

Insecticide Resistance Action Committee Update, September 2007

Alan McCaffery



2nd Meeting of EPPO Permanent Panel on Resistance, St Petersburg, September 2007

- IRAC Membership and new structure
- IRAC team developments
- Website, publications
- IRAC MoA Scheme update
- Pollen Beetle working group
- Country Group developments
- Future activities and developments



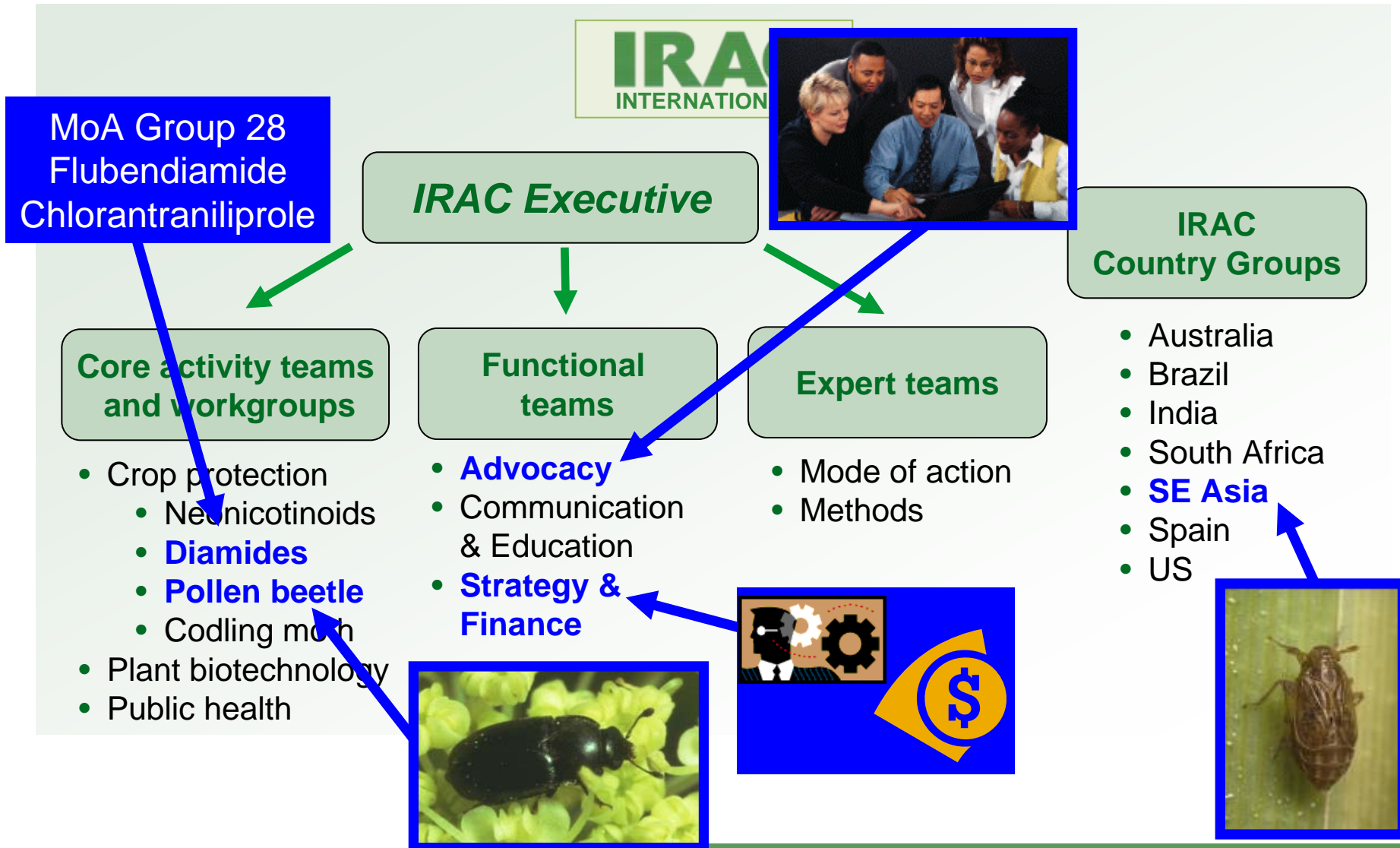
IRAC's growing membership

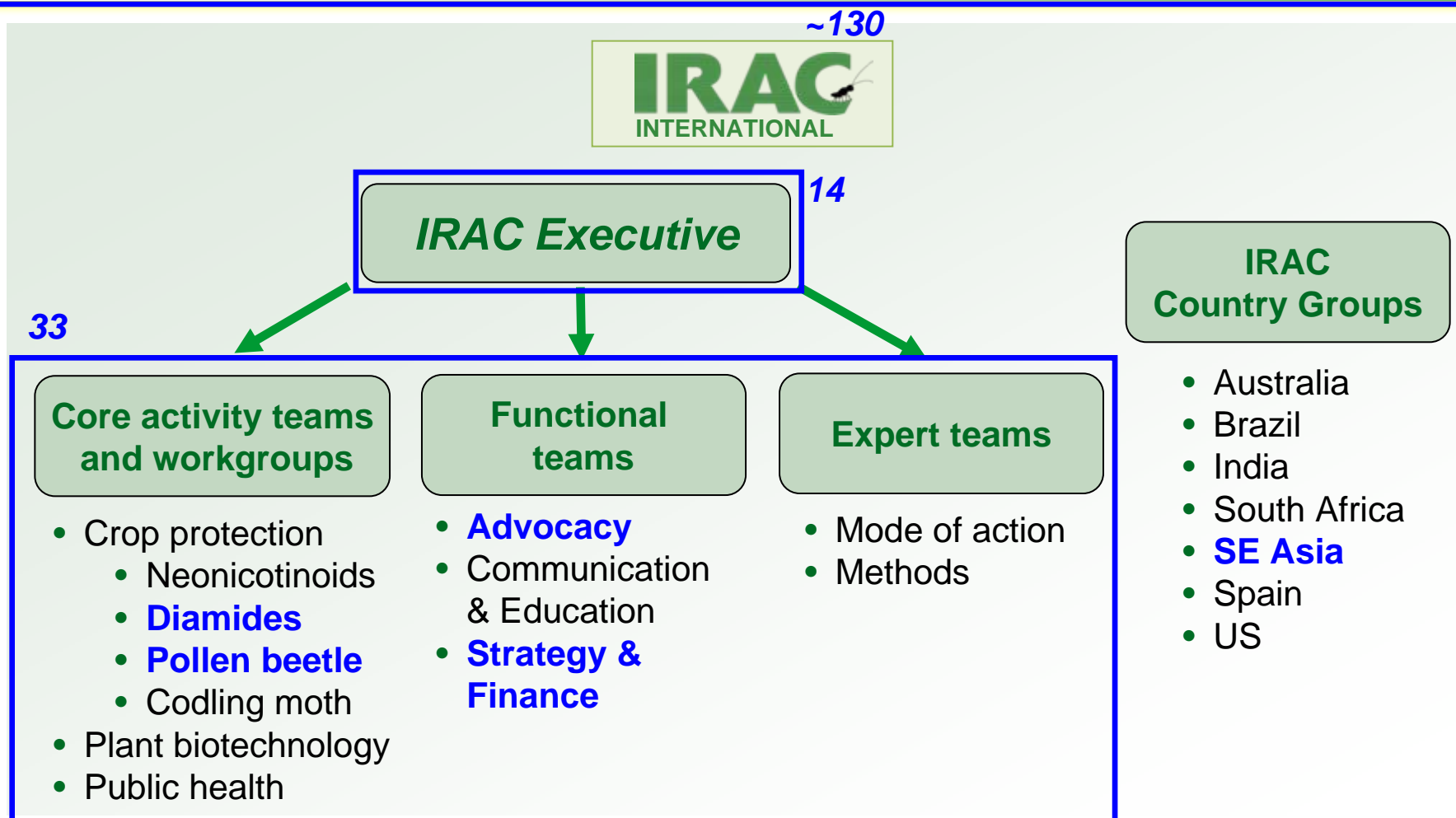
- Currently 9 IRAC Executive member companies + international coordinator
- Makhteshim Agan and Monsanto joined in the past year
- Ongoing recruitment drive
 - IRAC is actively negotiating with 3 potential new members
 - One current focus is on Neonicotinoid producers





Also a new constitution including code of conduct and anti-trust guidance







Insecticide Resistance Action Committee

Resistance Management for Sustainable Agriculture and Improved Public Health

username password Go

Country Groups

Overview Core Activities eTools Membership Downloads

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Site Map
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- >> Introduction
- >> Committee
- >> Links to Furt
- >> Next Exec. C
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- >> Next Concal

Next Event:

- >> October 15 -
IPPC Glasg

Full Diary

Help us help you:

Where would you like to see more information?

Latest News Items

IRAC Pollen Beetle WG with EPPO for Workshop
Members of the IRAC Pollen Beetle Working Group participated with around 40 others in an 'Ad hoc EPPO Workshop on insecticide resistance of *Meligethes spp* (Pollen beetle) on oilseed rape' that was held at the BBA headquarters in Berlin from 3-5 September 2007. The biology, control and resistance ma...read more

New IRAC Whitefly Test Method
The latest addition to the IRAC Test Method series is Method No. 12a for adult whiteflies (*Trialeurodes vaporariorum* IRAC Method by

documents can be
nel.

