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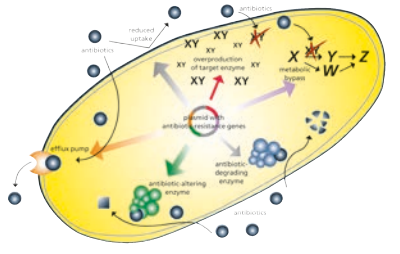
Science & Solutions

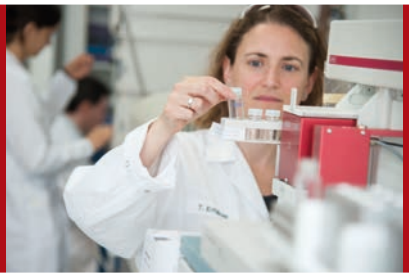
Resisting antibiotics

Reduce bacterial resistance & promote growth



Antibiotic-free in Europe

The European experience in the “post-antibiotics” era



EU registration

What this means in terms of product quality

Editorial

Antimicrobials – What's next?

The earliest use of antimicrobial substances dates back to the ancient Egyptians who used moldy bread as wound disinfectant. With today's standard of human and animal health, life without antimicrobials, like Penicillin, would be unthinkable.

But there is growing public concern over the spread of bacterial resistances and their negative consequences on human health. Several countries have implemented programs with the aim of reducing the overall use of antimicrobials, particularly in food-producing animals, especially the use of antimicrobial growth promoters (AGPs) as well as veterinary drugs. The Netherlands took on a pioneering role in this remark. As a result of strict legal policies, the sales of antibiotics licensed for therapeutic use in animals decreased by 51% (244 vs. 495 tonnes).

The US Food and Drug Administration has also aimed for stricter rules for veterinary drugs and the phasing out of AGPs (FDA Guidances 209 and 213).

Within our industry, it is reasonable to expect that the public and legal pressure to reduce the use of antimicrobials in animal production will increase further. For this reason, Biomin finds itself at the right place at the right time. Since its inception in 1983, Biomin has led the way in providing natural solutions for animal health and nutrition issues, with an emphasis on R&D excellence.

Our solutions are developed to help animals better achieve their genetic potential for performance, with a focus on improving the overall health status. This strategy includes minimizing the impact of challenges caused by mycotoxins, pathogens, dysbiosis and suboptimal nutrient digestibility.

More on this topic in this issue of **Science & Solutions** that focuses on swine production, the natural way.

Christine Hünger

Christine HUNGER PhD
Product Manager

Contents

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Addressing antibiotic resistance in swine

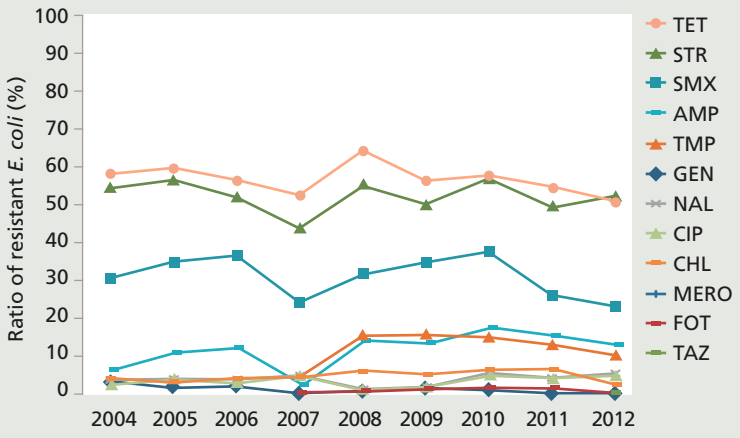
Reducing antibiotic resistant bacteria in swine farms positively influences swine production and helps address problems of antibiotic resistance and residues in meat. Reduced resistance to pathogenic *E.coli* contributes to successful antibiotic treatment during disease outbreaks.

Worldwide, antibiotics are used in animal production at therapeutic levels for the treatment of infections and for growth promotion or prophylaxis. The disadvantage of antibiotics is the emergence and spread of resistant bacteria. Resistant bacteria have become a major concern for both animal health and the public as human medicine is running out of antibiotics that are still effective in treating certain infections.

