CropLife
INTERNATIONAL

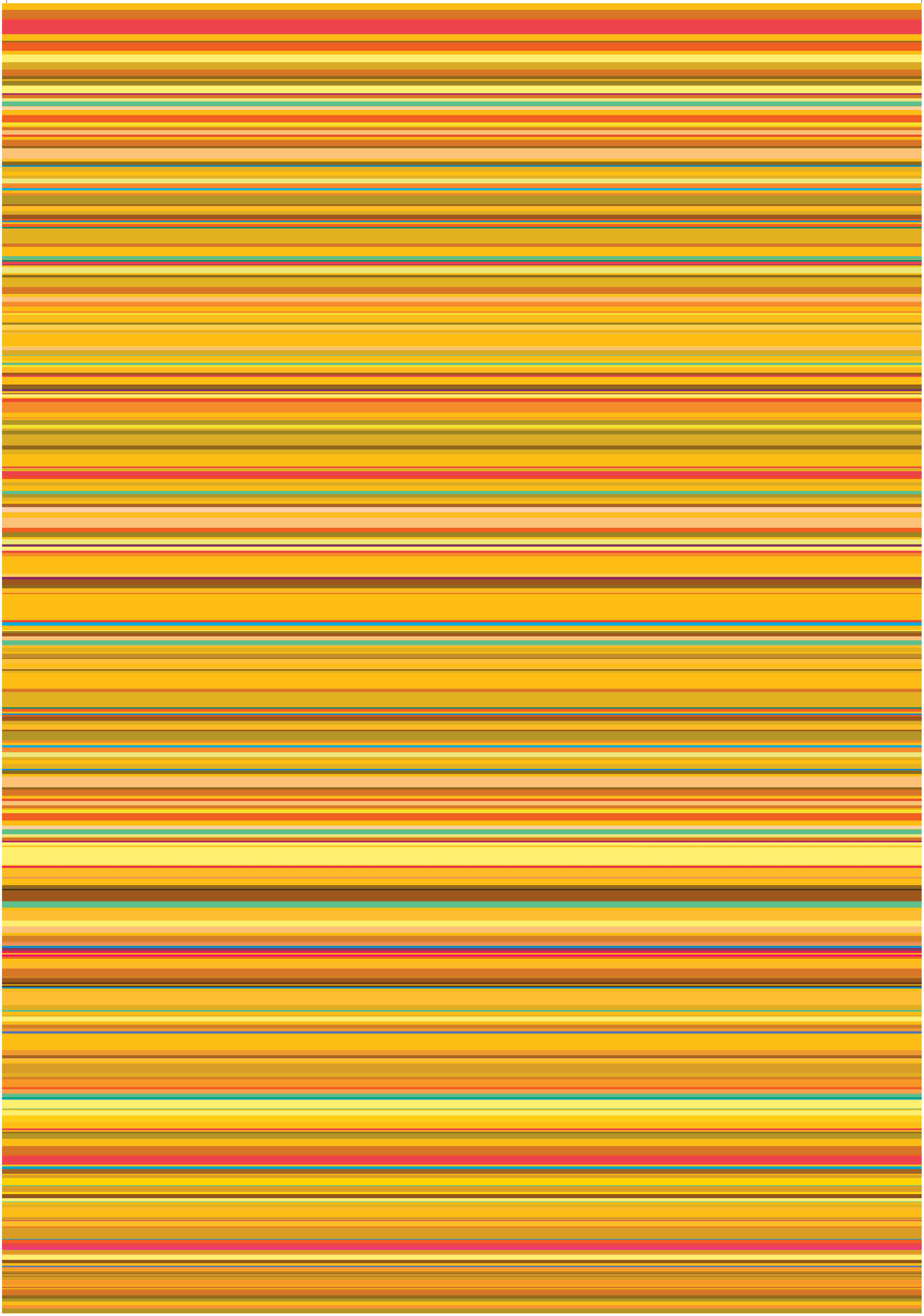
Representing the Plant Science Industry

Insecticide Resistance Action Committee

Insecticide
Resistance
Action
Committee

Resistance Management for Sustainable Agriculture and Improved Public Health

IRAC



Insecticide Resistance Action Committee

Resistance Management for Sustainable Agriculture and Improved Public Health

April 2007

Contents

Contents

Foreword

Foreword

Effective insecticide resistance management (IRM) in conjunction with integrated pest management (IPM) is vital to global crop protection, sustainable agriculture and improved public health, and it is an essential element of responsible product stewardship. The industry's understanding of insecticide resistance and its application of this knowledge to maintain the efficacy of its products is a huge success story that is not realised by the general public and other stakeholders.

The Insecticide Resistance Action Committee (IRAC) was formed in 1984 and works as a specialist technical group of the industry association CropLife International to provide a coordinated crop protection industry response to prevent or delay the development of resistance in insect and mite pests. There are now IRAC country group committees in many parts of the world researching and responding to local resistance issues as well as the parent IRAC International group that provides a coordinating and supporting role at the global level (see also www.irac-online.org).

Developing new insecticides is becoming increasingly difficult and more costly, so it is vital to protect those effective products in the marketplace from the development of resistance. Moreover, with fewer new insecticides being discovered and regulatory pressures reducing the number of older commercial chemistries available, the 'toolbox' of usable insecticides is being reduced, making effective IRM more important than ever.

IRAC and CropLife International have together produced this publication to emphasize the importance of IRM for sustainable agriculture and improved public health and to highlight examples of success stories from around the world.

1. Introduction and background

1. Introduction and background

Effective management of pest insect populations in most of the world's agriculture, horticulture, public health and animal health is dependent on a variety of inputs including a ready supply of safe, highly efficacious insecticides. With their abundant numbers and short life-cycles, populations of pest insects can readily develop resistance to the insecticides used against them with the result that once-effective insecticides are no longer able to control the pests for which they were intended. Accordingly, resistance may be defined as: 'a heritable change in the sensitivity of a pest population that is reflected in the repeated failure of a product to achieve the expected level of control when used according to the label recommendation for that pest species'. The crop protection industry views resistance as an extremely serious threat and an issue that needs a proactive approach. This is also reflected by the fact that European regulatory authorities request data on resistance based on EPPO (European and Mediterranean Plant Protection Organization) guideline PP 1/213(2) "Resistance Risk Assessment" when a new pesticide is registered while regulatory authorities around the world require resistance management practices be followed for crops with insect protection through biotechnology (see also below Regulatory Support and Advocacy). For both new and established insecticidal products, effective IRM is essential.

Insects and mites compete with humans and other animals for food, fibre and forage. Entomologists calculate that crop damage caused by insects has doubled in the last 50 years, in part due to intensified farming efforts to feed a growing world population (Figure 1). The crop protection industry has tried to curtail this destruction with new and novel chemical and biotechnology solutions. As a result, more than 200 different insecticides make up the active ingredients in some 40,000 commercial chemical products today, all targeted at reducing insect damage. However, despite the 'armoury' of products available, more than 500 arthropod pests worldwide have developed resistance to insecticides.

Rice crops are readily attacked by a broad range of insect pests, many of which are resistant to the insecticides used to control them. Most recently, the Rice brown planthopper, *Nilaparvata lugens*, has developed resistance to the neonicotinoid insecticides across much of SE Asia. IRAC member companies are working with growers and government agencies to find solutions to this problem.

