

IRAC MoA Classification Scheme

Issued, February 2014

Version 7.3

Prepared by: IRAC International MoA Working Group

Approved by: IRAC Executive

Contents:

1. Introduction	3
2. What is resistance?.....	3
3. MoA, Target-site resistance and Cross-resistance	3
4. Use of alternations or sequences of different MoAs	3
5. Non-target site resistance mechanisms	4
6. The MoA Classification Scheme	4
6.1 Rules for inclusion of a compound in the MoA list	4
6.2 Classification Table	5
6.3 Criteria for descriptors of the quality of MoA information	11
6.4 Notes regarding Sub-groups	12
6.5 General notes & MoA Classification Scheme Updates	12

Appendix 1

Product labels: Indication of MoA of active ingredient and accompanying IRM advice	14
---	----

Appendix 2

IRM principles recommended and endorsed by IRAC	15
---	----

Appendix 3

MoA Group Descriptors	16
-----------------------------	----

Appendix 4

Procedure for allocation of new insecticidal materials to the MoA Classification	19
---	----

Appendix 5

Active Ingredients in alphabetical order with their MOA Classification	22
--	----

1. Introduction

The IRAC Mode of Action (MoA) classification provides 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.

2. 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 growers. Resistance arises through the over-use or misuse of an insecticide or acaricide against a pest species and results from the selection of resistant forms of the pest and the consequent evolution of populations that are resistant to that insecticide or acaricide.

3. MoA, Target-site resistance and Cross-resistance

In many cases, not only does resistance render the selecting compound ineffective, it 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 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 group share a common MoA, there is a high risk that existing or developing target-site resistance will confer cross-resistance to all compounds in the same group. It is this concept of cross-resistance within a family of chemically related insecticides or acaricides that is the basis of the IRAC MoA classification.

4. Use of alternations or sequences of different MoAs

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 from 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 successive generations of the pest should not be treated with compounds from the same MoA group.

Three groups in the classification are exceptions in that they do not contain compounds acting at a common target site and are therefore exempt from the proscription against rotation of compounds within a group. These are Group 8, Miscellaneous non-specific (multi-site) inhibitors; Group 13, Uncouplers of oxidative phosphorylation via disruption of the proton gradient; and Group UN, Compounds of unknown or uncertain MoA.

5. 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.

6. The MoA Classification Scheme

The MOA classification scheme developed and endorsed by IRAC is based on the best available evidence of the MoA 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 MoA 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.

6.1. Rules for inclusion of a compound in the MoA list

- Chemical nomenclature is generally based on that appearing in *The Pesticide Manual*, 16th edition, November 2012, Ed. Colin MacBean, published by The British Crop Protection Council. ISBN 9781901396867
- 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.
- 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 may be used

6.2. Classification Table

IRAC MoA Classification v 7.3, February 2014		
See section 6.4 for further information on sub-groups. See section 6.3 for criteria for descriptors of the quality of MoA information.		
Main Group and Primary Site of Action	Chemical Sub-group or exemplifying Active Ingredient	Active Ingredients
1 Acetylcholinesterase (AChE) inhibitors Nerve action {Strong evidence that action at this protein is responsible for insecticidal effects}	1A Carbamates	Alanycarb, Aldicarb, Bendiocarb, Benfuracarb, Butocarboxim, Butoxycarboxim, Carbaryl, Carbofuran, Carbosulfan, Ethiofencarb, Fenobucarb, Formetanate, Furathiocarb, Isoprocarb, Methiocarb, Methomyl, Metolcarb, Oxamyl, Pirimicarb, Propoxur, Thiodicarb, Thiofanox, Triazamate, Trimethacarb, XMC, Xylylcarb
	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, Imicyafos, 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- methyl, Profenofos, Propetamphos, Prothiofos, Pyraclofos, Pyridaphenthion, Quinalphos, Sulfotep, Tebupirimfos, Temephos, Terbufos, Tetrachlorvinphos, Thiometon, Triazophos, Trichlorfon, Vamidathion
2 GABA-gated chloride channel antagonists Nerve action {Strong evidence that action at this protein is responsible for insecticidal effects}	2A Cyclodiene organochlorines	Chlordane, Endosulfan
	2B Phenylpyrazoles (Fiproles)	Ethiprole, Fipronil
3 Sodium channel modulators Nerve action {Strong evidence that action at this protein is responsible for insecticidal effects}	3A Pyrethroids Pyrethrins	Acrinathrin, Allethrin, <i>d-cis-trans</i> Allethrin, <i>d-trans</i> Allethrin, Bifenthrin, Bioallethrin, Bioallethrin S-cyclopentenyl isomer, Bioresmethrin, Cycloprothrin, Cyfluthrin, <i>beta</i> -Cyfluthrin, Cyhalothrin, <i>lambda</i> -Cyhalothrin, <i>gamma</i> -Cyhalothrin, Cypermethrin, <i>alpha</i> -Cypermethrin, <i>beta</i> -Cypermethrin, <i>theta</i> -cypermethrin, <i>zeta</i> -Cypermethrin, Cyphenothrin, (<i>1R</i>)- <i>trans</i> - isomers], Deltamethrin, Empenthrin (<i>EZ</i>)- (<i>1R</i>)- isomers], Esfenvalerate, Etofenprox, Fenpropathrin, Fenvalerate, Flucythrinate, Flumethrin, <i>tau</i> -Fluvalinate, Halfenprox, Imiprothrin, Kadethrin, Permethrin, Phenothrin [(<i>1R</i>)- <i>trans</i> - isomer], Prallethrin, Pyrethrins (pyrethrum), Resmethrin, Silafluofen, Tefluthrin, Tetramethrin, Tetramethrin [(<i>1R</i>)-isomers], Tralomethrin, Transfluthrin,

