Ionophores Q&A

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Introduction

This document answers some commonly asked questions about the use of ionophores by the UK broiler industry. It is to be used as a resource for the industry to align messaging and provide detailed responses to some of the more challenging questions. These range from questions relating to the basic understanding of the role of ionophores and the issues around coccidiosis in poultry to more technical questions and questions which draw on the global picture to address issues such as resistance and any risks for human health.

Positioning statement

Coccidiosis is a common and potentially severe intestinal disease in poultry, caused by *Eimeria* species, that can significantly impact bird health, welfare, and performance. It can lead to enteritis, impaired nutrient absorption, increased incidence of pododermatitis due to wet litter, and elevated mortality rates if not effectively controlled.

Multiple strategies are available to manage coccidiosis, including biosecurity, vaccination, and the use of anticoccidial compounds. Among these, ionophores remain a cornerstone of prevention and control, providing an effective, reliable, and economically viable option for poultry producers. Ionophores act directly on *Eimeria* parasites during their intestinal development phase, reducing disease severity and spread.

Ionophores are a class of antimicrobials categorised as animal-only antimicrobials, meaning they are not authorised or used in human medicine, and are not structurally or functionally related to any antibiotics considered critical for human health[1,2]. They have unique mechanisms of action, making them distinct from and unlikely to drive resistance to antibiotics critical for human health[i3] Although recent studies have identified ionophore resistance genes occasionally found alongside resistance genes for medically important antibiotics, there is no direct evidence that ionophore use in animals leads to clinically significant resistance in humans[4].

Based on current peer-reviewed evidence, ionophores remain a low-risk, effective, and responsible tool in managing coccidiosis.

Q&A

What is coccidiosis?
Coccidiosis is a severe parasitic disease that can affect poultry, cattle, sheep and pigs.

Why is it a problem for poultry in particular?
Coccidia (Eimeria species) oocysts are highly resistant and are always present in the birds' environment. Coccidiosis can affect all growing poultry, including outdoor flocks. Immunity can develop, but in some cases can be short lived, and concurrent diseases may make birds more susceptible again.

How do birds become infected?
Coccidiosis is a disease caused by microscopic parasites known as coccidia, which are ubiquitous in the environment and commonly affect livestock and poultry. Ionophores are anticoccidial substances used to control these infections. Unlike antibiotics monitored through the European Sales and Use of Antimicrobials for Veterinary Medicine (ESUAvet) programme, ionophores have not been included in ESVAC data collection.

The parasite can destroy the cells of the bird's intestine, causing enteritis, and potentially leading to other intestinal diseases,[5] as well as negatively impacting optimal growth of the animal. Coccidia have an oocyst life cycle stage which exists in the environment and, as they are highly resistant to cleaning and disinfection, it is virtually impossible to destroy and remove them. This means coccidia are constantly present in poultry environments with birds being continuously re-infected and potentially diseased until birds develop their own immunity.

How does the disease manifest itself?
Birds with coccidiosis can suffer from severe diarrhoea and other related diseases, affecting their health and well-being. In heavy burdens with the most pathogenic species, coccidiosis can be fatal[6].

How can farmers protect poultry from coccidiosis?
Since coccidiosis is naturally occurring, best management practices and hygiene may not be sufficient to prevent the disease. Management practices, hygiene and vaccination may help to reduce the risk of disease. However, as coccidia have huge replicative potential and cannot be eliminated from the environment, coccidiosis remains a constant risk for poultry. For the health and welfare of infected birds, anticoccidials are a suitable option to prevent coccidiosis and to limit the build-up and further spread of coccidia in the environment.

Farmers and veterinarians need access to appropriate products to treat the animals and limit the build-up and spread of the coccidia.

Licensed doses of anticoccidials can be supplemented in feed for the preventative control of coccidiosis[7].

Vaccination is also an option to be used to reduce clinical signs and intestinal lesions caused by coccidiosis.

Why are anticoccidials so important in this context?
Poultry production without anticoccidials or vaccination can cause bird suffering by compromising health and welfare.

Why is coccidiosis harmful?

Coccidiosis damages intestinal epithelial cells resulting in inflammatory changes, reducing the normal digestive processes and causing increased mucus production, which can in turn allow bacteria to proliferate leading to enteritis. Effects of enteritis can include:

- Reduced absorptive capacity –reduced performance
- Diarrhoea leading to wet litter – can lead to poor environment with increased podo-dermatitis and negative welfare outcomes for birds
- Mortality

When is coccidiosis a threat to the birds?