Source: Alan Mc Caffery

Source: Syngenta

Resistance to pesticides in insect and mite pests is thus one of the most economically damaging situations growers and pest control professionals face, and no commodity, farmer or region of the world is exempt. The crop protection industry is aware of the consequences of the development of resistance and is proactively taking the lead in tackling the problem, and IRAC is the leader in this effort. It is actively developing strategies to prevent or minimise the chances of the development of resistance to valuable new insecticide classes. Resistance management tactics that reduce these risks are especially important for any new product that is commercialised by the industry. IRM approaches are also important for the long-term maintenance of efficacy of all chemical and biotechnology crop protection technologies available to farmers and pest control operators. As well as protecting new products from resistance, the industry is working to reduce the severity and incidence of resistance to established classes of insecticides that may have been used by farmers and pest control operators for 30 years or more.

Resistance has been documented in many major pests and in many countries of the world. From tobacco budworms (*Heliothis virescens*) in Louisiana cotton, to aphids (*Myzus persicae*) in Europe, and malaria-carrying mosquitoes in disease endemic countries, the devastating effects of insecticide resistance have caused major losses of crops, income and even lives. Resistance to insecticides has now arisen in various species of whiteflies, including the tobacco whitefly (*Bemisia tabaci*) and even more recently control of the rice brown planthopper (*N. lugens*) in India and South-east Asia has become increasingly difficult due to the development of resistance to the most effective products. In all cases, this has resulted in a serious economic impact on crop yields.

The impact of such losses extends beyond the boundaries of one farmer's fields. Sometimes it directly impacts consumers a continent away. In China, for example, cotton yields fell by one third between 1991 and 1993, largely due to the development of resistance to the synthetic pyrethroids and other insecticide groups in the cotton bollworm (*Helicoverpa armigera*). Such a dramatic drop in production threatened not only the Chinese cotton farmers, but the country's textile mills and mill workers, too. Ultimately, even the price of U.S. clothing imported from China increased. In a similar manner, cotton production in Thailand virtually ceased in the late 1980's, due to resistance to insecticides in the cotton bollworm, and this had a severe impact on the country's economy. In contrast, this same problem of resistance in cotton pests was tackled in Australia through the implementation of a well-designed, scientifically-validated and appropriately funded IRM strategy. This landmark action saved the cotton industry from certain demise, and enabled the foundation of the highly successful industry that exists in Australia today.

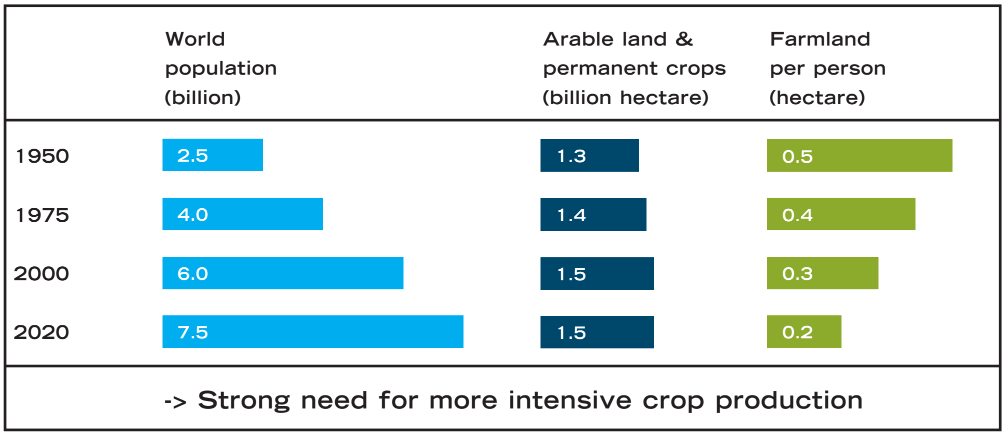


Figure 1. Trends in global population and farmland area
Source: United Nations

Many chewing pest and sucking pest species attack cotton and, without effective control, loss of yield can be very substantial. Both insecticides and GM insect-control varieties are used to control these pests and IRAC is involved in developing sustainable resistance management solutions for them.

Source: Bayer

2. Insecticide Resistance Action Committee

2. Insecticide Resistance Action Committee

Background and Aims

IRAC was formed in 1984 to provide a co-coordinated crop protection industry response to prevent or delay the development of resistance in insect and mite pests. The main aims of IRAC are firstly to facilitate communication and education on insecticide resistance and secondly to promote the development of resistance management strategies in crop protection and vector control so as to maintain efficacy and support sustainable agriculture and improved public health. It is IRAC's view that such activities are the best way to preserve or regain the susceptibility to insecticides that is so vital to effective pest management. In general, it is usually easier to proactively prevent resistance occurring than it is to reactively regain susceptibility.

Organisation

IRAC is an inter-company organisation that operates as a Specialist Technical Group under the umbrella of CropLife International. IRAC is also recognised by The Food and Agriculture Organization (FAO) and the World Health Organization (WHO) of the United Nations as an advisory body on matters pertaining to resistance to insecticides. The group's activities are coordinated by IRAC International and Country or Regional Committees with the information disseminated through conferences, meetings, workshops, publications, educational materials and the IRAC website (www.irac-online.org).

IRAC International comprises of key technical personnel from the crop protection companies affiliated with CropLife through membership in the relevant national associations and currently eight companies are represented: BASF, Bayer CropScience, Dow AgroSciences, DuPont, FMC, Makteshim, Sumitomo and Syngenta. The International Committee supports resistance management project teams and also provides a central coordination role to regional, country and technical groups around the world. IRAC Country Groups frequently include additional member companies outside of those in the International Committee as well as non-industrial members as appropriate for tackling local resistance issues. Clearly, not every insecticide manufacturer is a member of IRAC, and a particular challenge that the organisation faces is how to maintain effective resistance management in markets where generic insecticides are widely used and where effective IRM is not considered a priority by all.

Focus

The current focus of IRAC is on education and communication of resistance issues, a role well suited to its technical foundation. Much of this activity is channelled through the IRAC website. In addition, the gathering momentum for increased regulation of pesticides, especially in Europe, demanded supportive advocacy for IRM based on the availability of a broad range of insecticidal materials with different modes of action. IRAC has thus strived to influence and provide advice to those bodies involved in regulation in order to maintain the chemical tools needed for successful IRM. IRAC is tackling resistance on a broad range of fronts and these wide-ranging activities are summarised below.

Insecticide Mode of Action

In consultation with technical experts from the industry and academia, IRAC has developed a definitive classification of insecticides based on mode of action (MoA). This is based on the fact that in the majority of cases, not only does resistance to an insecticide render the selecting compound ineffective, but it often also confers cross-resistance to other chemically related compounds. This is because compounds within a specific chemical group usually share a common target site within the pest, and thus share a common MoA.

This MoA list is updated periodically as new insecticides enter the market or when new, scientifically validated, information becomes available on the MoA of commercial products. The IRAC MoA classification has become the definitive reference for insecticide classification and is recognised by farmers, scientists and regulators worldwide. More information on this and an up to date IRAC MoA poster is available on the IRAC website. Figure 2 shows an extracted example of part of the IRAC MoA classification list.

The concept of cross-resistance between chemically related insecticides or acaricides is the fundamental basis of the IRAC mode of action classification. Experience has shown that all effective IRM strategies seek to minimise the selection for resistance from any one type of insecticide or acaricide. In practice, alternations, sequences or rotations of compounds from different MoA groups provide growers and pest control professionals with sustainable and effective IRM options. This ensures that repeated selection with compounds from any single MoA group is minimised.

The IRAC classification thus ensures that insecticide and acaricide users are aware of MoA groups and that they have a sound basis on which to implement season-long, sustainable resistance management strategies. Of course, to help delay resistance it is strongly recommended that growers also integrate other control methods into their insect or mite control programmes.

