Status of Insecticide Resistance and Monitoring Needs in Asia Pacific

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Acknowledgement

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APMEN
asia pacific malaria elimination network

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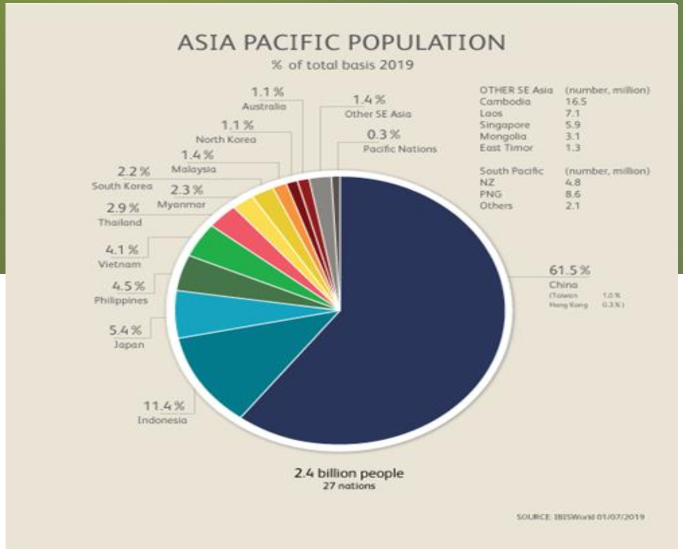
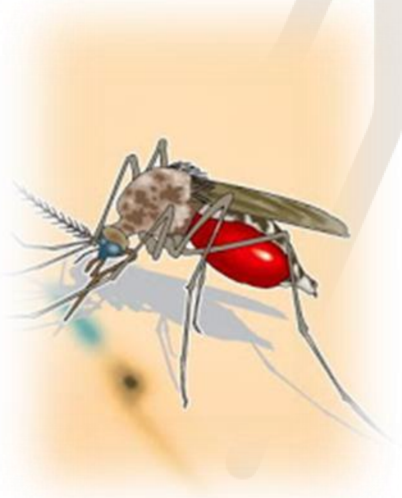


The Asia and the Pacific region is home to 60 per cent of the world's population – more or less 4.3 billion people – and includes the world's most populous countries, China and India.

Recently, the World Health Organization estimates that over 400 million people in Southeast Asia and the Pacific were at risk of vector borne disease infection, and 3.5 million people contracted malaria.

Disease	Vector	Distribution within the Asia Pacific	Prevention measures	More details
Dengue	Aedes mosquitoes • Mostly day biting though can bite in evening an night • Indoor and outdoor biting	Widely throughout the Asia Pacific often in urban areas.	• Repellents • Long clothing / treated clothing • Room screening • Removal of breeding sites	http://wwwnc.cdc.gov/travel/diseases/dengue
West Nile Virus	Mosquitoes, mostly Culex though local variation in dominant vector	West and central Asia	Depending on local vector • Repellents • Long clothing / treated clothing • Room screening • Insecticide treated nets	http://wwwnc.cdc.gov/travel/diseases/west-nile-virus
Murray Valley Encephalitis	Culex mosquitoes	Papua New Guinea, remote NW or SE Australia	• Repellents • Long clothing / treated clothing • Room screening Insecticide treated nets	http://wwwnc.cdc.gov/travel/diseases/murray-valley-encephalitis-virus
Chikungunya	Aedes mosquitoes • Mostly day biting though can bite in evening an night • Indoor and outdoor biting	Widely throughout the Asia Pacific often in urban areas.	• Repellents • Long clothing / treated clothing • Room screening • Insecticide treated nets	http://wwwnc.cdc.gov/travel/diseases/chikungunya
Japenese Encephalitis	Culex Mosquitos • Mainly dusk to dawn biting • Mainly outdoor biting	Widely throughout Asia Pacific. Often in rural areas associated with rice production or flooding, and near urban areas where these areas are neighbouring.	• Vaccine • Repellents • Long clothing / treated clothing • Room screening • Insecticide treated nets	http://wwwnc.cdc.gov/travel/diseases/japanese-encephalitis



Currently, no specific therapeutic drugs OR **effective vaccines** are available for important vector borne diseases, including dengue, Zika, malaria etc.

Vector control remains the potential method for reducing transmission

Several vector control tools to target mosquitoes have been proposed

Fabric impregnated with pyrethroids-spatial repellent

DEET or botanical oil- topical repellents

Insecticidal space spray (fogging or ultra-low volume applications)

Larval habitat source management

Push–pull system" using combinations of spatial repellents and attractant traps

Sterile insect techniques

Attractive toxic sugar bait systems (ATSB) use a strategy of "attract and kill"

Chemical insecticides and resistance

Types of synthetic insecticides

Organophosphorus insecticides	TEEP - tetraethyl pyrophosphate Dianizion Parathion Paraoxon Trichlorfon Malathion	FYFANON 440EW ANTHON BOVINOX PROXOL DANEX
Polychlorinated insecticides	Bischlorophenyl: DDT Metoxychlorine Derivatives cyklodiene: Aldrin Dieldrin Ceptachlorine Endosulfan Chlordon Derivatives cycloparaffinic: Hexachlorocyklohexane Lindane Chlorinated terpenes: Camphenes Pinenes	AZOTOX DITOX TRIOX ANOTEX CESAREX CHLOROPHENOTHANI DEDELO DINOCIDE DIDIMAC DIGMAR GENITOX GUESAPON IXODEX NEOCID R50
Carbamate insecticides	Carbanil Carbofuran Primor Izolan Aldikarb Bindokarb	PRIMOR 500W MARSHAL 250DS PRIFLOR AE PRIMIX AL PRIMIX AE

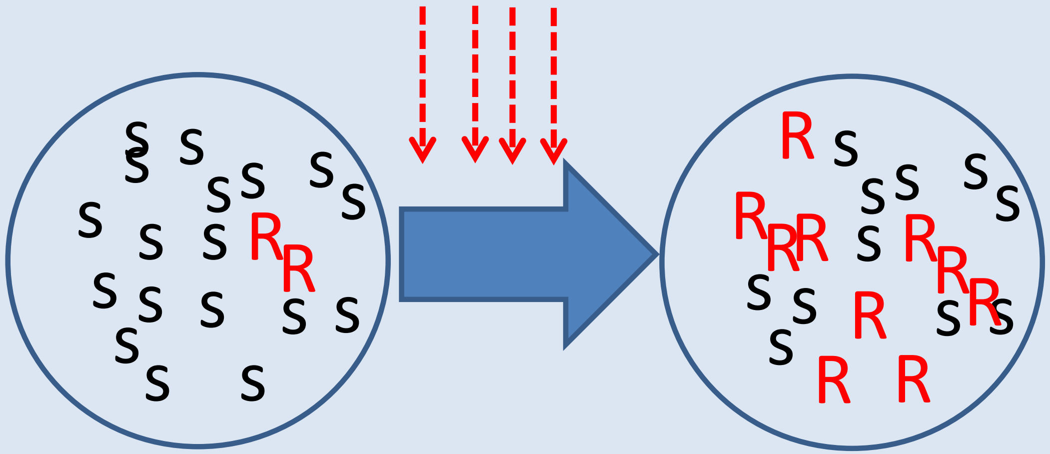
Pyrethroids	Pyrethrins Jasmolin Cynarin Synthetic: Allethrin Alphamethrin Bioresmethrin Cyfluthrin Cypermethrin Deltamethrin Permethrin Rosmethrin Trousfluthrin Fenvalerate	CYFLOK 50EW K-OTHRINE BROS INSECT SPRAY ABC AC INSEKTUM A 01 AL SPRUZIT 04EC DECIS 2.5EC

Neonicotinoids	Imidaclopirid Firponil Clothianidin Natural:	ACTARA 25WG MOSPILAN 20SP

