IRAC Mode of Action Classification

Revised & re-issued, September 2006

Version: 5.2

The IRAC Mode of Action (MoA) classification provides farmers, growers, advisors, extension staff, consultants and crop protection professionals with a guide to the selection of insecticides or acaricides for use in an effective and sustainable insecticide or acaricide resistance management (IRM) strategy. In addition to presenting the MoA classification, this document outlines the background to, and purposes of, the classification list and provides guidance on how it is used for IRM purposes. The list is reviewed and re-issued at intervals as required.

What is resistance

Resistance to insecticides may be defined as '*a heritable change in the sensitivity of a pest population that is reflected in the repeated failure of a product to achieve the expected level of control when used according to the label recommendation for that pest species*' (IRAC). This definition differs slightly from others in the literature, but IRAC believes it represents the most accurate, practical definition of relevance to farmers and growers. Resistance arises through the over-use or mis-use of an insecticide or acaricide against a pest species and results in the selection of resistant forms of the pest and the consequent evolution of populations that are resistant to that insecticide or acaricide.

MoA, Target-site resistance and Cross-resistance

In the majority of cases, not only does resistance render the selecting compound ineffective but it often also confers cross-resistance to other chemically related compounds. This is because compounds within a specific chemical group usually share a common target site within the pest, and thus share a common mode of action (MoA). It is common for resistance to develop that is based on a genetic modification of this target site. When this happens, the interaction of the selecting compound with its target site is impaired and the compound loses its pesticidal efficacy. Because all compounds within the chemical sub-group share a common MoA, there is a high risk that the resistance that has developed will automatically confer cross-resistance to all the compounds in the same sub-group. It is this concept of cross-resistance within chemically related insecticides or acaricides that is the basis of the IRAC mode of action classification.

Effective IRM strategies use alternations or sequences of different modes of action (MoA)

The objective of successful Insecticide Resistance Management (IRM) is to prevent or delay the evolution of resistance to insecticides, or to help regain susceptibility in insect pest populations in which resistance has already arisen. Effective IRM is thus an important element in maintaining the efficacy of valuable insecticides. It is important to recognize that it is usually easier to proactively prevent resistance occurring than it is to reactively regain susceptibility. Nevertheless, the IRAC MoA classification will always provide valuable guidance to the design of effective IRM strategies.

Experience has shown that all effective insecticide or acaricide resistance management strategies seek to minimise the selection for resistance from any one type of insecticide or acaricide. In practice, alternations, sequences or rotations of compounds from different MoA groups provide a sustainable and effective approach to IRM. This ensures that selection from compounds in any one MoA group is minimised. The IRAC classification in this document is provided as an aid to insecticide selection for these types of IRM strategies.

Applications are often arranged into MoA spray windows or blocks that are defined by the stage of crop development and the biology of the pest(s) of concern. Local expert advice should always be followed with regard to spray windows and timings. Several sprays of a compound may be possible within each spray window but it is generally essential to ensure that successive generations of the pest are not treated with compounds from the same MoA group.

Non-target site resistance mechanisms

It is fully recognized that resistance of insects and mites to insecticides and acaricides can, and frequently does, result from enhanced metabolism by enzymes within the pest. Such metabolic resistance mechanisms are not linked to any specific site of action classification and therefore they may confer resistance to insecticides in more than one IRAC MoA group. Where such metabolic resistance has been characterized and the cross-resistance spectrum is known, it is possible that certain alternations, sequences or rotations of MoA groups cannot be used. Similarly, mechanisms of reduced penetration of the pesticide into the pest, or behavioural changes of the pest may also confer resistance to multiple MoA groups. Where such mechanisms are known to give cross-resistance between MoA groups, the use of insecticides should be modified appropriately.

Where the resistance mechanism(s) is unknown, the intelligent use of alternations, sequences or rotations of compounds from different MoA classes remains an entirely viable resistance management technique since such a practice will always minimise selection pressures.

The Mode of Action (MoA) classification

The following classification scheme developed and endorsed by IRAC is based on the best available evidence of the mode of action of available insecticides. Details of the listing have been agreed by IRAC companies and approved by internationally recognized industrial and academic insect toxicologists and biochemists.

