



Insecticide Resistance Action Committee

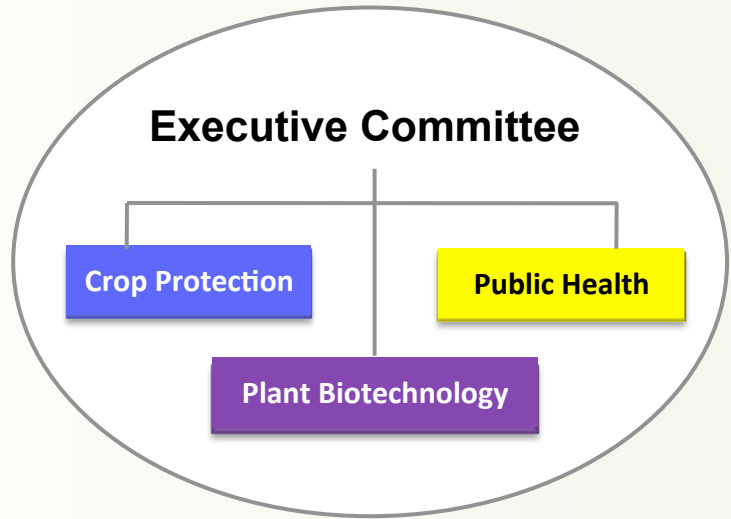
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# The challenge of insecticide resistance – an industry perspective

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13  
Companies



- Steering Group
- Outreach
- R. Database (MSU)
- Methods
- Mode of Action
- Public Health
- Biotechnology
- Coleoptera
- Sucking Pest
- Lepidoptera

- Insecticide Resistance Action Committee
  - Formed in 1984 – now in its 32nd year and still growing
  - Specialist technical expert group for the agrochemical and Public Health industry
  - Part of CropLife International Stewardship Committee
  - Provides a coordinated industry approach to help manage resistance in insect and mite pests
  - Promotes the development and facilitates implementation of IRM strategies (communication tools, educational workshops etc).
  - Around 70 industry representatives and specialist members in different working groups
  - 7 Country/Regional Groups with a further 70-80 representatives

1992-London



## Public Health Team : 6 companies represented:

- Mark Hoppé: Syngenta (Chair)
- James Austin: BASF
- Ronda Hamm: Dow
- Sebastian Horstmann, Ralf Nauen: Bayer Crop Science
- John Invest, John Lucas: Sumitomo Chemical
- Helen Pates Jamet, Melinda Hadi: Vestergaard
  
- Non industry observers: David Malone IVCC
- Alan Porter APA

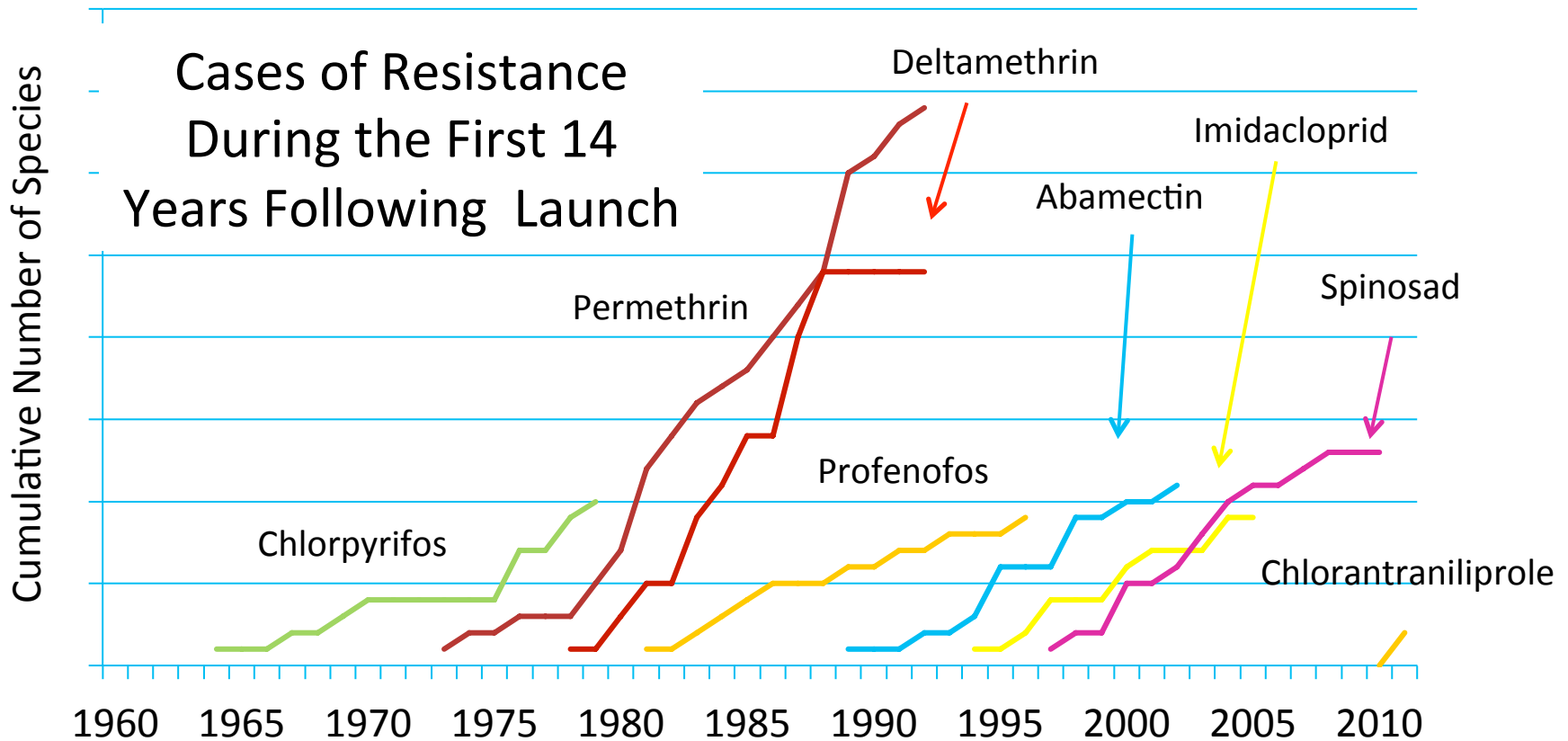
### PH Team Activities



Initiatives and groups IRAC PH team members are involved with include:

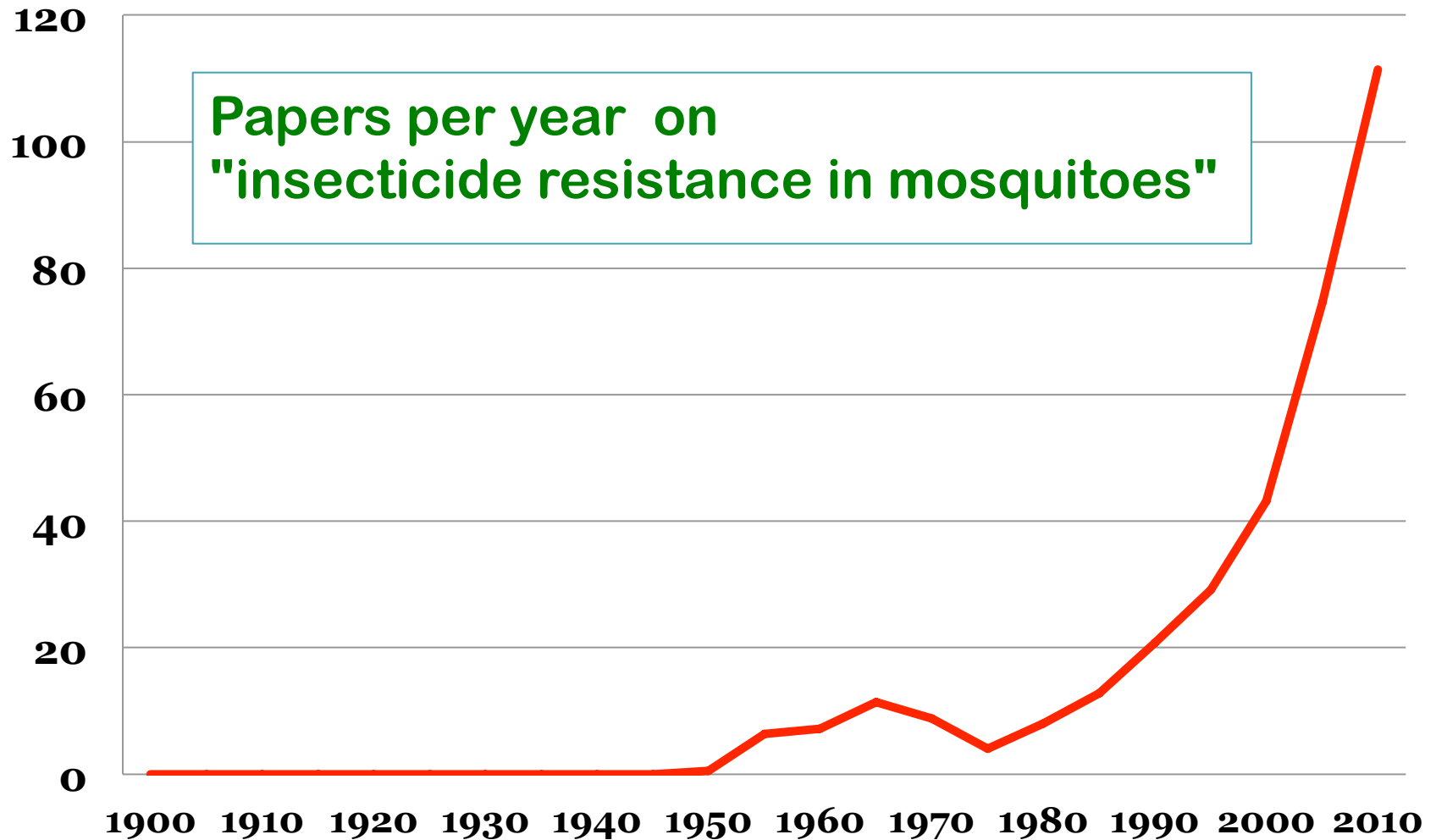
- WHO
- RBM Vector Control Work Group
- Innovation 2 Impact (i2i)
- Working party to update WHO test procedures for monitoring insecticide resistance
- Academic institutes
- Etc

# Insecticide Resistance can, and will, eventually develop to any insecticide



Disease	Insect	Vector Control Intervention
<b>Malaria</b>	<i>Anopheles</i>	LLIN and IRS
<b>Dengue</b>	<i>Aedes</i>	larvicides, space sprays, IRS
<b>Lymphatic filariasis</b>	<i>Anopheles Culex &amp; Aedes</i>	MDA plus vector control LLINs and IRS
<b>Leishmaniasis</b>	Sandflies	IRS
<b>Chagas</b>	Kissing Bugs	IRS
<b>Onchocerciasis</b>	Biting Blackflies	MDA. Larviciding

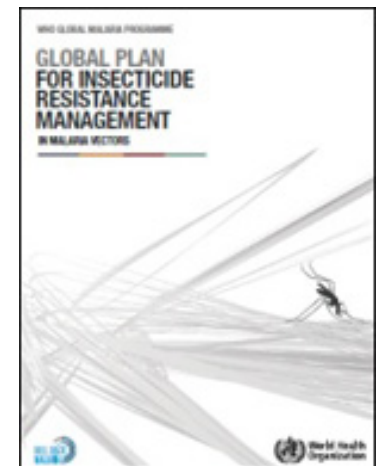
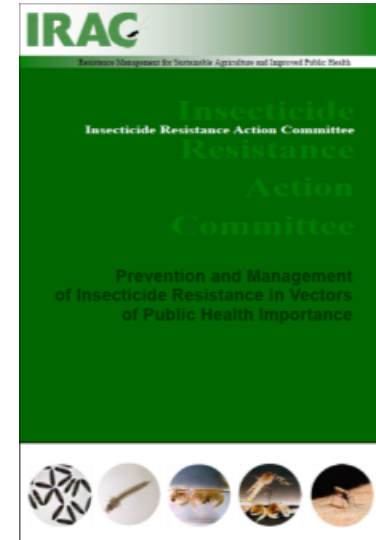




Source: Medline search, Trina Padoll 2013

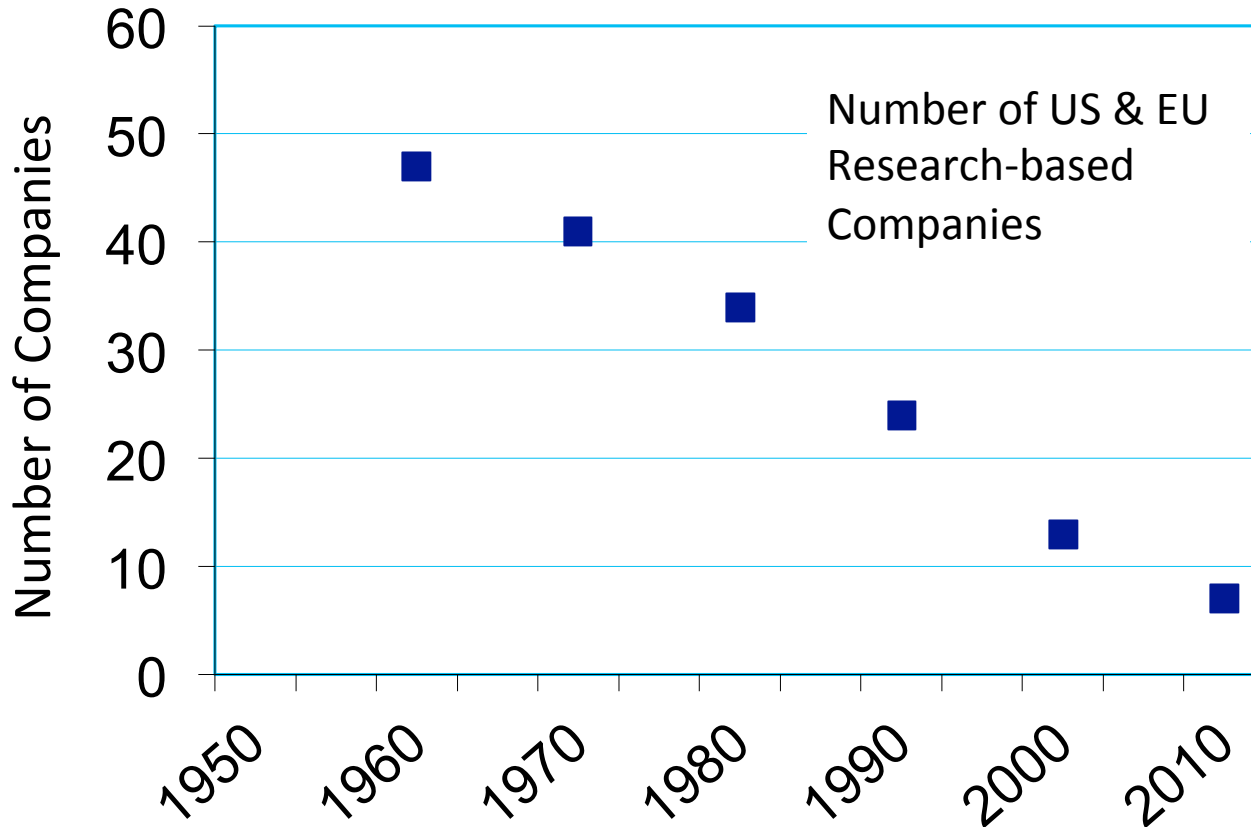
# Insecticide Resistance Management

- Rotations
- Mosaics
- Mixtures
  - of insecticides with different modes of action, to which the target population is susceptible
  - However, this implies that you have multiple effective insecticides with different MoA