It is known that resistance of insects and mites to insecticides and acaricides can, and frequently does, result from enhanced metabolism by detoxifying enzymes within the pest. Such metabolic resistance mechanisms are often not linked to any specific site of classification and therefore they may confer cross-resistance to insecticides in more than one IRAC MoA group (also called multi-resistance). Where such mechanisms are known to give cross-resistance between MoA groups, it is clear that the use of insecticides should be modified appropriately. In the absence of such information, the use of windows, sequences or alternations of MoA classes are effective anti-resistance tactics that can be employed.

IRAC Mode of Action Classification v5.1, September 2005

Main Group and Primary Site of Action	Chemical Sub-group or exemplifying Active Ingredient	Active Ingredients
3 Sodium channel modulators	DDT	DDT
	Methoxychlor	Methoxychlor
	Pyrethroids	Acrinathrin, Allethrin, d-cis-trans Allethrin, d-trans Allethrin, Bifenthrin, Bioallethrin, Bioallethrin S-cylclopentenyl, Bioresmethrin, Cycloprothrin, Cyfluthrin, beta-Cyfluthrin, Cyhalothrin, lambda-Cyhalothrin, gamma-Cyhalothrin, Cypermethrin, alpha-Cypermethrin, beta-Cypermethrin, thetacypermethrin, zeta-Cypermethrin, Cyphenothrin , (1R)-transisomers], Deltamethrin, Empenthrin , (EZ)- (1R)- isomers], Esfenvalerate, Etofenprox, Fenpropathrin, Fenvalerate, Flucythrinate, Flumethrin, tau-Fluvalinate, Halfenprox, Imiprothrin, Permethrin, Phenothrin [(1R)-trans- isomer], Prallethrin, Resmethrin, RU 15525, Silafluofen, Tefluthrin, Tetramethrin, Tetramethrin [(1R)-isomers], Tralomethrin, Transfluthrin, ZXI 8901

Figure 2. Extract from IRAC Mode of Action classification

Resistance Monitoring Methods

Reliable data on resistance, rather than anecdotal reports or assumptions, are essential to successful resistance management and key to this is the availability of sound baseline data on the susceptibility of the target pest to the toxicant. A large number of bioassay and biochemical tests are used to characterise resistance, but they are not necessarily comparable because different parameters and criteria are often used. IRAC has evaluated, validated and published a wide range of standard resistance testing methods and these are available on the IRAC website. Importantly, they provide consistent and comparable methods for evaluating the status of resistance in insect populations, and a means of assessing the success of IRM strategies. Most of these methods require only basic equipment and are suitable for use in laboratories worldwide. New methods and alternative options such as biochemical and molecular methods are being considered and if approved these will be added to the website.

Effective resistance management relies on sound information about the extent and intensity of resistance problems. IRAC has evaluated, validated and published a wide range of standard resistance assays to enable this information to be obtained.

Source: Syngenta

Regulatory Support and Advocacy

IRAC has taken a leading role as an expert group providing industry responses to proposals from government regulatory authorities. For example, there is now a regulatory requirement in the European Union under Directive 91/414/EEC for companies to provide an assessment of the potential risk of resistance being developed by target organisms and for management strategies to be introduced to address such risks (McNamara and Smith, 2000). This is necessary to sustain the performance of as many active ingredients with different modes of action as possible over a long time period through the use of alternate spray regimes, rotation and efficient application techniques.

The recently published guidelines (PP 1/213(2) on Resistance Risk Assessment from EPPO outline the requirements for research and recommendations on resistance issues in order to obtain re-registration of established insecticides or approval of new ones. Baseline susceptibility studies (testing several strains of a target species that has had no prior exposure to the particular chemical class under evaluation), monitoring (periodic studies to determine if susceptibility has changed in the target species by simple bioassays after the launch of a new compound or for re-registration purposes), and possible resistance management strategies (how insecticides across different classes be rotated (or sometimes mixed) during the crop season to prevent resistance), have now to be provided by the crop protection companies as a required part of the registration dossier (OEPP/EPPO, 1999). The Fungicide, Herbicide and Insecticide Resistance Action Committees (FRAC, HRAC and IRAC) have been instrumental in developing workable guidelines for companies, resulting in the publication of an official Guidance Document (EPPO Std. PP 1/213(1) and (2)).

Similarly, the U.S. Environmental Protection Agency (EPA) and the Pest Management Regulatory Agency of Canada have been developing a voluntary pesticide resistance management labelling scheme based on MoA. The IRAC MoA classification scheme is used as the framework for this IRM labelling. Development has been carried out under the auspices of the North American Free Trade Association and has resulted in the issue of a Pesticide Registration (PR) Notice in the United States. A similar labelling scheme operates in Australia and other countries are considering similar schemes.

IRAC has been highlighting its concern at the removal of many crop protection insecticides from the European market, especially where this results in a reduction in the availability of MoA classes for specific economic pest problems. IRAC strongly believes that this continuing reduction in the toolbox of available insecticides inevitably leads to an increased risk of the development of resistance to the remaining market products. For example, the deregulation of a number of organophosphate (op) insecticides that were very effective for the control of the pollen beetle (*Meligethes aeneus*), in oilseed rape crops in many European countries has resulted in almost total reliance on the synthetic pyrethroids, and exclusive use of this group of insecticides has led to the rapid development of resistance.

Oilseed rape is grown widely in Europe, but is readily attacked by the Pollen beetle, *M. aeneus*. Following the withdrawal of OP insecticides from this market, control has recently relied almost exclusively on synthetic pyrethroids, and this has resulted in widespread resistance. IRAC is helping to tackle this problem. This issue is particularly acute for minor crops where few products are registered for use and where rotation and alternation options are limited. An example is hops where the hop aphid (*Phorodon humuli*), has developed resistance to pyrethroids and there are few other registered products for its control.

Source: Syngenta

3. The nature of insecticide resistance

3. The nature of insecticide resistance

Evolution of insecticide resistance

As indicated above, resistance may be defined as ‘a heritable change in the sensitivity of a pest population that is reflected in the repeated failure of a product 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. Clearly, because pest insect populations are usually large in size and they breed quickly, there is always a risk that insecticide resistance may evolve, especially when insecticides are misused or over-used.

Following the introduction of synthetic organic insecticides such as DDT in the 1940’s, it was not long before the first cases of resistance were detected and by 1947, resistance to DDT was confirmed in houseflies. Thereafter, with every new insecticide group that was introduced, including cyclodienes, organophosphates, carbamates, formamidines, pyrethroids, *Bacillus thuringiensis*, spinosyns and neonicotinoids, cases of resistance appeared some 2 to 20 years after their introduction in a number of key pest species. This phenomenon has been described as the ‘pesticide treadmill’, and the sequence is familiar. As a result of continued applications over time a pest may evolve resistance to an insecticide with the result that the resistant strain becomes increasingly difficult to control at the labelled rate and frequency. This in turn may lead to more frequent applications of the insecticide. As a consequence of this, both the intensity of the resistance and the frequency of insecticide-resistant individuals in the population may increase still further and problems of control continue and are certain to worsen as yet more product is applied. Eventually users are obliged to switch to another insecticide if one is available. The genetics of these heritable resistance traits and the intensive repeated application of pesticides, together are responsible for the rapid build-up of resistance in most insects and mites. Natural selection by an insecticide allows some initially very rare, naturally occurring, pre-adapted insects with resistance genes to survive and pass the resistance trait on to their offspring. Through continued application of insecticides with the same MoA, selection for the resistant individuals continues so the proportion of resistant insects in the population increases, while susceptible individuals are eliminated by the insecticide.