Insecticide Resistance

Physiological resistance

Insecticides



Behavioral avoidance

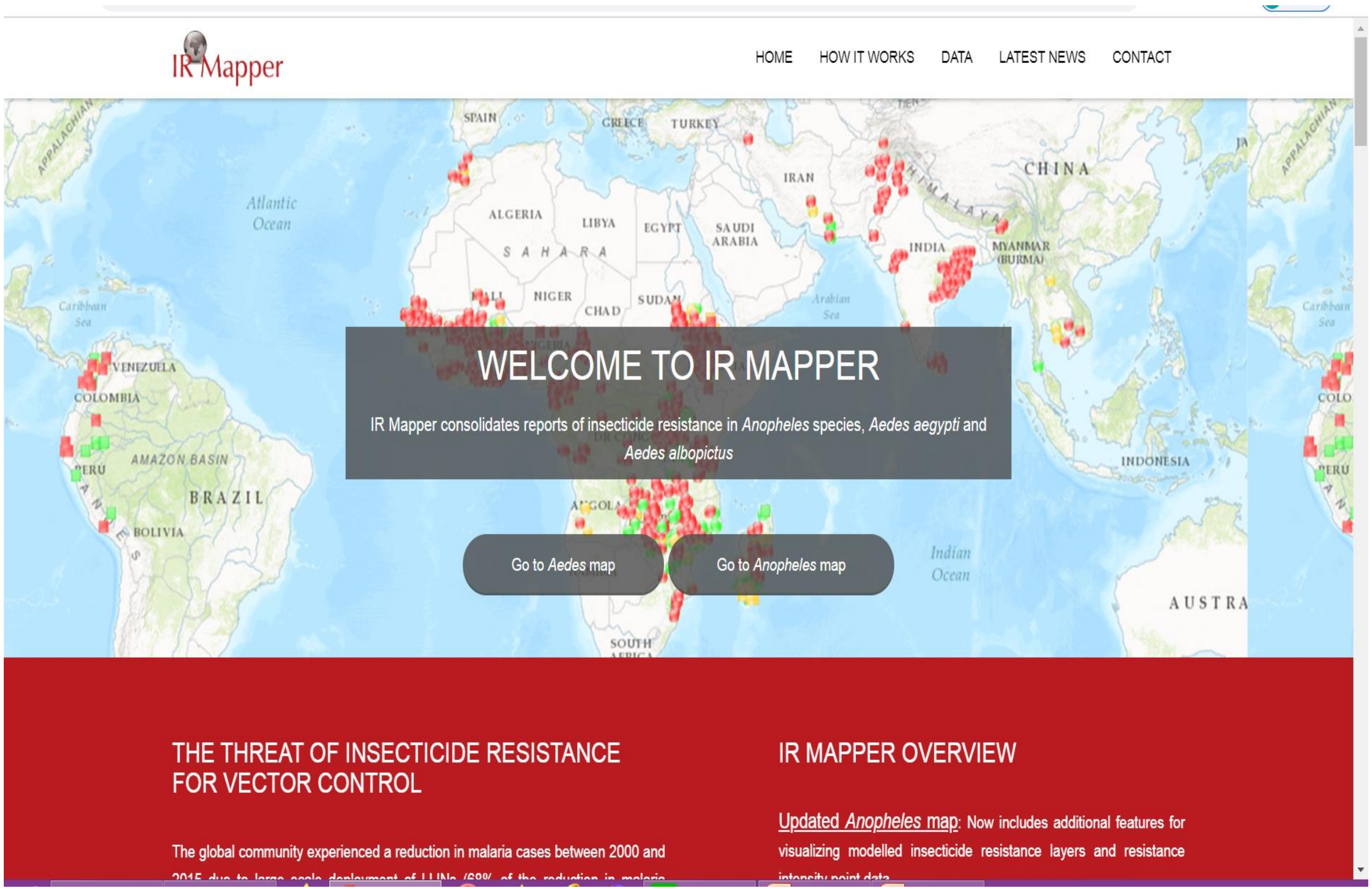
Moving away from treated surfaces

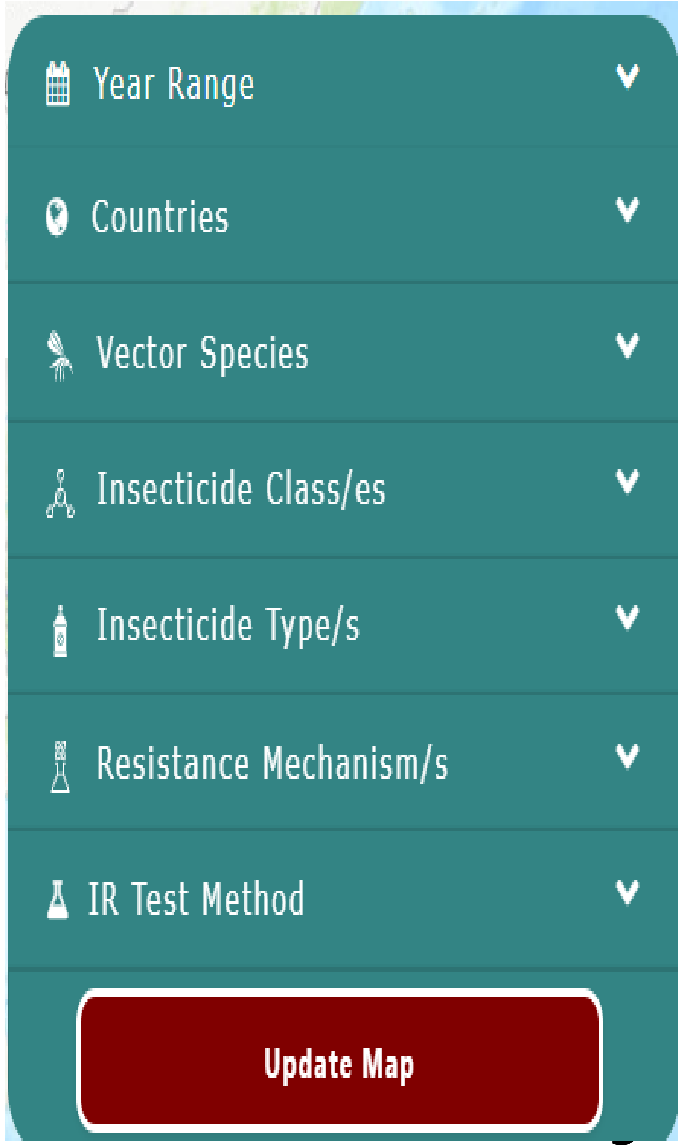
Spatial repellent

Contact irritant

Physiological resistance

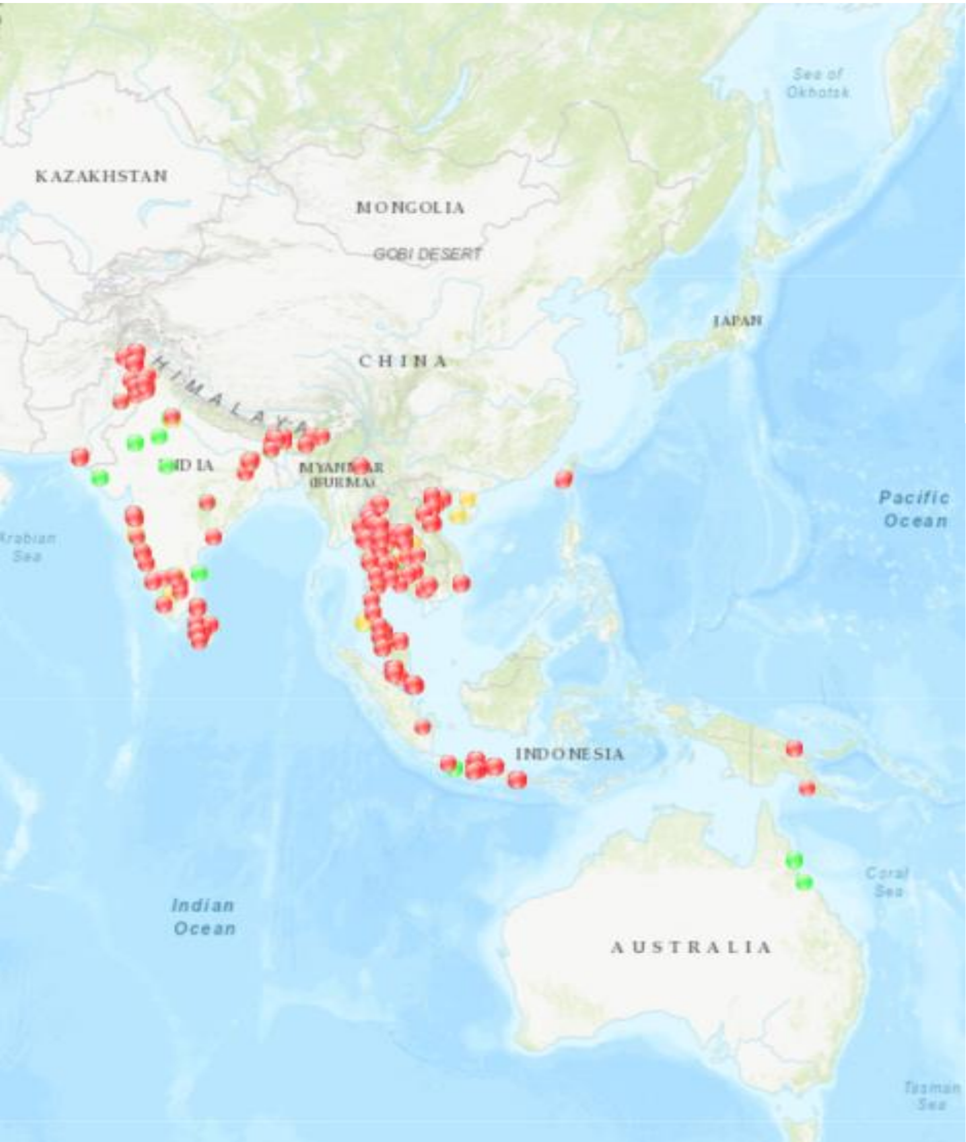
https://www.irmapper.com/





2005-2020: Resistance in *Aedes* mosquitoes for all compounds