It is our aim to ensure that insecticide and acaricide users are aware of mode of action groups and that they have a sound basis on which to implement season-long, sustainable resistance management through the effective use of alternations, sequences or rotations of insecticides with different modes of action. To help delay resistance it is strongly recommended that growers also integrate other control methods into insect or mite control programmes. Further advice is given in Appendix 2.

Note: Inclusion of a compound in the MoA list does not necessarily signify regulatory approval.

Rules for inclusion of a compound in the MoA list:

- Chemical nomenclature is based on that appearing in *The Pesticide Manual*, 13th edition, 2003, Ed. C.D.S. Tomlin, published by The British Crop Protection Council. 1250pp., ISBN 1 901396 13 4
- To be included in the active list, compounds must have, or be very close to having, a minimum of one registered use in at least one country. Superseded, obsolete or withdrawn compounds with no current registration are listed separately (see Appendix 3 – in preparation)
- In any one MoA classification sub-group, where more than one active ingredient in that chemical sub-group is registered for use, the chemical sub-group name is used.
- In any one MoA classification sub-group, where only one active ingredient is registered for use, the name of that exemplifying active ingredient is used
- Where more than one chemical sub-group or exemplifying active ingredient appears in a single mode of action group, each is named according to the above rules; chemical sub-groups having precedence over single active ingredients

IRAC Mode of Action Classification v5.2, September 2006 [1]

Main Group and Primary Site of Action	Chemical Sub-group or exemplifying Active Ingredient	Active Ingredients
1 Acetylcholine esterase inhibitors	**1A** Carbamates	Aldicarb, Alanycarb, Bendiocarb, Benfuracarb, Butocarboxim, Butoxycarboxim, Carbaryl, Carbofuran, Carbosulfan, Ethiofencarb, Fenobucarb, Formetanate, Furathiocarb, Isoprocarb, Methiocarb, Methomyl, Metolcarb, Oxamyl, Pirimicarb, Propoxur, Thiodicarb, Thiofanox, Trimethacarb, XMC, Xylylcarb
	Triazemate	Triazemate
	1B Organophosphates	Acephate, Azamethiphos, Azinphos-ethyl, Azinphos-methyl, Cadusafos, Chlorethoxyfos, Chlorfenvinphos, Chlormephos, Chlorpyrifos, Chlorpyrifos-methyl, Coumaphos, Cyanophos, Demeton-S-methyl, Diazinon, Dichlorvos/ DDVP, Dicrotophos, Dimethoate, Dimethylvinphos, Disulfoton, EPN, Ethion, Ethoprophos, Famphur, Fenamiphos, Fenitrothion, Fenthion, Fosthiazate, Heptenophos, Isofenphos, Isopropyl *O*-methoxyaminothio=phosphoryl) salicylate, Isoxathion, Malathion, Mecarbam, Methamidophos, Methidathion, Mevinphos, Monocrotophos, Naled, Omethoate, Oxydemeton-methyl, Parathion, Parathion-methyl, Phenthoate, Phorate, Phosalone, Phosmet, Phosphamidon, Phoxim, Pirimiphos-, ethyl, Profenofos, Propetamphos, Prothiofos, Pyraclofos, Pyridaphenthion, Quinalphos, Sulfotep, Tebupirimfos, Temephos, Terbufos, Tetrachlorvinphos, Thiometon, Triazophos, Trichlorfon, Vamidothion
2 GABA-gated chloride channel antagonists	**2A** Cyclodiene organochlorines	Chlordane, Endosulfan, gamma-HCH (Lindane)
	2B Phenylpyrazoles (Fiproles)	Ethiprole, Fipronil
3 Sodium channel modulators	DDT	DDT
	Methoxychlor	Methoxychlor
	Pyrethroids	Acrinathrin, Allethrin, d-cis-trans Allethrin, d-trans Allethrin, Bifenthrin, Bioallethrin, Bioallethrin S-cylclopentenyl , Bioresmethrin, Cycloprothrin, Cyfluthrin, beta-Cyfluthrin, Cyhalothrin, lambda-Cyhalothrin, gamma-Cyhalothrin, Cypermethrin, alpha-Cypermethrin, beta-Cypermethrin, theta-cypermethrin, zeta-Cypermethrin, Cyphenothrin , (1*R*)-*trans*-isomers], Deltamethrin, Empenthrin , (*EZ*)- (1*R*)- isomers], Esfenvalerate, Etofenprox, Fenpropathrin, Fenvalerate, Flucythrinate, Flumethrin, tau-Fluvalinate, Halfenprox, Imiprothrin, Permethrin, Phenothrin [(1*R*)-trans- isomer], Prallethrin, Resmethrin, RU 15525, Silafluofen, Tefluthrin, Tetramethrin, Tetramethrin [(1*R*)-isomers], Tralomethrin, Transfluthrin, ZXI 8901
	Pyrethrins	Pyrethrins (pyrethrum)