eConnection eClassification

>>Latest issue of eConnection<<

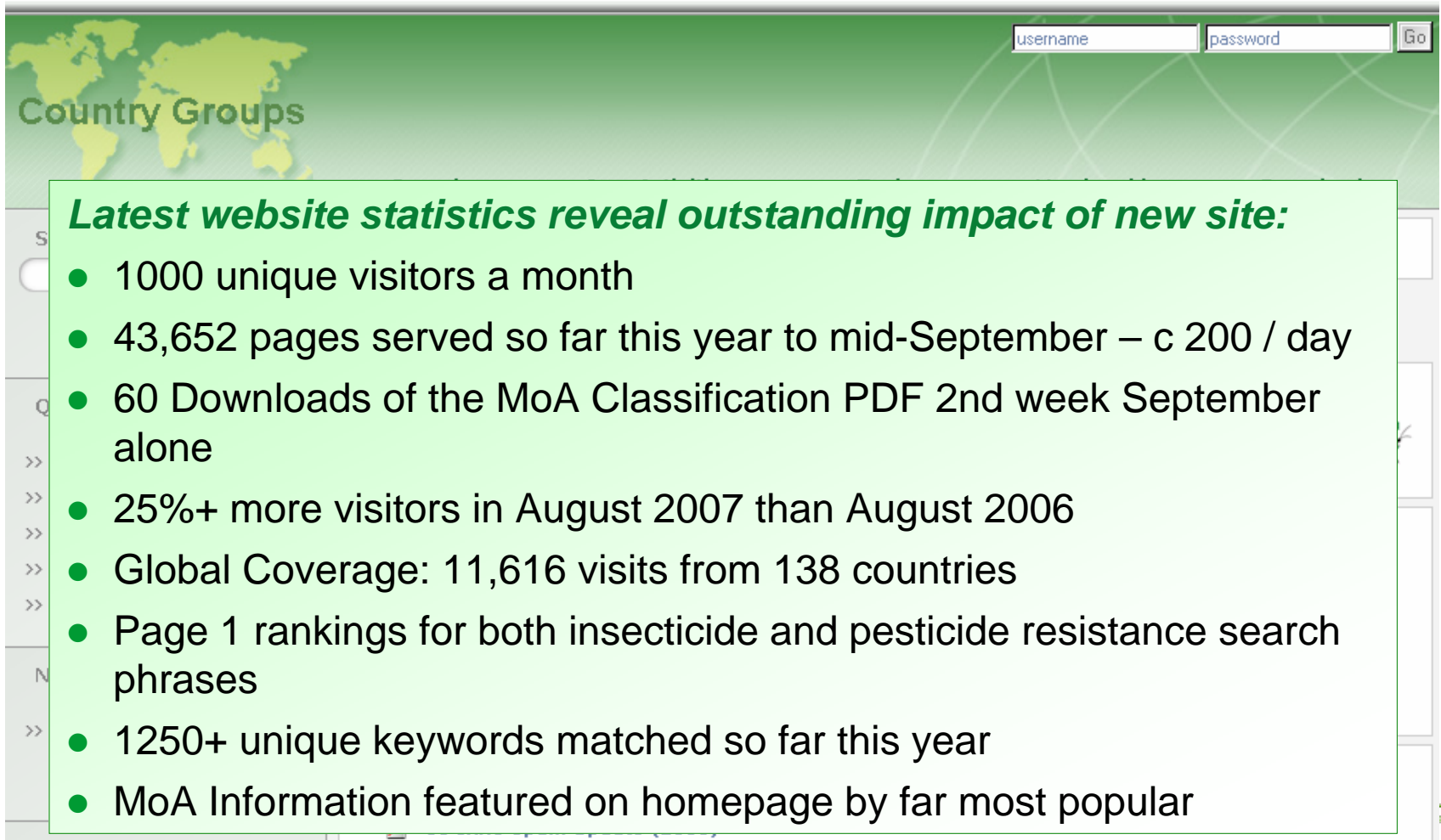
Full Listing of IRAC MoA Documents

SusceptibilityTest Methods

IRAC Country Groups

Australia Brazil India

- IRAC's key communication vehicle
- Completely new website launched Spring 2007
- To coincide with Resistance 2007 Conference at Rothamsted Research, April 2007
- Serves whole of IRAC International - both IRAC Executive and IRAC Country Groups



