Effective insecticide resistance management:

The agrochemical industry's approach to ensuring the sustained efficacy of insecticides

Alan McCaffery[1] and Ralf Nauen[2]

[1]Syngenta, Bracknell, UK

Chairman, Insecticide Resistance Action Committee

[2]Bayer CropScience, Monheim, Germany

Vice-Chairman, Insecticide Resistance Action Committee

IUPAC, Kobe, August 10, 2006: Resistance Management and IPM. S12-5

Outline

Why effective Resistance Management is essential

What industry is doing?

- At a Company level
  - Example Resistance Management Strategy – A typical responsible company approach to IRM
- At an Inter-company level
  - Example Collaborative Industrial Approach to IRM – An industry partnership to ensure sustainability
- At an All-industry level
  - Role of Insecticide Resistance Action Committee (IRAC)





Why Effective Resistance Management is essential

- Sustaining effective commercial life of current insecticides requires intelligent use of presently available compounds
  - Insecticide Resistance Management (IRM)

- For any crop / pest situation, effective IRM requires the availability of a broad range of modes of action

- IRM is made much more difficult by loss of modes of action through resistance development caused by misuse or overuse of insecticides

- We cannot always rely on having a steady stream of new modes of action to circumvent resistance problems…….

Cost of discovering new AIs

- Finding and developing new insecticides is extremely costly & difficult
- We cannot accept losing them to resistance! – So, IRM is vital!

Cost of developing and registering a new chemical crop protection AI in year 2000 ($M) [Source: ECPA, 2003]

Category	Sub-category	Costs	Total Cost
Research	Chemistry	41	94
	Biology	44	
	Toxicology / Environmental Chemistry	9	
Development	Chemistry	20	79
	Field Trials	25	
	Toxicology	18	
	Environmental Chemistry	16	
Registration			11
Total			184

What is industry doing at a company level?

Example Resistance Management Strategy - for a Neonicotinoid

Responsible companies have clear guidelines to manage resistance to Neonicotinoids. E.g.:

To prevent the development and spread of resistance, applications of neonicotinoid insecticides should be applied in 'block' applications where, e.g.:

The total duration of the neonicotinoid 'blocks' does not exceed more than half of the crop cycle (Syngenta approach). The duration of a block application should be based on either:

- **The generation time of the target pest (Where possible each block should treat a single generation of the target pest)**
- **The period of insect control that is provided by a single application of the insecticide (Applicable to insects with a short generation time).**

Wherever possible it is recommended that the application of an insecticide 'block' should not immediately be followed by an application of an insecticide 'block' of the same chemical class.

Baselines and Resistance Monitoring

- Each company establishes baselines for its products
- And undertakes regular susceptibility monitoring for key at-risk pests e.g. :
  - Cotton aphid, Peach-potato aphid, Tobacco whitefly, Glasshouse whitefly, Rice brown planthopper, Diamondback moth, Fall armyworm, Cotton bollworm, Tobacco budworm, Colorado potato beetle, Pollen Beetle, Spider mites, Thrips spp. etc.

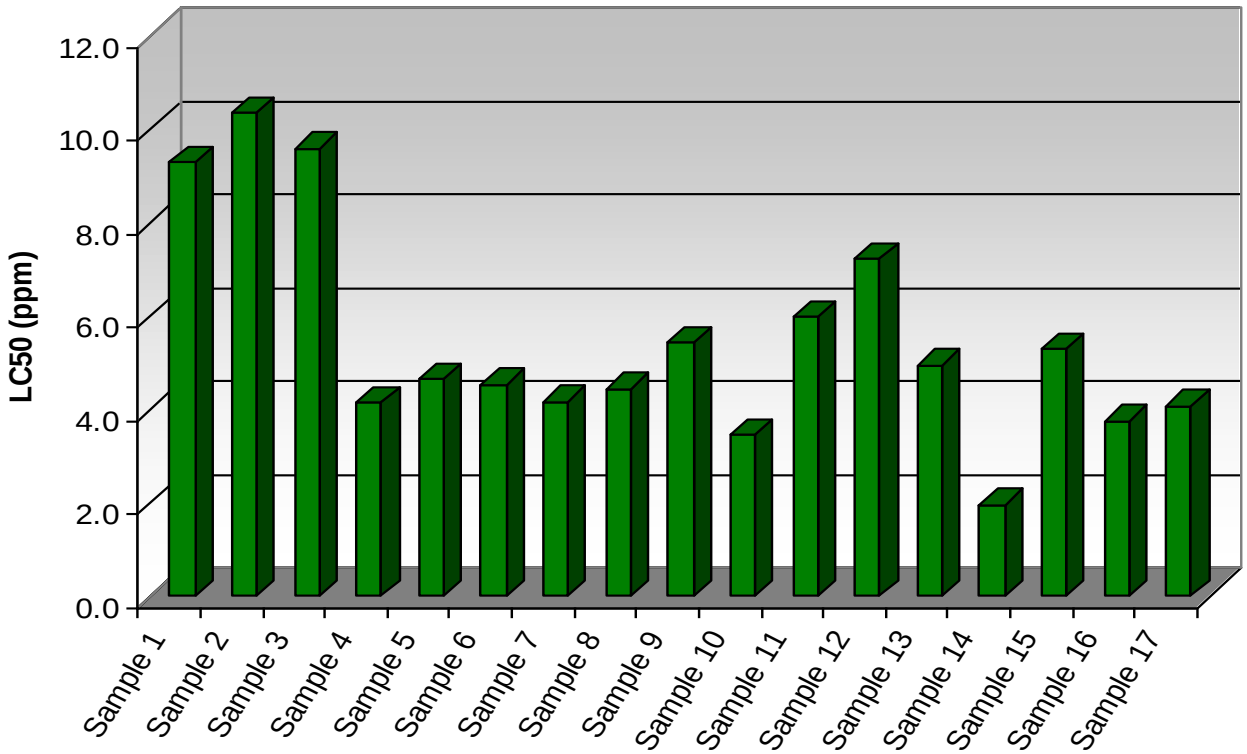
Ensures we know current status of susceptibility to key insecticides

EPPO-Guideline PP1/213 (Resistance risk assessment)