IRAC MoA Classification v 7.3, February 2014

*See section 6.4 for further information on sub-groups.
See section 6.3 for criteria for descriptors of the quality of MoA information.*

Main Group and Primary Site of Action	Chemical Sub-group or exemplifying Active Ingredient	Active Ingredients
	3B DDT Methoxychlor	DDT Methoxychlor
4 Nicotinic acetylcholine receptor (nAChR) agonists Nerve action {Strong evidence that action at one or more of this class of protein is responsible for insecticidal effects}	4A Neonicotinoids	Acetamiprid, Clothianidin, Dinotefuran, Imidacloprid, Nitenpyram, Thiacloprid, Thiamethoxam,
	4B Nicotine	Nicotine
	4C Sulfoxaflor	Sulfoxaflor
	4D Butenolides	Flupyradifurone
5 Nicotinic acetylcholine receptor (nAChR) allosteric activators Nerve action {Strong evidence that action at one or more of this class of protein is responsible for insecticidal effects}	Spinosyns	Spinetoram, Spinosad
6 Chloride channel activators Nerve and muscle action {Strong evidence that action at one or more of this class of protein is responsible for insecticidal effects}	Avermectins, Milbemycins	Abamectin, Emamectin benzoate, Lepimectin, Milbemectin
7 Juvenile hormone mimics Growth regulation {Target protein responsible for biological activity is unknown, or uncharacterized}	7A Juvenile hormone analogues	Hydroprene, Kinoprene, Methoprene
	7B Fenoxycarb	Fenoxycarb
	7C Pyriproxyfen	Pyriproxyfen

IRAC MoA Classification v 7.3, February 2014

See section 6.4 for further information on sub-groups.
See section 6.3 for criteria for descriptors of the quality of MoA information.

Main Group and Primary Site of Action	Chemical Sub-group or exemplifying Active Ingredient	Active Ingredients
8 * Miscellaneous non-specific (multi-site) inhibitors	8A Alkyl halides	Methyl bromide and other alkyl halides
	8B Chloropicrin	Chloropicrin
	8C Sulfuryl fluoride	Sulfuryl fluoride
	8D Borates	Borax
	8E Tartar emetic	Tartar emetic
9 Modulators of Chordotonal Organs Nerve action {Target protein responsible for biological activity is unknown, or uncharacterized}	9B Pymetrozine	Pymetrozine
	9C Flonicamid	Flonicamid
10 Mite growth inhibitors Growth regulation {Target protein responsible for biological activity is unknown, or uncharacterized}	10A Clofentezine Hexythiazox Diflovidazin	Clofentezine, Hexythiazox, Diflovidazin
	10B Etoxazole	Etoxazole
11 Microbial disruptors of insect midgut membranes (includes transgenic crops expressing <i>Bacillus thuringiensis</i> toxins, however specific guidance for resistance management of transgenic crops is not based on rotation of modes of action)	11A <i>Bacillus thuringiensis</i> and the insecticidal proteins they produce	<i>Bacillus thuringiensis</i> subsp. <i>israelensis</i> <i>Bacillus thuringiensis</i> subsp. <i>aizawai</i> <i>Bacillus thuringiensis</i> subsp. <i>kurstaki</i> <i>Bacillus thuringiensis</i> subsp. <i>tenebrionis</i> <i>B.t.</i> crop proteins: (* Please see footnote) Cry1Ab, Cry1Ac, Cry1Fa, Cry1A.105, Cry2Ab, Vip3A, mCry3A, Cry3Ab, Cry3Bb, Cry34Ab1/Cry35Ab1
	11B <i>Bacillus sphaericus</i>	<i>Bacillus sphaericus</i>

IRAC MoA Classification v 7.3, February 2014

*See section 6.4 for further information on sub-groups.
See section 6.3 for criteria for descriptors of the quality of MoA information.*