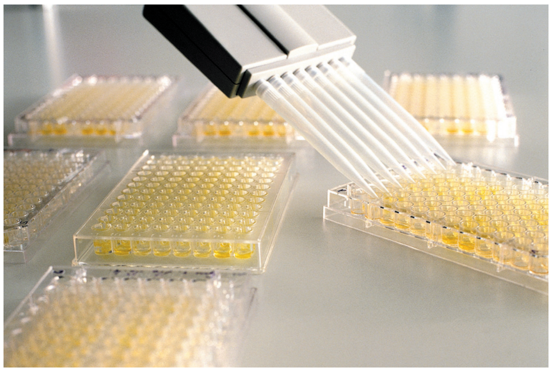
Under permanent selection pressure, resistant insects outnumber susceptible ones and an insecticide is no longer effective. The speed with which resistance develops depends on several factors, including how fast the insects reproduce, the migration and host range of the pest, the availability of nearby susceptible populations, the persistence and specificity of the crop protection product, and the rate, timing and number of applications made.
Resistance increases fastest in situations such as greenhouses, where insects or mites reproduce quickly, there is little or no immigration of susceptible individuals and the user may spray frequently.

Mechanisms of resistance

There are a number of ways insects can become resistant to insecticidal crop protection and public health products:

- **Metabolic resistance**. Using enhanced levels of metabolism by enzymes, resistant insects may detoxify a particular insecticide faster than susceptible insects, and quickly eliminate the insecticidal compounds.
- **Target-site resistance**. The target site where the insecticide acts in the insect may be genetically modified to prevent the insecticide binding or interacting at its site of action thereby reducing or eliminating the pesticidal effect of the insecticide.
- **Penetration resistance**. The insecticide may penetrate through the cuticle of resistant insects more slowly than susceptible insects.
- **Behavioural resistance**. Resistant insects may detect or recognise the presence of the insecticide and avoid it.

Insects may simultaneously possess several mechanisms of resistance to a single compound or group of related compounds (e.g. target site resistance and multiple metabolic mechanisms of resistance to pyrethroids in Heliothine pests of cotton). In addition, by having a range of resistance mechanisms, insects may possess multiple resistances to a number of unrelated insecticide groups. For example, individual resistant peach-potato aphids (*M. persicae*) in Europe may possess *kdr* (knockdown resistance) and super-*kdr* resistances to pyrethroids, esterase resistance primarily to organophosphates and to some extent to pyrethroids and carbamates, and MACE (modified acetylcholinesterase) resistance to pirimicarb and triazamate. In order to help develop effective IRM strategies, it is important that resistance mechanism studies are undertaken by specialist laboratories to distinguish between these possibilities.



Source: Syngenta

Understanding the nature of individual resistance cases is essential if effective solutions to resistance problems are to be developed. IRAC is working to add further biochemical and molecular techniques to its portfolio of resistance monitoring methods in order to help characterise resistance problems. Such information is especially important in helping to develop strategies to tackle resistance problems. IRAC is also working to ensure that the concept of using sequences or alternations of insecticides with different modes of action is widely understood and put into practice so that, as far as possible, such problems can be avoided.

Metabolic resistance

Metabolic resistance is often the most common mechanism and it may present the greatest challenge, especially as such mechanisms may confer resistance to multiple MoA classes of insecticides. All insects use their detoxifying enzyme systems to break down or sequester foreign compounds including insecticides. In this regard, many polyphagous insects that feed on a broad range of host plants are especially well adapted to feeding on a range of natural plant toxins and are often readily able to detoxify foreign compounds as well as insecticides. Resistant strains of pests with metabolic resistance may express more abundant amounts of or have more efficient forms of these enzymes. Common metabolic resistance mechanisms include monooxygenases (mixed function oxidases [MFOs]), carboxylesterases and glutathione-S-transferases. In addition to being more efficient, these enzyme systems may also have a wide substrate specificity, with the result that they are able to detoxify a broad spectrum of insecticides, including those from different MoA groups.

Carboxylesterases often have a strong affinity for insecticidal substrate molecules, and through a mechanism of amplification they may act to sequester insecticidal molecules and hence confer high levels of resistance. For example, enhanced carboxylesterase activity in the aphid M. persicae resulting from gene amplification may give resistance to pyrethroids, OPs and carbamates. Similar amplification of esterases has been shown to be responsible for resistance in *Culex* mosquitoes.

Switching to a different compound, ideally in a different MoA group to combat this type of resistance is likely to succeed only if the second compound is metabolised by a different enzyme within the target pest. Compounds within specific MoA groups tend to be metabolised by similar enzyme systems, so using another compound within a mode of action group is much less likely to overcome resistance than using one in a different MoA class, where metabolic cross-resistance is less likely. Occasionally, it may be possible to use a metabolic inhibitor, such as the monooxygenase synergist piperonyl butoxide (PBO) or esterase inhibitors such as DEF (S, S,S-tributylphosphorothioate) or some other organophosphorus compounds, to overcome certain forms of metabolic resistance.

Target-site resistance

Insects possessing target site resistance have resistance alleles that lead to expression of a modified form of the target site receptor, or in some way affect receptor abundance. This modification of the receptor prevents the normal interaction of the insecticide with its target site and hence prevents its action. Compounds from any one MoA class are all usually affected (at least to varying degrees) by a specific target site resistance. This is the basis for the MoA classification that IRAC has developed to aid in designing IRM strategies that use sequences or alternations and sometimes mixtures of MoAs. For example, the synthetic pyrethroids, pyrethrum and DDT are all affected by kdr (knockdown) resistance which involves a modification of the sodium channel that is involved in the propagation of action potentials in the insect nervous system.This mechanism is known to occur for example in a range of pest Lepidoptera including the tobacco budworm *H. virescens* and the bollworms *Helicoverpa zea* and *H. armigera* and in a range of public health pests such as *Musca domestica*, *Culex* spp., *Anopheles* spp. and *Aedes aegypti*. Resistance to one pyrethroid in any of these insects will usually confer resistance to all other pyrethroids.

Other well-known target site resistances include modified acetylcholinesterase (MACE) (an enzyme responsible for controlling the propagation of nerve signals at synapses) and giving resistance to certain carbamate and organophosphorus insecticides (e.g. aphids, houseflies, mosquitoes), *rdl* (a modification of the receptor involved in the action of the inhibitory neurotransmitter, GABA) which gives resistance to cyclodienes (e.g. cockroaches), and modification of a Cry toxin receptor on the midgut membrane leading to resistance to certain forms of *B. thuringiensis* (e.g. diamondback moth *Plutella xylostella*). Target site resistance may be effectively managed by using different classes of insecticides (see IRAC MoA classification) that target different sites of action. Various molecular assays (e.g. analyses of SNPs (single nucleotide polymorphisms and various PCR techniques) are available to detect the molecular changes associated with these types of mechanism).

Reduced penetration

Penetration resistance is known to occur in insects such as the housefly (*M. domestica*) or the cotton bollworm (*H. armigera*). It is characterised by a much slower entry of an insecticide into the resistant insect than that into a comparable susceptible insect. This is because the cuticle has been modified in a way which delays the uptake of the insecticide. Penetration resistance usually provides only quite modest levels of protection to the insect, but it may act as a powerful contributing factor or modifier when expressed in the presence of other mechanisms such as metabolic resistance. Because of its rather general nature, this mechanism can protect insects from a wide range of insecticides.