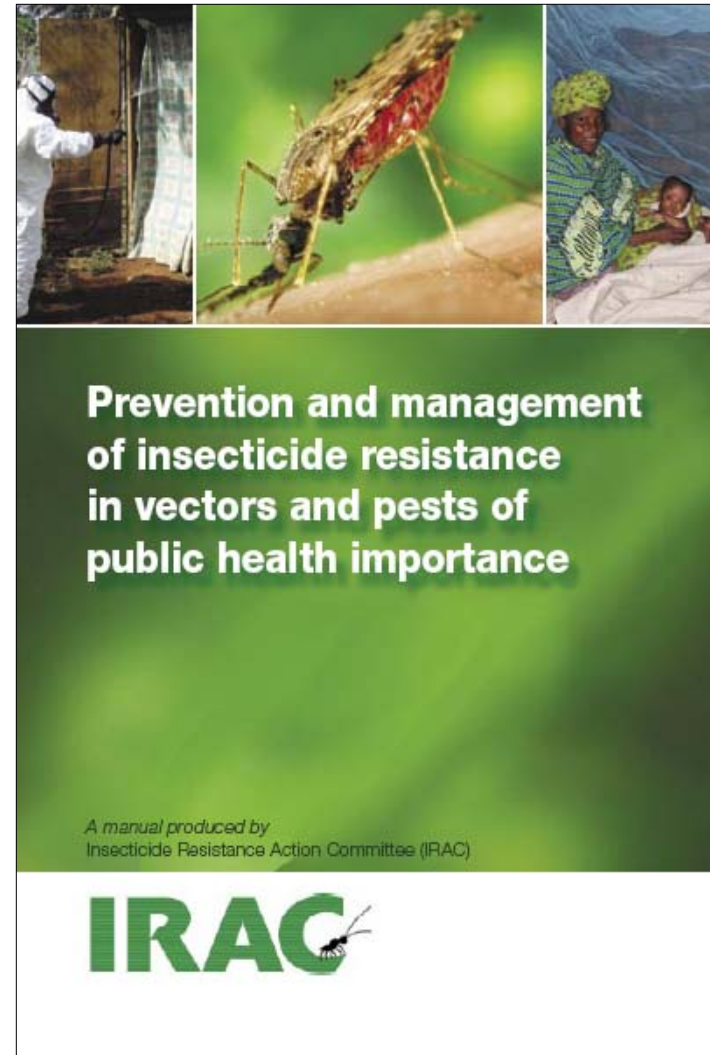
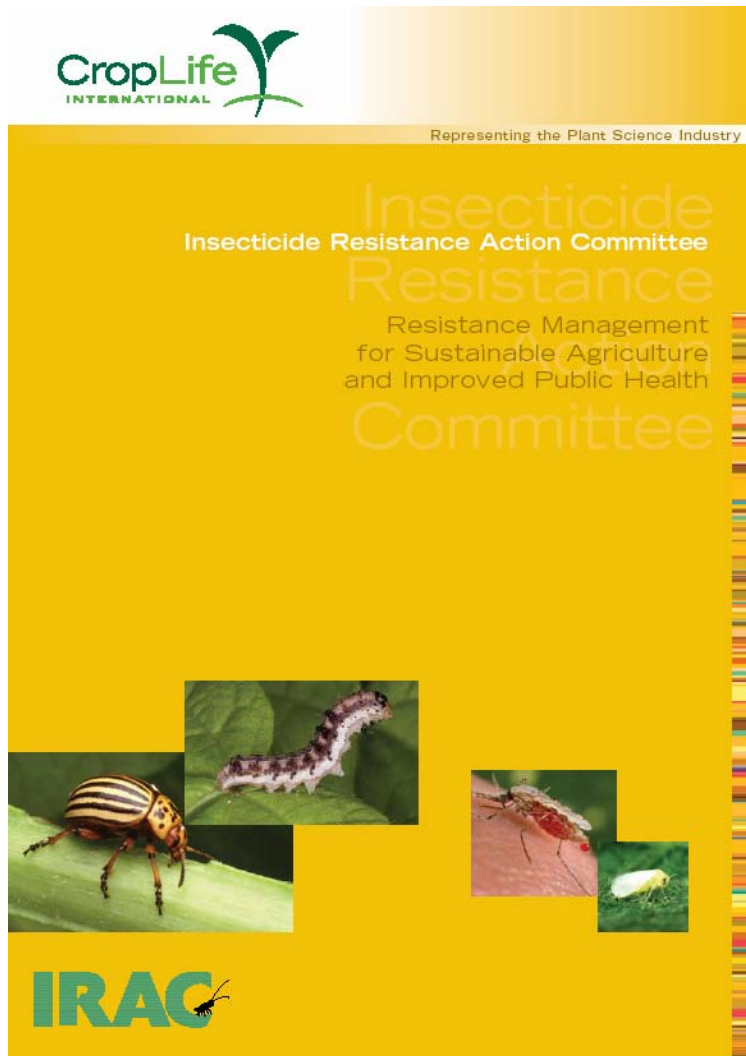
The screenshot shows the IRAC website homepage. At the top left is a world map with the text "Country Groups" below it. At the top right are two input fields labeled "username" and "password", followed by a "Go" button. A large green box with a white border is overlaid on the page, containing the following text:

Latest website statistics reveal outstanding impact of new site:

- 1000 unique visitors a month
- 43,652 pages served so far this year to mid-September – c 200 / day
- 60 Downloads of the MoA Classification PDF 2nd week September alone
- 25%+ more visitors in August 2007 than August 2006
- Global Coverage: 11,616 visits from 138 countries
- Page 1 rankings for both insecticide and pesticide resistance search phrases
- 1250+ unique keywords matched so far this year
- MoA Information featured on homepage by far most popular

In the bottom right corner of the screenshot, there is a small logo for "life" with a stylized plant icon.

Recent IRAC Publications



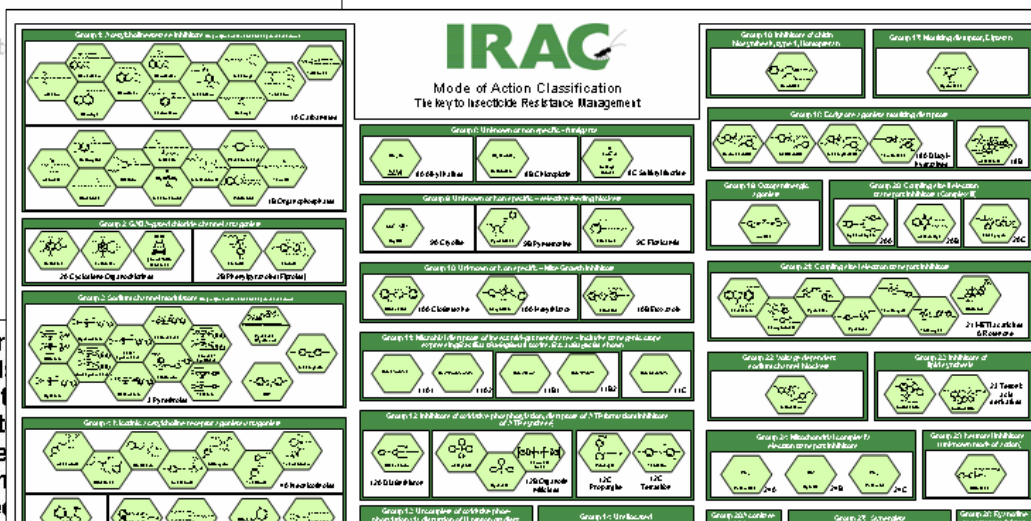


IRAC Mode of Action Classification

Revised & re-issued, July 2007

The IRAC Mode of Action (MoA) classification provides farmer extension staff, consultants and crop protection professional selection of insecticides or acaricides for use in an effect insecticide or acaricide resistance management (IRM) strat presenting the MoA classification, this document outlines the purposes of, the classification list and provides guidance on h purposes. The list is reviewed and re-issued at intervals as re

Insecticide Resist



IRAC MoA Scheme

- Definitive, scientifically rigorous, global scheme developed by IRAC technical experts and researchers as ultimate authority on MoA
- All current insecticides allocated to a Mode of Action group or sub-group - MoA groups 1 to 28
- Key tool for selection of insecticides for effective IRM
- Latest version July 2007. Fundamental review underway
- MoA Structure poster extremely popular

IRAC has an on-going programme of poster development

Lepidopteran Insecticide Mode of Action Classification: A key to effective insecticide resistance management

www.irc-online.org



Introduction and background

A great many of the world's key pest insect species belong to the order Lepidoptera. It is for this reason that the agrochemical industry has developed a wide range of very effective insecticides that can be used to control these insects. Unfortunately, as a consequence of the intensive use of some of these insecticides, many Lepidoptera species have developed resistance to them. The dominant factor behind this is the ability of certain species, particularly in the lepidoptera, having developed resistance to virtually every insecticide used against it, but there are many others.

