Identify the most effective molecules for the existing problem

One of the most important points within the control and prevention measures for coccidiosis in broiler chickens is selecting the right anticoccidial product and correctly implementing into the operation.

At Phibro we believe this decision is complex. While on the surface it might appear the only factors to consider are: the molecule to be used, the best price and then mixing it in the birds' feed throughout. The evaluation of all factors need to be considered to provide a high efficiency program for your poultry production.

There are two major aspects to review – safety and resistance.

Safety

Anticoccidial drugs might cause adverse effects in target species when overdosed. Some of the anticoccidials (e.g. ionophores, halofuginone, nicarbazin) when accidentally fed to other species might cause detrimental effects and even mortality. Withdrawal periods for each drug should be followed to ensure drug residues are below safe levels in end consumer product.

Resistance

Resistance is the ability of a parasite strain to multiply or to survive in the presence of concentrations of a drug that normally destroy parasites of the same species or prevent their multiplication (Chapman, 1997).

Resistance development is a natural selection process. After a period of use of any given product the *Eimeria* population in the field develops resistance thus, the efficacy of the product declines.

Resistance development initiates with a genetic shift (single or multiple mutations) allowing the parasite to escape or resist the drug MoA (Mode of Action). Spreads in the parasite population enforced by the selection pressure of using the given product (the longer the drug is used the more resistance is enforced among the field *Eimeria* population - Peek and Landman, 2011)

Resistance development is an inevitable consequence of the use of any product. It could be partial or even complete and should be distinguished from the subtle differences in sensitivity of different native strains of *Eimeria* species to different products.

Resistance is reversible when the selection pressure is removed (Chapman, 1997).

Ionophore anticoccidials

Since their first introduction on the market in the 1970s, ionophores have been the backbone of anticoccidial programs worldwide.

They are produced by fermentation and share a similar mode of action – affect cell membrane permeability and facilitate the ion transport across, thus impair the normal cell metabolism. They have dose dependent effect against extracellular forms of the parasite – sporozoites and merozoites.

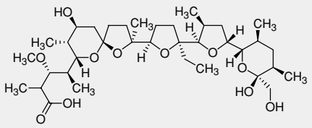
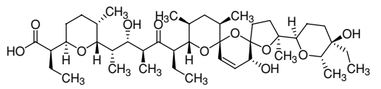
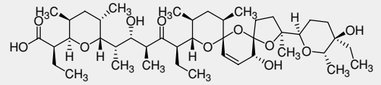
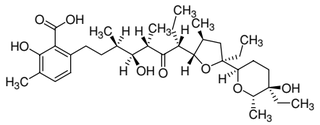
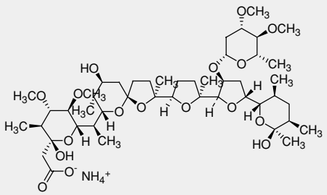
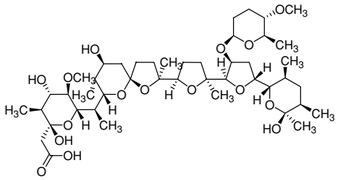
Ionophores don't completely block the development of the parasite, allowing also sensitive individuals to proliferate, which reduces the selection pressure, therefore resistance is built slowly and allows for immunity development.

Based on their chemical structure and properties, ionophores are divided into 3 groups – monovalent, divalent and glycosides (Peek and Landman, 2011; Noack et al., 2019). Due to the shared mode of action there is certain cross resistance between different ionophores, though there are differences in sensitivity between the different classes of ionophores e.g. a given *Eimeria* isolate could develop resistance towards monovalent ionophores (monensin, salinomycin and narasin), but still be sensitive towards a glycoside ionophore or the other way around (Bedrnik et al., 1989).

