



Insecticide Resistance Action Committee

---

# MoA WG 2016/2017

51st IRAC International Meeting, Philadelphia  
March 28th, 2017

---



# MoA WG Team Members: 2016-2017

Team increased by 4 members

- ADAMA            Danny Karmon
- AgBiTech        Holly Popham\*
- BASF             Vince Salgado & Barbara Wedel\*
- Bayer             Ralf Nauen & Ulli Ebbinghaus-Kintscher
- DuPont           **Dan Cordova** (Team Leader)
- Dow               Tom Sparks & Jerry Watson
- Mitsui            Toshifumi Nakao\* & Shinchi Banba\* (guest members)
- NNI               Shinsuki Fujioka\* & Kazuyuki Sakata (outgoing)
- Sumitomo        Shigeru Satio
- Syngenta         **Andrew Crossthwaite** (Deputy Team Leader) & Ferus Earley
  
- Excellent support from Alan Porter

# MoA WG Activities

## Four conference calls (# of participants)

January 2016 (8)

August 2016 (7)

November 2016 (12)

January 2017 (11)

## Focus

## Enhancing external awareness of MoA Classification and changes

Group	Mode of Action	Hyperlinked References		
1	Acetylcholinesterase (AChE) inhibitors	Eukalyo TR Mechanism of action of organophosphorus and carbamate insecticides. <i>Environmental Health Perspectives</i> 87:245-254 (1990).		
2	GABA-gated chloride channel antagonists	Salgado VL, Schwesinger S and Hines KA. Ligand-gated chloride channel antagonists. <i>Wiesche M, Wiley-VCH Verlag, Weinheim, pp. 1353-1395 (2012).</i> Chen L, Durkin KA and Casida JE. Structural model for $\alpha$ -aminobutyric acid receptor. <i>PLoS ONE</i> (2006). Zhao X, Salgado VL, Yen JF and Narahashi T. Differential Actions of Fipronil and Dieldrin. <i>PLoS ONE</i> (2011). Gallea F and Sattelle DB. Single channel analysis of the blocking actions of EBDN. <i>Pharm</i> 130:1833-1842 (2009). Hartel D and Casida JE. Fipronil insecticide: Novel photochemical desulfurization via... Howe AM, Sheldahl HA, Buckingham SD and Sattelle DB. Actions of the insecticide fipronil. <i>PLoS ONE</i> (2010). Cole LM, Nicholson RA and Casida JE. Action of Phenylpyrazole Insecticides at the... Branch-Crawford RH, Stachan JD, Rocheau TA, Anonim K and Ravall RT. A novel... 3	Sodium channel modulators	Dames TGE, Field LM, Usherwood PNR and Williamson MS. DDT, Pyrethrins, Pyrethroids... Bakeland DM. Pyrethroids, knockdown resistance and sodium channels. <i>Pest Manag Sci</i>

### IRAC

Insecticide Resistance Action Committee

#### Understanding Insecticide Resistance

The key to effective insect resistance management www.iraconline.org

**Introduction**

- IRAC provides the use of a Mode of Action (MoA) classification of insecticides and acaricides as the basis for effective and sustainable resistance management.
- Insecticides are allocated to specific groups based on their target site.
- The IRAC MoA Classification Scheme provides farmers, growers, advisors, extension staff, consultants and crop protection professionals with a guide to the selection of acaricides and insecticides in resistance management programs.
- Effective resistance management preserves the utility and diversity of available insecticides.

**1. What is Resistance?**

- Resistance is a heritable change in the sensitivity of a pest population that is reflected in the reproductive rate of a group to achieve the expected level of control when used according to the label recommendation for that pest species.
- Cross-resistance occurs when resistance to one insecticide confers resistance to another insecticide, even where the insect has not been exposed to the latter product.

**2. How does resistance arise?**

- Insect populations benefit from naturally variant genes over time due to changes in their DNA sequence and/or randomly occurring point mutations of the natural gene pool (metamutagenesis).
- Further, individuals within a population can respond to insecticide exposure by increasing the expression of detoxifying enzymes.
- Continued exposure, especially through misuse or overuse of an insecticide, favours survival of those individuals with the lowest insecticide sensitivity.
- Those insects are more likely to produce offspring, resulting in a population shift to increased insecticide resistance.



