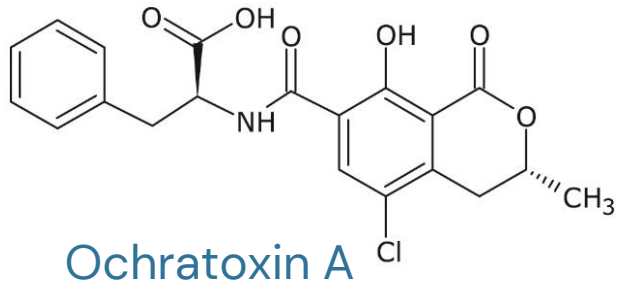


Trichothecenes





Aflatoxins

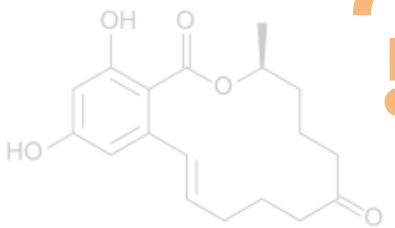


Ochratoxin A

Mycotoxin Research

Ergot alkaloids

Fumonisins



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Trichothecenes

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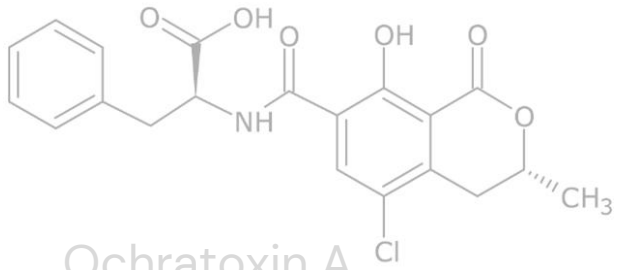
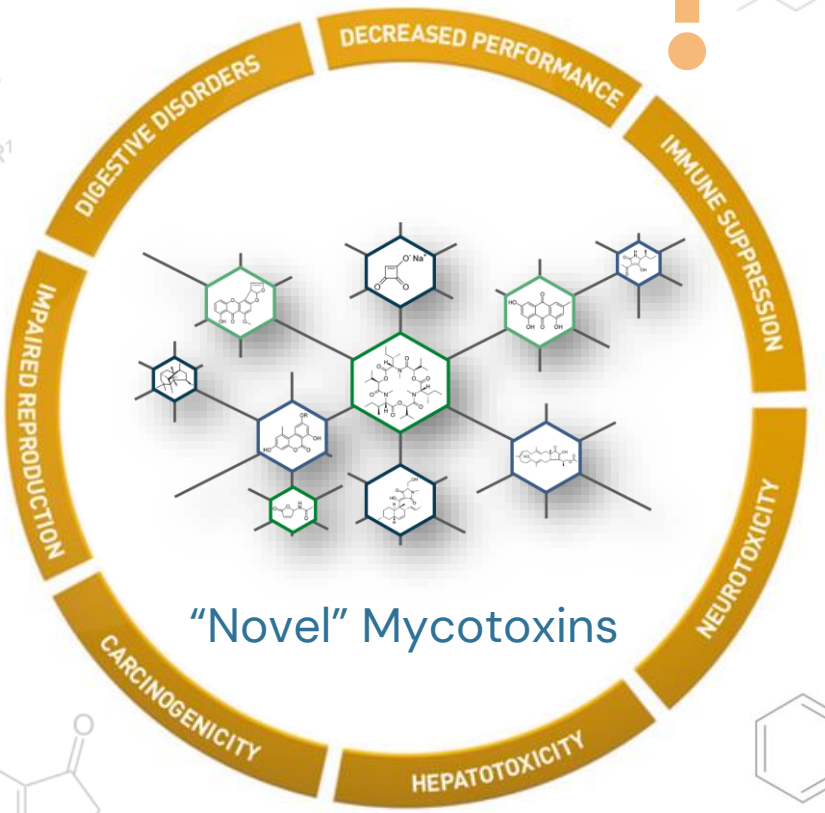


Ochratoxin A



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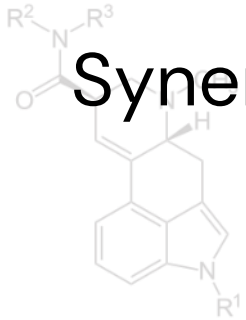
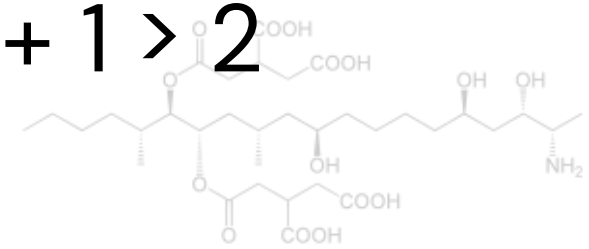
Mycotoxin Research

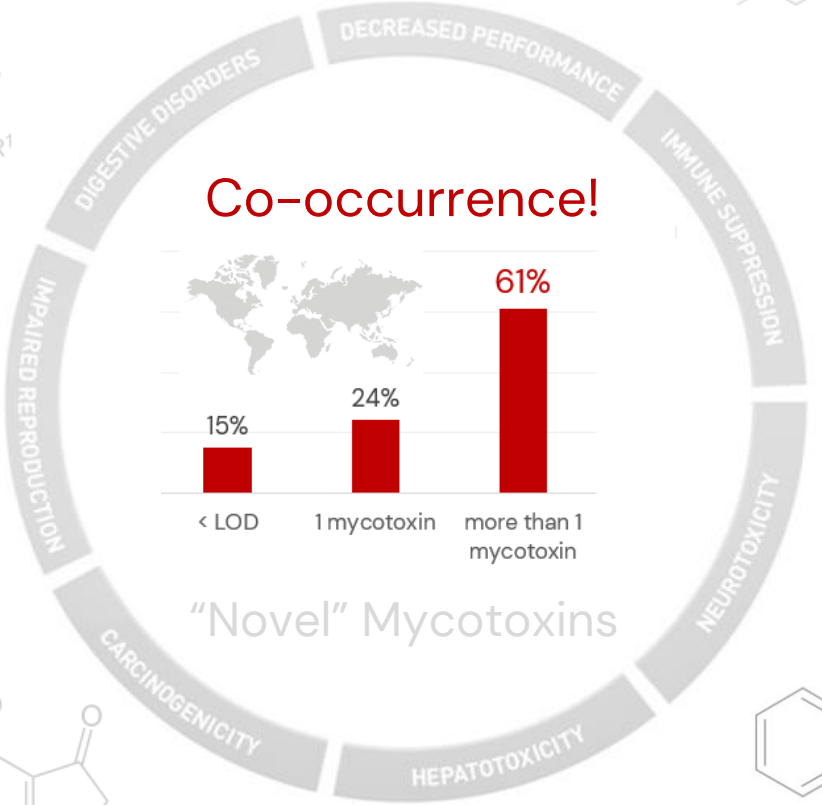
Synergistic effects?! → 1 + 1 > 2



Ergot alkaloids



Fumonisins



Zearalenone

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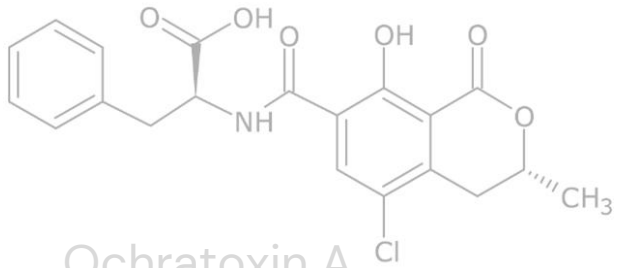


Ochratoxin A

Mycotoxin Research

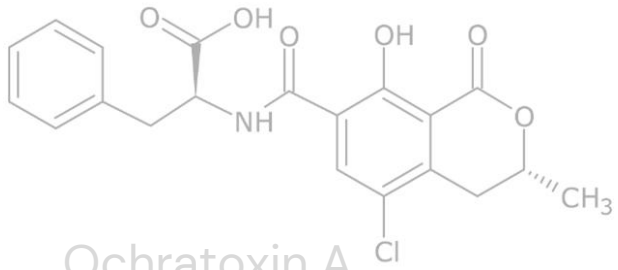
Ergot alkaloids

Fumonisins

Zearalenone

Trichothecenes

Aflatoxins



Ochratoxin A

Mycotoxin Research

NO
"one fits all"
solution!

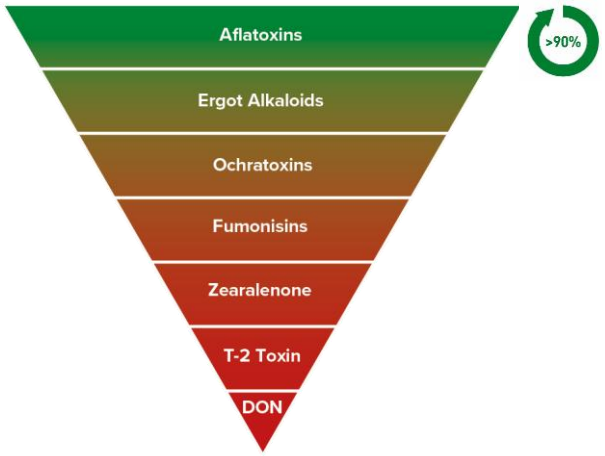
1985

1st mycotoxin **binder** launched by BIOMIN

ADSORPTION

WHY

not successful outside Asia?



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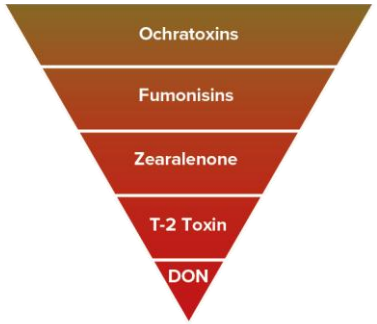
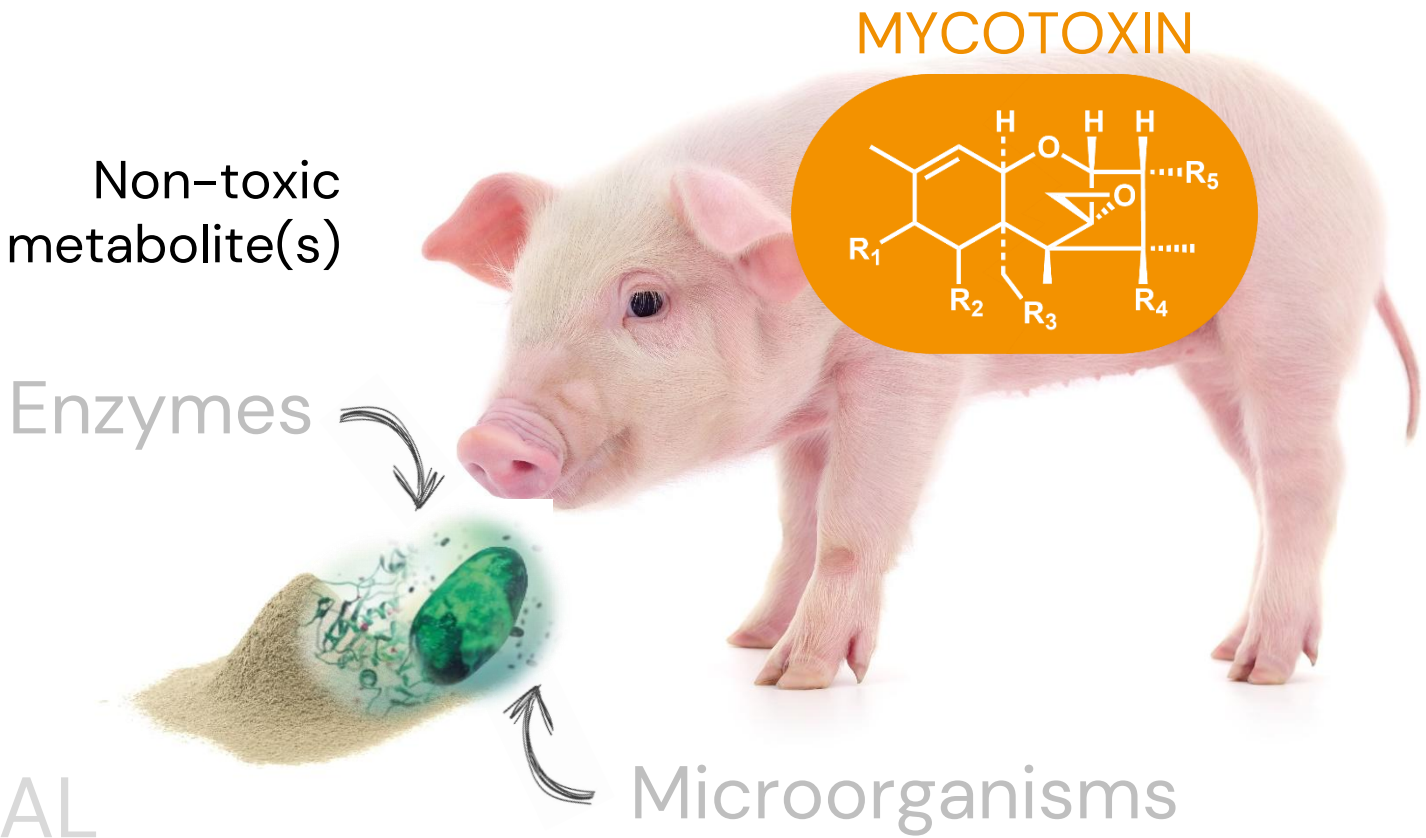
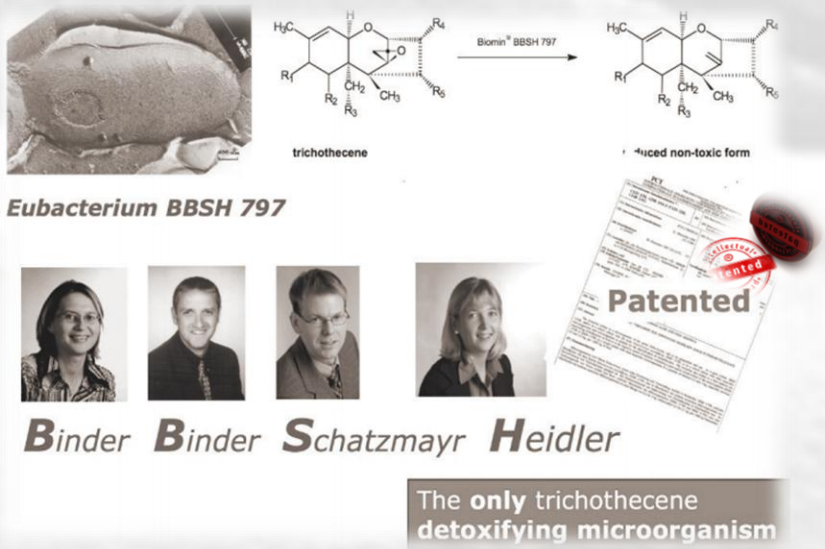