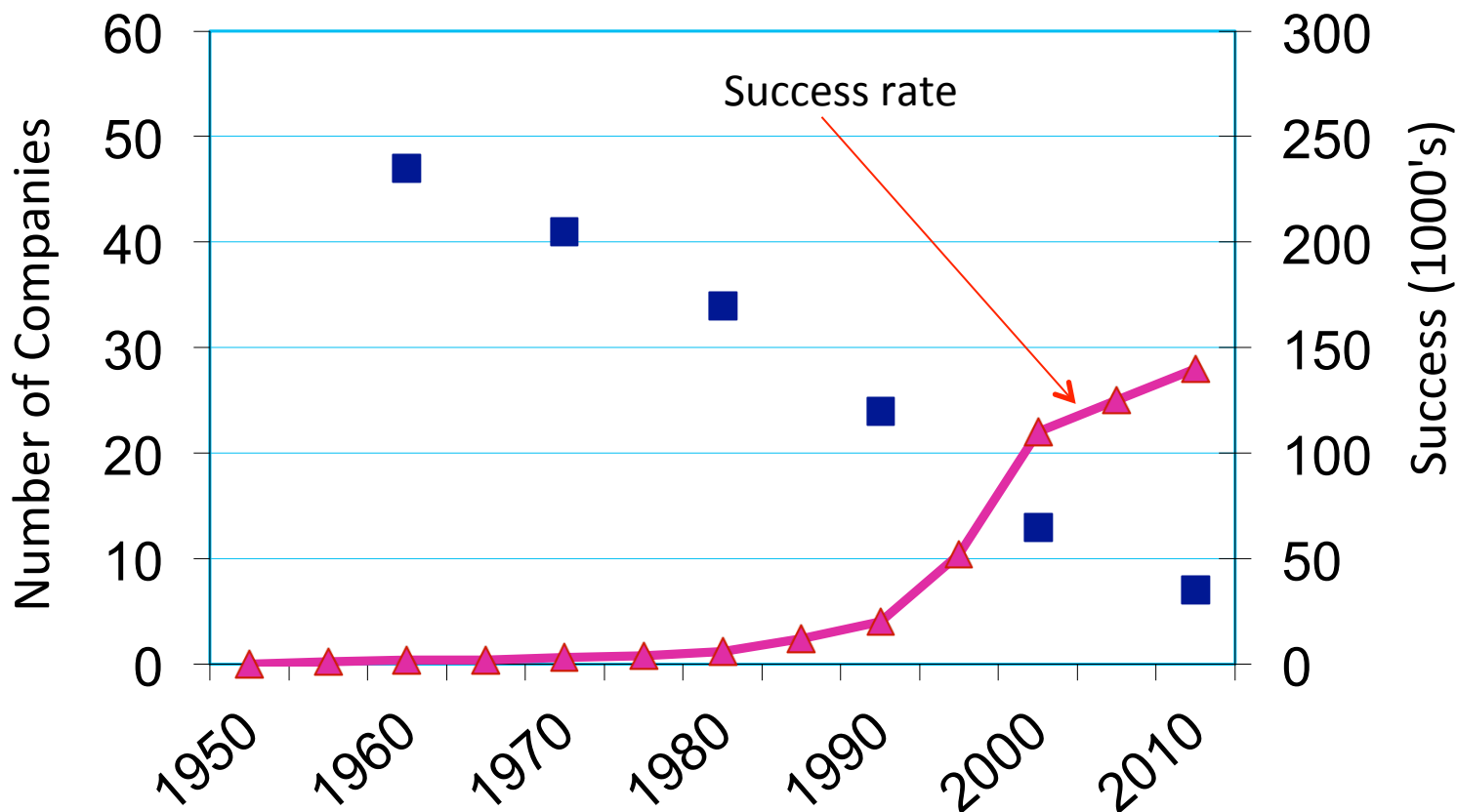
## Specific Challenges Facing Vector Control

# Fewer Companies involved in developing new insecticides



Data from GT Brooks 1974, RL Metcalf 1980, W. Klassen 1995 Philips McDougal, 2003, CropLife 2011

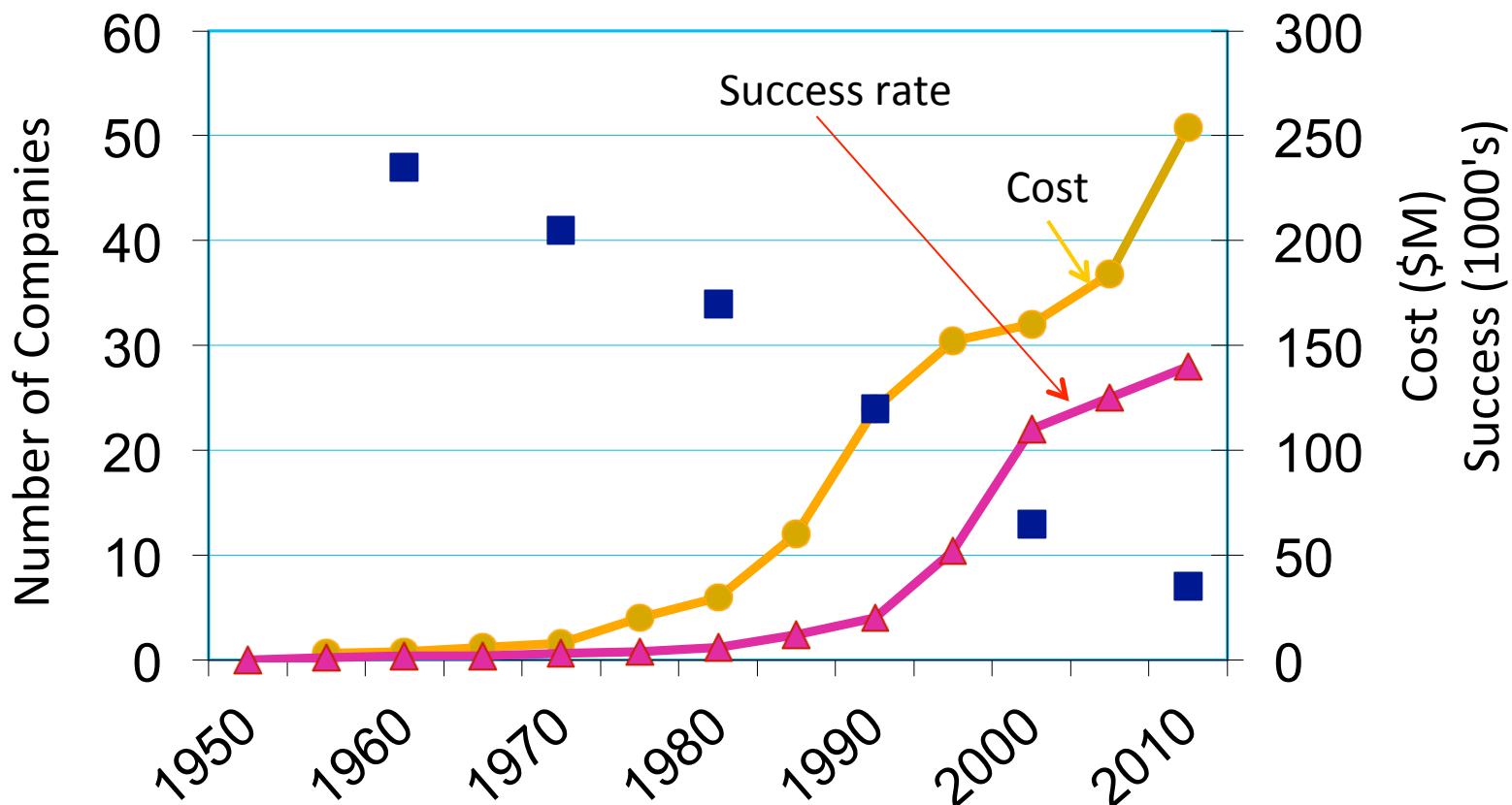
# Harder to discover insecticides (easy ones already found!)



