

Session 3

International Working Group & Country Group Review

46th Meeting of IRAC International, Brussels, Belgium

Wednesday - March 30th, 2011

IRAC Public Health team

2010 a review...

Mark Hoppé





Team Membership

Insecticide Resistance Action Committee



Chair: Mark Hoppé Syngenta
Deputy chair: Georgina Bingham Zivanovic Vestergaard Frandsen



Members:

James Austin	BASF
Luigi Avella	Chemtura
Karin Horn	Bayer Crop Science
John Invest	Sumitomo chemical UK
Chris Longhurst	Dow
Chouaibou Mouhamadou	Vestergaard Frandsen
Ralf Nauen	Bayer Crop Science
Helen Pates Jamet	Vestergaard Frandsen
Alan Porter	APA

Non industry observers:

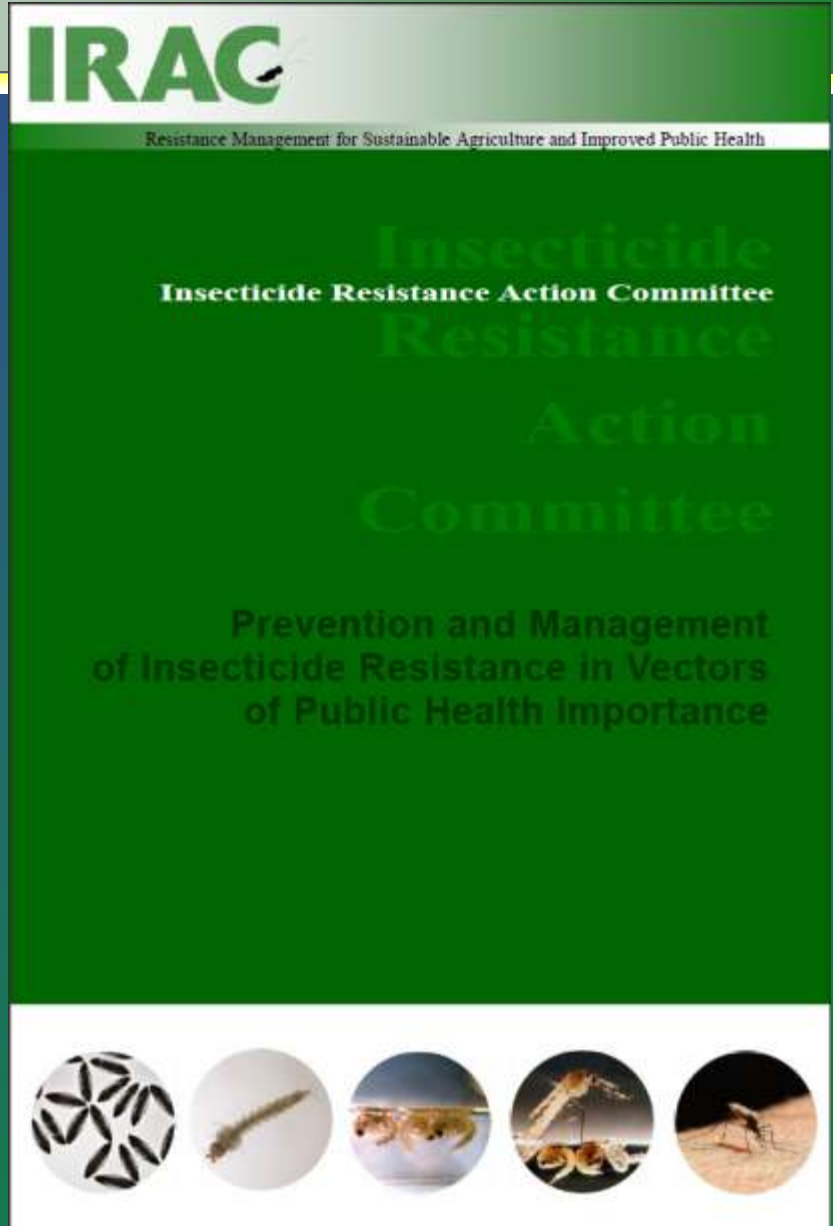
Kate Aultman	BMGF
Jo Lines	WHO
Bob Wirtz	CDC

