IVCC
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Creating Solutions
Saving Lives

Vector Control in the Indo-Pacific: Technical, Regulatory and Market Access Landscapes

INNOVATIVE VECTOR CONTROL CONSORTIUM

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Contents

Glossary

APLMA	Indo-Pacific Malaria Leaders Alliance
API	Annual Parasite Incidence
APMEN	Indo-Pacific Malaria Elimination Network
ATSB	Attractive toxic sugar bait
BMGF	Bill & Melinda Gates Foundation
CRCT	Cluster randomized controlled trial
DFAT	Department of Foreign Affairs and Trade (Australia)
DIY	Do It Yourself
DPRK	Democratic People's Republic of Korea
EUP	Experimental Use Permit
GMS	Greater Mekong Subregion
HRP	High risk population
IOM	International Office of Migration
IRS	Insecticide residual spraying
ITC	Insecticide treated clothing
ITM	Insecticide treated material
ITN	Insecticide treated net
IVCC	Innovative Vector Control Consortium
IVM	Integrated vector management
JE	Japanese encephalitis
LF	Lymphatic filariasis
LLIHN	Long last insecticide treated hammock net
LLIN	Long lasting insecticide treated net
LSM	Larval source management
MAP	Malaria Atlas Project
MOH	Ministry of Health
ORS	Outdoor residual spraying
PBO	piperonyl butoxide
PCO	Pest control operator
PCR	Polymerase Chain Reacton
PMI	President's Malaria Initiative (US)
PQ	Pre-Qualification (WHO)
RAI2E	Global Fund Regional Artemisinin Initiative to Eliminate Malaria
RIDL	Release of Insects with Dominant Lethal
s.l.	senso lato
s.s.	senso stricto
SEARO	South East Asia Regional Office (WHO)
SIT	Sterile Insect Technique
UCSF	University of California, San Francisco
ULV	Ultra-low volume (spraying)
USEPA	United States Environmental Protection Agency
VCAG	Vector Control Advisory Group (WHO)
VL	Visceral leishmaniasis
WHO	World Health Organization
WPRO	Western Pacific Regional Office (WHO)

Acknowledgements:

With funding from the Department of Foreign Affairs and Trade (DFAT), Australia, IVCC commissioned the three related landscape analyses:

Technical Landscape Analysis: Report prepared by the University of California, San Francisco (UCSF) Global Health Group's Malaria Elimination Initiative. The research team included: Allison Tatarsky, UCSF Malaria Elimination Initiative; Michael Macdonald, Consultant; Neil Lobo, UCSF Malaria Elimination Initiative and University of Notre Dame; Elodie Vajda, UCSF Malaria Elimination Initiative; Tom Burkot, James Cook University.

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Regulatory Landscape Analysis: Report prepared by Vasanthan Paul John, Consultant for IVCC.

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Market Access Landscape Report: Report prepared by FutureBridge (FB) Asia Pacific Market Access Team, India.

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Background and objectives

In 2018, the IVCC received a five-year grant from the Australia Department of Foreign Affairs and Trade (DFAT) to develop and disseminate vector control technologies for malaria and other vector-borne diseases in the Indo-Pacific region. As a first step, IVCC commissioned the University of California, San Francisco, Global Health Group's Malaria Elimination Initiative (MEI) to conduct a vector control technical landscape analysis; Vasanthan John Paul to conduct a regulatory landscape; and FutureBridge to conduct a Market Access landscape.

Technical Landscape objectives include:

1. Describe mosquito-borne disease transmission ecology across the region and by country, including the biological challenges to controlling disease
2. Document ministry of health vector borne disease strategic and technical priorities and gaps, capacity, and emergency response
3. Gather information on vector control products available by market type and delivery pathways
4. Identify gaps in protection based on disease transmission and implemented intervention strategies
5. Develop broad target product profiles based on gaps in protection

Regulatory Landscape objectives include:

1. Map the regulatory requirements and processes in the focus countries.
2. Collate the information on the regulatory authority and the framework of regulations in the country for Vector Control Products
3. To compare and evaluate the registration processes in the various focus countries and their outlook on regulating Vector Control Products.
4. To ascertain the influence of WHO or other regional regulatory authorities in the registration process in the country.
5. To analyze the barriers and the gaps in the regulatory process that hinder the registration of the products

Market Access landscape objectives include:

1. To study the vector control market, and market access landscape, by type of market, vector control implementing organizations, and consumers, including an understanding of regulatory pathways.
2. To map and provide a better understanding of procurement channels for vector control products and their barriers.
3. To perform a detailed market study for 6 countries in the Indo-Pacific region, namely, Indonesia, Myanmar, Cambodia, Vietnam, Malaysia, and Papua New Guinea (PNG).

Methods

Technical Landscape

The inclusion criteria for the analysis included three mosquito genera (*Anopheles*, *Aedes*, and *Culex*) and five mosquito-borne diseases (malaria, dengue, Zika, chikungunya, lymphatic filariasis, and Japanese encephalitis). We used a mixed-methods approach in a three-part analysis:

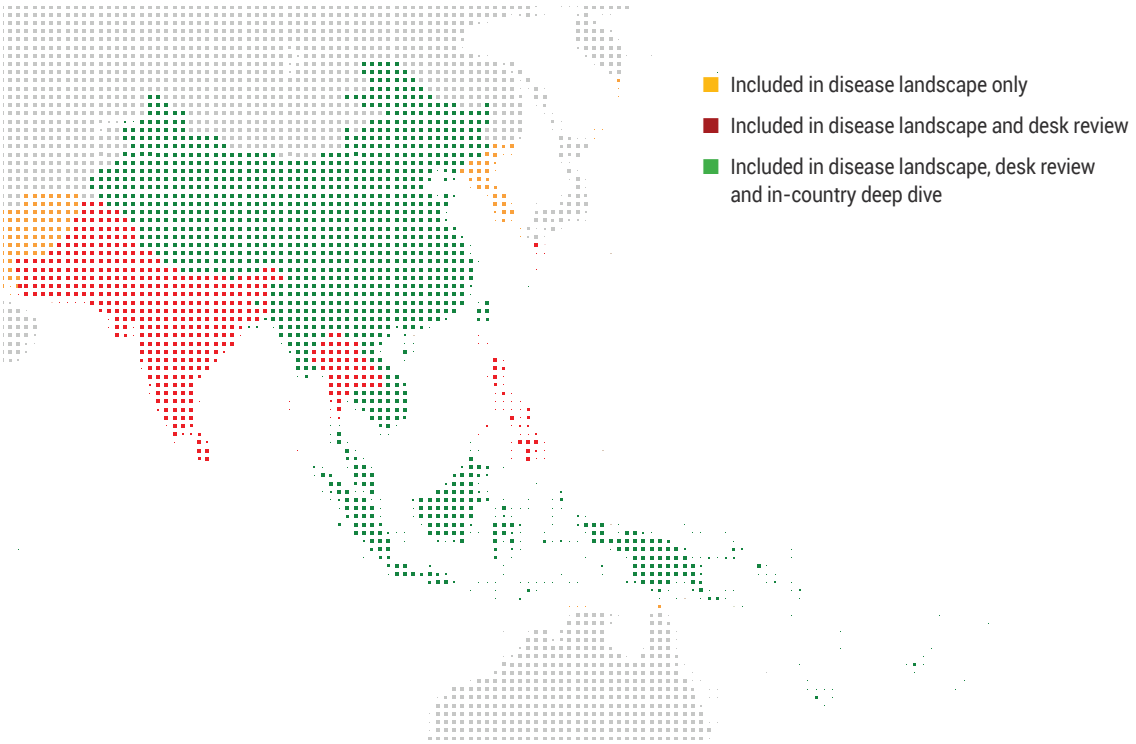
Disease landscape: UCSF mapped and analyzed descriptive statistics of diseases and vectors across the region based on data from the Malaria Atlas Project, World Health Organization (WHO), and United States and European Centers for Disease Control and Prevention (CDC), country reports, and peer-reviewed literature.

Desk review: Grey and peer-reviewed literature were reviewed and remote and in-person consultations conducted with key stakeholders and subject matter experts. Grey literature included WHO regional reports and reviews and resources from WHO Pre-Qualification (PQ) and the Vector Control Advisory Group (VCAG); ministry of health (MOH) reports, including malaria program reviews, annual reports, presentations, and Global Fund concept notes; Indo-Pacific Malaria Elimination Network (APMEN) reports; donor and partner reports; and Walter Reed Bioinformatics Unit (WRBU) reports, among others. Peer-reviewed literature was searched based on key information gaps, with a focus on systematic reviews of the vector control toolbox for malaria and *Aedes*-borne diseases. We conducted consultations with key stakeholders and subject matter experts at the American Society for Tropical Medicine and Hygiene (ASTMH) conference in October 2018 and Roll Back Malaria (RBM) Vector Control Working Group (VCWG) meeting in January 2019, as well as remotely by Skype.

In-depth country reviews: UCSF travelled to select countries (based on consultation with IVCC and DFAT) to conduct comprehensive key informant interviews based on a semi-structured interview guide and made site visits to research facilities where possible. The interview guide included specific questionnaires by key informant category: government, research institution, NGO implementing partner, private sector implementing partner (e.g. extractives industry, pest control operator, etc.), retail vendor, and vector control manufacturer. We also collected additional relevant grey literature. Twenty-four countries in the Indo-Pacific region were included in the disease landscape, 19 countries in the desk review, and eight countries in the country deep-dives (Figure 1).[1]

[1] In-depth country reviews: Cambodia, China, Indonesia, Malaysia, Myanmar, Papua New Guinea, Sri Lanka, Vietnam; Additional countries for desk review: Bangladesh, Bhutan, India, Lao PDR, Nepal, Pakistan, Philippines, Solomon Islands, Thailand, Timor Leste, and Vanuatu. Additional countries only for disease landscaping: Afghanistan, Fiji, North Korea, Samoa, and South Korea.

FIGURE 1. COUNTRIES INCLUDED IN THIS TECHNICAL LANDSCAPE ANALYSIS



Regulatory Pathways Landscape

The methodology adopted for collating information on regulatory pathways included:

1. A detailed questionnaire was developed taking into consideration all parameters of the regulatory processes
2. Questionnaires were shared with Vector control product manufacturers and suppliers, country agents / distributors, country regulatory contacts / experts
3. Information was also collected from country level regulatory websites, WHO portal, third party desk reviews.
4. The collected information was further validated by cross checking across industry and country level malaria elimination program leads

Market Access Landscape

Following methodology was adapted for market size estimation. It is a combination of desk research, primary research and analysis.

Step 1: Secondary Research

Secondary research involves desk research with respect to industry events, corporate activity, trends and new product introductions with the help of websites such as:

- National statistics offices
- National governmental and official sources
- National and international trade press
- National and international trade associations
- Industry study groups and other semi-official sources
- Company financials and annual reports
- Online databases e.g., Factiva, Bloomberg
- The financial, business and mainstream press

Step 2: Primary Research

Primary research involves interaction with global KOLs to gather local data, insights and also to validate findings from secondary research. The primary research will help to fill the gaps in remained after secondary research, generate a structure and strategic direction for data analysis and to gather expert's view on current trends and drivers.

Step 3: Company Analysis

With the use of secondary sources such as annual reports, broker reports, financial press and databases, we have built a top-down estimates of product sales of major key players at global and region level. For country level, we analysed national company database, local company websites along with insights from key opinion leaders.

Step 4: Data Validation

All data collected and derived, is subject to exhaustive review process using secondary and primary sources along with KOL analysis and country level modelling. Upon completion of the country data analysis, data was then reviewed on a comparative basis with trends of regional and global level. Comparative data checks are carried out on the basis of per capita consumption, spending capacity, growth rate, product category and sub-category and distribution of sales by channel. Top-down estimates are validated using bottom-up approach through regional and global market and company total sales.

Disclaimer and Limitations

The market size numbers are subjective as these are picked from multiple sources and these sources may have some limitation due to adopted methodology in terms of coverage, representation, and distribution. These numbers have been derived by FB analysis with inputs from primary and secondary research. Gaps were covered through assumptions which can always be challenged due to difference in approach, availability of base data, adopted methodology and coverage of primary research respondents.

Disease landscape

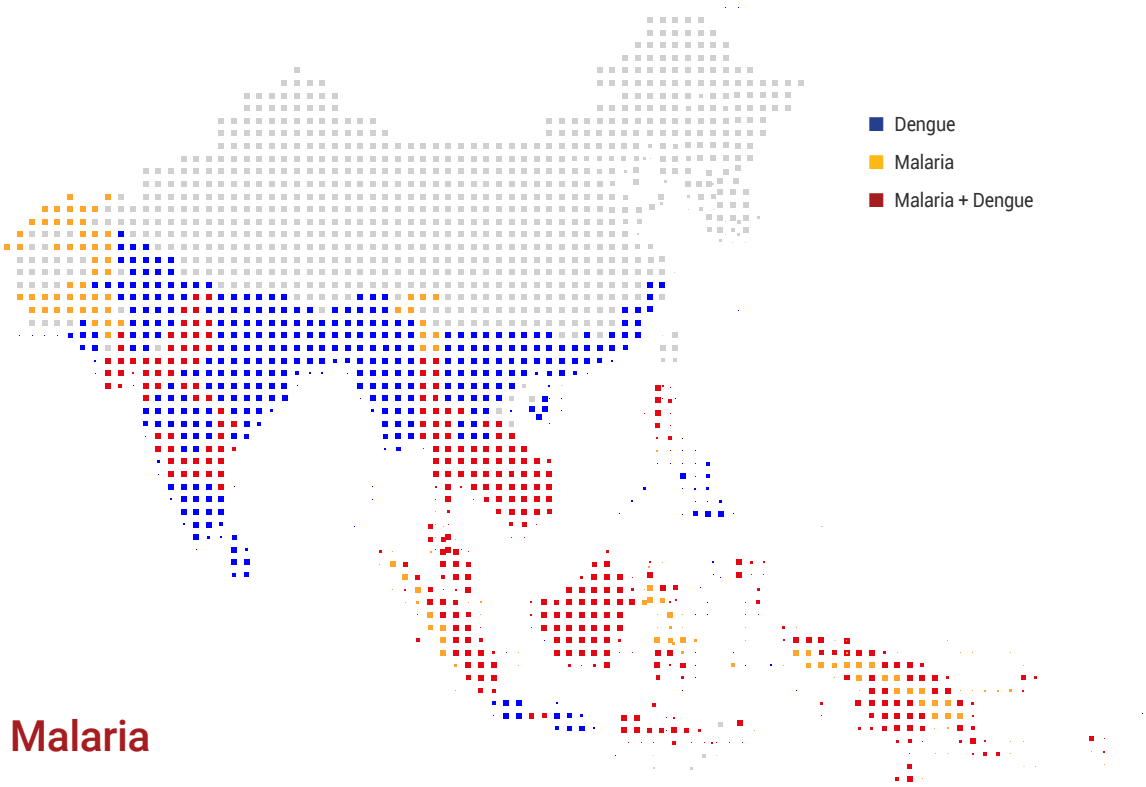
The epidemiology of malaria, dengue, chikungunya, Zika, lymphatic filariasis (LF), and Japanese encephalitis (JE) across the Indo-Pacific region is described below. Figure 2 illustrates areas where four of the diseases are co-endemic, and Figure 3 illustrates countries where malaria, dengue, or malaria and dengue are present. These maps are modelled predictions based on data of infection occurrence (or, in the case of *P. falciparum* and *P. vivax*, infection prevalence).

FIGURE 2. THE OVERLAP IN THE GEOSPATIAL DISTRIBUTIONS OF FOUR DISEASES: MALARIA (P. FALCIPARUM, P. VI-VAX, AND P. KNOWLESI), DENGUE, CHIKUNGUNYA AND LYMPHATIC FILARIASIS.[2]

[2] Malaria data from https://map.ox.ac.uk/. Dengue, chikungunya, and LF data from Catherine Moyes, Nick Golding, Josh Longbottom, Freya Shearer and Moritz Kraemer (University of Oxford). The binary map of LF infection occurrence was derived from Cano J, Rebollo MP, Golding N, et al. The global distribution and transmission limits of lymphatic filariasis: past and present. Parasites & Vectors. 2014; 7:466; https://doi.org/10.1186/s13071-014-0466-x as detailed in Golding N, Wilson AL, Moyes CL, et al. Integrating vector control across diseases. BMC Medicine. 2015; 13:249; https://doi.org/10.1186/s12916-015-0491-4. The binary map of dengue infection occurrence was derived from Bhatt S, Gething PW, Brady OJ, et al. The global distribution and burden of dengue. Nature. 2013; 496:504-507; https://doi.org/10.1038/nature12060 as detailed in Golding N, Wilson AL, Moyes CL, et al. Integrating vector control across diseases. BMC Medicine. 2015; 13:249; https://doi.org/10.1186/s12916-015-0491-4. The binary map of chikungunya infection occurrence was derived from Nsoesie EO, Kraemer MUG, Golding N, et al. Global distribution and environmental suitability for chikungunya virus, 1952 to 2015. Eurosurveillance. 2016; 21(20); https://doi.org/10.2807/1560-7917.ES.2016.21.20.30234 as detailed in Weetman D, Kamgang B, Badolo A, et al. Aedes mosquitoes and Aedes-borne arboviruses in Africa: Current and future threats. International Journal of Environmental Research and Public Health. 2018; 15(2), 220; https://doi.org/10.3390/ijerph15020220.