1988 Collaboration with vetmeduni vienna

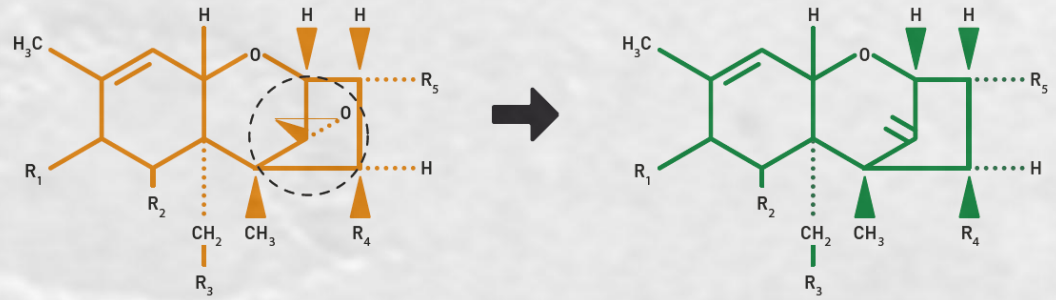
1993 In-house R&D **BIOTRANSFORMATION**



2001 Launch of BBSH® 797 containing Mycofix®

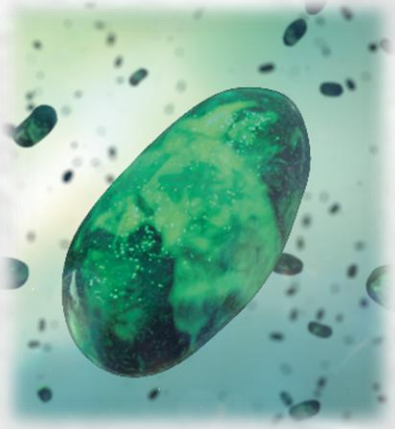


- Genus nov. (formerly *Eubacterium*) sp. nov., family *Coriobacteriaceae*
- produces de-epoxidases



Trichothecenes

detoxified form



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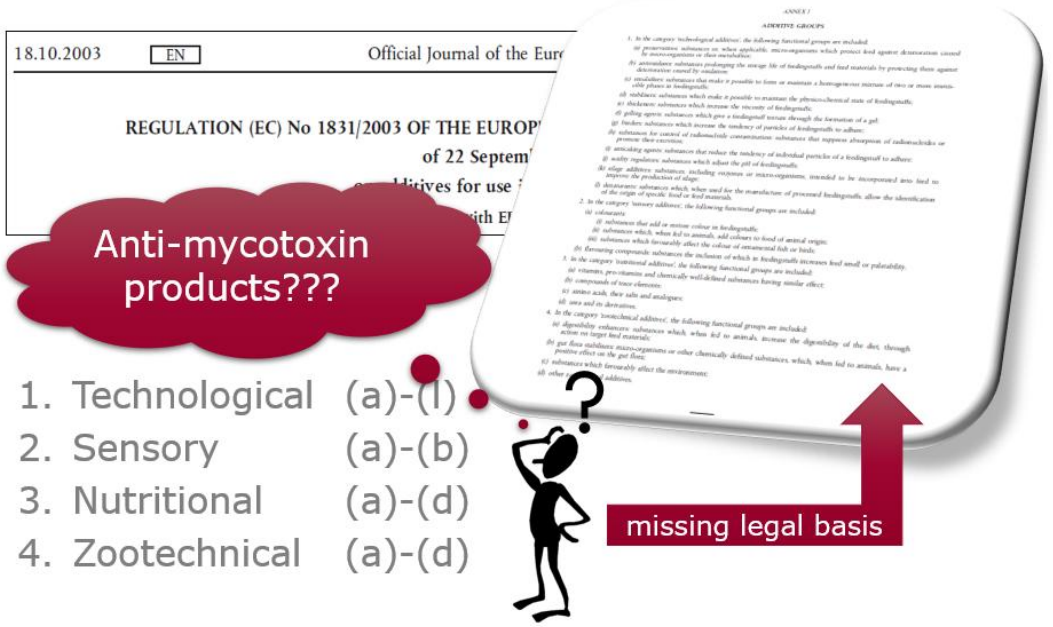


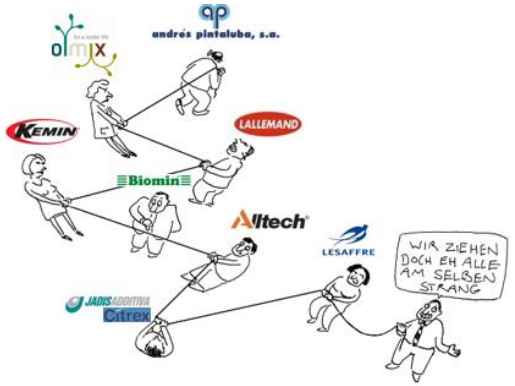
Missing legal basis for registration

Anti-mycotoxin products on market with **unspecific** (e.g., anticaking agent, pellet binders) or even **illegal claims** (e.g., mycotoxin-binding)

2005 Initiative started to establish legal basis

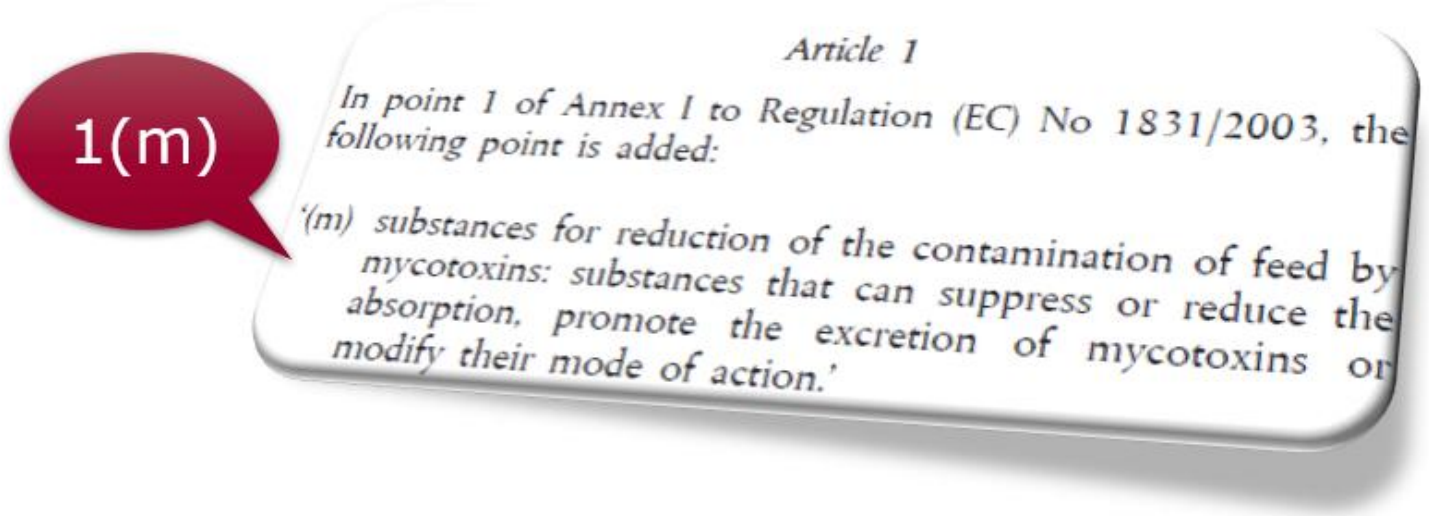
BIOMIN contacted FEFANA [1]

Task Force “Mycotoxins” founded with the aim to open a new functional group in the category of technological feed additives



[1] represents interests of the European feed additives industry

2009 Legal basis established



New functional group established under the Regulation (EC) No. 1831/2003

Regulation (EC) No. 386/2009 of 12 May 2009 amending Regulation (EC) No. 1831/2003

2012

EFSA guidance document

Requirements for evaluation of identity, safety and efficacy:

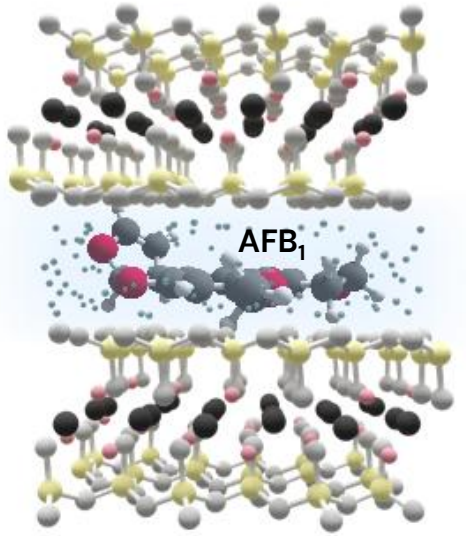
- ✓ target mycotoxin(s) must be specified
- ✓ product must not interfere with the analytical determination of mycotoxins (MT) in feed
- ✓ **mode of action** must be demonstrated
- ✓ MT binders: binding capacity must be determined
- ✓ MT degraders: effects of the mycotoxin degradation product(s) on the safety of the target animals and consumers must be shown

- ✓ Mycotoxin content in feed used in studies must **not exceed legal limits[1]/official recommendations[2]**
- ✓ Minimum three *in vivo* studies with significant effects at the **lowest recommended dosage**
- ✓ Mycotoxin/metabolite excretion in feces/urine, concentration in blood, tissues or products (milk or eggs) or other **relevant biomarkers** must be taken as end-points for demonstration of efficacy

[1] Directive 2002/32/EC, [2] Commission Recommendation 2006/576/EC

2013

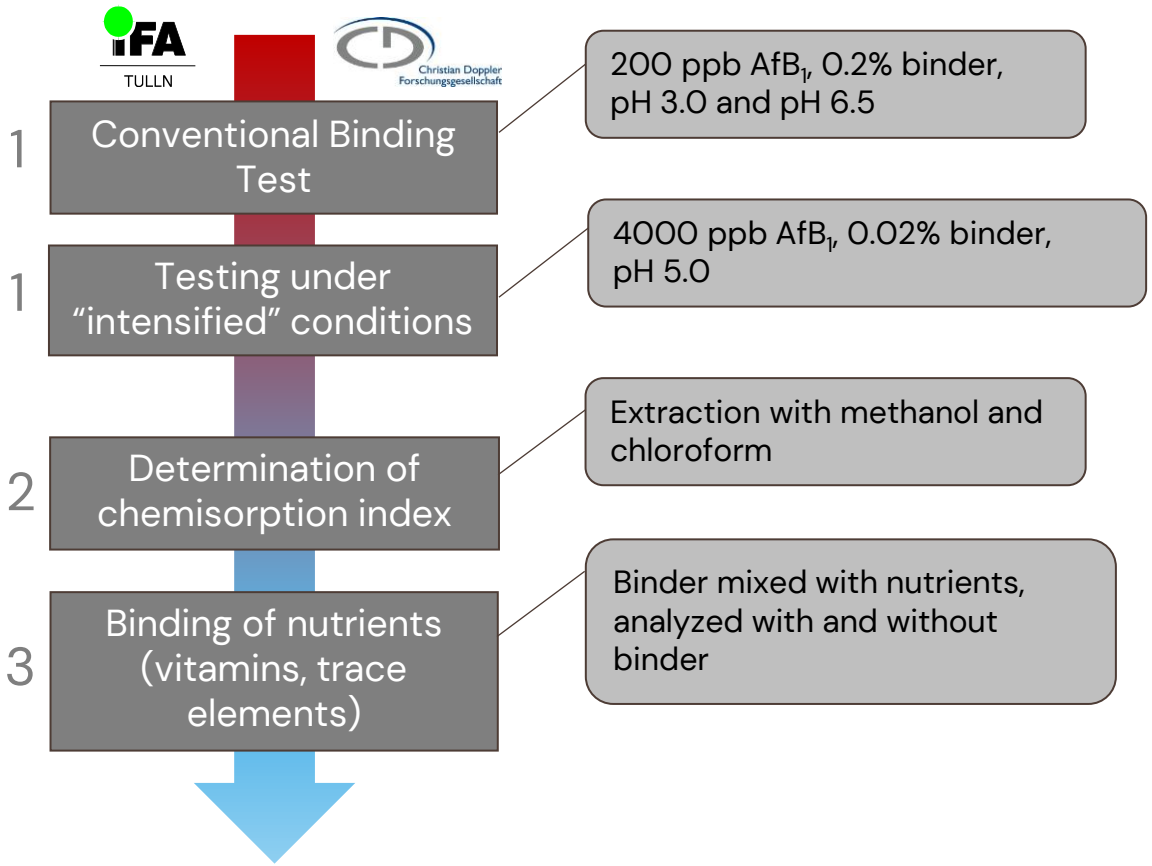
EU registration
Mycofix® Secure (AFLA-binder)