In recent years the industry has worked especially hard to develop new types of insecticide with novel modes of action, and currently there are more classes of compound available than ever before. Nevertheless, this process is becoming ever slower and more costly. It is therefore vital to ensure that effective insecticide resistance management (IRM) strategies are implemented to ensure that resistance does not develop to these new compounds and to equally ensure that susceptibility is regained where resistance develops to older chemicals.

In order to help prevent or delay the incidence of resistance, IRAC promotes the use of a Mode of Action (MoA) classification of insecticides in its active and sustained IRM strategies. Available insecticides are allocated to specific groups based on their target site as described below. By using sequences or alternations of insecticides from different modes of action classes, resistance is less likely. Available at the IRAC website www.irc-online.org, the IRAC MoA classification tool provides farmers, growers, advisors, extension staff, consultants and crop protection professionals with a guide to the selection of insecticides in IRM programs.

Midgut

Sprayable insecticides with specificity to Lepidoptera, and found from them that are expressed in the midgut, are active. Factors tend to midgut membrane and the leads to pore formation. Clearly results from membrane.

Group 7: Microbial disruptors of insect midgut membranes
Factors produced by the bacterium *Bacillus thuringiensis* (Bt) are expressed in the midgut of various insect species (specific cross resistance sub-group)

Metabolic Processes

Insecticides acting on a range of processes.

Group 23: Inhibitors of oxidative phosphorylation via disruption of H⁺ proton gradient
Chlorantraniliprole (chlorantraniliprole)

Group 27: Synergists
Synergists are used to inhibit detoxifying enzymes. They can act on metabolic resistance.

21a Pyridone-dependent monoamine oxidase inhibitors (e.g. Pyriproxyfen (PYP))
23a Calcium inhibitors (e.g. Flubron (FLB))

Cuticle synthesis

New cuticle is synthesized during the moult cycle. Inhibition of the process leads to insect death.

Group 29: Inhibitors of chitin biosynthesis, e.g. Fenoxypyr (FENOXYPYR)

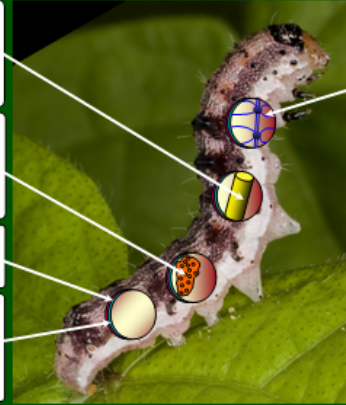
Group 30: Inhibitors of chitin biosynthesis, e.g. Fenoxypyr (FENOXYPYR)

Moulting and Metamorphosis

Moulting and metamorphosis are controlled by the hormones, ecdysone and juvenile hormone. Two groups of insecticides interfere with these processes.

Group 7: Juvenile hormone mimics
Group 15: Juvenile hormone antagonists (e.g. Fenoxypyr) applied in the pro-ecdysone phase, disrupt and prevent metamorphosis

Group 18: Ecdysone agonists (moulting disruptors)
20a Ecdysone agonists (e.g. Methoxyfenozide) act as ecdysone agonists



Effective IRM strategies: Sequences or alternations of MoA

All effective insecticide resistance management (IRM) strategies seek to minimize the incidence of resistance to any one type of insecticide. In practice, alternations, sequences or rotations of compounds from different MoA groups provide sustainable and effective IRM for pest Lepidoptera. This means that resistance from compounds in the same MoA group is minimized, and resistance is less likely to evolve. Example:



Sequence of insecticide MoA through season

Applications are often arranged into MoA groups, where the MoA groups that are defined by the stage of crop development and the biology of the Lepidoptera in an area of concern. Local expert advice should always be followed with regard to spray windows and timing. Several sprays may be possible within each spray window but it is generally essential to ensure that successive generations of the pest are not treated with compounds from the same MoA group.

Metabolic resistance mechanisms may give cross-resistance between MoA groups, and where this is known to occur, the above advice must be modified accordingly.

Nervous System

The nervous system is the target for most current insecticides. A range of insecticides with specific modes of action act on individual targets in the system. These insecticides are generally fast acting.

Stimulatory Nervous System Targets

Group 1: Acetylcholinesterases (AChE) inhibitors
1a Carbamates (e.g. Fenitrothion)
2a Organophosphates (e.g. Chlorpyrifos)
These compounds act as inhibitors of AChE at nerve synapses. This results in hyperactivity in the nervous system.

Group 3: Sodium channel modulation
DDT, Pyrethroids, Pyrethroids (e.g. Cypermethrin, Deltamethrin)
Sodium channels are involved in the propagation of action potentials along nerves. These compounds interfere with this action, causing hyperactivity & nerve block.

Group 4: nAChR agonists (Nicotinic) (nAChR agonists)
Spinosyns (e.g. Spinosad) act at the nicotinic acetylcholine receptor, interfering with the normal functioning of synapses.

Group 22: Voltage dependent sodium channel blockers
Indoxacarb blocks sodium channels and this leads to neural dysfunction.