Main Group and Primary Site of Action	Chemical Sub-group or exemplifying Active Ingredient	Active Ingredients
4 Nicotinic Acetylcholine receptor agonists / antagonists	**4A** Neonicotinoids	Acetamiprid, Clothianidin, Dinotefuran, Imidacloprid, Nitenpyram, Thiacloprid, Thiamethoxam
	4B Nicotine	Nicotine
	4C Bensultap Cartap hydrochloride Nereistoxin analogues	Bensultap Cartap hydrochloride Thiocyclam, Thiosultap-sodium
5 Nicotinic Acetylcholine receptor agonists (allosteric) (not group 4)	Spinosyns	Spinosad
6 Chloride channel activators	Avermectins, Milbemycins	Abamectin, Emamectin benzoate, Milbemectin
7 Juvenile hormone mimics	**7A** Juvenile hormone analogues	Hydroprene, Kinoprene, Methoprene
	7B Fenoxycarb	Fenoxycarb
	7C Pyriproxyfen	Pyriproxyfen
8 Compounds of unknown or non-specific mode of action (fumigants)	**8A** Alkyl halides	Methyl bromide and other alkyl halides
	8B Chloropicrin	Chloropicrin
	8C Sulfuryl fluoride	Sulfuryl fluoride
9 Compounds of unknown or non-specific mode of action (selective feeding blockers)	**9A** Cryolite	Cryolite
	9B Pymetrozine	Pymetrozine
	9C Flonicamid	Flonicamid
10 Compounds of unknown or non-specific mode of action (mite growth inhibitors)	**10A** Clofentezine Hexythiazox	Clofentezine Hexythiazox
	10B Etoxazole	Etoxazole

Main Group and Primary Site of Action	Chemical Sub-group or exemplifying Active Ingredient	Active Ingredients
11 Microbial disruptors of insect midgut membranes (includes transgenic crops expressing *Bacillus thuringiensis* toxins)	**11A1** *B.t.* subsp. *israelensis*	*Bacillus thuringiensis* subsp. *israelensis*
	11A2 *B. sphaericus*	*Bacillus sphaericus*
	11B1 *B.t.* subsp. *aizawai*	*Bacillus thuringiensis* subsp. *aizawai*
	11B2 *B.t.* subsp. *kurstaki*	*Bacillus thuringiensis* subsp. *kurstaki*
	11C *B.t.* subsp. *tenebrionis*	*Bacillus thuringiensis* subsp. *tenebrionis*
12 Inhibitors of oxidative phosphorylation, disruptors of ATP formation (inhibitors of ATP synthase)	**12A** Diafenthiuron	Diafenthiuron
	12B Organotin miticides	Azocyclotin, Cyhexatin, Fenbutatin oxide
	12C Propargite Tetradifon	Propargite Tetradifon
13 Uncouplers of oxidative phosphorylation via disruption of proton gradient	Chlorfenapyr DNOC	Chlorfenapyr DNOC
14 vacant		
15 Inhibitors of chitin biosynthesis, type 0, Lepidopteran	Benzoylureas	Bistrifluron, Chlofluazuron, Diflubenzuron, Flucycloxuron, Flufenoxuron, Hexaflumuron, Lufenuron, Novaluron, Noviflumuron, Teflubenzuron, Triflumuron
16 Inhibitors of chitin biosynthesis, type 1, Homopteran	Buprofezin	Buprofezin
17 Moulting disruptor, Dipteran	Cyromazine	Cyromazine
18 Ecdysone agonists / moulting disruptors	**18A** Diacylhydrazines	Chromafenozide, Halofenozide, Methoxyfenozide, Tebufenozide
	18B Azadirachtin	Azadirachtin