Behavioural resistance

Behavioural resistance occurs when insects or mites are able to prevent or minimise contact with insecticides through avoidance. This mechanism of resistance has been reported for several classes of insecticides, including organochlorines, organophosphates, carbamates and pyrethroids. Insects may simply cease feeding if they come across certain insecticides, or leave the area where spraying occurred (i.e., move to underside of a sprayed leaf, move deeper in the crop canopy or fly away from the treated area). With transgenic plants, insects can avoid feeding on the plant parts with the highest levels of insecticidal proteins. Behavioural resistances are hard to diagnose, and few management strategies are known; but rotating or alternating insecticides should delay their effects.

4. Strategies to prevent or delay resistance

4. Strategies to prevent or delay resistance

An integrated approach to prevent the evolution of resistance

The most effective strategy to combat insecticide resistance is to do everything possible to prevent it occurring in the first place. To this end, crop specialists recommend IRM programs as one part of a larger IPM approach covering three basic components: monitoring pest complexes in the field for changes in population density, focusing on economic injury levels and integrating multiple control strategies.

Monitoring pests

Scouting is one of the key activities that users of insecticidal products can implement as part of their insecticide resistance management strategy. Farmers should follow the progress of insect population development in their fields (with or without the assistance of a crop consultant or advisor), to determine if and when control measures are warranted. They should monitor and consider natural enemies when making control decisions. After treatment, they should continue monitoring to assess pest populations and the effectiveness of any control measures implemented. Similar considerations apply to the control of public health pests.

Economic injury levels

Insecticides should be used only if insects are numerous enough to cause economic losses that exceed the cost of the insecticide plus application, or where there is a threat to public health. Exceptions are in-furrow, at-planting or seed treatments for early season pests that from experience it is known usually reach damaging levels annually. Farmers are always encouraged to consult their local advisors about economic thresholds of target pests in their areas.

Integrated control strategies

Monitoring is just one element of an insecticide resistance management program. To avoid resistance, insecticide users should consider implementing the following major resistance management strategies.

- An integrated approach is always encouraged in which as many different control tactics as possible are incorporated. IPM-based programs may include the use of synthetic insecticides, biological insecticides, beneficial insects (predators / parasites), cultural practices, transgenic plants (where allowed), crop rotation, pest-resistant crop varieties and chemical attractants or deterrents. Insecticides must be selected with care and their impact on future pest populations considered. Broad-spectrum insecticides should always be avoided when a more specific insecticide will suffice. Even cultural practices, such as destroying overwintering stages of pests (e.g. pupal stages of the cotton bollworm (*H. armigera*) can play a role in managing resistance).
- Applications of insecticide must be timed correctly, targeting the most vulnerable life stage of the insect pest. The use of spray rates and application intervals recommended by the manufacturer and in compliance with local agricultural extension regulations is essential.
- It is important to mix and apply insecticides carefully. As resistance increases, the margin for error in terms of insecticide dose, timing, coverage, etc., assumes even greater importance. The pH of water used to dilute some insecticides in tank mixes should be adjusted to 6 to 8. Sprayer nozzles should be checked for blockages and wear, and should be able to handle the pressures required for good coverage.

- Spray equipment should be properly calibrated and checked on a regular basis. In tree fruits, proper and intense pruning will allow better canopy penetration and tree coverage. Application volumes and techniques recommended by the manufacturers and local advisors should always be used.
- A key element of effective resistance management is the use of alternations, rotations, or sequences of different insecticide MoA classes. Users should avoid selecting for resistance or cross-resistance by repeated use within the crop cycle, or year after year, of the same insecticide or related products in the same MoA class. By using alternations, rotations or sequences of insecticides across all available classes, selection pressure for the evolution of any one type of resistance is minimised and the development of resistance will be delayed or prevented. In addition, growers should avoid tank-mixing products from the same product class. The IRAC MoA scheme provides a classification of insecticidal MoA groups, and is key to the selection of appropriate insecticides.
- It is important to consider the impact of pesticides on beneficial insects, and use products at labelled rates and spray intervals to minimise undesired effects on parasitoids and predators. Insecticides should be selected in a manner that causes minimum damage to populations of beneficial arthropods and local extension service recommendations should be followed.
- Preserve susceptible genes. Some programs try to preserve susceptible individuals within the target population by providing a refuge or haven for susceptible insects, such as unsprayed areas within treated fields, adjacent refuge fields, or attractive habitats within a treated field that facilitate immigration. These susceptible individuals may out-compete and interbreed with resistant individuals, diluting the impact of any resistance that may have developed in the population. Such tactics are mandated for use with genetically modified corn and cotton crops in countries such as the US. In this case a combination of high dose expression of insecticidal toxins by the transgenic crop is combined with provision of associated, structured refuges that allow the development of susceptible individuals. These susceptible insects are available to mate with rare homozygous resistance insects emerging from the transgenic crop. The resultant heterozygote forms are killed by the high dose of toxin expressed in the transgenic crop. The effectiveness of this approach is underlined by the fact that resistance has not developed in over ten years of use of this technology in the US.
- Consider crop residue options. Destroying crop residues can deprive insects of food and overwintering sites. This cultural practice will kill pesticide-resistant pests (as well as susceptible ones) and prevent them from producing resistant offspring for the next season. However, farmers should review their soil conservation requirements before removing residues.

Causes of field failures not due to resistance

Poor control of a pest insect may arise from a number of causes, of which resistance may be just one. If field failures occur, it is therefore important that before resistance can be confirmed as the cause of failure, a number of other causes must be eliminated.

- Poor control may readily arise due to application errors. In this regard factors such as the timing of applications, the number of applications, the dosage, the use of correct product carriers, the correct application method, and the appropriate timing for treatment evaluation all need to be considered.
- Poor control may arise due to equipment failure. Blocked spray nozzles, improperly functioning applicators, incorrect calibration of spray equipment for use with recommended spray volumes and pressures, may all contribute to poor control and must be eliminated before resistance is suspected.
- Environmental conditions may also affect control efficacy. Rain or overhead irrigation too soon after application may cause loss of insecticide. Likewise, temperature, wind or other environmental conditions may be less than ideal for application and result in poor control.

Options for managing resistance

If resistance is suspected, there are several steps users can take to manage the problem. First and foremost, it is vital that there should be no respray with an insecticide with the same MoA or one that is known to have a metabolic cross-resistance with the insecticide to which resistance is suspected. Extension staff or company sales personnel should be contacted to help evaluate the cause of control failure. Additional expert inputs from specialist institute or university laboratories may be needed to accurately confirm insecticide resistance and to determine the nature of the resistance and possible alternative insecticidal solutions. To confirm resistance, an evaluation of the surviving insects for the level of detoxifying enzymes or the presence of resistant genes will be made by professionals using a number of methods. In some cases, diagnostic doses of a specific product are applied to surviving insects from the field. Depending on available resources, insects may be taken to a laboratory for biochemical or molecular diagnostic investigation. Producers should always work with local crop specialists to determine appropriate monitoring and diagnostic programs for their resistance-related situations. To manage resistant insect populations, control experts or consultants may advise users on short-term spray decisions (including spray options), resistance management tactics, evaluating the success of a resistance management program, tracking resistance status on a farm or field-by-field basis, and determining relative tolerance of pests and biocontrol agents.

5. Resistance management of transgenic insect-protected crops

5. Resistance management of transgenic insect-protected crops

Transgenic plants producing insecticidal proteins to provide built-in insect protection are the newest technologies to make their way into mainstream crop production. Transgenic crops provide high-levels of insect protection season long and throughout the plant, even in those tissues that are hard to reach with conventional sprays. The insecticidal proteins are target-pest specific, so populations of beneficial and other non-target insects are preserved. However, transgenic plants theoretically have a greater potential than traditional insecticides to foster resistance development since all of a pest population may be exposed to the insecticidal toxins for an extended period. Therefore, to counter these spatial and temporal selection pressures, careful resistance management is critical.

