Decoding the connection between stress, endotoxins, and poultry health

By Technical Team, EW Nutrition

Stress can be defined as any factor causing disruptions to homeostasis, which triggers a biological response to regain equilibrium. We can distinguish four major types of stressors in the poultry industry:

- Technological: related with management events and conditions
- Nutritional: involving nutritional disbalances, feed quality and feed management
- Pathogenic: comprising health challenges.
- Environmental: changes in environment conditions

In practical poultry production, multiple stress factors occur simultaneously. Their effects are also additive, leading to chronic stress. The animals are not regaining homeostasis and continuously deviate the use of resources through inflammation and the gut barrier-function, thus leading to microbiome alteration. As a consequence, welfare, health, and productivity are compromised.

What are endotoxins?

Bacterial lipopolysaccharides (LPS), also known as endotoxins, are the main components of the outer membrane of all Gram-negative bacteria and are essential for their survival. LPS have direct contact with the bacteria's surroundings and function as a protection mechanism against the host's immunological response and chemical attacks from bile salts, lysozymes, or other antimicrobial agents.

Gram-negative bacteria are part of animals' microbiota; thus, there are always LPS in the intestine. Under optimal conditions, this does not affect the animals, because intestinal epithelial cells are not responsive to LPS when stimulated from the apical side. In stress situations, the intestinal barrier function is impaired, allowing the passage of endotoxins into the blood stream. When LPS are detected by the immune system either in the blood or in the basolateral side of the intestine, inflammation and changes in the gut epithelial structure and functionality occur.

The gut is critically affected by stress

Even when there is no direct injury to the gut, signals from the brain can modify different functions of the intestinal tract, including immunity. Stress can lead to functional disorders, as well as to inflammation and infections of the intestinal tract. Downstream signals act via the brain–gut axis, trigger the formation of reactive oxygen and nitrogen species as well as local inflammatory factors, and circulating cytokines, affecting intestinal homeostasis, microbiome, and barrier integrity.

Stress then results in cell injury, apoptosis, and compromised tight junctions. For this reason, luminal substances, including toxins and pathogens, leak into the bloodstream. Additionally, under stress, the gut microbiome shows and increment on Gram-negative bacteria (GNB). For instance, a study by Minghui Wang and collaborators (2020) found an increase of 24% in GNB and lower richness, in the cecum of pullets subjected to mild heat stress (increase in ambient temperature from 24 to 30°C).

Both these factors, barrier damage and alterations in the microbiome, facilitate the passage of endotoxins into the blood stream, which promotes systemic chronic inflammation.

What categories of stress factors trigger luminal endotoxins' passage into the bloodstream?

Technological stress

Various management practices and events can be taken as stressors by the animals' organism. One of the most common examples is **stocking density**, defined as the number of birds or the total live weight of birds in a fixed space. High levels are associated with stress and loss of performance.

A study from the Chung-Ang University in 2019 found that broilers with a stocking density of 30 birds/m^2 presented two times more blood LPS than birds kept at half of this stocking density. Moreover, the body weight of the birds in the high-density group was 200g lower than the birds of the low-density group. The study concluded that high stocking density is a factor that can disrupt the intestinal barrier.

Nutritional stress

The feed supplied to production animals is designed to contribute to express their genetic potential, though some feed components are also continuous inflammatory triggers. **Anti-nutritional factors, oxidized lipids, and mycotoxins** induce a low-grade inflammatory response.

For instance, when mycotoxins are ingested and absorbed, they trigger stress and impair immunity in animals. Their effects start in gastrointestinal tract and extend from disrupting immunity to impairing the intestinal barrier function, prompting secondary infections. Mycotoxins can increase the risk of endotoxins in several ways:

- By inducing changes in the intestinal microbiota that increase gram-negative bacteria
- By disrupting the intestinal barrier function, allowing endotoxins (as well as other toxins and pathogens) to cross the gut barrier and pass into the bloodstream
- By alterations in the immune response, low doses of mycotoxins, such as trichothecenes, induce the upregulation of pro-inflammatory cytokines. A possible synergy can be inferred as when they are together, the effects may be prolonged and require a lower dosage to be triggered.

A study conducted by EW Nutrition (Figure 1) shows an increase in intestinal lesions and blood endotoxins after a mycotoxin challenge of 200pbb of Aflatoxin B1 + 360ppb Ochratoxin in broilers at 21 days of age. The challenged birds show two times more lesions and blood endotoxins than the ones in the unchallenged control. The use of the right mitigation strategy, a product based on bentonite, yeast cell walls, and phytogenics (EW Nutrition GmbH) successfully prevented these effects as it not only mitigates mycotoxins, but also targets endotoxins in the gut.

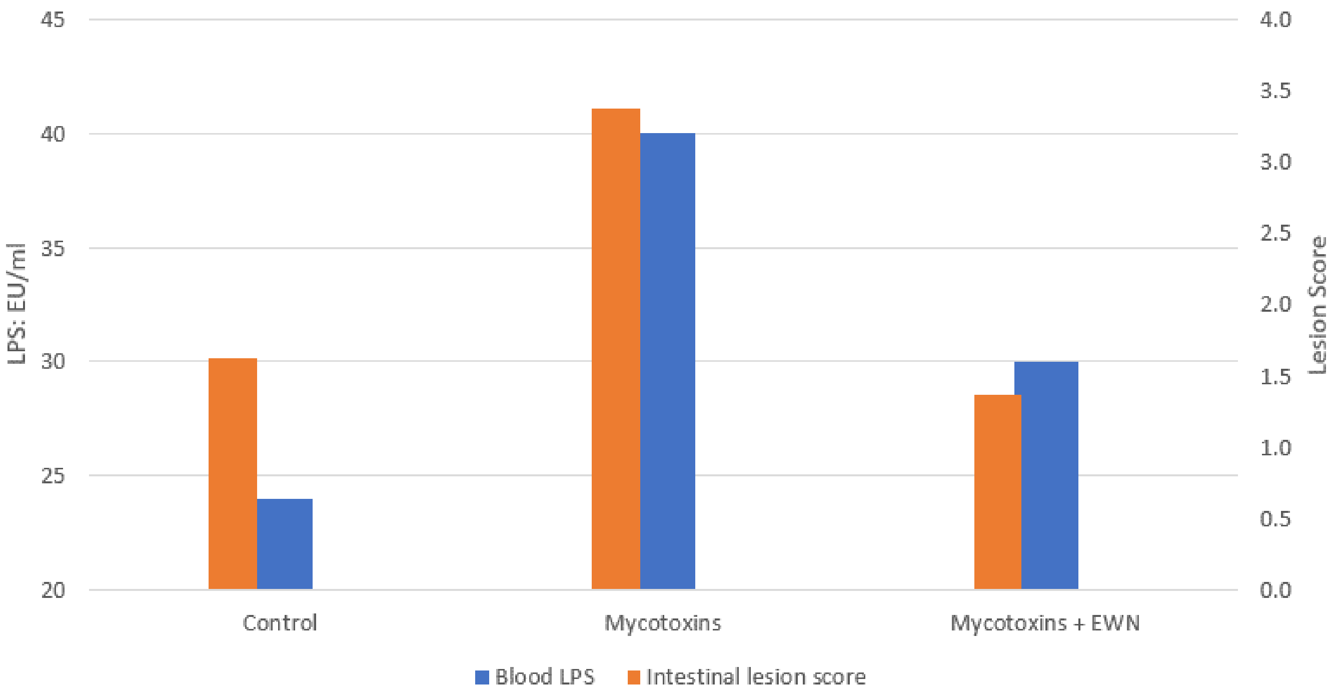


Figure 1 Blood LPS and intestinal lesion score of broilers challenged with 200ppb AFB1 + 350 ppb OTA from 1 to 21 days of age without and with an anti-toxin product from EW Nutrition GmbH (adapted from Caballero et al., 2021)

Pathogenic stress

Intestinal disease induces changes in the microbiome, reducing diversity and allowing pathogens to thrive. In clinical and subclinical necrotic enteritis (NE), the intestinal populations of GNB, including Salmonella and E.coli also increases. The lesions associated with the pathogen compromise the epithelial permeability and the intestinal barrier function, resulting in translocation of bacteria and LPS (Figure 5) into the bloodstream and internal organs.

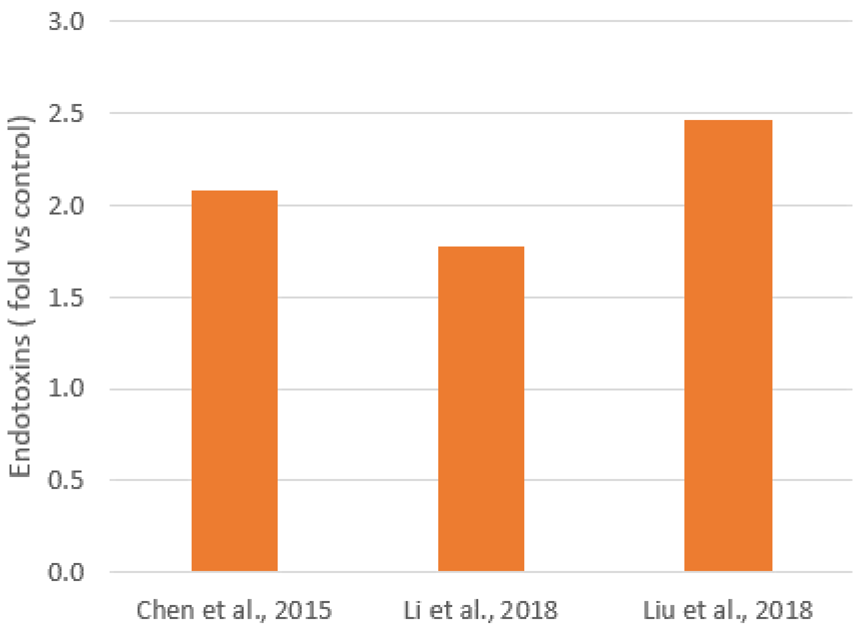


Figure 2 Increase in systemic LPS (vs a healthy control) after a NE challenge (adapted from Chen et al., 2015, Li et al., 2018 & Liu at al., 2018)

Environmental stress

Acute and chronic heat and cold stress increases gut permeability, by increasing intestinal oxidative stress and disrupting the expression of tight junction proteins. This results in the damage and destruction of intestinal cells, inflammation, and imbalance of the microbiota. An increased release and passage of endotoxins has been demonstrated in heat stress (Figure 3), as well as a higher expression of TLR-4 and inflammation.

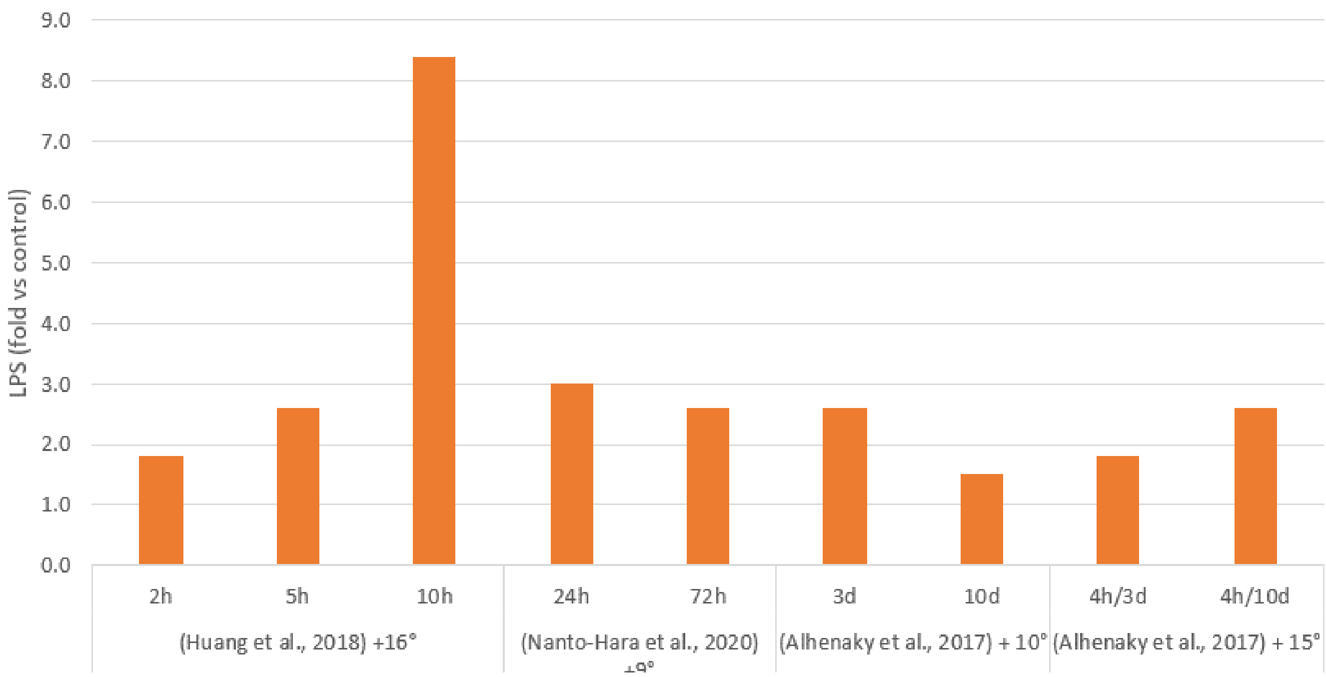
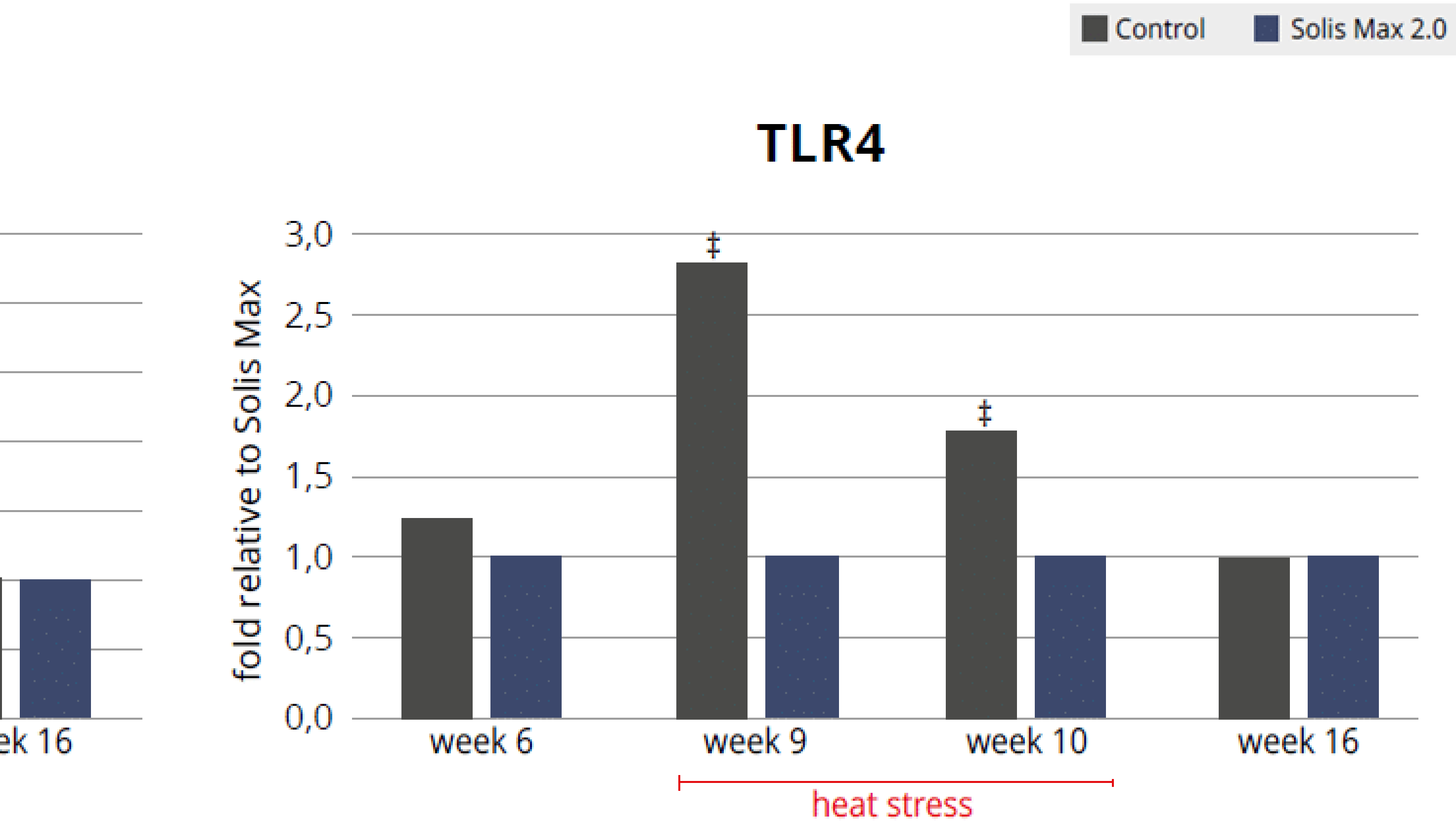


