Insecticide Resistance Action Committee

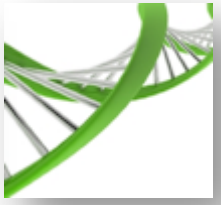
Mode of Action WG

49th IRAC International Meeting

18th March 2014

- Session -




IRAC

MoA WG Team Members: 2013-2014

- Dan Cordova – DuPont – Deputy Chair
- Andrew Crossthwaite – Syngenta
- Fergus Earley – Syngenta (Advisor)
- Danny Karmon - MAI
- David Kim – Vestergaard Frandsen
- Peter Luemmen - Bayer
- Ralf Nauen - Bayer
- Shigeru Saito – Sumitomo
- Vincent Salgado – BASF - Chair
- Tom Sparks – Dow
- Jerry Watson – Dow

- Excellent support from Alan Porter

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MoA WG Activities

2013 - 2014

- Jealott's Hill, UK F2F – 20 Mar 2013 (8 participants and ~12 guests)
- Four conference calls

  5 Jun 2013 (7 participants)
  19 Sep 2013 (10 participants)
  16 Jan 2014 (9 participants)
  27 Feb 2014 (9 participants)

- This week - face-to-face meeting

  Session 3C (Research Triangle Park, NC, March 19th)

Company participation has been relatively constant for the past 6 years - eight (8) companies

- BASF, Bayer, Dow, DuPont, Makhteshim-Agan, Sumitomo, Syngenta, Vestergaard Frandsen

MoA Classification Objectives

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.

MoA WG Activities

- **MoA Classification v. 7.3 issued February 2014**
  - New active flupyradifurone Group 4D - Butenolides
  - Renamed Sub-group 8D – Borax to Borates
  - Renamed Group 9 to Modulators of Chordotonal Organs
  - Simplified table notes and section 6.4 – notes regarding sub-groups.
  - New note: Actives in groups 8 (non-specific multi-site inhibitors), 13 (uncouplers) and UN 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.

MoA WG Activities

- Target site mutations Listings published 6/2013
  - Includes references for each listing / mutation
  - Will be reviewed annually
- Led by Dan Cordova

IRAC MoA Group	Target Site	Mutation	Subunit	Mutation Common Name	Affected Organisms	Field Relevance	Literature References
1A	Acetylcholinesterase (Carbamates)	S431F, A302S		MACE (S431F)	*Aphis gossypii, Myzus persicae*	Yes	Nabeshima et al. (2003) Biochem Biophys Res Comm, 307; 15; Nauen et al. (2004) Pest Manag Sci, 60;1051; 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
1B	Acetylcholinesterase (Organophosphates)	S431F, A302S		MACE (S431F)	*Aphis gossypii, Myzus persicae*	Yes	Nauen et al. (2004) Pest Manag Sci, 60:1051; 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*	Yes	Khajehali et al. (2010) Pest Manag Sci, 66:220; Carvalho et al. (2012) Pest Biochem Physiol, 104:143
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
		V410A/G		IS6	*Helicoverpa zea*	Yes	Hokins et al. (2010) Insect Biochem Mol Biol 40:385
		V410L		IS6	*Cimex lectularius*	Yes	Yoon et al. (2008) J Med Entomol 45, 1092-1101.
		V410M		IS6	*Heliothis virescens Helicoverpa zea*	Yes	Park et al. (1997) Biochem Biophys Res Comm 239:688; Hokins et al. (2010) Insect Biochem Mol Biol 40:385
		M918I		IIS4-S6	*Plutella xylostella*	Yes	Sonoda et al. (2012) Pest Biochem Physiol 102:142.
		M918L		IIS4-S5	*Aphis gossypii, Myzus persicae*	Yes	Fontaine et al. (2011) Pest Manag Sci 67:881.
		M918T		IIS4-S6	*Tetranychus evansi, Myzus persicae, Haematobia irritans, Liriomyza huidobrensis, Musca domestica, Myzus persicae, Thrips tabaci, Tuta absoluta*	Yes	Williamson et al. (1996) Mol Gen Genet 252, 51-60. Nyoni et al. (2011) Pest Manag Sci 239:688. Eleftherianos et al. (2008) Bull Entom Res 98:183. Toda and Morishita (2009) J Econ Entomol 102:2296. Haddi et al. (2012) Insect Biochem Mol 42:506
		M918V		IIS4-S6	*Bemisa tabaci*	Yes	Morin et al. (2002) Insect Biochem Mol 32:1781.
		L925I		IIS5	*Bemisa tabaci, Cimex lectularius, Rhipicephalus microplus*	Yes	Morin et al. (2002) Insect Biochem Mol 32:1781. Yoon et al. (2008) J Med Entomol 45, 1092-1101. Roditakis et al. (2006) Pest Biochem Phys 85:166. Morgan et al. (2009) Int J Parasit 39:775.