Timely awareness of any emerging problems

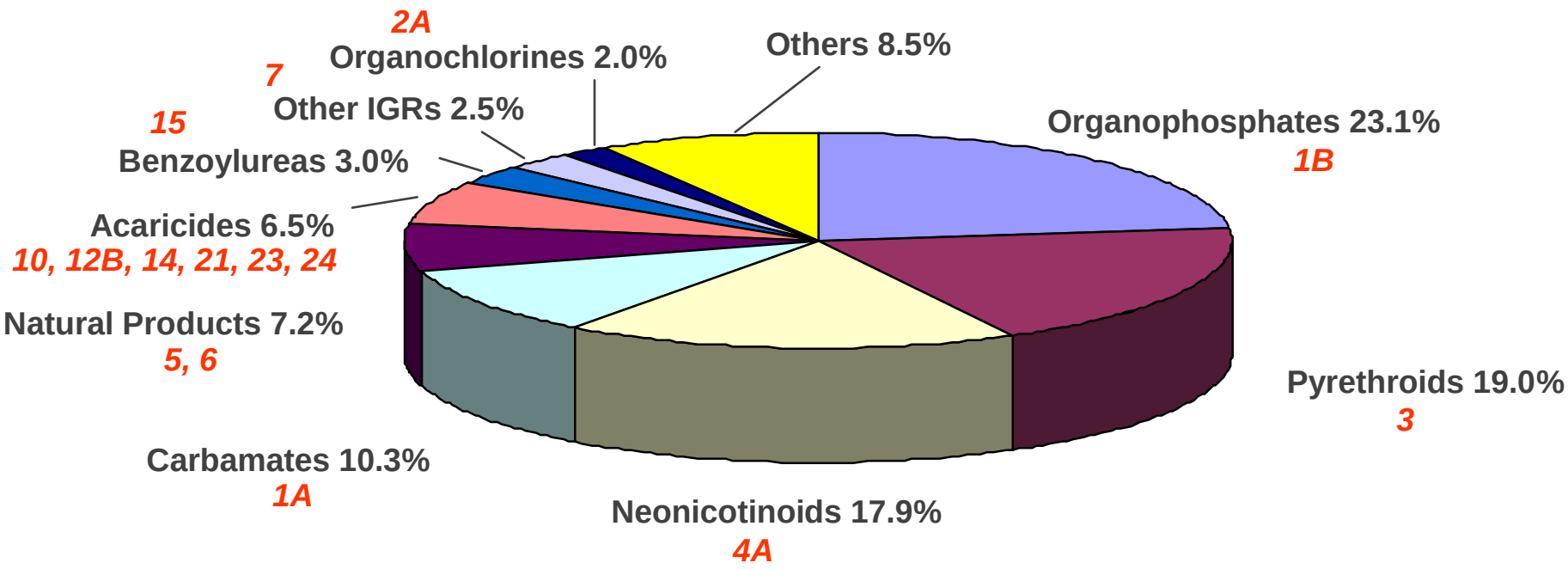
Example of Susceptibility Monitoring

- Adult Western Corn Rootworm (*Diabrotica virgifera virgifera*) ‘baseline’ susceptibility to a neonicotinoid
- Independent samples collected from USA Corn Belt



What is industry doing at an inter-company level?

Global Insecticide sales



Total Global Insecticide Sales 2004 = $7,690 million

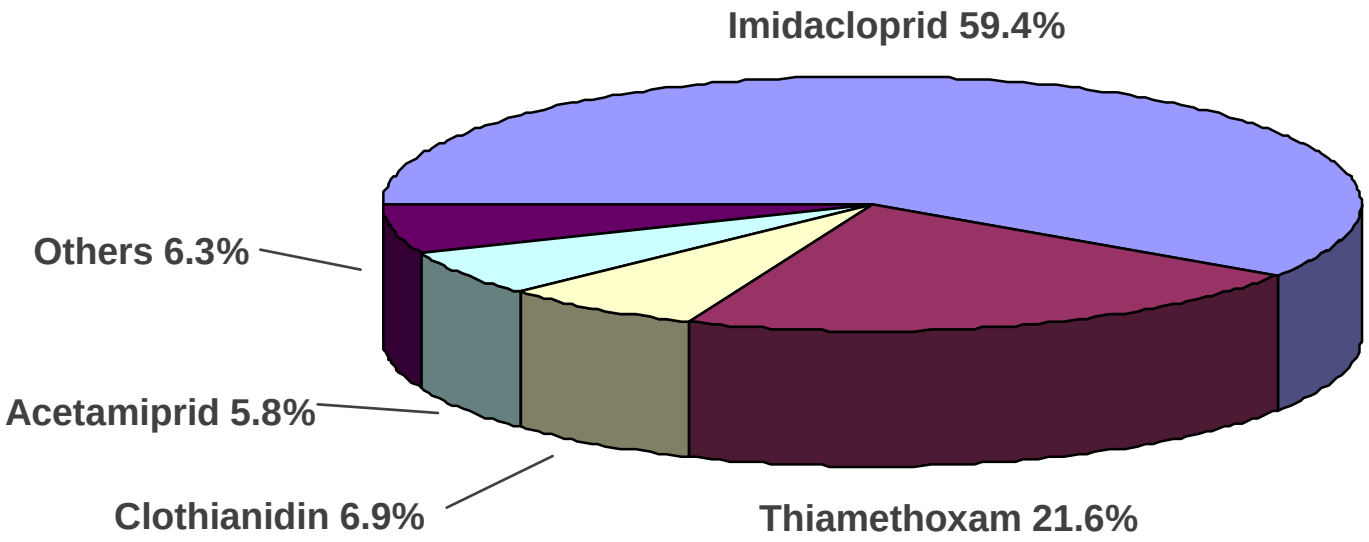
[Source Phillips McDougall, November 2005

[Natural products includes avermectins and spinosyns]

IRAC Mode of Action Classification Number

Neonicotinoids now 3rd largest group of insecticides based on global sales

Global Neonicotinoid sales



Global Neonicotinoid Sales 2004 = $1,380 million

[Source Phillips McDougall, November 2005]

IRAC Mode of Action Classification Number 4A

Imidacloprid and Thiamethoxam account for >80% of market

Bayer CropScience and Syngenta – Collaborative Neonicotinoid Stewardship Project

- Bayer CropScience: Imidacloprid, Thiacloprid, Clothianidin
- Syngenta: Thiamethoxam

- Two companies uniquely placed to take a lead in developing and delivering coherent and effective IRM strategies - at both a global and local level
- March 2005: Bayer CropScience and Syngenta agreed joint global stewardship project to manage Neonicotinoids, focussing on key at-risk pests
- Other companies invited to join – but so far declined