Main Group and Primary Site of Action	Chemical Sub-group or exemplifying Active Ingredient	Active Ingredients
12 Inhibitors of mitochondrial ATP synthase Energy metabolism {Compounds affect the function of this protein, but it is not clear that this is what leads to biological activity}	12A Diafenthuron	Diafenthuron
	12B Organotin miticides	Azocyclotin, Cyhexatin, Fenbutatin oxide
	12C Propargite	Propargite
	12D Tetradifon	Tetradifon
13 * Uncouplers of oxidative phosphorylation via disruption of the proton gradient Energy metabolism	Chlorfenapyr DNOC Sulfluramid	Chlorfenapyr DNOC Sulfluramid
14 Nicotinic acetylcholine receptor (nAChR) channel blockers Nerve action {Compounds affect the function of this protein, but it is not clear that this is what leads to biological activity}	Nereistoxin analogues	Bensultap, Cartap hydrochloride, Thiocyclam, Thiosultap-sodium
15 Inhibitors of chitin biosynthesis, type 0 Growth regulation {Target protein responsible for biological activity is unknown, or uncharacterized}	Benzoylureas	Bistrifluron, Chlorfluazuron, Diflubenzuron, Flucycloxuron, Flufenoxuron, Hexaflumuron, Lufenuron, Novaluron, Noviflumuron, Teflubenzuron, Triflumuron
16 Inhibitors of chitin biosynthesis, type 1 Growth regulation {Target protein responsible for biological activity is unknown, or uncharacterized}	Buprofezin	Buprofezin

IRAC MoA Classification v 7.3, February 2014

See section 6.4 for further information on sub-groups.
See section 6.3 for criteria for descriptors of the quality of MoA information.

Main Group and Primary Site of Action	Chemical Sub-group or exemplifying Active Ingredient	Active Ingredients
17 Moulting disruptor, Dipteran Growth regulation {Target protein responsible for biological activity is unknown, or uncharacterized}	Cyromazine	Cyromazine
18 Ecdysone receptor agonists Growth regulation {Strong evidence that action at this protein is responsible for insecticidal effects}	Diacylhydrazines	Chromafenozide, Halofenozide, Methoxyfenozide, Tebufenozide
19 Octopamine receptor agonists Nerve action {Good evidence that action at one or more of this class of protein is responsible for insecticidal effects}	Amitraz	Amitraz
20 Mitochondrial complex III electron transport inhibitors Energy metabolism {Good evidence that action at this protein complex is responsible for insecticidal effects}	20A Hydramethylnon	Hydramethylnon
	20B Acequinocyl	Acequinocyl
	20C Fluacrypyrim	Fluacrypyrim
21 Mitochondrial complex I electron transport inhibitors Energy metabolism {Good evidence that action at this protein complex is responsible for insecticidal effects}	21A METI acaricides and insecticides	Fenazaquin, Fenpyroximate, Pyrimidifen, Pyridaben, Tebufenpyrad, Tolfenpyrad
	21B Rotenone	Rotenone (Derris)

IRAC MoA Classification v 7.3, February 2014

*See section 6.4 for further information on sub-groups.
See section 6.3 for criteria for descriptors of the quality of MoA information.*

Main Group and Primary Site of Action	Chemical Sub-group or exemplifying Active Ingredient	Active Ingredients
22 Voltage-dependent sodium channel blockers Nerve action {Good evidence that action at this protein complex is responsible for insecticidal effects}	22A Indoxacarb	Indoxacarb
	22B Metaflumizone	Metaflumizone
23 Inhibitors of acetyl CoA carboxylase. Lipid synthesis, growth regulation {Good evidence that action at this protein is responsible for insecticidal effects}	Tetronic and Tetramic acid derivatives	Spirodiclofen, Spiromesifen, Spirotetramat
24 Mitochondrial complex IV electron transport inhibitors Energy metabolism {Good evidence that action at this protein complex is responsible for insecticidal effects}	24A Phosphine	Aluminium phosphide, Calcium phosphide, Phosphine, Zinc phosphide
	24B Cyanide	Cyanide
25 Mitochondrial complex II electron transport inhibitors Energy metabolism {Good evidence that action at this protein complex is responsible for insecticidal effects}	Beta-ketonitrile derivatives	Cyenopyrafen, Cyflumetofen
28 Ryanodine receptor modulators Nerve and muscle action {Good evidence that action at this protein complex is responsible for insecticidal effects}	Diamides	Chlorantraniliprole, Cyantraniliprole, Flubendiamide

IRAC MoA Classification v 7.3, February 2014

See section 6.4 for further information on sub-groups.
See section 6.3 for criteria for descriptors of the quality of MoA information.

Main Group and Primary Site of Action	Chemical Sub-group or exemplifying Active Ingredient	Active Ingredients
UN * Compounds of unknown or uncertain MoA {Target protein responsible for biological activity is unknown, or uncharacterized}	Azadirachtin	Azadirachtin
	Benzoximate	Benzoximate
	Bifenazate	Bifenazate
	Bromopropylate	Bromopropylate
	Chinomethionat	Chinomethionat
	Cryolite	Cryolite
	Dicofol	Dicofol
	Pyridalyl	Pyridalyl
	Pyrifluquinazon	Pyrifluquinazon

Table Notes:

- a) Inclusion of a compound in the classification above does not necessarily signify regulatory approval.
- b) MoA assignments will usually involve identification of the target protein responsible for the biological effect, although groupings can be made where compounds share distinctive physiological effects and have related chemical structures.
- c) Groups 26 and 27 are unassigned at this time and have therefore been omitted from the table.
- d) A compound with an unknown or controversial MoA or an unknown mode of toxicity will be held in group 'UN' until evidence becomes available to enable that compound to be assigned to a more appropriate MoA class.
- e) Actives in groups marked with a * are thought not to share a common target site and therefore may be freely rotated with each other unless there is reason to expect cross-resistance. These groups are 8, 13, and UN.