There was no geospatial data available on JE occurrent at the time of writing this report. Therefore, the relative probability of occurrence for Culex tritaeniorhynchus, the main vector for JE, is used as a proxy for JE risk but is not included in this map (see Figure 6).

FIGURE 3. SPATIAL DISTRIBUTION OF DENGUE (ALONE), MALARIA (ALONE) AND MALARIA + DENGUE INFECTION OCCURRENCE.[2] MALARIA INCLUDES P. FALCIPARUM, P. VIVAX, AND P. KNOWLESI.



Malaria

Epidemiology

In 2017, there were an estimated 23,320 malaria deaths and 13,147,000 malaria cases in the Indo-Pacific region (Figures 4 and 5), 86% of which were reported from the WHO SEARO[3] region, of which 65% was *P. vivax*.[4] Despite this, the region is celebrating some successes, with Sri Lanka certified malaria free in 2016 and China and Malaysia reporting zero human malaria cases since 2017 and 2018, respectively. While malaria has declined from 17 cases per 1,000 population at risk to 7 cases per 1,000 population in the SEARO region between 2010 and 2017, malaria cases have plateaued at 2.5 cases per 1,000 population at risk in the WPRO[5] region (although cases increased by over three-fold in Papua New Guinea and Solomon Islands during those years) and multi-drug resistance in malaria parasites remains a threat to elimination in the GMS.[6,7] Twenty-two countries have committed to the goal of malaria elimination by 2030, which is actively supported by the Indo-Pacific Malaria Elimination Network (APMEN)[8] and the Indo-Pacific Malaria Leaders Alliance (APLMA).[9]

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3 Bangladesh, Bhutan, DPRK, India, Indonesia, Myanmar, Nepal, Sri Lanka, Thailand, Timor-Leste (malaria at risk SEARO countries)

4 World Health Organization. World Malaria Report 2018. Geneva; Global Malaria Programme.

5 Cambodia, China, Lao PDR, Malaysia, Papua New Guinea, Philippines, Republic of Korea, Solomon Islands, Vanuatu, Vietnam (malaria at risk WPRO countries)

6 World Health Organization. World Malaria Report 2018. Geneva; Global Malaria Programme.

7 Imwong M, Suwannasin K, Kunasol C, Sutawong K, Mayxay M, Rekol H, et al. The spread of artemisinin-resistant Plasmodium falciparum in the Greater Mekong subregion: a molecular epidemiology observational study. Lancet Infect Dis. 2017; 17(5): 491-497.

8 APMEN http://www.apmen.org/

9 APLMA https://www.aplma.org/

FIGURE 4. ANNUAL MALARIA PARASITE INCIDENCE (API) (CASES PER 1,000 POPULATION AT RISK) FOR 2016 BY COUNTRY.[10]

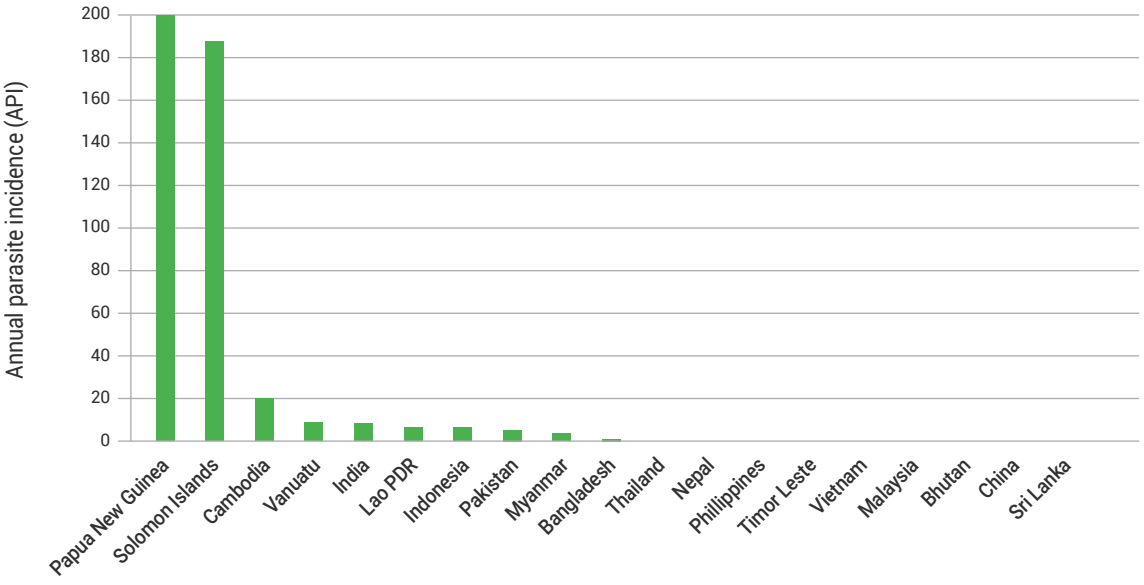
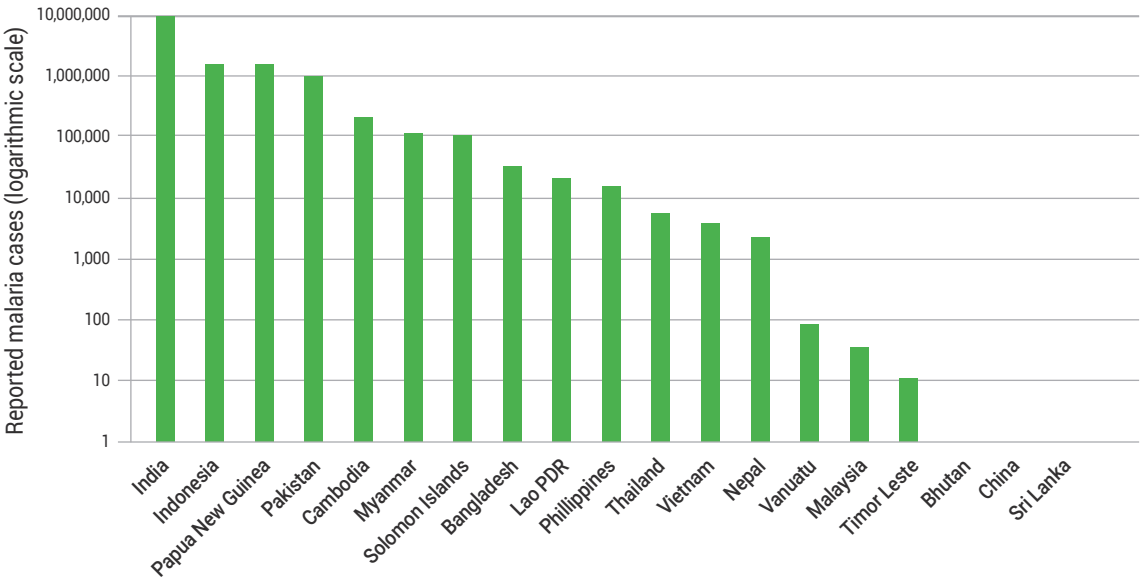


FIGURE 5. REPORTED MALARIA CASES (LOGARITHMIC SCALE) BY COUNTRY IN 2017.[11]

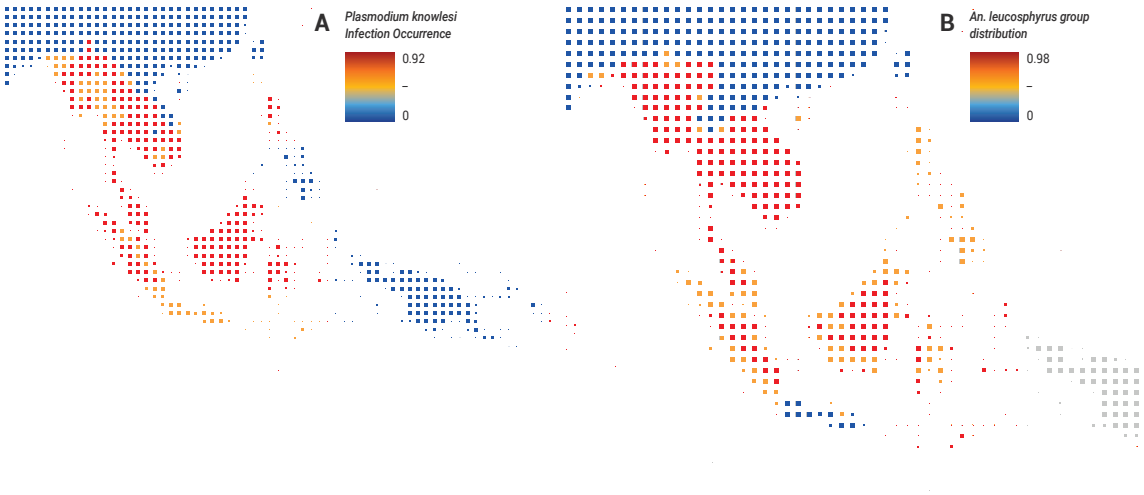


[10] World Health Organization. World Malaria Report 2017. Geneva, Global Malaria Programme.
[11] World Health Organization. World Malaria Report 2018. Geneva, Global Malaria Programme.

There are multiple drivers of malaria transmission across the Indo-Pacific region, including vector and human behaviors, and insecticide resistance, which are described further below, that significantly impact the effectiveness of vector control interventions, as do the environment, climate, and changing landscape ecology, which are beyond the scope of this analysis.

Plasmodium knowlesi, a zoonotic malaria parasite, is now the most common *Plasmodium* species infecting humans in Malaysia where cases are confirmed by polymerase chain reaction (PCR). *P. knowlesi* has been reported from several other countries but is likely under-reported due to misdiagnosis by microscopy as *P. falciparum* or *P. vivax*.[12] The rise of *P. knowlesi* is due in part to deforestation and land-use changes, prevalent throughout the region.[13] There are distinct parallels between *P. knowlesi* challenges and malaria in the GMS regarding the vectors (from the *An. leucosphyrus* group), transmission ecology, human ecology, and potential control strategies and tools. Moreover, there are operational research capacities in Malaysia that could be better linked to other regional efforts for control of "forest malaria." Estimates of *P. knowlesi* infection occurrence and distribution of the main vector group are mapped in Figure 6.

FIGURE 6. THE RELATIVE PROBABILITY OF OCCURRENCE OF (A) *P. KNOWLESI* INFECTION AND (B) *AN. LEUCOSPHYRUS* GROUP MOSQUITOES.[14]



[12] Barber BE, Rajahram GS, Grigg MJ, William T, Anstey NM. World Malaria Report: time to acknowledge Plasmodium knowlesi malaria. Malar J. 2017;16(1):135. Published 2017 Mar 31. doi:10.1186/s12936-017-1787-y

[13] Davidson, G., Chua, T.H., Cook, A. et al The Role of Ecological Linkage Mechanisms in Plasmodium knowlesi Transmission and Spread. EcoHealth (2019). https://doi.org/10.1007/s10393-019-01395-6

[14] The relative probability of occurrence of Plasmodium knowlesi infection is detailed in Shearer FM, Huang Z, Weiss DJ, et al. Estimating geographical variation in the risk of zoonotic Plasmodium knowlesi infection in countries eliminating malaria. PLoS NTD. 2016; https://doi.org/10.1371/journal.pntd.0004915. Vector data found on https://map.ox.ac.uk/ from Moyes CL, Shearer FM, Huang Z, et al. Predicting the geographical distributions of the macaque hosts and mosquito vectors of Plasmodium knowlesi malaria in forested and non-forested areas. Parasites & Vectors. 2016; 9:242; https://doi.org/10.1186/s13071-016-1527-0.

Vector ecology

Outdoor transmission driven by early evening and outdoor vector biting continues to pose the biggest challenge to malaria elimination in the Indo-Pacific.[15] Vector species are highly diverse in the region, with over 19 dominant vector species and many more secondary vectors.[16] The distributions of *An. dirus s.l., An. punctulatus, An. subpictus*, and *An. flavirostris* are shown in Figure 7. Many of the vectors are naturally exophilic and exophagic, while others have become more so over time, largely due to behavioral resistance to avoid insecticides used in indoor interventions. While many of the efficient vectors are anthropophagic (e.g. *An. dirus s.s., An. baimai, An. minimus s.s*., and *An. punctulatus*), other important vectors are more zoophagic or opportunistic, and still contribute significantly to malaria transmission (e.g. *An. farauti, An. culicifaces,* and *An. stephensi*) (Table 1).

Some of the greatest malaria vector biodiversity occurs in the South-East Asia region.[17] The main vectors in this region are *Anopheles dirus s.l., An. minimus s.l.,* and *An. sundaicus s.l*. Of the *An. dirus s.l. species, An. dirus s.s.* and *An. baimai* are dominant and considered forest and forest-fringe malaria vectors with anthropophilic and exophagic behaviors with larvae found in rain water pools and occasionally artificial containers, as well as in mono-agricultural environments. An. minimus s.l., including the two main vectors An. minimus and An. harrisoni, are widespread in hill forested areas, (with An. harrisoni more limited to the northern parts of the GMS and showing more exophagic and zoophilic behavior than An. minimus s.s.) and preferring slow running steams for larval habitats. Vectors in the An. sundaicus-related group are coastal; larvae prefer brackish water and adults exhibit both endo- and exophagy and anthropophagy behaviors. Note that *An. epiroticus*, usually reported on the Southeast Asia mainland, may also be found in Indonesia and is only distinguished by molecular methods.

In the Western Pacific region, the *An. punctulatus* complex dominates, including three primary vector species *An. farauti, An. punctulatus*, and *An. koliensis* and four secondary vectors.[18] *An. farauti* has the widest geographic distribution but is limited to coastal areas whose larvae are found in both brackish and fresh water swamps as well as temporary ground pools. *Anopheles farauti* adults are increasingly adapting to biting early and outdoors and to rest outdoors. *An. punctulatus* is mainly found in lowland regions and foothills, with larval habitats in temporary ground pools, rock pools, and pools in rivers and streambeds. *An. koliensis* is predominantly an inland species in the lowlands and river valley flood plains with larval habitats of wheel tracks, drains, swamps, and natural ground pools. Both *An. punctulatus* and *An. koliensis* feed indoors and outdoors but later at night than *An. farauti. Anopheles koliensis* may have been eliminated in the Solomon Islands by IRS.

In South Asia, *An. culicifacies*, found in a range of sunlit larval habitats, from agricultural drainage canals and borrow-pits in Punjab to rock pools in dry-season river beds in Sri Lanka, is the principal vector of rural malaria while *An. stephensi* is the main vector in urban areas where it had adapted to water cisterns and other human-made larval habitats. In India specifically, *An. fluviatilis* in found in the hills and foothills while *An. dirus, An. minimus*, and *An. nivipes* are in the northeastern states.[19]

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[15] Malaria vector control in the Greater Mekong Sub-region: an independent situation analysis and suggestions for improvement 21 September 2018 Prepared by Sean Hewitt PhD VBDC Consulting Ltd http://www.vbdc-consulting.com/files/180920.pdf

[16] Sinka ME, Bangs MJ, Manguin S, Chareonviriyaphap T, Patil AP, Temperley WH, et al. The dominant Anopheles vectors of human malaria in the Indo-Pacific region: occurrence data, distribution maps, and bionomics precis. Parasites & Vectors. 2011; 4(89).

[17] Suwonkerd W, Ritthison W, Ngo CT, Tainchum K, Bangs MJ, Chareonviriyaphap T. Vector biology and malaria transmission in Southeast Asia. IntechOpen. 2013; 10:273-325.