Figure 3 Systemic LPS increase (in comparison with a non-stressed control) after different heat stress challenges in broilers: 16°C increased for 2, 5 and 10 hours (Huang et al., 2018); 9°C increased for 24 and 72 hours (Nanto-Hara et al., 2020); 10°C continuously for 3 and 10 days, and 15°C 4 hours daily for 3 and 10 days (Alhenaky et al., 2017)

Zhou and collaborators (2021) showed that 72 hours of low temperature treatment in young broilers increased intestinal inflammation and expression of tight junction proteins, while higher blood endotoxins indicate a disruption of the intestinal barrier. As a consequence, the stress decreased body gain and increased the feed conversion rate.

An experiment conducted by EW Nutrition GmbH with the objective of evaluating the ability of a toxin mitigation product to ameliorate heat-stress induced LPS. For the experiment, 1760 Cobb 500 pullets were divided into two groups, and each was placed in 11 pens of 80 hens, in a single house. One of the groups received feed containing 2kg/ton of the product from the first day. From week 8 to week 12, the temperature of the house was raised 10°C for 8 hours every day.

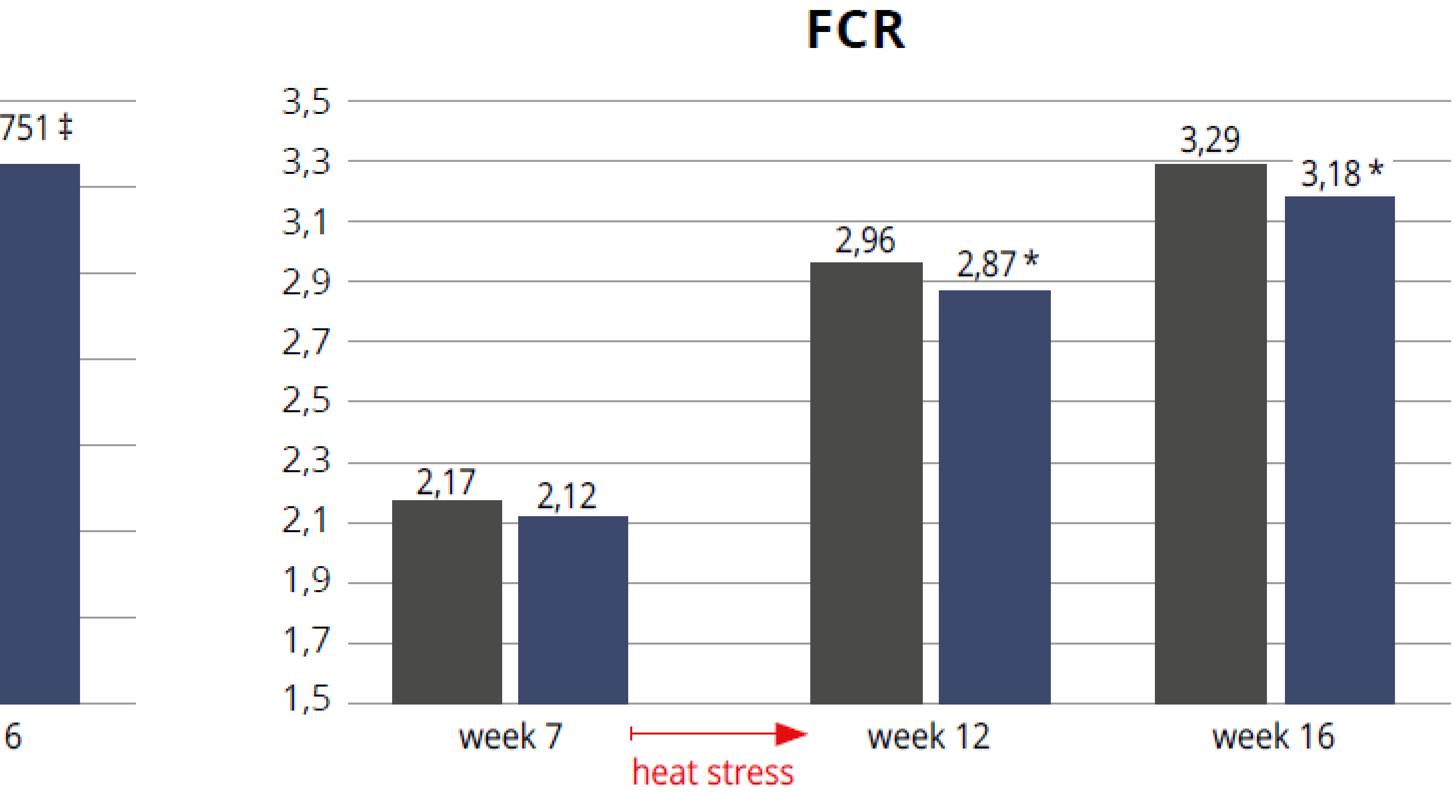
Throughout the heat stress period, blood LPS (Fig 4) was lower in the pullets receiving the product, which allowed lower inflammation, as evidenced by the lower expression of TLR4 (Fig. 5). Oxidative stress was also mitigated with the help of the combination of phytomolecules in the product, obtaining 8.5% improvement on serum total antioxidant capacity (TAC), supported by an increase in in superoxide dismutase (SOD glutathione peroxidase (GSH) and a decrease in malondialdehyde (MDH).



es of pullets before (wk 6) and during heat stress (wk 9 and 10). (*) indicates significant differences (P<0,05), and

In practice: there is no silver bullet

In commercial poultry production, a myriad stressors may occur at the same time and some factors trigger a chain of events that work to the detriment of animal health and productivity. Reducing the solution to the mitigation of LPS is a deceitfully simplistic approach. However, this should be part of a strategy to achieve better animal health and performance. In fact, EW Nutrition's toxin mitigation product alone helped the pullets to achieve 3% improvement in body weight and 9 points lower cumulative feed conversion (Figure 6).



Keeping the animals as free of stress as possible is a true priority for poultry producers, as it promotes animal health as well as the integrity and function of the intestinal barrier. Biosecurity, good environment, nutrition and good management practices are crucial; the use of feed additives to reduce the consequences of unavoidable stress also critically supports the profitability of poultry operations.

A guide to international sustainability regulations

*By **Ilinca Anghelescu**, Global Director Marketing Communications, EW Nutrition*

This may be the year that climate change has arrived in humanity's backyard, driving home the repercussions of human action and the finite nature of our planet's resources. More than ever, it is also becoming clear that we cannot fight climate change in our own backyard but that long-term cross-border action is imperative.

With the visible threat of extreme events nearer than ever, companies and countries feel pressured to show their commitment to sustainable practices. The shape this commitment takes is, however, very different. The slew of regulations and policies directly or indirectly aimed at promoting sustainability may take the shape of water or energy management, environmental protection, specific business practice regulations, and may or may not include reporting obligations and monitoring bodies. Some international initiatives are attempting to impose such obligations, with varying degrees of success. Reading between the lines, the number of regulations is not the problem; it is the competencies in standardizing and enforcing these regulations that prove more difficult.

Sustainability regulations in the European Union

The European Union is both the [fastest warming region] (with the exception of the Arctic) and probably the most advanced in terms of regulatory pressure. It has been steadily developing not just specific regulations aimed at green growth, but also specific reporting tools to avoid greenwashing and standardize the monitoring and measuring of this commitment.

The largest sustainability initiative, the EU's **Green Deal**, unveiled in 2019, is a comprehensive policy framework aimed at making Europe the world's first climate-neutral continent by 2050. Among its objectives are reducing greenhouse gas emissions, increasing energy efficiency, and promoting circular economy practices. Key regulations include:

- European Emissions Trading System (EU ETS): The EU ETS is a “cap and trade” scheme that aims to reduce greenhouse gas emissions in the European Union. It is the first and largest carbon market, covering around 45% of the EU’s greenhouse gas emissions, and is operational across the EU, Iceland, Liechtenstein, and Norway. The system works by setting a cap on the total amount of greenhouse gases that can be emitted by all participating installations. Within this cap, operators buy or receive emissions allowances, which they can trade with one another as needed. The fourth phase started in January 2021 and is to continue until December 2030, however the reduction target for 2030 needs to be reassessed.
- Single-Use Plastics Directive: This regulation aims to reduce single-use plastics and their impact on the environment by banning certain products and promoting recycling.
- Circular Economy Action Plan: Designed to reduce waste and promote recycling, this plan outlines initiatives to make products more durable and easier to repair. The plan includes measures on product design, waste management, and resource efficiency.
- Taxonomy Regulation: This regulation establishes an EU-wide classification system for environmentally sustainable economic activities. The taxonomy defines which economic activities can be considered environmentally sustainable, based on their contribution to environmental objectives such as climate change mitigation and adaptation, biodiversity, and water protection.

More recent but directly concerned with regulating and reporting sustainability in business practices are the following:

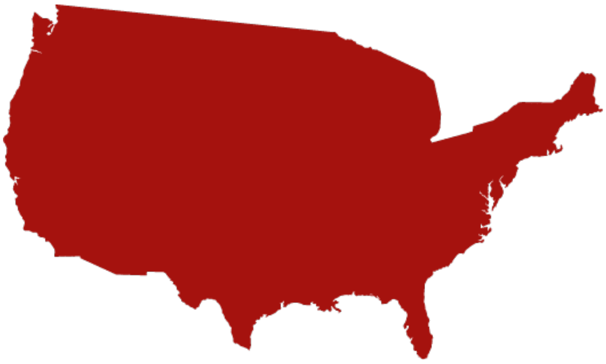
- Sustainable Finance Disclosure Regulation (SFDR): The SFDR requires financial market participants and advisers to disclose information about how they integrate sustainability risks into their investment decisions, consider and disclose the adverse impacts of their investments on sustainability factors.
- Corporate Sustainability Reporting Directive (CSRD): This requires companies to report on a wide range of sustainability issues, including environmental, social, and governance (ESG) factors. The reporting requirements will be phased in, starting from January 1, 2024, for certain large EU and EU-listed companies, and will apply to all in-scope companies by January 1, 2028.

In addition to these regulations, the EU also provides financial support for sustainable projects through its Horizon Europe research and innovation program. Horizon Europe has a budget of €95.5 billion for the period 2021-2027, and a significant portion of this funding will be used to support research and innovation in areas such as climate change mitigation, renewable energy, and sustainable agriculture.

Sustainability regulations in the United States

The United States traditionally has a more decentralized approach to regulations, with federal, state, and local governments all playing important roles. Key federal regulations and initiatives in the field of sustainability include:

1970. Clean Air Act: Enforced by the Environmental Protection Agency (EPA), this law aims to reduce air pollution and greenhouse gas emissions. This law regulates air pollution from a variety of sources, including power plants, factories, and vehicles. The Clean Air Act has helped to reduce air pollution in the US by over 70% since it was passed in 1970.
1971. Clean Water Act: Also administered by the EPA, this act sets standards for water quality, aiming to protect aquatic ecosystems. This law regulates water pollution from a variety of sources, including factories, farms, and sewage treatment



plants. The Clean Water Act has helped to improve water quality in the US by over 70% since it was passed in 1972.

1972. Renewable Energy Tax Credits: Also called Residential Clean Energy Credits, these incentives encourage the development and use of renewable energy sources like solar and wind power.

More recent, targeted sustainability actions and regulations in the US include:

- Executive Order 14057: Issued by President Biden in 2021, the Executive Order on Catalyzing Clean Energy Industries and Jobs Through Federal Sustainability requires federal agencies to take steps to reduce their greenhouse gas emissions and promote clean energy.
- ESG Disclosure Simplification Act: This bill, passed by the House of Representatives in 2021, would require public companies to disclose more information about their environmental, social, and governance (ESG) practices.
- Methane Emissions Reduction Plan: The White House Action Plan, together with the Supplemental Methane Proposal put forth by the Environmental Protection Agency (EPA) in 2022, would require primarily oil and gas companies to reduce methane emissions from their operations.
- Sustainable Electricity Plan: This plan, released by the Department of Energy in 2022, outlines the Biden administration's goals for increasing the use of renewable energy and reducing greenhouse gas emissions from the electricity sector.
- SEC Climate-Related Disclosures/ESG Investing: Prompted by the Climate Risk Disclosure Act of 2021, the Securities and Exchange Commission (SEC) has issued a rule proposal that would require US publicly traded companies to disclose annually how their businesses are assessing, measuring, and managing climate-related risks. This would include climate-related risks and their material impacts on the registrant's business, strategy, and outlook; governance of climate-related risks; greenhouse gas ("GHG") emissions; certain climate-related financial statement metrics and related disclosures; information about climate-related targets and goals, and transition plan, if any. Some companies would have to already start reporting in 2023 for 2023. However, it is likely the proposal will undergo several rounds of revisions.