Goals	Objectives	Timeline
<p>Identify potential, new or existing resistance issues. Set up Team Working Groups or Focal Points as necessary</p>	<p>Monitor and report to the Executive on any potential, new or existing national, regional or global resistance issues that could require action by IRAC e.g. Vectors and Hygiene Pests. Research the issues and report to the Executive on a recommended plan of action including the extent of the problem and whether and how it should be best tackled. Set up appropriate PH Team WGs as deemed appropriate for the 2010/11 year. Each WG should set up their own goals and SMART objectives.</p>	<p>Ongoing</p> 
<p>Provide expert input into IRM initiatives with identified partners.</p>	<p>Set up a schedule of IRAC PH Team conference calls, meetings for 2010/11. Identify and invite relevant experts and observers from groups interested in Public Health IRM e.g vectors, hygiene pests (WHO, Gates Foundation, IVCC) to participate and ensure that IRAC as an expert group provided input into relevant IRM initiatives. e.g. WHO proposal to Gates Foundation. Maintain, and build on, the role of Liaison Officers to report back to the Public Health Team on the activities of other groups active in the area</p>	<p>Ongoing</p> 

Goals	Objectives	Timeline
Preparation of Public Health communication material	Complete and produce VM in time for launch at ASTMH in November Produce a cut-down version for use by technicians Produce decision trees/charts for use by technicians	October 2010 
Develop IRAC methods for the housefly and mosquito	Provide approved methods for monitoring the susceptibility of mosquitoes and houseflies to the IRAC methods team. To be undertaken in conjunction with appropriate third parties, e.g. CDC, WHO	
Develop a position paper on WHOPES discriminating rates	In conjunction with appropriate experts, make recommendations on relevant discriminating doses to identify insecticide resistance in key species of adult mosquito. Produce an IRAC PH team position paper to communicate the team's view on discriminating doses to interested third parties.	End Q2 2010
Organise insecticide resistance symposium at the ASTMH 2010 conference	Invite speakers and coordinate symposium to promote best practice IRM in the context of IVM. Launch VM, possible at separate event during the ASTMH event.	October 2010 

■ Major success:

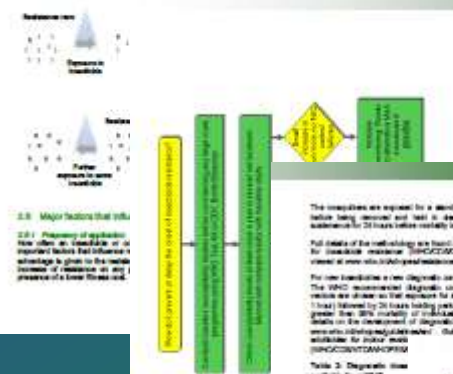
- Updated Vector manual...
- Many thanks to the team for writing and reviewing this
- Special thanks to Alan for the layout and formatting
- Online version available from November 2010
- Paper version in print
- Positive feedback from online version



- 72 pages of information, recommendations and advice
- Completely revised and updated from first edition
- Target audience: Those who plan, manage, fund or have influence on the design and implementation of mosquito vector control programmes
- Covers all aspects of IRM in an Integrated Vector Management (IVM) context
- Print run of 4000 copies to be made freely available to the Vector Control community

Insulation there is no reason for the resistance genes to be lost in the population and for resistance to stay near. For example, DDT was used extensively for malaria control over a 20 year period up to the 1950s. It is likely to control Anopheles subpictus and Anopheles gambiae. DDT was replaced by malathion in 1950s in the early 1970s when a hole was effective. Use of DDT was discontinued. Subsequent regular monitoring has shown that DDT resistance has remained very low, because of malathion. Around 80% of the adult mosquito population was resistant to the DDTs compared to about 20% in the 1950s. This rate of resistance is clearly too slow to establish any effective resistance management strategy involving the introduction of DDT.

Figure 2. Possible scenario for resistance development in a susceptible population



The mosquitoes are exposed for a specified period of time to the pyrethroids before being removed and held in their cages with net screens well maintained for 24 hours before mortality is assessed.

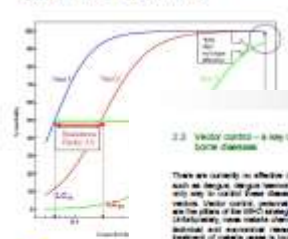
Full details of the methodology are found in the document 'The Procedure for Insecticide Resistance (INSECTICIDE) TESTS' which can be viewed at www.who.int/csr/don.

For new insecticides a new diagnostic concentration has to be determined. The WHO recommended diagnostic concentrations for most groups of insecticides are shown in the exposure for a specified period of time (usually 1 hour) followed by 24 hours holding period, can be reduced to 10 minutes to 1 hour (10% mortality of individuals from susceptible strains). Full details on the development of diagnostic concentrations can be found at www.who.int/csr/don.