MoA WG Activities – NovaSource Counter Mat

Rotate Insecticides to Control Resistant Insects Effectively

Rotate insecticides with different modes of action. Use chart below to identify the modes of action of commonly used insecticides.

Main Group and Primary Site of Action	Chemical Sub-group or exemplifying Active Ingredient	Active Ingredients
Group 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, Vamidothion
Group 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
Group 3 **Sodium channel modulators** Nerve action {Strong evidence that action at this protein is responsible for insecticidal effects}	3A Pyrethroids Pyrethrins	Acrinathrin, Allethrin, *d-cis-trans* Allethrin, *d-trans* Allethrin, Bifenthrin, Bioallethrin, Bioallethrin-S-cyclopentenyl isomer, Bioresmethrin, Cycloprothrin, Cyfluthrin, *beta*-Cyfluthrin, Cyhalothrin, *lambda*-Cyhalothrin, *gamma*-Cyhalothrin, Cypermethrin, *alpha*-Cypermethrin, *beta*-Cypermethrin, *theta*-cypermethrin, *zeta*-Cypermethrin, Cyphenothrin, (1R)-*trans*- isomers], Deltamethrin, Empenthrin (EZ)- (1R)- isomers], Esfenvalerate, Etofenprox, Fenpropathrin, Fenvalerate, Flucythrinate, Flumethrin, *tau*-Fluvalinate, Halfenprox, Imiprothrin, Kadethrin, Permethrin, Phenothrin [(1R)-*trans*- isomer], Prallethrin, Pyrethrins (pyrethrum), Resmethrin, Silafluofen, Tefluthrin, Tetramethrin, Tetramethrin [(1R)-isomers], Tralomethrin, Transfluthrin,
	3B DDT Methoxychlor	DDT Methoxychlor
Group 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
Group 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
Group 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
Group 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

Main Group and Primary Site of Action	Chemical Sub-group or exemplifying Active Ingredient	Active Ingredients
Group 8* **Miscellaneous nonspecific (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
Group 9 **Modulators of chordotonal organs** Nerve action {Target protein responsible for biological activity is unknown, or uncharacterized}	9B Pymetrozine	Pymetrozine
	9C Flonicamid	Flonicamid
Group 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
Group 11 **Microbial disruptors of insect midgut membranes** (includes transgenic crops expressing *Bacillus thuringiensis* toxins, however specific guidance for resistance management of transgenic crops is not based on rotation of modes of action)	11A *Bacillus thuringiensis* and the insecticidal proteins they produce	*Bacillus thuringiensis* subsp. *Israelensis* *Bacillus thuringiensis* subsp. *aizawai* *Bacillus thuringiensis* subsp. *kurstaki* *Bacillus thuringiensis* subsp. *tenebrionis* B.t. crop proteins: (*Please see footnote) Cry1Ab, Cry1Ac, Cry1Fa, Cry1A.105, Cry2Ab, Vip3A, mCry3A, Cry3Ab, Cry3Bb, Cry34Ab1/ Cry35Ab1
	11B *Bacillus sphaericus*	*Bacillus sphaericus*
Group 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 Diafenthiuron	Diafenthiuron
	12B Organotin miticides	Azocyclotin, Cyhexatin, Fenbutatin oxide
	12C Propargite	Propargite
	12D Tetradifon	Tetradifon
Group 13* **Uncouplers of oxidative phosphorylation via disruption of the proton gradient** Energy metabolism	Chlorfenapyr DNOC Sulfluramid	Chlorfenapyr DNOC Sulfluramid
Group 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
Group 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
Group 16 **Inhibitors of chitin biosynthesis, type 1** Growth regulation {Target protein responsible for biological activity is unknown, or uncharacterized}	Buprofezin	Buprofezin
Group 17 **Moulting disruptor, Dipteran** Growth regulation {Target protein responsible for biological activity is unknown, or uncharacterized}	Cyromazine	Cyromazine

Main Group and Primary Site of Action	Chemical Sub-group or exemplifying Active Ingredient	Active Ingredients
Group 18 **Ecdysone receptor agonists** Growth regulation {Strong evidence that action at this protein is responsible for insecticidal effects}	Diacylhydrazines	Chromafenozide, Halofenozide, Methoxyfenozide, Tebufenozide
Group 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
Group 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
Group 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)
Group 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
Group 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
Group 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
Group 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
Group 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
Group UN* **Compounds of unknown or uncertain MoA^** {Target protein responsible for biological activity is unknown,	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.

Source: IRAC MoA Classification Scheme v. 7.3, February 2014, with permission. Further information is available from www.irac-online.org.
IRAC is a specialist technical committee providing best resistance management practice and does not endorse the use of specific products.

