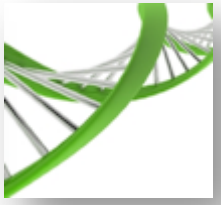
Insecticide Resistance Action Committee

MoA WG 2015/16

50th IRAC International Meeting, Dublin

April 5-8th, 2016




CropLife INTERNATIONAL

MoA WG Team Members: 2015-2016

- Dan Cordova – DuPont - Chair (as of Oct 2015)
- Andrew Crossthwaite – Syngenta - Deputy Chair (as of Oct 2015)
- Fergus Earley – Syngenta (Advisor)
- Ulli Ebbinghaus-Kintscher – Bayer
- Danny Karmon – Adama
- Ralf Nauen - Bayer
- Shigeru Saito – Sumitomo
- Kazuyuki Sakata – NNI
- Vince Salgado – BASF (outgoing Chair)
- Tom Sparks – Dow
- Jerry Watson – Dow
- Excellent support from Alan Porter

MoA WG Activities (since Mar 2014)

Six conference calls (# of participants)

14 Oct 2014 (8)
13 Nov 2014 (6)
24 Mar 2015 (8)
17 Sep 2015 F2F Rothamsted (8)
2 Nov 2015 (6)
28 Jan 2016 (8)

Classification Scheme updated (v8.1)

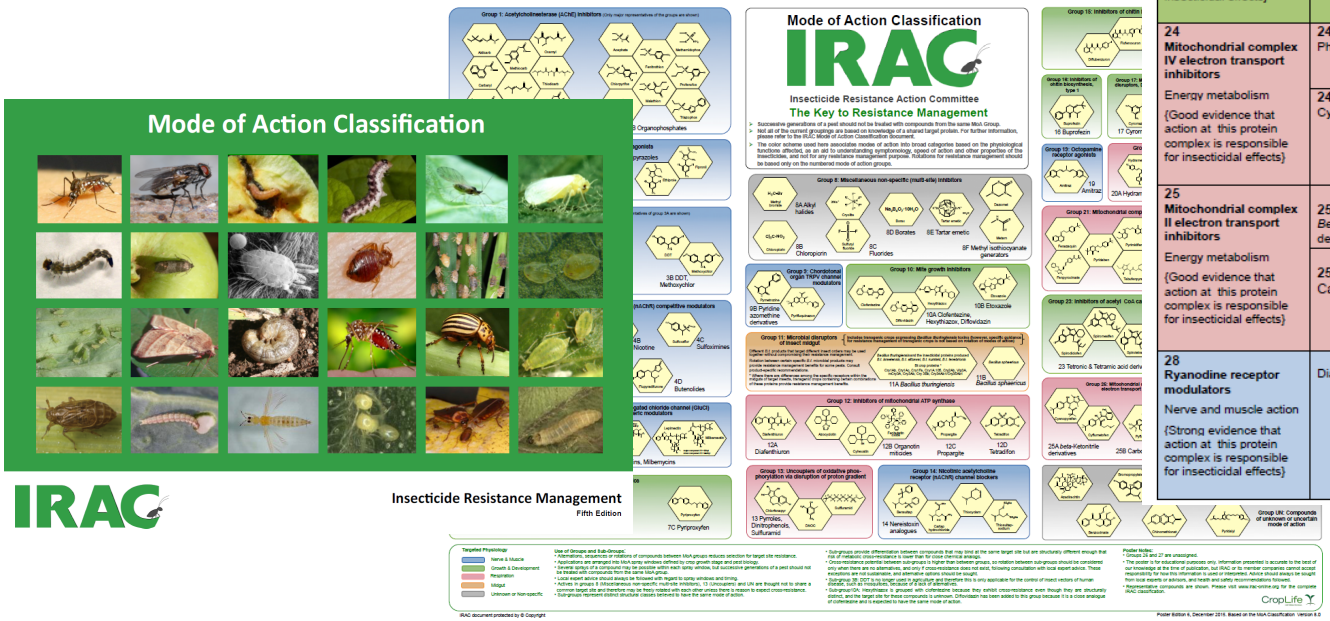
IRAC MoA Classification — *Version: 8.0*