In addition to these federal laws, there are also a number of state and local sustainability regulations. U.S. regulations generally lack cohesion, with the federal government's role fluctuating depending on the administration in power. Still, there is growing momentum towards sustainability, driven by grassroots movements and corporate initiatives.

Sustainability regulations in China

China, the world's largest polluter, faces significant sustainability challenges as it grapples with rapid industrialization, urbanization, and economic growth. It has made substantial progress, particularly in renewable energy adoption, but still faces challenges of implementation.

- Carbon Neutrality Commitment: In September 2020, Chinese President Xi Jinping announced China's commitment to achieving carbon neutrality by 2060. This ambitious goal involves reducing carbon emissions to net-zero by mid-century.
- Renewable Energy Development: China is a global leader in renewable energy deployment. It has set targets for increasing the share of renewable energy sources like wind, solar, and hydropower in its energy mix. Initiatives include the National Renewable Energy Development Plan and the 13th Five-Year Plan for Energy Development.

- Emissions Trading System (ETS): China has launched a national carbon emissions trading system, which is the world's largest such program. It caps emissions from certain industries and encourages emission reductions through trading of carbon allowances.
- Green Finance Initiatives: The country is promoting green finance to support sustainable development. Initiatives include green bond issuance, guidelines for green lending, and

incentives for sustainable investment.
- Air Quality Improvement: The "Blue Sky" campaign aims to reduce air pollution in Chinese cities through stricter emissions standards, promotion of cleaner energy sources, and transitioning from coal to natural gas. The campaign appears to have had significant impact.
- Sustainable transportation and circular economy: Initiatives to promote electric vehicles (EVs) and public transportation include subsidies for EV purchases, charging infrastructure development, and incentives for green vehicle production. China is also working on promoting a circular economy by reducing waste, improving resource efficiency, and encouraging recycling. The Circular Economy Promotion Law was passed in 2008.
- Environmental Protection Laws and Regulations: China has strengthened its environmental laws and regulations to address pollution and environmental degradation. This includes revisions to the Environmental Protection Law and stricter enforcement.

These sustainability regulations, plans, and actions reflect China's efforts to address pressing environmental challenges, transition to a more sustainable and low-carbon economy, and contribute to global efforts to combat climate change. Results are varied but the sheer scale of China's pollution make the success of these initiatives a matter of global concern.

Sustainability regulations in India

Prompted by very tangible threats, India, recently crowned the world's most populous country, has been fighting climate change for several decades, although not necessarily under one umbrella of sustainability. Moreover, there are currently no regulations that mandate sustainability reporting in India. However, Indian regulators are revising its existing environmental laws and plans, which will likely result in more stringent requirements for companies.

Instead of reporting requirements, India provides support through various sustainability-related programs and legislation.

- National Action Plan on Climate Change (NAPCC): Launched in 2008, the NAPCC outlines the country's strategy to combat climate change. It consists of eight national missions focused on various aspects of climate change mitigation and adaptation, including solar energy, energy efficiency, water, agriculture, and forestry.
- Renewable Energy Initiatives: India has set ambitious targets for increasing its renewable energy capacity, including solar and wind power. Initiatives like the National Solar Mission aim to promote clean energy sources and reduce greenhouse gas emissions.

- Sustainable Agriculture Initiatives: Programs like the National Mission for Sustainable Agriculture (NMSA) promote sustainable farming practices, soil health management, and water-use efficiency in agriculture.
- National Clean Air Program (NCAP): India's NCAP, launched in 2019, aims to improve air quality in major cities by reducing particulate matter and other air pollutants. It includes measures to control emissions from industries, vehicles, and biomass burning.
- National Biodiversity Strategy and Action Plan (NBSAP): India has developed an NBSAP to conserve biodiversity, protect ecosystems, and promote sustainable use of natural resources.
- Water Resource Management: India has various initiatives and programs to address water-related challenges, including river rejuvenation projects, watershed development, and efforts to improve water-use efficiency in agriculture.
- Sustainable Transportation: The Faster Adoption and Manufacturing of Hybrid and Electric Vehicles (FAME) scheme promotes the adoption of electric and hybrid vehicles to reduce air pollution and greenhouse gas emissions.
- Environmental Impact Assessment (EIA) Regulations: India has a regulatory framework for conducting EIAs for various development projects to assess and mitigate their environmental impacts.
- Plastic Waste Management Rules: India has implemented rules to manage and reduce plastic waste, including restrictions on single-use plastics.
- National Mission for Sustainable Habitat (NMSH): This mission focuses on promoting sustainable urban planning and development, energy efficiency in buildings, and waste management in urban areas.

India's approach is comprehensive but at the moment focuses on top-down actions. As in China, market players are at present not required to disclose any climate-related impact or information.

International sustainability regulations

International organizations play a crucial role in coordinating global sustainability efforts. The United Nations and its agencies, particularly the UN Framework Convention on Climate Change (UNFCCC), an international treaty and organization established to address the issue of global climate change adopted in 1992, have spearheaded international sustainability regulations, of which the most impactful are mentioned below.

- The Paris Agreement: Signed in 2015, the agreement represents a global commitment to combat climate change by limiting global warming to well below 2 degrees Celsius above pre-

industrial levels and aiming to limit it to 1.5 degrees Celsius. 196 nations have agreed on its goals, as well as committed to specific targets and standards of accountability. The Paris Agreement is part of the UNFCCC.
- The United Nations' Sustainable Development Goals (SDGs): The SDGs are a set of 17 goals that aim to end poverty, protect the planet, and ensure prosperity for all. They provide a framework for companies to align their business strategies with sustainable development objectives. These goals were adopted by all United Nations Member States in September 2015 as part of the 2030 Agenda for Sustainable Development.
- The Task Force on Climate-related Financial Disclosures (TCFD): The TCFD is a voluntary initiative that provides recommendations for companies to disclose climate-related risks and opportunities in their financial filings. The TCFD was founded by the Financial Stability Board (FSB), an international body that monitors and makes recommendations about the global financial system, in December 2015. The TCFD encourages organizations to conduct scenario analysis, which involves assessing the potential financial impact of different climate-related scenarios, including both transition risks (related to policy and market changes) and physical risks (related to climate impacts like extreme weather events).
- The International Sustainability Standards Board (ISSB) issued the first two sustainability standards, the IFRS S1 General Requirements for Disclosure of Sustainability-related Financial Information and the IFRS S2 Climate-related Disclosures. They will theoretically become effective on or after January 1, 2024. If jurisdictions challenge or delay bringing them into law, the effective date may well be later. IFRS S1 provides a set of disclosure requirements designed to enable companies to communicate to investors about the sustainability-related risks and opportunities they face over the short, medium and long term. IFRS S2 sets out specific climate-related disclosures and is designed to be used with IFRS S1. Both fully incorporate the recommendations of the Task Force on Climate-related Financial Disclosures (TCFD).

Conclusion

China, the US, and India have been, for a while now, the largest polluter nations. ***However, statistics do not look at the indirect pollution cost of countries that produce abroad for internal consumption.*** If we take that cost into consideration, it becomes evident that sustainability regulations at both national and international level are crucial for addressing environmental and social challenges.

Regulations alone are obviously not enough. Strict enforcement and monitoring are what is going to transform national and supra-national entities, regional authorities, businesses, communities, and individuals into responsible actors.

Salmonella in pigs: a threat for humans and a challenge for pig producers

*By **Dr. Inge Heinzl**, Editor, EW Nutrition*

Salmonellosis is third among foodborne diseases leading to death (Ferrari, 2019). More than 91,000 human cases of Salmonellosis are reported by the EU each year, generating overall costs of up to €3 billion a year (EFSA, 2023), 10-20% of which are attributed to pork consumption (Soumet, 2022). The annual costs arising from the resulting human health losses in 2010 were about €90 million (FCC Consortium, 2010). Take the example of Ireland, where a high prevalence of Salmonella in lymph nodes still shows a severe issue pre-slaughter and a big challenge for slaughterhouses to stick to the process hygiene requirements (Deane, 2022).

Several governments already have monitoring programs in place, and the farms are categorized according to the salmonella contamination of their pigs. In some countries, e.g., Denmark, an economic penalty of 2% of the carcass value must be paid if the farm has level 2 (intermediate seroprevalence) and 4-8% if the level is 3. Other countries, e.g., Germany, the UK, Ireland, or the Netherlands, use quality assurance schemes. The farmers can only sell their carcasses under this label if their farm has a certain level.

Let’s take a quick look at the genus of Salmonella

Salmonellas are rod-shaped gram-negative bacteria of the family of enterobacteria that use flagella for their movement. They were named after the American vet Daniel Elmer Salmon. The genus of Salmonella consists of two species (S. bongori and S. enterica with seven subspecies) with in total more than 2500 serovars (see Figure 1). The effects of the different serovars can range from asymptomatic carriage to severe invasive systemic disease (Gal-Mor, 2014). All Salmonella serovars generally can cause disease in humans; the rosa-marked ones already showed infections.

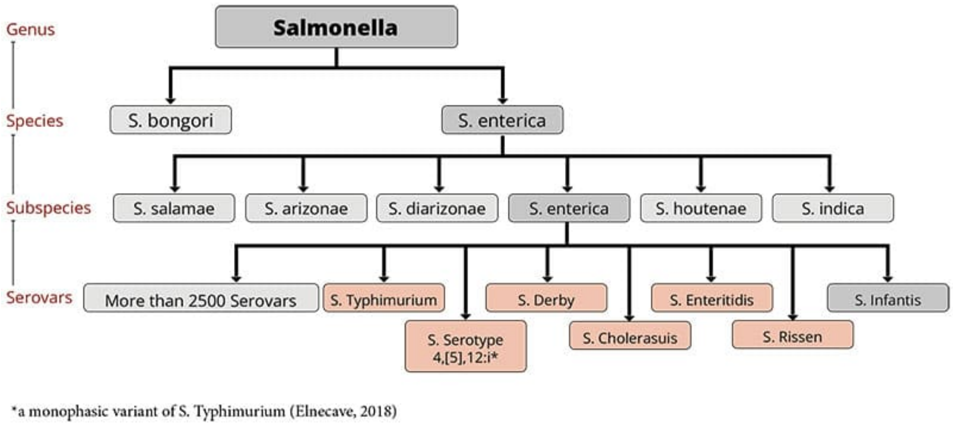


Figure 1: the genus of Salmonella with Salmonella serovars relevant for pigs (according to Bonardi, 2017: Salmonella in the pork production chain and its impact on human health in the European Union)

Within the group of Salmonella, some serovars can only reside in one or few species, e.g., S. enterica spp. enterica Serovar Dublin (S. Dublin) in bovines (Waldron, 2018) or S. Cholerasuis in pigs (Chiu, 2004). An infection in humans with these pathogens is often invasive and life-threatening (WHO, 2018). On the contrary, serovars like S. Typhimurium and S. Enteritidis are not host-specific and can cause disease in various species.

The serotypes S. Typhi and S. Paratyphi A, B, or C are highly adapted to humans and only for them pathogenic; they are responsible for the occurrence of typhus.

Serovars occurring in pigs and relevant for humans are, for example, S. Typhimurium (Hendriksen, 2004), S. Serotype 4,[5],12:I (Hauser et al., 2010), S. Cholerasuis (Chiu, 2004), S. Derby (Gonzalez-Santamarina, 2021), S. Agona (Brenner Michael, 2006) and S. Rissen (Elbediwi, 2021).

Transmission of Salmonella mostly happens via contaminated food

The way of transmission to humans depends on the serovar:
Human-specific and, therefore, only in humans and higher primates residing serovars S. Typhi and Paratyphi A, B, or C (typhoidal) are excreted via feces or urine. Therefore, any food or water contaminated with the feces or urine of infected people can transmit this disease (Government of South Australia, 2023). Typhoid and paratyphoid Salmonellosis occur endemic in developing countries with the lack of clean water and, therefore, inadequate hygiene (Gal-Mor, 2014).

Serovars which can cause disease in humans **and** animals (non-typhoidal), can be transmitted by
– animal products such as milk, eggs, meat
– contact with infected persons/animals (pigs, cows, pets, reptiles…) or
– other feces- or urine-contaminated products such as sprouts, vegetables, fruits….

Farm animals take salmonellas from their fellows, contaminated feed or water, rodents, or pests.

Symptoms of Salmonellosis can be severe

In the case of typhoid or paratyphoid Salmonellosis, the onset of illness is gradual. People can suffer from sustained high fever, unwellness, severe headache, and decreased appetite, but also from an enlarged spleen irritating the abdomen and dry cough.

A study conducted in Thailand with children suffering from enteric fever caused by the typhoid serovars S. Typhi and Paratyphi showed a sudden onset of fever and gastrointestinal issues (diarrhea), rose spots, bronchitis, and pneumonia (Thisyakorn et al., 1987)

The non-typhoid Salmonellosis is typically characterized by an acute onset of fever, nausea, abdominal pain with diarrhea, and sometimes vomiting (WHO, 2018). However, 5% of the persons – children with underlying conditions, e.g., babies, or people who have AIDS, malignancies, inflammatory bowel disease, gastrointestinal illness caused by non-typhoid serovars, and hemolytic anemia, or receiving an immunosuppressive therapy can be susceptible to bacteremia. Additionally, serovars like S. Cholerasuis or S. Dublin are apt to develop bacteremia by entering the bloodstream with little or no involvement of the gut (Chiu, 1999). In these cases, consequences can be septic arthritis, pneumonia, peritonitis, cutaneous abscess, mycotic aneurysm, and sometimes death (Chen et al., 2007; Chiu, 2004, Wang et al., 1996).

In pigs, S. Cholerasuis causes high fever, purple discolorations of the skin, and thereinafter diarrhea. The mortality rate in pigs suffering from this type of Salmonellosis is high. Barrows orally challenged with S. Typhimurium showed elevated rectal temperature by 12h, remaining elevated until the end of the study. Feed intake decreased with a peak at 48h after the challenge and remained up to 120h after the challenge. Daily gain reduced during the following two weeks after infection. A higher plasma cortisol level and a lower IGF-I level could also be noticed. All these effects indicate significant changes in the endocrine stress and the somatotropic axis, also without significant alterations in the systemic pro-inflammatory mediators (Balaji et al., 2000)

To protect humans, Salmonella in pork must be restraint

There are three main steps to keep the contamination of pork as low as possible:

1. Keeping Salmonella out of the pig farm
2. Minimizing spreading if Salmonella is already on the farm
3. Minimizing contamination in the slaughterhouse

1. How to keep Salmonella out of the pig farm?

To answer this question, we must look at how the pathogen can be transported to the farm. According to the Code of Practice for the Prevention and Control of Salmonella on Pig Farms (Ministry of Agriculture, Fisheries and Food and the Scottish Executive Rural Affairs Department), there are several possibilities to infiltrate the pathogen into the farm:

- Diseased pigs or pigs which are ill but don’t show any symptoms
- Feeding stuff or bedding contaminated with dung
- Pets, rodents, wild birds, or animals
- Farm personnel or visitors
- Equipment or vehicles

Caution with purchased animals!