Success rate = number of cpds that need to be screened for each product found

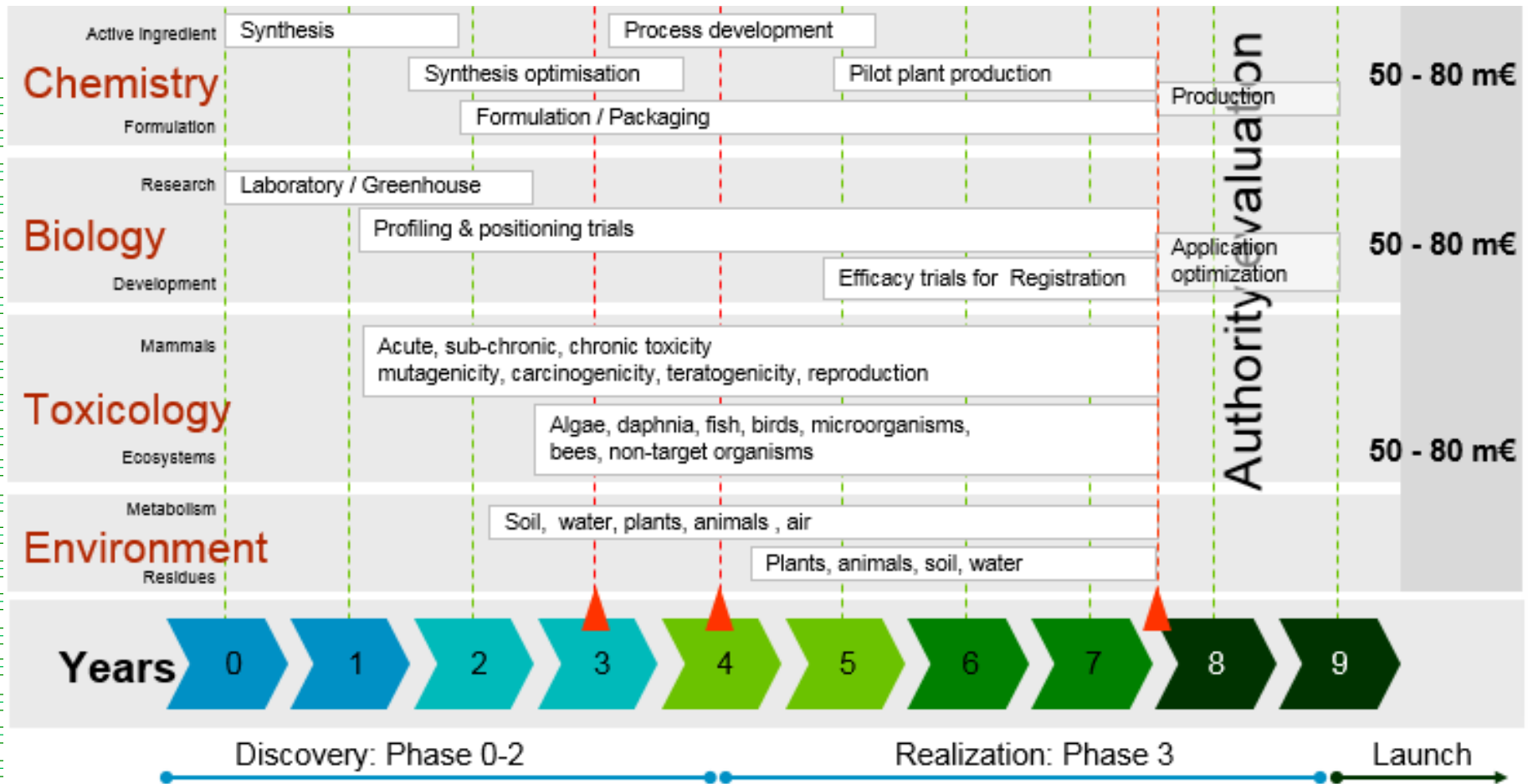
Data from GT Brooks 1974, RL Metcalf 1980, W. Klassen 1995 Philips McDougal, 2003, CropLife 2011

# The costs of discovering new insecticides has gone up



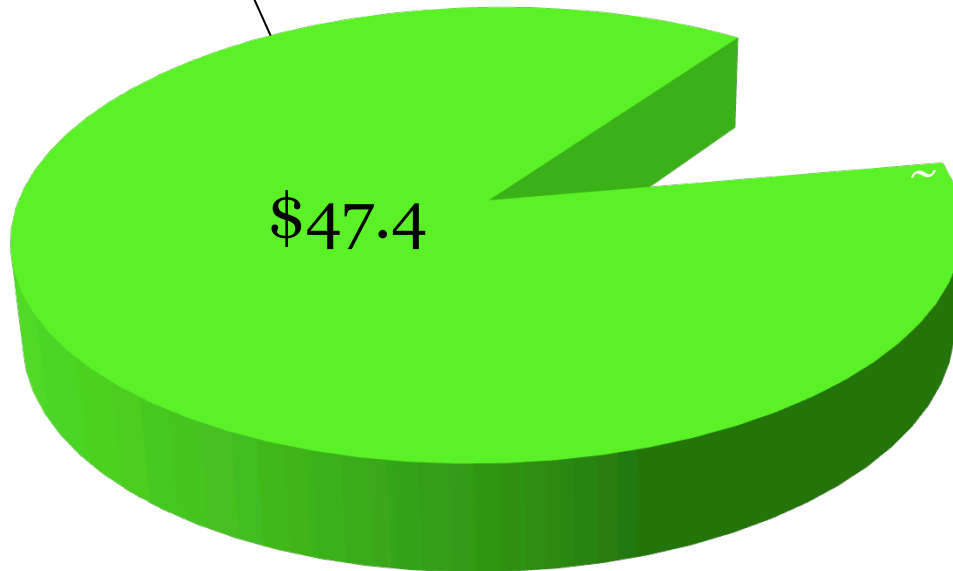
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## Vector Control : Small Market size, similar development costs