Main Group and Primary Site of Action	Chemical Sub-group or exemplifying Active Ingredient	Active Ingredients
19 Octopaminergic agonists	Amitraz	Amitraz
20 Mitochondrial complex III electron transport inhibitors (Coupling site II)	**20A** Hydramethylnon	Hydramethylnon
	20B Acequinocyl	Acequinocyl
	20C Fluacrypyrim	Fluacrypyrim
21 Mitochondrial complex I electron transport inhibitors	METI acaricides	Fenazaquin, , Fenpyroximate, Pyrimidifen, Pyridaben, Tebufenpyrad, Tolfenpyrad
	Rotenone	Rotenone
22 Voltage-dependent sodium channel blockers	Indoxacarb	Indoxacarb
23 Inhibitors of lipid synthesis	Tetronic acid derivatives	Spirodiclofen, Spiromesifen
24 Mitochondrial complex IV electron transport inhibitors	**24A** Aluminium phosphide	Aluminium phosphide
	24B Cyanide	Cyanide
	24C Phosphine	Phosphine
25 Neuronal inhibitors (unknown mode of action)	**25** Bifenazate	Bifenazate
26 Aconitase inhibitors	Fluoroacetate	Fluoroacetate
27 Synergists	**27A** P450-dependent monooxygenase inhibitors	Piperonyl butoxide
	27B Esterase inhibitors	Tribufos (DEF)
28 Ryanodine receptor modulators	Diamides	Flubendiamide, Chlorantraniliprole
un Compounds with unknown mode of action[2]	**una** Benzoximate	Benzoximate
	unb Chinomethionat	Chinomethionat

Main Group and Primary Site of Action	Chemical Sub-group or exemplifying Active Ingredient	Active Ingredients
	unc Dicofol	Dicofol
	und Pyridalyl	Pyridalyl
ns Miscellaneous non-specific (multi-site) inhibitors[3]	**nsa** Borax	Borax
	nsb Tartar emetic	Tartar emetic

Notes to be read in association with the above classification:

[1] Inclusion of a compound in the list above does not necessarily signify regulatory approval
[2] A compound with an unknown mode of action or an unknown mode of toxicity will be held in category 'un' until evidence becomes available to enable that compound to be assigned to a more appropriate mode of action class
[3] Category 'ns' is used for compounds or preparations with a non-specific, multisite action.

Groups and Sub-groups – Although sharing the same primary target site, it is possible that not all members of a single major MoA class have been shown to be cross-resistant. Different resistance mechanisms that are not linked to the target site of action, such as enhanced metabolism, may be common for such a group of chemicals. In such cases, the MoA grouping is further divided into sub-groups. For the purposes of this classification it should be assumed that cross-resistance exists between compounds in any one MoA sub-class. Alternation of compounds from different sub-groups within a class *may* be an acceptable part of an IRM strategy. Consult a local resistance expert for further advice.

Products containing multiple or stacked toxins will be differentiated from those containing single toxins only. This will be done by adding a suffix of "m" for multiple toxin products and "s" for single toxin products. Products containing spores will be differentiated from those without spores by adding "+" for spore-containing products and "-" for those which do not contain spores. For example, *Bacillus thuringiensis* subsp. *kurstaki* products containing multiple toxins and spores may be designated as 11Dm+, while the same product without spores and expressing only one toxin would be designated as Group 11Ds-

Superseded, obsolete or withdrawn compounds for which no current registration exists, and that are no longer in common usage, will be listed in Appendix 3 (in preparation).

General notes

This document has been prepared using the most up-to-date information available to IRAC. It is provided to user groups, grower organisations, extension personnel, regulatory authorities such as the US EPA and all those involved in resistance management, as an agreed definitive statement by the agrochemical industry on the mode of action of insecticides currently in use. Given the broad nature of this user community and the many uses that are demanded of this document, readers should be aware that IRAC has sought to provide a workable listing that serves the needs of as many of these users as possible.

In a continued effort to refine the list, readers are kindly asked to inform IRAC of factual errors or omissions, citing definitive evidence wherever possible. Such submissions should be directed to IRAC via the website at: www.irac-online.org. Suggestions for improvements are likewise welcome.