Group 25: Acetate inhibitors
Fluxusyns

Group 28: GABA-gated chloride channel modulation
Diamides (e.g. Flubron) and diamides, Chlorantraniliprole act at the neuromuscular junction and cause paralysis.

Inhibitory Nervous System Targets

GABA is an inhibitory neurotransmitter in the insect nervous system. The GABA receptor is a target for a number of insecticide groups.

Group 2: GABA-gated chloride channel antagonists
These compounds bind to the GABA receptor complex and inhibit the action of GABA, causing neuronal hyperactivity.

24 Cyclotene GABA-gate (e.g. Endosulfan)
25 Phenylpyrazoles (e.g. Fenoxypyr)

Group 5: GABA-gated chloride channel activation
Avermectins (e.g. Abamectin, Emamectin benzoate) bind to the GABA receptor complex, mimicking GABA and causing paralysis.

Insecticide Mode of Action Classification: A Key to Effective Insecticide Resistance Management in Mosquitoes

www.irc-online.org

Insecticides used to control adult mosquitoes

Mosquito larvae moult several times during their development and undergo complete metamorphosis when becoming adults.

Group 7: Juvenile hormone mimics
JH analogues (Group 7A) and Pyriproxyfen (Group 7C) interfere with the hormonal regulation of development.

Group 15: Inhibitors of chitin synthesis
Benzylureas, inhibit the production of chitin structures within the insect.

Group 17: Moulting disruptor, Dislone, Cyromazine, disrupts successful larval development.

Microbial disruptors of insect midgut membranes
Derived from bacteria, these toxins need to be ingested: Group 11: Microbial disruptors of insect midgut membranes: *Bacillus thuringiensis* var. *israelensis*, Bt (Group 11 A1) *Bacillus sphaericus*, Bt (Group 11 A2)

Insecticides acting on the nervous system

Group 1: Acetylcholinesterase (AChE) inhibitors
Organophosphates (Group 1B), and 2a AChE inhibitors at nerve synapses, resulting in hyperactivity in the nervous system.

Nicotinic acetylcholine receptor agonists

Group 5: Spinosyns, alter the function of nicotinic acetylcholine-gated ion channels, resulting in insect neuronal excitation, leading to neuron excitation.

Mosquitoes also use a range of other receptors, such as olfactory receptors. Insecticides are applied to the bodies of water where mosquitoes larvae develop.

Insecticides used to control mosquito larvae

Group	Mode of Action	Chemical sub-group	Example
1A	Acetylcholinesterase inhibitor	Carbamates	Carbaryl
1B		Organophosphates	Diazinon
2	Bacillus thuringiensis (Bt) spores	DEET, pyrethroids and pyriproxyfen	DEET, Permethrin, Fenoxypyr
3	Sodium channel modulation	Pyrethroids	Permethrin, Deltamethrin
4	nAChR agonists	Bacillus thuringiensis var. israelensis	Bacillus thuringiensis var. israelensis
5	Nicotinic acetylcholine receptor agonists	Spinosyns	Spinosad
7A	Juvenile hormone mimics	Juvenile hormone analogues	Pyriproxyfen
7C		Pyriproxyfen	Pyriproxyfen
11 A0	Microbial disruptors of insect midgut membranes	Bacillus thuringiensis var. israelensis	Bacillus thuringiensis var. israelensis
15	Inhibitors of chitin synthesis	Benzylureas	Benflupropstar
17	Moulting disruptor, Dislone	Cyromazine	Cyromazine

www.irc-online.org. Designed and produced by IRAC Public Health Team, July 2007. Photographs courtesy of Syngenta.



New CP posters e.g. Brown planthopper, Pollen Beetle will add to Leps and Whitefly



www.irc-online.org

- Formed in January 2007
- Established in response to request from EPPO Permanent Panel on Resistance (October 2006)
 - Coordinate European pollen beetle resistance monitoring with countries, regulators, researchers, other interested parties
- Regular teleconferences throughout year
- Face to face meetings in April, September




Industry Participants:

Russell Slater – Chair (Syngenta)
Ralf Nauen (Bayer CropScience)
Fabrice Robin (BASF)
Chris Longhurst (Dow AgroSciences)
Jean-Luc Rison (DuPont)
Marco Jegerings (FMC)
Gérald Huart (Makhteshim)

Advising participants:

Udo Heimbach (BBA, Germany)
Christer Nilsson (SLU, Sweden)

- Scope: Initially restricted to pollen beetle. Other OSR pests to be considered if needed
- 2007 Objectives:
Provide co-ordinated insecticide resistance monitoring in European populations of Pollen beetle
 - IRAC No 11 methodology for PB defined & published on IRAC website:
 - All encouraged to use this methodology & promote use outside the group
- Develop and publish agreed IRM strategy for Pollen Beetle



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

IRAC Susceptibility Test Methods Series Method No: 11
Version: 1

Details:

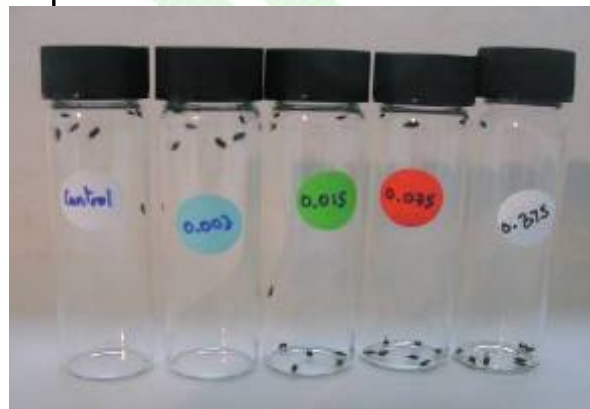
Method:	No: 11
Status:	Approved
Species:	Pollen Beetle, <i>Meligethes aeneus</i>
Species Stage:	Adults
Product Class:	Synthetic pyrethroids



Comments: The method was developed as a result of discussions within the German Expert Committee on Pesticide Resistance – Insecticides (ECPR-I), and is a modification of a monitoring method formerly used by Bayer Crop Science and Syngenta. It is currently being widely used in Western Europe for monitoring sensitivity of *Meligethes aeneus* populations in oilseed rape to synthetic pyrethroids.