Antibiotic use in animal production has been identified as a risk factor in the development of antibiotic resistant bacteria that can be transferred to humans via several routes. These include the consumption of animal products, exposure to resistant microorganisms from contact with animals, and the contamination of ground and surface waters by wastes containing antimicrobials and resistant microorganisms.

Exposure to antibiotics not only increases the level of antibiotic resistance among bacteria belonging to the normal intestinal flora of animals but also among pathogenic bacteria. Where high levels of resistant pathogenic bacteria are present, antibiotic treatments may no longer be effective against pathogens.

Figure 1. Microbiological resistance of *E. coli* to different antibiotics in Austria



TET—tetracycline; STR—streptomycine, SMX—sulfamethoxazol; AMP—ampicilline; TMP—trimethoprim; GEN—gentamicin; NAL—nalidixic acid; CIP—ciprofloxacin; CHL—chloramphenicol; MERO—meropenem; FOT—cefotaxim; TAZ—cefrazidim

Source: AURES, 2012

E. coli resistance in swine

Surveillance and monitoring studies on antimicrobial resistance provide information about the occurrence of resistances in pigs in different parts of the world. *E. coli* resistance in swine was described in the Austrian Resistance Report AURES, a yearly report published since 2004 on the levels of resistance in humans and the veterinary sector.

To date, a total of about 160 digesta samples from the large intestine of swine from 30 farms in Austria have

Nataliya Roth
Product manager, Acidifiers

Photo: Sebastian Kaulitzki

Results

Improvements in body weight and weight gain were seen in the group that received diets supplemented with Biotronic® Top3 (*Table 1*). Body weight at day 42 was 3% higher in the trial group compared to the control group. Average weight gain in the Biotronic® Top3 group was 4% higher than the control group.

Table 1. Performance characteristics of piglets.

Period	Body weight, kg		Weight gain, kg		Feed intake, g		FCR	
	Control	Biotronic®	Control	Biotronic®	Control	Biotronic®	Control	Biotronic®
Day 14 /Period 1-14	19.25	19.46	6.97	7.20	725	761	1.58	1.58
Day 28/ Period 1-28	29.10	29.27	16.83	17.00	974	1014	1.62	1.67
Day 42/ Period 1-42	37.71	38.75	25.45	26.48	1110	1161	1.83	1.84

Analysis of samples on day 14 showed no difference in the total *E. coli* count between groups but lower counts of resistant *E. coli* in the group fed Biotronic® Top3 (*Table 2*). Microbiological analysis at the end of the trial (day 42) showed that total *E. coli* counts in the fecal samples of the group fed Biotronic® Top3 was about 90% lower than the control group (*Table 3*).

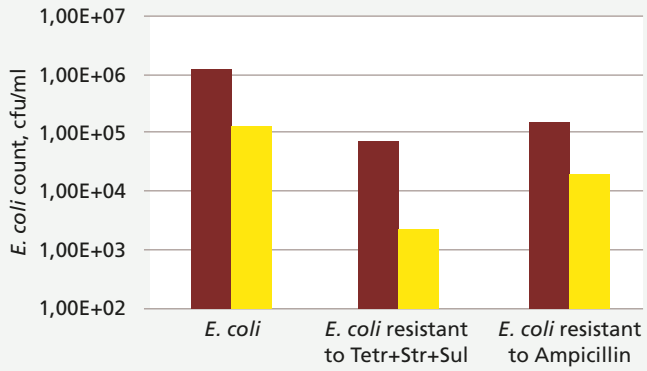
Table 2. *E. coli* in fecal samples on day 14, cfu/ml.