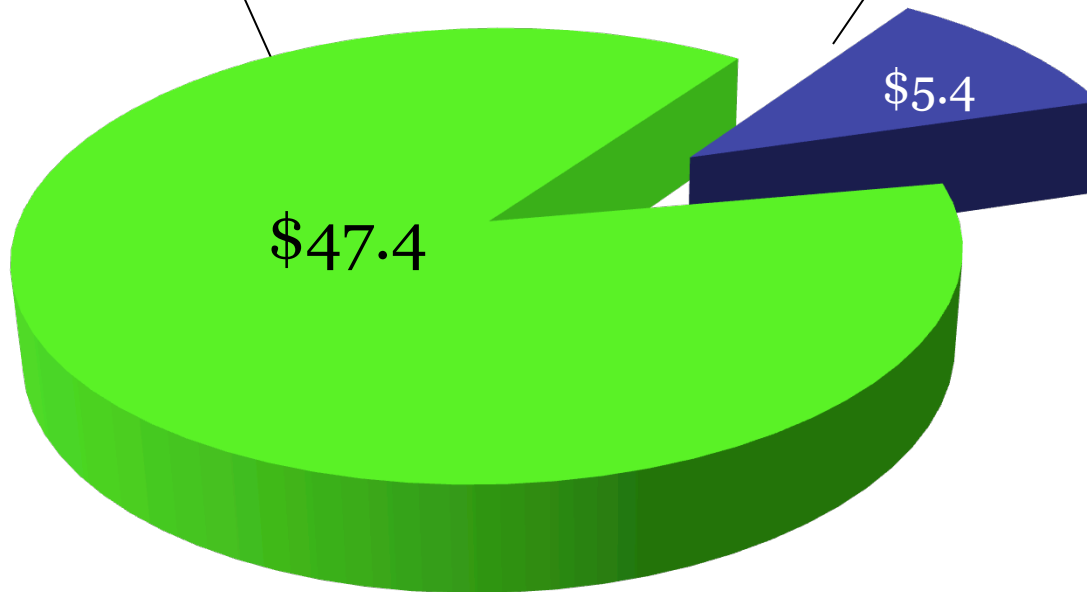


Estimated market size (Billion USD) at distributor level of chemical crop /no crop protection products (Source: Phillips McDougall May 2013, et al)





# Vector Control : Small Market size, similar development costs



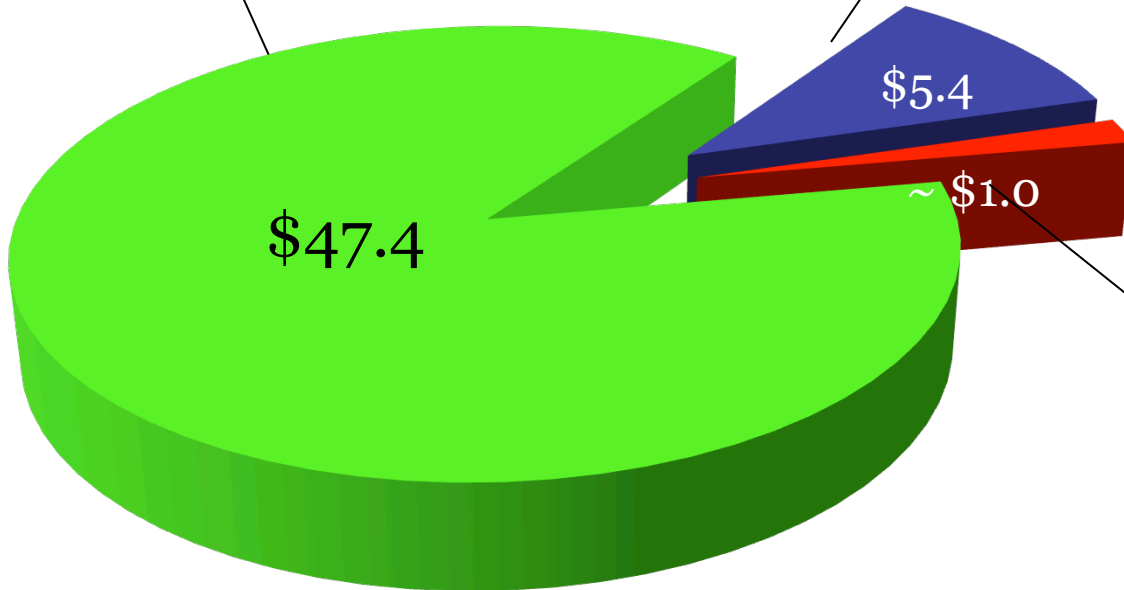
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# Vector Control : Small Market size, similar development costs



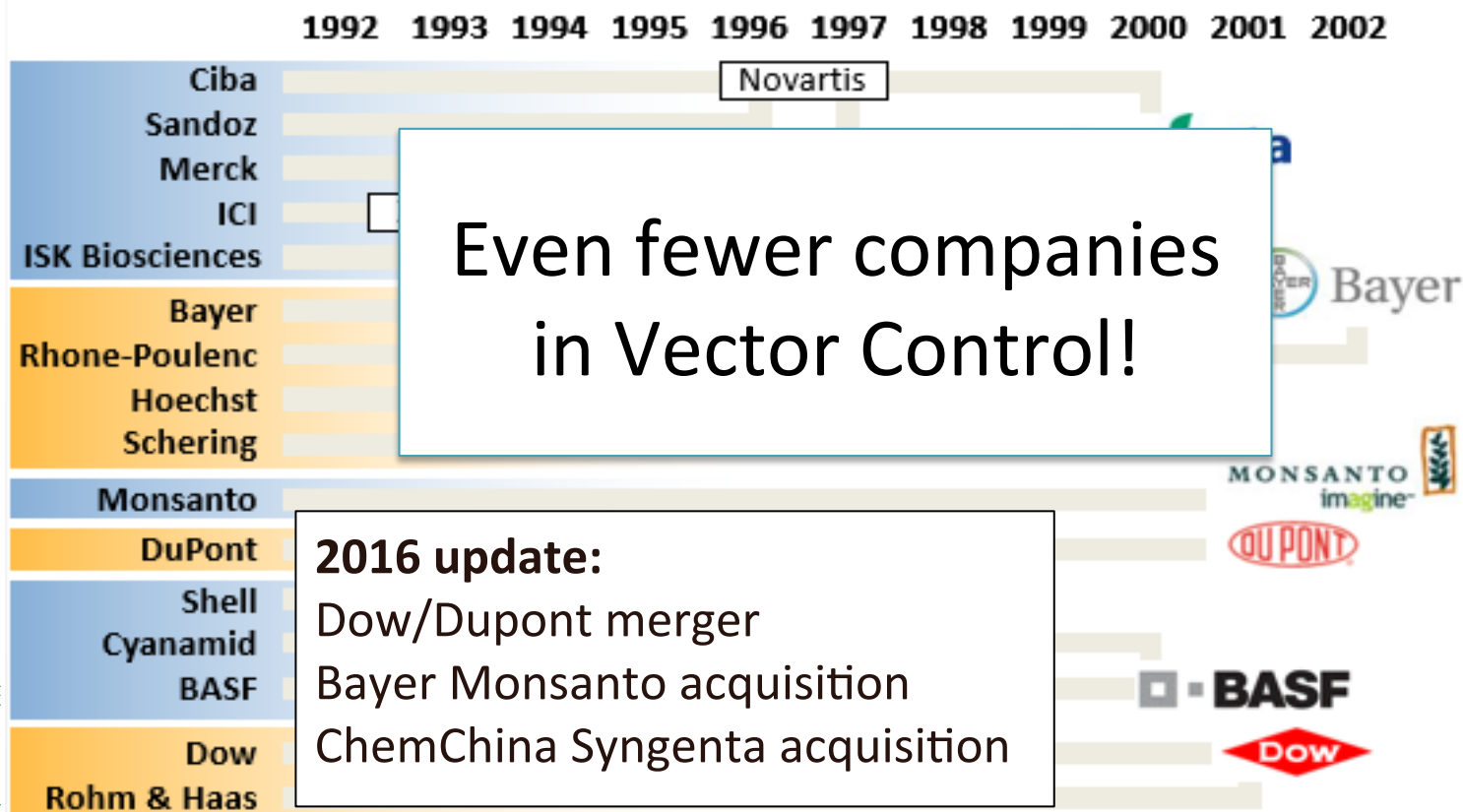
Vector Control insecticides are typically repurposed ag products