Coccidiosis is now a threat all the way through the life of a growing bird as it takes time for immunity to develop. Even when immunity has developed, in some cases it can be short lived.

What constitutes good intestinal integrity?

Intestinal integrity is the optimal functionality of the intestinal tract and the primary driver of bird health and performance. Coccidiosis can significantly compromise intestinal integrity often leading to enteritis. Preventing inflammation of the intestinal tract (enteritis) is essential for maintaining intestinal integrity.

How does intestinal integrity link to sustainability?

Good intestinal integrity is a key component of sustainable poultry production. By dealing with the most important component of health, farmers can address some of the important contributors to sustainability:

1. Economic – performance is not lost through disease
2. Social – bird health and welfare standards are maintained
3. Environment – in the absence of disease, better use of feed etc and thus a lower environmental footprint

What are the main causes for loss of intestinal integrity?

Intestinal integrity is balanced by the microbial flora and can be influenced by various infectious and non-infectious factors:

- Enteritis caused by coccidia, bacteria and viruses
- Diet high in salt
- Biogenic amines
- Non-starch polysaccharides such as xylans, glucans or mannans
- Poor fat quality
- Mycotoxins
- Poor farm management
- Lack of hygiene
- Lack of biosecurity measures
- All immunosuppressive diseases (e.g. Gumboro or Marek´s disease) create a favourable environment for the loss of intestinal integrity.

What are ionophores?

- Ionophores in use in the UK poultry industry are classed as specified feed additives not veterinary medicinal products.
- They cannot be used in human medicine and are unrelated to and **do not contribute** to shared class antibiotic resistance. They are therefore not considered important to human health by leading public health and regulatory agencies[6].
- Ionophores are not classified as veterinary medicinal products
- Ionophores are used to control and prevent coccidiosis and maintain intestinal integrity

Ionophores are used to control and prevent coccidiosis and maintain intestinal integrity and at this stage are considered a sustainable and economical solution to control coccidiosis and maintain bird health and welfare.

How are ionophores for poultry controlled?
Ionophores fall under the Food Standards Agency (FSA) jurisdiction with the retained EU Regulation 1831/2003. This regulation enables the FSA to monitor and control the use of anticoccidials. Under the current regulations, any variation to the recommended dosage is strictly prohibited. Although a veterinary prescription is not required, anticoccidials are always administered and controlled by qualified animal health personnel. All major poultry integrations contract and use expert poultry veterinarians to ensure that the best health and safety control measures are observed.

What are Maximum Residue Limits (MRLs)?

The maximum residue limit (MRL) is the maximum allowed concentration of a residue in a food product obtained from an animal that has received a veterinary medicine or that has been exposed to a biocidal product for use in animal husbandry[8]. In the process of establishing an MRL, firstly a No Observed (Adverse) Effect Level (NO(A)EL) is identified through scientific studies with the active substance. The NO(A)EL is the highest dose that does not cause adverse effects. This figure is then divided by an 'uncertainty' or 'safety factor' e.g. by 100-1000 to determine the Acceptable Daily Intake (ADI). The ADI is the amount of the residue that is considered safe for an individual to eat every day for their lifetime taking into account a number of safety factors. The MRLs are such that consumers can ingest generous amounts of animal foodstuffs every day without exceeding the ADI. A number of factors are taken into consideration here including the amounts of each food eaten per day and how the substance is metabolised and distributed in the various tissues.
For all registered ionophore coccidiostats, a MRL is set for each edible tissue and product to ensure the ADI is not exceeded.

How much chicken would a human have to eat to exceed the Maximum Residue Levels (MRLs) for ionophores?
All ionophores are licensed with established Maximum Residue Levels (MRLs) linked to the Average Daily Intake of meat by consumers, (ADI). Ionophore MRLs are such that consumers would have to consume 600kg or 300 whole chickens per day to reach a level where there remains no adverse effect.

Is there a withdrawal period?
Some ionophores have a withdrawal period, and some do not. Check the label for the product that is used.

Why do we need ionophores?
Prevention of coccidiosis is essential in order to maintain intestinal integrity, health and welfare and the efficient absorption of nutrients in poultry[9].