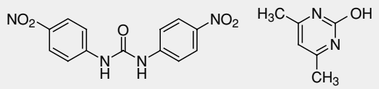
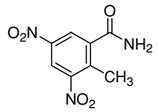
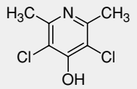
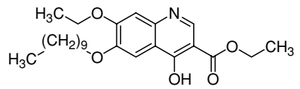
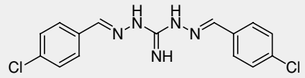
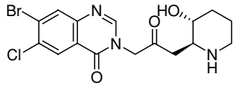
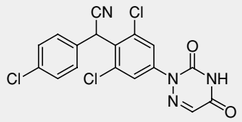
Indirect evidence of cross resistance is the resistance against narasin, described even before its introduction to the market, explained by resistance developed after use of monensin and salinomycin (other monovalent ionophores). (Chapman, 1997).

Ionophores exert the same effect over the host cell membranes, thus have low safety margin 10-20%.

Ionophores registered for use in broiler feed are listed in the table to the right, as well as doses and chemical structure.

Monovalent ionophores	Dose range	Chemical structure
Monesin*	100-120 ppm*	
Salinomycin*	50-70 ppm*	
Narasin	60-70 ppm	
Divalent ionophores	**Dose range**	**Chemical structure**
Lasalocid	75-125 ppm	
Glycoside ionophores	**Dose range**	**Chemical structure**
Maduramicin*	5-6 ppm*	
Semduramicin	20-25 ppm	

* Several suppliers. Always consult the label for approved dosage / supplier.

Chemical or synthetic	Dose range	Chemical structure
Nicarbazin*	100-120 ppm*	
Zoalene (DOT)*	40-125 ppm*	
Clopidol*	125 ppm*	
Decoquinate*	20-40 ppm*	
Robenidine*	30-36 ppm*	
Holofuginone*	2-3 ppm*	
Diclazuril*	1 ppm*	

* Several suppliers. Always consult the label for approved dosage / supplier.

Chemically synthetized anticoccidials

(Synthetics or Chemicals)

Chemically synthesized anticoccidials were launched commercially in the 1940's. Since then many new compounds have been introduced.

The main and important chemical anticoccidials (listed below) currently used are representatives of different chemical classes with different mode of actions (Peek and Landman, 2011; Kadykalo et all 2017). For this reason, they should not be generalized but reviewed separately.

Different chemicals develop resistance at a different pace – from very rapid (diclazuril and decoquinate); to rapid (robenidine and clopidol) to slow (nicarbazin and zoalene) (Chapman, 1997).

Due to the very different chemical structure and mode of action of the currently available chemical anticoccidials, there is no cross-resistance among them. The only exception is diclazuril which has cross-resistance with the in-water treatment toltrazuril (Chapman, 1997).

Synergistic combinations

Ionophores and nicarbazin are the most widely used anticoccidial molecules due to their effectiveness against the major *Eimeria* species in domestic poultry *Gallus gallus*, but also their ability to develop resistance slowly and allow for immunity development. In this respect they are perceived as reliable because the risk of a sudden outbreak is lower.

Unfortunately, both ionophores and nicarbazin have narrow safety margins. In addition, nicarbazin increases heat production and increases sensitivity to heat stress (Fowler, 1995).

In order to reduce their effective dose, synergistic combinations of different ionophores with nicarbazin have been developed. This allows for effective coccidiosis control with a lower risk of side effects of the drugs.

Combo drug	Dose range	Product Name
Narasin + Nicarbazin	40-50 ppm + 40-50 ppm	Maxiban
Monensin + Nicarbazin	40-50 ppm + 40-50 ppm	Monimax
Salinomycin + Nicarbazin	50 ppm + 50 ppm	Salinocarb
Maduramicin + Nicarbazin	3.75 ppm + 40 ppm	Gromax
Semduramicin + Nicarbazin	15-18 ppm + 40-48 ppm	Aviax® Plus
*Always consult the label for approved dosage / supplier.		