Table 3. Diagnostic insecticide concentrations from WHO

Insecticide	WHO	WHO
Organophosphates	0.1	0.1
Organochlorines	0.1	0.1
Carbamates	0.1	0.1
Pyrethroids	0.1	0.1

Figure 3. Showing a field to mosquito susceptibility as an early step by monitoring the population for resistance before being used in the field.



2.3 Vector control – a key component in managing vector-borne diseases

There are currently no effective drugs or vaccines for tropical diseases such as malaria, dengue, schistosomiasis, leishmaniasis and Chagas disease. The only way to control these diseases is to prevent transmission by insect vectors. Vector control, personal protection and community participation are the pillars of the IVM strategies for tropical infectious diseases control. Community-wide vector control programmes are fundamental for individual and population health, especially in Africa. The effective treatment of malaria needs to increasingly combine and improve due to drug resistance. In high transmission areas control include use of long-lasting insecticidal nets (LLINs) and indoor residual spraying (IRS). In low transmission areas, IRS is not warranted through very effective vector control and/or personal protection interventions. Vector control can also be targeted for diseases that are controlled primarily by transmission from drug administration (MCI). The current strategy of the World Health Organization (WHO) focuses on vector control activities to reduce transmission.



2.4 The need for chemical control

Insecticides remain the most important element of integrated approaches to vector control. The insecticide resistance in some of DDT by the Commission on Insecticide Resistance (CIR) has dramatically reduced the high degree of reliance on insecticides and programs in vector control. Insecticide resistance has also been a major barrier to the development of new insecticides and their use. To reduce the reliance on insecticides, WHO is promoting integrated vector and pest management, including alternative methods such as biological control or environmental management when and where they are effective and applicable. WHO also provides the skills and support for insecticide resistance management. For example, a very successful Dengue disease control programme in Singapore has been widely based on insect spraying of pyrethroid insecticides. Other countries (see below);

Activities 2010



- **First draft of “Mini-Vector Manual” produced**
 - Smaller pocket version, similar to MoA booklet, containing more practical advise
 - Will use more flow diagrams, decision trees, etc.



■ ASTMH meeting

- Proposal for a symposium rejected by organising committee
- Two papers submitted, accepted, but as posters
- Posters presented by Georgina
- Much interest in posters, which started lively discussions on IRM

The increase in the utility and importance of biomolecular techniques in resistance monitoring in insect vectors

www.irac-online.org

Monitoring Objectives

The monitoring of insecticide susceptibility in vector control programmes has three main objectives:

- **Baseline data collection:** Conducts 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 the population over time, comparing it with the pre-intervention baseline. Hence the impact of the control strategy on the proportion of susceptible individuals in the mosquito population can be evaluated.
- **Detection of resistance:** To detect resistant individuals when they arise at a low frequency in the population so that resistance management can be effectively introduced. Detection of resistance when a large proportion of the mosquito population are already resistant limits the potential effectiveness of IRM strategies.

Careful use of the information provided from the activities above will allow evidence based decisions to be made in the design of integrated vector management strategies in a specific locality.

Molecular Monitoring methods

Molecular tools can be used to complement bioassays. Their use is currently restricted to research laboratories but bioassays are still in use.

The following is a description of the currently available molecular techniques:

- **Genetic identification using a multiplex PCR assay:** The presence of each specific P450 gene is confirmed and an estimate of the relative proportion of P450s can be determined.
- **Identification of the use of insecticide resistance genes:** A gene can be identified using a real-time quantitative length polymorphism (RFLP) PCR assay. The frequency of an allele (allele) can be determined by measuring the length polymorphism (RFLP) PCR assay. The frequency of an allele (allele) can be determined by measuring the length polymorphism (RFLP) PCR assay.
- **Development of assays for molecular resistance:** Real-time quantitative PCR (qPCR) can be used to identify the presence of P450 genes in a population. The detection of P450 genes in a population can be used to identify P450 genes in a population.

Bioassay Monitoring methods

Bioassays can be used to monitor the susceptibility of mosquito populations. The bioassay can be used to monitor the susceptibility of mosquito populations. The bioassay can be used to monitor the susceptibility of mosquito populations.

Details for the bioassay can be found at www.irac-online.org.

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Biochemical Monitoring methods

The use of biochemical monitoring methods can be used to monitor the susceptibility of mosquito populations. The biochemical monitoring methods can be used to monitor the susceptibility of mosquito populations.

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The importance of Insecticide Resistance Management in the control of the mosquito vectors of malaria

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Insecticides have been extensively used since the 1940s to control the mosquito vectors of malaria, and have been a vital component in the fight against malaria. However, resistance has developed and is widespread in populations of the major mosquito vector species to the four classes of insecticide currently recommended for adult vector control. As insecticide resistance continues to develop and spread, there is a real danger that these valuable tools will be lost.