Description:

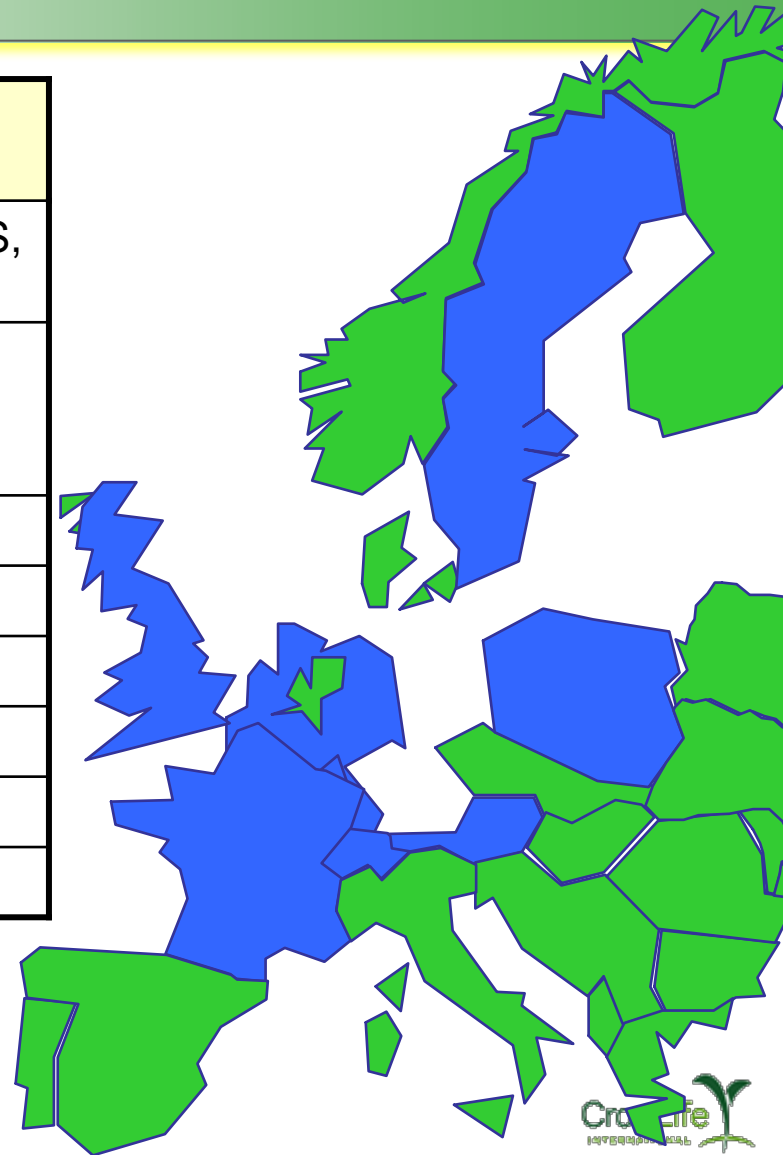
Materials:
 Insect-proof containers, fine pointed brush, beakers for test liquids, syringes/pipettes for liquids or weighing balance for solids, acetone, syringes/pipettes for making dilutions, 20ml glass vials, vial roller (or hotdog roller), small funnel to transfer beetles to vials, binocular microscope or hand lens, paper towels, maximum/minimum thermometer.