Aedes aegypti **IR MAPPER PROGRAM** ***Aedes albopictus***



On | Confirmed Resistance

On | Possible Resistance

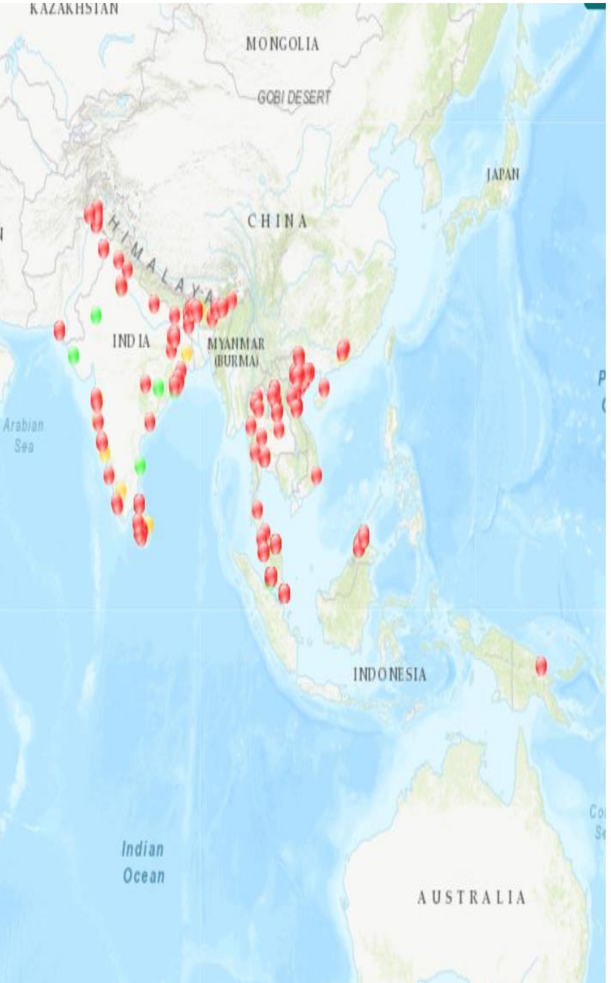
On | Susceptibility

CDC Bottle Assay

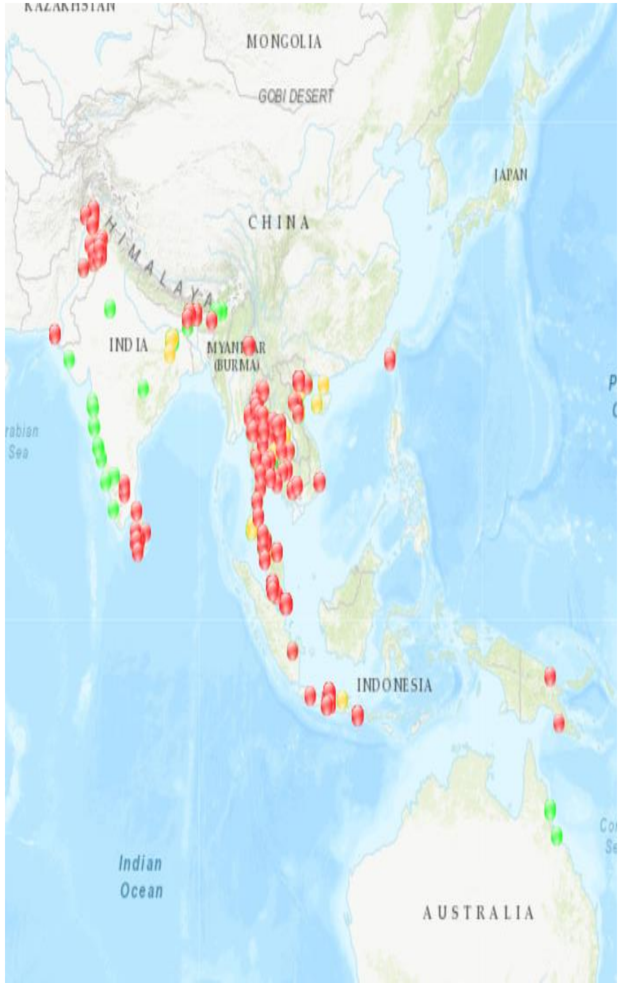
WHO Susceptible test

2005-2020: *Aedes aegypti* and *Aedes albopictus* resistance

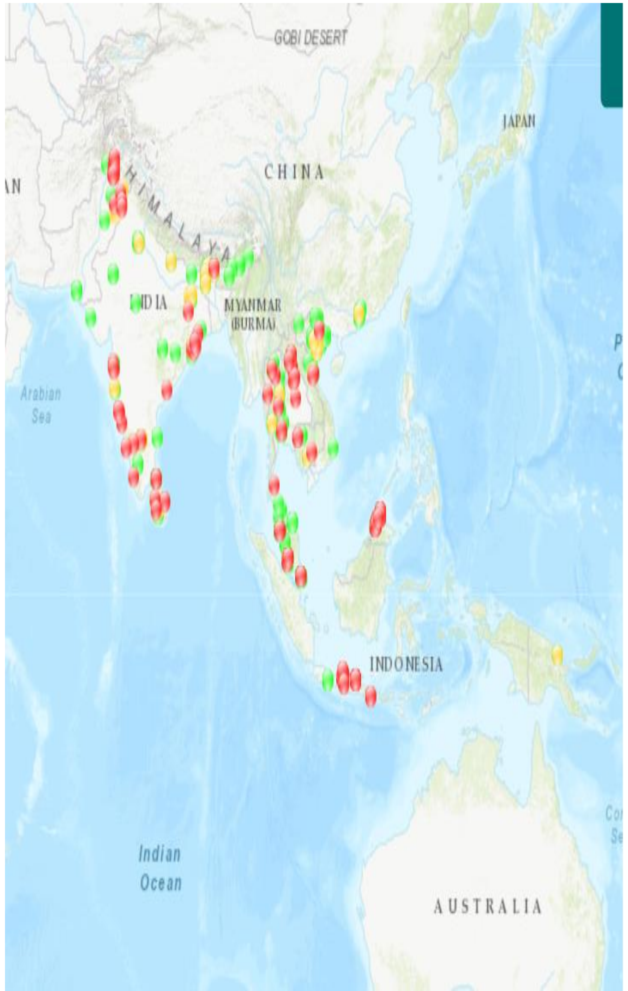
Organochlorines



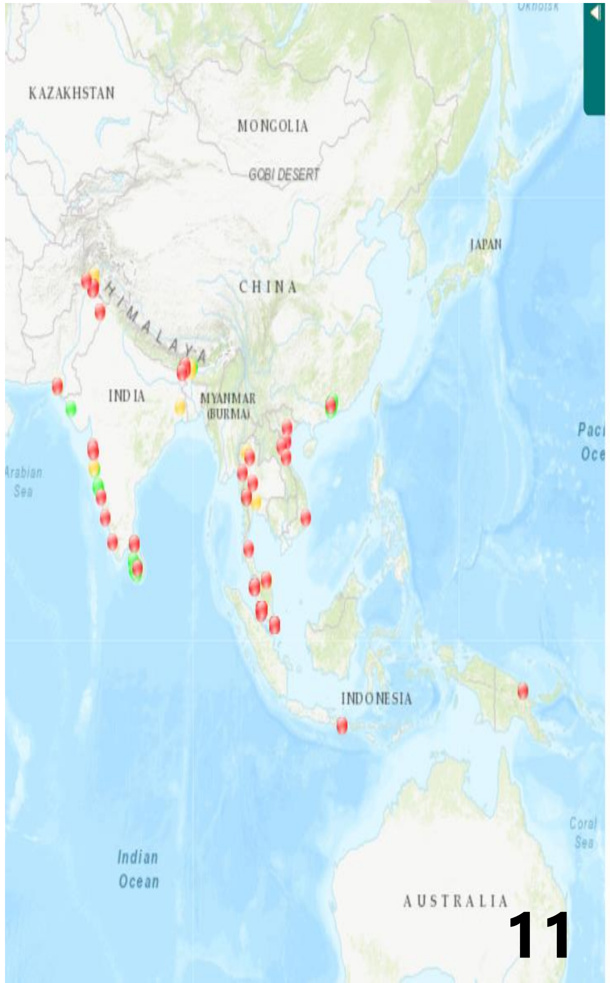
Pyrethrpoids