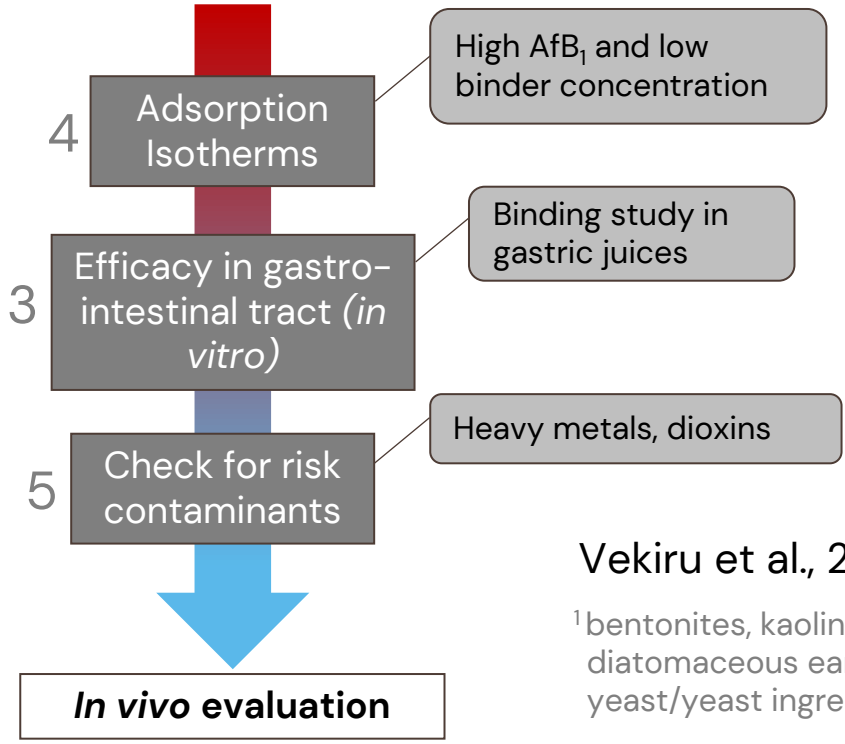


Mycofix® Secure

1. adsorption capability
2. strength of binding
3. affinity to mycotoxin
4. adsorption capacity
5. safety

Binder Project > 300 substances tested[1]





Vekiru et al., 2007

[1] bentonites, kaolinites, zeolites, diatomaceous earth, organoclays, charcoals, yeast/yeast ingredients, ...

Mycofix® Secure

Binder Project > 300 substances tested

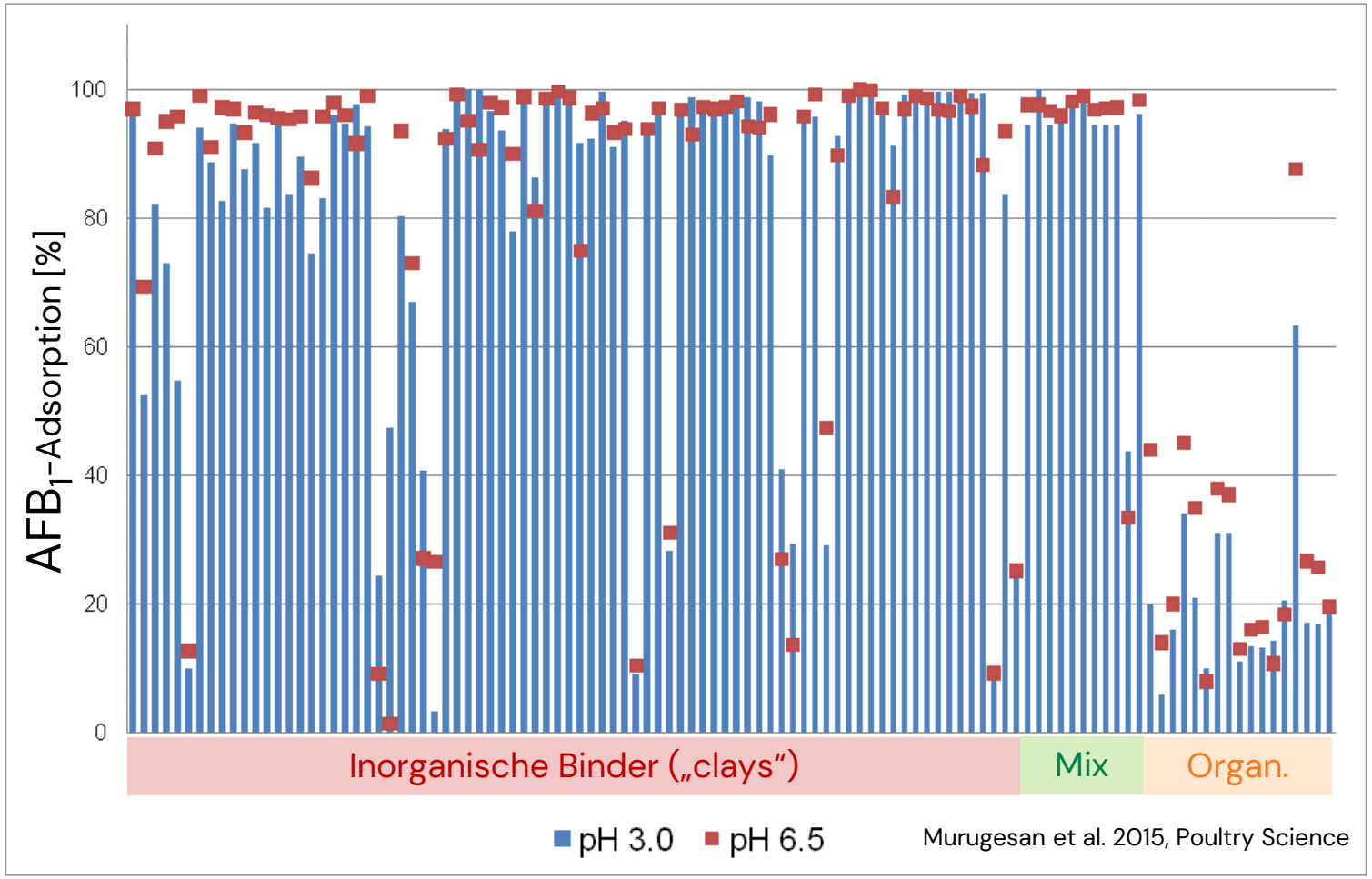
200 ppb AfB_1, 0.2% Binder, pH 3.0 und pH 6.5

1 Conventional Binding Test

1 Testing under "intensified" conditions

2 Determination of chemisorption index

3 Binding of nutrients (vitamins, trace elements)



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Mycofix® Secure

Binder Project > 300 substances tested

IFA TULLN

Christian Doppler Forschungsgesellschaft

1 Conventional Binding Test[1]

1 Testing under "intensified" conditions

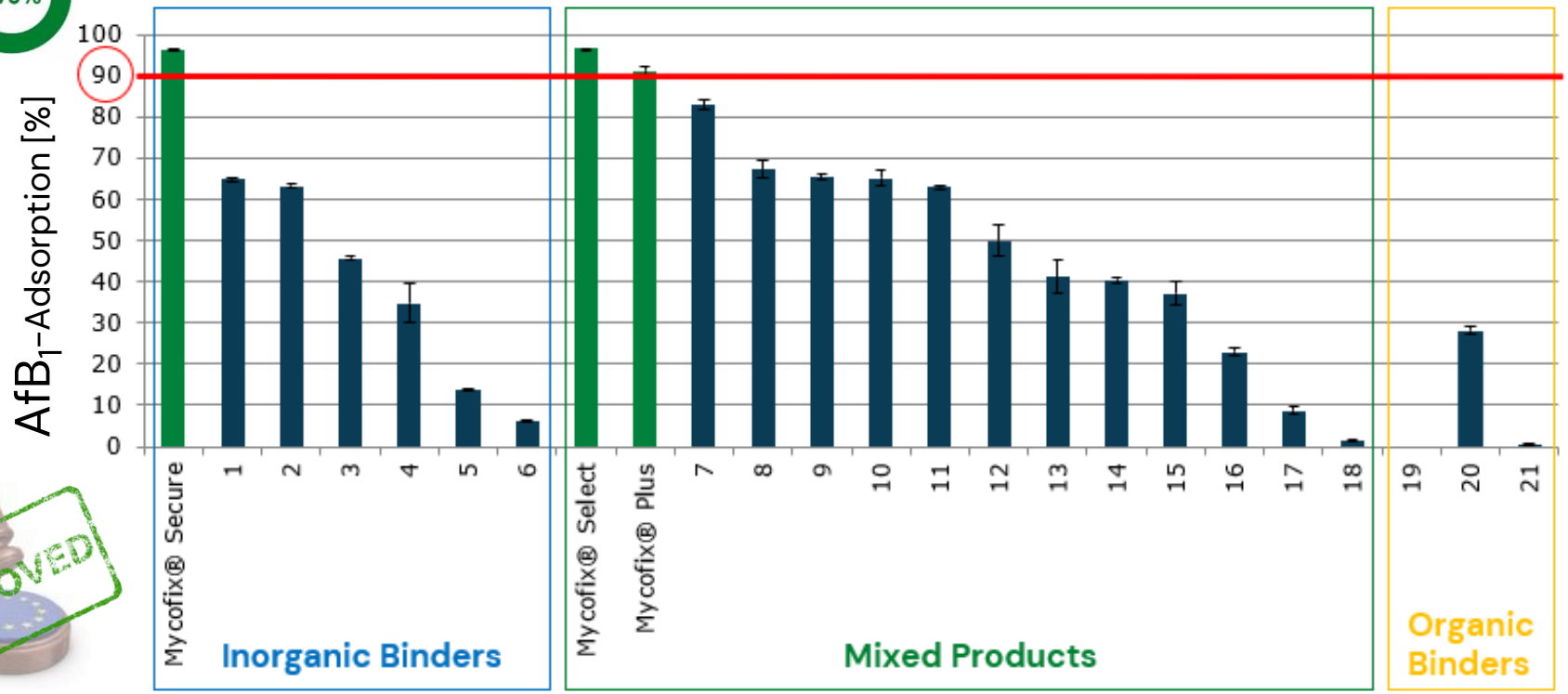
2 Determination of chemisorption index

3 Binding of nutrients (vitamins, trace elements)

>90%

EUROPEAN COMMISSION
JOINT RESEARCH CENTRE
Institute for Reference Materials and Measurements (Geel)
Standards for Food Bioscience Unit
European Union Reference Laboratory for Feed Additives - Authorisation

4000 ppb AfB_1, 0.02% binder, pH 5.0



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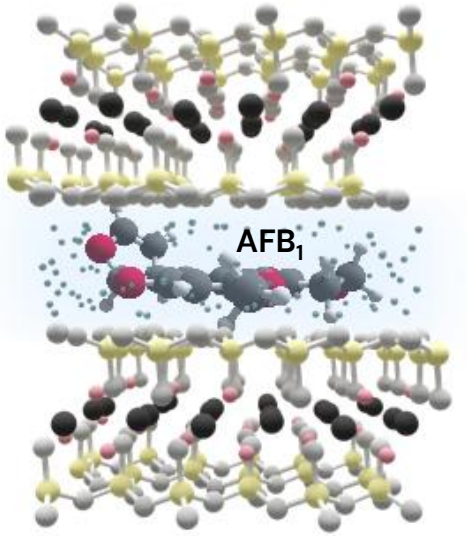
2013

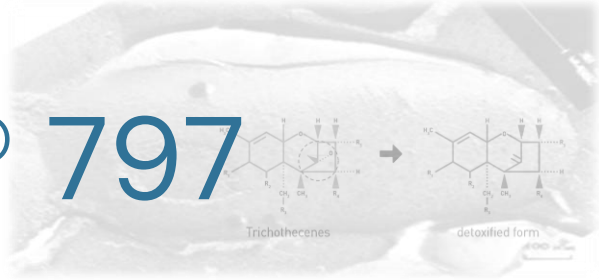
EU registration

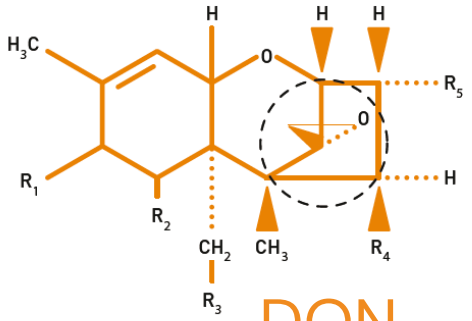
Mycofix® Secure (AFLA-binder)



