

### Introduction and background

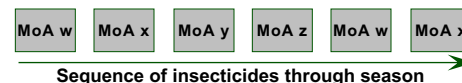
The agrochemical industry has developed a broad range of very effective insecticides for the control of lepidopteran pests. Unfortunately, as a consequence of the misuse or overuse of these insecticides, many species have developed resistance. Populations of *Plutella xylostella*, for example, have developed resistance to virtually every insecticide used against them. Additionally, there are numerous other species prone to resistance development. In recent years the industry has worked especially hard to develop new types of insecticides with novel modes of action, but this process is becoming ever harder and more costly. It is therefore vital that effective insecticide resistance management (IRM) strategies are implemented, to ensure that resistance does not develop to these new compounds, or to older chemistries that are still effective.

In order to help prevent or delay the incidence of resistance, IRAC promotes the use of a Mode of Action (MoA) classification of insecticides in effective and sustainable IRM strategies. Available insecticides are allocated to specific groups, based on their target site, as described below. By using sequences or alternations of insecticides from different MoA classes, resistance is less likely to occur. Available at the IRAC website [www.irac-online.org](http://www.irac-online.org), this IRAC MoA classification list provides farmers, growers, advisors, extension staff, consultants and crop protection professionals with a guide to the selection of insecticides in IRM programs.

### Effective IRM strategies: Sequences or alternations of MoA

Effective insecticide resistance management (IRM) strategies seek to minimize the selection of resistance to any one type of insecticide. In practice, alternations, sequences or rotations of compounds from different MoA groups provide sustainable and effective IRM.

Example:



Applications are often arranged into MoA spray windows or blocks that are defined by the stage of crop development and the biology of the lepidopteran species of concern. Local expert advice should always be followed with regard to spray windows and timing. Several sprays may be possible within each spray window, but it is generally essential that successive generations of the pest are not treated with compounds from the same MoA group. Metabolic resistance mechanisms may give cross-resistance between MoA groups; where this is known to occur, the above advice should be modified accordingly.

### Nerve and Muscle Targets – These insecticides are generally fast acting.

#### Group 1 Acetylcholinesterase (AChE) inhibitors

Inhibit AChE, causing hyperexcitation. AChE is the enzyme that terminates the action of the excitatory neurotransmitter acetylcholine at nerve synapses.

**1A Carbamates** (e.g. Methomyl, Thiodicarb) **1B Organophosphates** (e.g. Chlorpyrifos)

#### Group 2 GABA-gated chloride channel blockers

Block the GABA-activated chloride channel, causing hyperexcitation and convulsions. GABA is the major inhibitory neurotransmitter in insects.

**2A Cycloodiene Organochlorines** (e.g. Endosulfan) **2B Phenylpyrazoles** (e.g. Fipronil)

#### Group 3 Sodium channel modulators

Keep sodium channels open, causing hyperexcitation and, in some cases, nerve block. Sodium channels are involved in the propagation of action potentials along nerve axons.

**3A Pyrethrins, Pyrethroids** (e.g. Cypermethrin, λ-Cyhalothrin)

#### Group 4 Nicotinic acetylcholine receptor (nAChR) competitive modulators

Bind to the acetylcholine (ACh) site on nAChRs causing a range of symptoms from hyperexcitation to lethargy & paralysis. ACh is the major excitatory neurotransmitter in the insect central nervous system.

**4A Neonicotinoids** (e.g. Acetamiprid, Thiacloprid, Thiamethoxam)

#### Group 5 Nicotinic acetylcholine receptor (nAChR) allosteric modulators – Site I

Allosterically activate nAChRs, causing hyperexcitation of the nervous system.

**Spinosyns** (e.g. Spinosad, Spinetoram)

#### Group 6 Glutamate-gated chloride channel (GluCl) allosteric modulators

Allosterically activate glutamate-gated chloride channels (GluCl), causing paralysis. Glutamate is an important inhibitory neurotransmitter in insects.

**Avermectins, Milbemycins** (e.g. Abamectin, Emamectin benzoate, Lepimectin)

#### Group 14 Nicotinic acetylcholine receptor (nAChR) blockers

Block the nAChR ion channel, resulting in nervous system block and paralysis.

**Bensultap, Cartap**

#### Group 22 Voltage-dependent sodium channel blockers

Block sodium channels, causing nervous system shutdown and paralysis. Sodium channels are involved in the propagation of action potentials along nerve axons.

