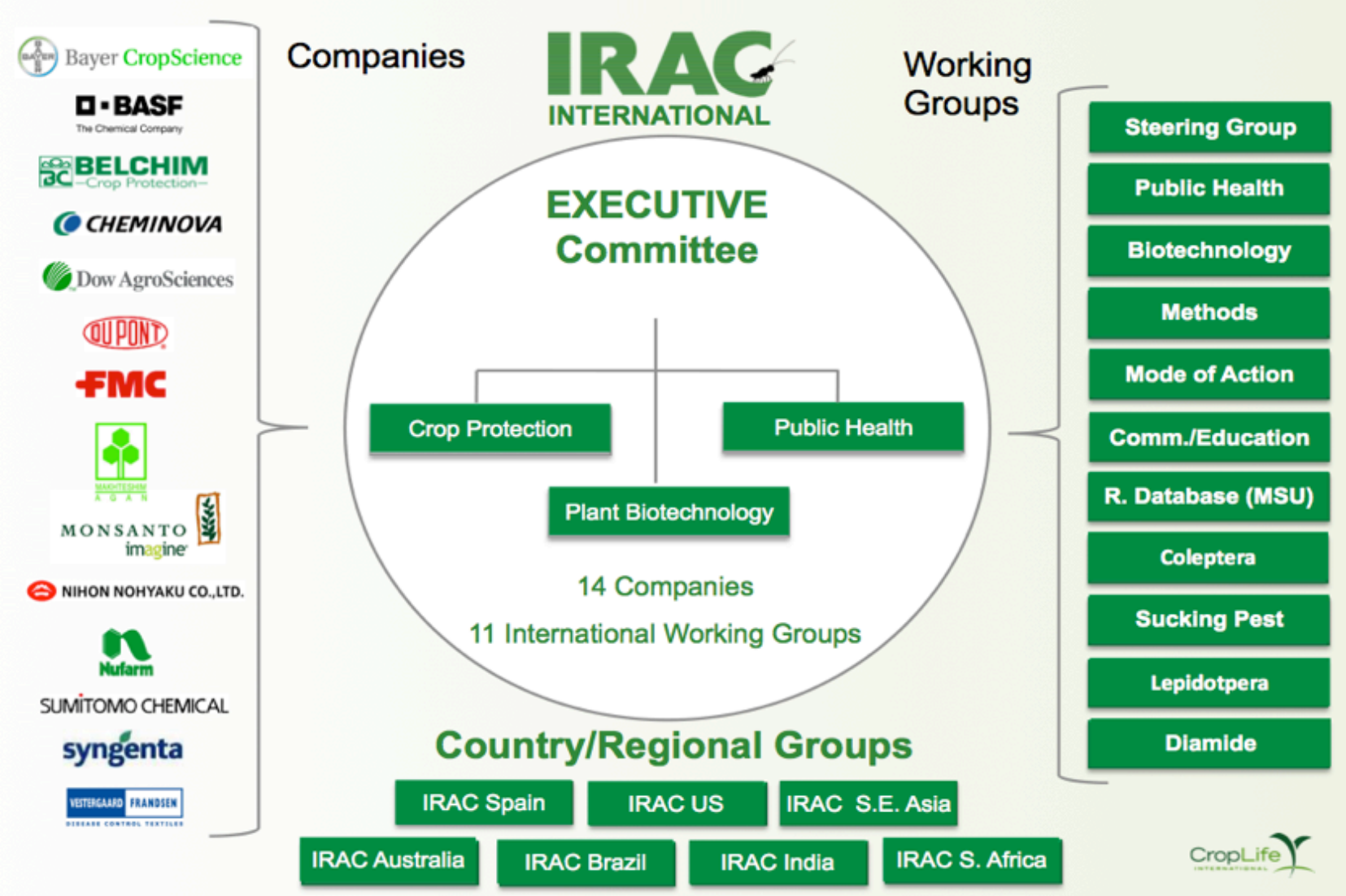
Insecticide Resistance Action Committee

Prevention and Management of Insecticide Resistance in Vectors of Public Health Importance