**3. Why is it important to minimise resistance?**

- The development of resistance to a class of insecticides often renders many, or sometimes all, of that class ineffective in controlling insect pest populations.
- Effective insecticides with new modes of action or chemical structures that are not affected by resistance mechanisms are very difficult to discover.
- It is possible that new product discoveries may not keep up with the development of resistance and therefore may not meet the needs of growers and farmers.
- Therefore, the best means of managing resistance development is to delay, or prevent its occurrence by practicing a sound resistance management strategy.

**4. Resources and further links**

- Comprehensive overview of IRAC MoA Classification Scheme: Sparks & Kaun, 2010. *Pest Biochem Phys* 121:122
- Comprehensive list of target site resistance mutations: <http://www.iraconline.org/iraconline/resistance/resistance-target-site/>
- Review on metabolic-based resistance: Li, et al., 2007. *Ann Rev Entomol* 52:231
- Examples of behavioural adaptation to insecticides: Fryxell et al., 2014. *PLoS Negl Dis* 7:1-8
- Wang et al., 2004. *J Econ Entomol* 97:2067
- Examples of codic acid alteration linked to resistance: Anonim, et al., 2006. *Pest Manag Sci* 62: 805
- Yoshida et al., 2007. *Insect Mol Biol*, 16:315

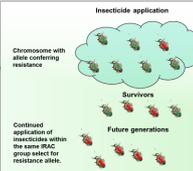
**Major Mechanisms of Resistance**

**Altered Target-Site**

Selection pressure can lead to survival of insects possessing a modified insecticide binding site or modified expression of the target protein. Mutation of a single or multiple amino acid residues can dramatically reduce insecticide potency at the binding site, which can be passed on to the offspring.

**Altered Metabolism**

All insects have enzymes to detoxify naturally occurring foreign materials. Enhanced/ altered/ amplified enzyme systems can metabolize or degrade insecticides before they can have a toxic effect. Enzyme systems include: Esterases, cytochrome P<sub>450</sub>, glutathione-S-transferases, peroxidases, ABC transporters



**Factors contributing to Resistance**

**Behavioural Changes**

Modification in insect behaviour to minimize contact so as to avoid lethal effects of an insecticide. This factor tends to be more of a contributing factor rather than an independent resistance mechanism.

**Altered Transport/Penetration**

Changes to insect cuticle, stomach lining or internal barriers (membranes protecting organs) can prevent or slow the absorption or penetration of insecticides. These factors tend to be more of a contributing factor rather than an independent resistance mechanism.

## Resistance Action Committee

## Action Classification Update

## Classification of Afidopyropen as Sub-phenes

Classification for afidopyropen was approved by the IRAC MoA WG and the IRAC structure (relative to pymetrozine and pyrifluquinazon) and lack of cross-pyropen will be added to the MoA Action Classification Scheme once a registration is filed in Appendix 6 of the Scheme (pending registration).

Find Out More

# MoA Classification Updates

## **GS-omega/kappa-Hxtx-Hv1a**

Vestaron requested dual MoA( $K_{Ca}$  &  $Ca_v$  channel blockers)  
Classified in UN due to insufficient data supporting dual MoA

## **Azadirachtin**

Reclassification request reviewed; maintained in UN as current evidence supports multiple actions without indication of target protein.

## **Etoxazole**

Evidence supporting chitin synthase MoA is strong.  
Concern for move to Group 15 given mite cross-resistance between certain 10A miticides. To be revisited

## **Nucleopolyhydrosis viruses**

AgBitech request for new Group 30 (NPVs). Implications of including “non-traditional” insecticides (i.e. biopesticides, dsRNA, biologicals) raised concern with several members. Agreed to delay classification decision.

## **Afidopyropen**

BASF request for Group 9D (Chordotonal organ – TRPV modulators) reviewed and approved

# MoA Poster & Website Updates

## Language posters

Spanish, Portuguese and Japanese posters updated; still waiting on Chinese update

## Pest-Specific Posters

Mite (Ebbinghaus-Kintscher), Vector Control (Saito), Lep (Sparks), Sucking Pest (Nauen)

## Resistance Mechanism Poster

Completed (Crossthwaite)

updates

## Website Upgrade

Subscription for classification

## Insecticide Resistance Action Committee

### Mode of Action Classification Update

### Mode of Action Classification of Afidopyropen as Sub-group 9D - Pyropenes

A 9D sub-grouping MoA classification for afidopyropen was approved by the IRAC MoA WG and the IRAC Executive based on its unique structure (relative to pymetrozine and pyrifluquinazon) and lack of cross-resistance to pymetrozine. Afidopyropen will be added to the MoA Classification Scheme once a registration is achieved. At the moment it is listed in Appendix 6 of the Scheme (pending registration).