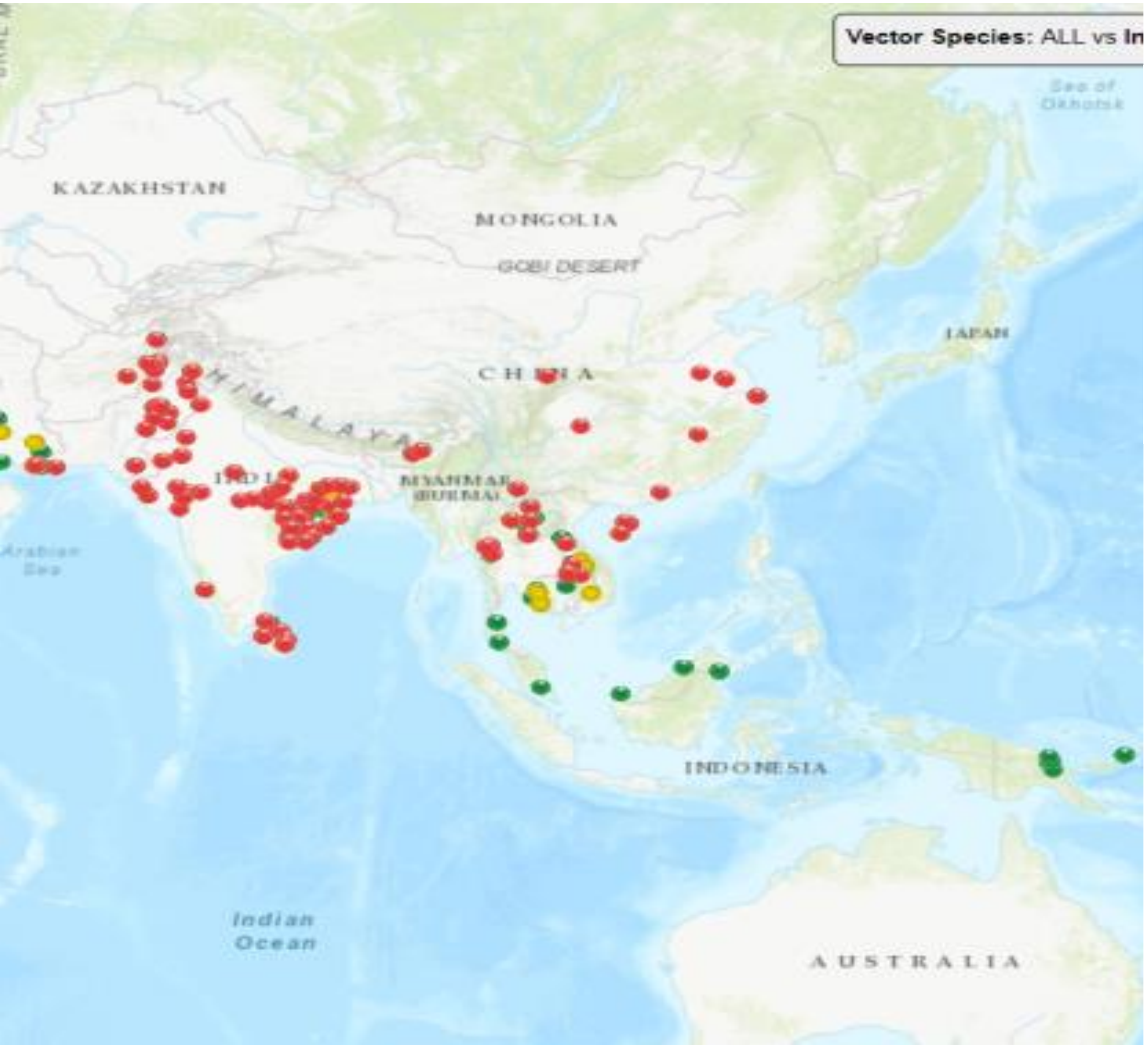
Organophosphates



Carbamates



2005-2020: Resistance in *Anopheles* for all compounds

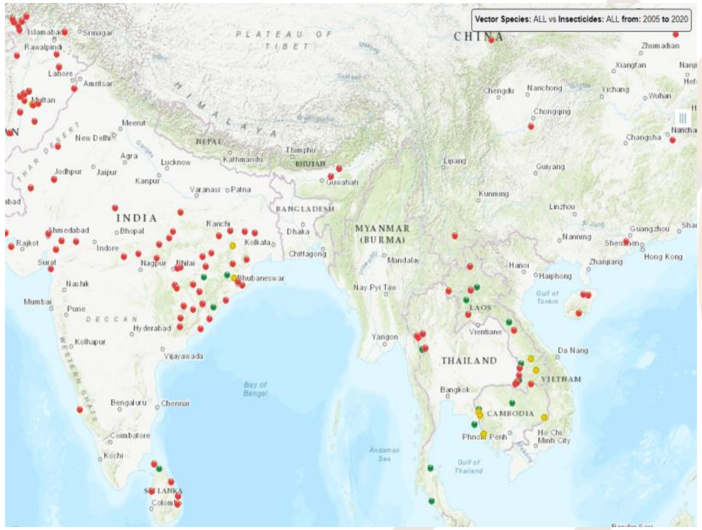


On | Confirmed Resistance

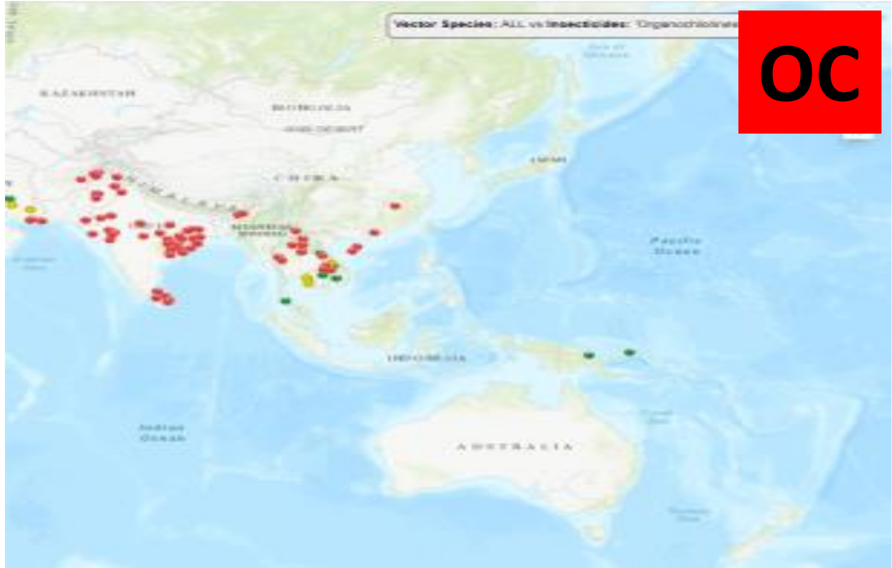
On | Possible Resistance

On | Susceptibility

All test assays



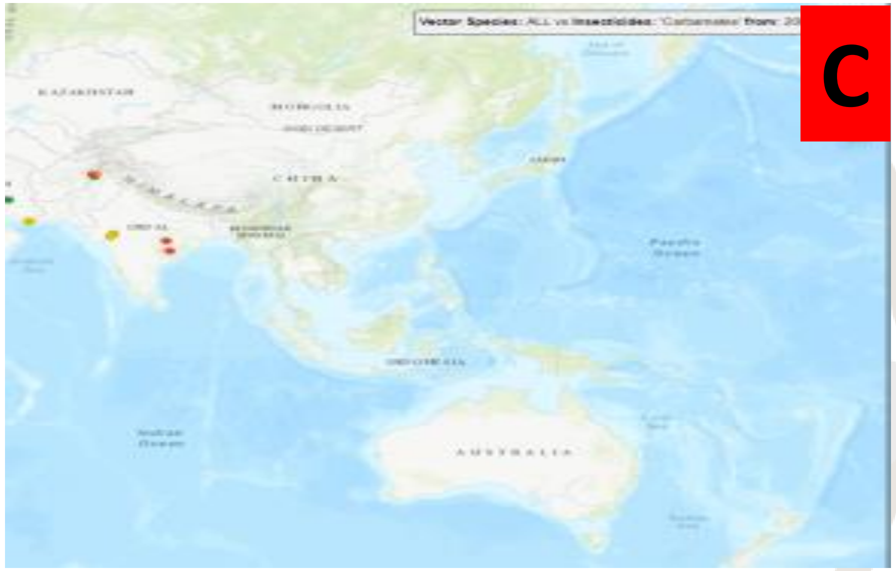
2005-2020: Resistance in *Anopheles* for all four insecticide classes



