

Sustainable antibiotic use strategies

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The industrialisation of livestock farming first saw the introduction of antibiotics in animal feed for poultry in the 1940's. Reports of up to 10% growth improvement continued to fuel their use as growth promoting agent during the following decades. Although the precise mechanisms of growth promotion triggered by antimicrobial agents still remain unclear, their use as a supplement in feed has been a defining characteristic of modern livestock farming. Nevertheless, the rise to prominence of AGPs in the animal industry came with its own share of criticism and controversy. In 1969 the Swann committee report suggested that intensive use of antibiotics in animal husbandry had led to a surge in the rate of antibiotic-resistant bacteria. During the 1990's, further evidence continued to pour in. In the 2000's in Europe, the growing awareness surrounding the risks of feed antibiotics, and the ensuing outbreaks of several animal disease led to the introduction of a range of new measures to ensure food safety. Europe enacted a total ban on the use of AGPs in animal feed, and restricted the use of antibiotics in animals to health reasons with a veterinary prescription. The drop in the sales volume of antibiotics that followed the ban of AGPs in Europe was matched by a reduction in actual exposure to antibiotics, which was measured by calculating the Animal Level of Exposure to Antimicrobials (ALEA) index. The ALEA index dropped because antibiotics today are far more efficient and require a lower dose and shorter treatment time than in the past. However, despite these improvements, the challenges associated with drug-resistant bacteria in animals persist, and continue to grow.

Returning to the dark age

In February 2019, Mr Andriukaitis, EU Commissioner for Health and Food Safety, rang the bell again. "The antimicrobial resistance shows no signs of slowing down" he said "and treatment for campylobacteriosis and salmonellosis are becoming less and less effective." Additionally, multidrug resistance (resistant to 2 to 3 antibiotics) is now found in about 30% of Salmonella in human. A review on antimicrobial resistance already reported an alarming increase of deaths related to antimicrobial resistant infections. An estimation of 10 million deaths in 2050 was given, placing this problem in

Poultry meat is the most popular source of animal protein around the world, owing to its affordability. Although AGPs were for a long time considered the most efficient solution to minimise production costs, their detrimental effects on the development of antibiotic-resistant strains of bacteria with tremendous implications for human health are worrisome.

the top position of the reasons of deaths worldwide. The associated costs will soar to \$ 100 trillion worldwide. Nowadays all specialists agree that the responsibilities of this problem are shared. From the agricultural point of view, an AGP ban by itself is not a sustainable, long-term solution, and it needs to be accompanied by appropriate biosecurity, monitoring and disease control supported by the use of modern nutritional strategies in the agricultural sector.

Biosecurity at the heart

In essence, biosecurity is all about preventing contact and the spread of microbes between animals and thus at the heart of antibiotic removal. Barns that house commercial birds should be considered a restricted access zone eligible for a tough cleaning programme.



PHOTO: JAN WILLEM SCHOUTEN

Studies showed that a selected blend of phytomolecules has the potential to be an alternative solution to antibiotics.



PHOTO: HOOS GROENWOLD

Managing birds, feed and last but not least people is of the essence. An important biosecurity measure is to limit visitors and make necessary visitors shower.

Avoiding visitors is a must! If a visit is required, visitors should have previously showered and changed clothing and footwear before entering barns. A field study led by Research Group on the Epidemiology of Zoonoses and Public Health from Montreal University was able to demonstrate that poultry operations that used external teams to remove litter or to vaccinate were respectively 8 to 13 times more at risk of having a flock infected than operations who use their internal and trained teams.

A proper cleaning and disinfection programme is essential! A complete cleaning programme between every productive cycle might require up to three entire days of work. Nevertheless, this time investment is critical to reduce the pathogenic load in the building. All steps of this process are important from wet to dry cleaning, soaking, washing, drying and disinfecting all installations (from the roof to individual equipment's feeder and water pipe system prone to biofilm development). The successive use of detergent and disinfectant will respectively guarantee the removal of all traces of organic matters together with the elimination of pathogens.

Management

Management comprises a wide range of actions to be set up once birds are placed in the barn. Among them, some critical

ones for antibiotic reduction can be highlighted

- **Management of density:** For decades, high stocking density coupled with the preventive use of antibiotics has been applied to maximise productivity. In certain regions of the globe (such as Europe) this is no longer permitted. This necessary change has pointed out that high stocking density has a negative effect on performance creating stress for animals and their intestinal microbiota. A reduction of stocking density can accompany the reduction in the use of preventive antibiotics, limiting pathogenic challenges.
- **Environmental management with ventilation:** Daily monitoring of the temperature, the humidity and associated ventilation inside the building is highly recommended. Indeed, pathogenic development is first dependent on these two parameters, that if are well controlled will avoid any over-proliferation and limit the use of therapeutic antibiotics. This monitoring being most of the time computerised, however the frequency of visits into the barn should not be underestimated.
- **Vaccination programme:** Infectious disease management with the use of vaccination is important. Vaccination programmes represent an important cost and may not totally protect birds. It also represents a particular stress for birds, inducing a reaction of the immune system most of the time generating a temporary inflammation. Circulating pro-inflammatory cytokines are known to affect voluntary feed intake. Even if this phenomenon lasts only few days, it may entail delays in growth performance first and depletion of gut mucosa by lack of nutrients. Birds will then divert energy from production to maintain gut integrity. Certain natural solutions based on plant compounds are now proven to limit the negative subclinical effects of vaccination programmes. The interest of the addition of such

Table 1 – Summary of meta-analysis of 38 broilers trials.