Bayer CropScience / Syngenta – Collaborative Neonicotinoid Stewardship Project

- Aim: To intensify the implementation of IRM by working together through contacts at country level
- Proposal to develop local IRM recommendations based on the two company global IRM recommendations for Neonicotinoids
  - Syngenta: Maximal exposure to Neonicotinoids is limited to 50% of the cropping cycle
  - Bayer CropScience: Neonicotinoids are limited to maximum of 3 applications per pest species and crop cycle
- Although slightly different, in practice it is expected that in most situations the time periods covered by neonicotinoids are similar for both company recommendations
- Agreed that local guidelines can be stricter than the global guidelines, but should not be more flexible (refer also to IRAC US Guidelines)

Bayer CropScience and Syngenta - Collaborative Neonicotinoid Stewardship Project – Targets

Agreed first list of key at-risk targets for co-operation:

Country	Target	Crop
Mexico	Whitefly	Vegetables
Guatemala	Whitefly	Melons & Tomatoes
India	Brown planthopper	Rice
Brazil	Whitefly	Beans
Morocco	Whitefly	Covered vegetables
Italy	Whitefly	Covered vegetables
Turkey	Whitefly	Covered vegetables
Japan	Thrips	Vegetables

BCS and Syngenta sponsor UK Neonicotinoid LINK project

- Bayer CropScience and Syngenta are jointly sponsoring [with others] :

  UK Department of Environment, Food and Rural Affairs, SA-LINK Project: Sustainability of Neonicotinoid Insecticides

  - To assess and manage increasing risk of resistance to Neonicotinoids in *Myzus persicae* (and other aphids)
  - Risk arises from rapid recent increase in uses of neonicotinoids in multiple host crops for *M. persicae*
  - Co-ordinating laboratory Rothamsted Research (Dr Ian Denholm, Dr Stephen Foster, et al.)

What is industry doing at an all-industry level?

Insecticide Resistance Action Committee

- IRAC formed in 1984 to provide a co-ordinated industry response to the development of resistance in insect and mite pests
  - A technical group reporting to CropLife
- Currently 7 IRAC International members:

BASF
Bayer CropScience
Dow AgroSciences
DuPont
FMC
Sumitomo
Syngenta

"Promote the development of resistance management strategies in crop protection and vector control to maintain efficacy and support sustainable agriculture and improved public health"

"Facilitate communication and education on insecticide and acaricide resistance"

International Committee Structure & Objectives

Insecticide Resistance Action Committee

Functional Teams:

- Communication & Education
- Regulatory

Expert Teams:

- Biotechnology
- Methods
- Mode of Action
- MSU Database & RPMN
- Public Health

Current Project Teams:

- Codling Moth
- Neonicotinoids

- Promote IRM to support sustainable agriculture and improved public health
- Emphasis on communication and education
- Development of international resources for IRM

CropLife

Roles of IRAC

Insecticide Resistance Action Committee

- Actively promote and support work of IRAC Country groups
- Interact effectively with and support IRAG groups
- Cooperate with CropLife International
- Interact with regulatory authorities responsible for insecticide registration

Liaison and coordination activities

IRAC International

A comprehensive approach to tackling resistance

Technical outputs

- Help to identify the scope and nature of resistance problems
- Provide methods for detecting and monitoring resistance
- Provide key resources to aid in developing effective IRM e.g. Mode of action scheme

Communication and education

- Develop IRAC website to provide communication and education on resistance to all stakeholders
- Develop educational resources to improve understanding of IRM
- Act as key global communicator on topical resistance issues

Role of Country groups

- Deal with key resistance issues at local level – supported by IRAC Intl. (liaison officer affiliated to each country group)
- Develop projects to support local problems –
  - e.g. IRAC-India developing project to tackle resistance in BPH
  - e.g. IRAC-Brazil developed local Mode of Action based IRM schemes
- Often include additional companies not involved in IRAC International
- May involve others from academia, research institutes & regulatory bodies
- Country groups can help with translation of IRAC materials & resources

Current IRAC Country groups:
- **IRAC Australia (AIRMG)**
- **IRAC Brazil**
- **IRAC India**
- **IRAC South Africa**
- **IRAC Spain**
- **IRAC US**

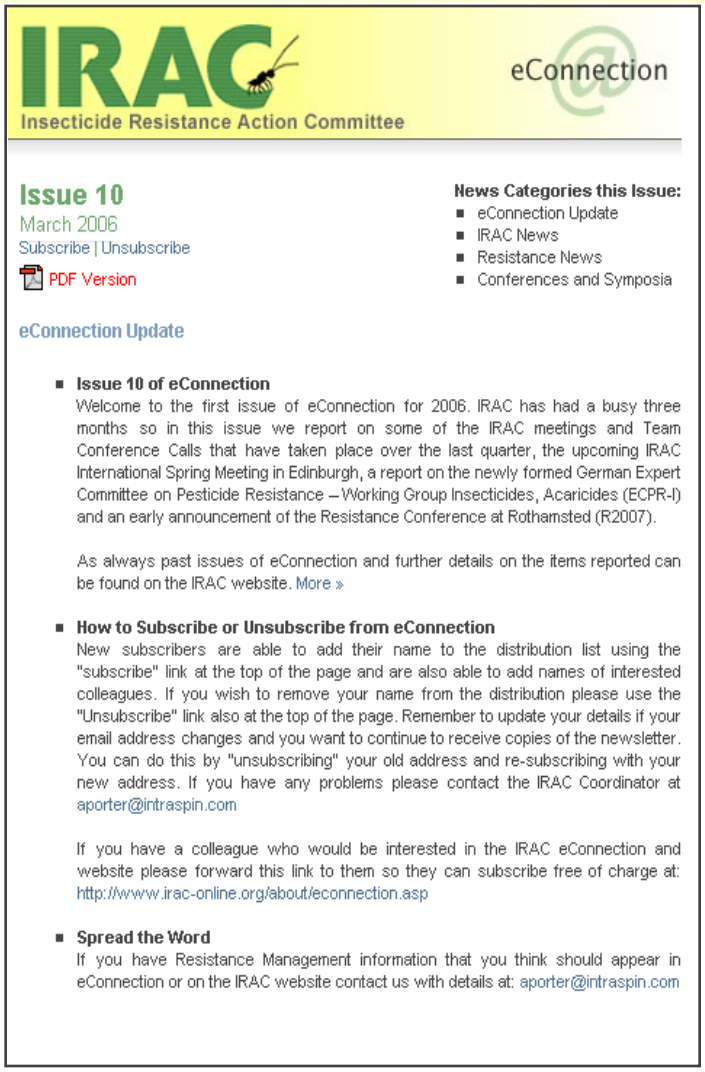
- ***IRAC is keen to see formation of IRAC-Japan as part of JCPA***