On | Confirmed Resistance

On | Possible Resistance

On | Susceptibility



Aedes mosquitoes: resistance to temephos in GMS countries

Journal of Medical Entomology, 57(4), 2020, 1207–1220
doi: 10.1093/jme/tjaa035
Advance Access Publication Date: 11 March 2020
Research

Vector Control, Pest Management, Resistance, Repellents

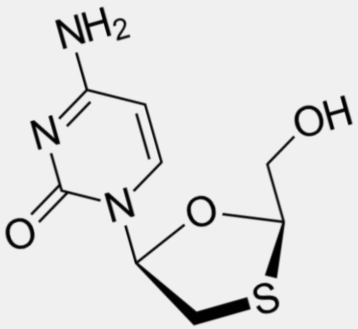
OXFORD

Susceptibility of *Aedes aegypti* and *Aedes albopictus* (Diptera: Culicidae) to Temephos in Thailand and Surrounding Countries

Manop Saeung,[1] Ratchadawan Ngoen-Klan,[1] Kanutcharee Thanispong,[2] Vithee Muenworn,[3] Michael J. Bangs,[1,4] and Theeraphap Chareonviriyaphap[1,5]

Aedes mosquitoes: resistance to temephos in GMS countries

"Temephos" remains the most commonly used compound to control immature stages of mosquitoes in the national dengue control program (Chareonviriyaphap *et al.*, 1999; 2013).



https://www.matichon.co.th/news-monitor/news_1543117

Aedes mosquitoes: resistance to temephos in GMS countries

Findings were interpreted following the WHO (2016) criteria; wherein

1. **Confirmed resistance** if mortality **< 90%**
2. **Suspected resistance** if **90 <** mortality < **97%**
3. **Susceptible** if mortality > **98-100%.**

An open-source **QGIS** program was used to map detected temephos resistance in *Ae. aegypti* and *Ae. albopictus* compiled from previous publications and survey data in Thailand as well as surrounding countries (1999-2019)

Distribution of *Aedes aegypti* found resistant to temephos:1999-2019

Published Source

Published sources: 34 (1999 - 2019)
Collection locations : 283

Thailand: 207 locations (17 pubs)
Lao PDR: 19 locations (3 pubs)
Cambodia: 10 locations (2 pubs)
Myanmar: 5 locations (2 pubs)
Malaysia: 35 locations (9 pubs)
Singapore: 7 locations (1 pub)

Locations with *Ae. aegypti* (262) and *Ae. albopictus* (39), respectively

Thailand: 206 and 11
Lao PDR: 12 and 7
Cambodia: 10 and 0
Myanmar: 5 and 0
Malaysia: 22 and 21
Singapore: 7 and 0

Locations with temephos resistance *Ae. aegypti* (100) and *Ae. albopictus* (22), respectively

Thailand: 73 and 3
Lao PDR: 9 and 3
Cambodia: 6 and 0
Myanmar: 0
Malaysia: 12 and 16
Singapore: 0

80% from Thailand

122

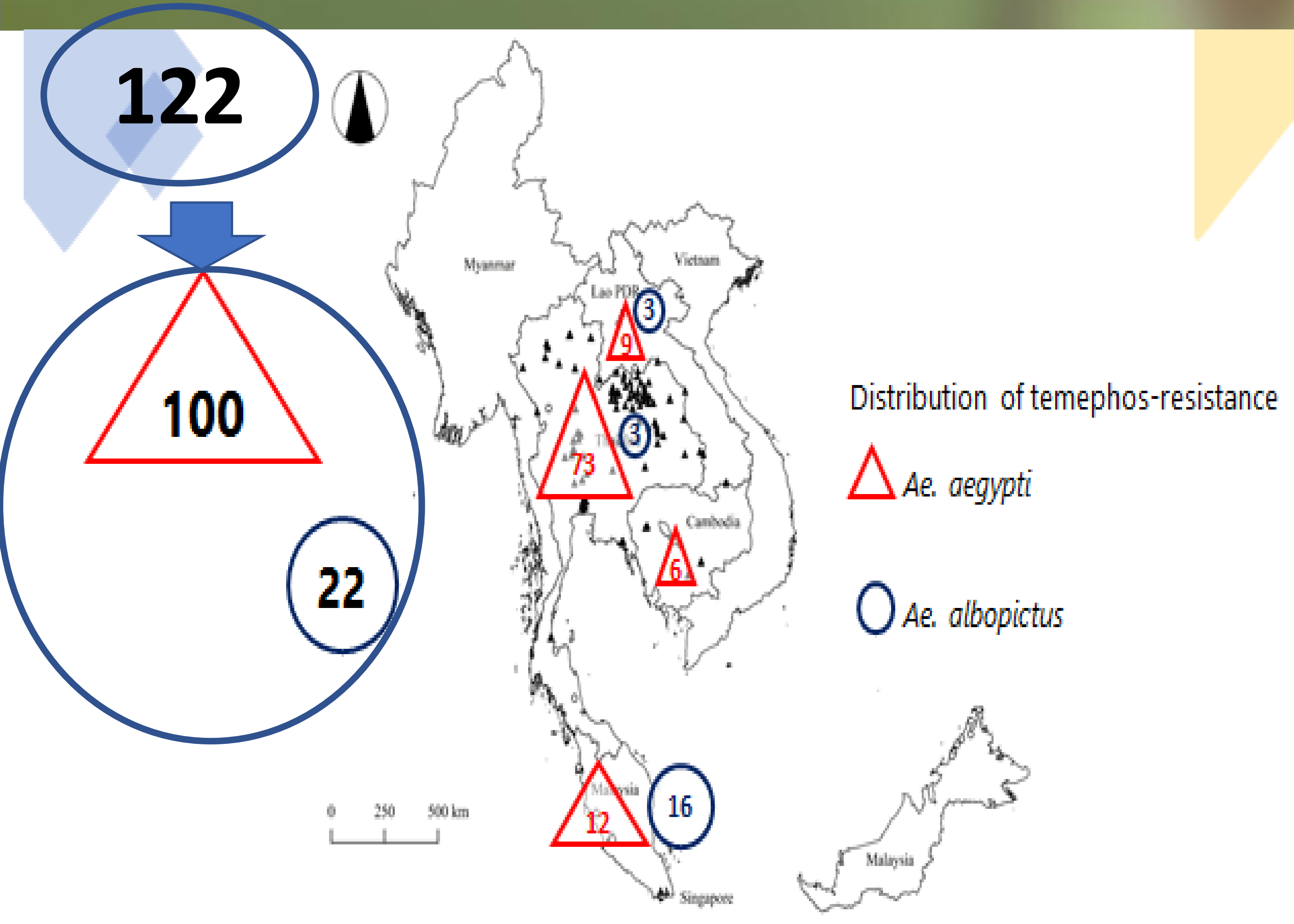
Experimental Data

Experimental data (2014-2018)
Collection locations: 62

Thailand - *Ae. aegypti* only.
Locations with temephos resistance: 15

62

Distribution of *Aedes aegypti* and *Aedes albopictus* found resistant to temephos in GMS countries (1999-2019)



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Susceptibility of *Aedes aegypti* and *Aedes albopictus* (Diptera: Culicidae) to Temephos in Thailand and Surrounding Countries

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Subject Editor: David Florin

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Abstract

Aedes-borne virus disease control relies on insecticides to interrupt transmission. Temephos remains a key chemical for control of immature stage *Aedes* in Thailand and much of Southeast Asia. However, repeated use of insecticides may result in selection for resistance in vector populations, thus compromising operational intervention. Herein, the phenotypic response to temephos by *Aedes aegypti* (L.) and *Aedes albopictus* (Skuse) collected in Thailand and surrounding countries is presented. Data from 345 collection sites are included: 283 from literature review (244 sites with *Ae. aegypti*, 21 with *Ae. albopictus*, and 18 having both species sampled), plus 62 locations with *Ae. aegypti* in Thailand conducted between 2014 and 2018. Susceptibility assays followed WHO guidelines using the recommended discriminating dose of temephos (0.012 mg/liter) against late third to early fourth instar *Ae. aegypti*. Findings revealed 34 locations with susceptible *Ae. aegypti*, 13 with suspected resistance, and 15 indicating resistance. Published data between 1999 and 2019 in Thailand found *Ae. aegypti* resistant in 73 of 206 collection sites, whereas 3 locations from 11 sampled with low-level resistant in *Ae. albopictus*. From surrounding countries conducting temephos assays (Cambodia, Lao PDR, Myanmar, Malaysia, and Singapore), resistance is present in *Ae. aegypti* and *Ae. albopictus* from 27 of 56 and 19 of 28 locations, respectively. Routine insecticide susceptibility monitoring should be an operational requirement in vector control programs. Given the wide distribution and apparent increase in temephos-resistance, alternative larvicidal compounds must be considered if chemical control is to remain a viable vector control strategy.