2013

EU registration BBSH® 797

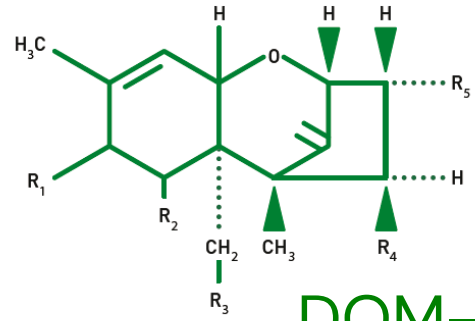




DON

Trichothecenes

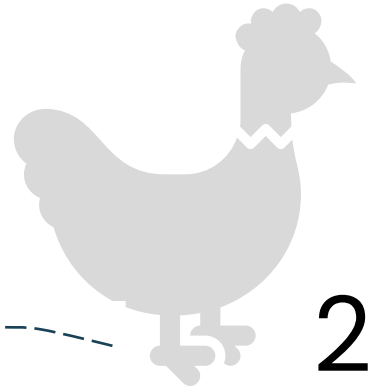
deoxynivalenol



DOM-1

detoxified form

de-epoxydeoxynivalenol



2017

CONFIDENTIAL

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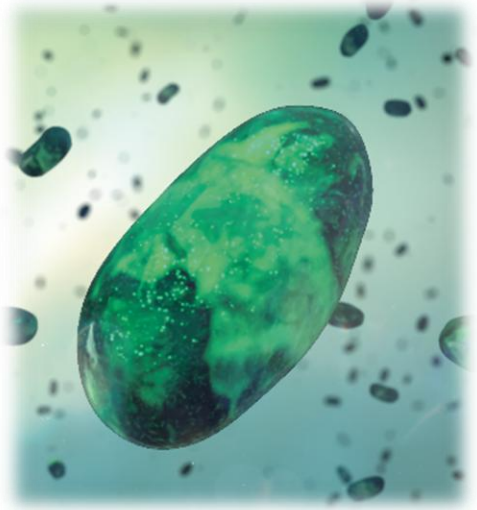
BBSH® 797

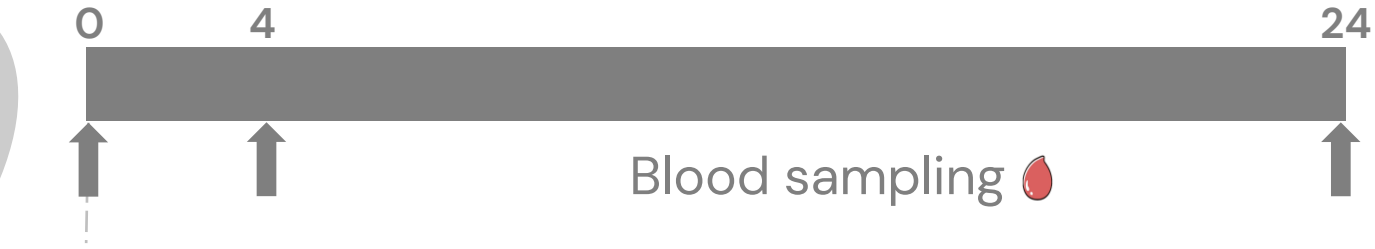


Safety & Efficacy evaluated by efsa

European Food Safety Authority

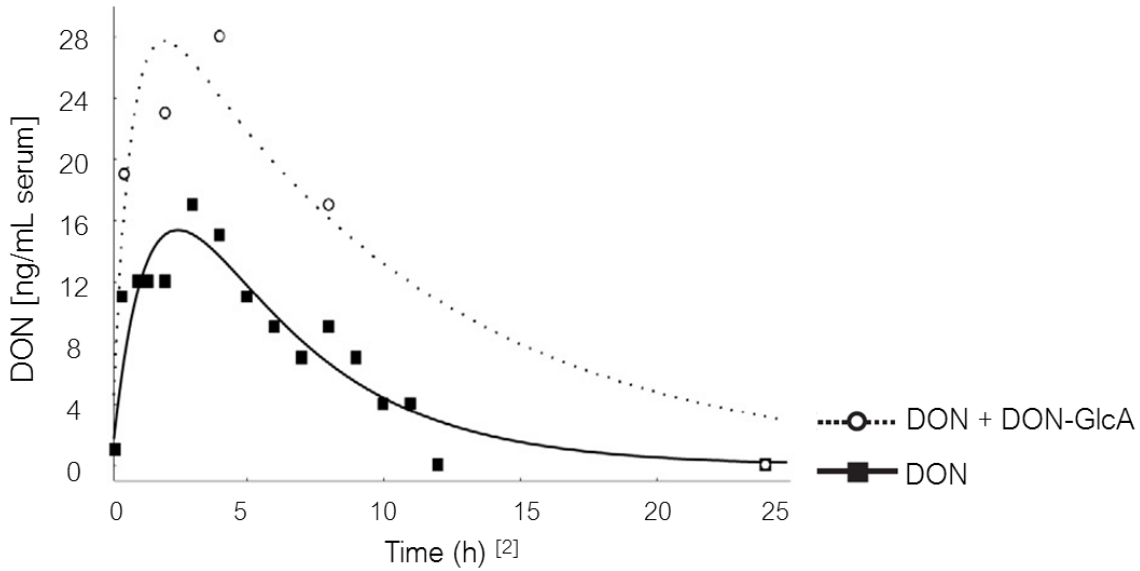
CAN Center for Applied Animal Nutrition

Piglet study



3 groups
- Control
- DON
- DON + BBSH

8 animals/group
2 replicates/group
DON 2 mg/kg
BBSH at min. dose



Dänicke & Brezina 2013. Food Chem. Toxicol. 60

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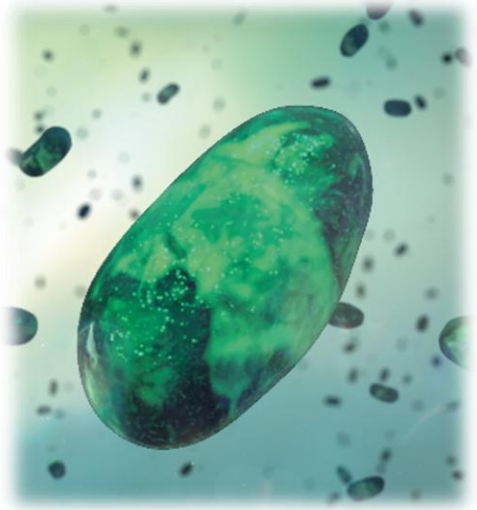
BBSH® 797



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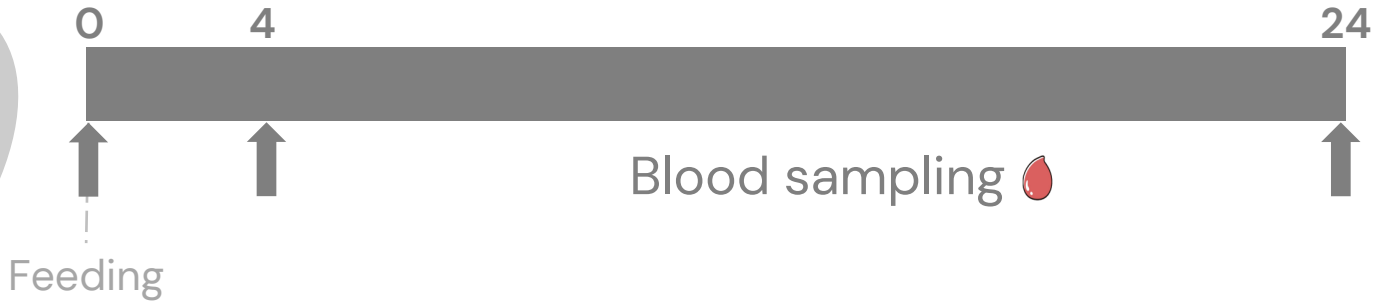

3 groups
- Control
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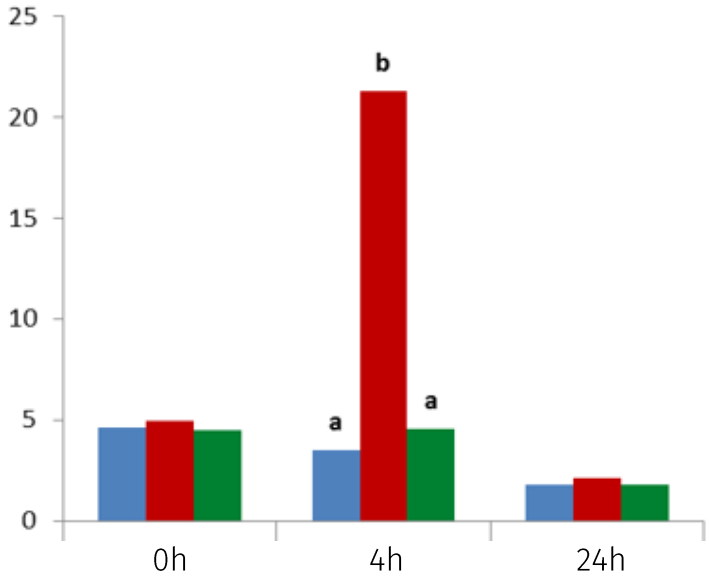
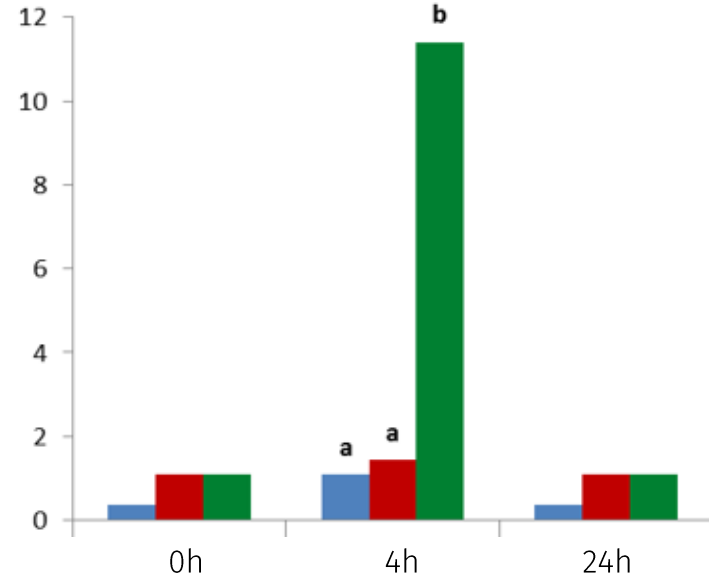
8 animals/group
2 replicates/group
DON 2 mg/kg
BBSH at min. dose

DON [ng/mL serum]

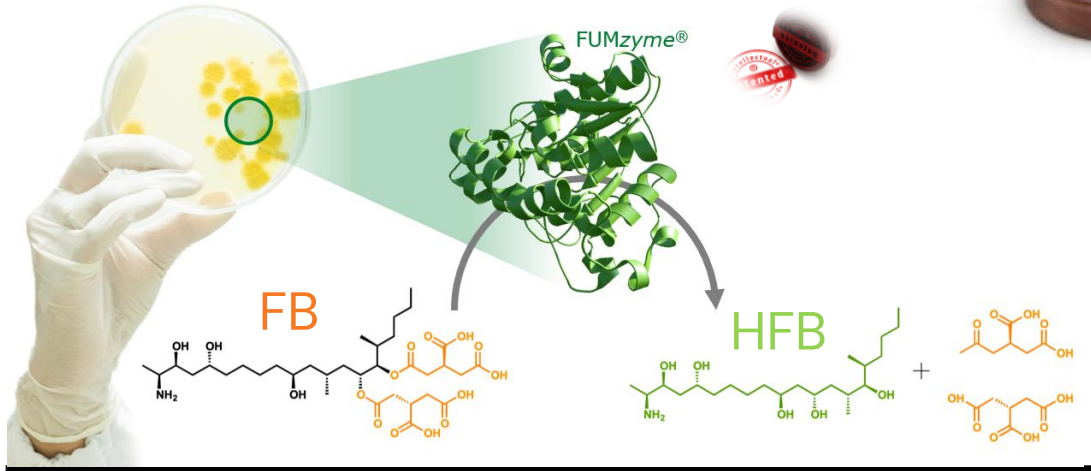


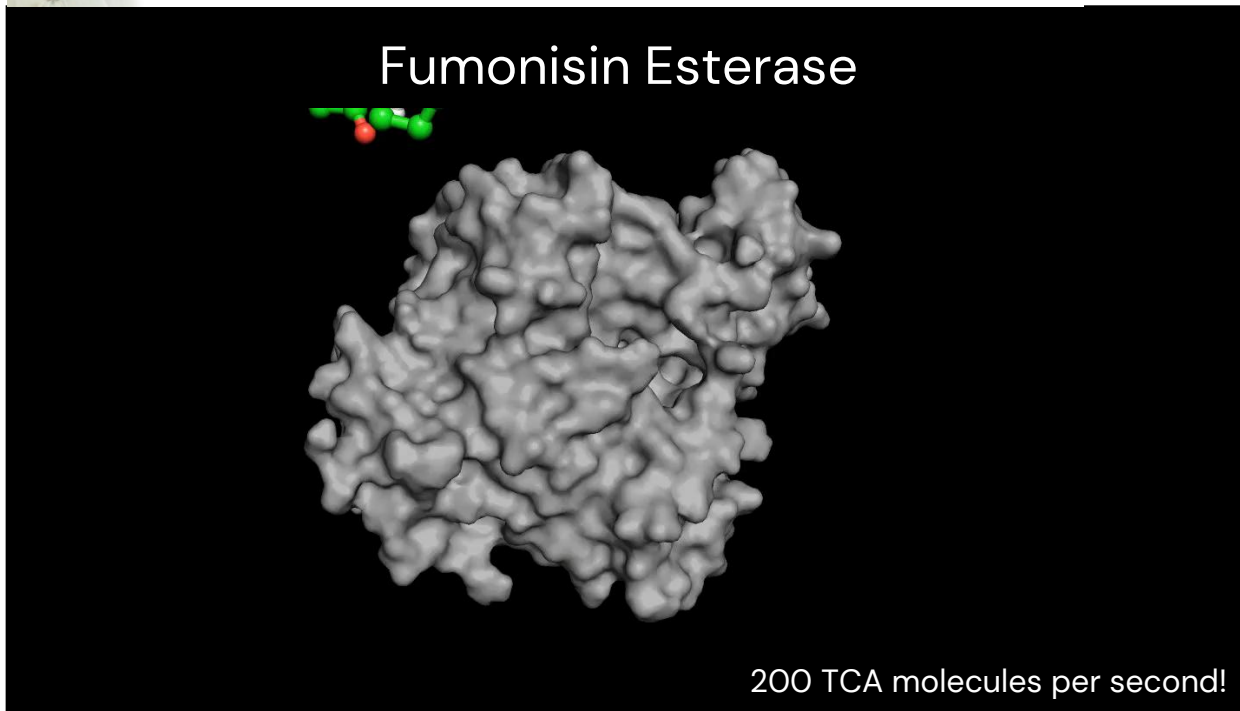
DOM-1 [ng/mL serum]