	Control			Biotronic®			Average	
	Sample 1	Sample 2	Sample 3	Sample 1	Sample 2	Sample 3	Control	Biotronic®
E.coli	1.14E+07	5.50E+04	2.08E+07	5.91E+05	3.62E+06	2.90E+07	1.08E+07	1.11E+07
E.coli resistant to Tetr+Str+Sul	7.64E+06	4.00E+03	4.06E+06	6.55E+05	7.66E+04	3.55E+05	3.90E+06	3.62E+05
E.coli resistant to Ampicillin	7.20E+05	9.00E+03	8.56E+05	0.00E+00	1.98E+05	4.42E+05	5.28E+05	2.13E+05

Table 3. *E. coli* in fecal samples on day 42, cfu/ml.

	Control			Biotronic®			Average	
	Sample 1	Sample 2	Sample 3	Sample 1	Sample 2	Sample 3	Control	Biotronic®
E.coli	2.20E+05	1.73E+06	1.59E+06	1.33E+05	1.13E+05	1.50E+05	1.18E+06	1.32E+05
E.coli resistant to Tetr+Str+Sul	9.41E+03	6.62E+03	2.01E+05	4.29E+02	1.82E+03	4.39E+03	7.23E+04	2.21E+03
E.coli resistant to Ampicillin	5.17E+04	6.62E+03	3.71E+05	4.18E+04	4.68E+03	1.15E+04	1.43E+05	1.93E+04

Figure 2. Average counts of *E. coli* in fecal samples of pigs.



The count of *E. coli* resistant to ampicillin in the trial group was 60% below the control group. The count of *E. coli* with multi-resistance to Tre+Str+Sul in the trial group was nearly 90% below the control group. *Figure 2* shows the average *E. coli* and resistant *E. coli* counts in the fecal samples of pigs at the end of the trial.

Average control
Average OCP

Source: Biomin, 2013

Nataliya Roth
Product manager, Acidifiers

The lower the counts of resistant bacteria in the intestinal flora, the lower the possibility that genes encoding resistance will be transferred to other bacteria, including pathogenic bacteria.

been analyzed for *E. coli*. Tests for antimicrobial susceptibility to different antibiotics were conducted. The microbiological resistance of *E. coli* using epidemiological cut-off values is shown in *Figure 1*. Epidemiological cut-off values are determined on the basis of the distribution of minimal inhibitory concentration for an antibiotic and a bacterial species. The cut-off values for different antibiotics are presented by the European Committee on Antimicrobial Susceptibility Testing (EUCAST).

Determining resistance

The ratio of resistant *E. coli* was determined as follows: [counts of resistant *E. coli* per year/ counts of tested *E. coli* per year] x 100. Ratios of *E. coli* resistant to tetracycline, streptomycine, sulfamethoxazol and ampicillin were between 15% and 50% in 2012. These percentages were higher than the ratio of *E. coli* resistant to other tested antibiotics.

For this reason, *E. coli* resistance to tetracycline, streptomycine, sulfamethoxazol and ampicillin were determined in the following swine trial. Multi-resistance includes resistances to tetracycline, streptomycine and sulfamethoxazol (Tet+Str+Sul).

Swine trial

A trial with weaned pigs showed that it was possible to minimize the incidence of resistant bacteria and reduce the number of multi-resistant bacteria in the gastrointestinal tract of swine with the help of a combined feed additive. This feed additive consisted of organic acids, cinnamaldehyde and a permeabilizer (OCP) in the form of a commercial product, Biotronic® Top3 (Biomin).

The trial was carried out at the Biomin Center of Applied Animal Nutrition in Mank, Austria, using 60 pigs [(Landrace x Large White) x Pietrain]. Pigs, two weeks after weaning (body weight 12.27 kg; 40 days) were assigned to two treatments. The negative control group diet contained no growth-promoting feed additives, whereas the diet of the trial group was supplemented with Biotronic® Top3 at the inclusion rate of 1.0 kg/t feed. No antibiotics were added to the feed.

The duration of the trial was 42 days. Body weight and feed intake were recorded, and feed conversion ratio was calculated. Fecal samples of 16 pigs per pen were collected and immediately frozen on day 14 and 42. The counts of *E. coli* as well as *E. coli* resistant to ampicillin and multi-resistant to Tetr+Str+Sul were determined in all fecal samples. The results of the trial are shown on page 3.