6.3. Criteria for descriptors of the quality of MoA information

{Strong evidence that action at this protein (or protein complex) is responsible for insecticidal effects}	Potent effects on the function of the target protein and either resistance due to mutation / overexpression / removal of this protein <u>or</u> correlation of potency between effects on the protein and biological activity for a set of analogues.
{Good evidence that action at this protein (or protein complex) is responsible for insecticidal effects}	Highly potent effects on the function of the protein combined with clearly consistent physiological effects
{Compounds affect the function of this protein, but it is not clear that this is what leads to biological activity}	Compounds (or their metabolites) have moderate or low potency on the function of the protein, and there is little or no evidence associating this effect with biological activity. Compounds may be grouped because of similarity of structure and distinctive physiological effect.
{Target protein responsible for biological activity is unknown, or uncharacterized}	Compounds may be grouped because of similarity of structure and distinctive physiological effect.

6.4. Notes regarding sub-groups

Sub-groups represent distinct chemical classes that are believed to have the same MoA but are different enough in chemical structure or mode of interaction with the target protein that the chance of selection for either metabolic or target-site cross-resistance is reduced compared to close analogs. Sub-groups may also distinguish compounds that are chemically similar but known to bind differently within the target or to have differential selectivity among multiple targets.

The cross-resistance potential between sub-groups is higher than that between different groups, so rotation between sub-groups should be avoided. In exceptional circumstances (i.e. where effective registered insecticides from other mode of action groups are unavailable) rotation may be considered following consultation with local expert advice and where cross-resistance does not exist. These exceptions should not be considered sustainable resistance management strategies, and alternative options should be sought to maintain pest susceptibility.

The following notes provide additional information about particular sub-groups.

Sub-groups	Notes
3A & 3B	Because DDT is no longer used in agriculture, this is only applicable for the control of human disease vectors such as mosquitoes.
4A, 4B,4C & 4D	Although these compounds are believed to have the same target site, current evidence indicates that the risk of metabolic cross-resistance between subgroups is low.
10A	Hexythiazox is grouped with clofentezine because they exhibit cross-resistance, even though they are structurally distinct, and the target site for these compounds is unknown. Diflovidazin has been added to this group because it is a close analogue of clofentezine and is expected to have the same mode of action.
11A	Different <i>Bacillus thuringiensis</i> products that target different insect orders may be used together without compromising their resistance management. Rotation between certain specific <i>Bacillus thuringiensis</i> microbial products may provide resistance management benefits for some pests. Consult product-specific recommendations. <u>B.t. Crop Proteins:</u> Where there are differences among the specific receptors within the midguts of target insects, transgenic crops containing certain combinations of the listed proteins provide resistance management benefits.
22A & 22B	Although these compounds are believed to have the same target site, current evidence indicates that the risk of metabolic cross-resistance between subgroups is low.

6.5. General notes & MoA Classification Scheme Updates

- Further details on the MoA Group Descriptors are given in Appendix 3.
- A list of active ingredients in alphabetical order with their respective MoA classification is given in Appendix 5.
- The Classification Scheme 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 MoA of insecticides currently in use.
- The IRAC MoA classification is reviewed and reissued at intervals as required. The latest version is always available for reference via the IRAC website (www.irac-online.org).
- Submissions for new active ingredients together with recommendations for their inclusion in specific new or existing MoA classes, together with citations or evidence for classification should be made to IRAC through the website.

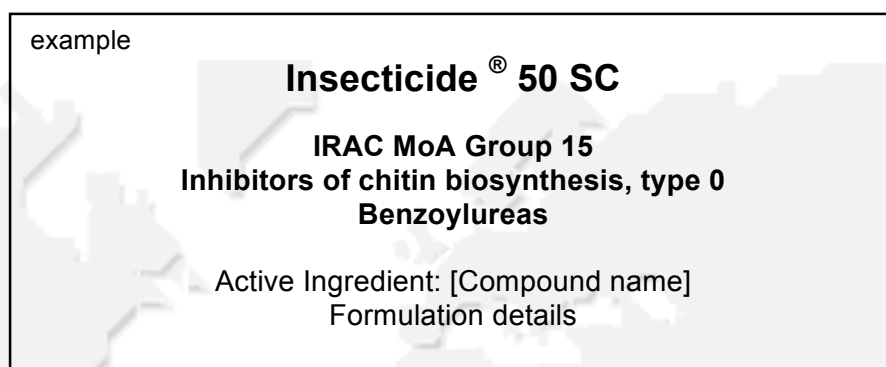
- IRAC member companies review draft versions before an agreed final version of any update is published. In addition, a number of internationally well-known insect toxicologists and biochemists can be consulted regarding additions, deletions or other changes to the list. Details of the procedures followed for allocation of new insecticidal materials to the MoA classification are given in Appendix 4.
- 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.
- Superseded, obsolete or withdrawn compounds for which no current registration exists, and that are no longer in common usage, are not listed.
- 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. Suggestions for improvements are likewise welcome.