Tips for Preventing Insecticide Resistance

- Use Integrated Pest Management (IPM) practices by monitoring pest pressure and choosing the correct insecticide.
- Identify the insect pest.
- Monitor pest populations and apply only when economic thresholds are reached.
- Rotate insecticides with different modes of action (MOA).
- Consider incorporating various management strategies of which insecticides may be only one method of control.
- Follow the application techniques stated on the label.
- Do not overuse insecticides.
- Do not apply insecticides in sub-lethal doses.
- Consider the presence of pollinators when planning spray timing. Follow pollinator precautions on product labels.
- Keep accurate records.

Consider using Sevin® carbaryl insecticide (Group 1A) in your pest control program. Visit www.novasource.com for a copy of the SEVIN label and for more information.

Always read and follow label directions.

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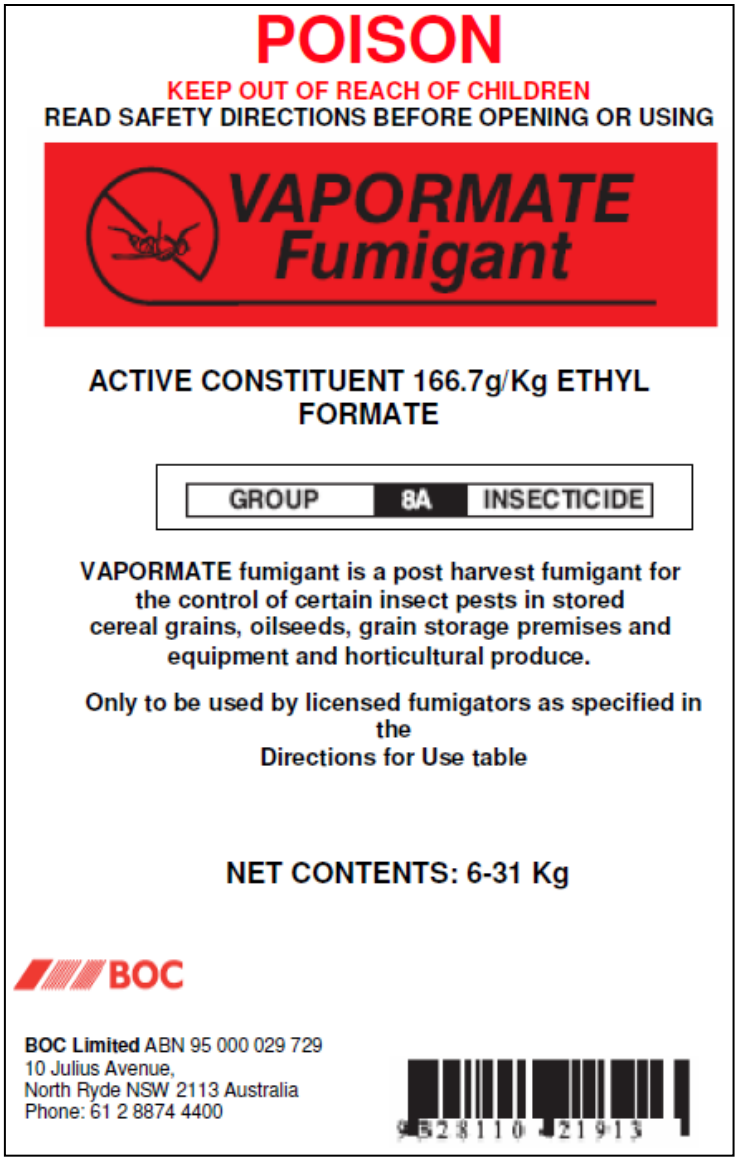
MoA WG Activities

- Projects in the works
  - Add v. 7.3 updates to MoA Classification Booklet
  - Add v. 7.3 updates to e-classification
  - Simplify and update MoA Structures poster
  - Mode of Action Presentation
    - On-hold pending outcome of UNL project
  - New Posters
    - Resistance Mechanisms
    - Coleoptera MoA poster
  - List of Key MoA References

MoA WG Activities

- New Issue – DIY "IRAC" classifications.
  - Group 8A – alkyl halides – is grossly incorrect. We would propose group UN.
  - IRAC must act to prevent DIY classifications immediately.



MoA WG Activities

- Other larger issues under discussion
  - Sub-Groups – should they exist?
  - Classification of microbials, soaps and oils.
    - Regulators are asking for a classification on all insect control products.