Insecticide Resistance Action Committee
- Organisation -

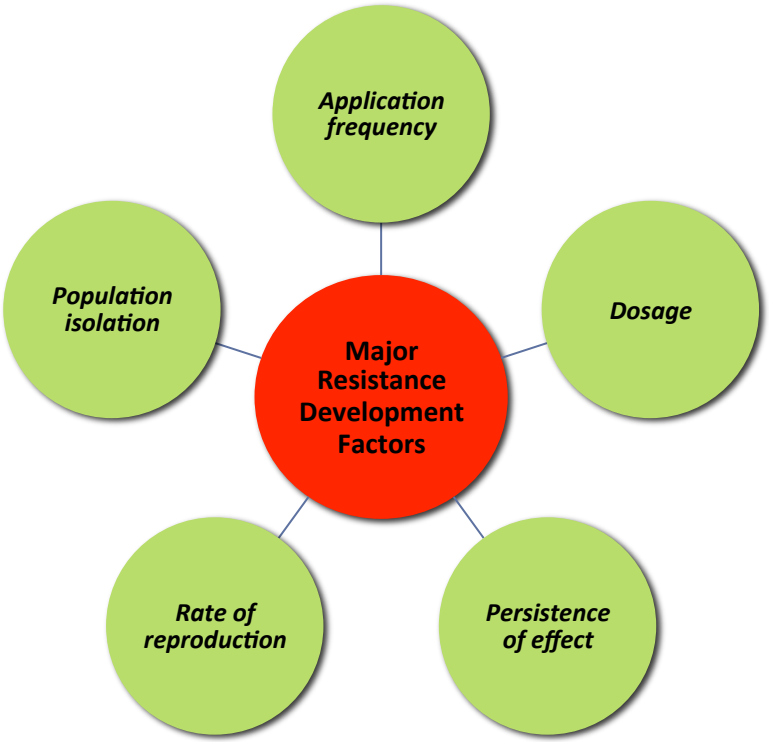


Insecticide Resistance Action Committee - Background -

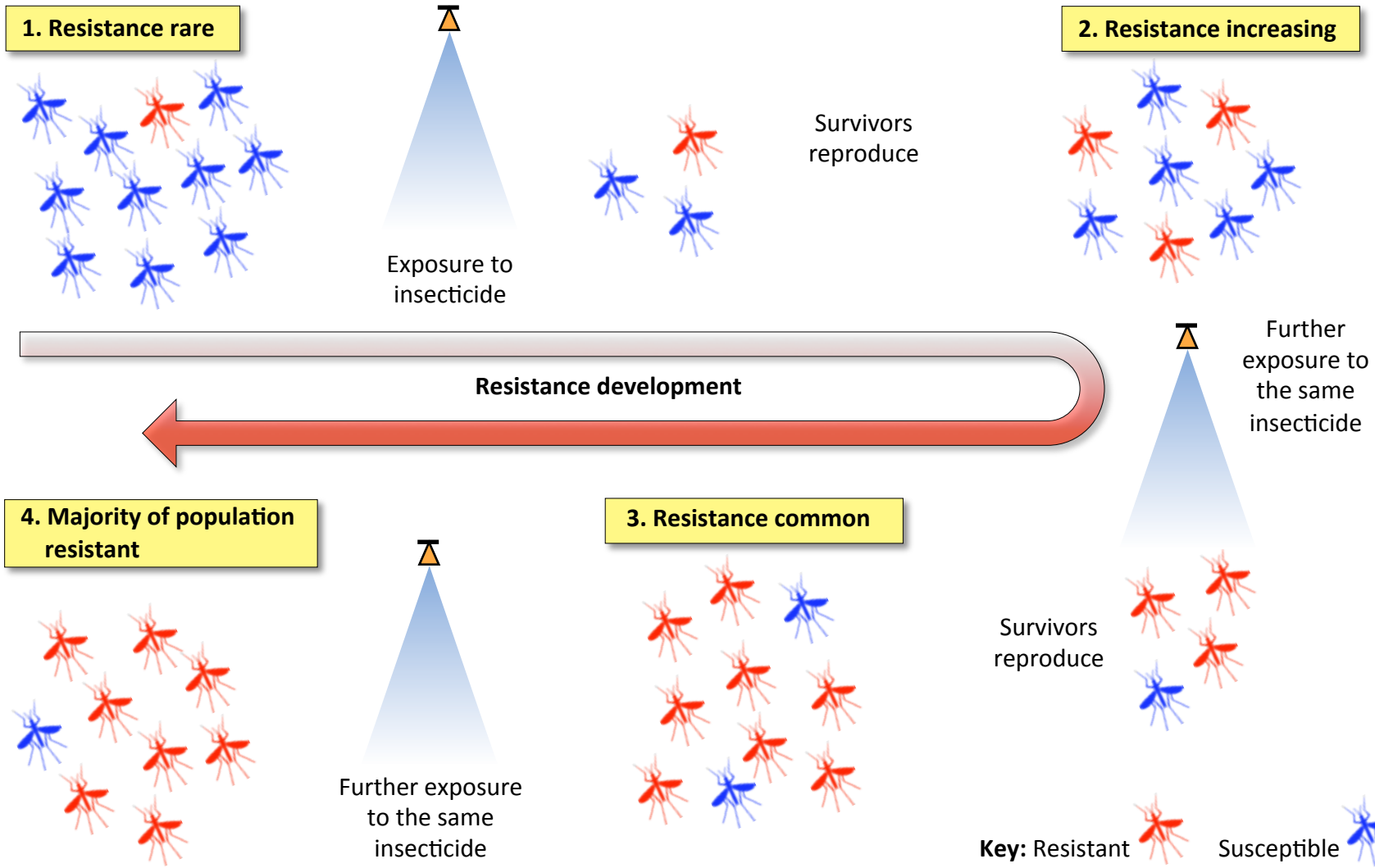
- Insecticide Resistance Action Committee
  - Formed in 1984 – now in its 28th year and still growing
  - Specialist technical expert group of the agrochemica and Public Health industry
  - Part of CropLife International Stewardship Committee
  - Provides a coordinated industry response to the development of resistance in insect and mite pests
  - Around 70 industry representatives and specialist members in different working groups
  - 7 Country/Regional Groups with a further 70-80 representatives

What is Resistance?

- Resistance:
  - Can 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'* (IRAC).