Fighting bacterial resistance

By reducing antibiotic resistant bacteria, natural feed additives provide a possible solution to the global problem of antibiotic resistance, as the swine trial shows. Moreover, the reduction in opportunistic pathogens and antibiotic resistant bacteria minimizes the risk of infections among animals and positively influences swine production.

The lower the counts of resistant bacteria in the intestinal flora, the lower the possibility that genes encoding resistance will be transferred to other bacteria including pathogenic bacteria. This will also reduce the dissemination of resistant bacteria in the farm environment. Reducing the resistance of pathogenic *E. coli* to antibiotics contributes to the successful treatment of animals during a disease outbreak.

E. coli – an indicator for resistance

It is necessary to reduce the use of antimicrobial drugs to control antibiotic resistance. Another way is to reduce the levels of resistant bacteria in the gastrointestinal tract of animal.
This lowers the load of resistant bacterial in the environment, which consequently reduces the transmission of resistance genes. Lowering antibiotic resistance is especially important for those bacterial species common in humans and animals.
For example, the bacteria *E. coli* found in food is ingested by humans every day. As antibiotic resistant strains of *E. coli* are ubiquitous in both human and animal isolates, *E. coli* is used as an indicator for resistance problems in both animals and humans.

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Antibiotic-free
The European experience

The EU has firmly established itself in a "post-antibiotic" era where antibiotics are administered only therapeutically. The process of banning antibiotics in the EU took place in stages over 30 years, before the complete ban in 2006.

The number of large animal-feeding operations in swine, poultry, and cattle has been increasing across Europe. With the growth in farm size come disease challenges that impact animal health and production.

As antibiotics enable animals to grow faster and gain weight more efficiently, their use in growth promotion became a common practice in animal husbandry. Different studies have shown the effects in the past of these antimicrobials on different species (*Table 1*). In the US, approximately 80 percent of total antibiotic usage is in food producing animals. The use of certain antibiotics as growth promoters is regulated regionally and/or by country.

Table 1. Effects of in-feed antimicrobial additives in various species (n=12,153).

Species	Weight gain (%)	FCR (%)
Broiler	+3.6	-3.4
Layer	+2.8	-2.7
Turkeys	+3.1	-2.2
Pigs	+8.1	-4.8
Fattening pigs	+3.2	-2.0
Piglets	+15.7	-8.6

Source: Rosen, 1995

Antibiotics in livestock

Antibiotics in livestock production can be used in two ways—therapeutically and sub-therapeutically. Therapeutic usage

The ban

Beginning in 1972, countries in the EU began their ban on different antimicrobials locally. This sequential ban ended in 2006 with the complete ban on AGPs in the EU.

