Are you really prepared for the post-antibiotic era?

by Rolando A. Valientes, DVM, Regional Category Manager – Eubiotics, DSM Nutritional Products Ltd.

That antibiotics used as in-feed growth promoting agents for all classes of livestock have been banned in the European Union is hardly news anymore. For more than one reason, antibiotics as growth promoters are now a part of the past there and animal producers in the EU have already made the transition to the post-antibiotic era, with difficulty but successfully. In the process, several valuable lessons have been learned.

What is news, indeed, is that several other countries, especially in Asia, are now actively pursuing legislations that will eventually ban the use of in-feed antibiotics for growth promoting purposes.

In fact, in 2004, South Korea adopted a policy of phasing down the number and the types of antibiotics allowed in animal feed. This eventually led to the complete ban on the use of antibiotic growth promotants which was implemented in July 2011. This is quite similar to the process followed in the European Union not so many years ago!

Once a few countries in a region start banning antibiotics, it is highly possible the whole region will follow suit, sooner or later. And, there are three good reasons for doing so:

- Exporters, who market their products in countries already banning antibiotics, need to abide by the policies of the importing country. Such an example is Thailand that has strong exports to the EU.
- Consumers worldwide have already become aware of the benefits of having antibiotic-free animal products, especially as this is something that has a direct impact on their long term health. Thus, there is a growing trend among consumer groups to push for a ban on antibiotics.
- For marketing purposes, offering animal products free of any antibiotic residues is considered a new opportunity for major food chains and restaurants. As such, these organisations already demand antibiotic-free products and consequently push for relevant legislation to pass in their home countries.

Thus, it is important to seriously consider the fact that a ban on antibiotics is more likely to happen than not, especially when neighbouring countries have already done so. This makes sense for consumers and businesses!

How to prepare

Once we accept the inevitable or rather, recognise the opportunities, the next logical step is to start early, before legislation is implemented.

Here, the example of the EU should be studied and experiences borrowed to avoid 'reinventing the wheel'. From such experience, the most important aspect in replacing antibiotics is first to understand that an integrated approach is required as no single intervention strategy can offer a quick solution.

We must realise that antibiotics kill bacteria and as such their use has allowed the creation of a production system that is suited to their use.

Without antibiotics we must reconsider the whole process. For that, there are three major areas that require attention:

- With antibiotics, a high level of biosecurity was desirable but not always necessary. Without antibiotics, whole farm biosecurity must be reevaluated and elevated as much as possible. Perfectly healthy animals do not require any antibiotics or other additives to grow and thrive. Under practical conditions, however, perfect health status is not possible, or even economical, to achieve, and as such we must still rely on certain additives. But, having a high hygiene status in the farm helps these additives work with maximum efficacy.
- Antibiotics allowed feed formulations to be high in crude protein, as excess bacterial growth (often pathogenic) due to undigested protein was easily controlled. Without antibiotics, it is imperative to adjust protein levels and ensure animals do not receive more protein (or any other nutrients) than they actually need. This will ensure gastrointestinal bacteria do not grow uncontrollably and any additives used in the feed do not have to work against (easily avoidable) obstacles. Of course, animal performance should not be sacrificed and fortunately, modern developments in animal nutrition (i.e. the use of the protease Ronozyme ProAct in broilers) have contributed in the process of removing antibiotics from animal feed.
- Even with a high(er) health status and diet reformulation, pathogenic bacteria are still expected to affect farm animal production as everything must be accomplished below the 'ideal' level. Thus, we must rely on certain additives to stop bacteria (especially pathogenic) from causing diseases that reduce animal performance and profitability.

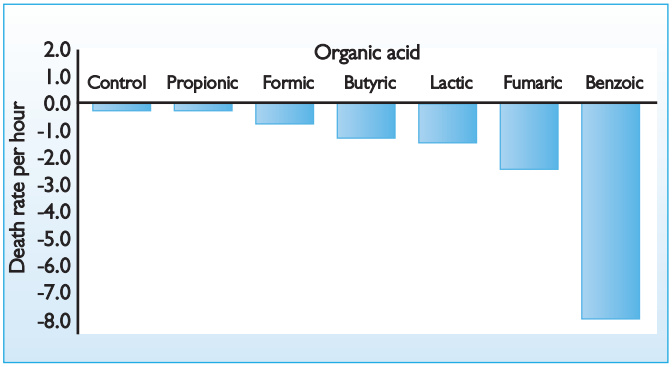

Fig. 1. Effect of various organic acids (100 mM) on death rate of coliform bacteria in stomach content at pH 4.5. Benzoic acid (VevoVitall) has the strongest antibacterial property (death rate refers to the bactericidal activity of acids against coliform bacteria at pH 4.5). Adapted from Knarreborg et al. (2002) Animal Feed Science and Technology 99:131.