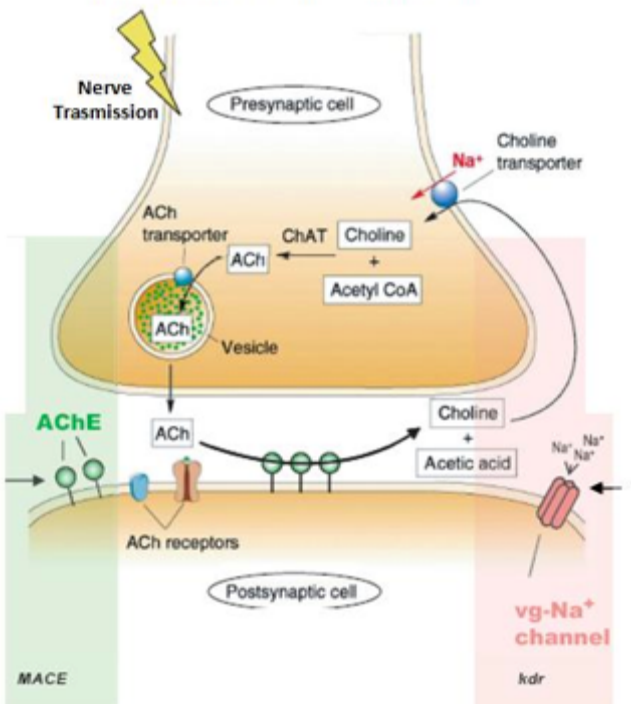


Resistance Development

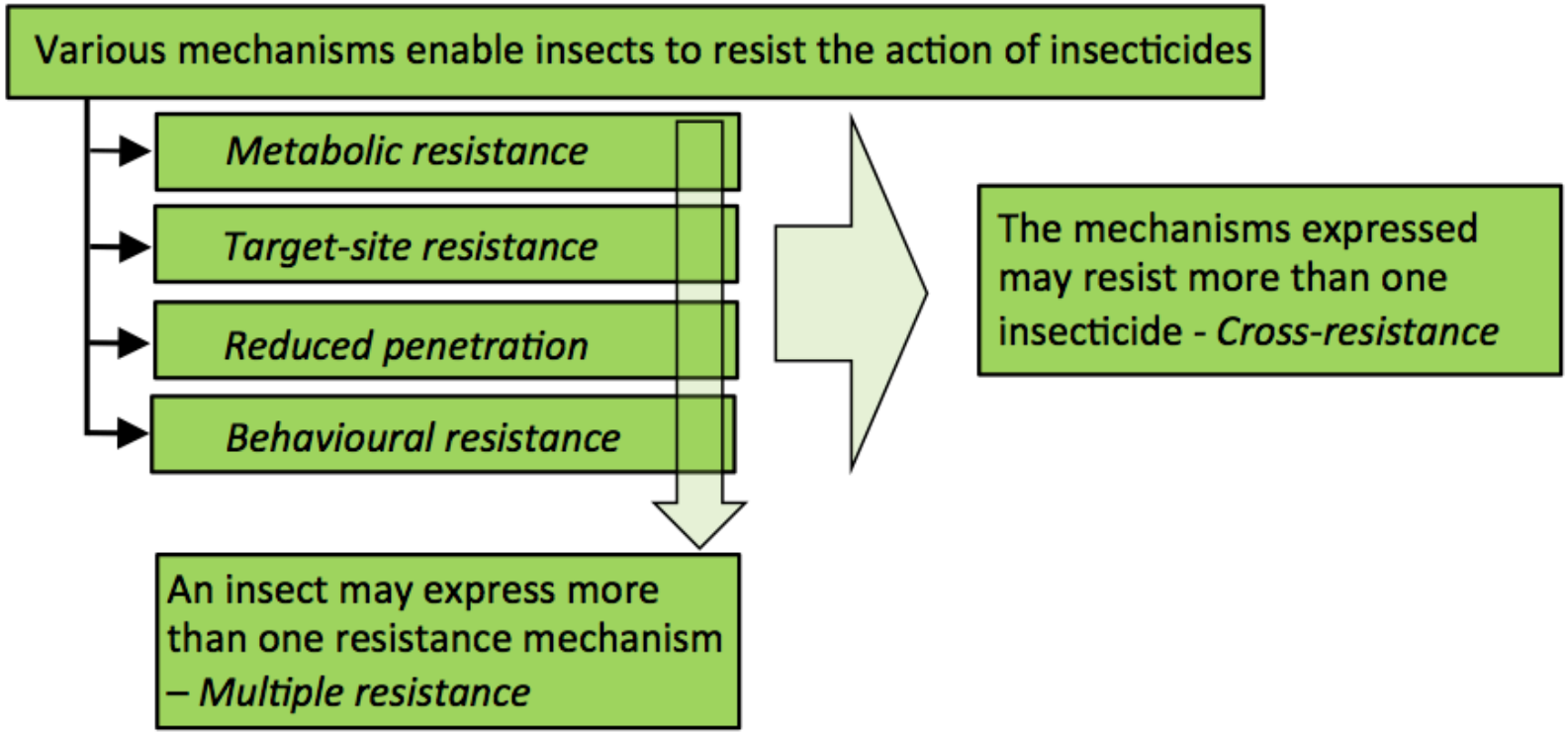


Insecticide Mode of Action

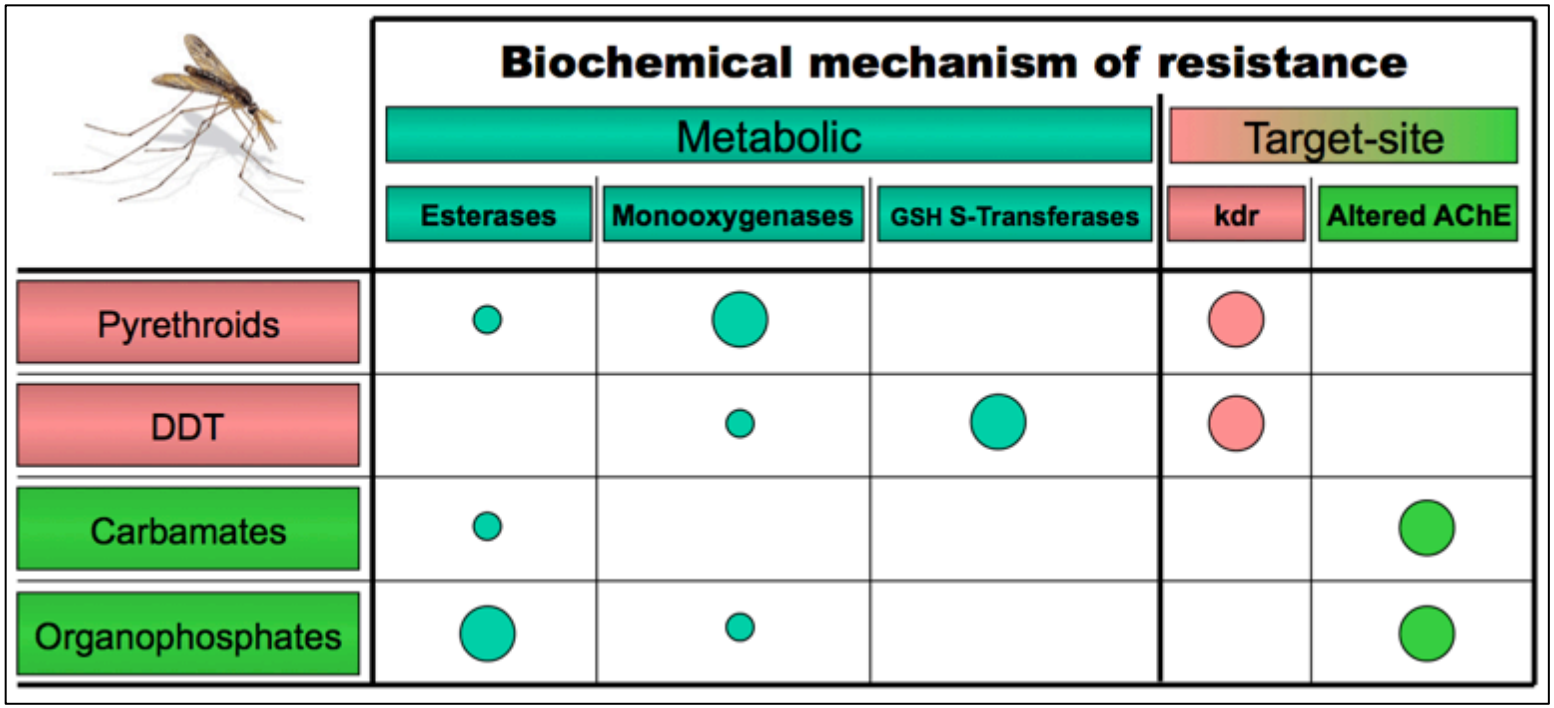
- Mode of Action:
  - Classification based on site of action.
  - Different insecticides can have the same target site within the insect.
  - Insecticides from the same chemical class, e.g. pyrethroids, will have the same MoA. There may be many different commercial products based on insecticides from the same chemical class.
  - The IRAC MoA Classification allocates each insecticide to a numbered group based on their target site. Chemical sub-groups are identified with a letter, for example, pyrethroids are given the IRAC MoA classification 3A