In countries such as the US and Australia, local regulatory bodies mandate and approve specific IRM strategies for use with transgenic insect-protected crops. For example, a high dose + refuge strategy for IRM has been adopted for Lepidoptera protected Bt corn (expressing Cry1 protein from the common soil bacterium *Bacillus thuringiensis*). This strategy assumes that resistance is a recessive trait and that the starting frequency of resistance alleles is low. Typically, plantings of the transgenic variety must be accompanied by a refuge area consisting of a given proportion of a conventional, non-GM, variety of that crop. Any rare homozygous resistant individuals that emerge from the transgenic variety are highly likely to mate with any of the much more abundant susceptible individuals from the refuge area. The resultant heterozygotes are killed by the high dose expressed in the transgenic variety.

Genetically modified crops expressing insecticidal toxins from *Bacillus thuringiensis* are now increasingly being cultivated around the world and these include cotton and maize. IRAC is involved in the development of effective IRM programs for these varieties.

Source: Syngenta

In the US, registrant companies are obliged to ensure that growers implement these IRM strategies through contractual obligations and they must assess grower's compliance with these regulations. Growers found to be repeatedly violating the requirements are subsequently denied access to the technology. Strong grower education programs, supported by registrants, grower organizations and public scientists, have been established to ensure IRM practices are implemented for the long-term benefit of the agricultural community. Just as monitoring for potential resistance is important with traditional plant varieties, growers who use transgenic varieties must watch closely for signs of resistance. In transgenic crops, this could be indicated by a small area of plants with pest damage typical of a non-transgenic plant. Such damage could result from the accidental presence of unprotected seed, from insects at non-susceptible life stages moving in from nearby weeds, or from feeding by insect species that are not affected by the insecticidal protein. If damage appears to be caused by a target pest, the population can be sampled and tested for resistance. In addition, registrants conduct random insect resistance monitoring, collecting pest populations and testing their sensitivity to the insecticidal proteins for comparison against baseline sensitivity. In US crops, growers are obligated to report suspected cases of resistance, and companies must investigate these cases and have remedial action plans in place in the event that resistance is confirmed. It is significant that in this highly regulated environment, resistance has not developed, despite the extensive and widespread use of this technology for over the past ten years.

As with insecticides, a multiple toxin approach may provide superior IRM. Modern varieties of a number of crops such as cotton are now becoming available in which two insecticidal toxins are expressed simultaneously. Theoretical studies and modeling suggest that the deployment of these stacked or pyramided varieties markedly increases the time taken for resistance to develop in pests feeding on such varieties, and this has been born out empirically in glasshouse studies. Moreover, it can be shown that resistance develops slower when the stacked variety is grown alone than when the stacked variety is grown in the presence of a variety expressing just one of the toxins. Smaller refuges or a complete absence of managed refuges may be possible once the potential of stacked varieties is fully known. The use of transgenic crop varieties is spreading rapidly around the world. In those countries like the US, where rigid, enforceable IRM strategies are mandated, the risks of resistance to insecticidal transgenic crop varieties currently seem low. In contrast, in other countries IRM strategies are less well organised and the threat of resistance may be greater. Nevertheless, in the small-scale farming systems of much of the developing world, the variety of available neighbouring [non transgenic] host plants may be huge for many pest species and these may act as natural refuges to provide a pool of susceptibility. Around the world these aspects of IRM for transgenic crops are being intensively studied.

6. Resistance management in public health

6. Resistance management in public health

Insecticide resistance in public health vectors can profoundly affect public health through the possible re-emergence of vector borne diseases. Surveillance wherever possible is essential to proactively react once a change in susceptibility of a public health pest to an insecticide is observed. To this end the World Health Organization has published methods for the surveillance of resistance development to insecticides, e.g. by simple, rapid diagnostic dose bioassays for mosquitoes. A comprehensive monograph on the Prevention and Management of insecticide resistance in vectors and pests of public health importance has been published by IRAC (IRAC, 2006).

An important aspect impacting resistance development in insect species important to public health is the availability of only a limited number of classes of insecticides registered for vector control. Since the advent of synthetic insecticides only four chemically different classes of insecticides are (or have been) used to treat adult mosquitoes, i.e. organochlorines (nowadays mostly banned), organophosphates, carbamates and pyrethroids. The synthetic pyrethroid permethrin for example was already introduced into the market more than 30 years ago. It is important to note that these four chemical classes are members of only two different modes of action, so there is little opportunity for MoA rotation in public health pests compared with the agricultural sector. Insecticides used to control malaria vector mosquitoes have to meet stringent requirements, i.e. potent contact action, a rapid knock-down effect and be selectively safe to humans and the environment. For these reasons the synthetic pyrethroids have been the mainstay for adult mosquito control and the organophosphate temephos as a larvicide over the last decades because no other insecticides fully meet these requirements.

Resistance to pyrethroid insecticides and DDT in mosquitoes is either conferred by a mutation in the voltage-gated sodium channel or by elevated levels of microsomal monooxygenases. DDT resistance is additionally specifically conferred by a so-called DDTdehydrochlorinase, a form of glutathione S-transferase. Unlike in agricultural pests, esterases have not yet been shown to play a major role in conferring pyrethroid resistance in mosquitoes. In contrast to pyrethroids, an over-expression of esterases by gene amplification provides considerable organophosphate (and to a certain extent carbamate) resistance in mosquitoes and has been reported as an evolutionary response to selection by organophosphates and carbamates. A second mechanism of importance is MACE and both organophosphates and carbamates are affected by this target site mutation in acetylcholinesterase.

The effective management of malaria vectors, i.e. mosquitoes by only a limited number of chemical classes of insecticides is a challenge in itself. Therefore management of insecticide resistance in public health pests is crucial, and should be considered as one of the most challenging issues in modern applied entomology.

As with agricultural practices, the best option currently is the rotation of different modes of action rather than alternating members of one chemical class or different chemical classes addressing the same target site. The presence of kdr resistance renders DDT and pyrethroids less effective, whereas carbamates and organophosphates can still be used. If MACE as a mechanism is not present, rotational use of such chemicals can be considered where product labelling and local regulations permit. In addition, the use of larvicides such as the organophosphate temephos in conjunction with pyrethroids can support resistance management through rotation of MoA across different life stages. Effective long-term resistance management is necessary, but many factors need to be considered (including regional availability of insecticides) to successfully implement strategies in order to effectively control insect vectors. This is not only achieved by making insecticides available but also driven by other factors, e.g. training courses and educational material on disease prevention, and by educating vector control personnel in insect management principles. Of course new active ingredients with new MoAs would be most welcome in order to diversify the tool-box for vector control and to extend the life-cycle of all available insecticides, thus lowering the risk of re-emerging vector-borne diseases. IRAC member companies are actively engaged in research in this area.

7. Conclusions

7. Conclusions

Many insect pests have developed widespread, insecticide-defeating resistance to many traditional insecticide treatments, and the industry is finding it increasingly difficult, time consuming and expensive to continually develop and supply the market with new products with different modes of action precisely when needed to replace old ones which are no longer effective. Moreover, it is becoming ever-more difficult to find new insecticides which conform to increasingly stringent environmental and regulatory standards. Importantly, all stakeholders are realising that susceptibility is a valuable commodity that cannot, and must not, be squandered by the indiscriminate over-use or mis-use of insecticides. The concept of using valuable insecticidal products until they fail because of resistance is no longer acceptable. It is imperative that the effectiveness of available insecticides and new technologies is conserved by users through the adoption of effective resistance management strategies.