Estimated market size (Billion USD) at distributor level of chemical crop /no crop protection products (Source: Phillips McDougall May 2013, et al)

## Industry consolidation...

(5 top companies represent 73% of the Ag market vs. 28% of the pharma market)



# 29 different MOA Insecticides available but.... Control

## TPP Vector ≠ Ag coming ...

## Bti/Bs

## Plus IVCC...

### Chitin Synthesis Inhibitors

15 Benzoxazolines

### Carbamates, Ops

1A Carbamates

1B Organophosphates

### Pyrethroids, DDT

Pyrethroids  
Pyrethrins

3B DDT,  
Methoxychlor

### Clothianidin

4A Neonicotinoids

4D Butenolides

4E Mesoionics

### Spinosyns

5 Spinosyns

6 Avermectins, Milbemycins

### JH mimics

7A Juvenile hormone analogues

7B Fenoxycarb

7C Pyriproxyfen

### Chlorfenapyr

13 Pyriroles,  
Dimethoates,  
Sulfonamides

14 Nereistoxin analogues

- Targeted Physiology
- Neurotoxicity
  - Growth & Development
  - Feeding
  - Molt
  - Unknown or Nonspecific

Use of Groups and Sub-Groups:

- Alphabetical sequence is a series of compounds within MOA groups reduces selection to target site resistance.
- Applications are assigned to MOA groups in order of their stage and pest biology.
- Several groups of a compound may be possible when each group works, but successive generations of a pest should not be treated with compounds from the same MOA group.
- Localized applications should always be taken with respect to crop age, volume and timing.
- Active in group 3 (Mitochondrial complex I electron transport inhibitors) and UN are thought not to show a common target site and this may be likely related to which other insects have a similar target site or resistance.
- Sub-groups represent defined sub-categories believed to have the same mode of action.

- Sub-groups provide differentiation between compounds that may bind at the same target site but are structurally different enough that risk of resistance is less than a close chemical analog.
- Cross-resistance potential between sub-groups is higher than between groups, so action between sub-groups should be considered only when there is no alternative, and only if cross-resistance doesn't occur, taking consultation with technical advice. These exceptions are not sustainable, and alternative options should be sought.
- Sub-group UN/UCF are large volume applications and therefore the only applicable to the control of most vectors of human disease, such as mosquitoes, because of a lack of alternatives.
- Sub-group UN/UCF are grouped with chitinase because they inhibit cross-resistance even though they are structurally different, and the target site is these compounds is unknown. Oxydemeton has been added to the group because it is a close analogue of chitinase and is expected to have the same mode of action.

Pest Insects:

- Groups 2B and 2C are unassigned.
- The goal is to educational purposes only. Information presented is accurate to the best of our knowledge at the time of publication, but ILC is not responsible for any errors or omissions. Always consult your local regulatory authority for the most current information on insecticide use.
- Representative compounds are shown. Please visit [www.crop-life.com](http://www.crop-life.com) for the complete POC database.

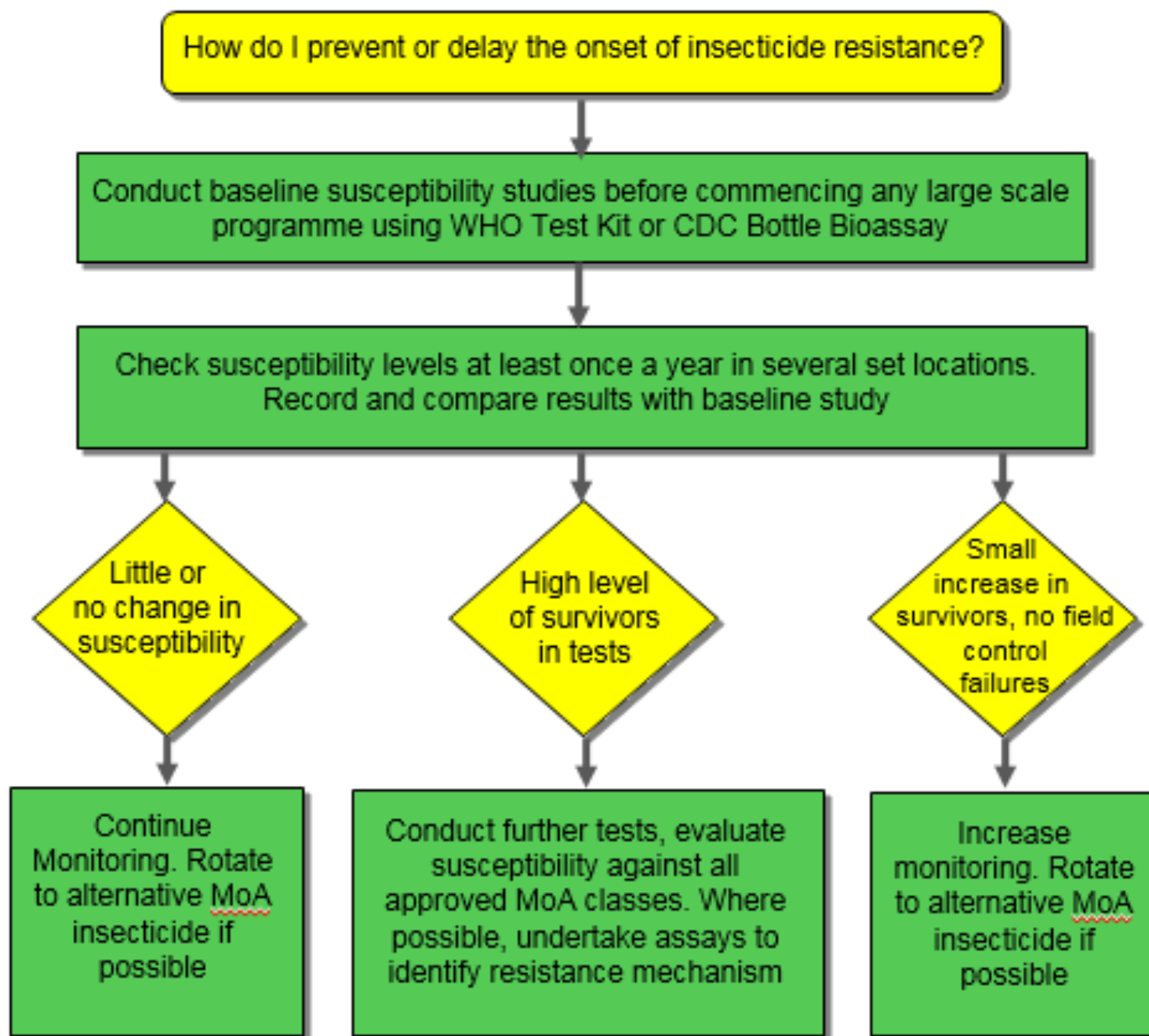
There are limited options in the Vector Control Insecticide toolbox