Resistance Mechanisms



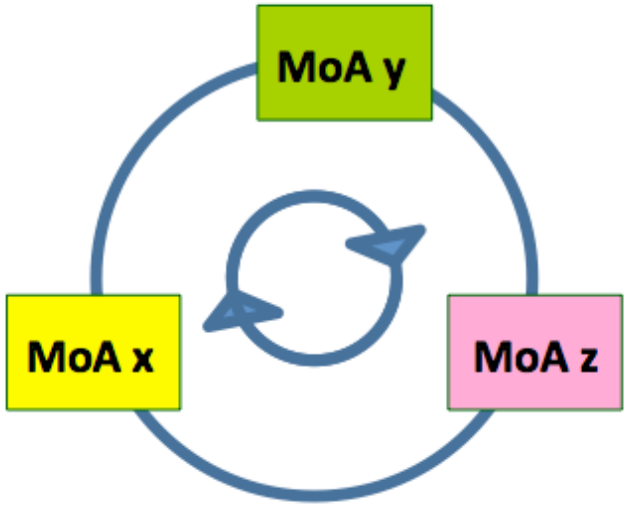
Resistance Mechanisms



Circle size reflects the relative impact of the mechanism on resistance

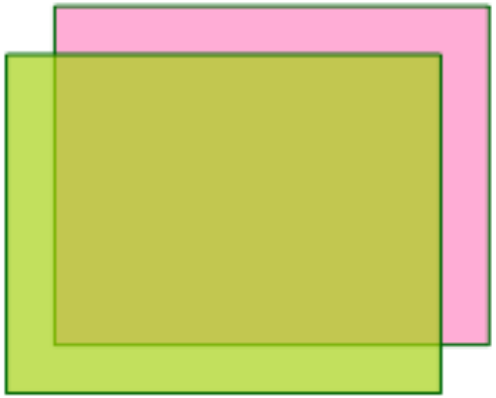
Resistance Management
- Strategies and Tactics -

- Rotation:
  - Strategy based on the rotation over time of two or more insecticide classes with different Modes of Action (MoA).
  - This approach assumes that if resistance to each insecticide is rare, then multiple resistance will be extremely rare.



Resistance Management
- Strategies and Tactics -

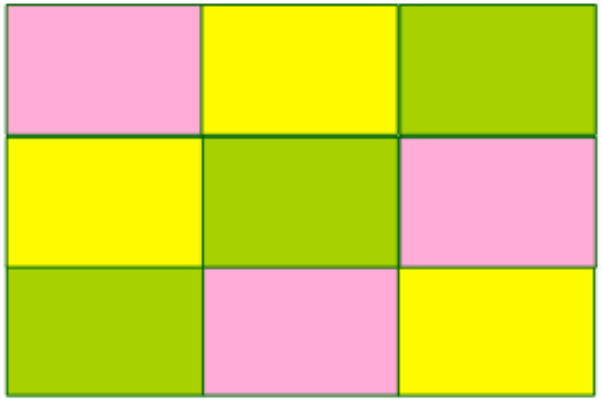
- Mixtures:
  - A single formulation containing two or more insecticides, or different insecticide formulations being applied in the same spray tank, or an LN* or ITM* treated with two or more insecticides with different MoA.
  - It can also include the combination of an LN or ITM with an IRS application in the same dwelling. This approach assumes that if a mosquito survives one insecticidal MoA, it will be killed by the other, and that if resistance to one is rare, resistance to both will be extremely rare.



** LN (Long lasting insecticide treated Net), ITM (Insecticide Treated Material)*

Resistance Management
- Strategies and Tactics -

- Fine-scale Mosaic
  - Spatially separated applications of different MoA insecticides against the same mosquito population. e.g. using two different MoA insecticides in different dwellings within the same village.
  - Mosquitoes are therefore likely to come into contact with a second insecticides during their lifetime, if they survive exposure to the first. This reduces the selection pressure for both insecticides.



Mode of Action Classes
Vector Control - Adults

- Nerve and Muscle Targets
  - *Group 1: Acetylcholinesterase (AChE) inhibitors* 1A Carbamates, 1B Organophosphates
  - *Group 3: Sodium channel modulators* 3A Pyrethrins, Pyrethroids, 3B DDT

Adulticides WHOPES Approved Uses	MoA	Class	Insecticide or Product	IRS	ITN	LN
	1A	Carbamate	Bendiocarb, Propoxur	✓	X	X
	1B	Organophosphate	Malathion, Fenitrothion, Pirimiphos-methyl	✓	X	X
	3A	Pyrethroid	Alphacypermethrin	✓	✓	✓
			Deltamethrin	✓	✓	✓*
			Permethrin	X	✓	✓*
			Etofenprox	✓	✓	X
			Lambdacyhalothrin	✓	✓	✓‡
			Bifenthrin	✓	✓	X
			Cyfluthrin	✓	X	X
			Deltamethrin + PBO	X	X	✓
	3B	Organochlorine	DDT	✓	X	X

** Indicates Full WHOPES approval as an LN (NB: Those without * indicates Interim approval only.)*
‡ Indicates interim approval as long lasting net treatment

Mode of Action Classes
Vector Control - Larvae

- Nerve and Muscle Targets
  - *Group 1: Acetylcholinesterase (AChE) inhibitors, 1B Organophosphates*
  - *Group 5: Nicotinic acetylcholine receptor (nAChR) allosteric modulators, Spinosyns*
- Growth and Development Targets
  - *Group 7: 7A Juvenile hormone mimics, 7C Pyriproxyfen*
  - *Group 15: Inhibitors of chitin biosynthesis Type 0, Benzoylureas*
- Midgut
  - *Group 11: Microbial disruptors insect midgut membranes, 11A B. thuringiensis var. Israeliensis, 11B B. sphaericus*