Website: www.irac-online.org

Accessed by over 129 countries

- IRAC's key communication vehicle
- Av. 1,169 hits, 212 visits, 330 page views per day (Q1, 2006)
- Ranked 1st in Google and Yahoo for Insecticide Resistance and IRM
- IRAC Country group information
- Information on IRAC, Mode of Action, advice on IRM
- Education modules
- Resources - key papers, posters, etc.
- Links for growers
- Home, diary and other general pages
- Team and group areas
- 215 coded pages, 100 viewable pages, 3 databases. 157 document files, 135 image/graphic files

eConnection



IRAC Insecticide Resistance Action Committee

eConnection

Issue 10
March 2006
Subscribe | Unsubscribe
PDF Version

News Categories this Issue:
- eConnection Update
- IRAC News
- Resistance News
- Conferences and Symposia

eConnection Update

- **Issue 10 of eConnection**
  Welcome to the first issue of eConnection for 2006. IRAC has had a busy three months so in this issue we report on some of the IRAC meetings and Team Conference Calls that have taken place over the last quarter, the upcoming IRAC International Spring Meeting in Edinburgh, a report on the newly formed German Expert Committee on Pesticide Resistance – Working Group Insecticides, Acaricides (ECPR-I) and an early announcement of the Resistance Conference at Rothamsted (R2007).

  As always past issues of eConnection and further details on the items reported can be found on the IRAC website. More »

- **How to Subscribe or Unsubscribe from eConnection**
  New subscribers are able to add their name to the distribution list using the "subscribe" link at the top of the page and are also able to add names of interested colleagues. If you wish to remove your name from the distribution please use the "Unsubscribe" link also at the top of the page. Remember to update your details if your email address changes and you want to continue to receive copies of the newsletter. You can do this by "unsubscribing" your old address and re-subscribing with your new address. If you have any problems please contact the IRAC Coordinator at aporter@intraspin.com

  If you have a colleague who would be interested in the IRAC eConnection and website please forward this link to them so they can subscribe free of charge at: http://www.irac-online.org/about/econnection.asp

- **Spread the Word**
  If you have Resistance Management information that you think should appear in eConnection or on the IRAC website contact us with details at: aporter@intraspin.com

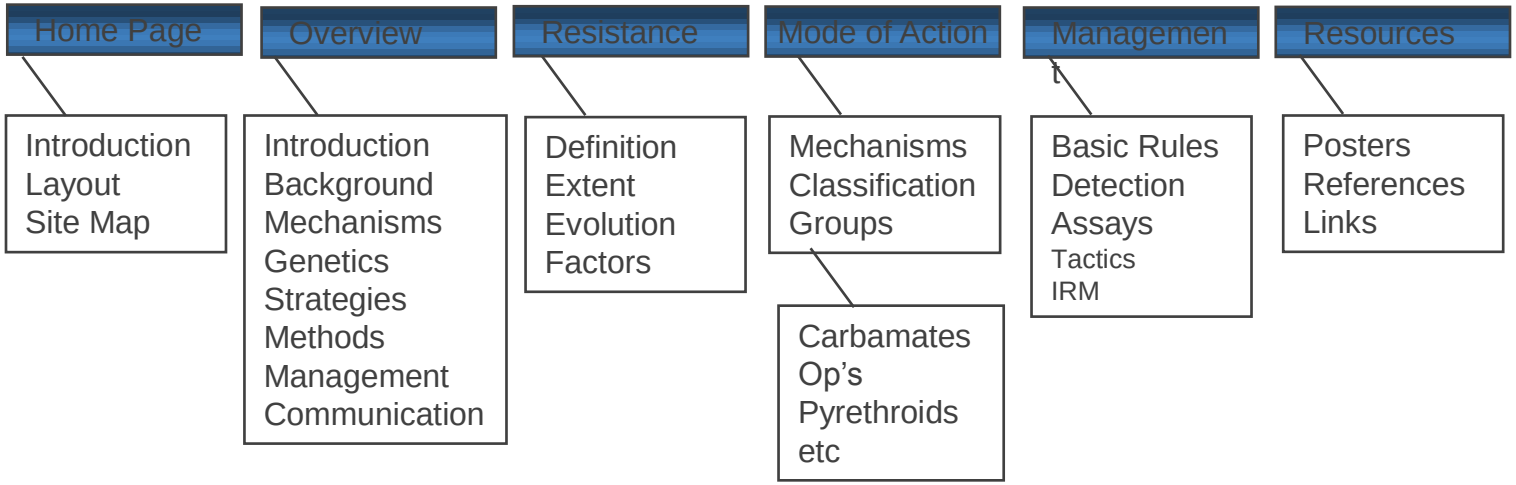
- Free IRAC newsletter distributed by e-mail - part of IRAC Communications Plan
- Raise awareness of importance of IRM
- Promote IRAC's reputation, expertise & resources
- Publicise and encourage IRAC website [links]
- 3 to 4 issues a year (10 to date)
- Current distribution 550 to 650
- 2005 / 2006 articles included:
  - EPPO standard on RRA
  - New MoA Scheme
  - MoA scheme for US cotton
  - Loss of AIs in EU for minor crops
  - Brown Planthopper & neonicotinoids
  - IRAC US neonicotinoids symposium
  - *Bemisia tabaci* biotype Q on the move
  - New IRAC communications pack

eLearning

Insecticide Resistance Action Committee

- New IRAC resource still in development
- Provides Education and Training modules on resistance & IRM
- Graphic provides a diagrammatic representation of layout and content