infested field.
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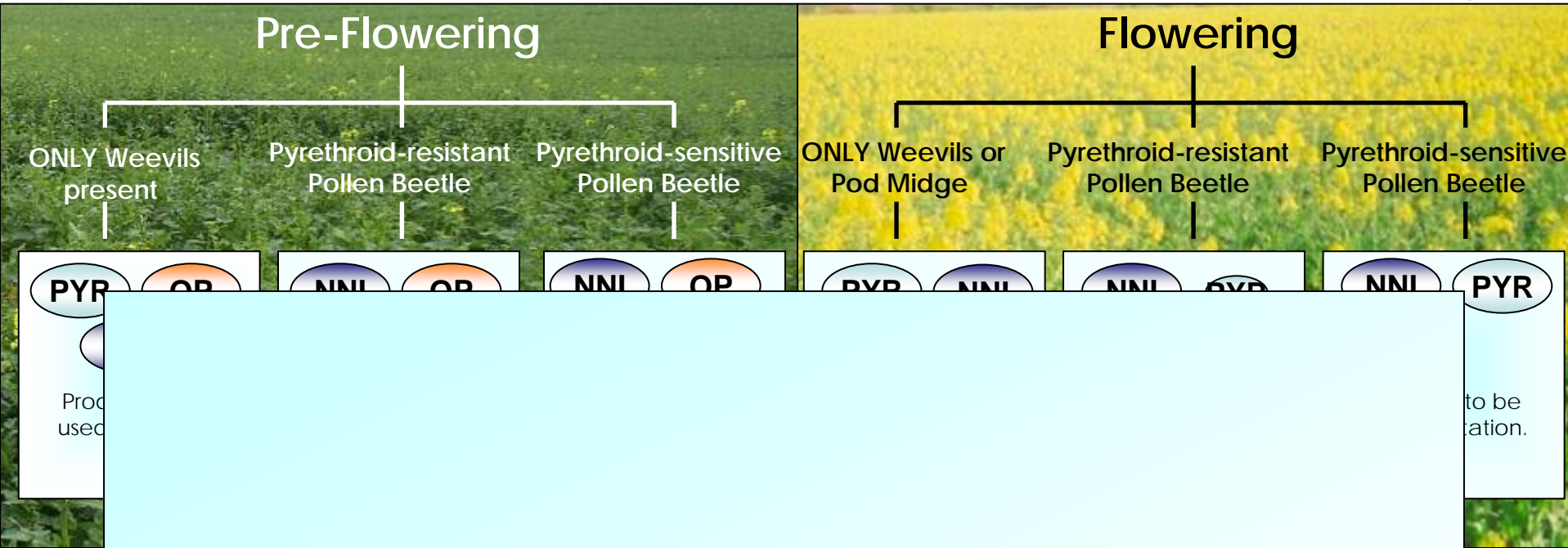
Country	No. of populations	Participant
United Kingdom	75+	Syngenta, BASF, ADAS, FMC
Germany	500+	BBA, Bayer, BASF, FMC, Regional agricultural bodies
France*	10+	Makhteshim
Belgium/Lux	10	BASF
Switzerland	40+	Syngenta, ACW
Poland	15	Bayer
Sweden	tbc	SLU
Austria	15	Bayer

* France covered by CETIOM/INRA survey using different methodology



IRAC Oilseed Pest Management Decision Tree

Version 0.3, Sept 2007



Final version under discussion

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- If aph
- to the neonicotinoid (4A), organophosphate (1B) and pyrethroid (3) MoA class are recommended when possible.
- Where possible alternative methods of oilseed rape pest management should be employed.

- Widespread, strong resistance to neonicotinoids recently reported in Brown Planthopper (*Nilaparvata lugens*) from SE Asia: China, India, Thailand, Bangladesh, Vietnam, Indonesia & Malaysia
- IRAC SE Asia group set up 2007 to work with local organisations and regulators
- Active resistance monitoring underway in key countries
- IRAC companies urgently working on alternative solutions and investing in collaborations with key universities and institutes to understand the nature of the resistance
- IRAC planning a series of SE Asia regional IRM training courses (Funding from CropLife applied for)
- IRAC working with CropLife to engage additional Neonicotinoid producers

Only a concerted, co-ordinated approach will work



- International Plant Protection Congress / British Crop Protection Conference, Glasgow, October 2007
 - Platform presentations by IRAC members
 - IRAC Neonicotinoid team presentation
 - IRAC Exhibition stand with CropLife International and European Crop Protection Association
 - A day of IRAC team meetings preceding conference
- Entomological Society of America, San Diego, December 2007
 - IRAC Symposium ‘Prevention and management of vectors and pests of public health importance’
- IRAC-US / CropLife America meeting, Washington DC, April 2008
 - IRAC Executive face-to-face meeting
 - Joint IRAC Exec, IRAC-US, CLA meeting
- International Congress of Entomology, Durban, July 2008
 - IRAC International meeting planned – depending on member availability

- Continued support for new Country / Regional groups such as IRAC SE Asia
- Continued drive to encourage additional companies to join – especially for off-patent, multi-brand compounds
- Advocacy team developing key focussed, strategic initiatives in Crop Protection, Plant Biotechnology and Public Health that will make a real impact on IRM
- Continued website and Communication & Education initiatives including eLearning material
- Crop Protection team focus on developing and publishing IRM guidelines for key pest groups and on guidance for use of mixtures
- Plant Biotechnology team focus on influencing IRM in emerging markets
- Public Health team focus on education on IRM and on application for Gates Foundation funding

Effective IRM is vital: IRAC is as active as it has ever been in efforts to ensure this happens

Insecticide Resistance Action Committee Feedback on EPPO Resistance Alerts Proposal, September 2007

Alan McCaffery



2nd Meeting of EPPO Permanent Panel on Resistance, St Petersburg, September 2007

IRAC's approach

- IRAC, and its members companies wish to discuss the concept and validity of the EPPO Alerts list proposal
- We have a number of very clear concerns
 - Detailed in the following slides
- Note: IRAC supports valid databases of confirmed cases of resistance

EPPO Alerts List – Quality of data and responses

- ‘Corrective measures needed early on - impossible to wait for definite confirmatory results’
- Inherently there is danger of inaccuracy and false identification of resistance
 - Proposal admits information needed early on is clearly not totally reliable
 - IRAC is concerned at this
- Only definitive scientifically and technically rigorous data are acceptable
- Wider applicability?
- Who is generating information?
- Labels?
- Techniques?

EPPO Alerts list – Confidentiality and Liability

- Idea is that the EPPO resistance alerts list will be used solely by the panel and the closed nature of the list will avoid alarmist action
 - How can this be guaranteed? May easily happen
- Where the panel identifies a suspected case of resistance it will be communicated to relevant national bodies, pesticide regulatory authorities, national resistance groups, agricultural boards, etc
- In theory, if an unconfirmed resistance case is formally documented on a (even private) private website, and if this then resulted in an unjustified loss of confidence in a product, there is a strong potential for liability, if the case is later found to be false
- There could be critical impacts on markets for products for which there is not a real resistance problem
- IRAC companies might be justified in legal challenge