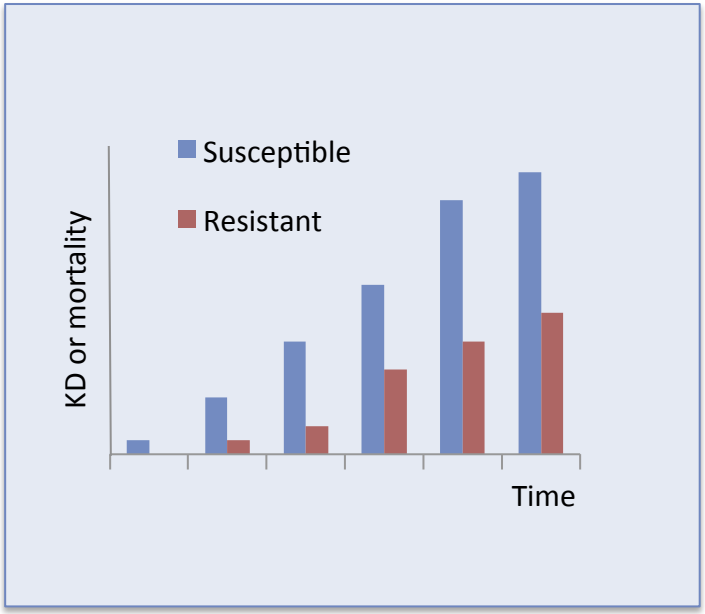
Larvicides WHOPES Approved

MoA	Class	Insecticide or Product
1B	Organophosphate	Temephos, Chlorpyriphos, Pirimiphos-methyl, Fenthion
5	Spinosyns	Spinosad
7A	Juvenile Hormone Mimics	Methoprene, Hydroprene
7C	Pyriproxyfen	Pyriproxyfen
15	Benzoylureas	Diflubenzuron, Novaluron
11A	Bacterial Larvicide	*Bt var. israeliensis*
11B	Bacterial Larvicide	*Bacillus sphaericus*

Monitoring of Vector Susceptibility

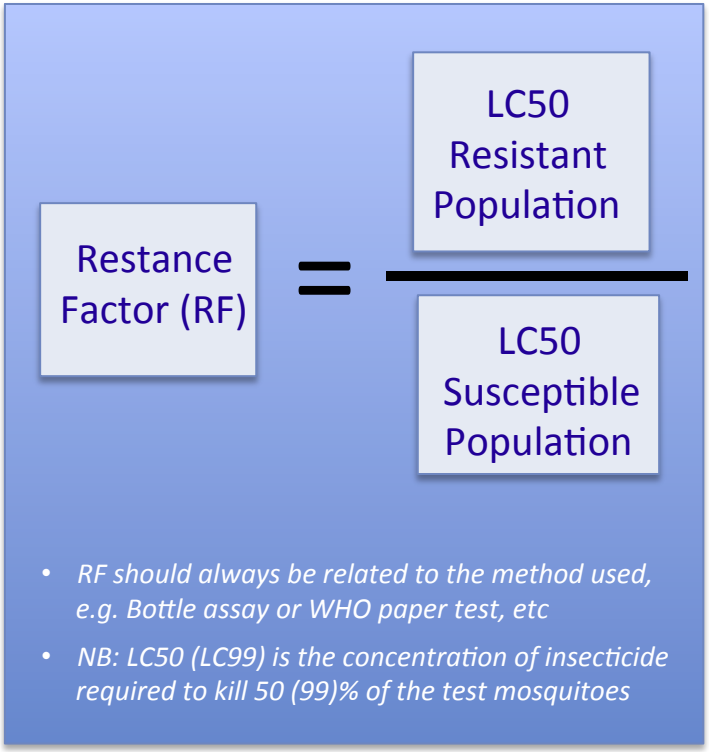
- Monitoring Objectives
  - **Baseline data collection:** Conducted prior to the start of a control programme in order to provide baseline data to inform planning and insecticide choice.
  - **Monitoring of susceptibility over time:** To evaluate the proportion of susceptible mosquitoes in population over time, comparing it with the pre-intervention baseline.
  - **Detection of resistance:** To detect resistant individuals when they are at a low frequency in the population so that resistance management can be effectively introduced.

Chnages in susceptibility over time



Discriminating Dose & Detection of Resistance

- Discriminating Dose
  - Discriminating Dose (DD) = 2 x LC99
  - Resistance may go unnoticed for a long time providing the LC99 is not affected.
  - An increase in the number of heterozygous resistant individuals however, would cause a shift in the LC50.
- Early Resistance Detection
  - Dose mortality including LC50 enables detection of a shift in vector susceptibility, before reduced insecticide efficacy occurs in the field.
- Resistance Factor (RF)
  - Provides susceptibility comparison of a vector population over time, or to compare between strains.



Monitoring Methods
WHO Test Kit - Adults

- Principle is exposure of adult mosquitoes for a given time in a plastic tube lined with a treated filter paper
- The dose rate on the paper (diagnostic conc.) is 2x the lethal dose estimated to kill 100% of mosquitoes of a susceptible strain.
- Mosquitoes are generally exposed for one hour and mortality is assessed after 24 hours.
- Approach designed to avoid spurious reports of resistance in the field where none may exist.
- The kit/papers with intructions can be purchased See: www.who.int/whopes/resistance/en/

$$\text{24 Hour \% Mortality} = \frac{100 \times (\%\ \text{test mortality} - \%\ \text{control mortality})}{100 - \%\ \text{control mortality}}$$

98 – 100% mortality	**Susceptible population**
80 – 97% mortality	**Resistant individuals in population suspected, but verification/confirmation required**
<80% mortality	**Resistant individuals in population present**

Monitoring Methods
CDC Bottle Assay - Adults

- Principle is exposure of adult mosquitoes for a given time in a 250 ml glass bottle coated with insecticide.
- The internal surfaces are coated with the insecticide diluted in acetone or ethanol. Once the solvent has evaporated, 10-20 adult mosquitoes are added.
- Assessments of knockdown/mortality are made at 10 minute intervals and plotted against time. Changes in the slope of this graph over time are indicative of changes in the susceptibility of the mosquito population.
- A diagnostic dose should be calculated at the start of the monitoring programme using a rate range study.
- CDC will furnish, at no cost, premeasured amounts of WHOPES approved IRS and LLIN insecticides, sufficient to conduct approximately 100 bottle assays for each For further details see: www.cdc.gov/ncidod/wbt/resistance/assay/bottle/index.htm.