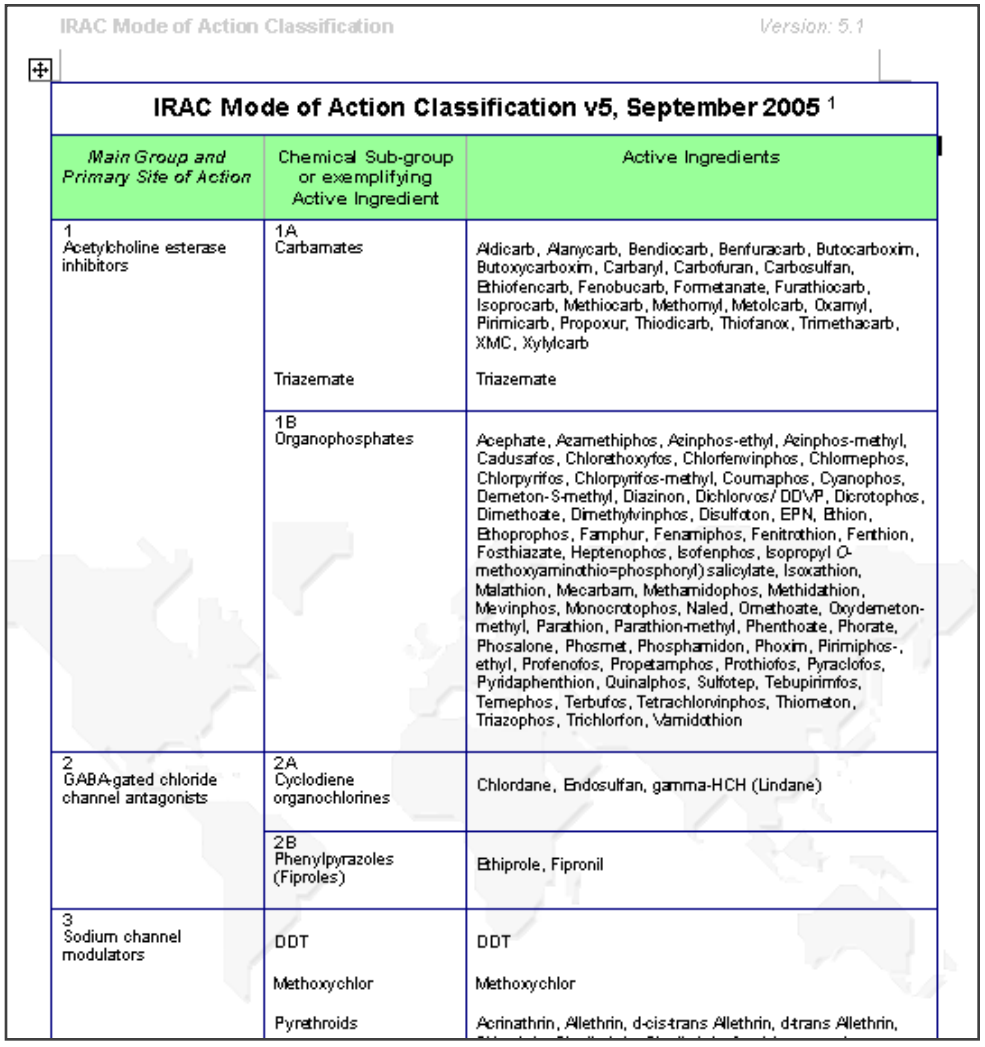
Proposed Website Menu Headings and Sub-Headings



CropLife

Mode of Action Classification

Insecticide Resistance Action Committee



IRAC Mode of Action Classification — Version: 5.1

IRAC Mode of Action Classification v5, September 2005 [1]

Main Group and Primary Site of Action	Chemical Sub-group or exemplifying Active Ingredient	Active Ingredients
1 Acetylcholine esterase inhibitors	1A Carbamates	Aldicarb, Alanycarb, Bendiocarb, Benfuracarb, Butocarboxim, Butoxycarboxim, Carbaryl, Carbofuran, Carbosulfan, Ethiofencarb, Fenobucarb, Formetanate, Furathiocarb, Isoprocarb, Methiocarb, Methomyl, Metolcarb, Oxamyl, Pirimicarb, Propoxur, Thiodicarb, Thiofanox, Trimethacarb, XMC, Xylylcarb
	Triazamate	Triazamate
	1B Organophosphates	Acephate, Azamethiphos, Azinphos-ethyl, Azinphos-methyl, Cadusafos, Chlorethoxyfos, Chlorfenvinphos, Chlormephos, Chlorpyrifos, Chlorpyrifos-methyl, Coumaphos, Cyanophos, Demeton-S-methyl, Diazinon, Dichlorvos/ DDVP, Dicrotophos, Dimethoate, Dimethylvinphos, Disulfoton, EPN, Ethion, Ethoprophos, Famphur, Fenamiphos, Fenitrothion, Fenthion, Fosthiazate, Heptenophos, Isofenphos, Isopropyl O-methoxyaminothio=phosphoryl) salicylate, Isoxathion, Malathion, Mecarbam, Methamidophos, Methidathion, Mevinphos, Monocrotophos, Naled, Omethoate, Oxydemeton-methyl, Parathion, Parathion-methyl, Phenthoate, Phorate, Phosalone, Phosmet, Phosphamidon, Phoxim, Pirimiphos-, ethyl, Profenofos, Propetamphos, Prothiofos, Pyraclofos, Pyridaphenthion, Quinalphos, Sulfotep, Tebupirimfos, Temephos, Terbufos, Tetrachlorvinphos, Thiometon, Triazophos, Trichlorfon, Vamidothion
2 GABA-gated chloride channel antagonists	2A Cyclodiene organochlorines	Chlordane, Endosulfan, gamma-HCH (Lindane)
	2B Phenylpyrazoles (Fiproles)	Ethiprole, Fipronil
3 Sodium channel modulators	DDT	DDT
	Methoxychlor	Methoxychlor
	Pyrethroids	Acrinathrin, Allethrin, d-cis-trans Allethrin, d-trans Allethrin,

- Definitive scheme developed and endorsed by IRAC in consultation with key researchers
- Worldwide distribution
- All current insecticides allocated to a Mode of Action group or sub-group
  - MoA groups 1-28
- A key tool for selection of insecticides in effective IRM programs
- Updated as required
- Latest version Sept 2005
- Next revision, Q3, 2006