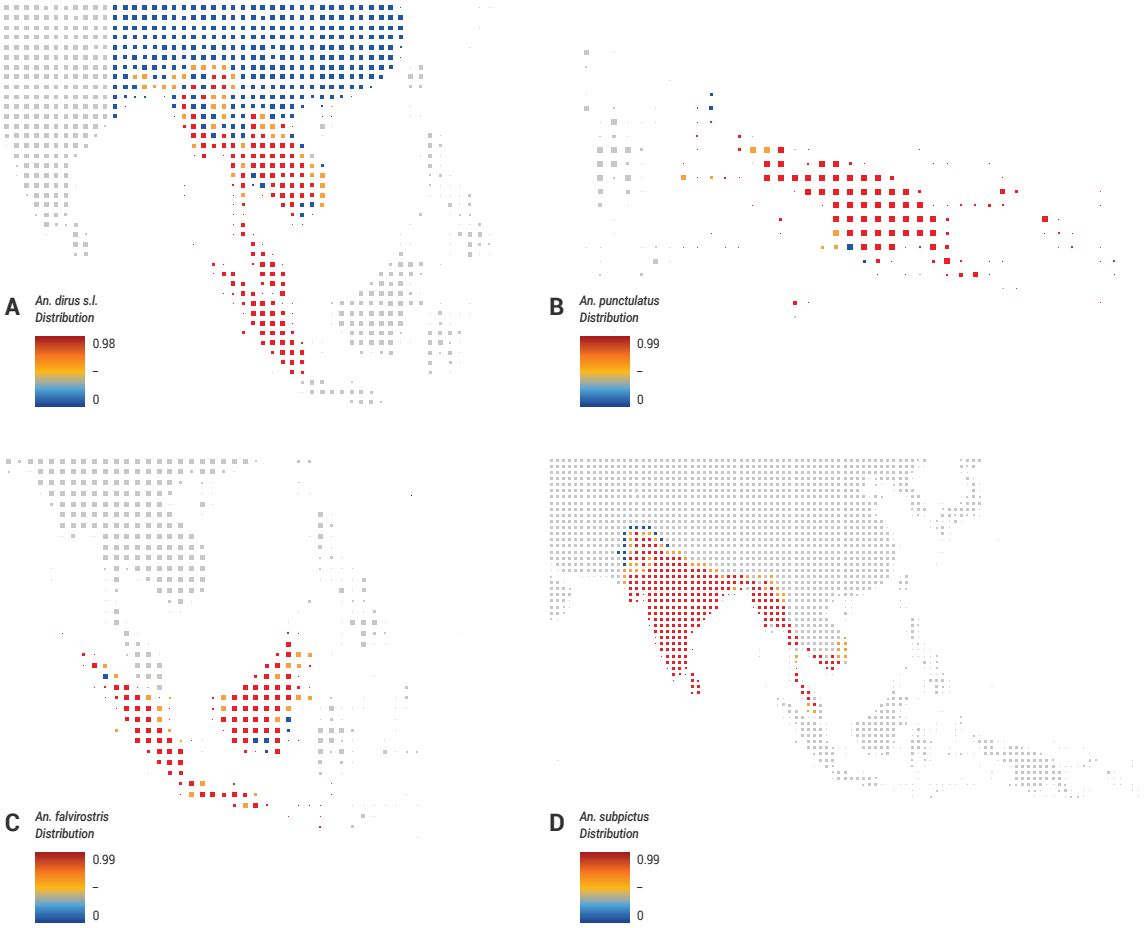
[18] Beebe NW, Russell TL, Burkot TR, Lobo NF, Cooper RD. The Systematics and Bionomics of Malaria Vectors in the Southwest Pacific, Anopheles mosquitoes - New insights into malaria vectors, Prof. Sylvie Manguin (Ed.), ISBN: 978-953-51-1188-7, InTech. Available from: http://www.intechopen.com/books/anopheles-mosquitoes-new-insights-into-malaria-vectors/the-systematics-and-bionomics-of-malaria-vectors-in-the-southwest-pacific.

[19] Kumar A, Chery L, Biswas C, Dubhashi N, Dutta P, Dua VK, et al. Malaria in South Asia: Prevalence and control. Acta Trop. 2012; 121(3).

TABLE 1. DOMINANT VECTOR SPECIES AND BIONOMICS FOR THREE KEY SUB-REGIONS IN THE INDO-PACIFIC

	Dominant species	Distribution	Human vs. animal preference	Feeding preference (indoors vs. outdoors)	Resting preference (indoors vs. outdoors)	Larval habitats
Southeast Asia (GMS, Indonesia, Malaysia, Philippines)	*An. dirus, An. balabacensis*	Forest, forest fringe, mature rubber plantations	Human (and An. balabacensis primate preference)	Outdoors	Both, now mostly outdoors	Shaded rain pools and occasionally artificial containers
	An. minimus, An. harrisoni, An. flavirostris	Forest hills, plantations	Both	Outdoors	Outdoors, with *An. minimus* preferring both	Slow running streams
	An. epiroticus, An. sundaicus	Coastal	Human	Both	Indoors	Brackish and fresh water
	An. vagus, An. aconitus	Agricultural areas	Both	Outdoors	Both	Rice fields, swamps
South Asia (Bangladesh, Bhutan, India, Nepal, Sri Lanka, Pakistan)	*An. culicifacies*	Rural, rice fields	Animal	Outdoors	Mostly indoors	Early rice, drainage canals
	An. stephensi	Urban, peri-urban	Human (urban) Animal (rural)	Both	Both	Man-made (urban); ponds, canals, streams, wide range (rural)
	An. subpictus	Rural, rice fields	Animal	Both	Indoors	Wide range
Western Pacific (Papua New Guinea, Solomon Islands, Vanuatu)	*An. farauti*	Coastal	Both	Both	Outdoors	Brackish and fresh water; permanent and temporary water pools
	An. koliensis	Lowlands and river valley flood plains	Both (but human preference)	Both	Outdoors	Wheel tracks, drains, natural ground pools
	An. punctulatus	Lowland regions, foothills	Both (but human preference)	Both	Outdoors	Rock pools, pools in rivers and streams

FIGURE 7. ESTIMATED SPATIAL DISTRIBUTION OF AN. DIRUS S.L. (A), AN. PUNCTULATUS (B), AN. FLAVIROSTRIS (C), AN. SUBPICTUS (D).[20]



Insecticide resistance

There is limited physiological insecticide resistance data reported for many Indo-Pacific countries, especially for the major vectors in the GMS.[21] Despite this, trend analyses indicate that the frequency of pyrethroid resistance in *Anopheles* increased globally between 2010 and 2016. Similar trends are not yet observed for the other three classes of insecticide, although resistance to organophosphates and carbamates is more common in SEARO and WPRO. In 2017, 47 of 89 endemic countries reported data into the WHO Malaria Threats Map, and Figure 8 below is a snapshot of the Malaria Threats Map for the Indo-Pacific region as of February 2019. Note that the lack of insecticide resistance data may be due not to the lack of regional tests being conducted for specific species but a failure to report results from resistance tests.

[20] Sinka M, Bangs MJ, Manguin S, et al. The dominant Anopheles vectors of human malaria in the Indo-Pacific region: occurrence data, distribution maps and bionomic précis. Parasites & Vectors. 2011; 4:89. https://doi.org/10.1186/1756-3305-4-89.

[21] WHO. Global report on insecticide resistance in malaria vectors: 2010-2016. Global Malaria Programme. 2018.

FIGURE 8. ESTIMATES OF INSECTICIDE RESISTANCE AMONG ANOPHELES POPULATIONS IN THE INDO-PACIFIC TO THE FOUR INSECTICIDE CLASSES.[22]

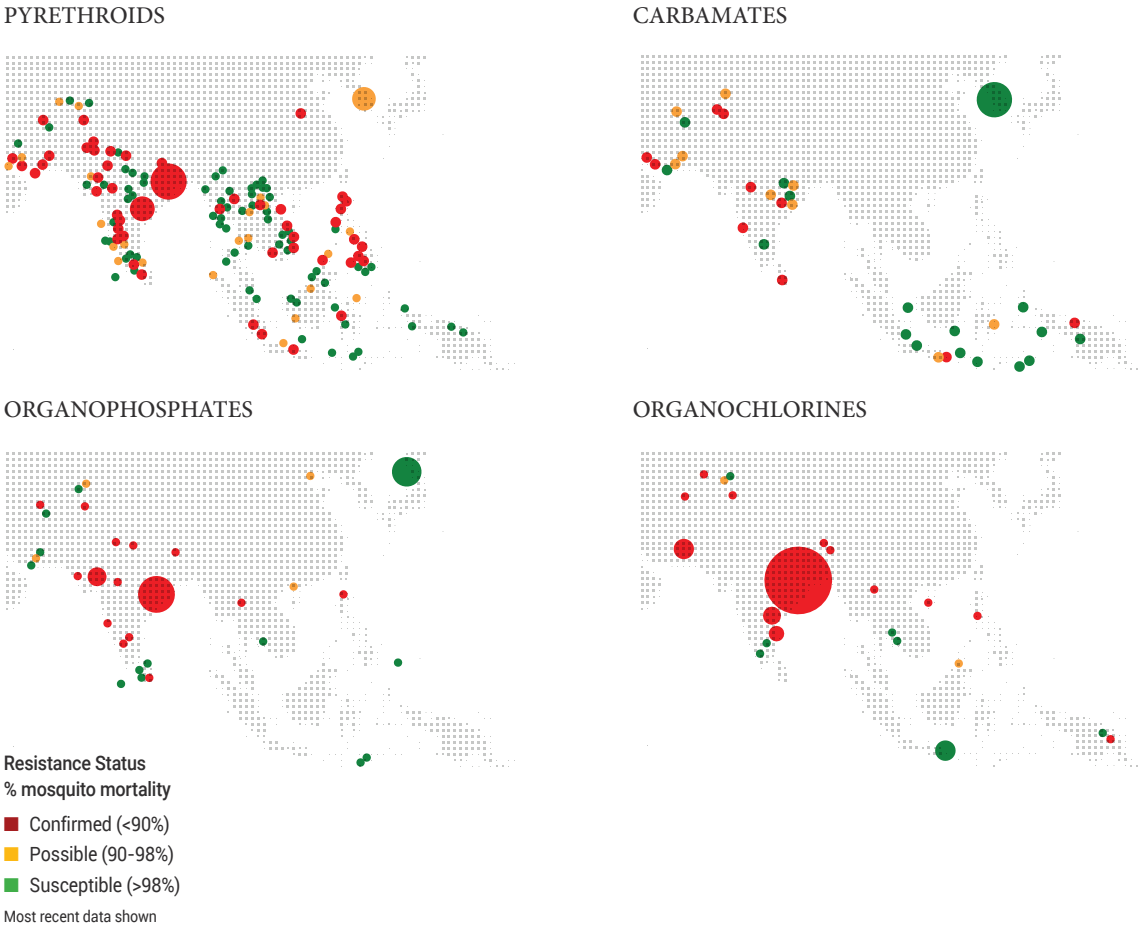


Table 2 below summarizes the physiological resistance data reported to the WHO between 2010 and 2016 across the Indo-Pacific region by country, insecticide class, resistance mechanism, and vector species. Only a handful of countries monitored all four classes, and of those, China, India, Pakistan, and Myanmar reported resistance to at least three insecticides.

It is important to note that the resistance shown for the GMS is largely for secondary vectors like *An. barbaristrosis, An. annularis* and *An. epioriticus*, not *An. dirus s.l.* (except for an isolated report from Lao PDR[23] and *An. balabacensis* in Malaysia) and only rarely for *An. minimus* and *An. dirus* (northern Vietnam, southern China). While physiological insecticide resistance is a major challenge in South Asia, it does not appear to be significant concern at present for malaria elimination in the rest of the region, although resistance may be emerging and close monitoring is critical.

[22] WHO Malaria Threats Map. Accessed February 2019. http://apps.who.int/malaria/maps/threats/

[23] Marcombe S, Bobichon J, Somphong B, et al. Insecticide resistance status of malaria vectors in Lao PDR. PLoS One. 2017;12(4):e0175984. Published 2017 Apr 24. doi:10.1371/journal.pone.0175984

TABLE 2. PHYSIOLOGICAL RESISTANCE STATUS TO FOUR INSECTICIDE CLASSES AND RESISTANCE MECHANISMS TESTED OR DETECTED (OR BOTH) FOR ADULT MALARIA VECTORS, FOR 2010-2016.[24]

Country*	Resistance status				Resistance mechanisms							Species exhibiting resistance
					Metabolic			Target site				
	Pyrethroids	Organochlorines	Carbamates	Organophosphates	Monooxygenases	Esterases	GSTs	kdr L1014	kdr L1014S	kdr (unspecified)	Ace-1R	
Bangladesh	R	-	-	-	-	-	-	-	-	-	-	An. philippinensis, An. vagus
Bhutan	S	-	-	-	-	-	-	-	-	-	-	
Cambodia	R	R	-	-	-	-	-	-	-	-	-	An. barbirostris, An. maculatus s.l., An. vagus
China	R	R	R	R	-	-	-	D	-	-	D	An. minimus s.l., An. sinensis s.l., An. vagus
DPRK	S	S	S	S	-	-	-	-	-	-	-	
India	R	R	R	R	D	D	-	D	D	-	-	An. culicifacies s.l., An. fluviatilis, An. stephensi
Indonesia	R	S	R	S	-	-	-	-	-	-	-	An. aconitus, An. barbirostris, An. peditaeniatus, An. vagus
Lao PDR	R	R	-	-	-	-	-	-	-	-	-	An. aconitus, An. dirus s.l., An. kochi, An. maculatus s.l., An. minimus s.l., An. neivai, An. nivipes, An. philippinensis, An. umbrosus s.l., An. vagus
Malaysia	S	-	-	-	-	-	-	-	-	-	-	
Myanmar	R	R	-	R	-	-	-	-	-	-	-	An. aconitus, An. annularis, An. hyrcanus s.l., An. minimums s.l., An. peditaeniatus, An. philippinensis, An. sinensis s.l., An. vagus
Nepal	-	R	S	S	-	-	-	-	-	-	-	An. annularis, An. culicifaces s.l.
Pakistan	R	R	-	R	-	-	-	-	-	-	-	
Papua New Guinea	S	-	-	-	-	-	-	-	-	-	-	An. farauti
Philippines	R	S	-	S	-	-	-	-	-	-	-	
Republic of Korea	-	-	-	-	-	-	-	D	D	-	D	An. sinensis s.l.
Solomon Islands	R	R	-	S	-	-	-	-	-	-	-	An. farauti s.l.
Thailand	R	-	-	-	-	-	-	-	-	-	-	An. barbirostris
Vanuatu	S	-	-	-	-	-	-	-	-	-	-	
Vietnam	R	S	-	-	-	-	-	-	-	-	-	An. aconitus, An. annularis, *An. epiroticus*, An. kochi, An. maculatus s.l., An. minimus s.l., An. nivipes, An. philippinensis, An. sinensis s.l., An. vagus

[24] WHO. Global report on insecticide resistance in malaria vectors: 2010-2016. Global Malaria Programme 2018.

Human behavior and high-risk populations for malaria

In areas of higher transmission such as eastern Indonesia, Papua New Guinea, Solomon Islands, and central-east India, nearly the entire population is at risk for malaria. These populations are often in remote villages where access to health services is more limited. To some extent in these areas and to a large extent in other areas like the GMS, transmission is highest among specific risk groups characterized to varying extents by ministries of health and partners. Broadly, this risk is often associated with occupation, including 1) forest-goers (for logging, rubber tapping, etc.), 2) construction and mine workers, 3) security personnel, 4) border crossers, and 5) seasonal workers.[25] The majority of these populations are men between the ages of 15 and 60, as evidenced by malaria case data across the region. Given that much of the work is outdoors and often during peak *Anopheles* biting, individuals have a higher risk of malaria infection. Other groups such as people displaced by conflict or disasters are also at elevated risk and often includes families.

In considering a "precision vector control" approach in the Indo-Pacific, understanding human behavior and its intersection with vector behavior is critical. We therefore considered high risk populations (HRPs) and their behaviors from the perspective of mosquito-borne disease prevention and control in Table 3 below that summarizes use cases for new tools.

In this context, it is important to understand perceived risk among these HRPs. A recently published systematic review by Nofal et al. of qualitative literature on interventions for forest-goers in the GMS acknowledges that individuals' understanding of malaria and perceived risk is critical to designing intervention packages.[26] In some areas, going into the forest is perceived to increase risk of contracting malaria (e.g. in Myanmar, malaria was referred to as "forest-sickness"), but individuals take the risk because they need income. In other settings, malaria was perceived as an insignificant risk since mosquitoes in the forest were not seen as malaria vectors. Nuisance biting was often the driver of use of personal protection measures.

Rudimentary protection measures, including wearing long shirts and trousers, were used but were often impractical because of the strenuous nature of forest work, although preferences vary by setting. Burning leaves to repel mosquitoes was popular but was recognized as inadequate and potentially harmful. The strong smell and high cost of repellents were reasons that they weren't readily used. Authors concluded that current vector control tools have limitations and that human-centered approaches should be used to design appropriate vector control tools for these populations; authors also recommended further research on chemoprophylaxis as a potential alternative.

[25] WHO, IOM. Population mobility and malaria. 2017.

[26] Nofal SF, Peto TJ, Adhikari B, Tripura R, Callery J, Bui TM, et al. How can interventions that target forest-goers be tailored to accelerate malaria elimination in the Greater Mekong Subregion? A systematic review of the qualitative literature. Malaria Journal. 2019; 18(32).