To minimize/prevent the entry of Salmonella into the livestock, bought-in animals must come from reputable breeding farms with a salmonella monitoring system in place. As possible carrier animals are more likely to excrete Salmonella when stressed; they should be kept in isolation after purchasing. Additionally, the animals must go through a disinfectant foot bath before entering the farm.

Keep rodents, wild animals, and vermin in check!

Generally, the production site must be kept clean and as unattractive as possible for all these animals. Rests of feed must be removed, and dead animals and afterbirths must be promptly and carefully disposed of. A well-planned baiting and trapping policy should be in place to effectively control rodents.

Only selected people should enter the hog houses

In any case, the number of persons entering the hog house must be kept as low as possible. Farmworkers should be trained in the principles of hygiene. They should wear adequate clothing (waterproof boots and protective overalls) that can be easily cleaned/laundered and disinfected. The clothes/shoes should always be used only at this site. Thorough hand washing and the disinfection of the boots when entering and leaving the pig unit are a must.

If visits are necessary, the visitors should take the same measures as the farm workers. And, of course, they should not have had contact with another pig farm during the last 48 hours.

Keep pens, farm equipment, and vehicles clean!

Farm equipment should not be shared with other farms. If this cannot be avoided, it must be cleaned and disinfected before re-entering the farm. Also, the vehicles for the transport of the animals must be cleaned and disinfected as soon as possible after usage, as contaminated transporters always pose the risk of infection.

Feed should be Salmonella-free!

To get high feed quality, the feed should be purchased from feed mills/sources with a well-functioning bacterial control to guarantee the absence of Salmonella. It is essential that birds, domestic and wild animals cannot enter the feed stores.
It is also advised to keep dry feed dry as possibly contaminating Salmonella can multiply in such humid conditions. Additionally, all feed bins and delivery pipes for dry and wet feed must be consciously cleaned, and the damp feed pipes also disinfected.
The change from pellets to mash could be helpful as the pellets facilitate Salmonella colonization by stimulating the secretion of mucins (Hedemann et al., 2005).

For sanitation of the feed, we offer organic acids (Acidomix product range) or mixtures of organic acids and formaldehyde in countries where formaldehyde products are allowed (Formycine) to decrease the pathogenic load of the feed materials. In vitro trials show the effectiveness of the products:

For the in vitro trial with Formycine, autoclaved feed samples were inoculated with Salmonella enteritidis serovar Typhimurium DSM 19587 strain to reach a Salmonella contamination of 10^6 CFU/g of feed. After incubating at room temperature for three hours, Formycine Liquido was added to the contaminated feed samples at 0, 500, 1000, and 2000 ppm. The control and inoculated feed samples were further incubated at room temperature, and Salmonella counts (CFU/g) were carried out at 24, 48, 72 hours and on day 15. The limit of Salmonella detection was set at 100 CFU/g (10^2). Results are shown in figure 2.

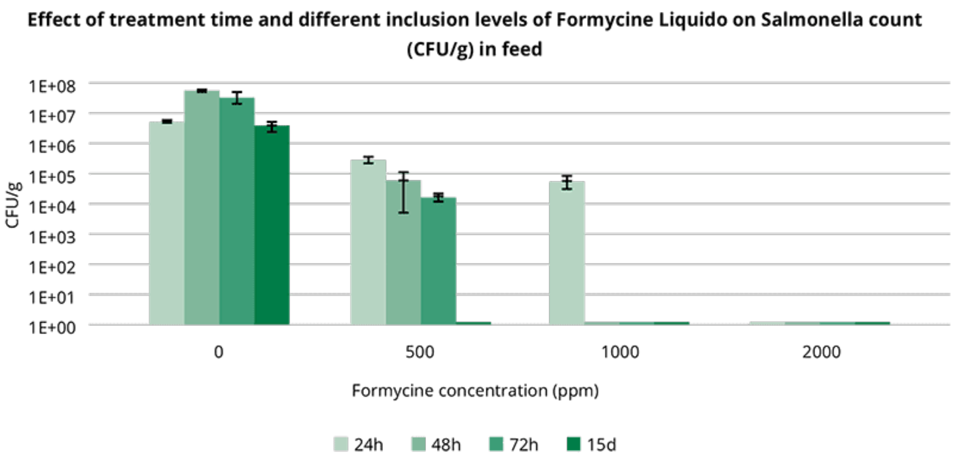


Fig. 2: Effect of treatment time and different inclusion levels of Formycine Liquido on the Salmonella count in feed

As important as uncontaminated feed is clean water for drinking. It can be achieved by taking the water from a main or a bacteriologically controlled water borehole. Regular cleaning/disinfection of the tanks, pipes, and drinkers is essential.

Bedding should be Salmonella-free

Straw material containing feces of other animals (rodents, pets) always carries the risk of Salmonella contamination. Also, wet or moldy bedding is not recommended because it is an additional challenge for the animal. To optimize the quality of bedding, the straw should be bought from reliable and as few as possible sources. The material must be stored dry and as far as practicable from the pig buildings (Ministry of Agriculture, Fisheries and Food & Scottish Executive Rural Affairs Department, 2000).

Vaccination is a beneficial measure

For the control of Salmonella in swine herds, vaccination is an effective tool. De Ridder et al. (2013) showed that an attenuated vaccine reduced the transmission of Salmonella Typhimurium in pigs. The vaccination with an attenuated S. Typhimurium strain, followed by a booster vaccination with inactivated S. Cholerasuis, showed better effects than an inactivated S. Cholerasuis vaccine alone (Alborali et al., 2017). Bearson et al. (2017) could delimitate transmission through less shedding and protect the animals against systemic disease.
To achieve the best effects, the producer must understand the diversity of Salmonella serovars to choose the most promising vaccination strategy (FSIS, 2023).

2. How to minimize the spreading of Salmonella on the farm?

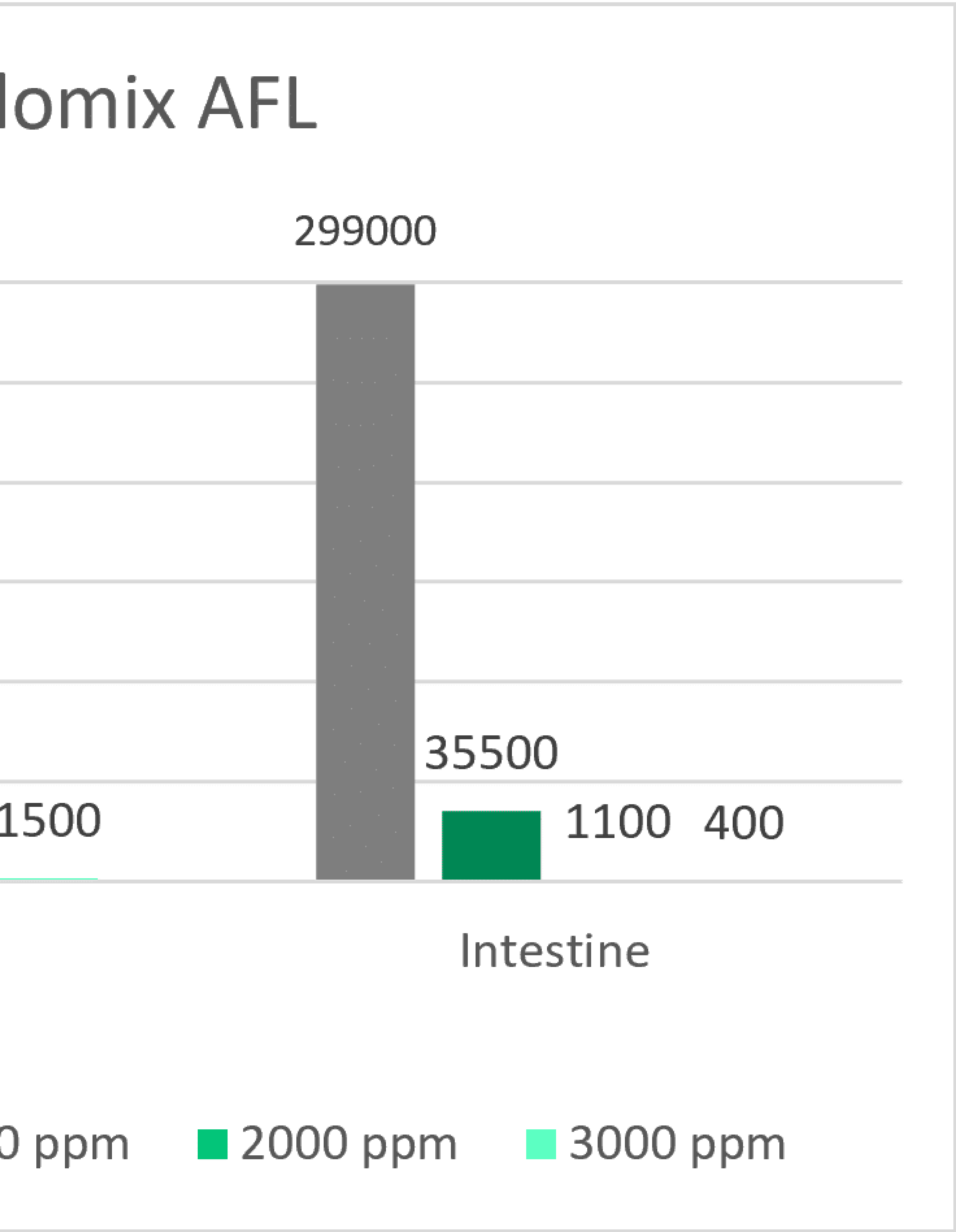
If there are already cases of Salmonella on the farm, infected animals must be separated from the rest of the herd. Small batch sizes are beneficial, as well as not mixing different litters after weaning. If feasible, separate units for different production phases with an all-in/all-out system could break the reinfection cycle and help reduce Salmonella contamination on the farm. And also in this case, vaccination is helpful.

Salmonella doesn’t like acid conditions

An effective tool is acidifying the feed with organic acids, as Salmonella doesn’t like acid conditions. A trial was conducted with Acidomix AFG and Acidomix AFL to show their effects against Salmonella. For the test, 10^5 CFU/g of Salmonella enterica ser. Typhimurium was added to feed containing 1000 ppm, 2000 ppm, and 3000 ppm of Acidomix AFG or AFL. The stomach and intestine were simulated in vitro by adjusting the pH with HCl and $NaHCO_3$ as follows:

Stomach	2.8
Intestine	6.8-7.0

After the respective incubation, the microorganisms were recovered from feed and plated on an appropriate medium for CFU counting. The results are shown in figures 3 and 4.



lomix AFL
299000
35500
1500
1100
400
Intestine
0 ppm
2000 ppm
3000 ppm

Figures 3 + 4: Effects of different concentrations of Acidomix AFG and Acidomix AFL against Salmonella enterica ser. Typhimurium in feed

Phytomolecules can support pigs against Salmonella

Plant compounds or phytomolecules can also be used against Salmonella in pigs. Some examples of phytomolecules to be used are Piperine, Allicin, Eugenol, and Carvacrol. Eugenol, e.g., increases the permeability of the Salmonella membrane, disrupts the cytoplasmic membrane, and inhibits the production of bacterial virulence factors (Keita et al., 2022; Mak et al., 2019). Thymol and Carvacrol interact with the cell membrane by H bonding, also resulting in a higher permeability.

An already published in vitro trial conducted with our product Ventar D also showed excellent effects against Salmonella while sparing the beneficial gut flora. A further trial once more demonstrated the susceptibility of Salmonella to Ventar D. It showed that Ventar D controls Salmonella by suppressing their motility and, at higher concentrations, inactivating the cells (see figures 5 + 6):

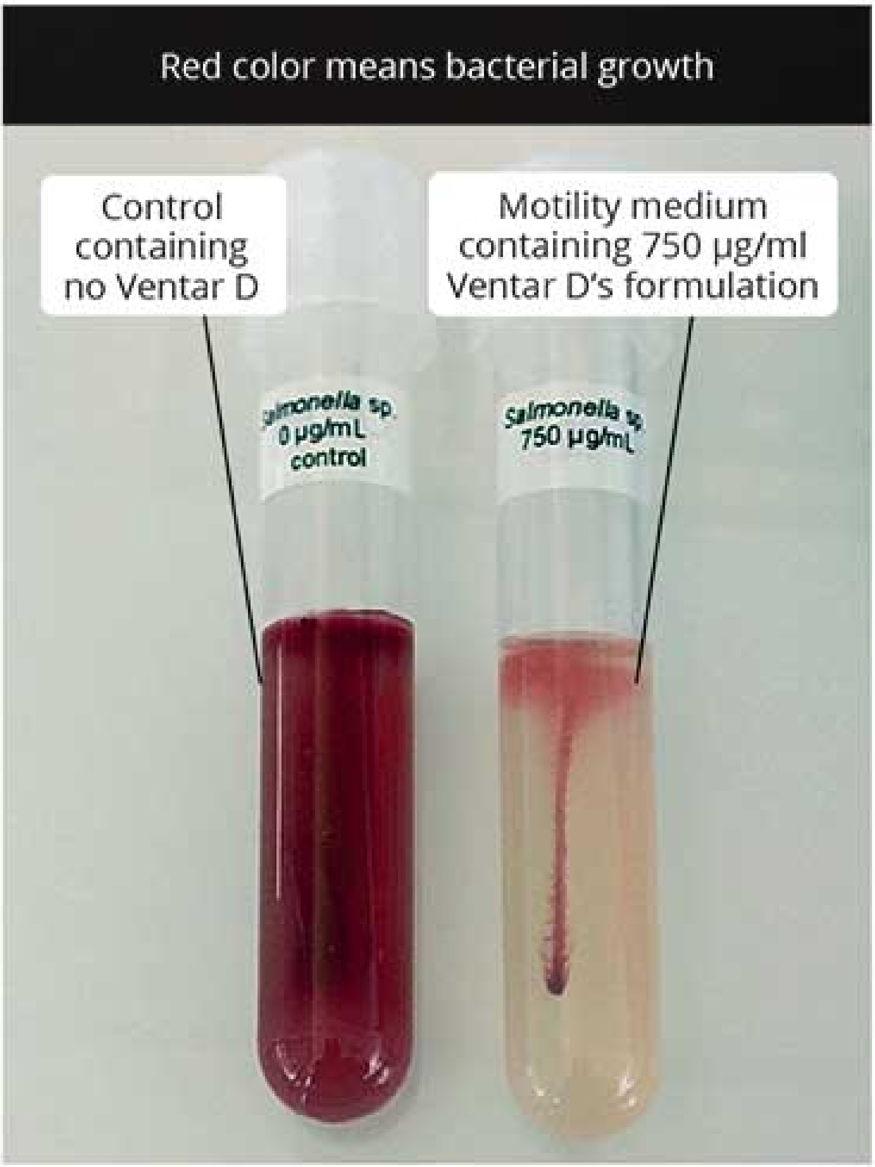


Figure 5: S. enterica motility test: on the left side – control; on the right side – motility medium containing.750 µg/mL of Ventar