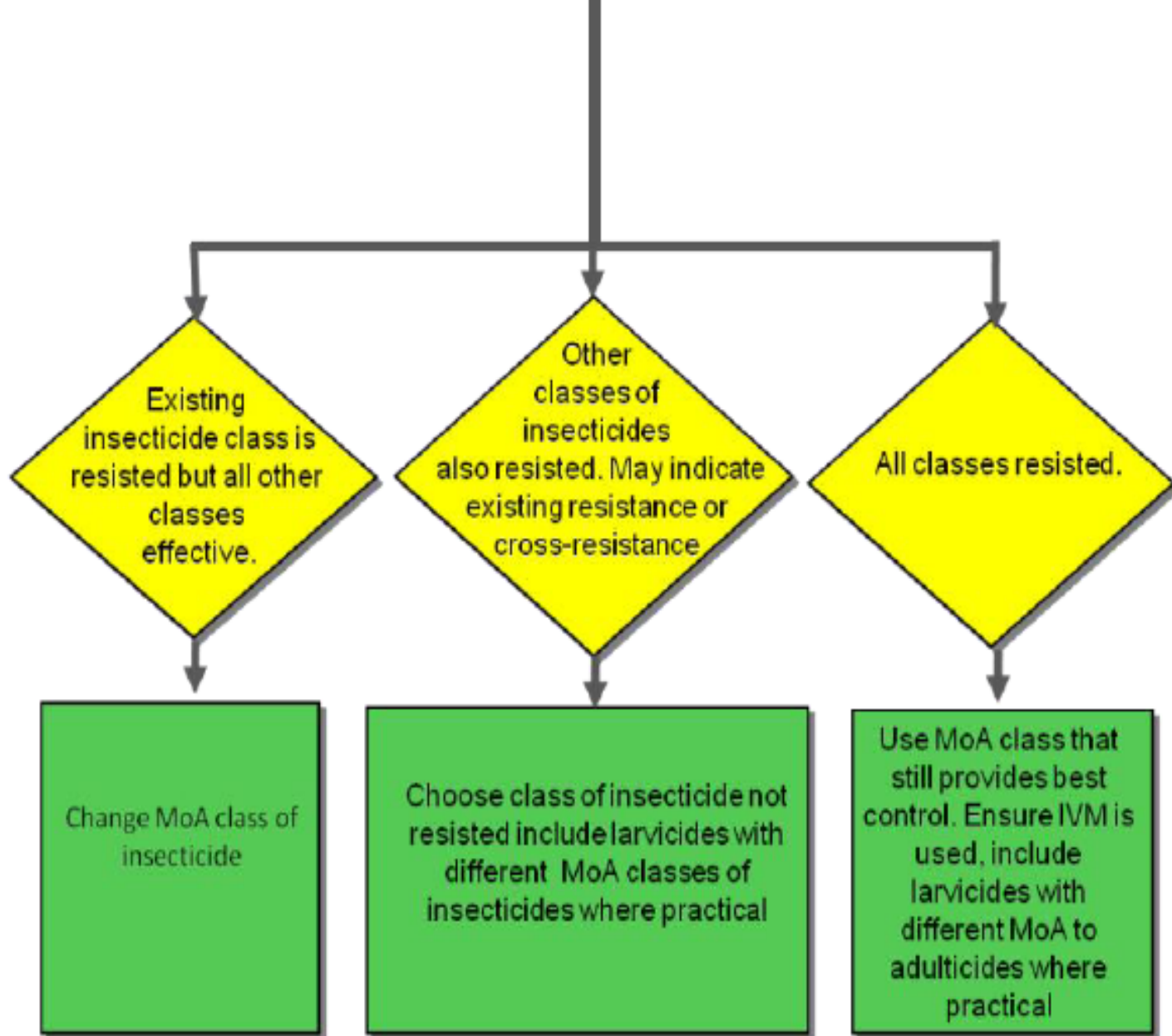
Insecticides should not be the only intervention to be considered

We need to ensure we maintain susceptibility through Integrated Vector Management best practices

Need to maintain susceptibility wherever possible and *before* resistance develops (proactive not reactive)

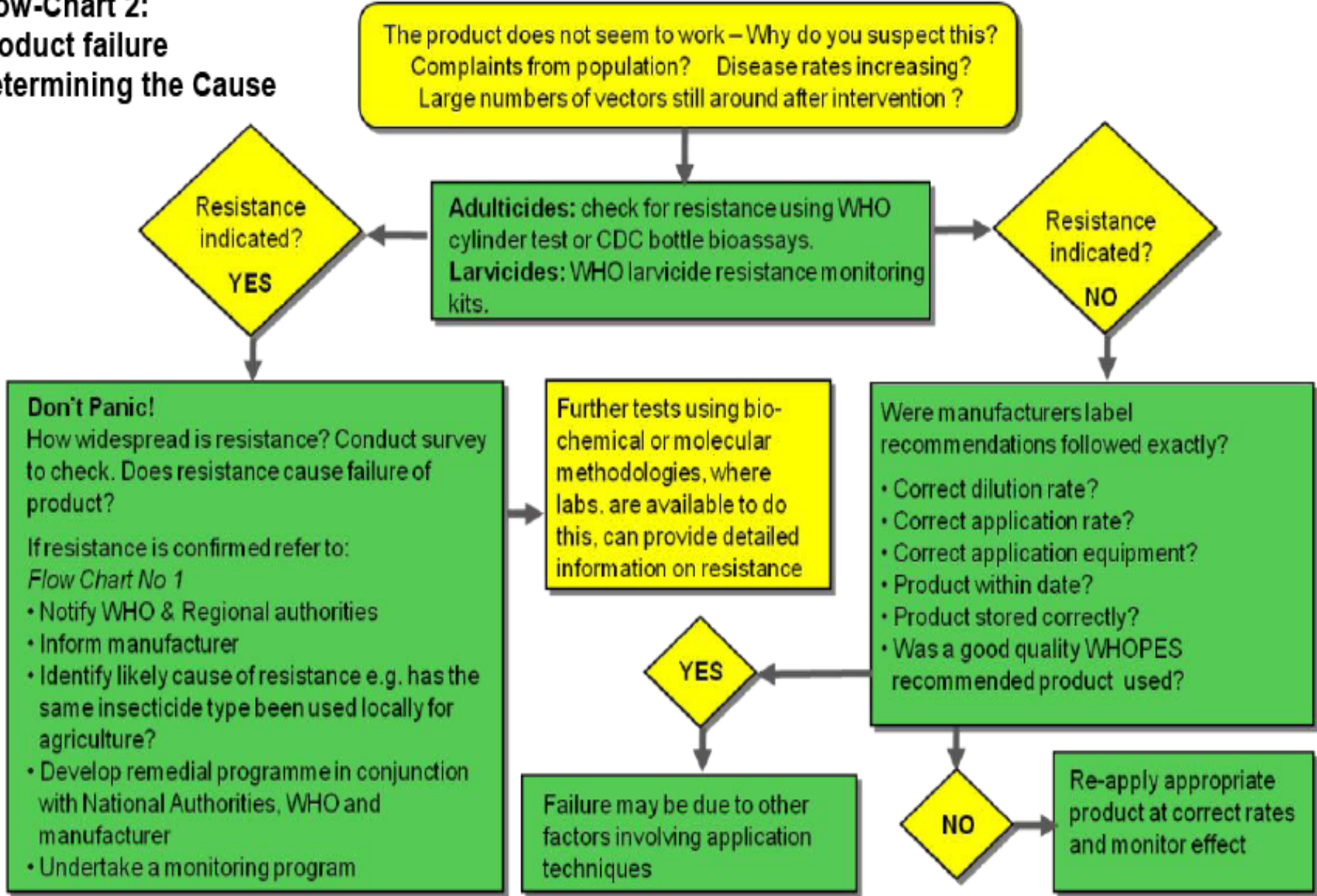
**Flow-Chart 1:  
Resistance  
Management  
Best Practice**