TABLE 3. SUMMARY OF USE CASES FOR NEW TOOLS

Movement	Target human population	Risk profile	Indoor exposure to mosquito biting	Outdoor exposure to mosquito biting	Existing vector control tools (use/ uptake is variable)	Potential new tools and approaches
More static	Village-based, accessible	All ages (in higher transmission areas), adult men (lower transmission areas)	Generally higher coverage of interventions; exposure outside protection of LLINs	Cooking, studying, gathering during peak biting times; overnight fishing	LLINs, focal IRS, community-based LSM	Spatial repellents, ivermectin-treated livestock, insecticide-treated paints, conventional net retreatment and improved application of adulticides (IRS, ORS), larviciding (including area-wide application), house improvements (e.g. screening, barrier fences)
	Village-based, remote/ tribal/ conflict areas	All ages (in higher transmission areas), adult men (lower transmission areas)	Generally lower coverage of interventions	Cooking, studying, gathering; overnight fishing	LLINs	Spatial repellents, house improvements (e.g. screening, barrier fences), insecticide-treated paints, DIY IRS, DIY repellent treatment kit
	Forest/ farm-based (seasonal), semi-permanent structures*	Adult men, sometimes families	Open structures; exposure outside protection of LLINs and/or LLIHNs	Work activities at peak biting times	LLINs, LLIHNs, topical repellents (limited)	Spatial repellents (if more closed structure), DIY IRS (farm huts that are more closed), longer-lasting topical repellents, bite proof clothing/ITC, DIY repellent treatment kit, ITM (e.g. blankets, mats)
	Internally displaced populations	All ages	Generally higher coverage of interventions; exposure outside protection of LLINs and/or ITM	Cooking, studying, gathering during peak biting times	LLINs, ITM	Spatial repellents, ATSBs,[27] area-wide adulticiding and larviciding, improved ITM (e.g. shelters, blankets)
	Long-term, formal project-based (construction, mines, dams)	Adult men, sometimes families	Generally higher coverage of interventions; exposure outside protection of LLINs, screening, and other interventions	Gathering during peak biting times	LLINs, focal IRS, small-scale LSM, space spraying, improved housing	Spatial repellents, ATSBs, area-wide adulticiding and larviciding
	Security, defense force, and forest ranger camps	All ages	Generally higher coverage of interventions; exposure outside protection of LLINs and/or IRS	Cooking, studying, gathering during peak biting times	LLINs, IRS	Spatial repellents, LLIHNs, improved application of adulticiding (IRS, ORS, area-wide) and larviciding
More mobile	Frequent movement between village and forest/ farm and/ or informal/ illegal mines*	Adult men	Often sleeping/ working outdoors in forest; if indoors, LLINs are often left in villages so no protection in forest/ farm/ mines	Sleeping and/ or working outdoors	LLINs, LLIHNs	Spatial repellents (if in enclosed area), long-lasting topical repellents, bite proof clothing/ITC, ITM (shelters, mats, blankets), DIY repellent treatment kit
	Security and defense force personnel and forest rangers	Adult men	Often working overnight	Working during peak biting hours	Topical repellents, bite proof clothing, LLITH	Longer lasting topical repellents, bite proof clothing/ITC, DIY repellent treatment kit, ITM
	Border crossers	Adult men	Generally sleeping outdoors and/or in temporary shelters	Outdoors during peak biting hours	IEC	Longer lasting, low cost topical repellents through consumer market, LLIHNs

*Delivery/distribution often at the village, at nearby towns, and/or along main roads.
DIY=do it yourself; IEC=information, education, communication; ITC=insecticide treated clothing;
ITM=insecticide-treated materials (e.g. blankets, tarpaulins); LLIHN=long lasting insecticide treated hammocks.

The focus in this analysis is vector control. Given this, other existing and important interventions and potential gaps in protection related to access to quality and effective diagnosis and treatment and other preventive interventions (e.g. chemoprophylaxis) are not included.

Accurately determining drivers of transmission, and therefore the appropriate response, requires a deeper, site-specific analysis.

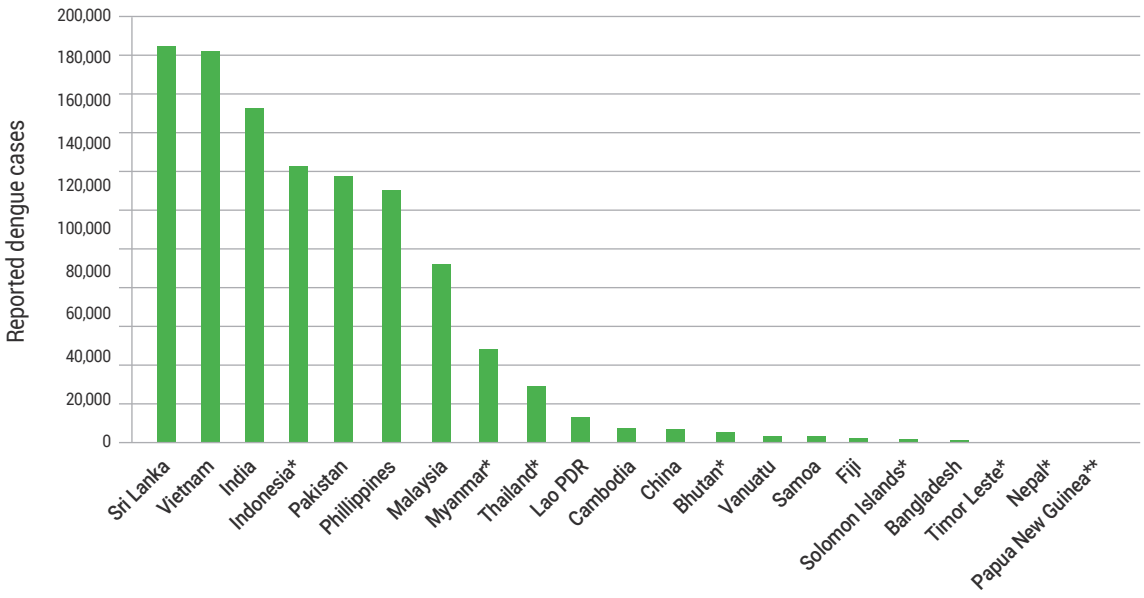
[27] ATSBs: early consensus from this landscape analysis was that most malarious areas offered too many alternative sugar sources for ATSBs to be effective against Anopheles. The exceptions may be displaced persons camps, some development projects (e.g. mines), or in urban areas (for Aedes).

Dengue, Zika, and chikungunya

Epidemiology

Over the past five decades, the global dengue incidence has increased 30-fold.[28] As many as 400M people are infected annually, with 40% of the world's population at risk in more than 100 endemic countries, with further spread to previously unaffected areas.[29] Each year, there are an estimated 20,000 deaths and 264 DALYs lost per million population.[30] In the Indo-Pacific region, there is a dearth of consolidated data on dengue incidence, but based on the analysis for this report, over 1M cases were reported in 2017 or preceding years (between 2010 and 2016), although we believe this to be widely underestimated and under-reported, particularly due to asymptomatic infections. A systematic analysis of the global economic burden of dengue by Shepard and colleagues (2016) compiled reported dengue episodes and projected nearly a 20-fold increase in estimated true burden in 2013, with an estimate of 22.85 million dengue cases in South Asia (39.1% of cases globally) and 23.21 million dengue cases in Southeast Asia, East Asia, and Oceania (39.7% of cases globally).[31] Of reported dengue episodes (not modelled and likely a significant underestimate), Sri Lanka, Vietnam, India, Indonesia, Pakistan, and the Philippines have recorded some of the highest numbers of dengue in the region (Figure 9). See Annex 1 for the detailed statistics and maps of dengue infection occurrence in Figures 2, 3 and 10.

FIGURE 9. REPORTED DENGUE CASES, 2017 (DATA SOURCES IN ANNEX 2). AS NOTED ABOVE, TRUE BURDEN IS ESTIMATED TO BE MUCH HIGHER.



*Data from other years (preceding 2017).

**Dengue cases in Papua New Guinea are rarely reported, but a study published by Senn et al (2011) indicates a seroprevalence of 8% among patients presenting to Madang clinics with acute febrile illness. According to Luang-Sarkia et al (2018), dengue surveillance is generally not undertaken and patients with acute febrile illness not regularly tested for dengue.

[28] WHO. Global Strategy for Dengue Control & Prevention 2012-2020.

[29] CDC. Dengue. Accessed February 2019. https://www.cdc.gov/dengue/index.html.

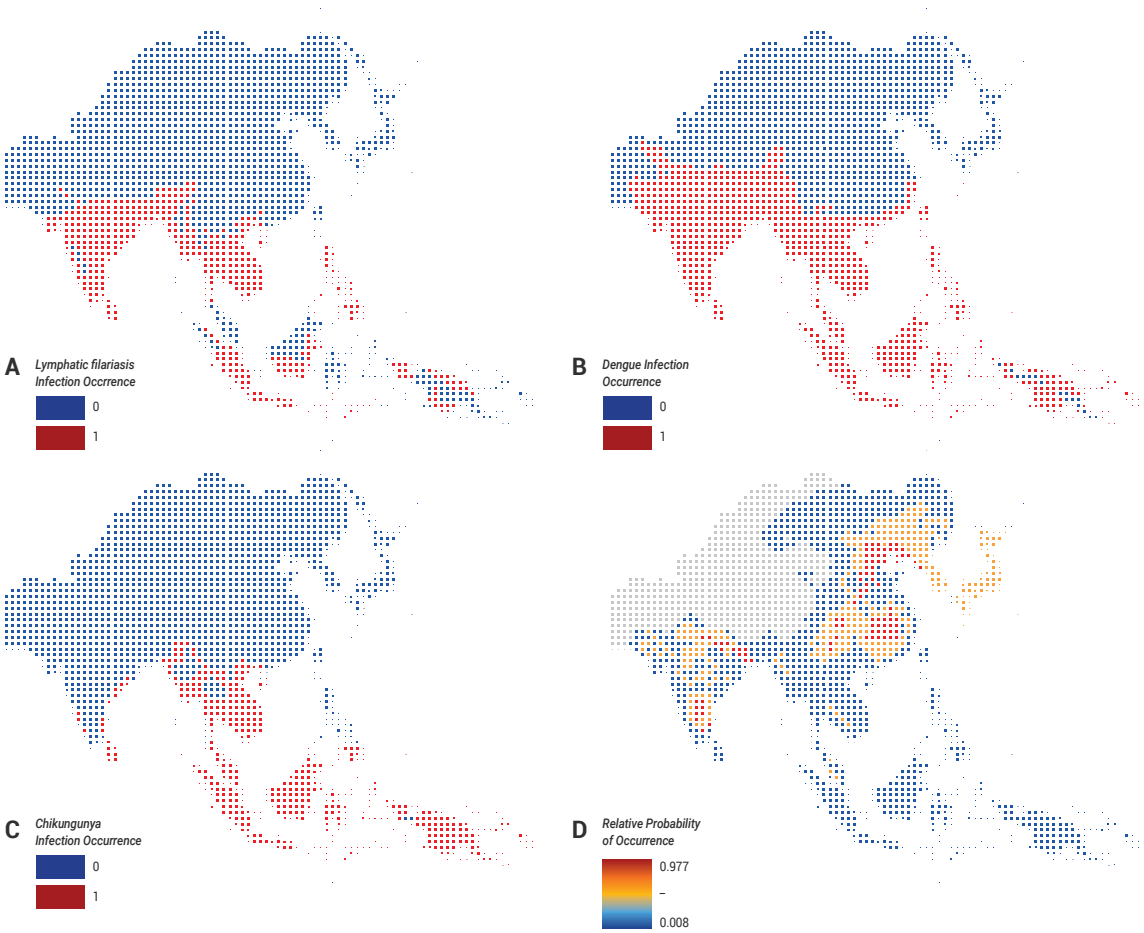
[30] WHO. Global Strategy for Dengue Control & Prevention 2012-2020.

[31] Shepard DS, Undurraga EA, Halasa YA, Stanaway JD. The global economic burden of dengue: a systematic analysis. Lancet Infectious Diseases. 2016; 16:935-941. Appendix, page 15.

Chikungunya is similarly not well documented, often because the symptoms resemble dengue and co-infection with dengue is common, so chikungunya goes misdiagnosed and under-reported. Additionally, chikungunya epidemics exhibit fluctuating and cyclical trends; such epidemics are marked by severe outbreaks interspersed by silent periods spanning several years to a few decades.[32] According to our analysis, there were over 184,000 cases of chikungunya reported over the last several years in the Indo-Pacific (Figure 10), although it is likely a significant underestimate for the reasons mentioned above. Indonesia, Sri Lanka, India, and Bangladesh have reported some of the highest numbers of chikungunya in the region (Annex 1).

As described in the Annex, Zika epidemiology is categorized based on reports of transmission with only a handful of cases reported across the region, although Zika may also be under-diagnosed and under-reported. According to the last update by the WHO in March 2018, Samoa and Solomon Islands reported new introduction or reintroduction of cases (Category 1) and 12 other countries in the region reported ongoing virus transmission (Category 2).

FIGURE 10. BINARY MAPS OF INFECTION OCCURRENCE FOR LF (A), DENGUE (B), AND CHIKUNGUNYA (C). MAP D IS THE RELATIVE PROBABILITY OF *CULEX TRITAENIORHYNCHUS* OCCURRENCE WITHIN THE JE ENDEMIC ZONE, USED AS A PROXY FOR JE RISK.[33]



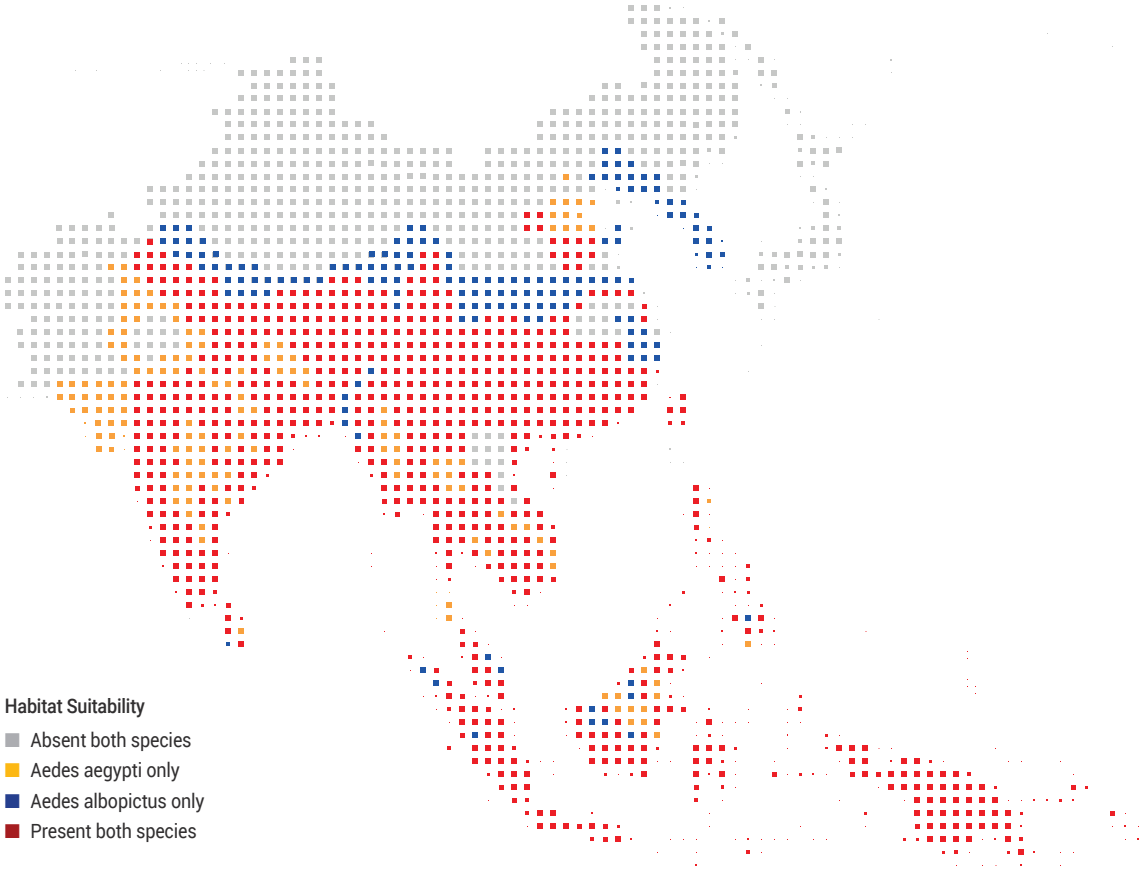
[32] WHO. Guidelines for Prevention & Control of Chikungunya Fever. 2009.

[33] The binary map of LF infection occurrence was derived from Cano J, Rebollo MP, Golding N, et al. The global distribution and transmission limits of lymphatic filariasis: past and present. 2014; 7:466.

Vector ecology

Aedes aegypti is the primary vector of dengue and has evolved to mate, feed, rest and lay eggs in and around human habitation.[34] *Although Ae. aegypti* is commonly reported as a daytime biter with peaks early morning and before dusk, feeding continues throughout the night in Papua New Guinea and the Solomon Islands (C Butafa, unpublished data). *Ae. albopictus* is usually a secondary vector of dengue but can be very competent for chikungunya. Concerningly, *Ae. albopictus* is increasing in relative proportion as the spatial distribution spreads north and south (Figure 11). There are other *Aedes* species that have been incriminated as dengue vectors, although they are geographically limited. Habitat suitability estimates for *Ae. aegypti* and *Ae. albopictus* are provided in Figure 11.