**22A Indoxacarb 22B Metaflumizone**

#### Group 28 Ryanodine receptor modulators

Activate muscle ryanodine receptors, leading to contraction and paralysis. Ryanodine receptors mediate calcium release into the cytoplasm from intracellular stores.

**Diamides** (e.g. Chlorantraniliprole, Cyantraniliprole, Cyclaniliprole, Flubendiamide, Tetrilaniliprole)

#### Group 30 GABA-gated chloride channel allosteric modulators

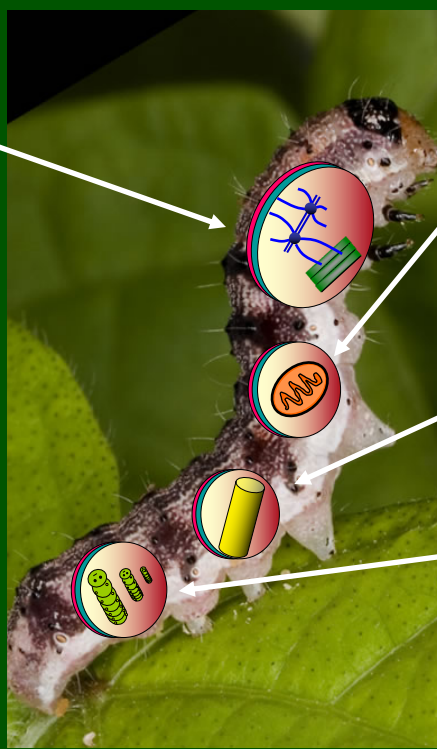
Allosterically block the GABA-activated chloride channel, causing hyperexcitation and convulsions.

**Meta-diamides** (e.g. Broflanilide, Fluxametamide, Isocycloseram)

#### Group 32 Nicotinic acetylcholine receptor (nAChR) allosteric modulators – Site II

Allosterically activate nAChRs, causing hyperexcitation of the nervous system.

**GS-omega/kappa HXTX-HV1A peptide**



#### Key to Targeted Physiology

- Nerve & Muscle
- Growth & Development
- Respiration
- Midgut
- Unknown or Non-specific

### Respiration Targets

Mitochondrial respiration produces ATP, the molecule that energizes all vital cellular processes. In mitochondria, an electron transport chain uses the energy released by oxidation to charge a proton gradient battery that drives ATP synthesis. Several insecticides are known to interfere with mitochondrial respiration by the inhibition of electron transport and/or oxidative phosphorylation. Insecticides that act on individual targets in this system are generally fast to moderately fast acting.

#### Group 13 Uncouplers of oxidative phosphorylation via disruption of the proton gradient

Protonophores that short-circuit the mitochondrial proton gradient so that ATP can not be synthesized.

**Chlorfenapyr**

#### Group 21 Mitochondrial complex I electron transport inhibitors

Inhibit electron transport complex I, preventing the utilization of energy by cells.

**21A Tolfenpyrad**

### Midgut Targets

Lepidopteran-specific microbial toxins that are sprayed or expressed in transgenic crops.

#### Group 11 Microbial disruptors of insect midgut membranes

Protein toxins that bind to receptors on the midgut membrane and induce pore formation, resulting in ionic imbalance and septicemia.

**11A Bacillus thuringiensis 11B Bacillus sphaericus**

#### Group 31 Baculoviruses

Host-specific occluded pathogenic viruses

**Granuloviruses, Nucleopolyhedroviruses**

### Growth and Development Targets

Insect development is controlled by the balance of two principal hormones: juvenile hormone and ecdysone. Insect growth regulators act by mimicking one of these hormones or by directly affecting cuticle formation/deposition or lipid biosynthesis. Insecticides that act on individual targets in this system are generally slowly to moderately slowly acting.

#### Group 7 Juvenile hormone mimics

Applied in the pre-metamorphic instar, these compounds disrupt and prevent metamorphosis.

**7B Juvenile hormone analogues** (e.g. Fenoxycarb)

#### Group 15 Inhibitors of chitin biosynthesis, Type 0

Incompletely defined mode of action leading to inhibition of chitin biosynthesis.

**Benzoylureas** (e.g. Flufenoxuron, Lufenuron, Novaluron)

#### Group 18 Ecdysone receptor agonists

Mimic the moulting hormone, ecdysone, inducing a precocious moult.

**Diacylhydrazines** (e.g. Methoxyfenozide, Tebufenozide)

**Unknown** Several insecticides are known to affect less well-described target-sites or functions, or to act non-specifically on multiple targets.

**Azadirachtin, Pyridaly**