Ionophore based anticoccidials have been the mainstay of protection against coccidiosis since 1970s.

Q: Is there an environmental benefit to using coccidiostats?

A: Yes, evidence suggests that ionophores can help by managing coccidiosis which causes health and welfare issues and leads to a higher environmental burden.

In a 2021 a published paper by Parker et al., predicted that if coccidiostats were removed from the UK broiler industry, and the demand for chicken stayed the same, there would be a need for 3% more land and the carbon emission would increase by 3.96%. This would be an increase of 84,000 tons of CO2 equivalent per year. Additionally, the amount of food required to feed the chickens would increase by 4.2%[10].

The U.S. poultry industry's shift toward No Antibiotics Ever (NAE) and Raised Without Antibiotics (RWA) production, which also precluded the use of ionophores, between 2017 and 2019 provides a practical example of how withdrawing ionophores can negatively affect environmental sustainability. During this transition, producers reported poorer feed conversion, higher mortality, and increased incidence of necrotic enteritis compared with conventional or No Antibiotics Important to Human Medicine (NAIHM) programs where ionophores could still be used[11,12]. Reduced feed efficiency increases feed consumption, manure production, land use, and water use per kg of chicken produced, thereby increasing the environmental footprint of production [13]. In addition, severe necrotic enteritis outbreaks in some flocks created animal welfare concerns and often necessitated therapeutic antibiotic intervention despite NAE program objectives[11].

In light of the increased mortality rates and reduced FCR experienced when ionophores are withdrawn it can be concluded that through controlling coccidiosis, through ionophore use, has the potential to increase the productivity on farm and reduce the associated greenhouse gas emissions.

How do ionophores in poultry work?
Ionophores act directly on the coccidial parasite when it is in the intestines of the bird resulting in the death of the parasite and preventing the intestinal damage that it causes. Ionophores are unique in their action as instead of trying to eliminate coccidiosis entirely, they allow a small number of coccidia to replicate in the intestine and enable birds to develop their own immune response.

Are ionophores considered medically important for humans?
No. The World Animal Health Organisations (OIE) did not include ionophores in their global survey on antibiotic use[2].

Is there likely to be any future use of ionophores in human medicine?
Whilst ionophores offer both a direct and in-direct antimicrobial properties against a broad spectrum of bacterial, viral, fungal and parasitic pathogens compounds, issues surrounding toxicity, bioavailability or lack of in vivo efficacy studies have been a barrier to their use in human medicine. For these reasons, ionophores are unlikely to be considered as a major therapeutic class for use in human medicine[12].

What are the differences between the US production system and the UK production system?
The methods of poultry production and processing in the US are quite different to the UK.
Animal health products are classified by the FDA which is different to the European classification. Due to the US classification system some companies removed ionophores from their diets as part of specific marketing campaigns. Some producers who removed them from their diets are now reintroducing ionophores

What alternatives are there to ionophores?
Live vaccines can be used to stimulate immunity against coccidiosis in poultry. This can be a successful approach in layers and breeders. The growing cycle of broilers is short, and care needs to be taken to make sure that immunity from vaccines develops in time to be an effective and sustainable option. Vaccination can be used in broilers, either on its own or in rotation with ionophores and other in feed anticoccidials.

It is worth noting that at present there are no vaccines available in the UK for poultry other than chickens and that ionophores form the mainstay of coccidiosis control for turkeys and gamebirds. Due to the relatively small sizes of the markets for these other bird types there is little incentive for vaccine development.

Synthetic coccidiostats can be used to control coccidiosis, however resistance to these products can build up relatively quickly, necessitating close monitoring and rotation practices.
Finally, there are several 'alternative' products which claim to be effective at helping managing coccidiosis. While some of these products have been shown to help reduce the impact of coccidiosis, these alternatives generally offer a supplementary support in addition to an existing coccidiosis program (ionophore, chemical or vaccine).

In broilers, pullets and turkeys immunity development after field challenge alone may not develop fast enough and be strong enough to protect against coccidiosis. The broiler industry also needs continued access to synthetic coccidiostats as well as ionophores to control coccidiosis.

Removing ionophores could decrease the health and welfare of the birds, by decreasing the number of options there are for controlling a disease that will always be present in farmed poultry. This could in turn increase the cost to consumers and have a detrimental impact on the sustainability of the poultry industry which provides high quality protein for all consumers

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