	Negative control	AGP treatment	XTRACT 6930	P-value
Feed intake (g/d)	81.99	84.04	84.09	0.40
Average daily gain (g/d)	48.9b	50.4a	51.3a	0.001
FCR (g/g)	1.73a	1.71ab	1.68b	0.01

additives made of turmeric and chilli pepper oleoresins (XTRACT Nature) as an adjuvant to a vaccination programme, was first evaluated by the USDA (United State Department of Agriculture) Animal Parasitic Diseases Laboratory in 2011. Results in broilers have demonstrated a boosting effect of the coccidiosis vaccination and an increase in the pool of antibodies produced in reaction to a second infection. A well controlled coccidiosis programme also opens possibilities for the reduction of coccidiostats use. Similar results were obtained with other types of vaccination programme in pullets.

Nutrition deeply involved in intestinal health

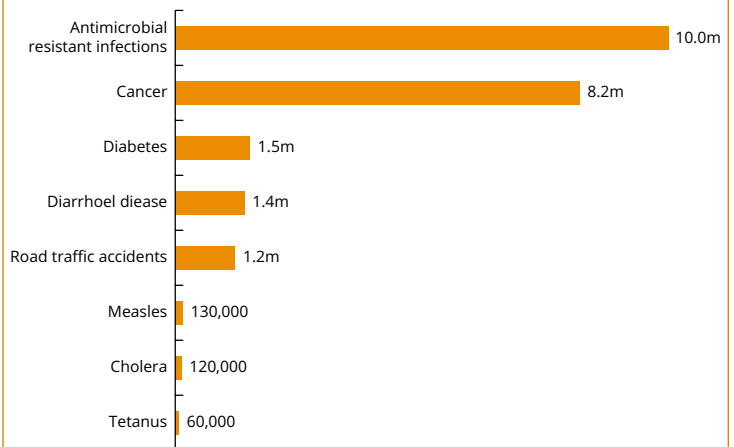
Nutrition is not only a matter of fulfilling birds' nutritional requirements. Nutrition plays an important role on birds' metabolic functions and represents an important angle of attack for a sustainable use of antibiotics.

- **Water:** a.k.a "the first nutrient": Water quality and accessibility are the first factors to be considered. Beyond its nutritional value, a proper monitoring of drunken quantities of water can be a first indicator of upcoming pathogenic outbreaks. A delicate balance between shortage of water (negatively impacting FCR) and wasted (negatively impacting litter quality) must be found. Water management is a tool to reduce the use of both preventive and therapeutic antibiotic.
- **Precision feeding:** In common practice, safety margins in nutrients are used to make sure all animals' requirements are covered. This impacts the formulation costs, increased excretion in manure and sometimes too high levels of nutrients that can affect intestinal health and require the use of an antibiotic. The withdraw of antibiotics used as preventive is frequently associated with a change in protein sources. Indeed, recent formulation models tend to recommend the use of individual synthetic amino-acids in order to reduce crude protein inclusion. This change aims to reduce the intestinal challenges associated with the digestion of proteins (e.g: intestinal inflammation, generation of heat...) and to orientate to more bioavailable amino-acids, limiting their availability for microbial fermentation.
- **Modern additives to complement precision feeding:** Poultry general health status is critical to the limitation of the use of antibiotics and intestinal health is conditioning it. Indeed it is now commonly accepted that mucosal tissues and microbial populations (super organism) are connected. Intestinal mucosa and microbiota are therefore a gateway to the internal media. The use of acidifiers to control water pH has become a common practice worldwide. There is no doubt they are essential in the elimination of antibiotics.

Additive targeting intestinal lumen

Probiotic, prebiotic and post-biotic metabolites are mainly intended to equilibrate gut microflora acting on the content of the intestinal lumen. Directly providing beneficial strains or

Figure 1 - Deaths from drug-resistant infections set to skyrocket.
Deaths from antimicrobial resistant infections and other causes in 2050



Source: Review on Antimicrobial Resistance

organic substrate to their development, their inclusion in feed is providing a potential competitive exclusion to pathogenic floras. In addition to lumen microbiota balance, optimal gut integrity is crucial. Among selected mode of actions, antioxidant and anti-inflammatory substances can be beneficial. Some natural compounds encompass these properties and thus also support global poultry immune system and its capacity to cope with any challenges.

Studies showed that a selected blend of phytomolecules consisting of carvacrol (from oregano), cinnamaldehyde (from cinnamon) and capsicum oleoresin (from red chilli pepper) has the potential to be an alternative solution to antibiotics. Data gathered for over 20 years from field trials, have shown that the inclusion in poultry diets enables chickens to achieve similar levels of growth and performance compared to diets supplemented with antibiotic growth promoters (be they avilamycin, bacitracin, flavophospholipol, or enramycin. A comprehensive overview of the effects of this blend is presented under a meta-analysis format (*see table 1*), taking into account 38 broiler trials, comparing negative controls or AGP-supplemented poultry feed to the natural solution.

Phytomolecules promising

The European experience has shown that a simple ban on AGPs is not enough to restrict their use, and that additional measures are required to provide a comprehensive solution. In light of the total AGP ban in Europe, the potential of phytomolecule to provide an alternative solution to AGPs in promoting growth and improving feed conversion ratios, while remaining a viable economical alternative, is promising. The results of these studies are even more interesting in its application as an alternative to AGPS, in light of signs suggesting tighter regulations or a near total ban on AGPs in other parts of the world.