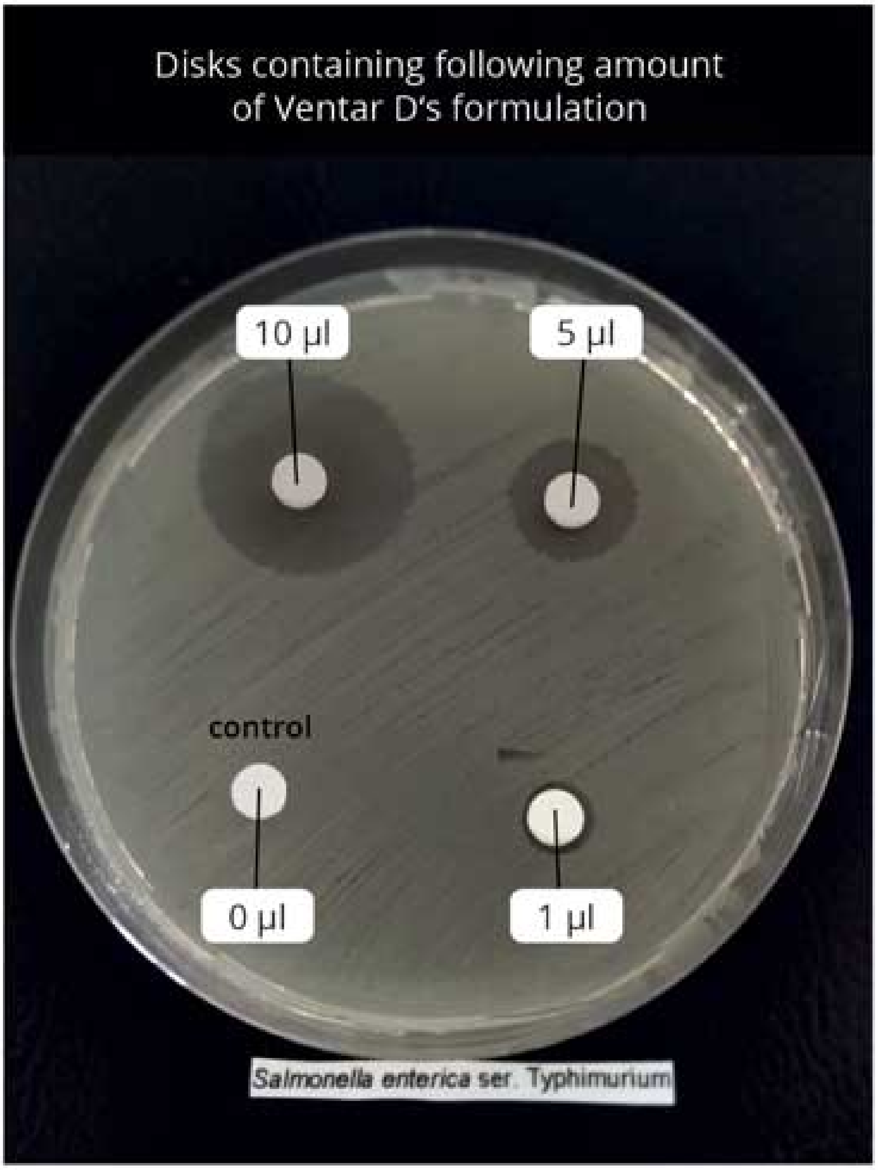


Fig 6 . Disk diffusion assay employing S. enterica. upper left side – disk containing 10 µL of Ventar; upper right – 5 µL; lower left – control; lower right – 1µL.

In addition to the direct Salmonella-reducing effect, essential oils / secondary plant compounds / phytomolecules improve digestive enzyme activity and digestion, leading to increased nutrient absorption and better feed conversion (Windisch et al., 2008).

3. How can the farmer keep Salmonella contamination low in the slaughterhouse?

In general, the slaughterhouse personnel is responsible for adequate hygiene management to prevent contamination of carcasses and meat. However, also the farmer can make his contribution to maintain the risk of contamination in the slaughterhouse as low as possible. A study by Vieira-Pinto (2006) revealed that one Salmonella-positive pig can contaminate several other carcasses.

According to a trial conducted by Hurd et al. (2002), infection and, therefore, “contamination” of other pigs can rapidly occur, meaning that cross-contamination is a topic during transport to the slaughterhouse and in the lairages when the pigs come together with animals from other farms. The stress to which the pigs are exposed influences physiological and biochemical processes. The microbiome and animal’s immunity are affected, leading to higher excretion of Salmonella during transport and in the lairages. So, the animals should not be stressed during loading and unloading or transportation. The trailer poses a further risk of infection if it was not cleaned and disinfected before. So, reliable people who treat the animals well and keep their trailers clean should be chosen for transportation.

Pig producers are obliged to keep Salmonella in check – phytomolecules can help

At least in the EU, pig producers have the big duty to keep Salmonella low in their herds; otherwise, they will have financial losses. They are not only responsible for their farm, but also the slaughterhouses count on them. Besides the standard strict hygiene management and vaccination, farmers can use products provided by the industry to sanitize feed but also to support their animals directly with phytomolecules acting against pathogens and supporting gut health.

All these measures together should be a solution to the immense challenge of Salmonella, to protect people and prevent economic losses.

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No revision of the Feed Additives law, says the European Commission

The authorization and marketing of feed additives in the European Union is currently governed by Feed Additives Regulation (EC) No 1831/2003, which came into effect in 2004. In 2021, the European Commission formalized an initiative to revise it, stating as reasons both the focus brought by the Farm to Fork Strategy, as well as inherent complexities in phrasing, process, and more. Representatives of the EC's responsible unit, DG SANTE Unit G5, have now confirmed to EW Nutrition that, following consultations and analysis, **the revision of the legislation on the authorisation of feed additives will not happen under the current Commission's mandate**.

The revision was initially deemed necessary on several grounds:

- Not enough focus on sustainable animal farming
- Lack of flexibility in promoting technical and scientific innovation
- A lengthy authorization process
- Unnecessary administrative burden
- Ineffective imports control leading to unfair competition between EU and non-EU operators
- Dependency on imports from third countries for some additives (e.g., vitamins)
- Restrictions on the circulation of feed additives only intended for export
- Insufficient legal clarity and consistency for a few aspects of the Regulation, e.g. use of certain additives in drinking water or labelling provisions for worker safety provisions in various complementary but unclear Regulations
- Extensive, unnecessary labeling regulations that create physical and administrative burdens

Near the end of the two-year assessment process, however, the response of European governmental, supra-national, and non-governmental bodies appears to have been lukewarm. Overall, the conclusion of the EC unit overseeing the process was that "**while a review of the framework would be useful, it does not appear necessary, considering the possibilities already granted by the existing legal framework**." In other words, applicants will have to use the existing mechanisms for applications, with no prospect for change in the near future.

Other strategies and regulations have also fallen through the cracks. For instance, the EU Animal Health Strategy 2007-2013 has not been updated in 10 years and there are no plans to renew the initiative. This is likely because the Green Deal and the flurry of new or upcoming regulations related to it are expected to supplant the framework for protein production in the European Union.

As the mandate of the current EC ends in 2024, there is a slim chance that the feed additive authorization process might be made less cumbersome once a new commission takes over.

Ketosis: the most critical metabolic disease in dairy cows

***Judith Schmidt**, Product Manager On-Farm Solutions*

Improvements in genetics, nutrition, and management continue to enhance dairy cows' performance. However, being high-performance athletes comes at a cost, putting an extremely high burden on the animals' energy metabolism. Especially around calving and during the first eight weeks of lactation, dairy cows can experience many stress factors: subclinical hypocalcemia, abomasum displacements, herd composition changes, or lameness. The more stress factors put the cows' organism under pressure, the more likely they will become sick. A common consequence of stress is the occurrence of metabolic diseases, especially ketosis.

Both in terms of animal health and economic aspects, ketosis is probably the most critical dairy cow disease when also considering the correlated diseases. In this article, we explore the causes and consequences of ketosis and highlight prevention strategies that keep this issue under control.

Ketosis: causes and consequences

How ketosis develops

A restricted feed intake capacity and/or reduced energy concentration in the ration lead to a deficit in the animal's energy balance. This situation occurs, for instance, at calving when the mother animal focuses her resources on the calf and its care. To compensate for the energy deficit, body fat is broken down for energy production. This process creates free fatty acids that accumulate in the liver and are partially converted into ketone bodies. These ketone bodies are a “transport medium” for energy, which various organs can use as an alternative energy source.

The problem arises when the deficiency lasts too long: more and more body fat is broken down, more and more fatty acids reach the liver, which leads to a fatty liver, and too high an amount of ketone bodies is formed and released into the blood. The ketone bodies in the blood inhibit appetite, resulting in less feed consumption and an energy deficit – the vicious cycle of ketosis begins.

Subclinical ketosis

Subclinical ketosis is defined as the stage of the disease at which an increased level of ketone bodies can be detected in the blood, urine, and milk. Furthermore, signs of hypoglycemia, increased levels of non-esterified fatty acid, and decreased hepatic gluconeogenesis can be seen in the blood. These conditions are typically not detected because there are no clinical signs.

Subclinical ketosis is a problem as it does not cause visible symptoms but leads to an increased incidence of subsequent diseases such as lab stomach displacement, clinical ketosis, and uterine inflammation. In addition, there may be loss of milk and fertility problems. Subclinically ill animals cannot be identified by the farmer by observation alone. Therefore, subclinical ketosis must be detected at an early stage to be able to act at the right time: prophylaxis instead of therapy.

There are several test possibilities to find out if an animal suffers from ketosis:

1. **Milk**: Milk test for ketosis detection has been available for many years. The results are to be obtained based on a color gamut. In contrast to blood analysis, the milk test does not evaluate exact values but shows a color change of the contained indicator. However, an increased milk cell content of the feeding of poorly fermented silages with a high butyric acid content significantly influences the result. The test often does not adequately reflect the actual conditions.
2. **Urine**: Another possibility is the examination of urine samples. Urine can be obtained spontaneously or with the help of a catheter. The results can also be read on a color scale of the urine test stripes. Like the milk test, the urine test only distinguishes different concentration ranges, but these are more finely graded than in the milk tests.
3. **Blood**: The most accurate but also most complex and expensive method is a blood test. It has the advantage that not only ketone bodies but also other parameters such as free fatty acids, minerals, and liver enzymes can be analyzed. In addition, the blood analysis results are evaluated in numbers and are more comparable than the color changes of test stripes. A good alternative is a rapid test by using a rapid test device, which is also used for measuring human blood sugar. A result is displayed with a drop of blood on a test strip within a few seconds.

Clinical ketosis

Depending on why there are elevated ketone body levels in the blood, we distinguish between primary and secondary clinical ketosis. For the primary form of clinical ketosis, the energy deficit itself (due to high performance and/or incorrect feeding) causes the condition. This form mainly occurs in susceptible, high-yielding dairy cows between the second and seventh weeks of lactation (Vicente et al., 2014). Secondary ketosis is caused indirectly by other diseases disease. A cow suffering from, for example, a claw disease might no longer consume a performance-based feed ration, leading to an energy deficit.

Typical symptoms

Typical of metabolic diseases, ketosis leads to a broad spectrum of symptoms. The classic symptoms at the beginning of the disease are a loss of appetite and decreased milk performance. As the disease develops, motor skills may be affected, and the excrement’s consistency becomes firmer and darker in color. The respiratory rate of sick animals increases, and they show dyspnea. Dyspnea is the medical description for breathing difficulties. Affected animals suffer from air shortage, which can occur in different situations. Due to the excretion of ketone bodies via the mucous membranes, the animals’ breath smells more or less strongly of acetone (Robinson and Williamson, 1977).

In addition, the animals undergo rapid and severe weight loss, and their general body conditions deteriorate noticeably. Furthermore, cows suffering from ketosis show increased milk fat content or an increased milk fat/protein quotient. Clinical symptoms include reduced general well-being, apathy, blindness, staggering, persistent "absent-minded" licking of the environment or overexcitability, muscle tremors, and aggressiveness (Andersson, 1984).

Effects on animal health and performance

Even in its subclinical form – if untreated – ketosis will engender health risks and reduced performance, negatively impacting milk yield and cows' fertility. For clinical cases, typical effects include infertility, udder and hoof problems, and a fatty liver. Ketosis during early lactation is usually associated with fatty liver disease. In severe cases, the liver becomes enlarged and more fragile. It then no longer performs its detoxification function, toxic compounds increase, and the central nervous system is damaged. Anorexia or even a total loss of consciousness, the so-called hepatic coma, might ensue, ending in a complete liver function failure.

Direct economic costs range from high veterinary costs to the total loss of the dairy cow, i.e., approximately € 600 to € 1.000 per cow. Moreover, producers face indirect costs from secondary diseases such as fatty liver disease, increased postpartum behavior such as uterine infections, abomasum dislocations, or claw diseases.

Ketosis prevention: feeding and targeted supplementation

Feeding strategy

As part of the preparatory feeding, both dry and pregnant cows should receive rations that lead to an optimal (and not maximum) body condition at the time of calving. Animals with a poorer nutritional status do not have enough body fat reserves to compensate for lack of energy in the first phase of lactation. In more cases, animals have a too high BCS, leading to a risk of difficult births, and the cows have too little appetite at the beginning of lactation. These cows tend to show an excessive mobilization of fat reserves and develop a fatty liver. So prevention of ketosis of the current lactation starts with preventing a too-high BCS in the middle of the previous lactation.

The aim of feeding measures is to keep the lactating cow's discrepancy between nutrient requirements and nutrient uptake as low as possible when the genetically determined performance potential is exhausted. For this reason, the ration must have a certain minimum energy density (high-quality forage and appropriate concentrate supplements). Also, anything that prevents the cows from ingesting the maximum amount of dry matter should be avoided.

Ket-o-Vital bolus for metabolic support

Another important preventive measure is the specific support of the calving cow's liver, rumen, and immune system. EW Nutrition's Ket-o-Vital Bolus was explicitly designed to reduce the risk of ketosis. It contains fast-available glucogenic substances, positively influencing the cow's energy metabolism. Another advantage the bolus offers is the slow release of the contained cobalt, selenium, niacin, and active yeast:

- Cobalt is a trace element important to form cobalamin, the so-called vitamin B12. It is essential for blood formation and the functioning of the nervous system.
- Selenium protects cells from oxidative damage and ensures an intact immune defense;
- Niacin is a B vitamin that intervenes in energy metabolism and prevents fatty liver syndrome;
- And active yeast supports rumen health, preventing rumen acidosis and increasing feed intake.

The application of the Ket-o-Vital Bolus is profitable and straightforward. Only one bolus per application is required.