Behavioral avoidance

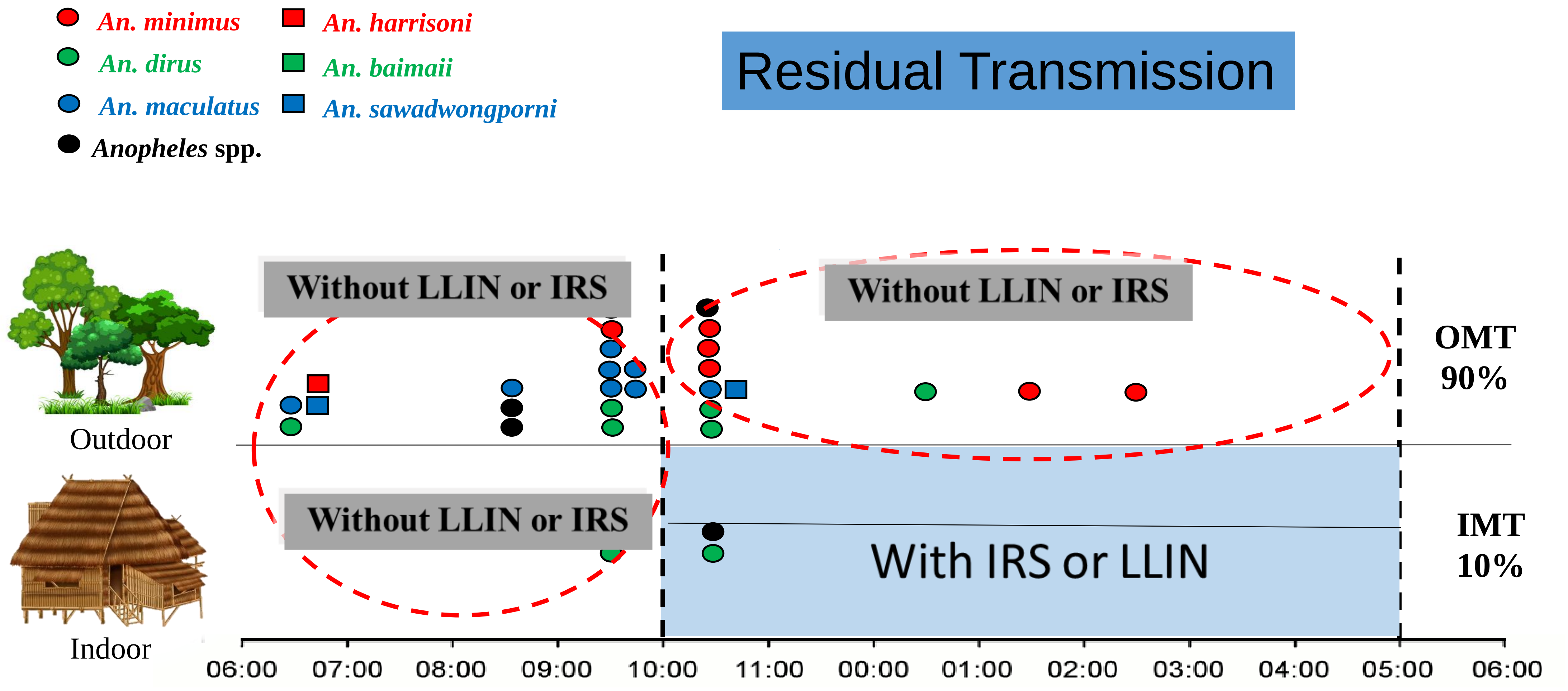
Moving away from treated surfaces → Contact irritant

Moving away from treated surfaces → Spatial repellent

Bed net and Indoor Residual Spray

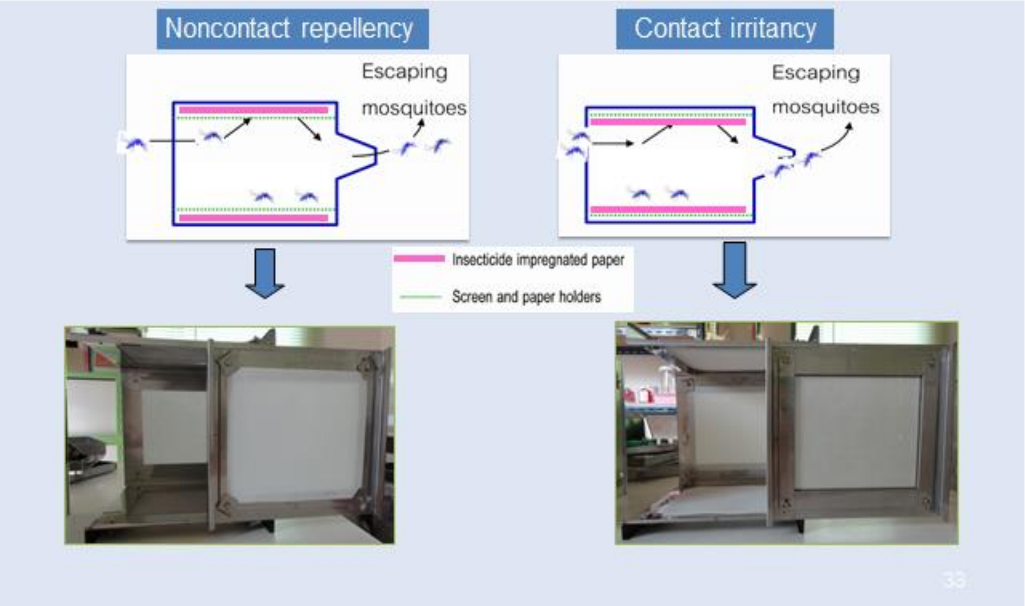
GMS: Malaria transmission has no longer been protected by LLIN or IRS

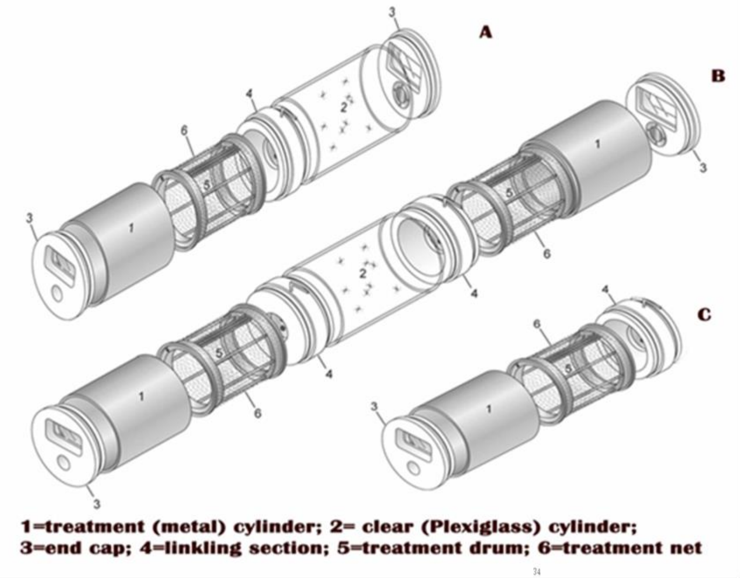
Residual Transmission



Behavioral traits of *Anopheles* mosquitoes in the Greater Mekong Sub-region (GMS)

Behavioral avoidance





Contact irritant

Spatial repellent

Toxicant

Journal of Vector Ecology
Volume 27, Issue 2, December 2002, Pages 250-252

An improved excito-repellency test chamber for mosquito behavioral tests (Article)