FIGURE 11. HABITAT SUITABILITY ESTIMATES FOR AE. AEGYPTI, AE, ALBOPICTUS, AND BOTH COMBINED.[35]



https://doi.org/10.1186/s13071-014-0466-x as detailed in Golding N, Wilson AL, Moyes CL, et al. Integrating vector control across diseases. BMC Medicine. 2015; 13:249; https://doi.org/10.1186/s12916-015-0491-4. The binary map of dengue infection occurrence was derived from Bhatt S, Gething PW, Brady OJ, et al. The global distribution and burden of dengue. Nature. 2013; 496:504-507; https://doi.org/10.1038/nature12060 as detailed in Golding N, Wilson AL, Moyes CL, et al. Integrating vector control across diseases. BMC Medicine. 2015; 13:249; https://doi.org/10.1186/s12916-015-0491-4. The binary map of chikungunya infection occurrence was derived from Nsoesie EO, Kraemer MUG, Golding N, et al. Global distribution and environmental suitability for chikungunya virus, 1952 to 2015. Eurosurveillance. 21(20); https://doi.org/10.2807/1560-7917.ES.2016.21.20.30234 as detailed in Weetman D, Kamang B, Badolo A, et al. Aedes mosuqitoes and Aedes-borne arboviruses in Africa: current and future threats. International Journal of Environmental Research and Public Health. 2018; 15(2): 220; https://doi.org/10.3390/ijerph15020220. The relative probability of Cx tritaeniorhynchus occurrence within the JE endemic zone is detailed in Longbottom J, Browne AJ, Pigott DM, et el. Mapping the spatial distribution of the Japenese encephalitis vector, Culex tritaeniorhynchus Giles, 1901 (Diptera: Culicidae) within areas of Japanese en-cephalitis risk. Parasite & Vectors. 2017; 10:148; https://doi.org/10.1186/s13071-017-2086-8.

[34] WHO. Global Strategy for Dengue Control & Prevention 2012-2020.

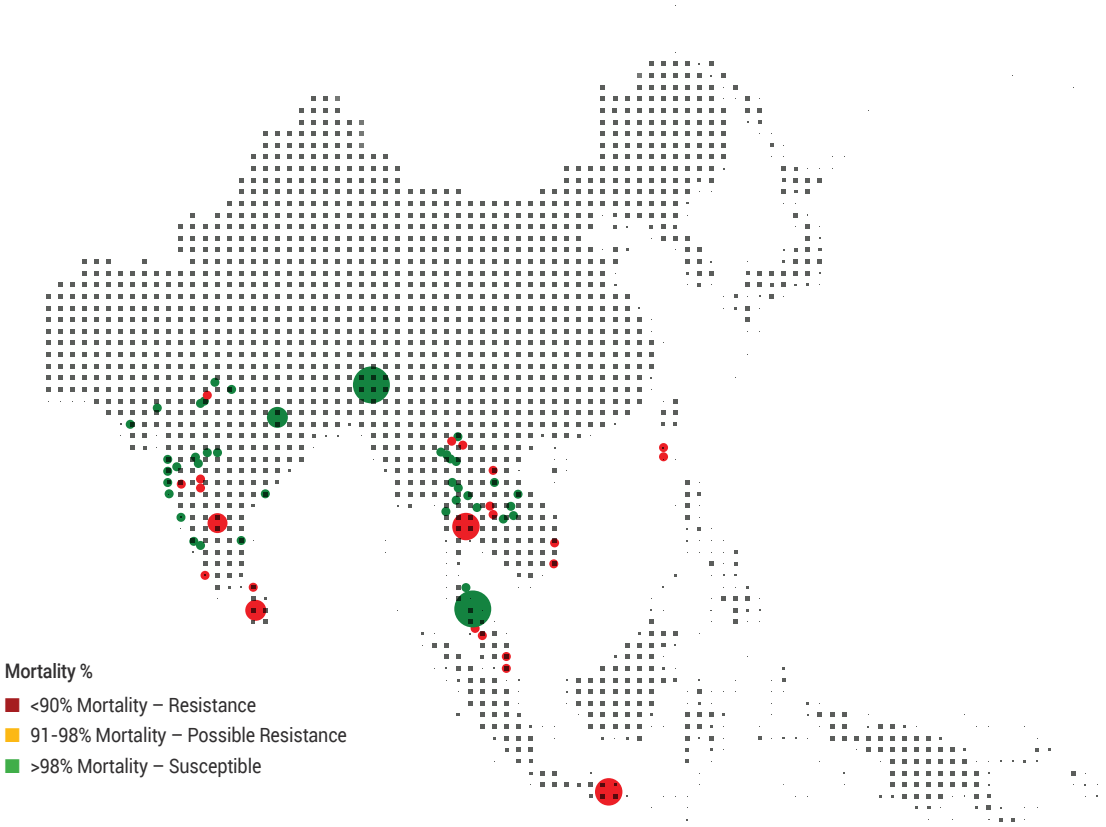
[35] Binary maps created by Catherine Moyes using predicted habitat suitability data from Kraemer MUG, Sinka ME, Duda KA, et al. The global distribution of the arbovirus vectors Aedes aegypti and Ae. albopictus. eLIFE. 2015; 4:e08347; https://doi.org/10/7554/eLife.08347.

Kraemer et al. (2019) recently released an analysis on the future spatial distribution of *Ae. aegypti* and *Ae. albopictus*, which concludes that spread is occurring in combination with human movement, including urbanization, and the presence of suitable climate.[36] Authors note that, even under current climate conditions and population density, both vector species will continue to spread globally, posing a significant risk to human health and global health security.

Insecticide resistance

Globally, insecticide resistance to all four classes of insecticides, including temephos, has been on the rise in *Ae. aegypti* while the levels of resistance in *Ae. albopictus* is relatively low, although resistance is expected to increase.[37] Figure 12 describes point data for pyrethroid resistance detected in *Ae. aegypti* populations across the Indo-Pacific region in 2017. Not shown on the map due to lack of data published or reported to the WIN Network is high levels of pyrethroid resistance in *Aedes* in Papua New Guinea (S Karl, personal communication) and reported high levels of pyrethroid and temephos resistance among several *Aedes* populations throughout Cambodia.[38]

FIGURE 12. GEOGRAPHIC DISTRIBUTION OF PYRETHROID RESISTANCE IN *AEDES AEGYPTI* AND *AEDES ALBOPICTUS* IN THE INDO-PACIFIC.[39] DATA INCLUDES ALL STANDARD TESTS, DOSAGES, AND MOSQUITO LIFE STAGES (BOTH LARVAE AND ADULTS).



[36] Kraemer MUG, Reiner Jr RC, Brady OJ, Messina JP, Gilbert M, Pigott DM, et al. Past and future spread of the arbovirus vectors Aedes aegypti and Aedes albopictus. Nature Microbiology. 2019.

[37] Vontas J, Kioulos E, Pavlidi N, Morou E, della Torre A, Ranson H. Insecticide resistance in the major dengue vectors Aedes albopictus and Aedes aegypti. Pesticide Biochemistry and Physiology. 2012; 104(2):126-131.

[38] Boyer S, et al Resistance of Aedes aegypti (Diptera: Culicidae) Populations to Deltamethrin, Permethrin, and Temephos in Cambodia. Asia Pac J Public Health. 2018 Mar;30(2):158-166. doi: 10.1177/1010539517753876. Epub 2018 Mar 4.

[39] Moyes CL, Vontas J, Martins AJ, et al. Contemporary status of insecticide resistance in the major Aedes vectors of arboviruses infecting humans. PLoS NTD. 2017. https://doi.org/10.1371/journal.pntd.0005625.

Other mosquito-borne diseases

Lymphatic filariasis

An estimated 120 million people in 81 countries are infected currently with lymphatic filariasis (LF), caused by parasitic worms transmitted by mosquito vectors, and 1.34 billion people live in areas where filariasis is endemic and are at risk of infection.[40] Of all filariasis infections, 90% are caused by *Wuchereria bancrofti* and the remaining caused by *Brugia malayi* and *B. timori* worms.

In 2000, the WHO established the Global Programme to Eliminate Lymphatic Filariasis, which has a stated goal of eliminating LF as a public health problem by 2020. The strategy includes 1) interrupting transmission using combinations of albendazole and diethylcarbamazine (DEC) delivered through mass drug administration (MDA) and 2) alleviate suffering and disability by introducing basic measures, such as improved hygiene and skin care to people living with disabling clinical manifestations of the disease.

Approximately 55.7% of the 1.34 billion people at risk globally are in the Indo-Pacific where LF is caused by *W. bancrofti* and *B. malayi*. The genera of vectors responsible for transmission vary by geographic area with *Culex quinquefasciatus* and *Anopheles* dominating in Asia and Papua New Guinea, respectively, with some contributions from *Mansonia* and *Aedes* vectors and *B. timori* transmitted by *Cx. quinquefasciatus*.[41,42] According to this analysis, LF is still endemic in Bangladesh, India, Indonesia, Lao PDR, Malaysia, Myanmar, Papua New Guinea, Philippines, and Timor Leste (Figure 10). A number of countries have eliminated LF in the region.

Japanese encephalitis

Japanese encephalitis (JE) is the leading cause of vaccine-preventable encephalitis in the Indo-Pacific region[43] and causes an estimated 68,000 clinical cases in the region each year with a case-fatality rate as high as 30%, although less than 1% of people infected with JE develop clinical illness.[44] JE is a flavivirus, related to West Nile and St. Louis encephalitis viruses, and is transmitted by *Cx. tritaeniorhynchus* to humans through a transmission cycle between mosquitoes and non-human hosts, including pigs and birds. Humans do not usually develop sufficient viremia to infect mosquitoes. JE transmission occurs primarily in rural agricultural areas associated with rice production and flooding irrigation. Because these settings are the primary larval habitats for *Cx. tri-taeniorhynchus*, the spatial distribution of the vector is used as a proxy for JE risk across the region (Figure 10, D).

The WHO reports 24 countries in the WHO SEARO and WPRO regions have endemic JE virus, with more than 3 billion at risk of infection (Figure 10, D). According to this analysis, there were an estimated 4,652 cases of JE reported in the Indo-Pacific region with the highest reports from India, China, Myanmar, Philippines, Indonesia and Vietnam (Annex 2).

Recommended prevention tools include repellents, insecticide treated clothing, and a vaccine. The WHO recommends that JE vaccination be integrated into national immunization schedules in all areas where JE disease is recognized as a public health issue.[45]

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[40] WHO. Lymphatic filariasis progress report 2000-2009 and strategic plan 2010-2020. WHO Global Programme to Eliminate Lymphatic Filariasis. 2010.

[41] Sudomo M, Chayabejara S, Duong S, Hernandex L, Wu WP, Bergguist R. Elimination of lymphatic filariasis in Southeast Asia. Adv Parasitol. 2019;72:205-33.

[42] Dickson BFR, Graves PM, McBride WJ. Lymphatic filariasis in mainland Southeast Asia: a systematic review and meta-analysis of prevalence and disease burden. Trop med and Infect Dis. 2017; 2(32).

[43] CDC. Japanese encephalitis. Accessed February 2019. https://www.cdc.gov/japaneseencephalitis/transmission/index.html

[44] WHO. Japanese encephalitis. 2015. https://www.who.int/news-room/fact-sheets/detail/japanese-encephalitis

[45] WHO. Japanese encephalitis. 2015. https://www.who.int/news-room/fact-sheets/detail/japanese-encephalitis

Summary of vector control evidence, opportunities, and recommendations

WHO recommendations, evidence on the *Anopheles* and *Aedes* control toolboxes, a summary of interventions in use across the Indo-Pacific region, and recommendations from this landscape analysis are summarized below.

WHO recommendations for control for *Anopheles* and *Aedes* vectors

For *Anopheles* control, the WHO recommends ITNs and IRS as the core vector control methods, as detailed in the new Guidelines for Malaria Vector Control released in February 2019.[46] In specific settings and circumstances, the core interventions can be supplemented by other measures including larval source management and scale-up of personal protection measures.

For *Aedes* control, the WHO recommends larval source management through chemical control, biological control, and/or environmental management and recommends additional interventions for individual and household protection; including bite-proof clothing; repellents; ITNs for people sleeping during the day; indoor coils, aerosols, and vaporizers; and household fixtures including window and door screening and air-conditioning. The effectiveness of IRS for *Aedes* control is not well documented according to WHO.[47] It should be noted that increasing reports of nighttime biting *Aedes* makes use of ITNs and IRS more relevant.

Evidence synthesis of the malaria vector control toolbox

In 2015, the UCSF Malaria Elimination Initiative conducted a systematic review of the availability and quality of evidence for 21 malaria vector control tools, excluding ITNs and IRS, describing an expanding pipeline of research on supplementary tools while identifying important gaps in the evidence base.[48] Of 17,912 studies screened, 155 were eligible for inclusion in the review. Of 21 vector control tools, only seven had at least one Phase III community-level evaluation (Figure 13).[49] Phase III trials were conducted on LSM, mosquito proofed housing, topical repellents, spatial repellents, insecticide-treated clothing and blankets, insecticide treated hammocks, and insecticide-treated livestock, all with varying impact on malaria transmission.[50] Systematic reviews of LSM and mosquito-proofed housing concluded that both interventions can offer population level protection from malaria while the systematic review and meta-analysis on topical repellents concluded that topical repellents are unlikely to provide effective population level protection against malaria. Two insecticide-treated hammock Phase III trials in Venezuela and Vietnam and one trial of insecticide-treated livestock in Pakistan reduced malaria incidence and prevalence, while two Phase III trials of insecticide-treated blankets and clothing had variable results. Spatial repellent Phase III trials included one in Indonesia using metofluthrin coils and another in China using transfluthrin coils, both demonstrating reductions in malaria prevalence. The remaining 14 tools were supported by at least one Phase II or Phase I evaluation. A meta-analysis was not possible due to the heterogeneity of the studies.

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[46] WHO. Guidelines for Malaria Vector Control. Global Malaria Programme. 2019.

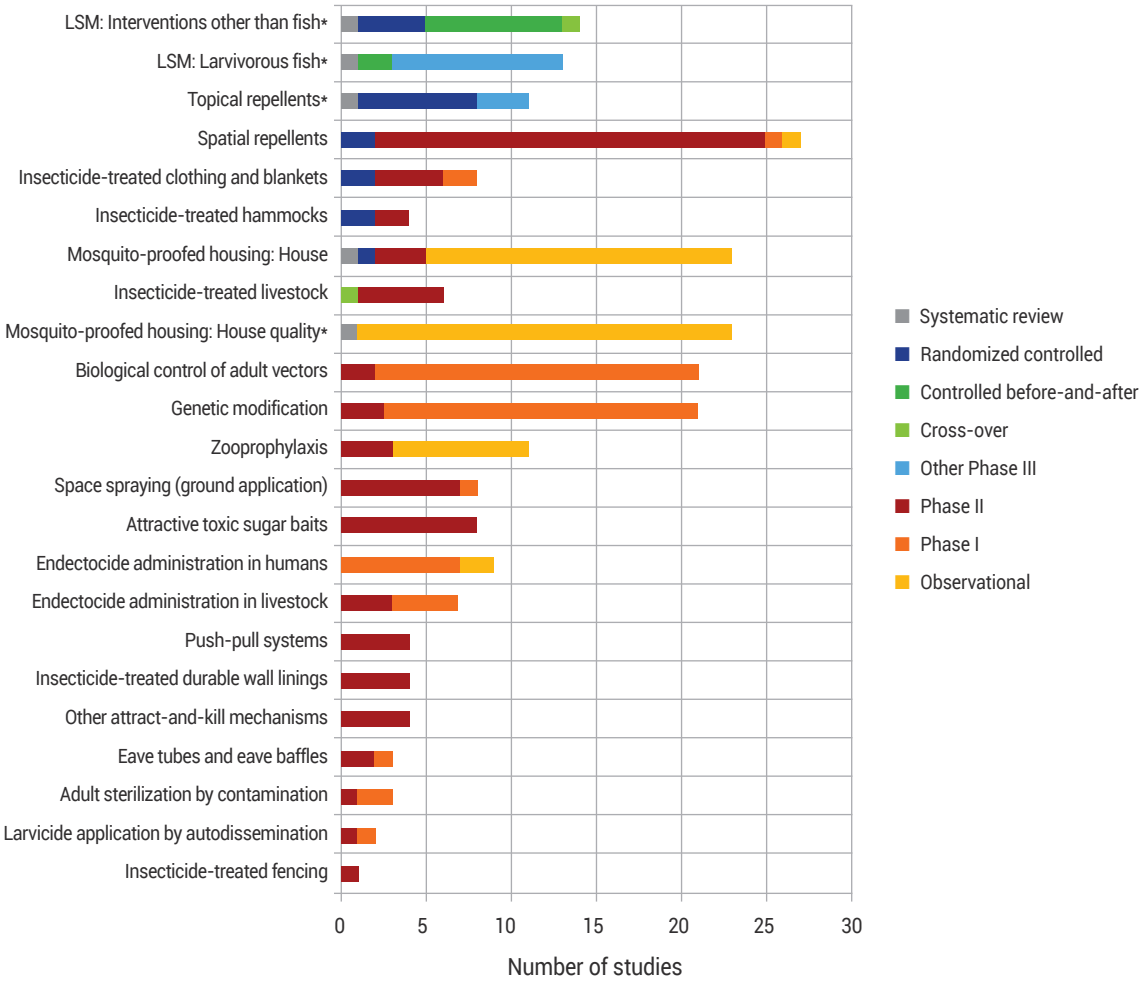
[47] WHO. Global Strategy for Dengue Control & Prevention 2012-2020.

[48] Williams YA, Tusting L, Hocini S, Graves PM, Killeen GF, Kleinschmidt, et al. Expanding the vector control toolbox for malaria elimination: a systematic review of the evidence. Adv in Parasit. 2018; 99:345-379.