Ketosis control: be one step ahead

High-performance dairy cows are at risk of ketosis, which results in involuntary culling, poor health, and performance losses. Advanced feed management practices combined with the targeted use of the Ket-o-Vital bolus offer a solution for preventing this debilitating disease. The bolus protects the cows from clinical and subclinical ketosis, reduces metabolic disorders, increases appetite, and improves health – leading to a quick recovery and ensuring profitable production.

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Respiratory disease – the biggest problem in horses

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The respiratory tract in horses is prone to various problems, ranging from allergic reactions and inflammation to infections. Through early diagnosis, appropriate treatment, and preventive measures, horse owners can help maintain the respiratory health of their horses and promote their well-being and performance.

Respiratory diseases are a constant topic of suffering and irritation among horse owners. According to a study published in 2005, respiratory diseases account for about 40 % of all equine internal diseases recorded worldwide (Thein 2005).

The high-performance organ: the horse’s lung

The respiratory tract of our horses is a high-performance system with a large exchange surface between the inside of the body and the environment. The lungs enable the so-called gas exchange, i.e., the transfer of oxygen from the air into the horse´s bloodstream. Only when this gas exchange functions properly can the horse supply its muscles with sufficient oxygen.

Even at rest, about 50 to 80 liters of air per minute enter the lungs of a 600 kg horse. With increasing load, this value can rise up to 2.000 liters per minute at maximum load. If a horse is healthy, it breathes calmly and slowly and takes eight to sixteen deep breaths per minute.

In order to protect the lungs as best as possible from harmful influences, the entire respiratory tract is equipped with a special mucous membrane. When irritated by pathogens or foreign bodies, for example, this mucous membrane forms more mucous and transports it towards the mouth cavity with the help of the finest cilia. In this way, most harmful particles are usually intercepted quickly, reliably and, above all, effectively and, if necessary, coughed up before they can even reach the alveoli and cause damage there.

The most common causes of respiratory diseases in horses

Chronic obstructive bronchitis

Chronic obstructive bronchitis is better known as COB or equine asthma. COB is more common in horses that are regularly kept in dusty or poorly ventilated environments, such as cramped stables or pastures with high levels of mold. Inhalation of dust particles and allergens can cause inflammation of the respiratory tract, resulting in coughing, increased mucus expectoration and breathing difficulties. The clinical picture of COB can vary greatly. From occasional poor performance in show horses to chronic coughing with purulent nasal discharge or significant weight loss.

Tracheitis

Another common respiratory disease in horses is tracheitis. This disease is often caused by bacterial or viral infections. Young horses, older horses or those with a weakened immune system are particularly susceptible to tracheitis. Besides infections, irritating factors such as dust, smoke or chemicals can also irritate the mucous membrane of the trachea and trigger inflammation.

Hay fever

Hay fever, also know as allergic respiratory disease or allergic rhinitis, is a common condition that can also affect horses. Like humans, it is an allergic reaction to certain pollens, molds or other environmental allergens that are suspended in the air. Common signs include sneezing, a runny nose and itchy eyes. However, some horses may also suffer from coughing or respiratory symptoms. Hay fever in horses can occur seasonally, depending on the pollen seasons. Depending on the region and season, the symptoms may be more serve during spring, summer or autumn.

Asthma

Asthma in horses, also known as equine asthma or heaves, is a chronic respiratory disease that occurs mainly in horses. It is similar to in many ways to asthma in humans. The main cause of this disease is hypersensitivity of the respiratory tract to dust, allergens or mold spores in the horse´s environment.

Respiratory distress or harmless rattling?

Horse owners know it – the four-legged friends have an impressive range of breathing sounds. But which are harmless, such as the exited trumpeting through the nostrils during a fright? And which ones could be symptoms of a respiratory disease?

Diagnosing respiratory problems in horses can be challenging because symptoms can often be non-specific and/or show signs similar to several diseases.

Snorting: When horses snort, it is a sign of relaxation. There is usually no cause for concern. Quite the opposite.

Snorting at gallop: Many horses snort rhythmically at a gallop. This is also considered harmless. Snorting is particularly common in thoroughbreds.

Coughing, for example when trotting: Occurs so often that it is often perceived as normal. But it is not. Coughing is always an alarm sign and can indicate an allergy, asthma or a viral or bacterial infection.

Whistling when inhaling: To be on the safe side, a veterinarian should be consulted.

Consequences of respiratory disease

Respiratory disease in horses can have significant economic consequences. If a horse suffers from chronic obstructive bronchitis or another respiratory disease, this can lead to various problems:

- Veterinary costs: The diagnosis and treatment of respiratory diseases often require veterinary visits, medication, and possibly further examinations such as x-rays or endoscopy.
- Reduced performance: A horse with respiratory problems may be severely limited in its performance. It may have difficulty breathing, which can have a negative effect on its athletic performance, equestrian work, or other activities.
- Downtime: During the treatment or recovery period, horses may have to take a break or be taken out of training. This may result in loss of income, especially if the horse was intended for competition or showing.
- Decrease in value: A horse with chronic respiratory problems may lose its value as a sport or breeding horse. Selling price might decrease and the demand for such a horse might decrease too.

To minimize economic impact, early diagnosis and treatment is important, as the implementation of appropriate preventive measures to reduce the risk of respiratory disease.

Prevention

Prevention of equine cough is of big importance to reduce the incidence and severity of the disease.

Clean stable environment

Dust is a common trigger of respiratory symptoms in horses. Regular removal of dust, dirt and mold spores from the stable and horse boxes can help to improve air quality and reduce respiratory stress.

Pasture management

When possible, horses should be allowed access to fresh pastures. The natural outdoor environment helps horses breathe cleaner air and inhale fewer harmful particles.

Hay feeding

Choosing high quality, low dust hay can reduce exposure to allergens. Moist soaking of hay before feeding can also help reduce dust levels.

Ventilation in the stable

Good ventilation in stables is essential to avoid stagnant air and dust accumulation. The use of fans or natural ventilation systems can improve air circulation.

Feed management

Feeding high quality feed that is free of mold and allergens can reduce the risk of respiratory problems. It is important to adjust feed rations to the individual needs of each horse.

Supplements

Supplements can play a positive role in the prevention of respiratory problems in horses if they are used selectively and with expert advice.

- Immune system support: Supplements such as vitamins, minerals and antioxidants can strengthen the immune system. A healthy immune system helps the horse to better defend itself against infections and inflammation of the respiratory tract.
- Certain supplements contain ingredients with anti-inflammatory properties, such as omega-3-fatty acids or herbal extracts. These can help reduce inflammation in the respiratory tract and thus reduce the risk of respiratory problems.
- Supporting respiratory health: Some supplements on the market have been specially designed to support respiratory function. They can help to regulate mucus production, improve respiratory protection, and facilitate the expectoration of mucus.
- Strengthening lung capacity: Certain ingredients in supplements can support the horse´s lung capacity and promote better oxygen uptake, which is important for performance and respiratory health.

Conclusion

If there are noticeable breathing sounds, coughing, fever or a drop in performance, the vet should come quickly. A respiratory disease tends to develop into a long-term problem if it is not treated appropriately. Without treatment, it can become chronic in some cases. Fresh air and species-appropriate husbandry, as well as feed that is free of mold und dust, are the first steps to supporting the normal function of your horse´s respiratory tract. Supplements can be an excellent tool for prevention. A holistic approach to equine health is crucial. This includes proper stable and feed hygiene, sufficient exercise, and good air quality in stables.

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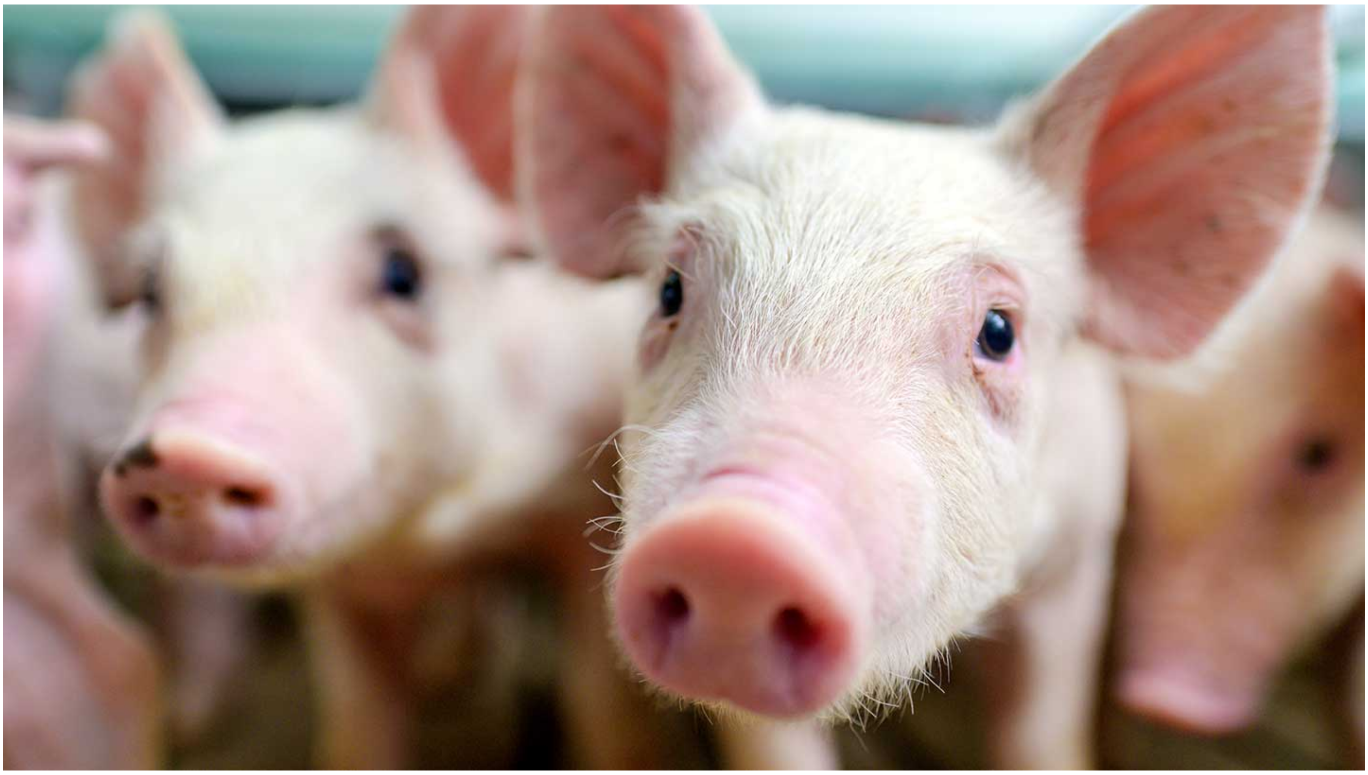
Minimizing Collateral Effects of Antibiotic Administration in Swine

Farms: A Balancing Act



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We care for our animals, and antibiotics are a crucial component in the management of disease due to susceptible pathogens, supporting animal health and welfare. However, the administration of antibiotics in pig farming has become a common practice to prevent bacterial infections, reduce economic losses, and increase productivity.

All antibiotic applications have collateral consequences of significance, bringing a deeper consideration to their non-essential application. This article aims to challenge the choice to administer antibiotics by exploring the broader impact that antibiotics have on animal and human health, economies, and the environment.

Antibiotics disrupt microbial communities

Antibiotics do not specifically target pathogenic bacteria. By impacting beneficial microorganisms, they disrupt the natural balance of microbial communities within animals. They reduce the microbiota diversity and abundance of all susceptible bacteria – beneficial and pathogenic ones… many of which play crucial roles in digestion, brain function, the immune system, and respiratory and overall health. Resulting microbiota imbalances may present themselves in animals showing health performance changes associated with non-target systems, including the nasal, respiratory, or gut microbiome[10, 9, 16]. The gut-respiratory microbiome axis is well-established in mammals. Gut microbiota health, diversity, and nutrient supply directly impact respiratory health and function[15]. In pigs specifically, the modulation of the gut microbiome is being considered as an additional tool in the control of respiratory diseases such as PRRS due to the link between the digestion of nutrients, systemic immunity, and response to pulmonary infections[12].

The collateral effect of antibiotic administration disrupting not only the microbial communities throughout the animal but also linked body systems needs to be considered significant in the context of optimal animal health, welfare, and productivity.

Antibiotic use can lead to the release of toxins

The consideration of the pathogenesis of individual bacteria is critical to mitigate potential for direct collateral effects associated with antibiotic administration. For example, in cases of toxin producing bacteria, when animals are medicated either orally or parenterally, mortality may increase due to the associated release of toxins when large numbers of toxin producing bacteria are killed quickly[3].

Modulation of the brain function can be critical

Numerous animal studies have investigated the modulatory role of intestinal microbes on the gut-brain axis. One identified mechanism seen with antibiotic-induced changes in fecal microbiota is the decreased concentrations of hypothalamic neurotransmitter precursors, 5-hydroxytryptamine (serotonin), and dopamine[6]. Neurotransmitters are essential for communication between the nerve cells. Animals with oral antibiotic-induced microbiota depletion have been shown to experience changes in brain function, such as spatial memory deficits and depressive-like behaviors.

Processing of waste materials can be impacted

Anaerobic treatment technology is well accepted as a feasible management process for swine farm wastewater due to its relatively low cost with the benefit of bioenergy production. Additionally, the much smaller volume of sludge remaining after anaerobic processing further eases the safe disposal and decreases the risk associated with the disposal of swine waste containing residual antibiotics[5].

The excretion of antibiotics in animal waste, and the resulting presence of antibiotics in wastewater, can impact the success of anaerobic treatment technologies, which already could be demonstrated by several studies[8, 13]. The degree to which antibiotics affect this process will vary by type, combination, and concentration. Furthermore, the presence of antibiotics within the anaerobic system may result in a population shift towards less sensitive microbes or the development of strains with antibiotic-resistant genes[1, 14].

Antibiotics can be transferred to the human food chain

Regulatory authorities specify detailed withdrawal periods after antibiotic treatment. However, residues of antibiotics and their metabolites may persist in animal tissues, such as meat and milk, even after this period. These residues can enter the human food chain if not adequately monitored and controlled.

Prolonged exposure to low levels of antibiotics through the consumption of animal products may contribute to the emergence of antibiotic-resistant bacteria in humans, posing a significant public health risk.

Contamination of the environment

As already mentioned before, the administration of antibiotics to livestock can result in the release of these compounds into the environment. Antibiotics can enter the soil, waterways, and surrounding ecosystems through excretions from treated animals, inappropriate disposal of manure, and runoff from agricultural fields. Once in the environment, antibiotics can contribute to the selection and spread of antibiotic-resistant bacteria in natural bacterial communities. This contamination poses a potential risk to wildlife, including birds, fish, and other aquatic organisms, as well as the broader ecological balance of affected ecosystems.

