

Introduction and background

Mosquitoes are vectors of many of the world's key human diseases, including malaria. The emergence of species resistant to insecticides widely used in vector control has the potential to impact severely on the control of these disease vectors. This may have a dramatic effect in Africa, as few affordable alternative insecticides are available for vector control. The extensive use and misuse of insecticides for agriculture and vector control has contributed to this problem. The lack of available suitable alternative insecticides for vector control has also been an issue, for example only pyrethroids are currently recommended by WHO for use on long lasting insecticide treated mosquito nets. Industry is now working in collaboration with the Innovative Vector Control Consortium (IVCC) to find new classes of insecticides with novel modes of action for use in public health. However the identification and approval process of a new active can take up to 10 years and ~\$200 million. It is therefore vital that effective insecticide resistance management (IRM) strategies are implemented to ensure that the efficacy of existing compounds can be maintained for as long as possible.

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.ircac-online.org, this IRAC MoA classification list along with the IRAC Vector Manual provides NGOs, ministers, advisors, extension staff, consultants and public health professionals with a guide to the selection of insecticides and planning of IRM programs.

Effective IRM strategies

Sequences or alternations of MoA

All effective insecticide resistance management (IRM) strategies seek to minimise the selection of resistance to any one type of insecticide. It is recommended that alternations, mosaics or rotations of compounds from different MoA groups can provide sustainable and effective IRM for mosquitoes. This ensures that selection by compounds in the same MoA group is minimised, and resistance less likely to evolve. The practice of using an insecticide until resistance occurs becomes a limiting factor in public health and is rapidly eroding the number of suitable insecticides for vector control. The limitations of current public health interventions such as IRS and LNs mean that successive generations of the mosquito are exposed to compounds from the same MoA group. This makes IRM in public health more challenging than in agriculture. Therefore insecticide resistance monitoring is of vital importance, this can be done using bioassays (WHO¹ and/or CDC² standard test kits and procedures) and also biochemical/ molecular methods. This testing should ideally be conducted annually to monitor any changes in susceptibility that may occur and thus allow timely intervention of alternative vector control methods.

(Web sites: 1. www.who.int/whopes/resistance/en/ 2. www.cdc.gov/ncidod/wbt/resistance/assay/bottle/index.htm)

Nerve and Muscle Targets

Most current insecticides act on nerve and muscle targets. These are generally fast acting.

Group 1 Acetylcholinesterase (AChE) inhibitors (Adults or Larvae)

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

1A Carbamates (e.g. propoxur & bendiocarb),

1B Organophosphates (e.g. Temephos, malathion, fenitrothion, pirimiphos-methyl)

Group 3 Sodium channel modulators (Adults only)

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. deltamethrin, permethrin, cypermethrin, alpha-cypermethrin, lambda-cyhalothrin, bifenthrin, etofenprox)

3B DDT

Group 5 Nicotinic acetylcholine receptor (nAChR) allosteric modulators Site I (Larvae only)

Allosterically activate nAChRs, causing hyperexcitation of the nervous system.

Acetylcholine is the major excitatory neurotransmitter in the insect central nervous system.

5 Spinosyns (e.g. spinosad,)



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 directly perturbing cuticle formation/deposition or lipid biosynthesis. Insecticides that act on individual targets in this system are generally slow to moderately slow acting.

Group 7 Juvenile hormone mimics

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

7A Juvenile hormone mimics (e.g. Methoprene, Hydroprene)

7C Pyriproxifen

Group 15 Inhibitors of chitin biosynthesis affecting CHS1

Incompletely defined MoA leading to inhibition of chitin biosynthesis

15 Benzoylureas (e.g. Diflubenzuron, Novaluron)

Midgut

Derived from bacteria, these toxins need to be ingested and disrupt the insect midgut membranes

Group 11 Microbial disruptors of insect midgut membranes
Bacillus thuringiensis var. *israeliensis* and *Bacillus sphaericus*



Adulticides WHOPES Approved Uses	MoA	Class	Insecticide or Product	IRS	ITN	LN
	1A	Carbamate	Bendiocarb, Propoxur	✓	X	X
1B	Organophosphate	Malathion Fenitrothion Pirimiphos-methyl	✓	X	X	
3A	Pyrethroid	Alphacypermethrin	✓	✓	✓	
		Deltamethrin	✓	✓	✓*	
		Permethrin	X	✓	✓*	
		Etofenprox	✓	✓	X	
		Lambda-cyhalothrin	✓	✓	✓	
Bifenthrin	Cyluthrin	Deltamethrin + PBO	✓	X	X	
			✓	X	X	
			X	X	✓	
3B	Organochlorine	DDT	✓	X	X	

* Indicates Full WHOPES approval as an LN
(NB: Those without * indicates Interim approval only.)

Larvicides WHOPES Approved	MoA	Class	Insecticide or Product
	1B	Organophosphate	Temephos, Chlorpyrifos, Pirimiphos-methyl, Fenthion
5	Spinosyns	Spinosad	
7A	Juvenile Hormone Mimics	Methoprene, Hydroprene	
7C	Pyriproxifen	Pyriproxifen	
15	Benzoylureas	Diflubenzuron, Novaluron	
11	Bacterial Larvicide	<i>Bt</i> var. <i>israeliensis</i> and <i>Bacillus sphaericus</i>	

Further reading:

Prevention and management of insecticide resistance in vectors and pests of public health importance
www.ircac-online.org

WHO (2006): Pesticides and their application.
WHO/CDS/NTD/WHOPES/GCDPP 6th edition, 114pp
www.who.int/whopes/en/

Targeted Physiology: Rotations for resistance management should be based only on the numbered mode of action groups.



Activity on pest lifecycle stage



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Designed by IRAC Public Health & MoA Teams, January 2019
Poster Version 3, Based on MoA Classification Version 9.1

For further information visit the IRAC website: www.ircac-online.org
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