Updates

The IRAC MoA classification is reviewed and reissued at intervals as required. The latest version is always available for reference via IRAC's website www.irac-online.org

Submissions for new active ingredients together with recommendations for their inclusion in specific new or existing MoA classes, togther with citations or evidence for classification should be made to IRAC through the website. IRAC member companies review draft versions before an agreed final version of any update is published. In addition, a number of internationally well-known insect toxicologists and biochemists are also consulted regarding additions, deletions or other changes to the list.

Changes to the listing may have serious consequences. In those countries where insecticide labels display the IRAC MoA number or class name as an aid to good IRM (see Appendix 1), changes may be especially costly to implement. In general, changes are therefore only endorsed when the scientific evidence supporting the change is compelling.

Appendix 1

Product labels: Indication of MoA of active ingredient and accompanying IRM advice

To assist users in the selection of insecticides for use in IRM strategies employing sequences, rotations or alternations of MoA groups, IRAC is encouraging producers to clearly indicate the IRAC MoA group number and description on the product label, and to accompany this with appropriate advice of the type indicated below. Thus, in addition to the detailed product information, handling, and safety information required by local regulations, a typical title label should clearly indicate the IRAC MoA Group number & description, and minimal, brief advice on IRM as indicated in the example below.

example

Insecticide ® 50 SC

IRAC MoA Group 15
Inhibitors of chitin biosynthesis, type 0, Lepidopteran Benzoylureas

Active Ingredient: [Compound name]
Formulation details

"For resistance management purposes, Insecticide 50SC is an IRAC Mode of Action Group 15 insecticide. Any insect population may contain individuals naturally resistant to Insecticide 50SC and other Group 15 insecticides. If these insecticides are used repeatedly, the resistant individuals may eventually dominate the pest insect population. These resistant insects may not be controlled by Insecticide 50SC or by other Group 15 insecticides. To delay the development of resistance:

- Avoid exclusive repeated use insecticides from the same chemical subgroup, (indicated by the IRAC Mode of Action Group number).
- Alternate with products from other IRAC Mode of Action Groups
- Integrate other control methods (chemical, cultural, biological) into insect control programs.

For further information on resistance management and advice on IRM programmes contact your local distributor."

Appendix 2

The following IRM principles are recommended and endorsed by IRAC:

a. Consult a local agricultural advisor or extension services in the area for up-to-date recommendations and advice on IPM and IRM programmes
b. Consider options for minimizing insecticide use by selecting early-maturing or pest-tolerant varieties of crop plants
c. Include effective cultural and biological control practices that work in harmony with effective IRM programmes. Adopt all non-chemical techniques known to control or suppress pest populations, including biological sprays such as Bt's, resistant varieties, within-field refugia (untreated areas) and crop rotation
d. Where possible select insecticides and other pest management tools which preserve beneficial insects
e. Use products at their full, recommended doses. Reduced (sub-lethal) doses quickly select populations with average levels of tolerance, whilst doses that are too high may impose excessive selection pressures
f. Appropriate, well-maintained equipment should be used to apply insecticides. Recommended water volumes, spray pressures and optimal temperatures should be used to obtain optimal coverage
g. Where larval stages are being controlled, target younger larval instars where possible because these are usually much more susceptible and therefore much more effectively controlled by insecticides than older stages
h. Use appropriate local economic thresholds and spray intervals
i. Follow label recommendations or local expert advice for use of alternations or sequences of different classes of insecticide with differing modes of action as part of an IRM strategy
j. Where there are multiple applications per year or growing season, alternate products of different MoA classes
k. In the event of a control failure, do not reapply the same insecticide but change the class of insecticides to one having a different mode of action and to which there is no [locally] known cross-resistance
l. Mixtures may offer a short-term solution to resistance problems, but it is essential to ensure that each component of a mixture belongs to a different insecticide mode of action class, and that each component is used at its full rate
m. Consideration should be given to monitoring for the incidence of resistance in the most commercially important situations and gauge levels of control obtained
n. Withholding use of a product to which resistance has developed until susceptibility returns may be a valid tactic if sufficient alternative chemical classes remain to provide effective control.

Appendix 3

IRAC Mode of Action Classification - Superseded or Obsolete Compounds
(Withdrawn compounds for which a registration no longer exists, but for which a searchable directory of MoA classification is historically of interest)

In preparation 2007