IRAC MoA Classification Version 8.0, December 2015

See section 7.4 for further information on sub-groups.
See section 7.3 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** Oxadiazines	Indoxacarb
	22B Semicarbazones	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** Phosphides	Aluminium phosphide, Calcium phosphide, Phosphine, Zinc phosphide
	24B Cyanides	Calcium cyanide, Potassium cyanide, Sodium cyanide
25 Mitochondrial complex II electron transport inhibitors Energy metabolism {Good evidence that action at this protein complex is responsible for insecticidal effects}	**25A** *Beta*-ketonitrile derivatives	Cyenopyrafen, Cyflumetofen
	25B Carboxanilides	Pyflubumide
28 Ryanodine receptor modulators Nerve and muscle action {Strong evidence that action at this protein complex is responsible for insecticidal effects}	Diamides	Chlorantraniliprole, Cyantraniliprole, Flubendiamide

MoA Booklets & Structure Posters printed



MoA Classification Updates (since Mar 2014)

Classification Scope statement added to Classification

The IRAC classification is intended to cover insecticides and acaricides acting at specific target sites where mutations could confer cross-resistance to all compounds acting at the same site. Some insecticides and acaricides also control nematodes, but selective nematicides are not included in the classification. Insecticidal oils, soaps, living organisms and viruses that are not known to act at specific target sites are currently not included. Uncouplers and non-specific (multi-site) inhibitors also do not act at specific target sites but are included.

Addition to Purpose Statement

Many countries now require including the IRAC group on labels, and this is recommended even if not required. Labeling guidelines are given in Appendix 1 and require that the active ingredient is listed in Appendix 5. Procedures for requesting IRAC classification of a new/unlisted active ingredient are found in Appendix 4.

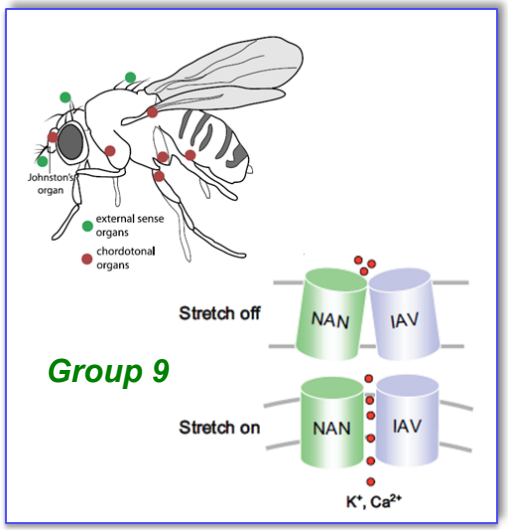
Addition to Appendix 1 – Labeling Guidelines

Inclusion of the IRAC group on the label is a warrant from the manufacturer that the insecticide has been classified by IRAC and is listed in Appendix 5 of this document, the only authoritative and comprehensive list of IRAC-classified insecticides. If an insecticide is not listed in Appendix 5 and falls within the scope of the IRAC classification as stated at the beginning of this document, please petition IRAC for classification of the product, as directed in Appendix 4, before drafting a label. Insecticidal materials falling outside the scope of the classification, including insecticidal oils, soaps, living organisms and viruses, may be labeled as “Exempt from IRAC Classification”.

MoA Classification Updates (since Mar 2014)

New additions

- triflumezopyrim (4E – mesoionic insecticides)
- dazomet, metam (8F – methyl isothiocyanate generators
- pyflubumide (25B – carboxanilides)
- GS-omega/kappa-HXTX-Hv1a, lime sulfur, sulfur (UN)



Major modifications

- Group 9 renamed "Chordotonal organ TRPV channel modulators"
  pymetrozine, pyrifluquinazon (9B – pyridine azomethine derivatives)
- Group 29 added "Chordotonal organ modulators – undefined target site
  flonicamid (29 – flonicamid)
- bifenazate – moved from UN to Group 20D
- Group 2 name – GABA-gated chloride channel antagonists
- Group 4 name – Nicotinic acetylcholine receptor (nAChR) competitive modulators
- Group 5 name – Nicotinic acetylcholine receptor allosteric modulators
- Group 6 name – Glutamate-gated chloride channel (GluCl) allosteric modulators

IRAC

MoA Classification Updates (since Mar 2014)

Minor modifications

- Group 4D descriptor – sulfoxaflor changed to sulfoximines
- Group 8C descriptor– sulfuryl fluoride changed to fluorides
- Group 13 descriptors
  - chlorfenapyr changed to pyrroles
  - DNOC changed to dinitrophenols
- Group 22 descriptors
  - indoxacarb changed to oxadiazines
  - metaflumizone changed to semicarbazones
- Group 24A descriptor – phosphine changed to phosphides
- Group 24B descriptor – cyanide changed to cyanides
  - addition of calcium cyanide, potassium cyanide, sodium cyanide