CropLife

Using the IRAC MoA Classification

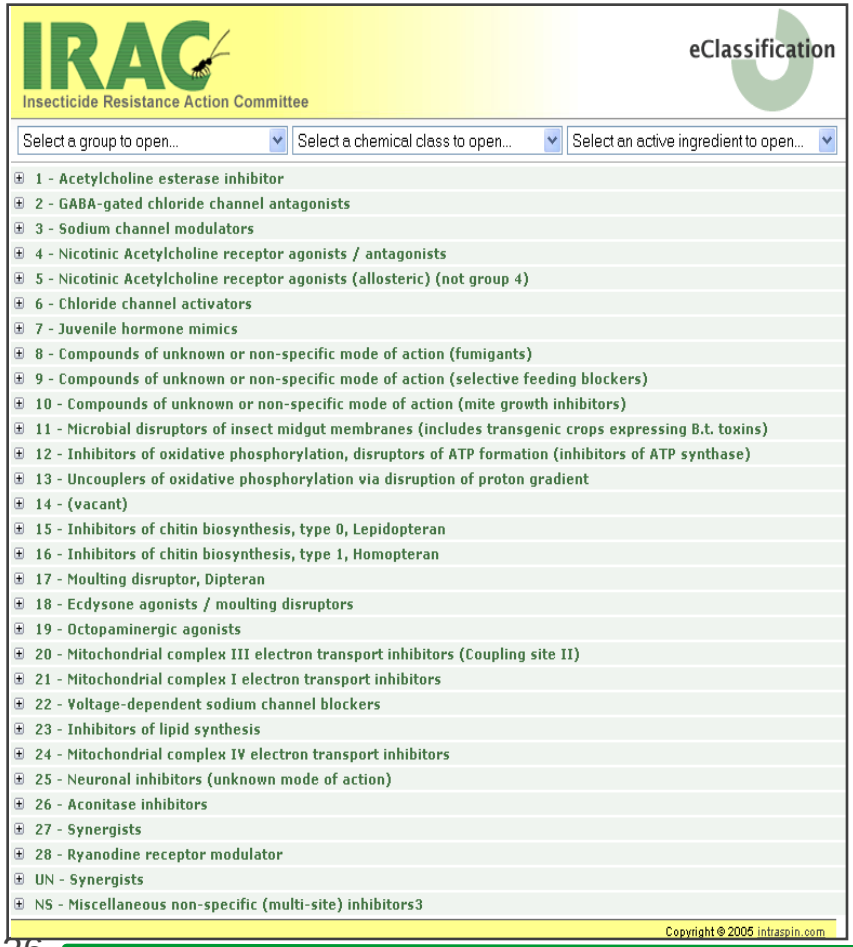
- The IRAC Mode of action scheme is central to developing effective IRM strategies
- Sequences, rotations or alternations of different MoA groups help prevent or delay resistance, or deal with existing resistance problems
- Modify locally to take account of known metabolic mechanisms conferring cross-resistance between MoA groups or insect populations with multiple resistances
- In the absence of any information, intelligent sequences of MoA groups will always reduce selection pressures and help prevent or delay resistance, and help regain susceptibility
- IRAC strongly supports MoA labelling schemes – e.g. US, Australia
  - And IRAC campaigns for wider use of such schemes
- Use of symbols and colours for MoA groups can help e.g. Brazil