Chareonviriyaphap, T.[a], Prabaripai, A.[b], Sungvornyothrin, S.[a]

Save all to author list

[a]Department of Entomology, Faculty of Agriculture, Kasetsart University, Bangkean, Bangkok 10900, Thailand
[b]Faculty of Liberal Arts and Science, Kasetsart University, Kamphaengsean Campus, Nakhon Fathom 73140, Thailand

PLoS ONE Open Access
Volume 2, Issue 8, 8 August 2007, Article number e716

A new classification system for the actions of IRS chemicals traditionally used for malaria control (Article) (Open Access)

Grieco, J.P.[a], Achee, N.L.[a], Chareonviriyaphap, T.[b], Suwonkerd, W.[c], Chauhan, K.[d], Sardelis, M.R.[a], Roberts, D.R.[a]

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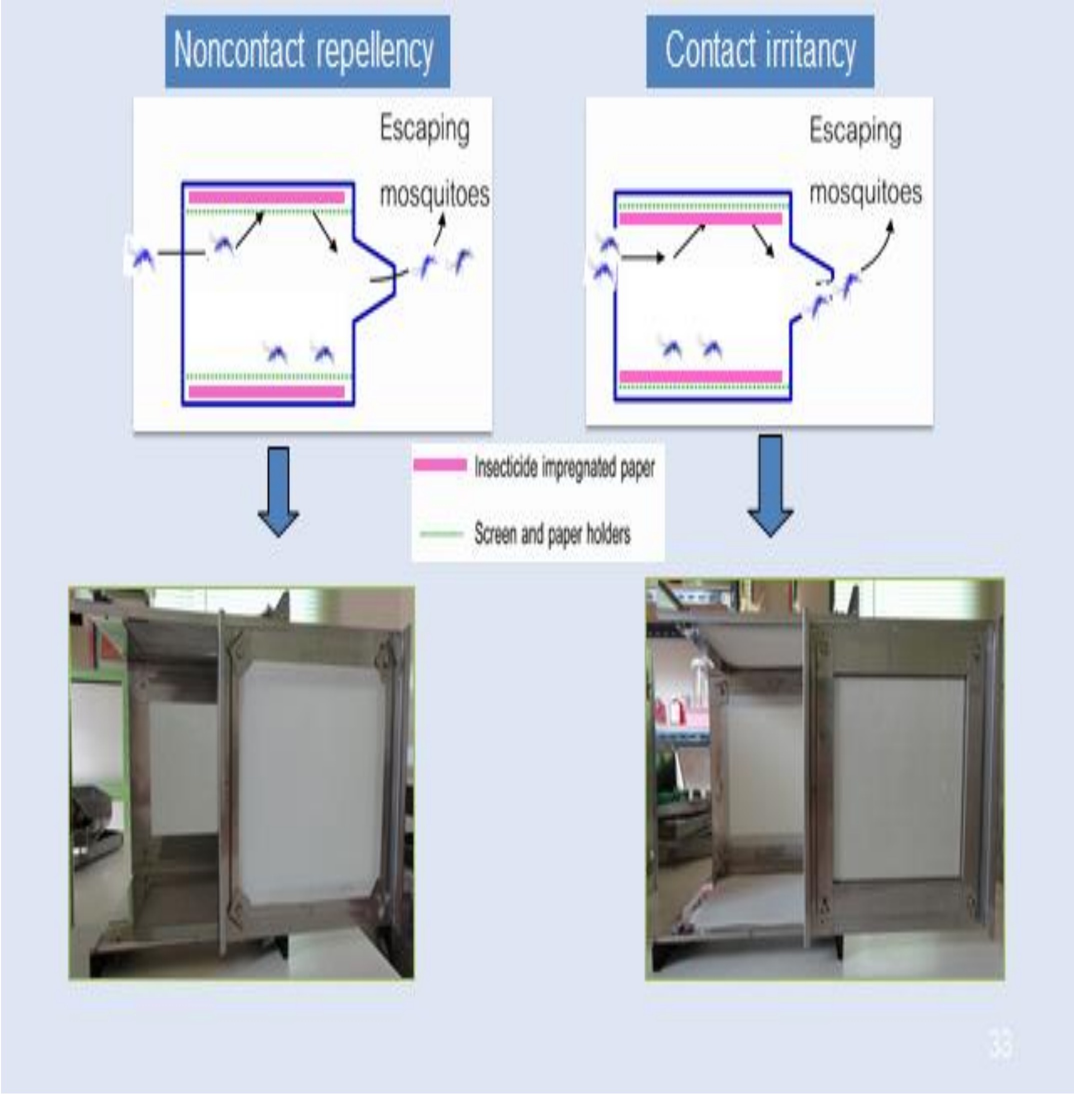
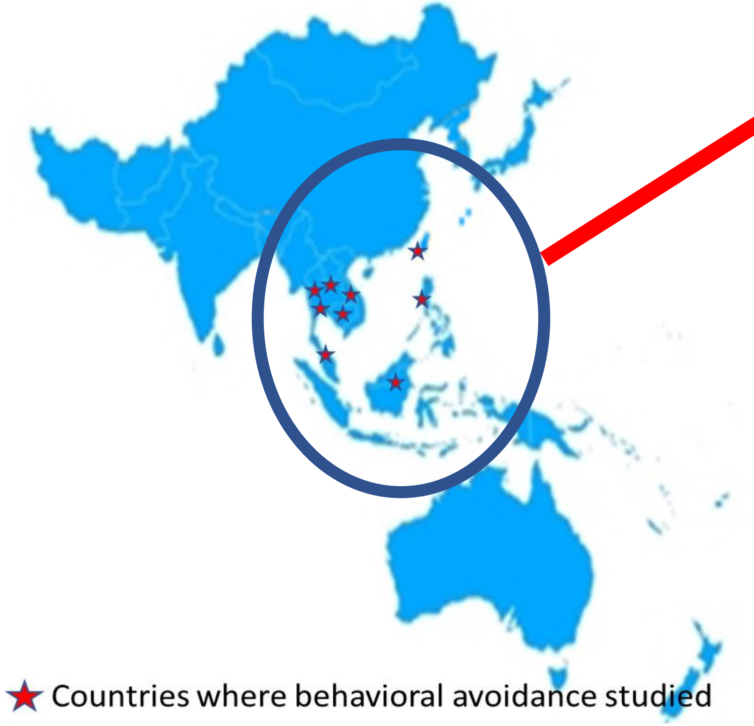
View additional affiliations

Behavioral avoidance





Aedes aegypti

Strong behavioral responses to all test compounds

Behavioral avoidance

Evidence of behavioral avoidance responses to insecticides in Anopheles populations

Species	Field/Lab	Dose	Insecticide	Location (province-district)	Published source
Anopheles minimus A*	Lab	2.00 g/m^2	DDT	Phrae-Rong Klang	Chareonviriyaphap *et al.* 2001[125]
		0.0625 g/m^2	Deltamethrin	Phrae-Rong Klang	
		0.0369 g/m^2	Lambdacyhalothrin	Phrae-Rong Klang	
Anopheles minimus complex	Field	2.00 g/m^2	DDT	Kanchanaburi-Pu Teuy	
		0.0625 g/m^2	Deltamethrin	Kanchanaburi-Pu Teuy	
		0.0369 g/m^2	Lambdacyhalothrin	Kanchanaburi-Pu Teuy	
Anopheles minimus A*	Lab	0.02 g/m^2	Deltamethrin	Phrae-Rong Klang	Chareonviriyaphap *et al.* 2004[70]
Anopheles dirus B†	Lab	0.02 g/m^2	Deltamethrin	Chantaburi-Ban Paung	
Anopheles minimus complex	Field	0.02 g/m^2	Deltamethrin	Kanchanaburi-Pu Teuy	
Anopheles maculatus B‡	Lab	0.02 g/m^2	Deltamethrin	Tak-Mae Sot	
Anopheles swadwongporni	Field	0.02 g/m^2	Deltamethrin	Kanchanaburi-Pu Teuy	
Anopheles dirus complex	Field	0.02 g/m^2	Deltamethrin	Kanchanaburi-Pu Teuy	
Anopheles minimus A*	Field	2.00 g/m^2	DDT	Tak-Mae-Sot	Potikasikorn *et al.* 2005[127]
		0.02 g/m^2	Deltamethrin	Tak-Mae-Sot	
		0.03 g/m^2	Lambdacyhalothrin	Tak-Mae-Sot	
Anopheles minimus C§	Field	2.00 g/m^2	DDT	Kanchanaburi-Pu Teuy	
		0.02 g/m^2	Deltamethrin	Kanchanaburi-Pu Teuy	
		0.03 g/m^2	Lambdacyhalothrin	Kanchanaburi-Pu Teuy	