Classification requests

- Grandevo/Venerate (Marrone Bio Innovations)
  - microbial mixtures fall outside of charter
- azadirachtin (LATAM Parry America) – inhibitors of gut enzymes
  remains in UN – toxicological MoA remains unclear
- GS-omega/kappa-HXTX-H1va (Vestaron) – inhibitors of B_K and Ca_v channels
  - added to UN – toxicological MoA remains unclear

GS-ω/κ-HXTX-H1va

MoA WG Activities (since Mar 2014)

PBP and eConnection Articles

Currently most downloaded paper

>10,400 views

cited in 23 other papers

Pesticide Biochemistry and Physiology 121 (2015) 122–128

Contents lists available at ScienceDirect

Pesticide Biochemistry and Physiology

journal homepage: www.elsevier.com/locate/pest

IRAC: Mode of action classification and insecticide resistance management

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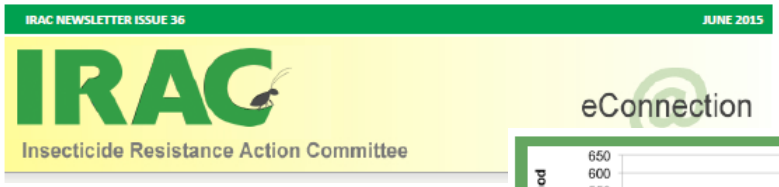

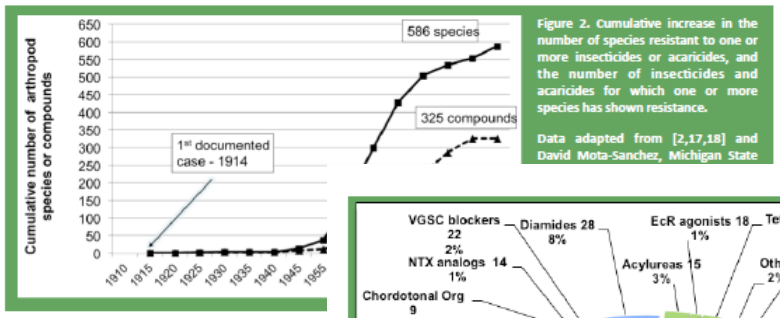

Figure 2. Cumulative increase in the number of species resistant to one or more insecticides or acaricides, and the number of insecticides and acaricides for which one or more species has shown resistance.

Data adapted from [2,17,18] and David Mota-Sanchez, Michigan State

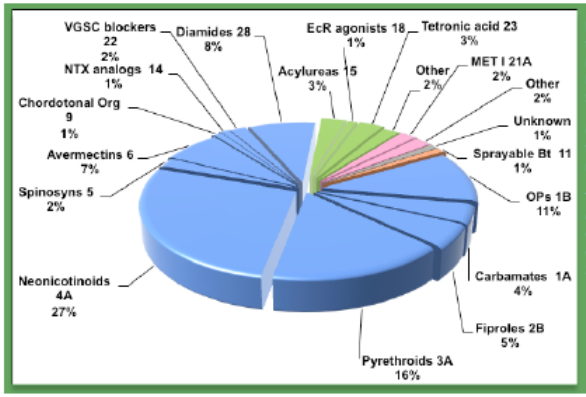

Figure 3. Distribution of total insecticide sales (percent of total value) by IRAC MoA Group or Subgroup.

Colors correspond to the targeted physiology shown in Table 2.

Total value = $17 billion, excludes fumigants. Based on 2013 End-user sales data from Agranova July 2014.