Please note that this is a simple guide and with some products such as LN's here is currently no alternative insecticide, however nets may still give protection through physical means and repellency.

**Flow-Chart 2:  
Product failure  
Determining the Cause**



The product does not seem to work – Why do you suspect this?  
Complaints from population? Disease rates increasing?  
Large numbers of vectors still around after intervention ?

Resistance indicated?  
**YES**

**Adulticides:** check for resistance using WHO cylinder test or CDC bottle bioassays.  
**Larvicides:** WHO larvicide resistance monitoring kits.

Resistance indicated?  
**NO**

**Don't Panic!**  
How widespread is resistance? Conduct survey to check. Does resistance cause failure of product?  
If resistance is confirmed refer to:  
*Flow Chart No 1*  
• Notify WHO & Regional authorities  
• Inform manufacturer  
• Identify likely cause of resistance e.g. has the same insecticide type been used locally for agriculture?  
• Develop remedial programme in conjunction with National Authorities, WHO and manufacturer  
• Undertake a monitoring program

Further tests using biochemical or molecular methodologies, where labs. are available to do this, can provide detailed information on resistance

Were manufacturers label recommendations followed exactly?  
• Correct dilution rate?  
• Correct application rate?  
• Correct application equipment?  
• Product within date?  
• Product stored correctly?  
• Was a good quality WHOPES recommended product used?

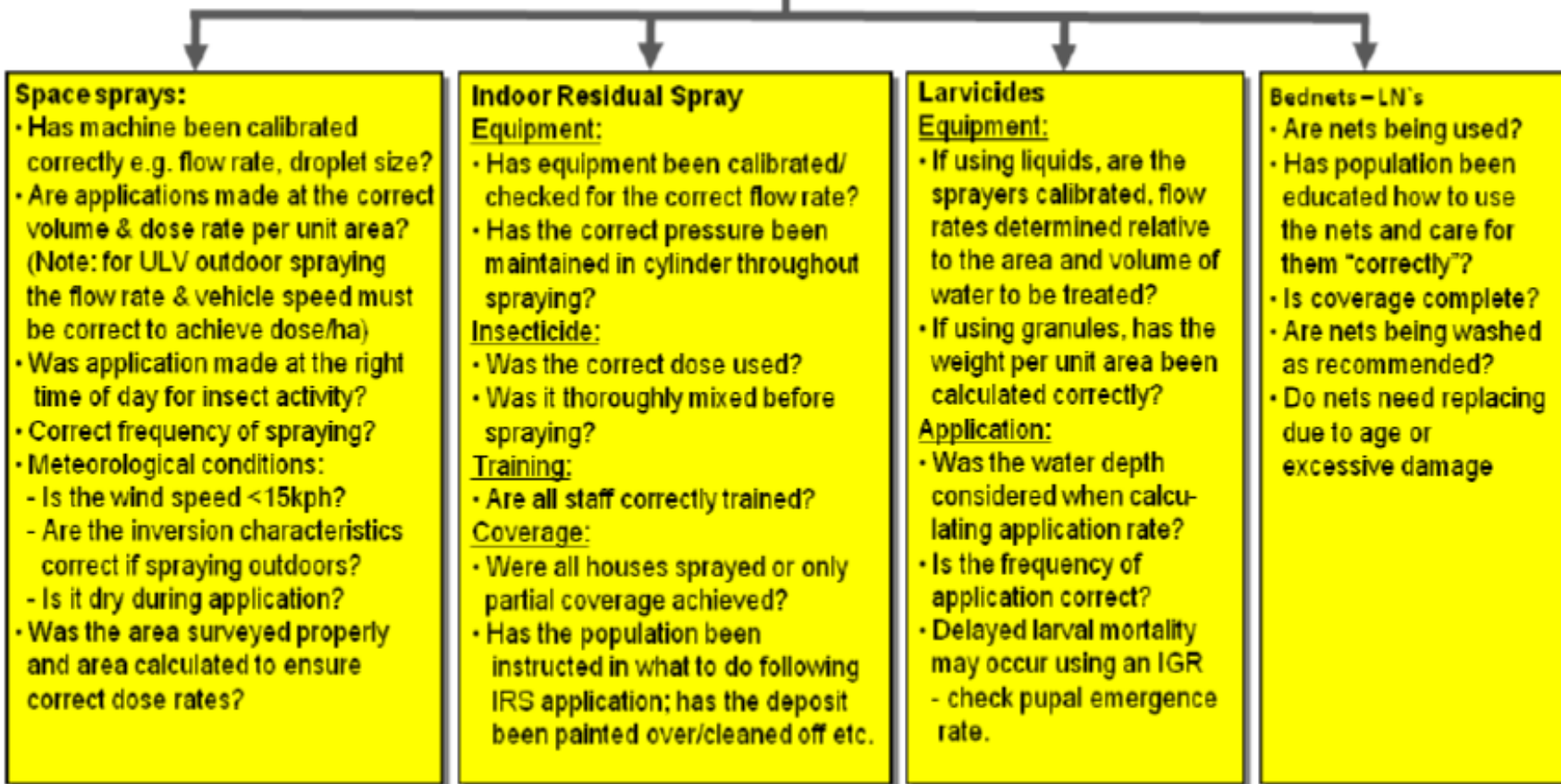
**YES**

Failure may be due to other factors involving application techniques

**NO**

Re-apply appropriate product at correct rates and monitor effect





For Further Details:  
[www.ircac-online.org](http://www.ircac-online.org)

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

**Insecticide Resistance Management**

**2. Resistance increasing**  
 Survivors reproduce  
 Further exposure to same insecticide  
 Survivors reproduce

**Key:** Resistant (red star) Susceptible (green star)

**Major mechanisms conferring resistance to important classes of insecticides in adult mosquitoes.**

	Pyrethroids	DDT	Carbamates	Organophosphates
Metabolic				
Target site				

**Flowchart Questions:**

- Resistance indicated? (NO)
- Were manufacturers label recommendations followed exactly? (e.g. Correct dilution rate? Correct application rate? Correct application equipment? Product within date? Product stored correctly? Was a good quality WHOPEIS recommended product used?)

**Outcomes:**

- Go to Page 22 for details
- Go to Page 20 and 21 for details
- Re-apply appropriate product at correct rates and monitor effect

**Common Resistance Mechanisms:**

- Small floats
- Exit skin when
- When it is dark

Copies available from IRAC via the website