2014

EU registration FUM*zyme*®



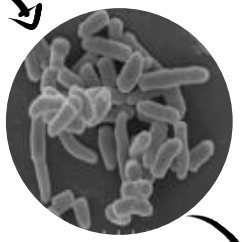


FUMzyme®

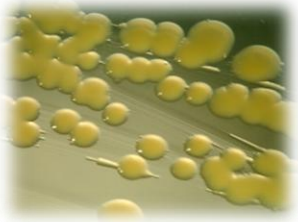
2014

Product formulation

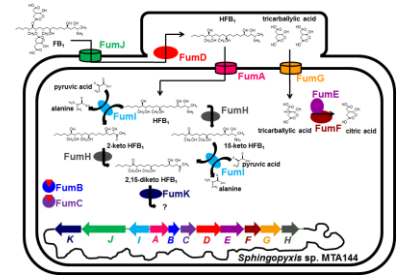
Soil 2004

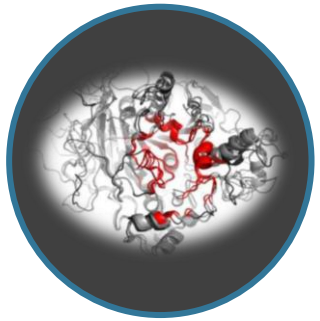


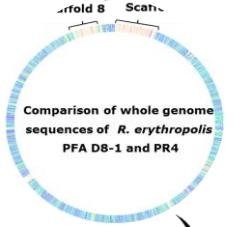
Strain



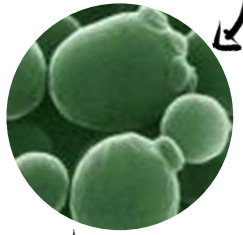
Sphingopyxis macrogoltabida



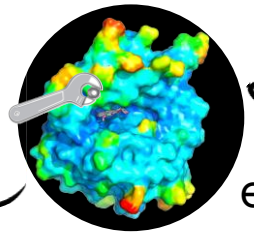




Genome



Expression

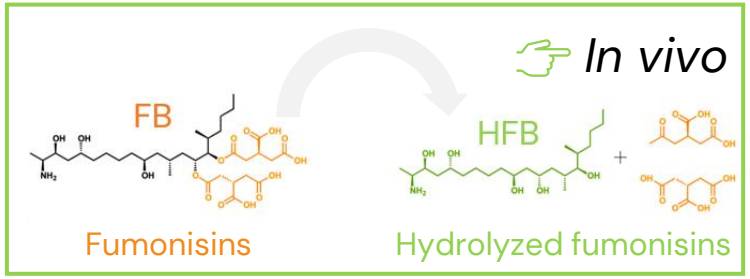


Enzyme engineering

Fermentation

In vitro

In vivo



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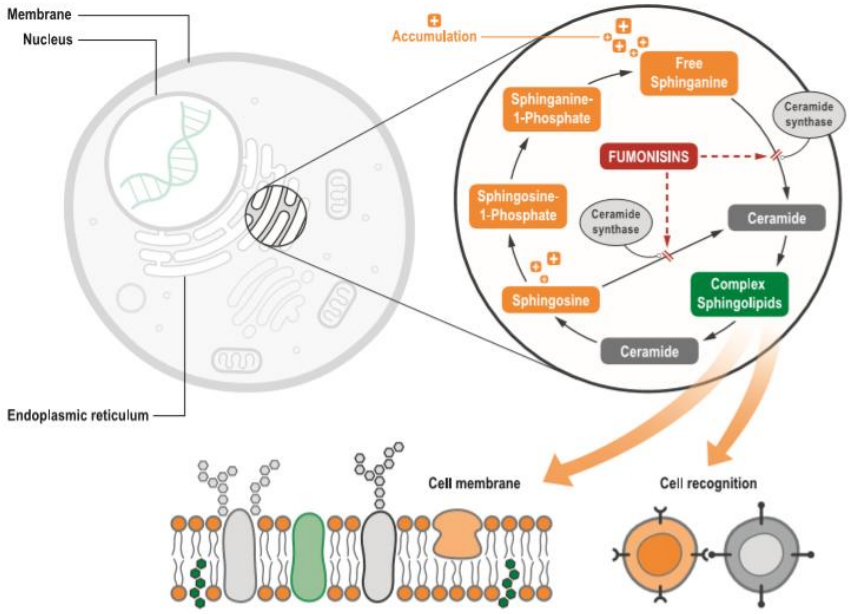
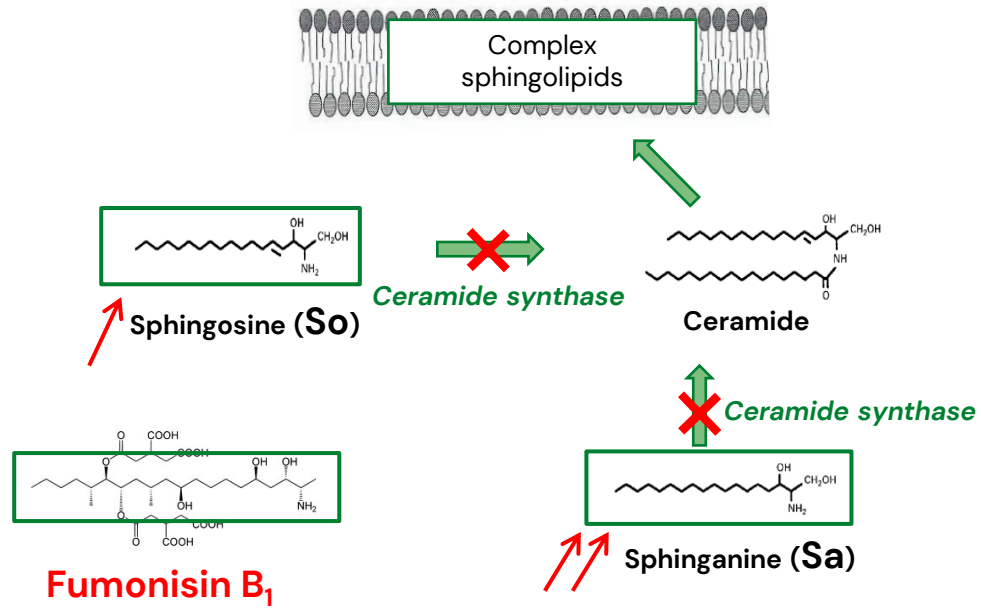
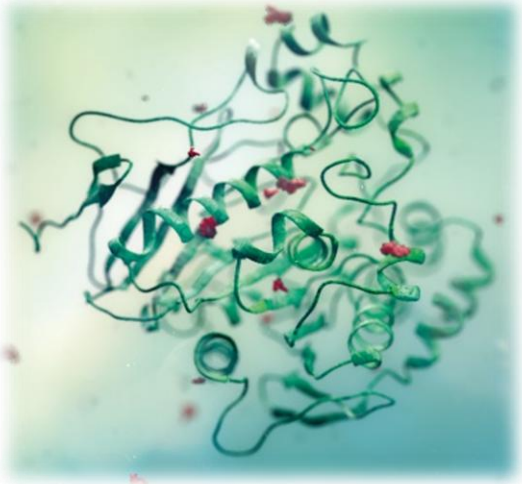
Fumonisins inhibit sphingolipid biosynthesis





Biomarker of effect: Sa/So ↑

FUM*zyme*®



Safety & efficacy evaluated by efsa

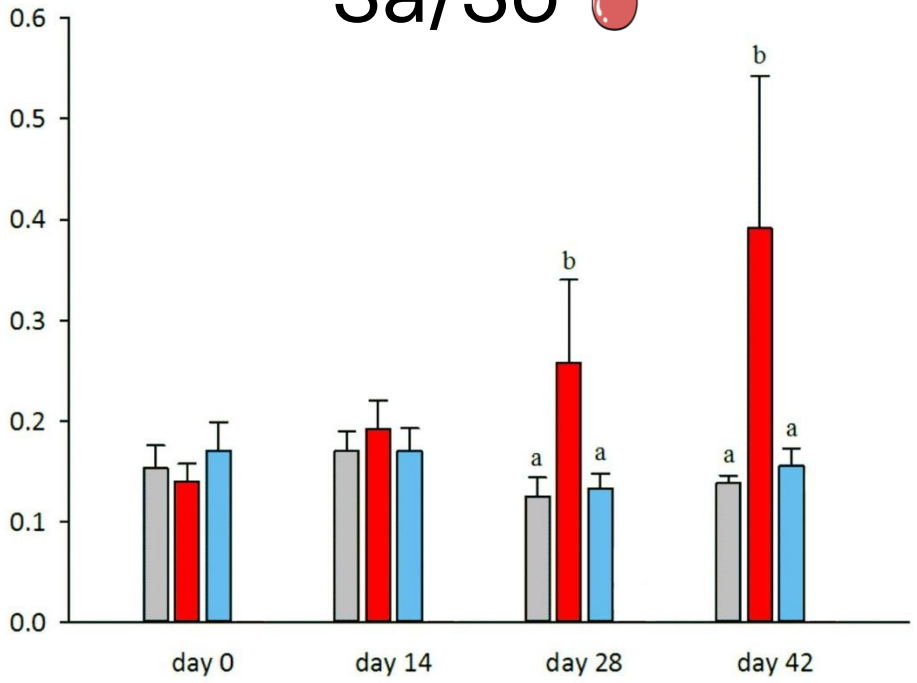
European Food Safety Authority

Piglet study

3 groups
- control
- FB_1
- FB_1 + FUM*zyme*

10 pigs/group
FB_1 2 mg/kg
FUM*zyme* 15 U/kg
Sa/So in serum

Sa/So



Masching et al., 2016. Toxins

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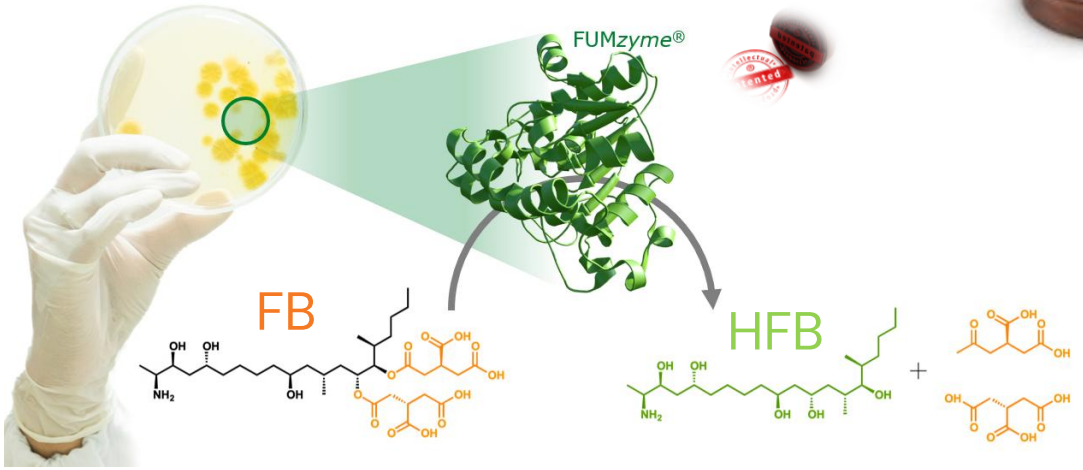
2014 EU registration FUM*zyme*®