[49] The level of evidence required for WHO policy recommendation is evidence of efficacy on malaria cases from two or more Phase III randomized control trials.

[50] Note: several tools listed are not currently recommended for public health use but are endorsed by WHO for personal protection (e.g. topical repellents and insecticide treated clothing).

FIGURE 13. FREQUENCY OF ELIGIBLE STUDIES FOR 21 VECTOR CONTROL TOOLS, STRATIFIED BY STUDY DESIGN (FROM WILLIAMS AND TUSTING, 2018). *STUDIES WITHIN THE SYSTEMATIC REVIEWS ARE DESCRIBED HERE.

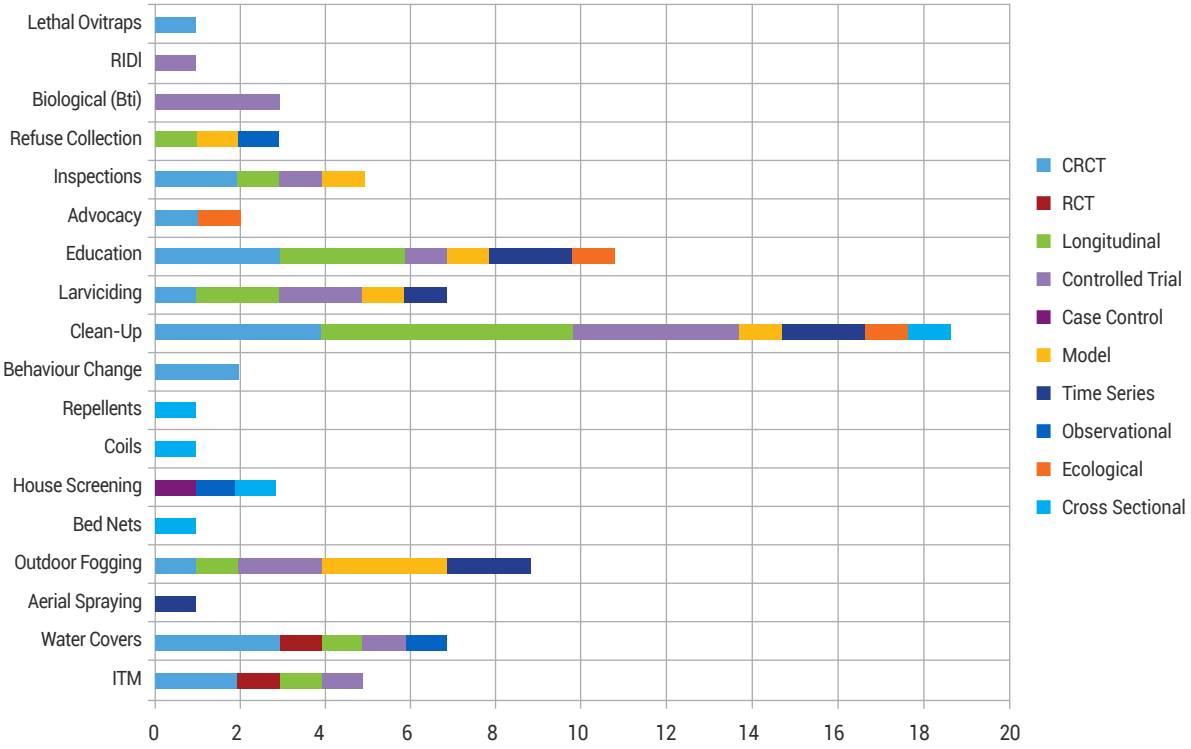


[50] Note: several tools listed are not currently recommended for public health use but are endorsed by WHO for personal protection (e.g. topical repellents and insecticide treated clothing).

Evidence synthesis of the Aedes-borne disease vector control toolbox

Bowman and colleagues from the University of Liverpool and Liverpool School of Tropical Medicine conducted a systematic review and meta-analysis of dengue vector control.[51] A total of 960 potentially relevant studies were identified, 41 studies were included in the final review, and 19 were included in the meta-analysis. Figure 14 illustrates the tools and approaches under review, stratified by study design. There were five Phase III studies, although none of them were randomized controlled trials. House screening was shown to significantly reduce the odds of dengue incidence, as did the combination of community-based environmental management with the use of water container covers. Indoor residual spraying reduced the odds of infection, but the results were not significant. The analysis found that there was no evidence that mosquito repellents, bed nets, or mosquito traps reduced the odds of dengue infection. The use of knockdown sprays and mosquito coils were both significantly associated with an increased odds of dengue infection (implying increased use was a response to *Aedes* nuisance and dengue, not a cause of increased infection).

FIGURE 14. FREQUENCY OF ELIGIBLE STUDIES FOR AEDES-BORNE DISEASE VECTOR CONTROL TOOLS, STRATIFIED BY STUDY DESIGN (FROM BOWMAN, 2016).



CRCT=cluster randomized controlled trial, RCT=randomized controlled trial. Ecological studies are studies in which the unit of observation is the population or community. Disease rates and exposures are measured in each of a series of populations and their relation is examined.[52]

[51] Bowman LR, Donegan S, McCall PJ. Is dengue vector control deficient in effectiveness or evidence?: Systematic review and meta-analysis. PLoS Negl Trop Dis. 2016; 10(3).

[52] The BMJ. Chapter 6: Ecological studies. (n.d.). Retrieved from https://www.bmj.com/about-bmj/resources-readers/publications/epidemiology-uninitiated/6-ecological-studies

Achee and colleagues reviewed alternative strategies for mosquito-borne arbovirus control, including traps, attractive toxic sugar baits (ATSB), insecticide-treated materials, classical sterile insect technique (SIT), release of insects with dominant lethality (RIDL), *Wolbachia*, and gene drives.[53]

Another systematic review and meta-analysis of cluster randomized controlled trials (CRCTs) for *Aedes aegypti* control was conducted by Alvarado-Castro and colleagues.[54] Eighteen studies met the inclusion criteria, and ten papers were included in the meta analysis based on entomological indices. Community mobilization (n=4 studies) was consistently effective based on entomological outcomes, one CRCT of biological control (copepods and *Bti*) showed a small impact, and the five studies of chemical control did not show a significant impact based on entomological outcomes. One CRCT of community mobilization measured the impact on dengue infection in Nicaragua and Mexico and found a significant impact on childhood dengue infection.[55]

Summary of interventions and tools used in the Indo-Pacific

Table 4 includes a summary of interventions and tools used in the Indo-Pacific region, as well as tools under evaluation by country. For malaria, nearly all programs rely on universal distribution of LLINs. Hammock culture is variable but some countries have started to scale up long-lasting insecticide treated hammocks with donor funding. IRS is in many national strategies, often for focal or outbreak response but is implemented at small scale, if implemented at all. Outdoor residual spraying (ORS) is increasingly being evaluated for both *Anopheles* and *Aedes* control but is not implemented at large scale by any program. Space spray, both indoors and outdoors, is commonly part of national dengue strategies, most often for outbreak response, but implementation is variable. LSM is widespread and often decentralized to districts and communities; larviciding is the main LSM intervention with some small-scale use of larvivorous fish and environmental management. The most common use of bite prevention tools for public health is through "forest packs" being delivered and evaluated by national malaria programs and partners in the GMS, which include a combination of topical repellents, hammocks, LLINs, and/or long sleeve clothing. There is other ongoing research, as described below.

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[53] Achee NL, Grieco JP, Vatandoost H, Seixas G, Pinto J, Ching-NG L, et al. Alternative strategies for mosquito-borne arbovirus control. PLoS Negl Trop Dis. 2019;13(1).

[54] Alvarado-Castro V, Solis-Paredes S, Nava-Aguilera E, Morales-Perez A, Alarcon-Morales L, Balderas-Vargas NA, et al. Assessing the effects of interventions for Aedes aegypti control: systematic review and meta-analysis of cluster randomized controlled trials. BMC Public Health. 2017;17(sup 1):384.

[55] Andersson N, Nava-Aguilera E, Arosteguí J, Morales-Perez A, Suaso-Laguna H, Legorreta-Soberanis J, et al. Evidence based community mobilization for dengue prevention in Nicaragua and Mexico (Camino Verde, the Green Way): cluster randomized controlled trial. BMJ. 2015;351:h3267.

TABLE 4. SUMMARY OF INTERVENTIONS USED ACROSS THE INDO-PACIFIC REGION BY MARKET AND DISEASE, ALSO NOTING INTERVENTIONS UNDER EVALUATION BY COUNTRY (NOT EXHAUSTIVE)

Tool	Public health		Community		Consumer	Military / forest rangers	Econ. dev zones	PCOs	Under evaluation	
	Malaria	Other VBD	Malaria	Other VBD	Non-specific	Non-specific	Non-specific	Nuisance	Malaria	Other VBD
LLIN	■						■		IDN	
Untreated nets					■	■				
ITH/LLITH	■								VNM	
Untreated hammocks					■	■				
Targeted IRS and / or IRS for foci and / or outbreak response	■	■				■				
Forest packs*	■								MMR, KHM, VNM	
Targeted larviciding and/or for outbreak response	■	■	■	■			■	■		
Small scale environmental management	■	■	■	■			■			
Targeted ORS	■	■							IDN, MMR	MYS
Small scale use of larvivorous fish	■	■		■				■		
Topical repellents (not including forest packs)		■			■	■	■		VNM	
ITC/bite-proof clothing (not included in forest packs)						■			MMR	
Space spray		■					■	■		
Community education and clean-up programs		■	■	■						
Coils					■					
Aerosols					■					
Candles					■				VNM, KHM	

IDN=Indonesia, KHM=Cambodia, LKA=Sri Lanka, MYS=Malaysia, MMR=Myanmar, SLB=Solomon Islands, THA=Thailand, VNM=Vietnam
*Forest packs include topical repellents and/or LLINs and/or long sleeve shirts and/or LLIHNs

TABLE 4. (CONTINUED) SUMMARY OF INTERVENTIONS USED ACROSS THE INDO-PACIFIC REGION BY MARKET AND DISEASE, ALSO NOTING INTERVENTIONS UNDER EVALUATION BY COUNTRY (NOT EXHAUSTIVE)

Tool	Public health		Community		Consumer	Military / forest rangers	Econ. dev zones	PCOs	Under evaluation	
	Malaria	Other VBD	Malaria	Other VBD	Non-specific	Non-specific	Non-specific	Nuisance	Malaria	Other VBD
Untreated house screens										
Controlled fires for smoke (as repellent)										
Waste management										
Lethal ovitraps										
Spatial repellents									IDN	LKA
Ivermectin in humans									THA, SLB	
Ivermectin in livestock									VNM	
Insecticide treated fencing / tarpaulins									IDN, VNM, KHM	
Wolbachia										IDN, MYS, LKA, MMR
Autodissemination traps										MYS
ULV adulticide and larvicide										MYS
Sterile insect technique										MYS, LKA
Insecticide treated paint										MYS

IDN=Indonesia, KHM=Cambodia, LKA=Sri Lanka, MYS=Malaysia, MMR=Myanmar, SLB=Solomon Islands, THA=Thailand, VNM=Vietnam
*Forest packs include topical repellents and/or LLINs and/or long sleeve shirts and/or LLIHNs

Technical challenges for vector control in the Indo-Pacific

Below is a summary of key challenges collated from the key informant interviews.

Malaria elimination

- Outdoor malaria transmission is the primary concern for most countries, including difficulty in accessing and providing appropriate, user-friendly malaria prevention tools for high risk populations, both in village settings with early/outdoor biting as well as among mobile and migrant populations, a highly heterogenous at risk population across the Indo-Pacific.
- There is limited attention to consumer preference for LLINs and LLIHNs, causing limited up-take in some areas and preference for conventional nets and hammocks. There is generally weak follow-up after distribution and weak quality control of large procurements.
- *P. knowlesi* transmission is increasing in some countries, raising new concerns about controlling this zoonotic malaria that parallels transmission of *P. falciparum* and *P. vivax* in the GMS.
- IRS is included in many national strategic plans, especially for foci and outbreak response, but its implementation is very limited with the exception of a few countries such as India where IRS is the primary vector control intervention.
- There is a lack of evidence on and resources for integrated vector control strategies, which is what will be required for elimination in the region.
- Global normative guidance is seen to hinder the ability of national malaria programs in the Indo-Pacific to incorporate supplemental vector control tools into national malaria strategy based on local transmission dynamics.

Aedes-borne disease control

- *Aedes* control (where present) is stalling in the wake of increasing dengue and other *Aedes*-borne disease transmission, including spread to more rural areas. There is a lack of suitable tools with heavy reliance on decades-old *stegomyia* indices and temephos-based strategies. Poor municipal waste management systems lead to larval habitat proliferation.
- There are large gaps in *Aedes* insecticide resistance monitoring and mapping, although pyrethroid resistance appears to be extensive in many countries.
- The *Aedes* control market is very different from the *Anopheles* control market, including some countries with large semi-regulated PCO sectors.

Surveillance, information management and targeting

- *Aedes* and *Anopheles* surveillance systems are antiquated in many countries, and data is often not being used for decision-making. This is often due to a lack of resources and capacity.
- Rapidly changing environments and transmission ecology in many countries is affecting both *Anopheles* and *Aedes* distribution and behavior. This combined with a lack of efficient vector surveillance results in suboptimal targeting and risk-area stratification.
- There is insufficient use of rapidly evolving information technology, including integrated electronic databases, mobile technology, GIS, remote sensing and 'big data' to monitor, target, and develop interventions. The lack of central databases for central decision-making may also contribute to less evidence-based decision-making. Conversely, the reliance and expectation of partners and donors on large databases and advanced decision-making tools may not match national or local capacity.

Operational

- Vector-borne disease control programs and strategies are often disparate or siloed, also with large gaps between control programs and national research institutions working in parallel with limited true collaboration in some settings.
- Some decision-makers require training in vector biology and transmission ecology to better adapt strategies to heterogenous and complex contexts.
- Vector control is often multi-sectoral involving agriculture, public works, and other ministries and also decentralized to district and/or community level, making accountability and measuring of impact difficult.
- There are inadequate resistance management plans, a lack of insecticide resistance data, and lack of registered alternate products for resistance prevention or management.
- Sub-optimal, low-cost products are available on retail and professional pest control markets in many places, disincentivizing companies to introduce higher quality yet higher cost products.
- Sluggish and challenging regulatory and policy processes exist with a reliance from key procurers on policy recommendations. The WHO is in the process of establishing new regulatory and policy processes that aims to address these challenges.
- There are significant challenges with national pesticide product registration, including Reliance on WHO regulatory and policy guidelines/recommendations in some countries;
  - Very slow registration of new products;
  - Insecticides not considered medical in nature so there is a need to recategorize for health; and
  - Low volumes and/or unstable markets.

Vector control recommendations from landscape analysis

Broadly, IVCC can capitalize on its IVM portfolio to develop a vector control toolbox for the Indo-Pacific region with a focus on malaria elimination, *Aedes*-borne disease control, and regional health security. Outdoor transmission is considered the most pressing challenge by stakeholders and experts. It's important to note that, while the epidemiology of malaria in the Indo-Pacific is different from that in Africa, outdoor transmission – long understood as a challenge in the Indo-Pacific – is increasing in relative importance in sub-Saharan Africa so this report and consideration of IVCC's program of work in this space should consider the potential demand in Africa.[56,57] Similarly, there may be synergies between tool development for vector control in humanitarian emergencies, i.e. for displaced families in situations where traditional LLINs and IRS are not practical and where tools are needed for outdoor transmission.[58]

As shown in Figure 15, we describe tools by those that function outdoors versus indoors and by those that require area wide (i.e. community) application versus individual use for bite prevention. There is a growing toolbox for mosquito control, but each tool has both limitations and opportunities for development and optimization by IVCC and other partners, as noted in Figure 15. Given the small size in this document, this figure is also attached as an Annex to this report.