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.



For resistance management purposes, Insecticide 50SC is an IRAC MoA 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 of insecticides from the same chemical sub-group, (indicated by the IRAC MoA Group number).
- Alternate with products from other IRAC MoA 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

IRM principles recommended and endorsed by IRAC

- Consult a local agricultural advisor or extension services in the area for up-to-date recommendations and advice on IPM and IRM programmes.
- Consider options for minimizing insecticide use by selecting early-maturing or pest-tolerant varieties of crop plants.
- 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.
- Where possible select insecticides and other pest management tools, which preserve beneficial insects.
- 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.
- 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.
- 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.
- Use appropriate local economic thresholds and spray intervals.
- 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.
- Where there are multiple applications per year or growing season, alternate products of different MoA classes.
- In the event of a control failure, do not reapply the same insecticide but change the class of insecticides to one having a different MoA and to which there is no [locally] known cross-resistance.
- 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 MoA class, and that each component is used at its full rate.
- Consideration should be given to monitoring for the incidence of resistance in the most commercially important situations and gauge levels of control obtained.
- 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

MoA Group Descriptors

Nerve and Muscle Targets

Most current insecticides act on nerve and muscle targets. Insecticides that act on these targets 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.

Group 2 GABA-gated chloride channel antagonists

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

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.

Group 4 Nicotinic acetylcholine receptor (nAChR) agonists

Mimic the agonist action of acetylcholine at nAChRs, causing hyperexcitation. Acetylcholine is the major excitatory neurotransmitter in the insect central nervous system.

Group 5 Nicotinic acetylcholine receptor (nAChR) allosteric modulators

Allosterically activate nAChRs, causing hyperexcitation of the nervous system. Acetylcholine is the major excitatory neurotransmitter in the insect central nervous system.

Group 6 Chloride channel activators

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

Group 9 Modulators of Chordotonal Organs

Stimulate chordotonal proprioceptors by an unknown mechanism. This impairs fine motor control, resulting in disruption of feeding and other behaviors of Hemiptera and certain other insects.

Group 14 Nicotinic acetylcholine receptor (nAChR) channel blockers

Block the nAChR ion channel, resulting in nervous system block and paralysis. Acetylcholine is the major excitatory neurotransmitter in the insect central nervous system.

Group 19 Octopamine receptor agonists

Activate octopamine receptors, leading to hyperexcitation. Octopamine is the insect equivalent of adrenaline, the fight-or-flight neurohormone.

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.

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.

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.

Group 10 Mite growth inhibitors

Incompletely defined MoA leading to growth inhibition

Group 15 Inhibitors of chitin biosynthesis, type 0

Incompletely defined MoA leading to inhibition of chitin biosynthesis.

Group 16 Inhibitors of chitin biosynthesis, type 1

Incompletely defined MoA leading to inhibition of chitin biosynthesis in a number of insects, including whiteflies.

Group 17 Moulting disruptor, Dipteran

Incompletely defined MoA that leads to moult disruption.

Group 18 Ecdysone receptor agonists

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

Group 23 Inhibitors of acetyl CoA carboxylase

Inhibit acetyl coenzyme A carboxylase, part of the first step in lipid biosynthesis, leading to insect death.

Respiration Targets

Mitochondrial respiration produces ATP, the molecule that energizes all vital cellular processes. In mitochondria, an electron transport chain stores the energy released by oxidation in the form of a proton gradient, which 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 12 Inhibitors of mitochondrial ATP synthase

Inhibit the enzyme that synthesizes ATP.

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.

Group 20 Mitochondrial complex III electron transport inhibitors

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

Group 21 Mitochondrial complex I electron transport inhibitors

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

Group 24 Mitochondrial complex IV electron transport inhibitors

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

Group 25 Mitochondrial complex II electron transport inhibitors

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

Midgut Targets

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

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.

Unknown or non-specific targets

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

Group 8 Miscellaneous non-specific (multi-site) inhibitors**Group UN Compounds of unknown or uncertain MoA**

Appendix 4

Procedure for allocation of new insecticidal materials to the MoA classification

IRAC maintains the MoA Classification scheme as the definitive, globally-recognised, ultimate authority on insecticide modes of action. In order to provide the best possible information for resistance management purposes, IRAC also issues regular updates of the scheme, in which newly introduced insecticides are allocated to an appropriate MoA classification group and structural sub-group, and in which re-classification or the correction of errors or anomalies for specific compounds is undertaken in light of definitive new information. This document details how these processes are administered by IRAC.

Who is responsible for the process within IRAC?