Every use of antibiotics can create resistance

One of the widely researched concerns associated with antibiotic use in livestock is the development of antibiotic resistance. The development of AMR does not require prolonged antibiotic use and, along with other collateral effects, also occurs when antibiotics are used within recommended therapeutic or preventive applications.

Gene mutations can supply bacteria with abilities that make them resistant to certain antibiotics (e.g., a mechanism to destroy or discharge the antibiotic). This resistance can be transferred to other microorganisms, as seen with the effect of carbadox on Escherichia coli[7] and Salmonella enterica[2] and the carbadox and metronidazole effect on *Brachyspira hyodysenteriae*[16]. Additionally, there is an indication that the zinc resistance of Staphylococcus of animal origin is associated with the methicillin resistance coming from humans[4].

Consequently, the effectiveness of antibiotics in treating infections in target animals becomes compromised, and the risk of exposure to resistant pathogens for in-contact animals and across species increases, including humans.

Alternative solutions are available

To successfully minimize the collateral effects of antibiotic administration in livestock, a unified strategy with support from all stakeholders in the production system is essential. The European Innovation Partnership – Agriculture[11] concisely summarizes such a process as requiring…

1. Changing human mindsets and habits: this is the first and defining step to successful antimicrobial reduction
2. Improving pig health and welfare: Prevention of disease with optimal husbandry, hygiene, biosecurity, vaccination programs, and nutritional support.
3. Effective antibiotic alternatives: for this purpose, phytomolecules, pro/pre-biotics, organic acids, and immunoglobulins are considerations.

In general, implementing responsible antibiotic stewardship practices is paramount. This includes limiting antibiotic use to the treatment of diagnosed infections with an effective antibiotic, and eliminating their use as growth promotors or for prophylactic purposes.

Keeping the balance is of crucial

importance

While antibiotics play a crucial role in ensuring the health and welfare of livestock, their extensive administration in the agricultural industry has collateral effects that cannot be ignored. The development of antibiotic resistance, environmental contamination, disruption of microbial communities, and the potential transfer of antibiotic residues to food pose significant challenges.

Adopting responsible antibiotic stewardship practices, including veterinary oversight, disease prevention programs, optimal animal husbandry practices, and alternatives to antibiotics, can strike a balance between animal health, efficient productive performance, and environmental and human health concerns.

The collaboration of stakeholders, including farmers, veterinarians, policymakers, industry and consumers, is essential in implementing and supporting these measures to create a sustainable and resilient livestock industry.

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Coccidiostats in the European Union: Challenges and Perspectives

*by **Technical Team**, EW Nutrition*

Controlling coccidiosis has been and continuous to be a major concern for poultry operations. However, for decades, some of these control measures have been taking an increasingly visible toll on the overall health of the flocks, the economics of poultry production, and the environment itself. Regulations have been put in place to defend consumer health and animal welfare while maintaining profitability in poultry production.

In the European Union and elsewhere, coccidiostats or anticoccidials are an essential means of control and are categorized either as feed additives or as veterinary medicinal products. The category is dictated by the pharmacologically active substance, mode of action, pharmaceutical form, target species and route of application.

In the European Union, there are currently 11 different coccidiostats which have been granted 28 different authorizations as feed additives allowed for specific usage in chickens, turkeys, and rabbits.

Coccidiostats: the basics

Compounds designed to kill the coccidial population are known as coccidiocidal; those designed to prevent the replication and development of coccidia are known as coccidiostats. Quite often, coccidiostat or anticoccidial is the term used to describe both categories.

Coccidiostats are antimicrobial compounds which either inhibit or destroy the protozoan parasites that cause coccidiosis in livestock. Each coccidiostat has individual inhibitory mechanisms. In the case of ionophores, the compounds affect transmembrane ion transport. In the case of synthetic compounds, the molecules' mode of action is varied and, in some cases, not even entirely known (Patyra et al., 2023).

The production, manufacture, and marketing of coccidiostats, premixes with coccidiostats, and feed with coccidiostats are regulated by the Regulation (EC) No 183/2005 of the European Parliament and of the Council of 12 January 2005 laying down requirements for feed hygiene.

Coccidiostat categories

Coccidiostats fall under two categories:

Ionophores

Ionophores, sometimes called polyether ionophore antibiotics, are substances which contain a polyether group and are of bacterial origin. They are produced by fermentation with several strains of *Streptomyces* spp and *Actinomadura* spp. Six substances are allowed in the EU:

- monensin sodium (MON)
- lasalocid sodium (LAS)
- maduramicin ammonium (MAD)
- narasin (NAR)
- salinomycin sodium (SAL)
- semduramicin sodium (SEM)

Synthetic

Synthetic compounds include:

- decoquinate (DEC)
- diclazuril (DIC)
- halofuginone (HFG)
- nicarbazin (NIC)
- robenidine hydrochloride (ROB)

EU authorizations for ionophores are granted under specific conditions of usage, including animal category, minimum and maximum dosage, MRL (Maximum Residue Limits), and withdrawal periods.

Regulation (EC) No 1831/2003 [13] of the European Parliament and of the Council of 22 September 2003 distinguishes between coccidiostats and antibiotics used as growth promoters. Unlike the antibiotic growth promoters (forbidden in the EU since 2006), whose primary action site is the gut microflora, coccidiostats only have a secondary and residual activity against the gut microflora. That still signals that they have the potential to trigger resistance and to alter the natural balance and immune response of the farmed animals. Their potential to cause resistance has been widely acknowledged by science and practitioners alike (see below).

Why were some antimicrobial growth promoters withdrawn in 1997-1998 – but not others?

Five designated “antibiotic feed additives” were prohibited in 1997-98: Avoparcin, Bacitracin zinc, Spiramycin, Virginiamycin, and Tylosin phosphate. The EU withdrew their authorization in order to “help decrease resistance to antibiotics used in medical therapy”. The motivation specified that these antibiotics belonged to classes of compounds also used in human medicine.

On the other hand, the EU at the time allowed the remaining antibiotics for use in feed as they did not belong to classes of compounds used in human medicine. That, of course, did not mean that resistance did not develop in birds.

The Commission did acknowledge the need to phase out the remaining antibiotics. At the same time, it stated that the use of coccidiostats would not presently be ruled out “even if of antibiotic origin” (MEMO/02/66, 2022). The reason was that “hygienic precautions and adaptive husbandry measures are not sufficient to keep poultry free of coccidiosis. Modern poultry husbandry is currently only practicable if coccidiosis can be prevented by inhibiting or killing parasites during their development.”

In other words, the Commission acknowledged that the only reason ionophores were still authorized was that it believed there were no other means of controlling coccidiosis in profitable poultry production.

What issues are raised by current coccidiosis control measures?

In its 2022 Position Paper on Coccidia Control in Poultry, the European Veterinaries Federation states that “challenges in coccidia control are due to parasitic and bacterial drug (cross-)resistance. Coccidiostats also interact with other veterinary medicinal products and have a secondary residual activity against gram-positive bacteria” (FVE, 2022).

Resistance

Ever since 1939, when sulphanilamide was shown to cure coccidiosis in chickens, the industry increased the use of similar (chemical) compounds. It quickly added sulfaquinoxaline, then nitrofurazone and 3-

notroroxarsone, amprolium and nicarbazin (Martins et al., 2022).

Prior to the introduction of the first ionophore, monensin, in the early 1970s, producers only had synthetic (non-ionophores) coccidiostats, characterized by rapid parasite resistance development. With the addition of ionophores, poultry operations started to rotate products between production cycles, or to use shuttle programs, with the express purpose of controlling the development of resistance. Synthetic compounds can, however, result in increased resistance in the long run (Martins et al., 2022). Moreover, studies in farmed animals indicate that sometimes even single use of antibiotics can promote the selection of resistant bacterial strains.

Another issue is the design of the rotation system, which, some researchers claim, could only delay the appearance of resistance (Daeseleire et al., 2017).

To make matters worse, for instance in the case of broilers, coccidiostats are generally administered throughout life to protect against re-infection. This may also lead to the next item on the list.

Residues

Regulation (EC) No 1831/2003 establishes Maximum Residue Limits (MRLs) for residues of an additive in relevant foodstuffs of animal origin. The goal is to control the use of coccidiostats in feed and ensure that there is no excess residue that ends up on the consumers' plate.

Broilers can be fed with coccidiostats throughout life, with the exception of a certain withdrawal period before slaughter. Cross-contamination of feed batches and residue formation in edible tissues of nontarget species represent valid concerns for end consumers.

Coccidiostats in food have been regulated in the Commission Regulation (EC) No 124/2009, including maximum levels for meat ranging between 2 µg/kg (monensin, salinomycin, semduramycin, and manduramycin) and 100 µg/kg (nicarbazin in liver and kidney). However, Daeseleire et al. state that “in the period 2011–14, noncompliant results were reported for maduramycin, monensin, diclazuril, lasalocid, nicarbazin, robenidine, salinomycin, narasin, semduramicin, decoquinate, halofuginone, and toltrazuril. The matrices/animals species affected were in descending order eggs, poultry, farmed game, horses, pigs, and sheep/goat (EURL workshop, 2015)”. Residues in eggs are widely seen as a serious concern (Bello et al., 2023). The fact that regulations are in place constitute no safeguard against defective practices.

What alternatives to coccidiostats does the EU support?

Vaccination

Coccidiosis vaccines have been in use for the last three decades. They are based on precocious oocysts and are commonly used in breeding and laying birds, and the use in broilers is steadily increasing. There is a limited number of vaccines authorized in the EU. As vaccines are relatively costly to apply, vaccination is typically performed during 2-3 cycles only, afterwards reverting to the use of coccidiostats, which leads to a suppression of the precocious vaccine-origin strains, allowing persistent coccidiostat-resistant field strains to flourish.

Herbal products (phytomolecules)

Phytomolecules have been widely used for a variety of poultry gut health issues. Their usage in flocks at risk of coccidiosis is predicated on their ability to strengthen the natural defenses of the animal. Infection severity and consequences depend to a large extent on co-infections, gut health, and the general immunity of the bird.

Prescription veterinary medicines

Toltrazuril, amprolium, and some sulfamides (sulfamiderazin, sulfadimethoxin, trimethoprime) are used against (clinical) coccidiosis outbreaks. However, these medicines are also prone to triggering resistance and should not be widely used. Moreover, they are used when coccidiosis is already manifest on the farm, so they do not prevent economical and performance losses.

Other research

There is limited research on acidifiers, enzymes, prebiotics or probiotics acting as defenses against infection. Furthermore, oocysts are highly resistant to the common disinfectants, but there are some highly specialized types available. In general, producers are reluctant to use these methods as their benefits are limited or indemonstrable.

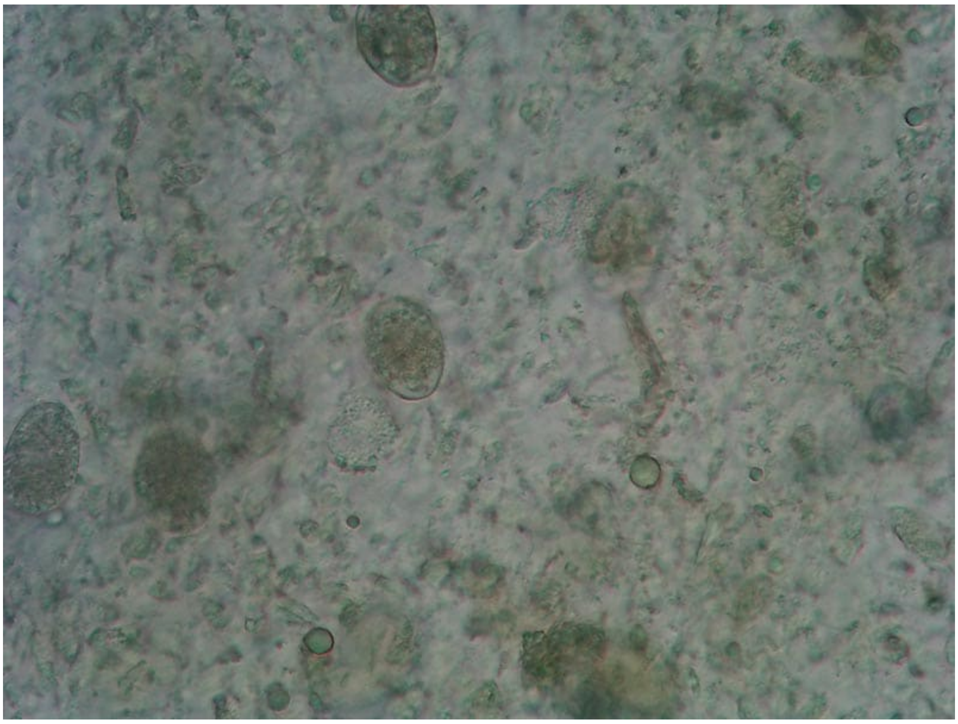
Genetic selection of the animals is also unable to offer solutions for the moment.

Ionophores as antibiotics: The U.S. case

Ionophores have demonstrated antibacterial activity (e.g., Rutkowski and Brzezinski, 2013). As opposed to their regime in the EU, where they are allowed as feed additives, in the United States, coccidiostats belonging to the polyether-ionophore class (ionophores) are not allowed in NAE (No Antibiotics Ever) and RWA (Raised Without Antibiotics) programs.

Instead of using ionophores, coccidiosis is approached by NAE/RWA US producers with a veterinary-led combination of live vaccines, synthetic compounds, phytomolecules, and farm management.

What are the perspectives of coccidiosis control?



In 2019, The European Medicines Agency (EMA) published the new Veterinary Medicinal Products Regulation (EU2019/6), emphasizing the necessity of fighting antimicrobial resistance. In response to the VMP Regulation, in November 2022, the FVE (European Veterinaries Federation) recommended tackling coccidiosis through “a combination of holistic flock health management, optimized stocking density, litter management, feeding and drinking regime as well as nutraceuticals, accompanied by appropriate biosecurity measures, vaccination and coccidiostats, where indicated”.

In its position paper, FVE advocates a “prudent and responsible use of coccidiostats”, as well as monitoring of polyether ionophores coccidiostats sales through ESVAC (European Surveillance of Veterinary Antimicrobial Consumption). European Union past experiences show that strong urges for monitoring are usually implemented and signal a need for regulation. As other countries and regions have shown excellent productivity in the absence of ionophores, it may be that, sooner or later, the EU will revise its lax attitude and embrace a stricter control of antimicrobial resistance.

FVE also recommends the development of rapid, low-cost and especially quantitative diagnostic tests for ongoing surveillance and monitoring purposes. Through fast, reliable, on-site oocyst counts, producers can cut cost and time resources and improve reaction time to preserve the health of their flocks.

From a scientific perspective, considering the range of micro-organisms affected, ionophores can be seen as antibiotics, with the usual associated risks for cross-resistance or co-selection (Wong 2019). While their current status in the European Union represents a concession to the economic security of a large and important industry, best practices in other regions show that coccidiosis can be approached holistically with solutions that reduce antimicrobial resistance and support the profitability of poultry operations.