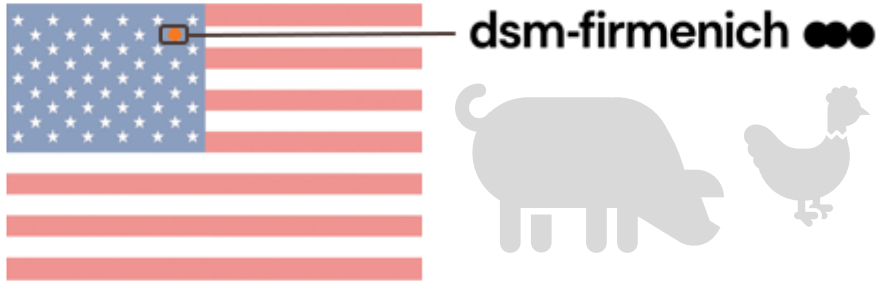
2017

2018 2nd generation

2021 silage application →

2022

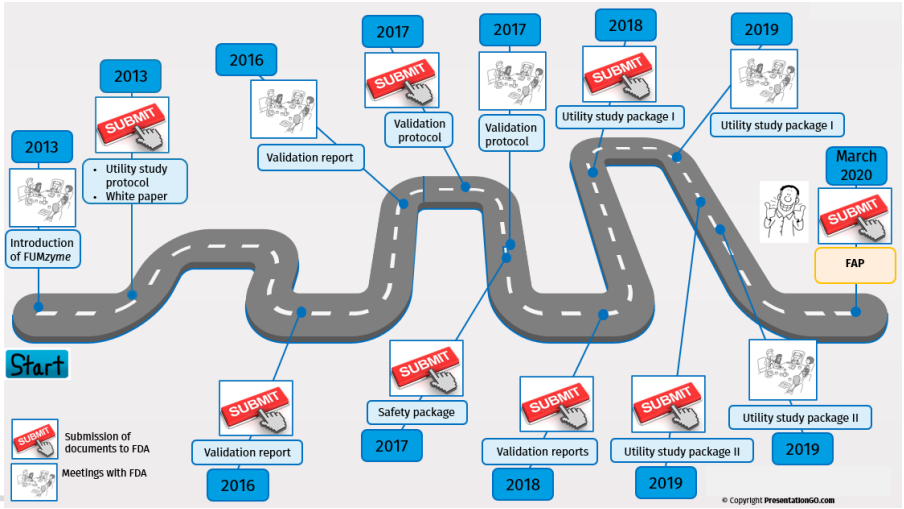
FDA approval FUM*zyme*®



First ever

FDA approved product against mycotoxins

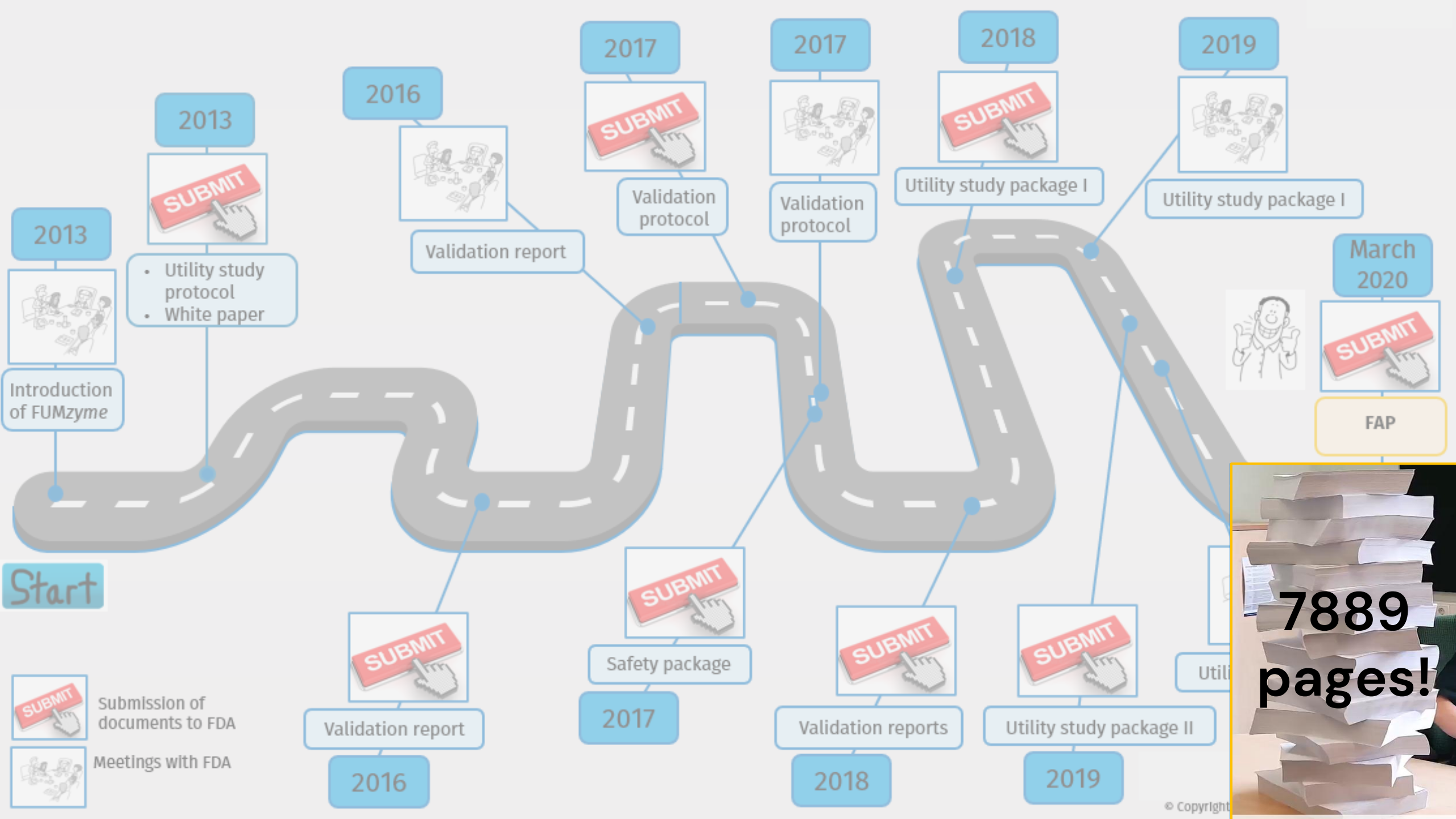
10-year process



No clear guidance

Step by step approach in dialogue with FDA

Long review times!


Start
2013
Introduction of FUMzyme
2013
SUBMIT
• Utility study protocol
• White paper
2016
Validation report
2016
SUBMIT
Validation report
2017
SUBMIT
Safety package
2017
2017
Validation protocol
Validation protocol
2018
SUBMIT
Validation reports
2018
2018
SUBMIT
Utility study package I
2019
SUBMIT
Utility study package II
2019
2019
Utility study package I
March 2020
SUBMIT
FAP
7889 pages!
SUBMIT
Submission of documents to FDA
Meetings with FDA
© Copyright

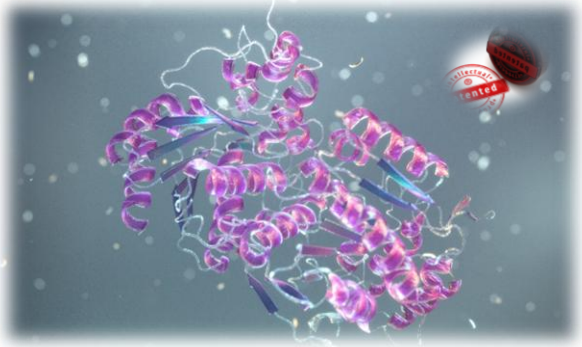
2023 EU dossier submitted for 3rd generation of FUM*zyme*®

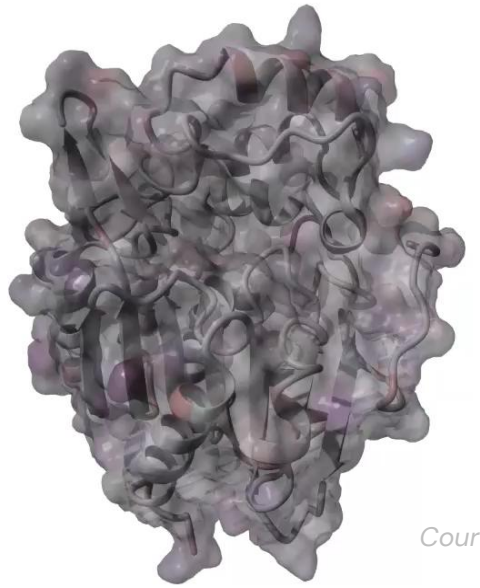
ALL animal species

2025 EU dossier & FAP submission ZEN*zyme*®

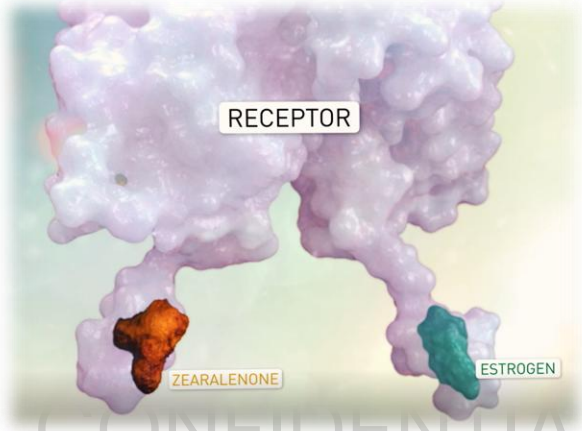
ZENzyme®

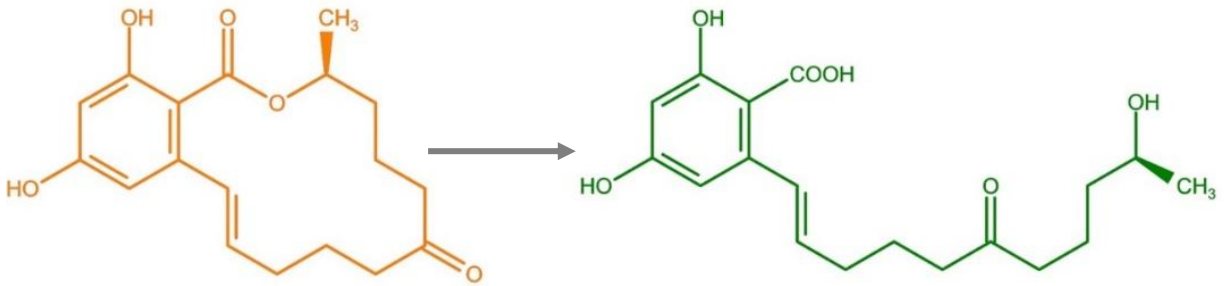
Zearalenone Hydrolase





Courtesy Sebastian Fruhauf & Andreas Höbartner-Gußl

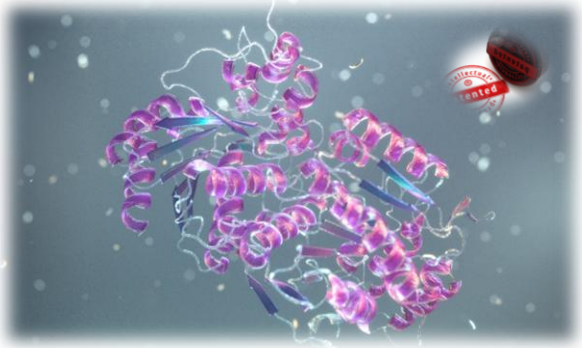




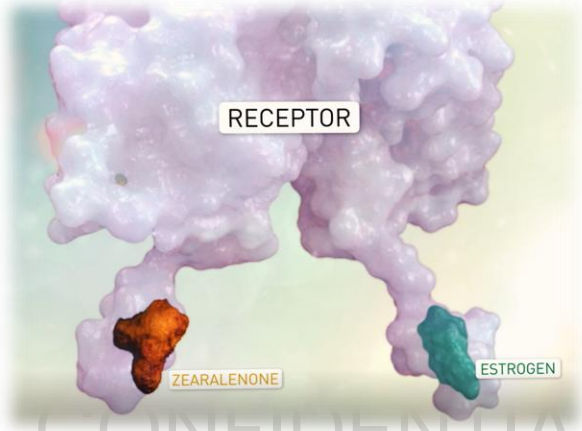
Zearalenone (ZEN) → hydrolyzed ZEN (HZEN)

ZENzyme®

Zearalenone Hydrolase



DSM Austria winner of the greatest award for companies in the field of innovation



Swine — ALL animal species

Work in progress

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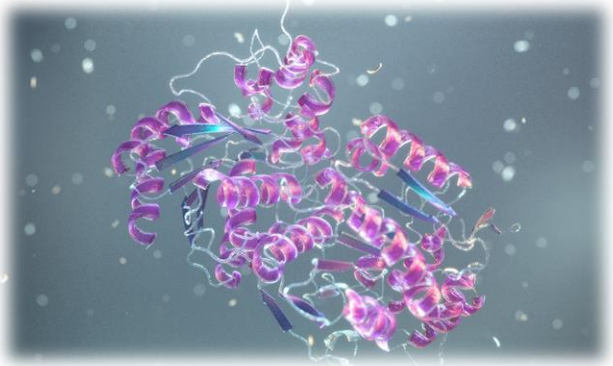
ZENzyme®