1972
European countries ban the use of Tetracycline, Penicillin and Streptomycin as AGPs

1986
Sweden bans the use of AGPs

1996/97
Germany and subsequently, the EU ban the use of Avoparcin

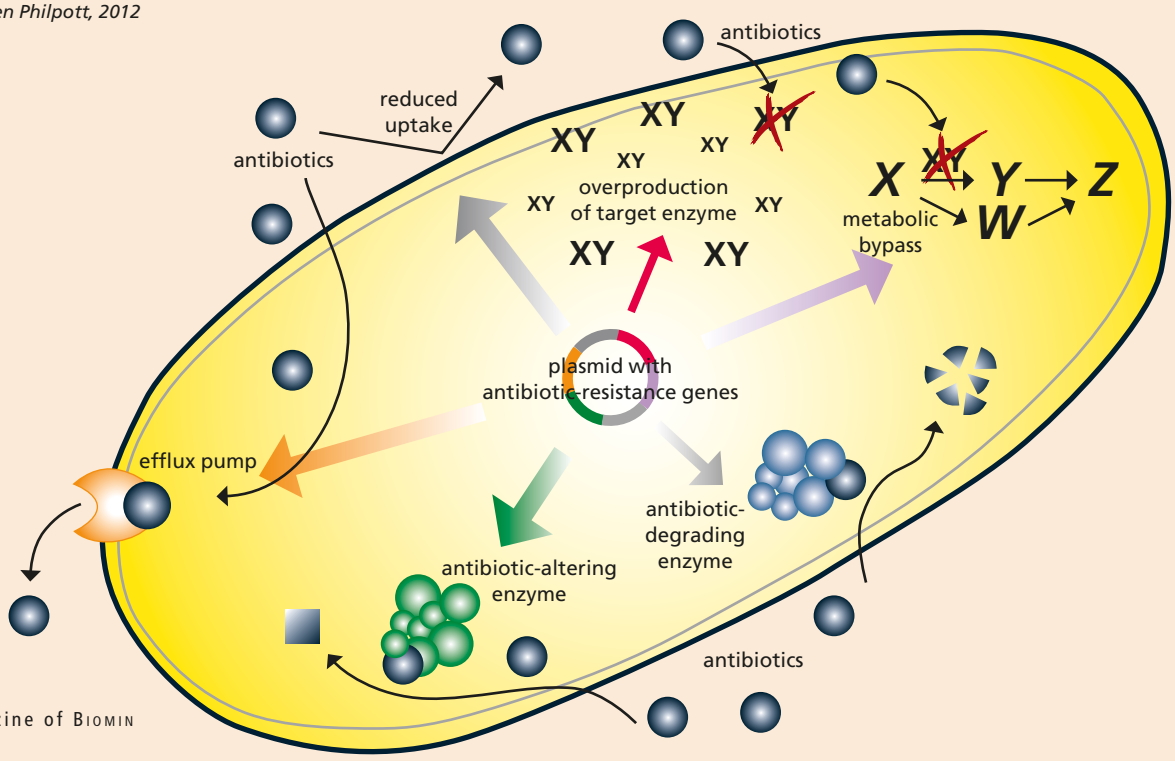
1998
Denmark bans the use of virginiamycin and sub-therapeutic use of AGPs

1999
The EU bans olaquindox and carbadox; suspends authorization of bacitracin, tylosin, spiramycin and virginiamycin

2006
The EU bans all AGPs

Source: Cogliani et al., 2011

Figure 1. Mechanisms of antibiotic resistance and their effects at the cellular level.
Source: Jen Philpott, 2012



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"It is not the strongest or the most intelligent who will survive but those who can best manage change."

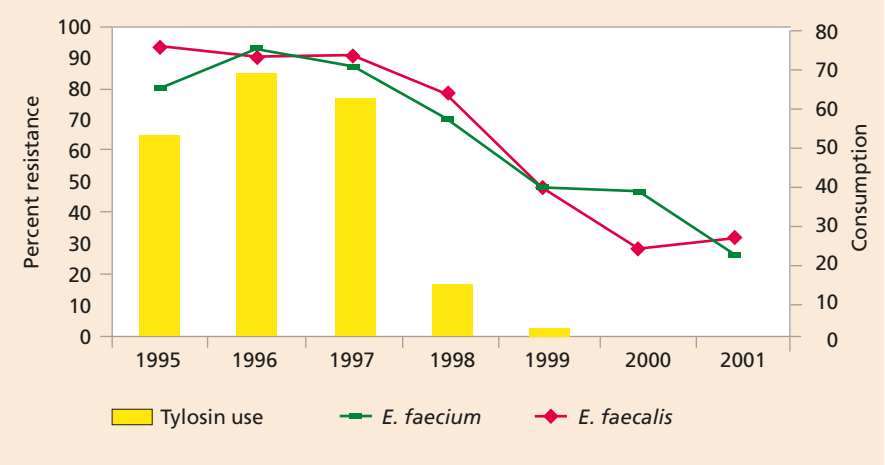
Charles Darwin

Photo: Sergii Figurnyi - Fotolia.com

involves a higher dosage over a shorter period in order to treat a specific disease. Sub-therapeutic usage requires a lower dosage over a longer period to prevent diseases, limit subclinical infections and improve growth rates. Until bacteria become antibiotic resistant, the use of antibiotics would limit subclinical diseases and improve performance.