The IRAC MoA Team comprises technical representatives of the member companies with expertise in insect toxicology, pharmacology or biochemistry. All IRAC companies are eligible to contribute technical expertise to the group. The group meets regularly to consider the content and detail of the MoA scheme and makes proposals on significant additions, deletions or reallocations of compounds within the scheme for consideration by the IRAC Executive.

Why and how often is the scheme updated?

New versions of the scheme are issued periodically as and when necessary, as a result of the MoA Team's consideration of new information. The introduction of major new MoA groups or the reallocation of compounds or groups would merit the issue of a new version (vN). Minor changes or corrections that do not significantly impact the scheme are undertaken automatically at intervals as necessary, and sub-versions are issued (vN.n). New sub-versions may be issued up to several times per year as required, while new full versions are not anticipated more than once per year. The potential impact of proposed significant changes on derived versions of the scheme around the world is fully appreciated, especially in countries where MoA labelling of products is used. The MoA team is cognisant of these impacts and revisions are only proposed when the evidence for change is scientifically compelling.

What evidence is needed to support MoA classification of a compound?

Proposals for additions to the MoA scheme or for amendments to the current scheme should be submitted to the IRAC MoA team (details below). These proposals will be considered by the Team and a decision on the outcome will be provided to the proposer in due course. Published material in high quality, front line, peer-reviewed, scientific journals is especially useful as a source of information for consideration by the team, and those companies, bodies or individuals submitting proposals for consideration by the team are strongly encouraged to provide such information wherever possible. Corroborating information is also especially welcome. Unpublished material may be submitted in evidence, and the MoA team will interpret this appropriately.

Several types of data can be used to establish MoA (including the activation of pro-insecticides to their actives). Convincing evidence to support the MoA hypothesis is needed. This includes the demonstration of a clear target effect (activation, inhibition, or modulation) at concentrations that can reasonably be expected in the intoxicated organism. Preferably, these data may be corroborated by physiological and/or symptomology studies to link insect mortality to the effect on the target site. A positive structure-activity correlation of *in vitro* efficacy with insecticidal potency, and/or target site mutations conferring resistance are required to further substantiate the proposed MoA.

What are the criteria for establishing MoA Sub-groups?

Sub-groups represent distinct chemical classes that are believed to have the same MoA but are different enough in chemical structure or mode of interaction with the target protein that the chance of selection for either metabolic or target-site cross-resistance is reduced compared to close analogs. Sub-groups may also distinguish compounds that are chemically similar but known to bind differently within the target or to have differential selectivity among multiple targets.

The cross-resistance potential between sub-groups is higher than that between different groups, so rotation between sub-groups should be avoided. In exceptional circumstances (i.e. where effective registered insecticides from other mode of action groups are unavailable) rotation may be considered following consultation with local expert advice and where cross-resistance does not exist. These exceptions should not be considered sustainable resistance management strategies, and alternative options should be sought to maintain pest susceptibility.

How are decisions made by the MoA Team?

Given the definitive nature of the IRAC MoA scheme, the MoA Team regards it as an absolute priority that the highest levels of scientific integrity are always employed in the consideration and discussion of allocation of compounds. In general, agreement on allocation of a compound is usually arrived at through consensus within the Team, following detailed discussion. Major decisions, for example the introduction of new MoA classes or sub-classes are proposed to the IRAC Executive for ratification. In the event that the Team cannot agree it may choose to place the case with a panel of external MoA experts to gain their written opinion before reconsidering the case. The composition of the expert panel is agreed in advance by the Team. If after reconsidering the particular case the team is still in disagreement, the matter will be passed to the IRAC Executive for further consideration. Where individual members of the Team are subject to a conflict of interests through company affiliation or other interests, they may choose to withdraw from discussion of particular compounds as they consider appropriate.