Path of a mosquito adulticide from decision to implement a programme to successful vector control

The path of a mosquito adulticide from decision to implement a programme to successful vector control is shown in the diagram. The path starts with the decision to implement a programme, followed by the implementation of the programme, and finally the successful vector control.

In the majority of cases, insecticide resistance develops against all members of a class of insecticides that share a common mode of action (MOA). It is therefore essential to talk about classes, or groups, of insecticides rather than individual insecticide products. IRAC has worked extensively with industry and non-industry experts to classify all insecticides into a comprehensive MOA Classification Scheme. The groups of insecticides with a MOA related to a common target site, are numbered groups. The IRAC MOA classification is regularly updated and can be found at www.irac-online.org and is available as a poster and booklet.

Insecticide Resistance Management

- Plan: IRM should be considered an integral part of any vector control programme, and should be a prerequisite for programme funding.
- Monitor: The susceptibility status of the target mosquito population should be monitored during the planning phase to guide choice of intervention. Monitoring should be continued to identify changes in susceptibility profile.
- Rotate: Where possible, guided by susceptibility monitoring data, plan to rotate insecticides by MOA class, either temporally or spatially. In the absence of susceptibility data, the rotation of products between IRAC MOA classes will reduce selection pressure for resistance development. Rotate mosquito treatments with alternative classes where appropriate.
- Resist: To reduce resistance, selection pressure from sublethal doses.
- Use: WHO PCT approved products that conform to specifications throughout programme cycle.
- Inform: Inform all key personnel at all locations about the IRAC MOA classification products.

Conclusion

Insecticide Resistance Management must be an integral part of all vector control programmes. Using insecticides in such a way that their effectiveness is maintained is a shared responsibility of the commercial organisations that sell them. It is also a shared responsibility of those who design and implement vector control programmes.

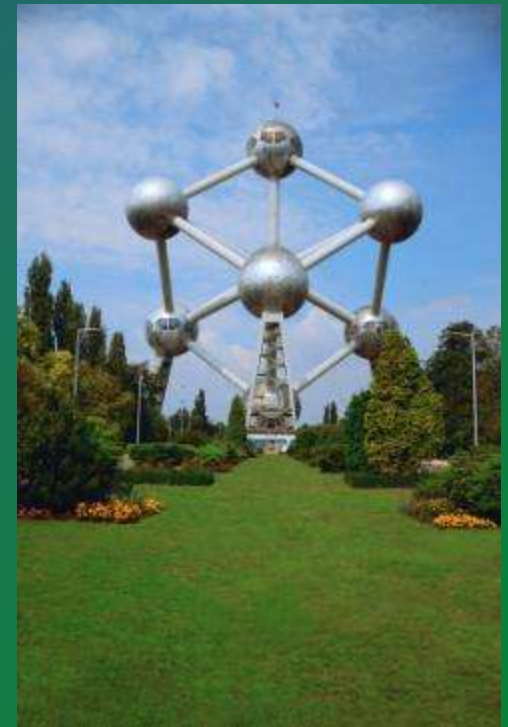
Further information on the IRAC MOA classification and management of insecticide resistance is available at www.irac-online.org.

■ ASTMH meeting

- Joined with CLI Vector Project Team in an “unofficial” symposium/meeting
- Paper presented by Bob Farlow (former IRAC PH team member, now consultant)
- Paper was well received by a large invited audience

- **IRAC PH team representation on expert panels:**
 - WHO meeting:
 - “The technical basis for coordinated action against insecticide resistance: preserving the effectiveness of modern malaria vector control” Geneva 4-6 May 2010
 - Core team of the RBM/Stockholm Convention insecticide resistance meeting:
 - “Developing a Global Strategy for the Prevention and Management of Insecticide Resistance” Liverpool 11-12 October 2010
 - WHO insecticide resistance project:
 - Continuing to support this ongoing project, with particular reference to susceptibility monitoring bioassays

- **6 teleconferences since last Spring meeting**
 - Average attendance 7
- **Face to face meeting postponed until Spring meeting**



2011 activities...

- Completion and publication of mini-Vector Manual
- Production of educational presentations, based on VM, that can be used by third parties
- Continue supporting WHO on their IR project
- Coordinate activities more closely with CLI VCPT
- Formulate position on mosquito larvicides
- Production of poster on IRM in mosquito larvicides
- Consider insecticide resistance risk assessment approach for VC interventions – in conjunction with Gates consultation
- Formulate position on mixtures
- Organise workshop with third parties to update team on latest status of insecticide resistance in Anopheline vectors