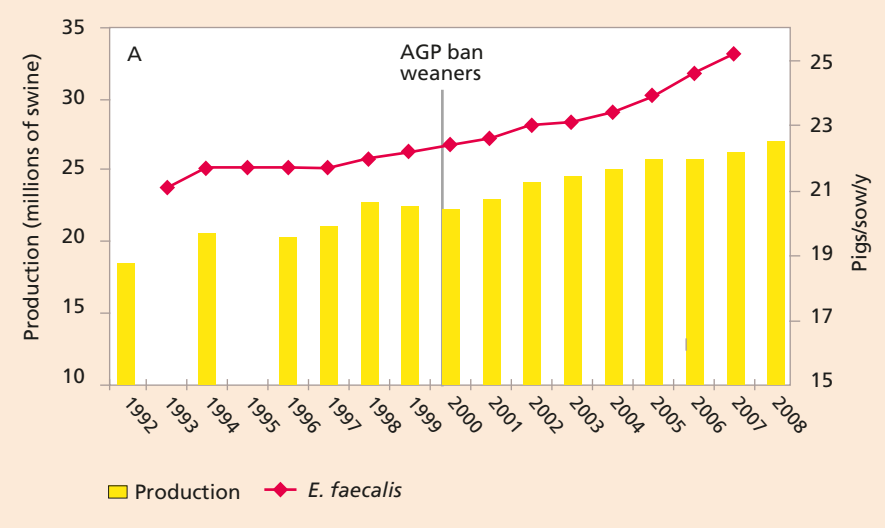
However, with antibiotic resistance, the farmer is faced with no other option but to increase the use of pharmaceuticals. Increased mortality, decreased body weight gain, and worsened feed conversion are further outcomes that would trigger an increase in production costs. In addition, bacterial resistance in animals may affect human disease control. The World Health Organization observed resistance among *Enterococcus faecalis* and *Enterococcus faecium* isolated from pigs at slaughter after long-term tylosin use for growth promotion (*Figure 2*).

Figure 2. Tylosin use for growth promotion and erythromycin resistance among *Enterococcus faecalis* and *Enterococcus faecium* isolated from pigs at slaughter from 1995 to 2001 in Denmark.



Source: World Health Organization, 2002

Figure 3. Swine production trend in Denmark after the AGP ban.



Source: Aarestrup et al., *2010*

Early responses

Resistance genes disseminated via the food chain, both from meat consumed and through the dispersion of antibiotics into soil and water, and can make their way into the digestive tract of humans. Therefore in 1986, Sweden became the first country in Europe to address the problem of antibiotic resistance and regulate the use of antibiotics in food-producing animals. Consequently, Swedish sales of in-feed antibiotics were reduced to one third, from 45 tonnes in 1986 to 15 tonnes by 2009.

Soon after, the Swedish agriculture ministry reported significant clinical problems emerging in piglets after the withdrawal of antibiotic growth promoters (AGPs). Post-weaning mortality increased by 1.5 percent and chickens took 5-6 days longer to reach 2.5 kg.

Despite these drastic consequences, other countries like Denmark, the United Kingdom, and the Netherlands soon followed the Swedish example. In Denmark, the use of AGPs fell from over 105 tonnes in 1996 to nil by 2000.

The European regulation also started to follow the Swedish and Danish examples. In 1997, the EU banned the use of avoparcin and remaining AGPs on the basis of the "'precautionary principle". In 1999, the EU put a ban on olaquindox and carbadox and suspended authorization of bacitracin, tylosin, spriamycin, and virginiamycin. From 2006, the EU enforced a complete ban on all AGPs.