250ml Glass Bottles

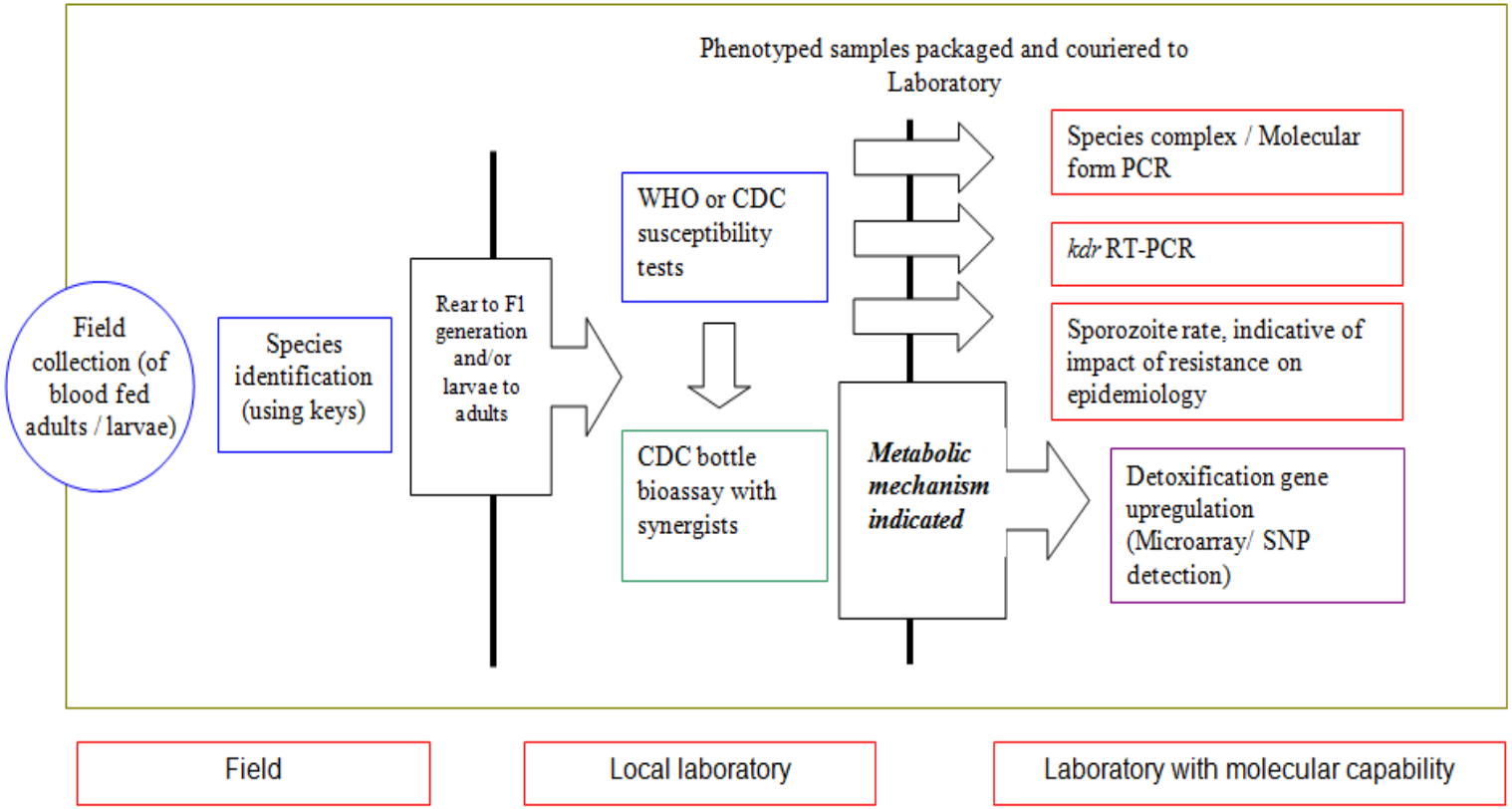
Monitoring Methods
WHO Test Kit - Larvae

- General Chemical:
  - Resistance determination in mosquito larvae is based on diagnostic concs. developed from dose response lines against susceptible species. The test assesses resistance to the insecticide used, but can also be used to determine if cross-resistance is present.
  - 3rd/4th wild instar larvae are used. Starting with a wide range of concs. an approximate dose response can be calculated. A narrower range of 4-5 concentrations yielding 10-95% mortality in 24 hour or 48 hours are used to determine LC50 and LC90 values.
- Insect Growth Regulators
  - Mortality may be slower with IGRs or not take place until the pupal stage. Assessment is every other day or every third day until the completion of adult emergence.
  - Result are expressed in terms of %larvae that do not develop into successfully emerging adults, or adult emergence inhibition.
- Bacterial larvicides
  - Larvicides such as Bti/Bs may be tested to determine resistance with the same methodology as for chemical larvicides, except in the preparation of stock solution.