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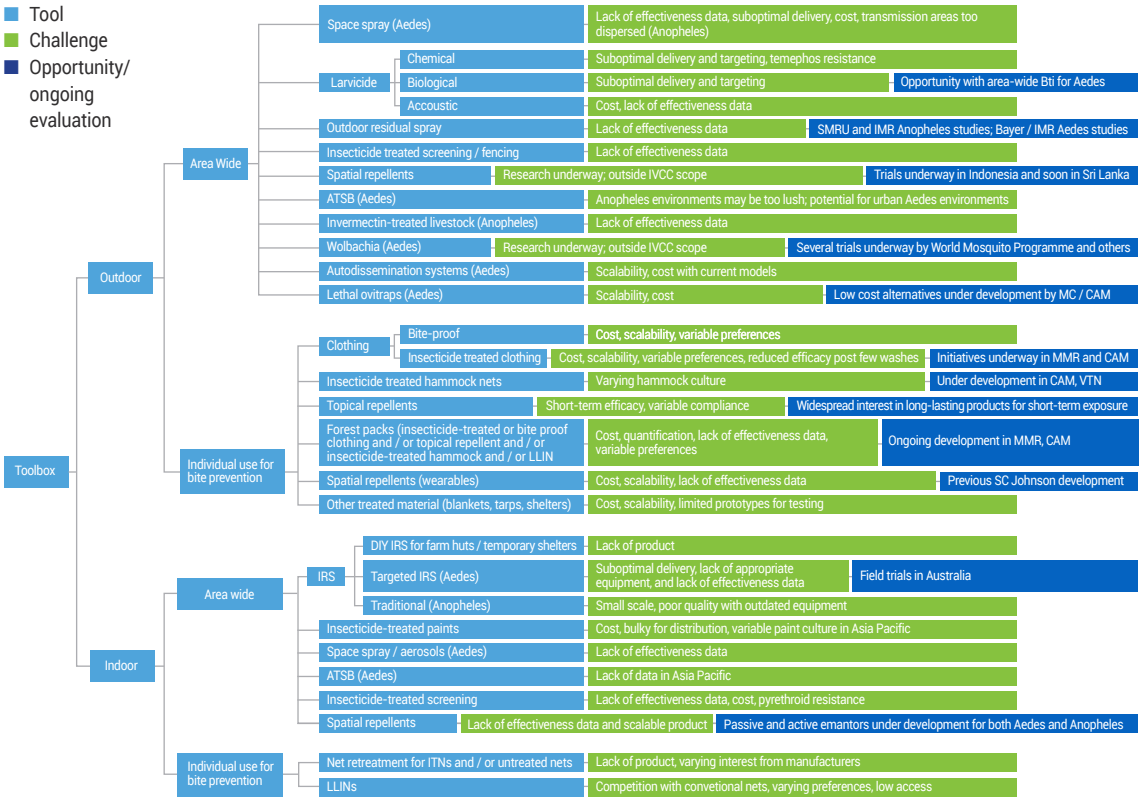
[56] Durnez L, Coosemans M. Residual transmission of malaria: an old issue for new approaches. Chapter 21, Anopheles mosquitoes – New insights into malaria vectors. IntechOpen. 2013; 671-704.

[57] Bier JC, Wilke ABB, Benelli G. Newer approaches for malaria vector control and challenges of outdoor transmission. Toward Malaria Elimination – A Leap Forward, IntechOpen. 2018

[58] https://endmalaria.org/sites/default/files/Vector-Control-Humanitarian-Emergency-meeting-report-.pdf

FIGURE 15. MIND MAP OF VECTOR CONTROL TOOLS FOR *ANOPHELES* AND *AEDES* CONTROL (SEE ATTACHMENT FOR FULL SIZE)



Below is a summary of our recommendations based on the desk review and key informant interviews, along with our consultations with industry and innovation partners.

LLINs. LLINs work on specific susceptible mosquito bionomic traits, including an overlap between mosquito time and place of biting and LLIN use (usually indoors) and susceptibility to the insecticide on the net. LLINs also provide a physical protective barrier against biting.

There is a strong net culture in the Indo-Pacific region, especially the GMS. LLIN access and coverage continue to be challenges, especially for families that have multiple living spaces (i.e. village and farm/forest) and populations that live in remote areas. There is also competition with conventional nets in many places where individuals prefer the colors, designs, and shapes of the conventional nets accessible through local shops. The disruption of the private market for ITNs with LLINs only distributed through public health mass campaigns has reduced access in some areas; continuous/routine distribution has helped fill gaps, and subsidized sales of nets may help fill gaps in more peri-urban settings where individuals seek out products from local shops. Community retreatment activities are still popular in some countries (e.g. Vietnam) where demand for retreatment kits remains strong. Until there is more insecticide resistance data from the Indo-Pacific, we would not yet recommend consideration of PBO or dual-AI[59] LLINs. Applicability of nets to migrant and mobile populations depends on housing consideration, with outdoor transmission incurring a gap in protective coverage from mosquito bites.

IVCC opportunity: explore market opportunities for long lasting retreatment strategies and subsidized sales of LLINs through the private sector to improve access to quality and effective products.

[59] PBO: piperonyl butoxide, a synergist (enhancing the functionality of insecticides) ; dual-AI: dual active ingredient.

IRS, ORS, and outdoor space spraying. IRS functions best on indoor resting mosquitoes susceptible to the active ingredient. ORS and outdoor space spraying effectiveness relies on contact between the active ingredient, susceptibility to the active ingredient, and an overlap between the mosquito (presence or resting behavior) and the space sprayed.

Across these interventions, there is a lack of epidemiological effectiveness data for both *Aedes*- and *Anopheles*-borne diseases. In many countries, IRS is in national strategies but is either not implemented, or is implemented at small scale, with the exception of India and Pakistan, and to a lesser extent in Vietnam. In India, given widespread insecticide resistance, innovation in IRS insecticide and application technology may have a significant impact on malaria, *Aedes*-borne diseases, and visceral leishmaniasis. Where IRS infrastructure exists, evidence should be generated on 1) targeted IRS for *Aedes* control and 2) IRS in malaria foci and for malaria outbreak response. For enclosed and semi-enclosed farm huts and semi-permanent structures, do-it-yourself (DIY) IRS could be effective depending on the local vector species.

There is increasing interest in ORS for malaria elimination across the Indo-Pacific. In Malaysia and Indonesia, ongoing entomological field evaluations of ORS targeting *P. knowlesi* vectors are funded by the MOHs. In Myanmar, a phase II entomological study of residual effect of ORS and knockdown from different insecticides is being funded by the Bill & Melinda Gates Foundation. None of the studies are looking at epidemiological impact (which, at present, will be required for a WHO policy recommendation).

Space spraying is often conducted without appropriate planning and monitoring, and the new WHO malaria vector control guidelines include a recommendation against space spraying given the very limited evidence; a similar lack of epidemiological evidence exists for *Aedes*-borne disease. Efforts are required to optimize the intervention (timing, frequency) with robust monitoring and evidence of effectiveness.

IVCC opportunity: generate epidemiological evidence on these interventions as part of an IVM approach based on local transmission dynamics and vector bionomics and explore product development for DIY IRS and application equipment.

ATSB. ATSB effectiveness is based on mosquito sugar feeding, which can occur at all times in a gonotrophic cycle. Access to the ATSB device is based on the abundance of alternative sugar sources will impact efficacy. There is significant interest and expanding research in ATSB for both *Aedes* and *Anopheles* control; epidemiological evidence of impact is lacking, although large clinical trials are underway. Several industry partners consulted as part of this landscape analysis noted an interest in developing attractants. The entomological impact of ATSBs are highly variable based on climate, alternative food-sources (i.e. local flora including plant species and flowering state), active ingredient, and the physiological state of the mosquitoes.[61] Given that most of the Indo-Pacific is tropical and lush, appropriateness of ATSB outdoors for *Anopheles* control may be limited, while *Aedes* environments may be much more suitable to ATSB.[62]

IVCC opportunity: develop and demonstrate impact of ATSB indoors for Aedes-borne disease control and malaria elimination in urban and peri-urban environments and in displaced persons camps.

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[60] Although the Myanmar study by the Shoklo Malaria Research Unit may include an evaluation of the SG6-P1 biomarker of human exposure to Anopheles saliva for monitoring the vector-control intervention.

[61] Florenzano JM, Koehler PG, Xue RD. Attractive toxic sugar bait (ATSB) for control of mosquitoes and its impact on non-target organisms: a review. Int J Environ Res Public Health. 2017; 14(4): 398.

[62] Sissoko F, Junnila A, Traore SF, Doumbia S, Dembele SM, Schlein Y, et al. Frequent sugar feeding behavior by Aedes aegypti in Bamako, Mali, makes them ideal candidates for control with attractive toxic sugar baits (ATSB). PLoS NTD. In review.

Bite prevention. For the purposes of this report, bite prevention strategies are interventions that prevent vector-host contact and include spatial repellents, both area wide and wearables, topical repellents, insecticide treated hammocks, insecticide treated clothing, bite-proof clothing, other insecticide treated materials (blankets, sheeting, tarps, tents), and LLINs (summarized above). All these tools require individual use and compliance, and all offer protection outdoors, which is the most significant gap in protection in the Indo-Pacific region, especially for malaria but also other mosquito-borne diseases. Spatial repellents, insecticide treated blankets, and LLINs can also be used indoors. Long lasting insecticide treated hammocks are the only products that have been procured and distributed through the public health sector to high risk populations in the GMS (Vietnam and, to a lesser extent, Cambodia). While hammock culture is variable across the region, there is a significant opportunity in optimizing and scaling hammock products following acceptability studies.

The key limitations of tools in the bite prevention space include compliance, longevity of effect, frequency of application/use required, delivery challenges, market size, low-cost competition in the consumer market, and lack of entomological and epidemiological evidence. Longer-lasting products (topical and spatial repellents) can help address compliance and delivery challenges related to replacement. Ensuring products are portable and designed to fit local needs and preferences will also improve compliance. Leveraging subsidized sales to the consumer market for free distribution through the public health sector, as well as leveraging the humanitarian, African, and Latin American markets increases the potential market size for these tools.

Other key gaps include consensus on testing guidelines and standardized screening methods, epidemiological evidence for various target product profiles and use cases, and identifying and developing new active ingredients.[63,64] There is interest from several industry partners in exploring product development with existing active ingredients and also in exploring new active ingredients.

There is increasing research and development in the bite prevention space, with significant opportunity for impact.[65] One approach is through forest packs, which are starting to gain traction in the GMS with funding from the Global Fund and PMI. These packs vary in specific products, but generally include a topical repellent, insecticide treated hammock, long sleeves and pants, and/or LLINs, alongside a flashlight and rucksack for transport. Another approach is through do-it-yourself (DIY) repellent treatment kit for various materials (e.g. blankets, eave ribbons, etc.) A kit could be adapted to setting and textile, making it highly versatile.

IVCC opportunity: building on the Outdoor Bite Prevention Innovation Workshop convened by IVCC in April 2017,[66] consolidate and manage the bite prevention roadmap; identify and further develop and evaluate key tools, including hammocks, longer lasting topical repellents, spatial repellents, DIY treatment kit, and clothing following more detailed review of the market landscape and product opportunities.

Other:

- **Insecticide treated paints**. Similar to IRS, insecticide treated paints rely on a mosquito resting on a painted surface and susceptibility to the active ingredient. Although epidemiological data is lacking for insecticide treated paints, entomological data is increasingly positive. Besides lack of evidence on public health impact, key limitations to scale up have been cost, bulkiness of the products, and pyrethroid resistance in some areas (relevant for the pyrethroid-only paints). Residual efficacy of the paints are about three years so as long as householders do not resurface/repaint the walls of their homes (as is customary in some Indo-Pacific countries), then paints have a much longer durability than IRS.

  IVCC opportunity: expand the evidence base for insecticide treated paints for Aedes-borne disease control and explore cost structures by leveraging the consumer and professional markets for the public health market.

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63 Arctec. Report for IVCC: an expert review of spatial repellents for mosquito control. 2018. LSHTM.

64 Richardson J. Presentation at RBM VCWG February 2019. Bite prevention tools roadmap: spatial protection with volatile pyrethroids.

65 Moore S. Presentation at RBM VCWG February 2019.

66 Systematic Inventive Thinking UK (SIT-UK). Outdoor Bite Prevention – Innovation Workshop. Report for IVCC. April 2017.

- **Chemical, biological, and acoustic larvicides**. Though there is considerable regional interest and a WHO recommendation for larviciding as a supplemental intervention, there is limited evidence on effectiveness in the Indo-Pacific region and lack of implementation resources (funding, manpower, knowhow) for *Anopheles* control. For *Aedes* control, there is widespread use of larviciding, often decentralized to district levels and to communities, thus making measuring impact difficult. New application technology may improve the scale of impact of larviciding, such as ULV spraying of Bti and other larvicides for *Aedes* control, currently being evaluated in Malaysia and elsewhere, and drone spraying of larviciding for *Anopheles* control. There is also increasing research on the use of drone and satellite remote sensing to map Anopheles larval habitats for LSM targeting. Acoustic larvicide technology is being used across the US and increasingly among private pest control operators in the Indo-Pacific region. At present, there is a lack of data on disease impact.

  IVCC opportunity: explore novel application methods for chemical and biological larvicides and increase the evidence base on effectiveness and best practices for implementation across the region.

- **Insecticide treated screening/barriers**: There are clear use cases for insecticide treated screens and barriers around villages and farm huts but further research is needed on entomological and epidemiological impact, as well more research to understand the impact of this tool on resistant vectors and in areas of pyrethroid resistance.

  IVCC opportunity: expand the evidence on effectiveness of insecticide treated screening and barriers, which could play an important role in an integrated vector management approach.

- **Ivermectin-treated livestock**. The efficacy of this intervention is based on the proportion of mosquitoes that will feed on treated animals. Evidence is still limited for this intervention but there is growing interest across Africa and the Indo-Pacific for malaria control (with ivermectin as well as other endectocides, including eprinomectin and fipronil). With a small-scale trial ongoing in Vietnam treating water buffalo with ivermectin for impact on *Anopheles*, this approach could be explored across the GMS, Papua New Guinea and elsewhere for pigs, as an example, which are very common across many communities in the region

  IVCC opportunity: expand the evidence base on livestock treated with ivermectin in areas with important exophagic and zoophagic vectors.

Disease Landscape Conclusion

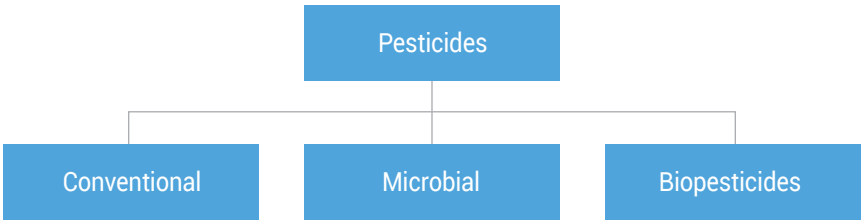
This report offers a snapshot of mosquito-borne diseases and opportunities for vector control product research, development, and access in the Indo-Pacific region. With the right set of tools targeted to the right populations at the right time in the right place, mosquito-borne diseases can be controlled and eliminated, improving health outcomes and health security for all.

Regulatory Landscape

Pesticide regulatory pathways in focus countries

The term "pesticides" includes Insecticides, Herbicides, Rodenticides, Antimicrobial products, Biopesticides, and other substances used to control a wide variety of pests. A pesticide product is defined as a pesticide in the particular form (including composition, packaging, and labelling) in which the pesticide is, or is intended to be, distributed or sold and includes any physical apparatus used to deliver or apply the pesticide if distributed or sold with the pesticide.[67]

The pesticide registration process includes many common elements, but some aspects are specific to the pesticide category. The categories that are important for the registration process are:

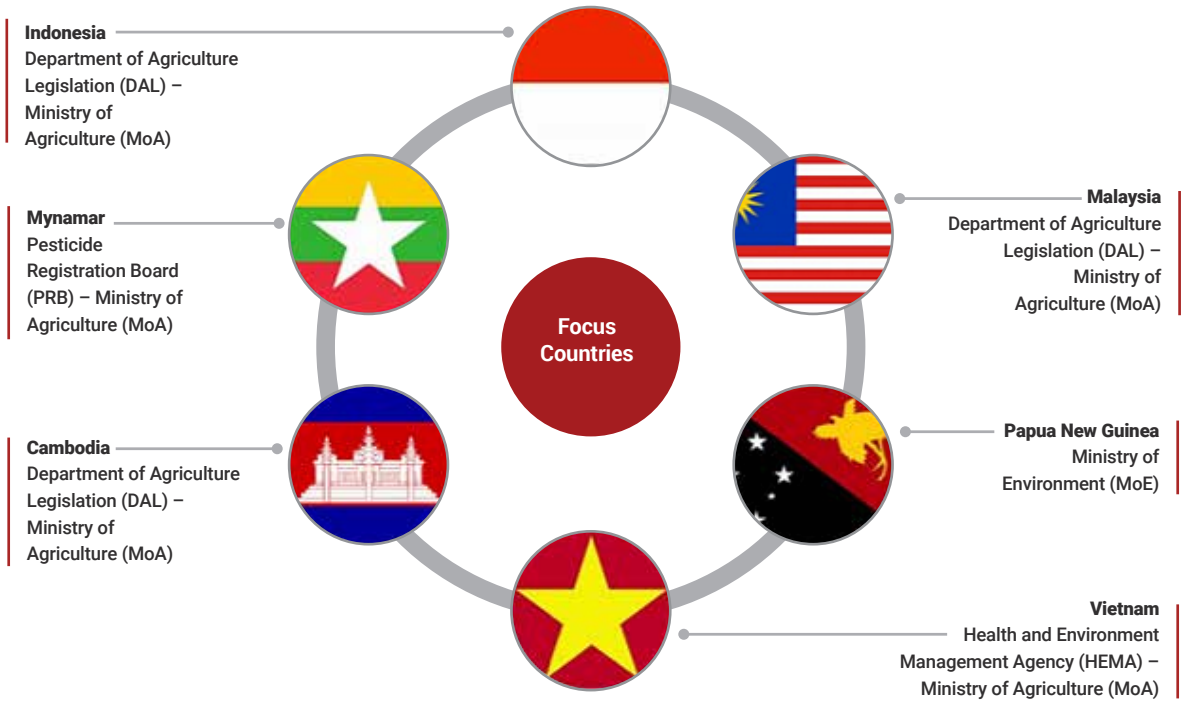


The registration process includes the following major steps for the first-time registration: (i) preparation and submission of the dossier by the applicant; (ii) initial administrative actions by the responsible authority; (iii) completeness check; (iv) technical and scientific evaluation; (v) preparation of summaries and conclusions; (vi) risk management and registration decision; (vii) publication and dissemination of registration decision; and (viii) label extension.[68]

[67] USEPA

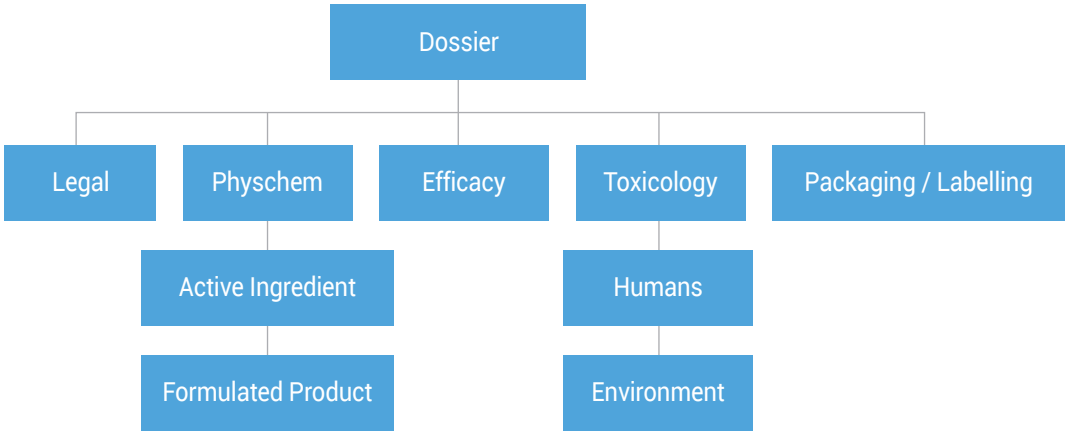
[68] WHO Guidelines on Pesticides Legislations - https://www.who.int/whopes/resources/9789241509671/en/

Regulatory Authority



Dossier Requirements

Product Registration is a careful evaluation of weighing the pesticides potential benefits of use vis-à-vis the potential adverse effects. A pesticidal product is evaluated for its (i) Quality (ii) Effectiveness against target pests (iii) Safety to Humans and (iv) Safety to non-target and environment and if its potential outweighs the adverse effects, then the product is approved for use. Therefore, for evaluation of product leading to regulatory approval, the following are components of the dossier.