The Danish experience

Globally, there are only limited studies that take into consideration antibiotic usage and their effect on the productivity of animals. Aarestrup *et al.* (2010) prepared a detailed study on the changes in anti-

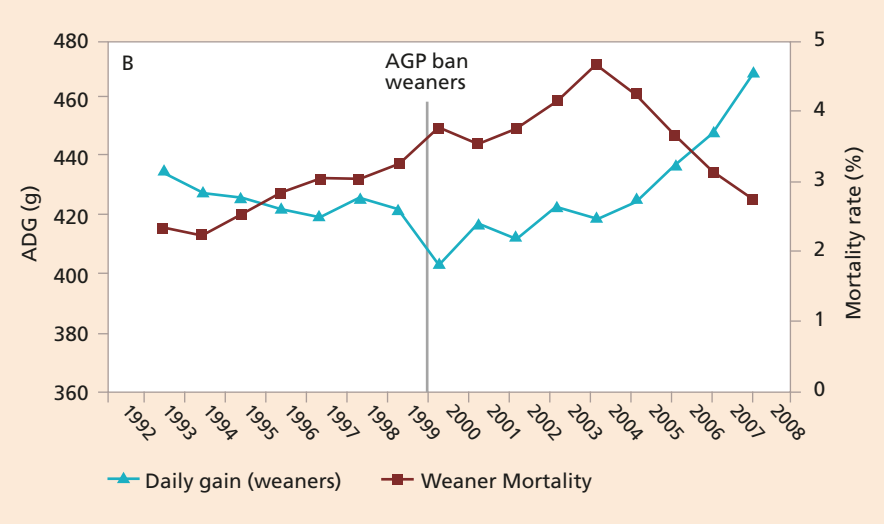
microbial consumption and productivity of Danish swine between 1992 and 2008.

According to their study, Danish pig production increased from 18.4 to 27.1 million head between 1992 and 2008. The average number of finishing pigs per sow per year also rose from 21.5 to 25 within 16 years (*Figure 3*). In 2008, the average consumption of antimicrobials was 49 mg/kg per hog, from 100 mg/kg in 1996. This decline was mainly due to the ban on the sub-therapeutic use of AGPs.

The average daily gain (ADG) of weaners (<35 kg) decreased from 1992 until shortly after the ban in 2000, and increased thereafter. In 2008, ADG was about 8% higher than before the AGP ban in 1992 (*Figure 4*). Average mortality of weaning pigs increased slightly from 1992 until 2004 when it reached its peak at almost 5% before falling back to 2.5% in 2008 which is close to the 1992 level. The mortalities were most probably influenced by porcine reproductive and respiratory syndrome (PRRS) and post-weaning multisystemic wasting syndrome (PMWS) which occurred in 1996 and 2001, respectively.

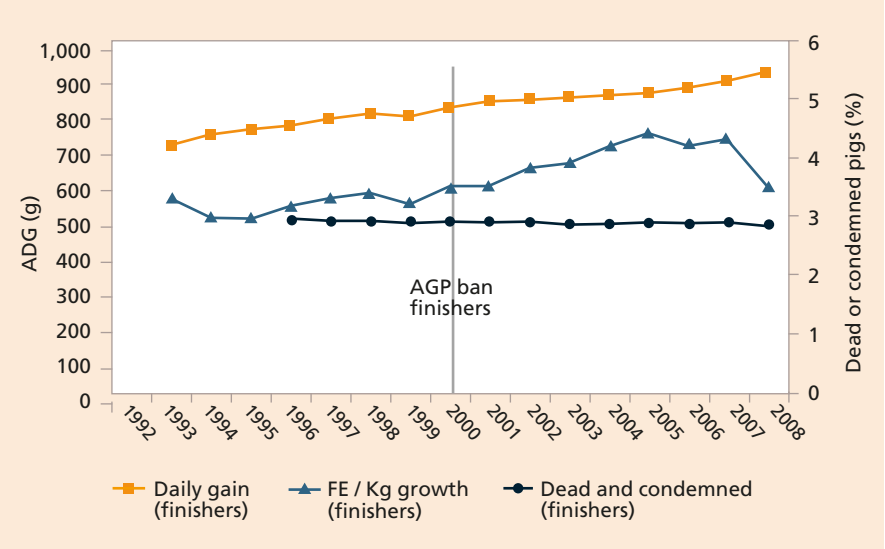
The ADG for finishing pigs (>35 kg) was higher (around +25%) in 2008 than in 1992, but mortality rates for weaning and finishing pigs were similar in both years (*Figure 5*). AGP consumption per kilogram of pig produced in Denmark fell by more than 50% between 1992 and 2008. With productivity showing improvements, the ban on AGPs is not seen to negatively impact swine production in the long term.