Broiler study

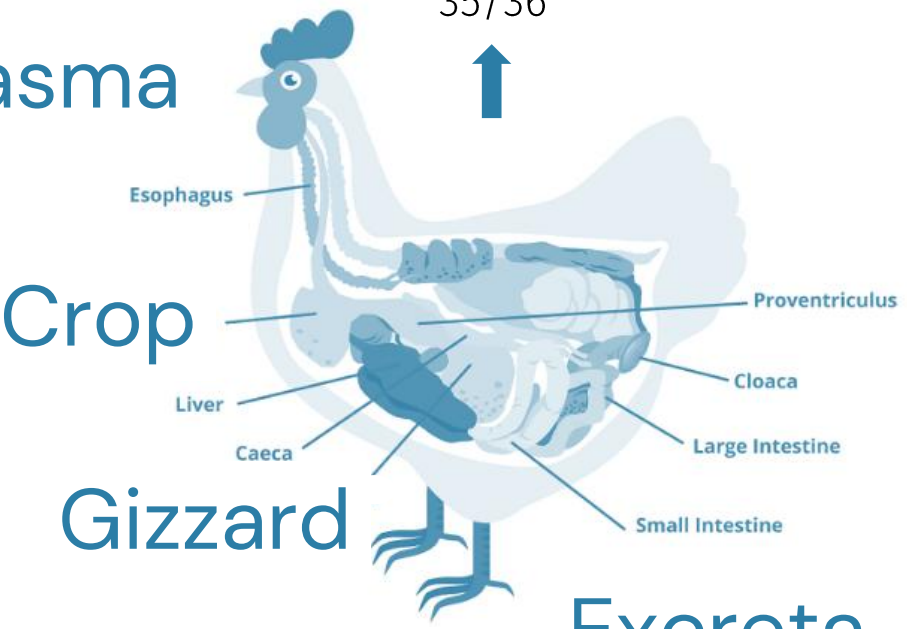
trial period

0 35/36

- Control
- ZEN
- ZEN + ZENzyme

256 animals
10/11 replicates/group
ZEN 1.5 mg/kg
ZENzyme 20 U/kg

Plasma

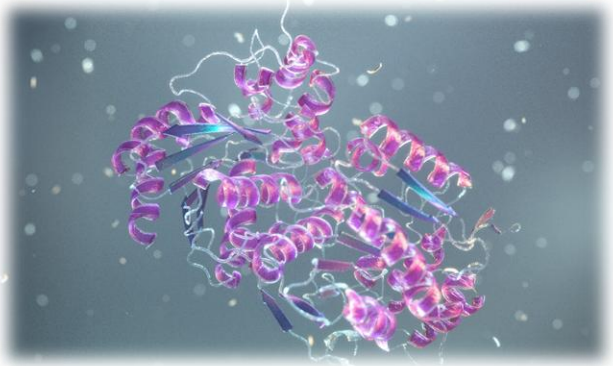


Crop

Gizzard

Excreta

ZENzyme®



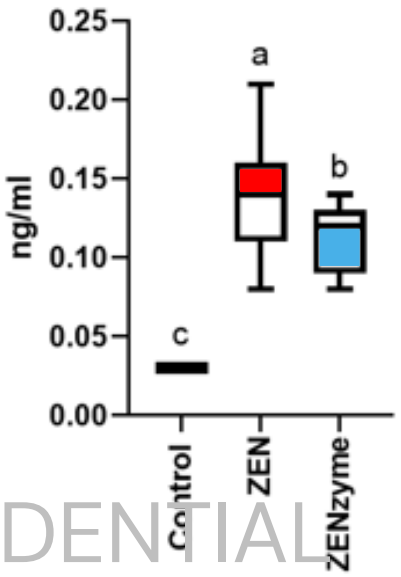
Broiler study

trial period

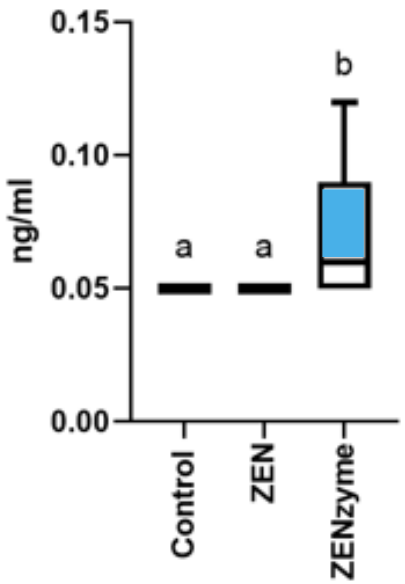
0 35/36

Plasma

ZEN

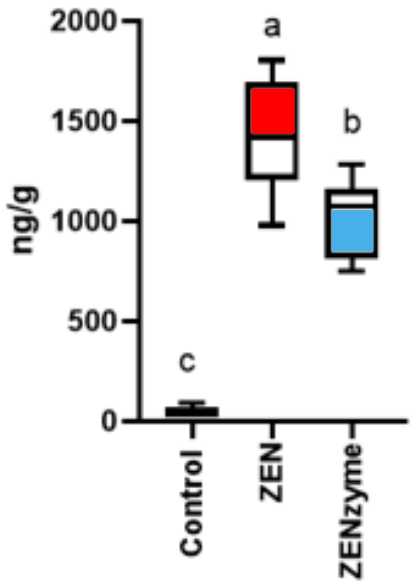


HZEN

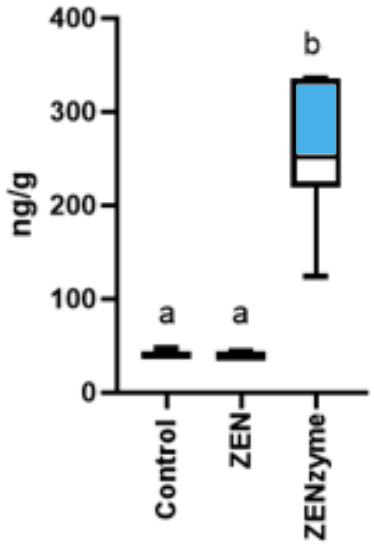


Excreta

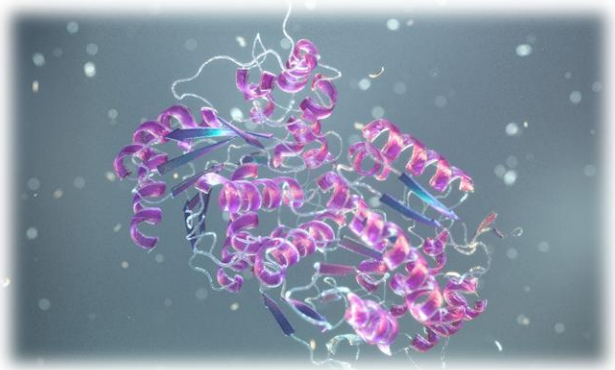
ZEN



HZEN



ZENzyme®



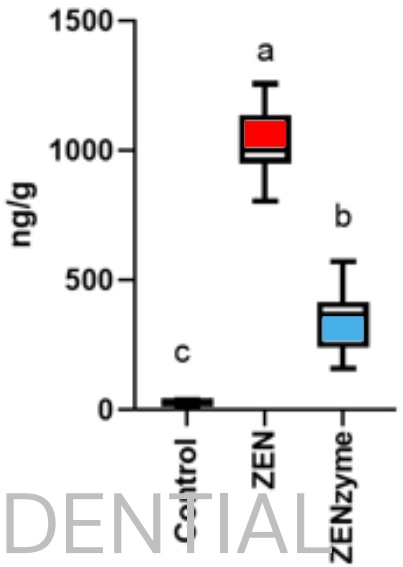
Broiler study

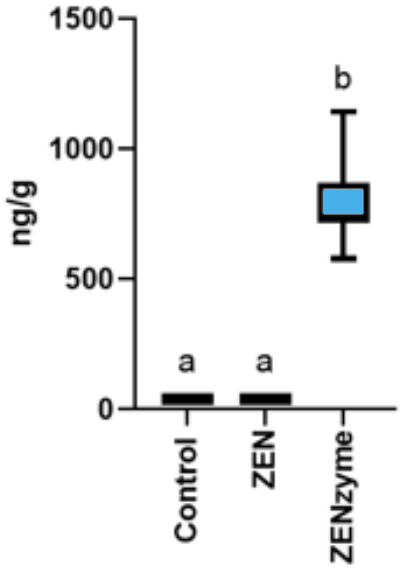
trial period

0 35/36

Crop

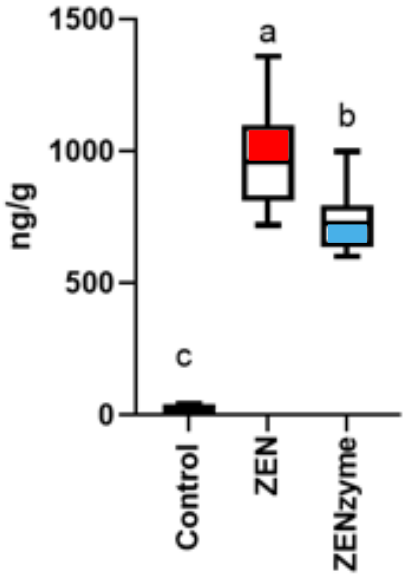
ZEN	HZEN

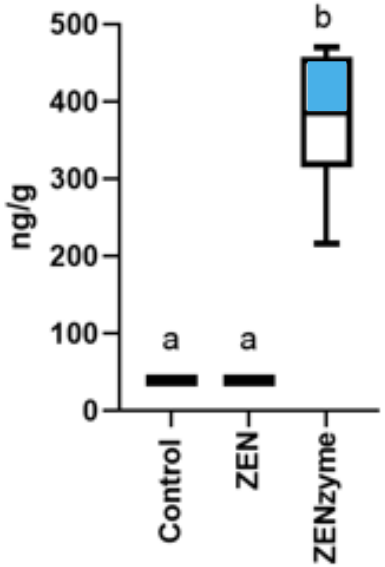




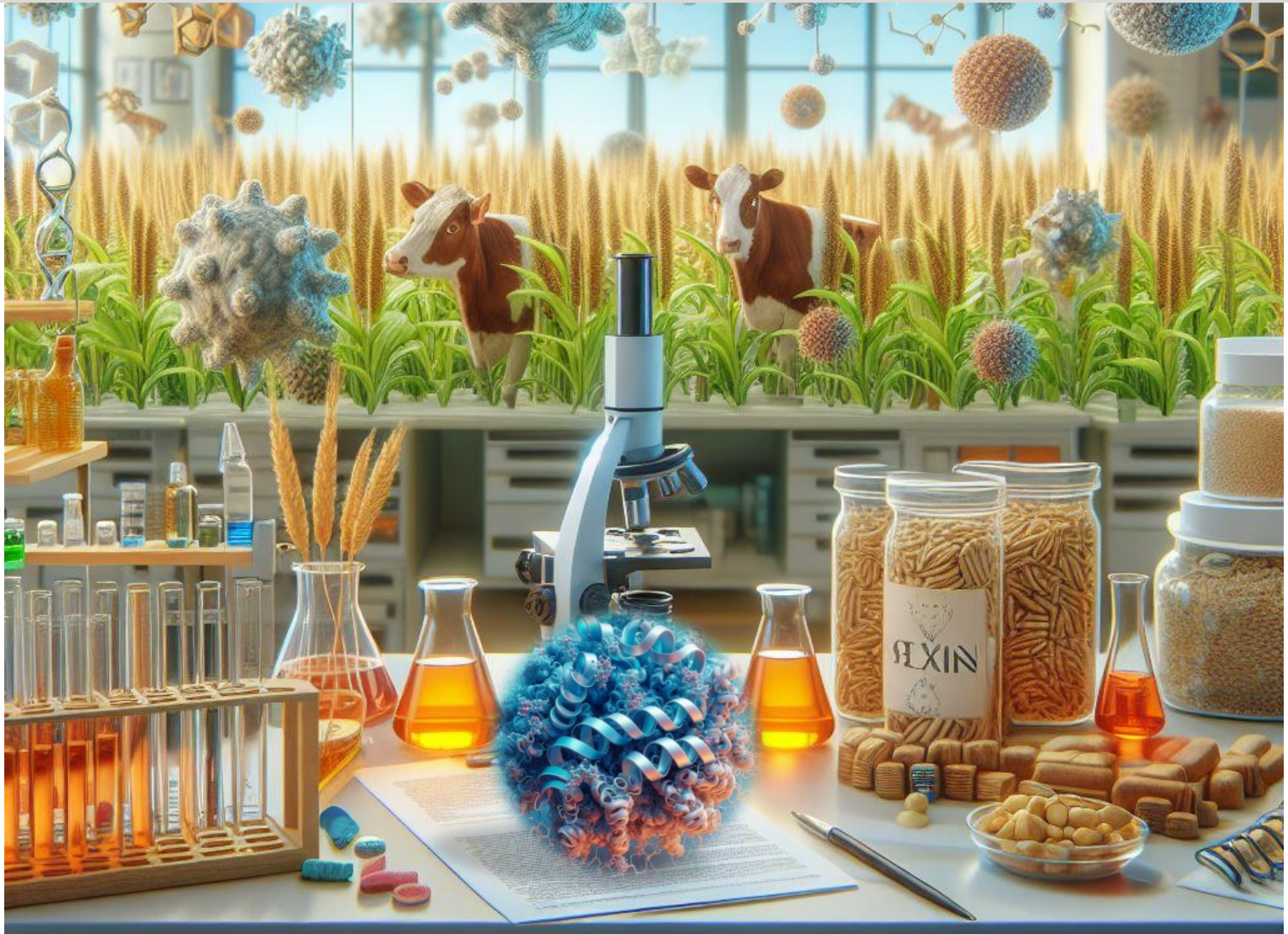
Gizzard

ZEN	HZEN





What’s there to come next?