Insecticide resistance remains one of the greatest challenges in modern agriculture and public health pest management, and it is crucial that it is tackled effectively. Indeed, resistance is everyone's problem and by working together, insecticide resistance can be successfully managed. IRAC and CropLife are playing a major role in this effort.

Source: IRAC

8. Further reading

8. Further reading

IRAC

IRAC (multi-authored), Prevention and Management of insecticide resistance in vectors and pests of public health importance. Monograph, 51pp (2006)

McCaffery A and Nauen R, The Insecticide Resistance Action Committee (IRAC): Public responsibility and enlightened industrial self interest. Outlooks on Pest Management 2: 11-14 (2006)

Wege PJ and Leonard PK, Insecticide resistance action committee (IRAC) fruit crops spider mite resistance management guidelines. Proc. Brighton Crop Protection Conf. - Pest and Diseases, 427-430 (1994)

Crop Protection

Insecticide mode of action

Dekeyser M, Acaricide mode of action, Pest Manag Sci. 61: 103-110 (2005)

Ishaaya I (Ed.) Biochemical Sites Important in Insecticide Action and Resistance, Springer Verlag, Heidelberg, (2001)

Ishaaya I, Horowitz R, Nauen R (Eds.) Insecticides Design Using Advanced Technologies, Springer Verlag, Heidelberg, (2007)

Khambay BPS, Pyrethroid insecticides. Pesticide Outlook 4: 49-54 (2002)

Nauen R and Bretschneider T, New modes of action of insecticides. Pesticide Outlook 12: 241-245 (2002)

Insecticide resistance

Ishaaya I (Ed.) Biochemical Sites Important in Insecticide Action and Resistance, Springer Verlag, Heidelberg, (2001)

McKenzie JA (Ed.) Ecological and Evolutionary Aspects of Insecticide Resistance. Austin, TX: RG Landes, Academic Press, (1996)

Nauen R and Denholm I, Resistance of insect pests to neonicotinoid insecticides: current status and future prospects. Arch Insect Biochem Physiol 58: 200-215 (2005)

Roush, R.T. and Tabashnik, B.E. (Eds.) 1990. Pesticide Resisatnce in Arthropods. Chapman and Hall, New York and London.

Sjut V (Ed.), Molecular Mechanisms of Resistance to Agrochemicals. Vol 13, Springer-Verlag Berlin Heidelberg, (1997)

Resistance management

Caprio, M.A. 1998. Evaluating resistance management strategies for multiple toxins in the presence of external refuges. J. Econ. Entomol. 91: 1021-1031.

Comins, H. 1986. Tactics for resistance management using multiple pesticides. Agric. Ecosyt. Environ. 16: 129-148.

Curtis, C.F. 1985. Theoretical models of the use of insecticide mixtures for the management of resistance. Bull. Entomol. Res. 75: 259-265.

Denholm I, Pickett JA, Devonshire AL (Eds.), Insecticide Resistance: From Mechanisms to Management. CABI Publishing, Wallingford, UK (1999)

Georghiou GP, Saito T (Eds.) Pest Resistance to Pesticides. Plenum Press, New York and London, (1983)

Hemingway J, Penilla PR, Rodriguez AD, James BM, Edge W, Rogers H, et al., Resistance management strategies in malaria vector mosquito control. A large-scale field trial in southern Mexico. Pestic Sci 51: 375-382 (1997)

Horowitz AR, Ishaaya I (Eds.), Insect Pest Management, Field and Protected Crops. Springer Verlag Berlin Heidelberg New York, (2004)

Mani, G.S. 1985. Evolution of resistance in the presence of two insecticides. Genetics 109: 761-783.

Roush RT, Designing resistance management programs: how can you choose? Pestic Sci 26: 423-441 (1989)

Regulatory

Anon. (2003) European and Mediterranean Plant Protection Organization Standard PP 1/213(2) Resistance Risk Analysis. Bull. OEPP/EPPO Bull. 33: 37-63.

Heimbach, U., Kral, G. and Niemann, P. EU regulatory aspects of resistance risk assessment. Pest Manag. Sci. 58: 935-938.

Leonard, P.K. (1997) There has never been a better time or a greater need for resistance management. Pestic. Sci. 51: 387-390.

Leonard, P.K. and Dutton, R. (2002) What impact will EPPO's new resistance risk assessment guideline have on selection pressure in the European Union? Pest Manag. Sci. 58: 939-943.

McNamara, D.G. (2001) Resistance risk analysis. Bull. OEPP/EPPO Bull. 31: 363-365.

Biotechnology

General

Bates, S.L., Zhao, J.-Z., Roush, R.T. and Shelton, A.M. 2005. Insect resistance management in GM crops: Past, present and future. Nature Biotech. 23: 57-62.

Carozzi, N. and Koziel, M. (Eds.) 1997. Advances in insect control: The role of transgenic plants. Taylor and Francis, London and Bristol. PA, USA.

Metz, M. (Ed.) 2003. Bacillus thuringiensis: A cornerstone of modern agriculture. Food Products Press, Binghampton, NY, USA.

Mode of Action

Aronson, A.I. and Shai, Y. 2001. Why Bacillus thuringiensis insecticidal toxins are so effective: Unique features of their mode of action. 2001. FEMS Microbiol. Lett. 195: 1-8.

Bravo, A., Gomez, I., Conde, J., Munoz-Garay, C., Sanchez, J., Miranda, R., Zhuang, M., Gill, S.S. and Soberon, M. 2004. Oligomerization triggers binding of a Bacillus thuringiensis cry1Ab pore-forming toxin to aminopeptidase N receptor leading to insertion into membrane microdomains. Biochim. Biophys. Acta 1667: 38-46

Gill, S.S., Cowles, E.A. and Pietrantonio, P.V. 1992. The mode of action of Bacillus thuringiensis endotoxins. Annu. Rev. Entomol. 37: 615-636.

Schnepf, E., Crickmore, N., Van Rie, J., Lereclus, D., Baum, J., Feitelson, J., Zeigler, D.R. and Dean D.H. 1998. Bacillus thuringiensis and its pesticidal crystal proteins. Microbiol. Molec. Biol. Rev. 62: 775-806.

<u>Mechanisms and genetics of resistance</u>
Ferre. J. and Van Rie, J. 2002. Biochemistry and genetics of insect resistance to Bacillus thuringiensis. Annu. Rev. Entomol. 47: 501-533.

Griffitts, J.S. and Aroian, R.V. 2005. Many roads to resistance: How invertebrates adapt to Bt toxins. Bioessays 27:614-624.

Tabashnik, B.E., Liu, Y.-B., Malvar, T., Heckel, D.G., Masson, L. and Ferre, J. 1998. Insect resistance to Bacillus thuringiensis: uniform or diverse. Phil. Trans. R. Soc. Lond. B 353: 1751-1756.

<u>Resistance Management</u>
Gould, F. 1998. Sustainability of transgenic insecticidal cultivars: Integrating pest genetics and ecology. Ann. Rev. Entomol 15: 11-23.

Roush, R.T. 1997. Managing resistance to transgenic crops. In Advances in insect control: The role of transgenic plants. Eds: N. Carozzi and M. Zoziel. Taylor and Francis, London, pp 271-294.

Roush, R.T. 1998. Two-toxin strategies for management of insecticidal transgenic crops: Can pyramiding succeed where pesticide mixtures have not? Phil. Trans. R. Soc. Lond. B 353: 1777-1786.

Tabashnik, B.E. 1994. Delaying insect adaptation to transgenic crops: Seed mixtures and refugia reconsidered. Proc. R. Soc. Lond. B 255: 7-12.