Figure 4. Danish productivity trends in weaners after the AGP ban.



Source: Aarestrup et al., *2010*

Figure 5. Danish productivity trends in finishers after the AGP ban.



Source: Aarestrup et al., *2010*

Life after AGPs

The Danish experience shows that there is life after AGPs but several measures have to be implemented. These include management, biosecurity, a well-balanced diet to reduce stress factors and mycotoxin risk management.

Over the last ten years, the ban on AGPs led to the need for a change in feed formulations. Today, there is greater knowledge on the use of additives in the different feed formulations. Alternatives to antibiotics, such as the use of phytogenics in combination with pro-, prebiotics and acidifiers have become better accepted.

Trials conducted with the Biomin phytogenic line Digestarom® showed that performance gains were comparable to gains achieved by AGPs but without any danger of antimicrobial resistance developing. Continual investments in research on non-antibiotic growth promoters can help overcome new challenges in animal production, and allow the industry to adapt to changing trends.

References are available on request.

Did you know...

...that growth performance from phytogenics equally rivals, if not surpasses that of antibiotics?

Read the story of phytogenics and piglet performance in this link!

Christina Schwab PhD
Product manager
Mycotoxin Risk Management

EU Regist

A worldwide

The EU registration for mycotoxin deactivation mycotoxin claims. It is also a detailed evalua- safety of a product. To date, Biomin® BBSH 797 the only products to have undergone the com- a final authorization. Why does this make a

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[1], Biomin submitted the first dossier.

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

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.

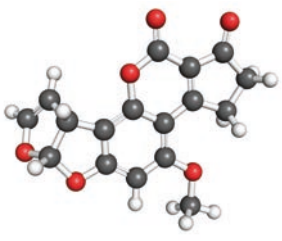
Bacteria and bentonite

The final authorization of Mycofix® Secure and Biomin® BBSH 797 is issued by the EU as non-holder specific authorization[2]. '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*).

It is different in the case of bentonite: The EU regulation[3] 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[2]. The claim "aflatoxin-binding" is allowed only for products that fulfill the main criteria[3].

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.

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.

[1] Regulation (EC) No 386/2009
[2] Regulation (EC) No 1016/2013
[3] Regulation (EC) No 1060/2013
[4] Main criteria in Regulation (EC) No 1060/2013:
smectite (dioctahedral montmorillonite) content ≥70% and aflatoxin B_1 binding capacity above 90% in a buffer solution at pH 5.0, with 4mg/l aflatoxin B_1 and 0.02% feed additive.

ration

quality benchmark

products is not only the legal basis for official
tion with high standards for the efficacy and
and the specific bentonite Mycofix® Secure are
plete registration procedure and succeeded in
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 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?

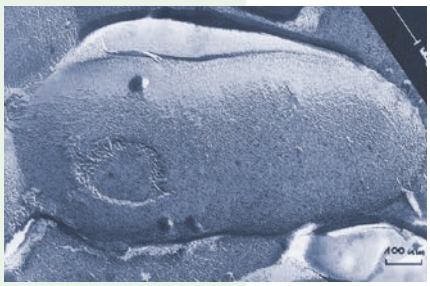
According to EFSA "In general, mycotoxin/metabolites excretion in feces/urine, concentration in blood/plasma/serum, tissues or products (milk or eggs) or other relevant biomarkers should be taken as end-points for demonstration of efficacy of substances for reduction of the contamination of feed by mycotoxins."[5]

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 M_1 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 vitro* 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.



Strain of Biomin® BBSH 797 under microscope
Source: Biomin

- 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.*

[5]EFSA Journal 2012;10(1):2528

Biotronic® Top3

the breakthrough in pathogen control

The **Biomin® Permeabilizing Complex** in Biotronic® Top3 damages the outer membrane of Gram-negative bacteria thus boosting the synergistic effect of its components, the organic acids and the phytochemical.

- Increase weight gain
- Improve feed conversion
- Maximize economic benefit

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