Full details of the tests can be found at: www.who.int/whopes/guidelines/en/

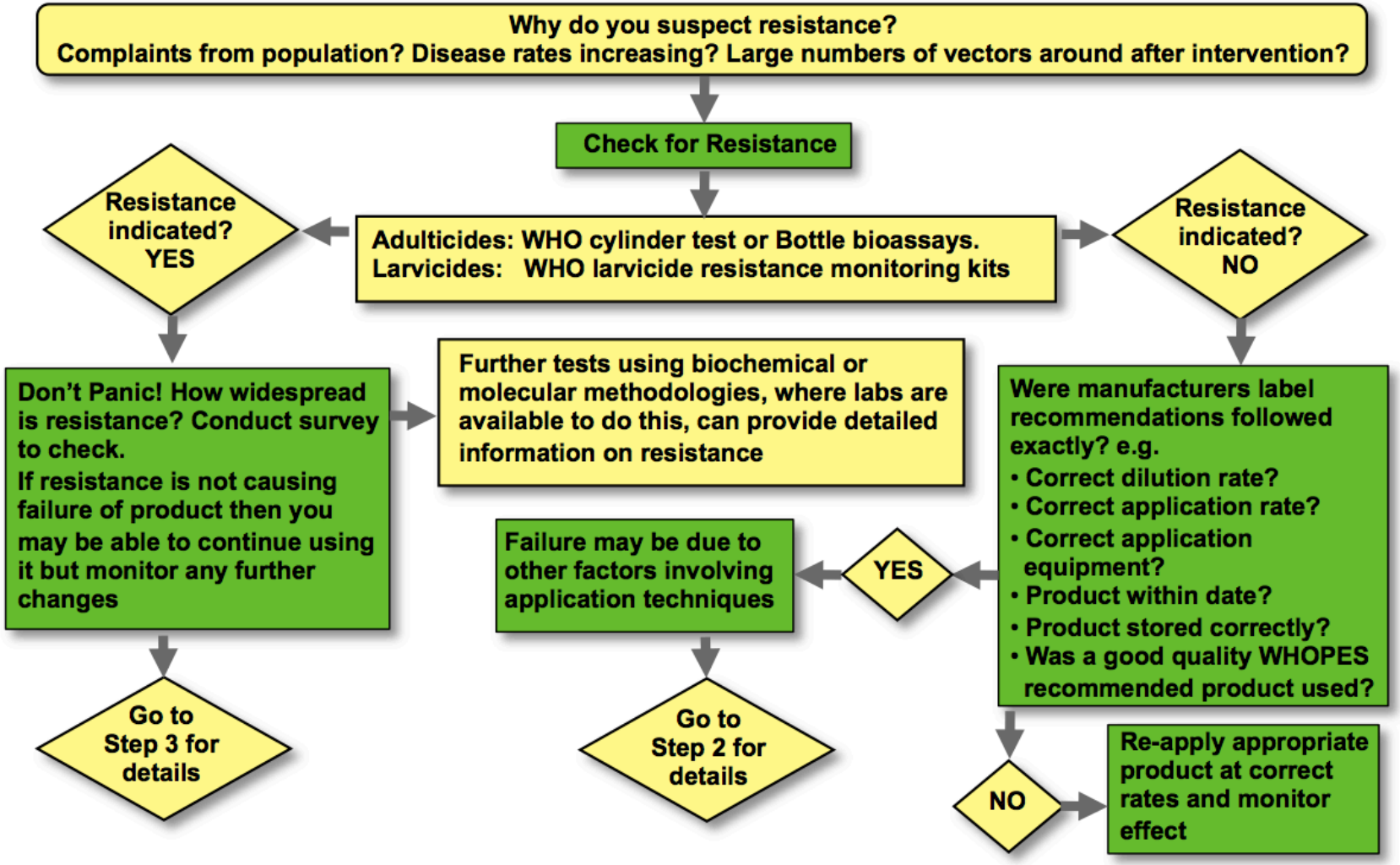
Monitoring Methods
- Summary -

Simplified diagram indicating possible steps in a resistance monitoring programme



Managing a Vector Control Programme – Step 1

The Product doesn't work - do I have Resistance?



Managing a Vector Control Programme – Step 2

The product doesn't work but bioassays show no resistance - check application techniques

Indoor Residual Spray

Training:
- Are all staff correctly trained?
- Has the population been instructed in what to do following an IRS application?
- Have spray team been trained in correct wall spraying technique?
- Refer to W.H.O. IRS Manual: http://www.who.int/whopes/equipment/en/

Equipment:
- Are the sprayers and nozzles in good condition e.g. able to maintain correct pressure no leaking hoses, unworn fan nozzles.
- Has equipment been calibrated and checked for the correct flow rate?
- Has the correct spray pressure been maintained throughout the spraying?

Application
- Was the correct insecticide dose used and thoroughly mixed before spraying?
- Were all houses sprayed or only partial coverage achieved?
- Has the deposit been painted over/cleaned off etc.
- Were applications made to coincide with transmission season?

Bednets – LN`s

Training
- Have the population been educated how to use and care for their nets correctly?

Application
- Are the nets being used?
- Is coverage of house and villages complete?
- Are the nets being washed as recommended? e.g. enough but not too often.
- Do nets need replacing due to age or excessive damage?

Managing a Vector Control Programme – Step 2 (Contd.)

The product doesn't work but bioassays show no resistance - check application techniques

Space sprays:

Training:

- Have staff been properly trained in space spraying methodology?
- Refer to Space Spray Application manual: http://www.who.int/whopes/equipment/en/

Equipment:

- Is the equipment properly maintained?
- Has the machine been calibrated correctly e.g. flow rate, droplet size?

Application:

- Are applications made at the correct volume and dose rate per unit area? (Note: for ULV outdoor spraying the flow rate and vehicle speed must be correct to achieve the required dose/ha)
- Was application made at the right time of day for insect activity?
- Was the frequency of spraying correct?
- Were meteorological conditions correct e.g. Wind speed <15kph and inversion characteristics considered if spraying outdoors?
- Was the area surveyed properly and area calculated to ensure the correct dose rates?

Larvicides:

Training:

- Have staff been fully trained in larvicide surveying and application methodology

Equipment:

- If using liquids, are the sprayers calibrated and flow rates determined relative to the area and volume of water to be treated?
- If using granules, has the weight/unit area been calculated correctly?

Application:

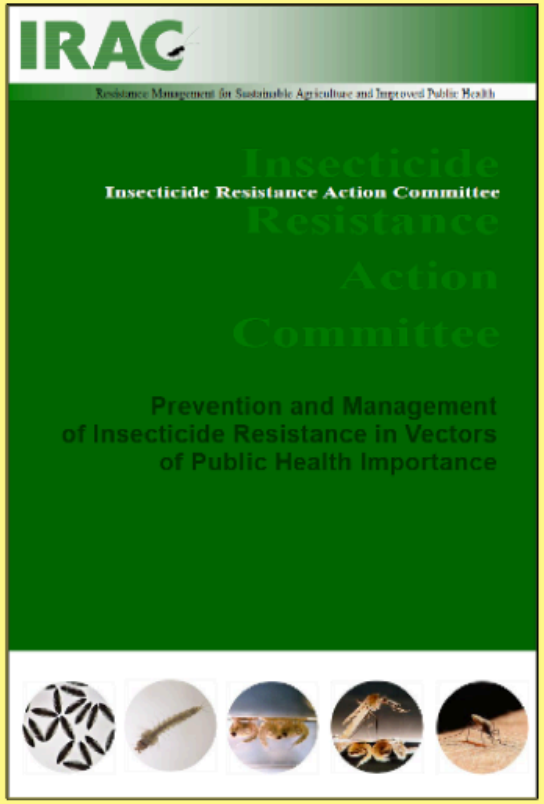
- Was the water depth considered when calculating the application rate?
- Is the frequency of application correct? (Regular monitoring of larval breeding sites is essential and re-application when new larvae re-appear).
- Delayed larval mortality may occur using an IGR - check pupal emergence rate.

Managing a Vector Control Programme – Step 3

Resistance is confirmed by bioassay – what now?