Journal of Animal Science, 2023, **101**, 1–11
https://doi.org/10.1093/jas/skad171
Advance access publication 23 May 2023
Animal Health and Well Being

Enzymatic degradation of ochratoxin A in the gastrointestinal tract of piglets

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[†]BIOMIN Research Center, DSM Animal Nutrition and Health, Tulln an der Donau, Austria

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Abstract

Animal feeds are often contaminated with ochratoxin A (OTA), a potent natural mycotoxin hazardous to animal and human health that accumulates in blood and tissues. To the best of our knowledge, this study is the first to investigate the in vivo application of an enzyme (OTA amidohydrolase; OAH) that degrades OTA into the nontoxic molecules phenylalanine and ochratoxin α (OTα) in the gastrointestinal tract (GIT) of pigs. Piglets were fed six experimental diets over 14 days, varying in OTA contamination level (50 or 500 µg/kg; OTA50 and OTA500) and presence of OAH; a negative control diet (no OTA added) and a diet containing OTα at 318 µg/kg (OTα318). The absorption of OTA and OTα into the systemic circulation (plasma and dried blood spots, DBS), their accumulation in kidney, liver, and muscle tissues, and excretion through feces and urine were assessed. The efficiency of OTA degradation in the digesta content of the GIT was also estimated. At the end of the trial, accumulation of OTA in blood was significantly higher in OTA groups (OTA50 and OTA500) in comparison to enzyme groups (OAH50 and OAH500, respectively). The supplementation of OAH explicitly reduced the absorption of OTA ($P < 0.005$) into plasma by 54% and 59% (from 40.53 ± 3.53 to 18.66 ± 2.28 ng/mL in piglets fed the 50 µg OTA/kg diets and from 413.50 ± 71.88 to 168.35 ± 41.02 ng/mL in piglets fed the 500 µg OTA/kg diets, respectively) and in DBS by 50% and 53% (from 22.79 ± 2.63 to 10.67 ± 1.93 ng/mL in piglets fed the 50 µg OTA/kg diets and from 232.85 ± 35.16 to 105.71 ± 24.18 ng/mL in piglets fed the 500 µg OTA/kg diets, respectively). The OTA concentrations in plasma were positively associated with the OTA levels detected in all tissues analyzed; adding OAH reduced OTA levels in the kidney, liver, and muscle ($P < 0.005$) by 52%, 67%, and 59%, respectively. The analysis of GIT digesta content showed that OAH supplementation led to OTA degradation in the proximal GIT where natural hydrolysis is inefficient. Overall, the data of present in vivo study demonstrated that supplementation of swine feeds with OAH successfully reduced OTA levels in blood (plasma and DBS) as well as in kidney, liver, and muscle tissues. Therefore, an approach to use enzymes as feed additives might be most promising to mitigate the harmful effects of OTA on the productivity and welfare of pigs and at the same time improving the safety of pig-derived food products.

Lay Summary

Ochratoxin A (OTA) is a potent toxin frequently present in animal feeds, which accumulates in the animal tissues for human consumption. This results in critical animal welfare issues, as well as food safety issues. To the best of our knowledge, the present study is the first to show that OTA can be degraded by an enzyme supplemented with pigs' feed. In the pig gut, this enzyme successfully breaks down the toxic OTA molecule into a nontoxic form that is excreted through urine and feces, which is applicable in supporting the pig's health, welfare, and productivity as well as assuring the safety of the pig meat for human consumption.

Key words: enzymatic hydrolysis, feed additive, mycotoxins, ochratoxin A, OTA amidohydrolase, piglet

Abbreviations: ACN, acetonitrile; CT, control group; DBS, dried blood spots; EC, European Commission; GIT, gastrointestinal tract; GLM, generalized linear models; HPLC, high-performance liquid chromatography; LC, liquid chromatography; ; ; MS, mass spectrometry; MS/MS, tandem mass spectrometry; OAH, OTA amidohydrolase; OTA, ochratoxin A; OTα, ochratoxin alpha

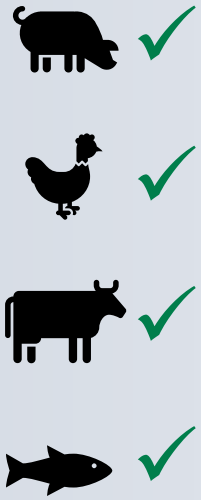
Introduction

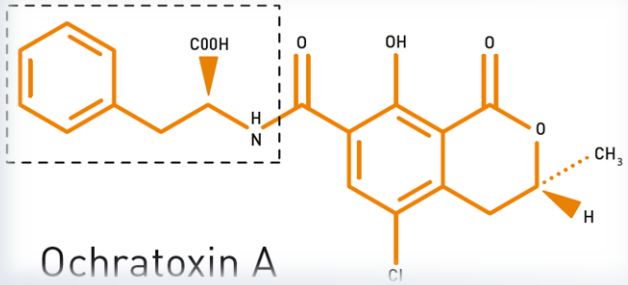
Ochratoxin A (OTA) is a naturally occurring mycotoxin potentially hazardous to animal and human health through feed/food contamination. Comprehensive evidence of the OTA carcinogenic effects in experimental animals has led the International Agency for Research on Cancer to classify this mycotoxin as a possible human carcinogen (group 2B) (IARC, 1993). Although OTA has been associated with the Balkan endemic nephropathy (Castegnaro et al., 2006; Milicevic et al., 2009), its mechanism of action is still unclear. Moreover, there is no direct evidence of OTA being acutely toxic to humans (European Food Safety Authority Panel on Contaminants in the Food Chain et al., 2020). Nevertheless, food safety issues arise due to the frequent presence of OTA in the feed of livestock and the transfer of OTA into meat and other animal-derived products for human consumption (Battacone et al., 2010; Vlachou et al., 2022).

The toxicological profile of OTA has been extensively investigated in various animal species and models. Such studies indicate that OTA is mainly nephrotoxic and hepatotoxic to rodents, poultry, and swine but OTA has also been described as carcinogenic, neurotoxic, and immunosuppressive (Weidenbach and Petzinger, 2004; Ringot et al., 2006; Sava et al., 2006; Pfohl-Leszkowicz and Manderville, 2007; Bernardini et al., 2014; Heussner and Bingle, 2015). The toxicity of OTA has also been reported to affect oocyte maturation and embryo development in mouse, swine, and sheep models

Received March 14, 2023 Accepted May 19, 2023.

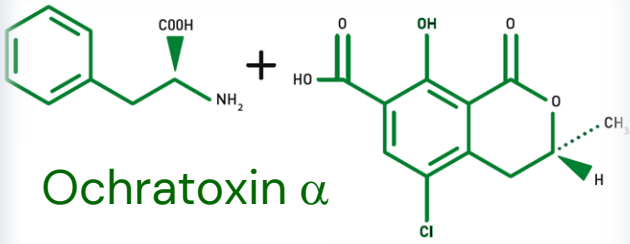
Proof-of-Concept



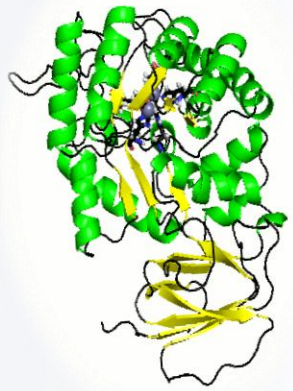


Ochratoxin A

OCHRAzyme®



Ochratoxin α



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Most recent Scientific Publications

OCHRA*zyme*

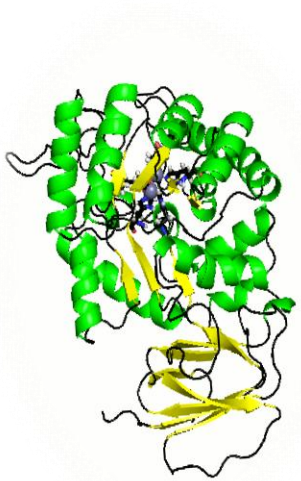
Toxins **2020**, 12(4), 258; https://doi.org/10.3390/toxins12040258
FEMS Microbiology Letters **2023**, Volume 370; https://doi.org/10.1093/femsle/fnad028
Journal of Animal Science **2023**, Volume 101; https://doi.org/10.1093/jas/skad171

ZEN*zyme*

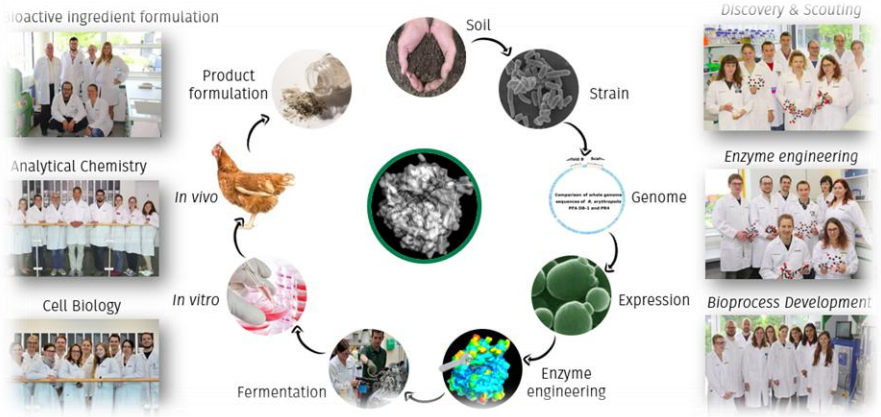
Toxins **2019**, 11(8), 481; https://doi.org/10.3390/toxins11080481
Toxins **2020**, 12(6), 405; https://doi.org/10.3390/toxins12060405
Toxins **2020,** 12(11), 712; https://doi.org/10.3390/toxins12110712
Toxins **2021**, 13(2), 84; https://doi.org/10.3390/toxins13020084
Toxins **2023**, 15(1), 48; https://doi.org/10.3390/toxins15010048
Mycotoxin Research **2023**, Volume 39; https://doi.org/10.1007/s12550-023-00486-2
ACS Catalysis **2024**, Volume 14; https://doi.org/10.1021/acscatal.4c00271

FUM*zyme*

Poultry Science **2017**, Volume 96; https://doi.org/10.3382/ps/pex280
World Mycotoxin Journal **2018**, 11(2), 201; https://doi.org/10.3920/WMJ2017.2265
Toxins **2018**, 10(4), 150; https://doi.org/10.3390/toxins10040150
Toxins **2018**, 10(7), 296; https://doi.org/10.3390/toxins10070296
Toxicology Letters **2019**, Volume 305; https://doi.org/10.1016/j.toxlet.2019.01.013
Toxins **2019**, 11(9), 523; https://doi.org/10.3390/toxins11090523
Toxins **2020,** 12(11), 712; https://doi.org/10.3390/toxins12110712
Food Control **2021**, Volume 123; https://doi.org/10.1016/j.foodcont.2020.107726
Food Research International **2021**, Volume 145; https://doi.org/10.1016/j.foodres.2021.110395
Journal of Agricultural and Food Chemistry **2023**, 71(4); https://doi.org/10.1021/acs.jafc.2c08217
Journal of Agricultural and Food Chemistry **2023**, 71(36); https://doi.org/10.1021/acs.jafc.3c01733
Toxins **2024**, *16*(1), 3; https://doi.org/10.3390/toxins16010003



What makes Mycofix® UNIQUE?

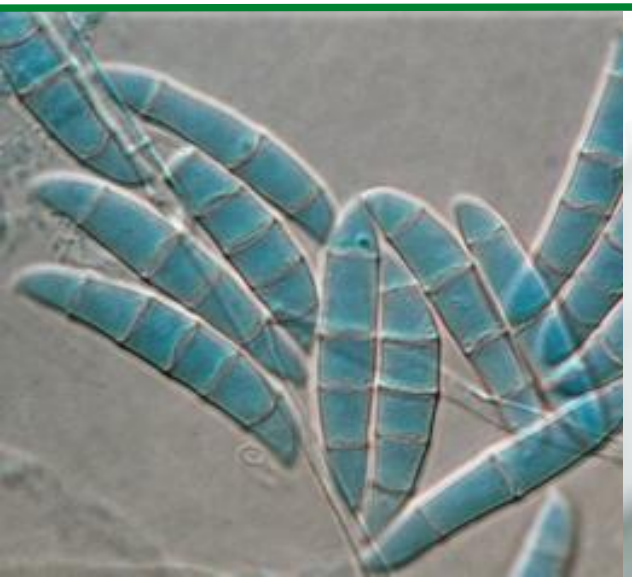


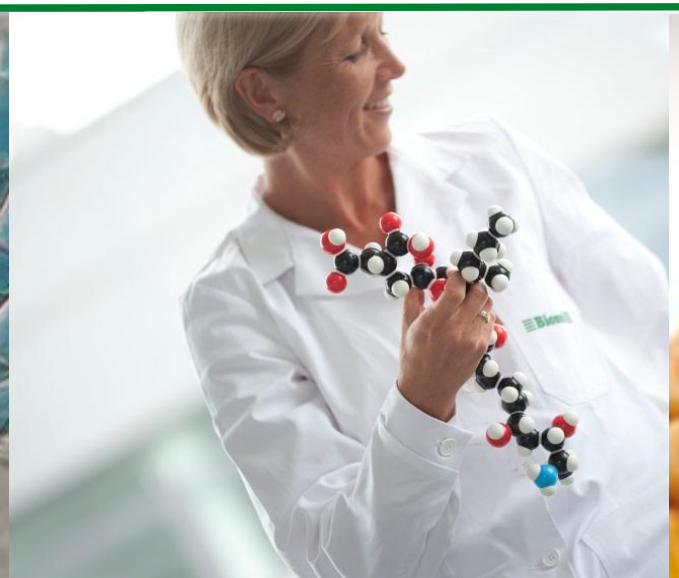
MYCOTOXIN RISK MANAGEMENT

MYCOFIX

THE Leading Expert

ANY Questions





MYCOTOXIN RISK MANAGEMENT

We bring progress to life™

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