Table 1. Intestinal digestive enzyme activities in chickens after 21 days on experimental diets. The combination of curcumin and piperine (Crina Poultry) enhances digestive enzyme secretion. Adapted from Lee et al. (2003), British Poultry Science 44 (3).

Enzyme unit/ mg of wet intestinal mucosa	Base diet	Thymol 100ppm	Cinnamaldehyde 100ppm	Crina Poultry 100ppm
Amylase	111±25[b]	129±9[ab]	111±18[b]	144±19
Lipase	40±7	40±13	43±6	51±13
Trypsin	14.1±3.2	13.3±2.5	14±1.3	15.9±2.5
Chymotrypsin	6.7±1.06	6.32±0.64	6.5±0.37	6.55±0.83

Antibiotic replacements

There is a great plethora of antibiotic replacements on the market. Even trying to run one single trial for

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each one would take many years of research (and a healthy budget) to test them all. Naturally, not all are of the same efficacy or even bring about the same return on investment.

DSM believe there is only a very small number of products that can actually replace antibiotics with success, and they have thus structured their business portfolio of products accordingly. They have experiences with three successful antibiotic replacement strategies:

● **Organic acids.**
Without doubt, organic acids are the most potent agents that can successfully reduce gastrointestinal pathogenic bacterial growth. The use of organic acids in this role is well known for centuries due to their widespread use in human foods. Today, food grade organic acids are available and indeed they are considered the most suitable additives for antibiotic-free diets.

But, not all organic acids are created equal. This has to do with their chemical properties and interactions with the acidic stomach and alkaline small intestine environment. Thus, some organic acids are clearly better than others.

To this end, DSM has identified benzoic acid to be the most efficacious and potent organic acid for use in animal feed (Fig. 1).

Consequently, benzoic acid was added to their portfolio under the commercial name of VevoVitall (a 99.9% pure benzoic acid).

Several field tests and experiences worldwide have proven the strong antimicrobial properties of benzoic acid.

● **Essential oil compounds derived from plants.**
Another strong additive with well known antimicrobial properties is a blend of essential oil compounds. Again, its use is well established in human nutrition.

With essential oil compounds, the available selection is even greater than with organic acids, and selecting the best and combining them, is an equal nightmare.

Needless to say, research has demonstrated that a blend of essential oil compounds works better than any single ingredient alone. DSM has identified the blend that works best and is now incorporated in their portfolio under the name Crina.

Under this range of products is Crina Poultry which is a blend of the following essential oil compounds: curcumin, piperine, thymol, and eugenol. The first two, curcumin and piperine, are known to stimulate the secretion of digestive enzymes (Table 1), thus enhancing nutrient digestibility.

This not only improves animal performance, but also deprives the pathogenic bacteria of nutrients that they would use to grow and proliferate.

The other two extracts, thymol and eugenol, have strong and direct antibacterial properties, that help regulate gut microflora (Table 2).

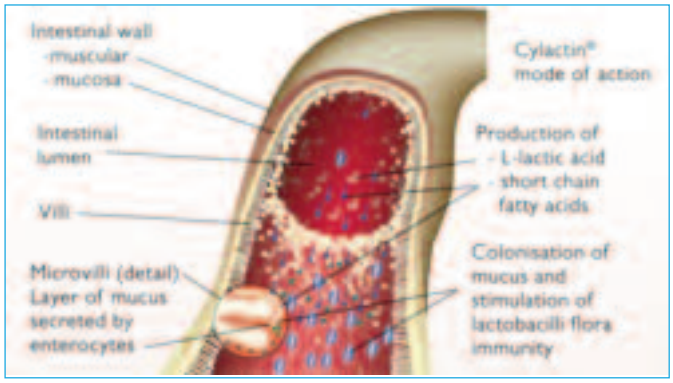


Fig. 2. The mode of action of Enterococcus faecium NCIMB 10415 in improving gastrointestinal health.