Bio-shuttle with natural anticoccidial additives: the all-encompassing solution

As producers optimize the use of biological interventions such as vaccines, their effect on broiler performance becomes more predictable and constant.

The current common practice of rotating coccidiostats fails to take advantage of the milder precocious Eimeria population that has developed within the broiler house. Instead, the use of new, natural feed additives with anticoccidial activity that is directly related to the coccidiostat-resistant Eimeria (field) strains, as well as the precocious Eimeria strains, can help to maintain a favorable ratio between mild precocious and more virulent field strains. This can help increase the number of cycles that benefit from the vaccinations applied, even when discontinuing vaccination. Careful monitoring of oocyst shedding patterns, preferably accompanied by gut health and coccidiosis lesion scoring and performance monitoring, can guide the producer on the right time to restart vaccination and repeat the same rotation program.

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From basketball to feed milling: a common tactic for winning in 2023

*By **Ivan Ilic**, Global Manager Technical Product Applications, EW Nutrition*

It has been a rough couple of years for the world. And from climate change to war, all negative impacts have reverberated down to feed millers.

- Climate change affected raw material prices and availability
- COVID-19 impacted shipping costs and manpower
- War impacted energy prices and raw material availability

And that´s without even considering market trends toward sustainability, shifting resources to biofuel, and so on.

With all these challenges going on, working to improve feed mill efficiency has lately kept me extremely busy. I´ve been traveling and talking to customers around the world about SurfAce and how we bring benefits in energy cost savings, process efficiency, moisture optimization, and so on. But when I am at home, I take a walk every evening in the woods near my house. I often use the time to reflect on personal and professional issues.

At some point, I found myself thinking about the European Basketball Championship (in Serbia, basketball is a national sport). Last year, the head coach of the Serbian national team decided not to call one of our best players to the national team. Lots of people criticized this decision, as for the past few years he had been one of the top players in Europe.

So, I started to think about choosing a team over a star. How do you balance your strong points to make sure of a win? (Yes, there is a connection to feed mills. I´m getting there.)

Winning through strategy rather than showmanship

Bozidar Maljkovic is a Serbian legend, who trained several winning teams, among which the European champion team Limoges. This was a French team he picked up mid-season, with moderate resources on the basketball court as well as outside it. The entire 1993 Euro season, Maljkovic chose to play extreme defense and score a very low number of points. In the finals, he played against a big favorite: Benneton Treviso, a wealthier team that, at that time, had a roster of excellent players. He won the game using the same strategy: tight defense, highly tactical game. A championship won not on artistic merit but on strategy.

After that final game, his good friend and well-known coach of Treviso, Petar Skansi, accused Maljkovic that he was destroying the basketball game with that tactic. Maljkovic answered to Skansi in more or less these words: you give me Kukoc (Treviso´s best player) and I´ll win on a different tactic.

When I remembered this episode during my walk, I suddenly saw a pattern in basketball coaching and feedmill management.

Know your objective

As in basketball, in feed milling you must be clear about your target, your main objective. In Maljkovic´s case, the objective was not to make basketball games attractive for the public, just as it was not to his objective to showcase his players. His target was to win the Euro title.

The same goes for the feed mill. Sure, you have several objectives, but there must be a main one. Say your primary objective is to maximize profit. If that is the case, then the next step is to be sure of what the market demands. This way you can avoid spending money for added value on something that the market is unwilling to pay for.

Know your players

Once you know what outcome you can deliver and what the market is prepared to pay for, the next step is analytics.

You must dive deep into your feed mill and get all the data on your “players”: raw materials, technology, people, machines, parameters, logistics etc. You must understand the current status and capabilities of your players, with advantages and limitations. Your job is to use them to the best of their capabilities in order to achieve your objective.

Know the interconnections between players

Just as every player depends on others, also feed mill processes are related and interdependent. If you want to have fine grinding, you will achieve better PDI, but it will cost more energy in milling and the result may not be as good for some categories of animals. Is this efficient and acceptable? It all depends on your main objective.

Balancing between pros and cons and walking that thin line is what efficiency means. With these challenges looming large, finding that balance will be the main task in feed milling.

Be curious

“Be curious” is one of the values of our company, but I would prompt anyone to adopt it. Play with parameters, support operators to do it, and find the point that yields maximum return for your specific objective.

Literature without your own data is fiction. In literature you can find data that says, for instance, that for every 15°C you have 1% more moisture. You can also find literature that says you have 1% more moisture for every 12°C or every 17°C. But what is the ratio in your feedmill? If you do not know, you are still not diving deep enough.

You need to figure out the interconnected factors in your own production. If you calculate by the books and official recommendations, you are adjusting work in some other feed mill, not yours. Yes: guidance is very important to understand relations and to be aware of margins. But inside those margins, you have to find your own numbers.

Find the least opportunity cost

Very often I see goals that are rebels without a cause. Take PDI, for instance. PDI is an important value, no doubt. It has been shown that better PDI correlates with better FCR etc.

However, when you set a target value for PDI you need to be sure that future investment in increasing PDI is relevant to your customers – and that they are willing to pay for that. Even if you are an integrator, first do the math on the benefits and the cost. With rising costs not just for you but also for your end customers, make sure the market can support the premium you are struggling to deliver. If you are sure, then find the most adequate way to win it. You can increase your PDI in lots of different ways, so you will need to calculate the least opportunity cost.

Production is a game of interdependencies. So is any team sport, in fact. When a coach makes a decision to put a star player in the spotlight, there may be a show but not always a win.

In a feed mill, the end game is always played around winning. It is a complex tactic of balancing all players and getting the most in your very specific circumstances. Our job is to identify and maximize these „synergies” in each specific case – and I can confirm that each case is different. In the end, Kukoc may have played the same game in Jugoplastika or Treviso, but no two feed mills are quite the same; even in same feed mill, no two lines will be adjusted the same way.

The future of coccidiosis control

*By **Madalina Diaconu**, Product Manager Pretect D, EW Nutrition and*

With costs of over 14 billion USD per year (Blake, 2020), coccidiosis is one of the most devastating enteric challenges in the poultry industry. With regard to costs, subclinical forms of coccidiosis account for the majority of production losses, as damage to intestinal cells results in lower body weight, higher feed conversion rates, lack of flock uniformity, and failures in skin pigmentation. This challenge can only be tackled, if we understand the basics of coccidiosis control in poultry and what options producers have to manage coccidiosis risks.

Current strategies show weak points

Good farm management, litter management, and coccidiosis control programs such as shuttle and rotation programs form the basis for preventing clinical coccidiosis. More successful strategies include disease monitoring, strategic use of coccidiostats, and increasingly coccidiosis vaccines. However, the intrinsic properties of coccidia make these parasites often frustrating to control. Acquired resistance to available coccidiostats is the most difficult and challenging factor to overcome.

Optimally, coccidiosis control programs are developed based on the farm history and the severity of infection. The coccidiostats traditionally used were chemicals and ionophores, with ionophores being polyether antibiotics. To prevent the development of resistance, the coccidiostats were used in shuttle or rotation programs, at which in the rotation program, the anticoccidial changes from flock to flock, and in the shuttle program within one production cycle (Chapman, 1997).

The control strategies, however, are not 100% effective. The reason for that is a lack of diversity in available drug molecules and the overuse of some molecules within programs. An additional lack of sufficient coccidiosis monitoring and rigorous financial optimization often leads to cost-saving but only marginally effective solutions. At first glance, they seem effective, but in reality, they promote resistance, the development of subclinical coccidiosis, expressed in a worsened feed conversion rate, and possibly also clinical coccidiosis.

Market requests and regulations drive coccidiosis control strategies

Changing coccidiosis control strategies has two main drivers: the global interest in mitigating antimicrobial resistance and the consumer's demand for antibiotic-free meat production.

Authorities have left ionophores untouched

Already in the late 1990s, due to the fear of growing antimicrobial resistance, the EU withdrew the authorization for Avoparcin, Bacitracin zinc, Spiramycin, Virginiamycin, and Tylosin phosphate, typical growth promoters, to "help decrease resistance to antibiotics used in medical therapy". However, ionophores, being also antibiotics, were left untouched: The regulation (EC) No 1831/2003 [13]of the European Parliament and the Council of 22 September 2003 clearly distinguished between coccidiostats and antibiotic growth promoters. Unlike the antibiotic growth promoters, whose primary action site is the gut microflora, coccidiostats only have a secondary and residual activity against the gut microflora. Furthermore, the Commission declared in 2022 that the use of coccidiostats would not presently be ruled out "even if of antibiotic origin" (MEMO/02/66, 2022) as "hygienic precautions and adaptive husbandry measures are not sufficient to keep poultry free of coccidiosis" and that "modern poultry husbandry is currently only practicable if coccidiosis can be prevented by inhibiting or killing parasites during their development". In other words, the Commission acknowledged that ionophores were only still authorized because it believed there were no other means of controlling coccidiosis in profitable poultry production.

Consumer trends drove research on natural solutions

Due to consumers' demand for antibiotic-reduced or, even better, antibiotic-free meat production, intensified industrial research to fight coccidiosis with natural solutions has shown success. Knowledge, research, and technological developments are now at the stage of offering solutions that can be an effective part of the coccidia control program and open up opportunities to make poultry production even more sustainable by reducing drug dependency.

Producers from other countries have already reacted. Different from the handling of ionophores regime in the EU, where they are allowed as feed additives, in the United States, coccidiostats belonging to the polyether-ionophore class are not permitted in NAE (No Antibiotics Ever) and RWE (Raised Without Antibiotics) programs. Instead of using ionophores, coccidiosis is controlled with a veterinary-led combination of live vaccines, synthetic compounds, phytomolecules, and farm management. This approach can be successful, as demonstrated by the fact that over 50% of broiler meat production in the US is NAE. Another example is Australia, where the two leading retail store chains also exclude chemical coccidiostats from broiler production. In certain European countries, e.g., Norway, the focus is increasingly on banning ionophores.

The transition to natural solutions needs knowledge and finesse

In the beginning, the transition from conventional to NAE production can be difficult. There is the possibility to leave out the ionophores and manage the control program only with chemicals of different modes of action. More effective, however, is a combination of vaccination and chemicals (bio-shuttle program) or the combination of phytomolecules with vaccination and/or chemicals (Gaydos, 2022).

Coccidiosis vaccination essentials

When it is decided that natural solutions shall be used to control coccidiosis, some things about vaccination must be known:

1. There are different strains of vaccines, natural ones selected from the field and attenuated strains. The formers show medium pathogenicity and enable a controlled infection of the flock. The latter, being early mature lower pathogenicity strains, usually cause only low or no post-vaccinal reactions.
2. A coccidiosis program that includes vaccination should cover the period from the hatchery till the end of the production cycle. Perfect application of the vaccines and effective recirculation of vaccine strains amongst the broilers are only two examples of preconditions that must be fulfilled for striking success and, therefore, early and homogenous immunity of the flock.
3. Perfect handling of the vaccines is of vital importance. For that purpose, the personnel conducting the vaccinations in the hatchery or on the farms must be trained. In some situations, consistent high-quality application at the farm has shown to be challenging. As a result**,** interest in vaccine application at the hatchery is growing.

Phytochemicals are a perfect tool to complement coccidiosis control programs

As the availability of vaccines is limited and the application costs are relatively high, the industry has been researching supportive measures or products and discovered phytochemicals as the best choice. Effective phytochemical substances have antimicrobial and antiparasitic properties and enhance protective immunity in poultry infected by coccidiosis. They can be used in rotation with vaccination, to curtail vaccination reactions of (non-attenuated) wild strain vaccines, or in combination with chemical coccidiostats in a shuttle program.

In a recent review paper (El-Shall et al., 2022), natural herbal products and their extracts have been described to effectively reduce oocyst output by inhibiting Eimeria species’ invasion, replication, and development in chicken gut tissues. Phenolic compounds in herbal extracts cause coccidia cell death and lower oocyst counts. Additionally, herbal additives offer benefits such as reducing intestinal lipid peroxidation, facilitating epithelial repair, and decreasing Eimeria-induced intestinal permeability.

Various phytochemical remedies are shown in this simplified adaptation of a table from El-Shall et al. (2022), indicating the effects exerted on poultry in connection to coccidia infection.

Bioactive compound	**Effect**
Saponins	*Inhibition of coccidia:* By binding to membrane cholesterol, the saponins disturb the lipids in the parasite cell membrane. The impact on the enzymatic activity and metabolism leads to cell death, which then induces a toxic effect in mature enterocytes in the intestinal mucosa. As a result, sporozoite-infected cells are released before the protozoa reach the merozoite phase.*Support for the chicken:* Saponins enhance non-specific immunity and increase productive performance (higher daily gain and improved FCR, lower mortality rate). They decrease fecal oocyst shedding and reduce ammonia production.
Tannins	*Inhibition of coccidia:* Tannins penetrate the coccidia oocyst wall and inactivate the endogenous enzymes responsible for sporulation.*Support for the chicken:* Additionally, they enhance anticoccidial antibodies’ activity by increasing cellular and humoral immunity.

Flavonoids and terpenoids	*Inhibition of coccidia:* They inhibit the invasion and replication of different species of coccidia.*Support for the chicken:* They bind to the mannose receptor on macrophages and stimulate them to produce inflammatory cytokines such as IL-1 through IL-6 and TNF. Higher weight gain and lower fecal oocyst output are an indication of suppression of coccidiosis.
Artemisinin	*Inhibition of coccidia:* Its impact on calcium homeostasis compromises the oocyst wall formation and leads to a defective cell wall and, in the end, to the death of the oocyst. Enhancing the production of ROS directly inhibits sporulation and also wall formation and, therefore, affects the Eimeria life cycle.*Support for the chicken:* Reduction of oocyst shedding
Leaf powder of Artemisia annua	*Support for the chicken:* Protection from pathological symptoms and mortality associated with Eimeria tenella infection. Reduced lesion score and fecal oocyst output. The leaf powder was more efficient than the essential oil, which could be due to a lack of Artemisinin in the oil, and to the greater antioxidant ability of A. annua leaves than the oil.
Phenols	*Inhibition of coccidia:* Phenols change the cytoplasmic membrane’s permeability for cations (H+ and K+), impairing essential processes in the cell. The resulting leakage of cellular constituents leads to water unbalance, collapse of the membrane potential, inhibition of ATP synthesis, and, finally, cell death. Due to their toxic effect on the upper layer of mature enterocytes of the intestinal mucosa, they accelerate the natural renewal process, and, therefore, sporozoite-infected cells are shed before the coccidia reaches the merozoite phase.

Table 1: Bioactive compounds and their anticoccidial effect exerted in poultry

Consumers vote for natural – phytochemicals are the solution

Due to still rising antimicrobial resistance, consumers push for meat production without antimicrobial usage. Phytomolecules, as a natural solution, create opportunities to make poultry production more sustainable by reducing dependency on harmful drugs. With their advent, there is hope that antibiotic resistance can be held in check without affecting the profitability of poultry farming.