MoA WG – Web Usage

Numbers shown are unique page views as distinct from total page views

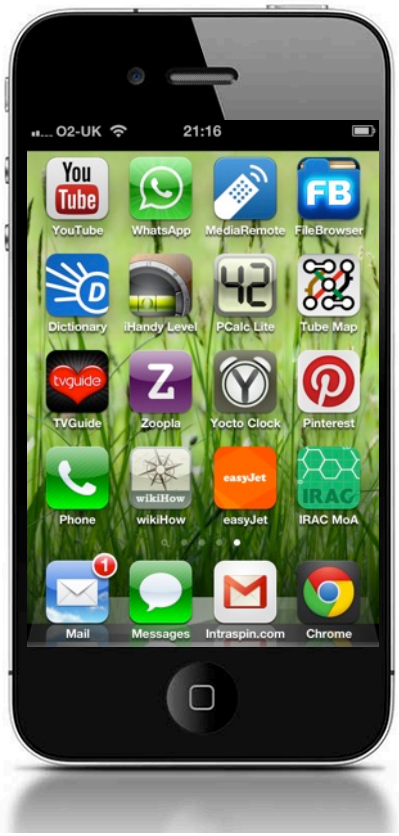
- MoA Team page – page views
  - 2011: 9484
  - 2012: 12, 376
  - 2013: 15,892
- Most Popular IRAC Pages

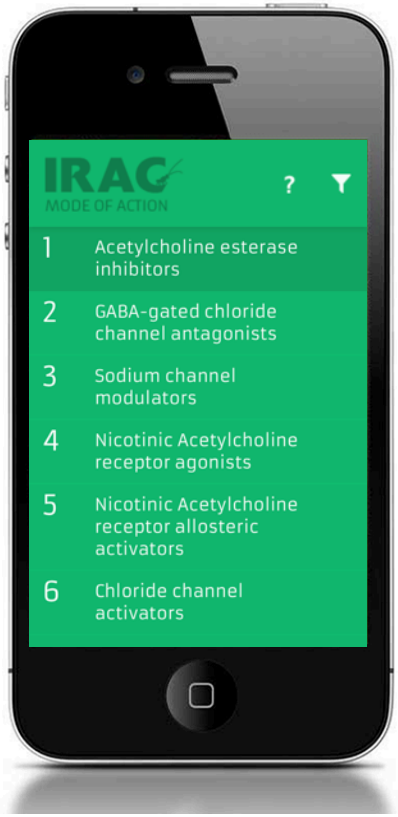
Rank	Page	Unique Views
1	IRAC Home	35K
2	MoA Team	16K
3	Pests	7K
4	About Resistance	5K

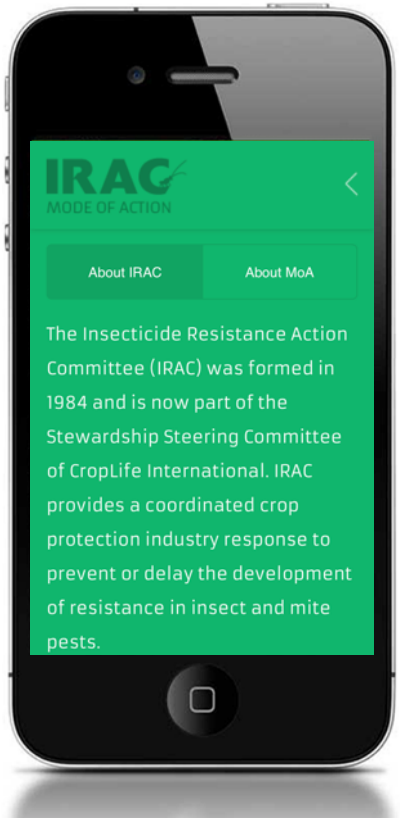
Data from Alan Porter

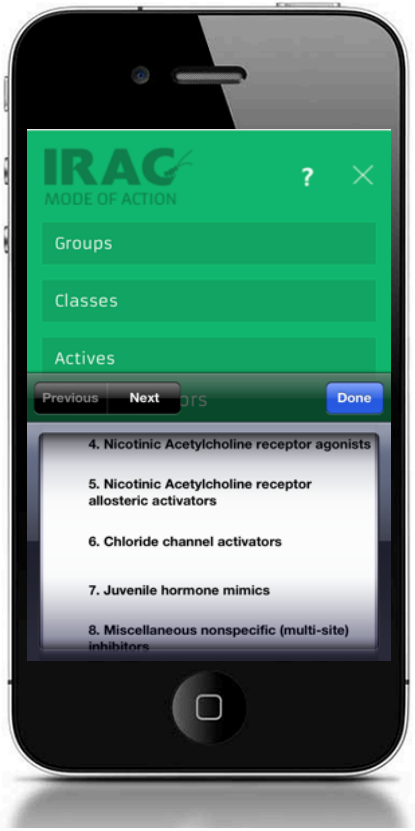
Phone/Tablet App

- Launched in March 2013 - 1330 downloads as of Feb 2014
- Some improvements in April 2013 but no change since then.
- Needs to be updated to replace blanks for some of the sub-groups
- Needs to be updated with the changes in the latest classification version (7.3)









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