● **Beneficial bacteria.**
Naturally, not all bacteria are pathogenic. Indeed, the majority of them are beneficial to the animal, not least because they compete and exclude other (pathogenic) bacteria.

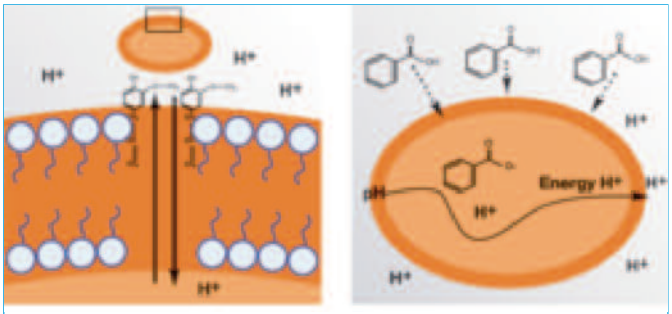
Thus, an integrated approach to replacing antibiotics calls for the use of specific in-feed bacteria (probiotics) that can realistically augment and support the indigenous bacterial population.

A probiotic containing live bacteria is considered the best option, and DSM has identified the strain of Enterococcus faecium NCIMB 10415 as the best one that stabilises the gut flora and improves animal health and welfare, improving overall performance (Fig. 2).

This strain is marketed under the name of Cylactin by DSM. Under commercial conditions, it enhances the in situ production of lactic acid (an organic acid also with antimicrobial properties) and short chain fatty acids (also with antimicrobial properties) in the gastrointestinal tract.

As a result, Cylactin enables the growth of beneficial bacterial (lactobacilli) and depresses that of pathogenic (colibacteria).

On average, the use of Cylactin in broiler diets increases growth by 3.2%, improves feed efficiency by 3.8%, and brings an estimated profit of €5871 per hundred thousand broilers (Table 3).



Other essential oils attack the cell walls of specific classes of bacteria, making the cell wall permeable so making it easier for benzoic acid to enter the cell.

Benzoic acid enters the bacteria cell and disrupts cell function by reducing the pH in the cell, depleting cell energy reserves.

Fig. 3. The mode of action of the combination of essential oil compounds and benzoic acid (Crina Poultry Plus).

A combination strategy

Here, it is important to note that most nutrition experts would agree in saying that a combination strategy of several but distinct additives works better than relying on any single product.

The best example is the combination of organic acids and a blend of essential oil compounds. It has been shown that the formulation combining benzoic acid (VevoVitall) and a blend of essential oil compounds (based on Crina Poultry) works even better than either product alone; thus DSM came up with an innovative product – Crina Poultry Plus.

It is known that organic acids must first cross the bacterial cell wall to enter in the cytosol where they exert their disrupting effect causing death. In that process, the essential oil compounds in Crina Poultry have been shown to actually increase the permeability of the bacterial outer membrane, thus making the work of VevoVitall even more efficacious as it can attack bacteria with a greater number of molecules (Fig. 3).

Conclusion

It is said that it is always better to be proactive than reactive. This could not be more in line with what is happening worldwide in the arena of antibiotics.

Even if in a certain country antibiotics are still allowed, there are telltale signs worldwide that a ban might be forthcoming. In other cases, it makes perfect business sense to adopt an antibiotic-free production system to capitalise on exports and other marketing opportunities.

To this end, using an integrated approach has been shown to give best results. Farm biosecurity, feed formulation, and additive selection are the three main areas of highest importance. Using a combination of certain, proven and efficacious, antibiotic replacing additives gives the best return on investment and ensures animal health, welfare, and productivity. ■

Days	Mean log_{10} Clostridium perfringens concentration/gram of sampled material	
	Control	Crina Poultry
14	3.33±1.48[a]	1.50±1.15[b]
21	3.25±0.67[a]	2.05±0.50[b]
30	3.95±1.18[a]	2.27±0.78[b]

Table 2. Effect of a blend of essential oil compounds (Crina Poultry) on Clostridium perfringens proliferation in faecal samples of broilers. Adapted from Mitsch et al. (2004), Poultry Science 83:669-675.

Table 3. The effect of Enterococcus faecium NCIMB 10415 on broiler performance and profitability (DSM internal data).

	Total broiler number	Live body weight (% improved)	Feed conversion rate (% improved)	Increased margin €/100,000 birds
Summary of 10 trials	306,660	3.2	3.8	5,871