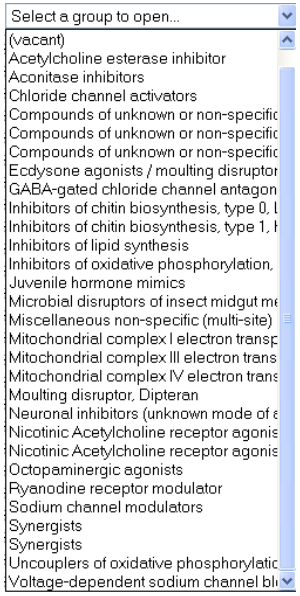
eClassification – interactive MoA

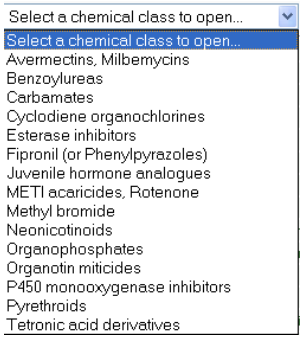
Insecticide Resistance Action Committee

New MoA interactive online tool

www.irac-online.org





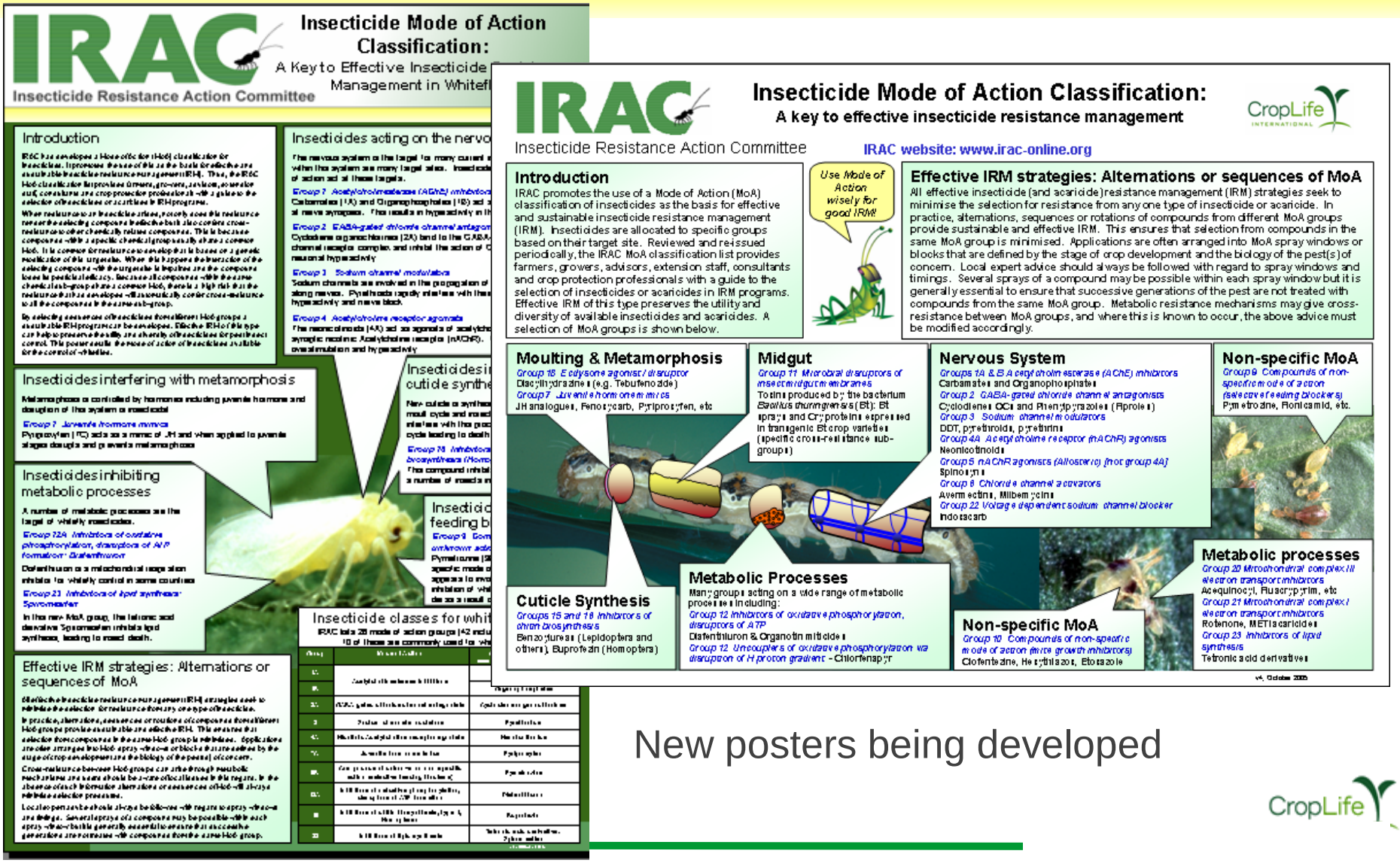


Drop down menu >> options

Data Sheets

MoA Posters

Insecticide Resistance Action Committee



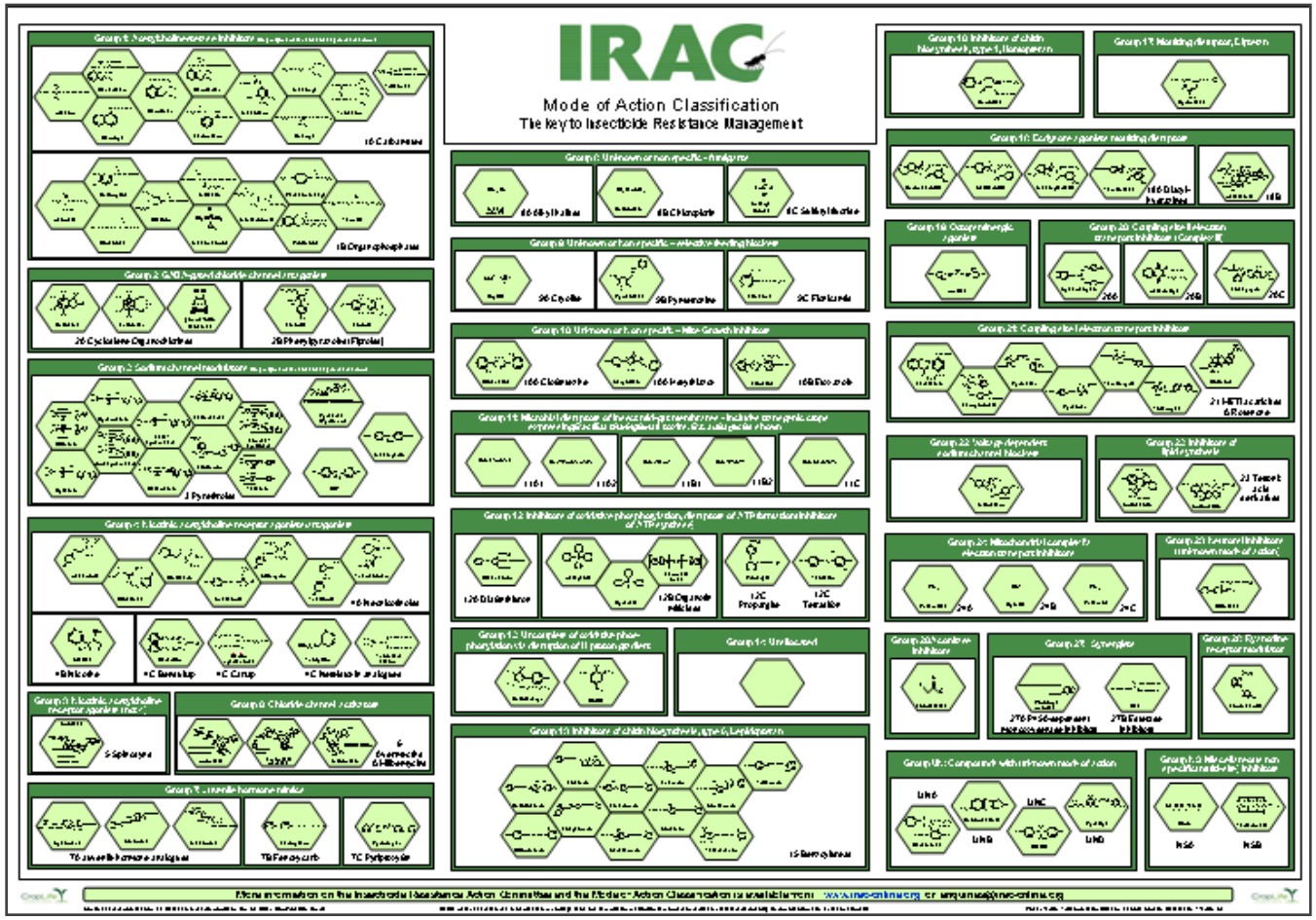
New posters being developed

CropLife

MoA Classification Poster

Insecticide Resistance Action Committee

IRAC Mode of Action Classification Groups and Structures



- Available as A1 posters
- First batch of 3000 printed
- Recently translated into Japanese - available soon

IRAC Susceptibility Test Methods

Insecticide Resistance Action Committee

Insecticide Resistance Action Committee
www.irac-online.org
Resistance Management for Sustainable Agriculture and Improved Public Health

IRAC Susceptibility Test Methods Series — Method No: 3
Version: 2

Details:

Method:	No: 3
Status:	Approved
Species:	*Panonychus ulmi* *Tetranychus spp*
Species Stage	*P. ulmi* (summer eggs) *Tetranychus* (eggs)
Product Class:	clofentezine hexythiazox tetradifon
Comments: None	

Photograph Courtesy of: Whitney Cranshaw, Colorado State University, Tetranychus spp

Description:

Materials:
Petri dishes (9-cm diameter), filter paper to fit Petri dishes, cotton wool, *untreated* apple or plum leaves, small scissors, small forceps, fine pointed brush or cocktail stick, beakers or glass jars (ca. 100-ml capacity) for test liquids, 1-ml disposable plastic syringes for liquids for weighing balance for solids, hand lens (minimum 10 x) or binocular microscope, maximum/minimum thermometer.