If resistance is confirmed:

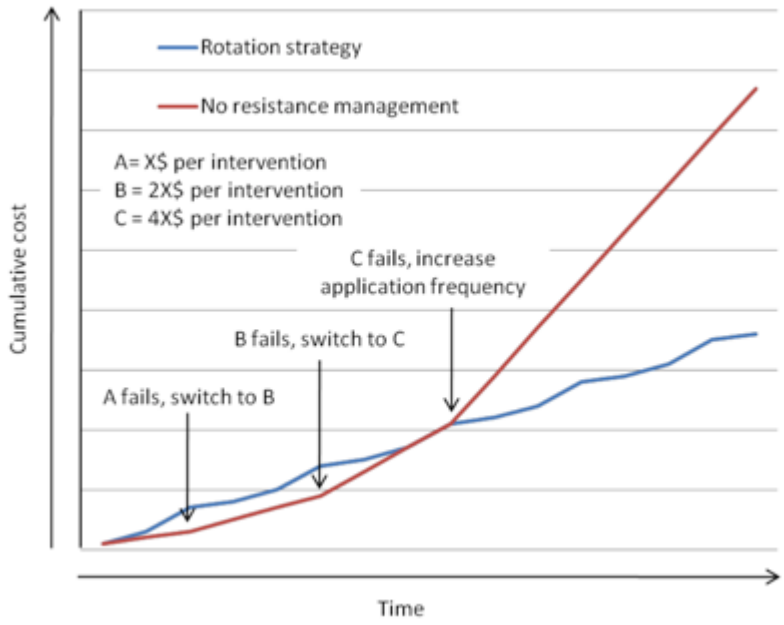
- Notify WHO & Regional Authorities
- Inform the manufacturer, they can often advise
- Identify likely cause of resistance e.g. has the same insecticide type been used locally for agriculture?
- If the existing class of insecticide is resisted but others are not, switch class (but check first that there is no cross resistance)
- If all adulticide classes are resisted, switch to larviciding where alternative MoA insecticides are available
- Undertake a continuous monitoring program
- Develop remedial programmes in conjunction with National Authorities, WHO and the manufacturer
- Read IRAC Prevention and Management of Insecticide Resistance in Vectors of Public Health Importance, for detailed advice



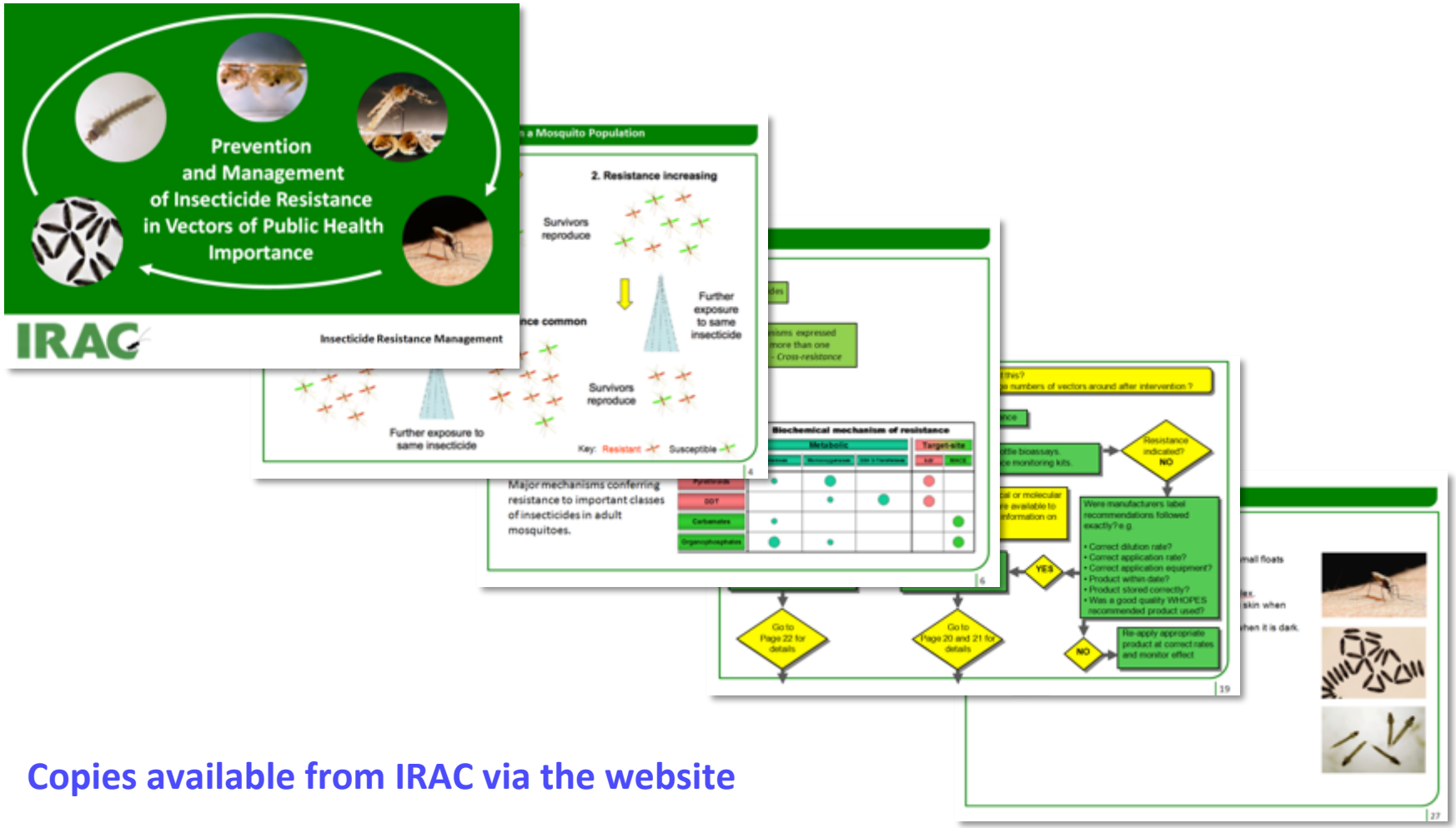
Key Consideration in Resistance Management - Summary -

- Prevention of resistance is much better than trying to resolve the problem once resistancehas developed. Insect susceptibility and effective products are both non-renewable valuable economic resources which should be preserved.
- Resistance management strategies are most effective when developed before control programmes are started.
- It is essential that the delivery of insecticide to the target insect is correct. This includes dose, application timing and technique.
- Insecticidal interventions should be part of a wider integrated vector management programme.
- If resistance occurs take immediate steps to contain it and reduce the selection pressure produced by the insecticide.
- Failure to successfully manage resistance has well documented financial implications and failure to implement an IRM programme on financial grounds is a false economy that will lead to increased costs in the future.

Hypothetical vector control programme cost with or without resistance management



For Further Details: www.irac-online.org



Copies available from IRAC via the website