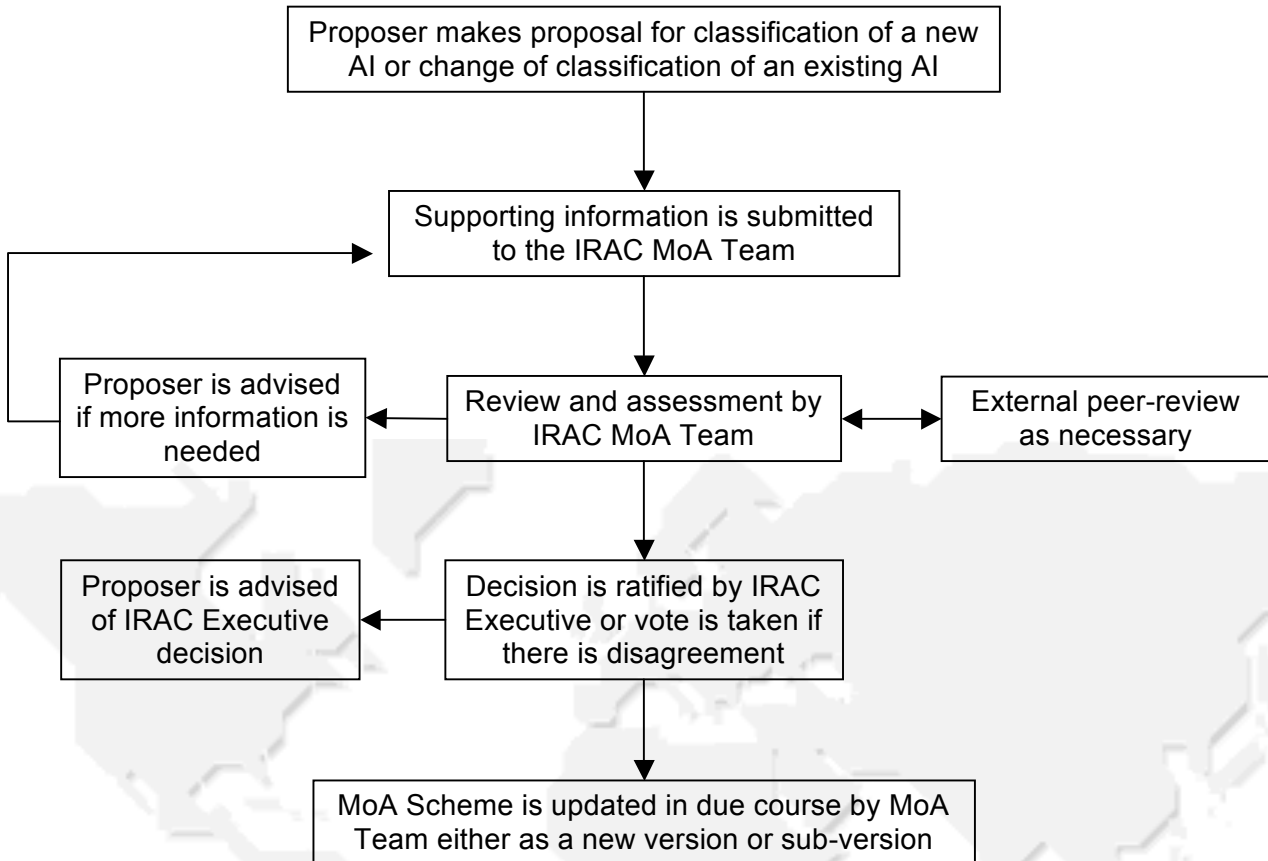
How long does this process take?

The MoA Team has a duty to make a definitive decision on allocation of a compound as quickly as possible following receipt of appropriate supporting evidence. For straightforward cases that do not require external consultation it should generally be expected that the Team could provide feedback to proposers within 3 months. The need for external consultants may extend the process to 6 months.

To whom should proposals be sent?

Proposals for new compounds or for changes to the current IRAC MoA scheme should be submitted to the IRAC MoA Team via the IRAC International Coordinator. A link to the coordinator is provided on the IRAC website (www.ircac-online.org) at the bottom of each page under 'Contact'.

Procedure for updates to IRAC MoA Classification Scheme



Appendix 5

Active Ingredients (Alphabetical Order) with MOA Classification

Active Ingredient	MOA No.	Active Ingredient	MOA No.
Abamectin	6	Carbosulfan	1A
Acephate	1B	Cartap hydrochloride	14
Acequinocyl	20B	Chinomethionat	UN
Acetamiprid	4A	Chlorantraniliprole	28
Acrinathrin	3A	Chlordane	2A
Alanycarb	1A	Chlorethoxyfos	1B
Aldicarb	1A	Chlorfenapyr	13
Allethrin	3A	Chlorfenvinphos	1B
<i>alpha</i> -Cypermethrin	3A	Chlorfluazuron	15
Aluminium phosphide	24A	Chlormephos	1B
Amitraz	19	Chloropicrin	8B
Azadirachtin	UN	Chlorpyrifos	1B
Azamethiphos	1B	Chlorpyrifos-methyl	1B
Azinphos-ethyl	1B	Chromafenozide	18
Azinphos-methyl	1B	Clofentezine	10A
Azocyclotin	12B	Clothianidin	4A
<i>Bacillus thuringiensis</i>	11A	Coumaphos	1B
<i>Bacillus sphaericus</i>	11B	Cryolite	UN
Bendiocarb	1A	Cyanide	24B
Benfuracarb	1A	Cyanophos	1B
Bensultap	14	Cyantraniliprole	28
Benzoximate	UN	Cycloprothrin	3A
<i>beta</i> -Cyfluthrin	3A	Cyenopyrafen	25
<i>beta</i> -Cypermethrin	3A	Cyflumetofen	25
Bifenazate	UN	Cyfluthrin	3A
Bifenthrin	3A	Cyhalothrin	3A
Bioallethrin	3A	Cyhexatin	12B
Bioallethrin S-cyclopentenyl isomer	3A	Cypermethrin	3A
Bioresmethrin	3A	Cyphenothrin (1 <i>R</i>)- <i>trans</i> -isomers]	3A
Bistrifluron	15	Cyromazine	17
Borax	8D	d- <i>cis-trans</i> Allethrin	3A
Bromopropylate	UN	DDT	3B
Buprofezin	16	Deltamethrin	3A
Butocarboxim	1A	Demeton-S-methyl	1B
Butoxycarboxim	1A	Diafenthiuron	12A
Cadusafos	1B	Diazinon	1B
Calcium phosphide	24A	Dichlorvos/ DDVP	1B
Carbaryl	1A	Dicofol	UN
Carbofuran	1A	Dicrotophos	1B