Methods:
(a) Cut square sections about 1.5 x 1.5 cm from chemically untreated apple or plum leaves. Use young leaves, but not before they are fully expanded. Leaves must be in good condition. Use a minimum of four replicates (leaf sections) per treatment.
(b) Place these sections, upper surface uppermost, on a sheet of moist filter paper on moist cotton wool in open Petri dishes.
(c) Collect apple leaves with adult mites, and with the fine pointed brush or cocktail stick transfer 10 – 15 females onto each leaf section. Maintain at a minimum temperature of 20°C, minimum photoperiod 16 h and a high light intensity, but not in direct sunlight.
(d) After 24 h, check that the female mites have laid eggs. Aim for at least 20 eggs per leaf section. If there are not enough eggs, leave for a further 24 h. Do not leave longer than 48 h.
(e) When sufficient egg numbers have been obtained, remove the mites with the fine pointed brush or cocktail stick. Record the time when this is done.
(f) Prepare appropriate test dilutions of formulations in water. The use of a wetter is not

For further information please contact: Alan Porter, IRAC International Coordinator
www.irac-online.org, email: aporter@intras.plm.com

IRAC Susceptibility Test Methods Series — Method No: 3
Version: 2

recommended.
(g) Agitate test liquids and then dip the leaf sections for 5 secs. Dip equal number of control leaf sections in water only.
(h) Record the number of eggs per leaf section.
(i) Return leaf sections to Petri dishes and maintain in conditions described above. Record maximum and minimum temperatures. Moisten cotton wool daily.
(j) Using a hand lens or binocular microscope observe leaf sections daily until there has been complete (or nearly complete) hatch on the untreated (water only) leaf sections. Record numbers of un-hatched eggs on treated and untreated leaf sections.
(k) Express results as percentage mortality and correct for untreated mortality using Abbott's formula. Untreated mortality should be recorded.

Precautions & Notes:

If the lids are left off, the leaf sections may dry out and, unless the cotton wool can be moistened at least daily, the test may be invalidated by excessive control mortality. In such circumstances, the method may have to me modified to suit the local conditions, e.g. use lids with holes cut in them to reduce water loss without creating a condensation problem.

For *Tetranychus* spp. which live mainly on the lower leaf surface, the leaf sections may need to be placed lower surface uppermost. Leaves of kidney beans are particularly suitable.

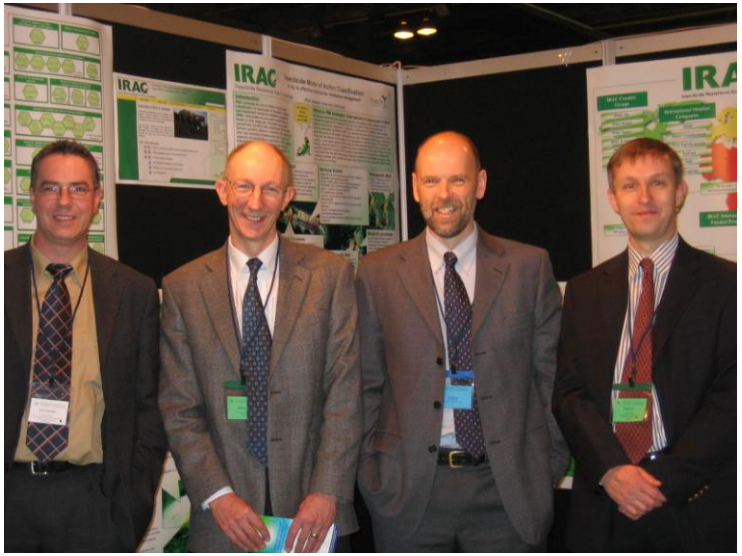
- IRAC provides validated test methods of proven ability to detect changes in susceptibility
- IRAC currently has a program to update the methods
- Intention to include methods for all pests in regulatory guidelines
- New methods will include biochemical and molecular methods

Conclusions

- The major insecticide manufacturers undertake extensive research to understand factors influencing the effectiveness of their compounds
- There is a large body of ongoing work to maintain awareness of susceptibility in key at-risk pests
- Key companies like Bayer CropScience and Syngenta are collaborating both internationally and at a local level to harmonise their guidelines for IRM for the neonicotinoids
- IRAC works for the industry to promote awareness of and solutions to resistance
  - Communication and education on IRM are vital
  - IRAC provides key resources such as the MoA scheme, methodologies, IRM advice to help manage resistance
  - IRAC country groups work to tackle local problems

Resistance is everyone's problem – managing it is vital!

The agrochemical industry is playing its part



IRAC representatives at the BCPC Conference in Glasgow in 2005

Example of Whitefly RM Strategy

Transplanting

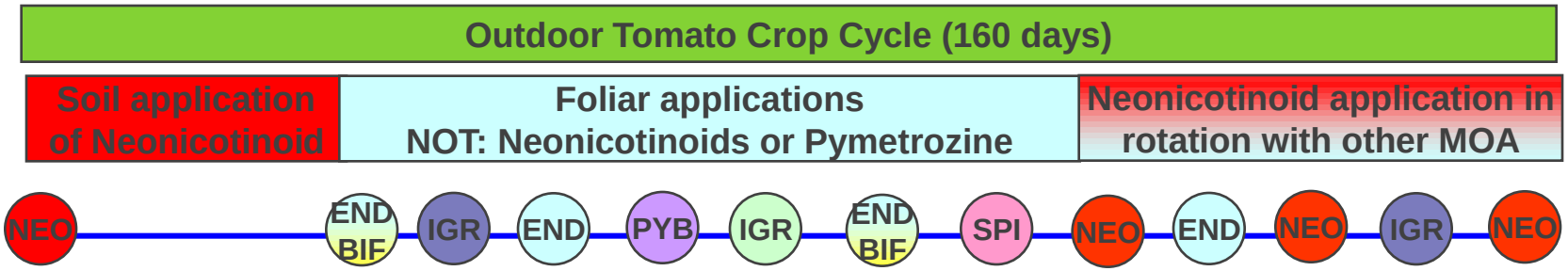
- Soil application of neonicotinoid provides good control for an extended period - with limited selection for resistance

First foliar applications made after soil application

- Avoid applications of neonicotinoids in this period
- Rotate other available AIs

Foliar applications at end of crop cycle

- Rotate available insecticides with different MoA including neonicotinoids.
- Avoid consecutive applications of same chemical class
- Limit total number of neonicotinoid applications as recommended by either company or IRAC guidelines



Bayer CropScience and Syngenta - Collaborative Neonicotinoid Stewardship Project

Key actions:

- Establish local contacts between nominated persons from both companies and set up joint meetings
- Establish agreed local IRM Neonicotinoid strategies taking into account the general guidelines of both companies
  - Agree and adopt positioning in high risk crops
  - Adapt for local conditions, positioning and availability of products
- Involve local regulatory authorities and encourage them to take ownership
- Involve key local academic groups and influencers
- Involve local IRAC groups
- Approach other local neonicotinoid companies
- Check possibility of implementing a labelling scheme (similar to US, Australia)