[Find Out More](#)

The poster is titled "IRAC Understanding Insecticide Resistance" and is subtitled "The key to effective insect resistance management". It is published by the Insecticide Resistance Action Committee (IRAC) and is available at [www.ircac-online.org](http://www.ircac-online.org). The poster is divided into several sections: Introduction, 1. What is Resistance?, 2. How does resistance arise?, Major Mechanisms of Resistance, 3. Why is it important to minimise resistance?, 4. Resources and further links, and Factors contributing to Resistance. The Major Mechanisms of Resistance section includes: Altered Target-Site (Selection pressure can lead to survival of insects possessing a modified insecticide binding site or modified expression of the target protein...), Altered Metabolism (All insects have enzymes to detoxify naturally occurring foreign materials...), and Behavioural Changes (Modification in insect behaviour to minimize contact so as to avoid lethal effects of an insecticide...). The Factors contributing to Resistance section includes: Altered Transport/Penetration (Changes to insect cuticle, stomach lining or internal barriers...), and Behavioural Changes (Modification in insect behaviour to minimize contact so as to avoid lethal effects of an insecticide...).

# New Additions to Website

## MoA reference document

Initiated by V. Salgado; prepared by WG members

Key literature reference for each MoA group with embedded hyperlinks

Group	Mode of Action	Hyperlinked References
1	<b>Acetylcholinesterase (AChE) inhibitors</b>	<a href="#">Fukuto TR Mechanism of action of organophosphorus and carbamate insecticides. Environmental Health Perspectives 87:245-254 (1990).</a>
2	<b>GABA-gated chloride channel antagonists</b>	<a href="#">Salgado VL, Schnatteter S and Holmes KA, Ligand-gated chloride channel antagonists (fiproles), in Modern Crop Protection Compounds 2nd edition, ed. by Kramer W, Schirmer U, Jeschke P and Witschel M, Wiley-VCH Verlag, Weinheim, pp. 1283-1305 (2012).</a> <a href="#">Chen L, Durkin KA and Casida JE, Structural model for <math>\gamma</math>-aminobutyric acid receptor noncompetitive antagonist binding; Widely diverse structures fit the same site. Proc Natl Acad Sci 103:5185-5190 (2006).</a> <a href="#">Zhao X, Salgado VL, Yeh JZ and Narahashi T, Differential Actions of Fipronil and Dieldrin Insecticides on GABA-Gated Chloride Channels in Cockroach Neurons. J Pharm Exp Ther 306:914-924 (2003).</a> <a href="#">Grolleau F and Sattelle, DB, Single channel analysis of the blocking actions of BIDN and fipronil on a Drosophila melanogaster GABA receptor (RDL) stably expressed in a Drosophila cell line. Br J Pharm 130:1833-1842 (2000).</a> <a href="#">Hainzl D and Casida JE, Fipronil insecticide: Novel photochemical desulfinylation with retention of neurotoxicity. Proc Natl Acad Sci 93:12764-12767 (1996).</a> <a href="#">Hosie AM, Baylis HA, Buckingham SD and Sattelle DB, Actions of the insecticide fipronil, on dieldrin-sensitive and -resistant GABA receptors of Drosophila melanogaster. Br J Pharm 115:909-912 (1995).</a> <a href="#">Cole LM, Nicholson RA and Casida JE, Action of Phenylpyrazole Insecticides at the GABA-Gated Chloride Channel. Pest Biochem Physiol 46:47-54 (1993).</a> <a href="#">French-Constant RH, Steichen JC, Rocheleau TA, Aronstein K and Roush RT, A single-amino acid substitution in a <math>\gamma</math>-aminobutyric acid subtype A receptor locus is associated with cyclodiene insecticide resistance in Drosophila populations. Proc Natl Acad Sci 90:1957-1961 (1993).</a>
3	<b>Sodium channel modulators</b>	<a href="#">Davies TGE, Field LM, Usherwood PNR and Williamson MS, DDT, Pyrethrins, Pyrethroids and Insect Sodium Channels. IUBMB Life 59:151-162 (2007).</a> <a href="#">Soderlund DM, Pyrethroids, knockdown resistance and sodium channels, Pest Manag Sci 64:610-616 (2008).</a>

# MoA WG Activities

## Establishing “comment period” for changes to existing MoA classifications

Include generic providers

Obtain list of key contacts

## MoA Training Module

Ongoing objective (since 2010)

Waiting on BASF response for use of existing training slides

Consideration for having external party generate IRAC version