Active Ingredient	MOA No.	Active Ingredient	MOA No.
Diflovidazin	10A	Halfenprox	3A
Diflubenzuron	15	Halofenozide	18
Dimethoate	1B	Heptenophos	1B
Dimethylvinphos	1B	Hexaflumuron	15
Dinotefuran	4A	Hexythiazox	10A
Disulfoton	1B	Hydramethylnon	20A
DNOC	13	Hydroprene	7A
<i>d-trans</i> Allethrin	3A	Imicyafos	1B
Emamectin benzoate	6	Imidacloprid	4A
Empenthrin [(E _Z)-(1 <i>R</i>)-isomers]	3A	Imiprothrin	3A
Endosulfan	2A	Indoxacarb	22A
EPN	1B	Isofenphos	1B
Esfenvalerate	3A	Isoprocarb	1A
Ethiofencarb	1A	Isopropyl O- (methoxyaminothio-phosphoryl) salicylate	1B
Ethion	1B	Isoxathion	1B
Ethiprole	2B	Kadethrin	3A
Ethoprophos	1B	Kinoprene	7A
Etofenprox	3A	<i>lambda</i> -Cyhalothrin	3A
Etoxazole	10B	Lepimectin	6
Famphur	1B	Lufenuron	15
Fenamiphos	1B	Malathion	1B
Fenazaquin	21A	Mecarbam	1B
Fenbutatin oxide	12B	Metaflumizone	22B
Fenitrothion	1B	Methamidophos	1B
Fenobucarb	1A	Methidathion	1B
Fenoxycarb	7B	Methiocarb	1A
Fenpropathrin	3A	Methomyl	1A
Fenpyroximate	21A	Methoprene	7A
Fenthion	1B	Methoxychlor	3B
Fenvalerate	3A	Methoxyfenozide	18
Fipronil	2B	Methyl bromide	8A
Flonicamid	9C	Metolcarb	1A
Fluacrypyrim	20C	Mevinphos	1B
Flubendimide	28	Milbemectin	6
Flucycloxuron	15	Monocrotophos	1B
Flucythrinate	3A	Naled	1B
Flufenoxuron	15	Nicotine	4B
Flumethrin	3A	Nitenpyram	4A
Flupyradifurone	4D	Novaluron	15
Formetanate	1A	Noviflumuron	15
Fosthiazate	1B	Omethoate	1B
Furathiocarb	1A	Oxamyl	1A
<i>gamma</i> -Cyhalothrin	3A	Oxydemeton-methyl	1B

Active Ingredient	MOA No.	Active Ingredient	MOA No.
Parathion	1B	Sulfoxaflor	4C
Parathion-methyl	1B	Sulfuramid	13
Permethrin	3A	Sulfuryl fluoride	8C
Phenothrin [(1 <i>R</i>)- <i>trans</i> - isomer]	3A	Tartar emetic	8E
Phenthoate	1B	<i>tau</i> -Fluvalinate	3A
Phorate	1B	Tebufenozide	18
Phosalone	1B	Tebufenpyrad	21A
Phosmet	1B	Tebupirimfos	1B
Phosphamidon	1B	Teflubenzuron	15
Phosphine	24A	Tefluthrin	3A
Phoxim	1B	Temephos	1B
Pirimicarb	1A	Terbufos	1B
Pirimiphos- methyl	1B	Tetrachlorvinphos	1B
Prallethrin	3A	Tetradifon	12D
Profenofos	1B	Tetramethrin	3A
Propargite	12C	Tetramethrin [(1 <i>R</i>)- isomers]	3A
Propetamphos	1B	<i>theta</i> -cypermethrin	3A
Propoxur	1A	Thiacloprid	4A
Prothiofos	1B	Thiamethoxam	4A
Pymetrozine	9B	Thiocyclam	14
Pyraclufos	1B	Thiodicarb	1A
Pyrethrins (pyrethrum)	3A	Thiofanox	1A
Pyridaben	21A	Thiometon	1B
Pyridalyl	UN	Thiosultap-sodium	14
Pyridaphenthion	1B	Tolfenpyrad	21A
Pyrifluquinazon	UN	Tralomethrin	3A
Pyrimidifen	21A	Transfluthrin	3A
Pyriproxyfen	7C	Triazamate	1A
Quinalphos	1B	Triazophos	1B
Resmethrin	3A	Trichlorfon	1B
Rotenone (Derris)	21B	Triflumuron	15
Silafluofen	3A	Trimethacarb	1A
Spinetoram	5	Vamidotion	1B
Spinosad	5	XMC	1A
Spirodiclofen	23	Xylylcarb	1A
Spiromesifen	23	<i>zeta</i> -Cypermethrin	3A
Spirotetramat	23	Zinc phosphide	24A
Sulfotep	1B		