Zhao, J.-Z., Cao, J., Li, Y., Collins, H.L., Roush, R.T., Earle, E.D. and Shelton, A.M. 2003. Transgenic plants expressing two Bacillus thuringiensis toxins delay insect resistance evolution. Nature Biotech. 21: 1493-1497.

Public Health

Hemingway J and Ranson H, Insecticide resistance in insect vectors of human disease. Ann Rev Entomol 45: 371-391 (2000)

Brogdon WG and McAllister JC, Insecticide resistance and vector control. Emerging Infectious Diseases 4: 605-613 (1998)

Liu N, Xu Q, Zhu F and Zhang L, Pyrethroid resistance in mosquitoes. Insect Science 13: 159-166 (2006)

Hemingway J, Hawkes NJ, McCarroll L and Ranson H, The molecular basis of insecticide resistance in mosquitoes. Insect Biochem Mol Biol 34: 653-665 (2004)

Weill M, Lutfalla G, Mogensen K, Chandre F, Berthomieu A, Berticat C, et al., Insecticide resistance in mosquito vectors. Nature 423: 137-138 (2003)

Enayati AA and Hemingway J, Pyrethroid insecticide resistance and treated bednets efficacy in malaria control. Pestic Biochem Physiol 84: 116-126 (2006)

Hemingway J, Beaty BJ, Rowland M, Scott TW and Sharp L, The Innovative Vector Control Consortium: improved control of mosquito-borne diseases. Trends in Parasitology 22: 308-312 (2006)
Cui F, Raymond M and Qiao C-L, Insecticide resistance in vector mosquitoes in China. Pest Manag Sci 62: 1013-1022 (2006)

Hemingway J, Penilla PR, Rodriguez AD, James BM, Edge W, Rogers H, et al., Resistance management strategies in malaria vector mosquito control. A large-scale field trial in southern Mexico. Pestic Sci 51: 375-382 (1997)

Zaim M and Guillet P, Alternative insecticides: an urgent need. Trends in Parasitology 18: 161-163 (2002)

David J-P, Strode C, Vontas J, Nikou D, Vaughan A, Pignatelli PM, et al., The Anopheles gambiae detoxification ship: A highly specific microarray to study metabolic-based insecticide resistance in malaria vectors. Proc Natl Acad Sci USA 102: 4080-4084 (2005)

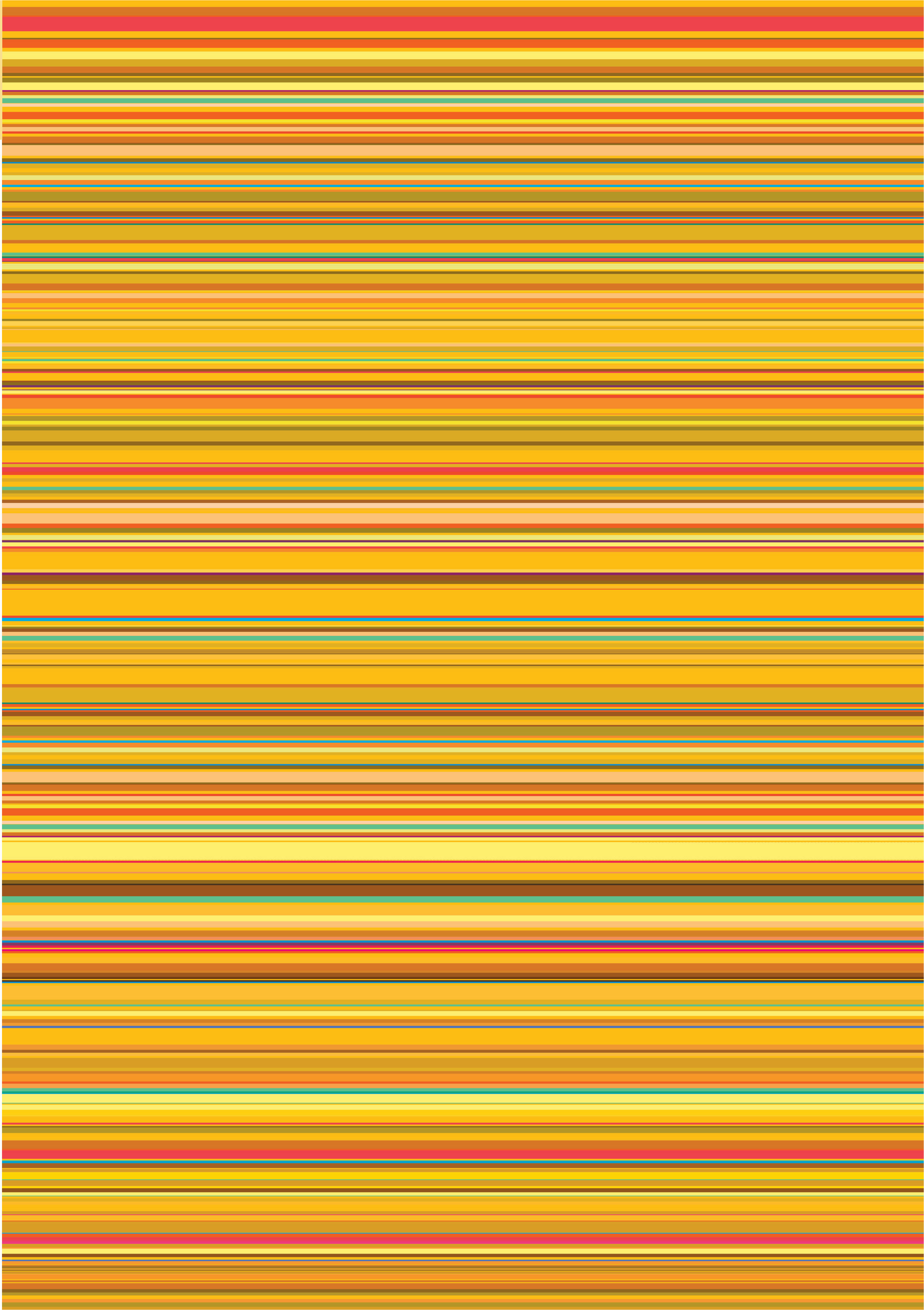
Ranson H, Claudianos C, Ortelli F, Abgrall C, Hemingway J, Sharakhova MV, et al., Evolution of supergene families associated with insecticide resistance. Science (Washington) 298: 179-181 (2002)

Vontas J, Blass C, Koutsos AC, David J-P, Kafatos FC, Louis C, et al., Gene expression in insecticide resistant and susceptible Anopheles gambiae strains constitutively or after insecticide exposure. Insect Mol Biol 14: 509-516 (2005)

Coleman M, Sharp B, Seocharan I and Hemingway J, Developing an evidence-based decision support system for rational insecticide choice in the control of African malaria vectors. J Med Entomol 43: 663-668 (2006)

Cover Pictures credits:
Colorado potato beetle, *Leptinotarsa decemlineata*, Source: USDA (Scott Baur)
Tobacco budworm, *Heliothis virescens*, Source: Nigel Armes
Mosquito, *Anopheles stephensi*, Source: CDC (J. Gathany)
Whitefly, *Bemisia tabaci*, Source: USDA (Scott Baur)

Notes



Graphic Design: NAos design

CropLife International aisbl
Avenue Louise 143
1050 Brussels, Belgium
tel +32 2 542 04 10
fax +32 2 542 04 19
croplife@croplife.org
http://www.croplife.org

For further information on Insecticide Resistance Management
visit the IRAC website:
www.irac-online.org or contact Alan Porter: aporter@intraspin.com.

www.irac-online.org www.croplife.org