Species	Field/Lab	Dose	Insecticide	Location	Published source
Anopheles maculatus B‡	Lab	0.02 g/m^2	Deltamethrin	Tak-Mae Sot	
Anopheles swadwongporni	Field	0.02 g/m^2	Deltamethrin	Kanchanaburi-Pu Teuy	
Anopheles dirus complex	Field	0.02 g/m^2	Deltamethrin	Kanchanaburi-Pu Teuy	
Anopheles minimus A*	Field	2.00 g/m^2	DDT	Tak-Mae-Sot	Potikasikorn *et al.* 2005[127]
		0.02 g/m^2	Deltamethrin	Tak-Mae-Sot	
		0.03 g/m^2	Lambdacyhalothrin	Tak-Mae-Sot	
Anopheles minimus C§	Field	2.00 g/m^2	DDT	Kanchanaburi-Pu Teuy	
		0.02 g/m^2	Deltamethrin	Kanchanaburi-Pu Teuy	
		0.03 g/m^2	Lambdacyhalothrin	Kanchanaburi-Pu Teuy	
Anopheles maculatus	Field	2.00 g/m^2	DDT	Kanchanaburi-Pu Teuy	Muenworn *et al.* 2006[137]
		0.5 g/m^2	Permethrin	Kanchanaburi-Pu Teuy	
Anopheles swadwongporni	Field	2.00 g/m^2	DDT	Kanchanaburi-Pu Teuy	
		0.5 g/m^2	Permethrin	Kanchanaburi-Pu Teuy	
Anopheles minimus A*	Field	0.04 g/m^2	Cypermethrin	Kanchanaburi-Pu Teuy	Pothikasikorn *et al.* 2007[138]
		0.04 g/m^2	Carbaryl	Kanchanaburi-Pu Teuy	
		0.19 g/m^2	Malathion	Kanchanaburi-Pu Teuy	
Anopheles minimus C§	Field	0.04 g/m^2	Cypermethrin	Kanchanaburi-Pu Teuy	
		0.04 g/m^2	Carbaryl	Kanchanaburi-Pu Teuy	
		0.19 g/m^2	Malathion	Kanchanaburi-Pu Teuy	
Anopheles harrisoni	Field	0.03 g/m^2	Bifenthrin	Kanchanaburi-Pu Teuy	Tisgratog *et al.* 2011[139]
Anopheles minimus	Field	0.03 g/m^2	Bifenthrin	Tak-Mae Sot	

With the exception of one population (*An. minimus* s.s. in Tak Province/Mae Sot District to DDT) all species show contact excitation (irritancy) as the predominant response versus noncontact spatial repellency.

*Published as *Anopheles minimus* A, now formally named *Anopheles minimus* s.s.; †*Anopheles dirus* B now as *Anopheles crascens*; ‡*Anopheles maculatus* B as *Anopheles maculatus* s.s.[66] and § *Anopheles minimus* C as *Anopheles harrisoni*.

Evidence of behavioral avoidance responses to insecticides in *Aedes aegypti and Culex quinquefasciatus* populations (2000–2011)

Species	Field/Lab	Dose	Insecticide	Location	Published source
Aedes aegypti	Field	0.02 g/m^2	Deltamethrin	Bangkok	Kongmee *et al.* 2004[126]
Aedes aegypti	Field	0.02 g/m^2	Deltamethrin	Pathum Thani	
Aedes aegypti	Field	0.02 g/m^2	Deltamethrin	Nonthaburi	
Aedes aegypti	Lab	0.02 g/m^2	Deltamethrin	Ayutthaya	
Aedes aegypti	Lab	0.02 g/m^2	Deltamethrin	Bangkok	
Aedes aegypti	Lab	0.25 g/m^2	Permethrin	Nonthaburi	Paeporn *et al.* 2007[97]
Aedes aegypti	Field	0.025 g/m^2	Alphacypermethrin	Kanchanaburi	Thanispong *et al.* 2009[140]
		2.00 g/m^2	DDT	Kanchanaburi	
Aedes aegypti	Field	0.025 g/m^2	Alphacypermethrin	Chiang Mai	
		2.00 g/m^2	DDT	Chiang Mai	
Aedes aegypti	Lab	0.025 g/m^2	Alphacypermethrin	USDA	
		2.00 g/m^2	DDT	USDA	
Aedes aegypti	Field	0.010%	Deltamethirn	Kanchanaburi	Mongkalagoon et al. 2009[141]
		0.0113%	Cyphenothrin	Kanchanaburi	
		2.091%	d-Tetramethrin	Kanchanaburi	
		2.377%	Tetramethrin	Kanchanaburi	
Aedes aegypti	Field	0.05%	Alphacypermethrin	Chiang Mai	Thanispong *et al.* 2010[142]
		0.05%	Deltamethrin	Chiang Mai	
		0.25%	Permethrin	Chiang Mai	
		4.00%	DDT	Chiang Mai	
Aedes aegypti	Field	0.05%	Alphacypermethrin	Kanchanaburi	
		0.05%	Deltamethrin	Kanchanaburi	
		0.25%	Permethrin	Kanchanaburi	

Species	Field/Lab	Dose	Insecticide	Location	Published source
Aedes aegypti	Field	0.05%	Alphacypermethrin	Khon Kean	
		0.05%	Deltamethrin	Khon Kean	
		0.25%	Permethrin	Khon Kean	
		4.00%	DDT	Khon Kean	
Aedes aegypti	Field	0.05%	Alphacypermethrin	Nonthaburi	
		0.05%	Deltamethrin	Nonthaburi	
		0.25%	Permethrin	Nonthaburi	
		4.00%	DDT	Nonthaburi	
Aedes aegypti	Field	0.05%	Alphacypermethrin	Songkhla	
		0.05%	Deltamethrin	Songkhla	
		0.25%	Permethrin	Songkhla	
		4.00%	DDT	Songkhla	
Aedes aegypti	Field	0.05%	Alphacypermethrin	Satun	
		0.05%	Deltamethrin	Satun	
		0.25%	Permethrin	Satun	
		4.00%	DDT	Satun	
Culex quinquefasciatus	Field	0.02 g/m^2	Deltamethrin	Nonthaburi	
		0.20 g/m^2	Fenitrothion	Nonthaburi	
		0.20 g/m^2	Propoxur	Nonthaburi	Sathantriphop *et al.* 2006[113]
Culex quinquefasciatus	Field	0.02 g/m^2	Deltamethrin	Tak	
		0.20 g/m^2	Fenitrothion	Tak	
		0.20 g/m^2	Propoxur	Tak	
Culex quinquefasciatus	Lab	0.02 g/m^2	Deltamethrin	Nonthaburi	
		0.20 g/m^2	Fenitrothion	Nonthaburi	

CONCLUSION

Insecticide resistances can be classified into **two categories: physiological (biochemical resistance) and behavioral avoidance.**

Mosquito vectors **resistance** (physiological) to the insecticides and types of resistance mechanisms are now well-documented on **the IR MAPPER program for all regions.**

Although the frequency and coverage in reporting insecticide resistance is incomplete and potentially skewed in geographical representation, there is evidence indicating an **increasing trend in the development of resistance** in the country.

Behavioral avoidance to all classes of insecticides has been documented in all mosquito species with the greatest responses to pyrethroids.

Perspectives and Recommendation

1.It is imperative that **routine insecticide susceptibility monitoring** be established and broadened in both coverage and frequency in the whole region.

2.Quite often, there is **insufficient wild caught Anopheles mosquitoes** that could be carried out to assess the susceptibility of populations of primary and secondary malaria vectors to insecticides or to carry out contact bioassays of LLINs and sprayed surfaces

3.Diagnostic dose for each local species by **determination of specific baseline discriminating concentration** of currently used insecticides for vector control is a crucial starting point for monitoring of resistance.

4.**Behavioral avoidance of mosquito vectors** to insecticides are important component of insecticide and disease control equation. **More field research is needed** on the responses of mosquito vectors from different geographic locations to various insecticides

Perspectives and Recommendation (Cont.)

5.Searching for **alternative interventions to minimize the further resistance evolution** as well as to preserve the efficiency of existing insecticides is needed.

6.Exploration of **next generation vector control tools in terms of nets and new classes of non-pyrethroid insecticide formulation** with new mode of action.

7.**Strenghthen partnerships** in the vector control from public health experts, policy-makers, researchers, public health entomologists and private sectors are crucial.

Thank you