Website Upgrade

Useful Mode of Action Links

- Procedure for classifying a new insecticide
- Online form for classifying a new insecticide
- MoA labeling guidelines

IRAC

MoA WG Activities (since Mar 2014)

Target Site Mutations Listings (led by Dan Cordova) Updated annually

IRAC MoA Group	Target Site	Mutation	Subunit	Mutation Common Name	Affected Organisms	Field Relevance	Literature References
1A	Acetylcholinesterase (Carbamates)	S431F, A302S			*Aphis gossypii*	Yes	Andrews et al, (2004) Insect Mol Biol, 13;555; Toda et al, (2004) Insect Mol Biol, 13:549;
		G119S, A201S, T280A, F331C/Y/W, G328A			*Tetranychus urticae, Tetranychus evansi*	Yes	Khajehali et al, (2010) Pest Manag Sci, 66:220; Carvalho et al, (2012) Pest Biochem Physiol, 104:143; Ilias et al (2014) Insect Biochem Mol Biol 48C:17-28
1B	Acetylcholinesterase (Organophosphates)	S431F, A302S			*Aphis gossypii*	Yes	Andrews et al, (2004) Insect Mol Biol, 13;555; Toda et al, (2004) Insect Mol Biol, 13:549;
		Δ3Q			*Bactrocera oleae*	Yes	Kakani et al, (2008) Insect Biochem Mol Biol, 38:781
		G119S, A201S, T280A, F331C/Y/W, G328A			*Tetranychus urticae, Tetranychus evansi; Apolugus lucorum*	Yes	Khajehali et al, (2010) Pest Manag Sci, 66:220; Carvalho et al, (2012) Pest Biochem Physiol, 104:143; Ilias et al (2014) Insect Biochem Mol Biol 48C:17-28; Wu et al (2015) Insect Biochem Mol Biol 65:75-82.
2	GABA-gated chloride channel	A302S/N	α	rdl	*Bemisia tabaci, Sogatella furcifera, Laodelphax striatellus*	Yes	Anthony et al, (1995) Pest Biochem Physiol, 51:220; Nakao et al, (2010) Pest Biochem Phys, 97:262; Nakao et al, (2011) J Econ Entom, 104:646
		A302S (A301G), T350M	α	rdl	*Drosophila melanogaster, Drosophila simulans,*	No	ffrench-Constant et al, (1993) Nature, 363:44; Le Goff et al, (2005) J Neurochemistry, 92:1295

MoA Key Reference Document (led by Vince Salgado)

Group	Mode of Action	References
1	Acetylcholinesterase (AChE) inhibitors	Fukuto TR (1990) Mechanism of action of organophosphorus and carbamate insecticides. Environmental Health Perspectives 87, 245-254
2	GABA-gated chloride channel antagonists	Salgado VL, et al, Ligand-gated chloride channel antagonists (fiproles), in Modern Crop Protection Compounds 2nd edition, ed. by Kramer W, Schirmer U, Jeschke P and Wiltschel M, Wiley-VCH Verlag, Weinheim, pp. 1283-1305 (2012). Chen L, et al, 2006, Proc Natl Acad Sci,103:5185-5190; Zhao X et al, 2003, J Pharm Exp Ther 306:914-924; Grolleau F and Sattelle DB, 2000, Br J Pharm, 130:1833-1842; Hainzl D and Casida JE, 1996, Proc Natl Acad Sci, 93:12764-12767; Hosie AM et al, 1995, Br J Pharm, 115:909-912; Cole LM, et al 1993, Pest Biochem Physiol 46:47-54; ffrench-Constant RH, et al, 1993, Proc Natl Acad Sci 90:1957-1961;
3	Sodium channel modulators	Khambay BPS, Jewess PJ (2005) Pyrethroids, in: L.I. Gilbert, K. Iatrou, S.S. Gill (Eds.), Comprehensive Molecular Insect Science,Elsevier Ltd, pp. 1–29. Soderlund DM (2008) Pyrethroids, knockdown resistance and sodium channels, Pest Manag Sci 64, 610–616
4	Nicotinic acetylcholine receptor (nAChR) agonists	Jeschke P, Nauen R, Beck ME (2013) Nicotinic acetylcholine receptor agonists: a milestone for modern crop protection. Angewandte Chemie International Edition 52, 9464-9485. Uvary I (1999) Nicotine and other insecticidal alkaloids, in *Neonicotinoid insecticides and the nicotinic acetylcholine recepto* r, ed. by Yamamoto I, Casida JE, Springer Press, Berlin Heidelberg New York, pp. 29-69. Sparks TC et al. (2013) Sulfoxaflor and the sulfoximine insecticides: chemistry, mode of action and basis for efficacy on resistant insects. *Pestic Biochem Physio* l 107, 1-7. Nauen et al. (2015) Flupyradifurone: a brief profile of a new butenolide insecticide. Pest Manag Sci 71, 850-862.

IRAC