Legal Requirements

These are administrative documents that are required to prove the authenticity of the registrant and the product. Under the legal part of the dossier the requirements are:

- Application form
- Company Registration Certificate
- Local Entity / Representative registration certificate
- Agreement with local representative
- Letter of Supply from Active Ingredient supplier
- Letter of Access
- Registration Certificates of the product registered in other countries
- Trademark registration

The above are commonly required documents but it is not the same in all the countries. There are differences in the requirement. Attachment in Appendix II provides details on specific country requirements.

Physicochemical

This component of the dossier comes under the technical requirement part. Herein, the required data is for the (i) Active Ingredient in the product and (ii) the end use or formulated product. The data requirements are related to product chemistry apply for technical material or formulated product. It includes data on physical characteristics of the technical material and/or formulated products. Additionally, it includes data on chemical information of technical and/or formulated products. They also include providing information about impurities, submitting an analytical method for enforcement and more.

- Physical Identity such as physical nature, Formulation type, colour,
- Chemical Identity such as nomenclature, CAS Registry number
- Chemical parameters such as Solubility, Specific Gravity, Melting Point, Boiling Point,
- 5 batch analysis of the active ingredient
- Impurity profile
- Storage Stability – Accelerated and or Real time
- Manufacturing process
- Analytical and validation methods
- Analytical Reports

Despite the commonality in the requirements, several countries in the region have their own list of requirements for physicochemical parameters. Some countries insist on test reports from GLP accredited laboratories and in some countries the tests are to be conducted from ISO 17025 accredited labs only; in other countries there is no specific requirement.

Additionally, regulatory authorities in the region do direct the applicant to any specific guideline or specification such as WHO (more relevant for public health pesticides), OECD or OPPTS guidelines for generating data. The attachment in the Appendix provides details on specific country requirements.

Efficacy

Product performance data are provided as a mechanism to ensure that pesticide products will control the pests listed on the label and that unnecessary pesticide exposure does not occur. Specific performance standards are used to validate the efficacy data in the public health areas, including:

Evaluation of pesticidal product is an essential part of the registration process. Proof of bio-effectiveness of the product on its intended target pest(s) is a mandatory component in the approval of a product to be used in a country. Pesticides, for use in Agriculture is tested for its effectiveness in institutes / laboratories on crops and pests for which its effectiveness is claimed on the label. The same yardstick is used for vector control products. The WHO has framed several guidelines for evaluating various vector control products such as Insecticides for IRS, Larvicide, Spatial sprays, LLINs, Mosquito coils, Vaporizers, repellents, Aerosols, Biological insecticides. However, many countries in the region insist on incountry evaluation of the product for its effectiveness regardless of the data available to adequately prove effectiveness of the product on the target pest. Moreover, some of the countries in the region do not specify the appropriate evaluation guideline to be followed and leave it to the manufacturer or the testing institute to decide upon the guideline to be followed. Attachment in the Appendix provides details on specific country requirements.

Toxicological

Data required to assess hazards to humans and domestic animals are derived from a variety of acute, sub-chronic, and chronic toxicity tests, and tests to assess mutagenicity and pesticide metabolism. The information required to assess hazards to non-target organisms is derived from tests to determine pesticidal effects on birds, mammals, fish, terrestrial and aquatic invertebrates, and plants. These tests include short-term acute, sub-acute, reproduction, simulated field, and full field studies arranged in a hierarchical or tier system that progresses from the basic laboratory tests to the applied field tests.

The results of each tier of tests must be evaluated to determine the potential of the pesticide to cause harmful effects and to determine whether further testing is required. A purpose common to all data requirements is to help determine the need for (and appropriate wording for) precautionary label statements to minimize the potential harm to non-target organisms.

Packaging & Labelling

A pesticide product's label is of utmost importance as the label is the primary mechanism to inform the end-user about how to use and apply the product to achieve the product's useful functions, as well as which precautions must be followed to protect both human health and the environment.

Types of Registration

Registration approval in countries comes in various categories. The categories of registration approval commonly granted in the region are (i) Full registration (ii) Provisional or Conditional Registration.

Under Full registration, the approval is granted for a defined period in some countries with no limit to the volume of pesticide that can be imported during the validity of the registration. The full registration in some countries is for a period of 3 years or 5 years. After this period, the registration is renewable for another period of 3 years or 5 years.

Provisional or conditional registration is valid for a period of 1 year or 2 years depending on the country. The provisional registration is granted for this specific period, and during this period additional data required for registration leading to full registration is to be generated. A limited volume is also permitted to be sold during this period. However, during this period of provision registration validity, the permitted volume cannot be exceeded. There is no renewal of provisional registration.

Country	Full Registration	Provisional / Conditional
Indonesia	5 years	2 years (No commercial)
Malaysia	5 years	No Provisional registration
Vietnam	5 years	No Provisional registration
Myanmar	10 years	5 years
Cambodia	No regulation for Public Health Pesticides	No regulation for Public Health Pesticides
Papua New Guinea	Permit – 1 year	No Provisional Permit

Cost of Registration

Cost of Registration differs from country to country in the region. The cost of registration includes (i) Cost of application (ii) Cost of registration (iii) Cost of in-country trials (if required) and (iv) Cost of Import Permit (if Product has to be imported into the country).

Though cost of registration in terms of application fees and registration fees are nominal, the cost gets inflated because of mandatory in-country efficacy trials in some countries in the region.

Flowchart on country registration processes

The registration process is a flow of different phases and it varies from country to country. From the time of submission of dossier to the final decision on the registration request, the process is known as registration process. The dossier goes through various stages such as pre-scrutiny, evaluation of dossier, evaluation of trial reports and then experts committee approval and final approval of ministerial board and grant of registration certificate.

The detailed flowchart examples are provided in the Appendix.

Validity of Registration Certificates

As described in the section below on types of registration, the validity of registration certificates may vary from country to country. Normally, for Full registration the validity is for a period of 3 years or 5 years in the focus countries. In countries, where provisional / conditional registration is granted, the validity is for a period of 1 or 2 years. More details on this can be referred under Section 6.3.

Requirements for Experimental Use Permits (EUP)[69]

Experimental Use Permit (EUP) or Trials Permit (TPs) are granted to a registrant to facilitate the importation of a small quantity of the pesticide to be registered or for any trial to be conducted by an institute or company for research purposes. EUP is granted on the basis of an application to be provided by the registrant of the product or by the trial scientist who is interested in importing an unregistered pesticide for the purposes of research.

Country specific EUP processes are detailed in the Appendix.

Post Registration Requirement

Once the registration is approved and a certificate is issued as proof of registration, the registrant is eligible for importing, stocking and selling of the Vector Control Product. However, each activity has to be authorized by the regulatory department in the country. Following regulatory approval, if the product is imported, then an Import Permit is to be obtained. For Selling and Stocking the pesticide in different provinces or states, a Selling and Stocking License is to be obtained. In addition to this monitoring and reporting of pesticide imports and sales should also be done on an annual basis.

Import Permit: An import permit is a mandatory requirement for a foreign manufacturer who has secured a registration in the country and now is ready to import the product into the country. To facilitate the import of the product, the registrant has to apply for an import permit to the respective regulatory department. The main document required for import permit to be granted is the Certificate of Registration (CoR).

Selling and Stocking License: A local manufacturer of Vector Control products or an importer of vector control products has to fulfil another statutory requirement – Stocking and Selling permit / license. This is a permit to be accorded by the respective regulatory authority who grants the registration or an allied ministry under which local trading laws come under. Only with a stocking and selling license would the product be allowed to be placed in pesticide shops or retail outlets.

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[69] Source: http://www.pertanian.go.id/ – INDONESIA; http://vihema.gov.vn/ – VIETNAM ; http://ppdmyanmar.org/ – MYANMAR; http://www.doa.gov.my/index.php/pages/view/302?mid=141 – MALAYSIA

Reporting: One of the most important activities which is normally required on an annual basis is for the pesticide manufacturer, supplier, registrant, importer or distributor to file an annual report on the volume of pesticide manufactured, reformulated, imported, repackaged or in stock to the regulatory authority, either on a prescribed form or online. The regulatory authority can then maintain a check on the pesticides that are being manufactured or shipped into the country. This is an important tool in providing information to the appropriate authority to curb unregulated pesticides in the market.

Pesticides and Public Health Programs

In country level Public Health programs, the use of pesticides is an indispensable tool for vector control. However, for inclusion as a recommended vector control product the pesticide should have regulatory approval in the country for use against the intended target pest. In addition to this it is also mandatory to be in the WHO (World Health Organization) Pre-Qualified List.

It is not mandatory to be under the WHO PQ list for registration of product for use in Vector Control in the country but to be included in Public Health Programs for procurement by country level funded vector borne disease control programs or global donor funded disease control programs, the product should be PQ listed. Many focus countries in the region are not aware of the change from WHOPES to WHO PQ. Country regulatory authorities who do not keep abreast with changes happening in the guidelines for vector control should be made aware of this significant change.

Various Country level Vector borne disease programs and have their specific requirements for vector control products as per their Vector Borne diseases Program.

Importance of Stringent Regulatory Authorities and International bodies in country regulatory processes

The regulatory authorities in the focus countries do not have any cooperation with any Stringent Regulatory Authorities (SRA), such as US EPA or the EU, nor have any collaborative registration process between the regulatory authorities in the countries. In addition to this, the regulatory authorities in this region such as CIBRC (India), ICAMA (China), NEA (Singapore), APVMA (Australia), MAFF (Japan) do not have any influence in expediting the registration in the focus countries.

Therefore, there is no significant influence by any other regional or global regulatory authority on the registration process in the region.

Regulations on Pest Control Operators (PCOs)

Pest Control Operators play an important part in the control of vectors causing life threatening diseases such as Malaria, Dengue, Zika, Chikungunya and other mosquito borne diseases. Pest control operators are trained to handle hazardous chemical pesticides that play an indispensable role in vector control programs.

The Pest Control Operators (PCOs) are trained to handle and use pesticides in the restricted pesticides list. It is pertinent to provide quality training to personnel on safe handling of pesticides, proper spraying of the pesticide on target areas and safe disposal of pesticides. The PCOs are also trained on first aid and the use of Personal Protective Equipment (PPE).

In the focus countries in the region, some of the countries such as Malaysia and Indonesia have robust training procedures for Pest control operators whereas in some of the other countries the training and certification is not very structured.

Proper training and sharing of information are lacking in many countries in the region and due to this proper and effective delivery of insecticides on the target areas and insects is not done. Proper training and periodic inspection would ensure effective delivery of insecticides and thereby an effective control of insect pests.

Regulations on disposal of pesticides

Disposal of pesticides that have expired or used should be carried out in a proper manner. Disposal is an important issue especially in mass distribution of LLINs or mass spraying of pesticides. In many of the focus countries disposal plans are not properly framed and there are no clear guidelines provided. It is left to the discretion of the manufacturers as well as the end users.

Comparison of registration process in the focus countries vis-à-vis African registration process

Parameter	Indo-Pacific	Sub Saharan African
Regulatory Authority	Primarily Ministry of Agriculture (MoA) regulates Pesticides for Public Health use.	Predominantly, Regulatory authority in Eastern Africa is under Ministry of Agriculture. In Western Africa especially in CILSS countries though regulations would be under MoA, authorizations have to be obtained from MoH too.
Harmonization	No regional harmonization between regulatory authorities	There are several regulatory harmonization processes in Sub Saharan Africa. SEARCH – East Africa SADC – South Africa CILSS – West Africa
Role of WHO Specifications	Not mandatory for registration.	Mandatory in many countries.
In Country testing	Several countries insist on in-country evaluation of efficacy & chemical content for registration	Many regulatory authorities in East Africa insist on in-country evaluation of efficacy In West Africa, in-country evaluation is not mandatory. Other regional country evaluation or WHO recommendation would suffice.
Testing Facilities	Several countries have good GLP / ISO certified testing facilities whereas in some countries testing capacity and capability is severely challenged	Very limited GLP / ISO certified laboratories / testing facilities in Sub Saharan Africa except in a few countries
Registration Timelines	Timelines depends on testing period and review time. In some countries the timelines can be very lengthy spanning over 15 – 20 months and some countries it is 3 – 6 months	Timelines would be based on testing and review period. Average time for regulatory approval would be 6 – 8 months. However, in some countries, the need for long in-country trials and slow review process may make the regulatory approval process very long – 18 – 20 months
Types of registration	Full / Provisional / EUP	Full / Provisional / EUP
Manufacturing capability	Good manufacturing capability in many countries However, some countries depend on importation of pesticides	Manufacturing capability is not available. All types of pesticides are imported into Africa.
Pest Control Operators	Better PCO training and certifications in many countries	Un-regulated PCO certification needs to be strengthened.
Validity of certificate	3, 5, 10 or indefinite period (till recall) Renewal of registration available	1 – 3 years only. Renewal of registration available
Labelling	Globally Harmonized System of Labelling guidelines followed. Labelling in English / Country specific language (1 or more)	Guidelines not specific. Labelling in English / Country specific language
Post Registration Inspection	Post registration inspection of goods is not required in many countries. Import permit may have to be obtained	Inspection of consignments prior to import is mandatory in many countries. 3rd party inspection agencies conduct inspection on behalf of country. Import permits are mandatory in some countries but not prevalent.

List of Registered Pesticides

A list of registered / approved pesticides for use in Public Health in the focus countries is attached in the Appendix.

Identified Gaps in Regulatory Processes in Focus Countries:

The regulatory systems in all countries have certain gaps and grey areas and that's the reason there are constant attempts on streamlining the process as well as work on legislations are ongoing. Some of the gaps that have been broadly identified are as follows:

Fragmented Registration Process:

The countries in the region are in the process of strengthening pesticide legislation in line with international standards. There are continuous efforts by the governments to bring in newer regulations and systems. Despite, the several efforts undertaken to streamline the registration process and with advances in the processes, there are several areas of lacunae.

There are great differences between the countries in the region. The pesticide regulations are more lopsided towards regulating for use in Agriculture and the strengthening of legislations for pesticides in use for other areas especially Public Health Use is meted out with little or no change.

No Standardized guidelines and specifications:

There are no specific guidelines recommended for public health pesticides in many of the countries in the region. There are no guidance documents available for specific categories of vector control products. The end use products range from indoor products such as mosquito coils, vaporizers / emanators, Indoor residual sprays of insecticides, aerosols / spatial repellents, insecticide treated mosquito nets and outdoor products such as insecticides used for outdoor residual sprays etc. Each product would require specific physical and chemical characteristics and specifications, specific testing requirements, toxicological requirements, packaging and labelling requirements. However, this specific guidance document is lacking in almost all the regulatory authorities. More disabling is the lack of a provision in the legislation to provide justification or request for waiving tests that are irrelevant for a particular type of pesticide. Since the regulatory authorities in many of the countries are under the Ministry of Agriculture, very little about the products and pests in public health domain is known to the regulatory authority. Due to this lack of awareness, the requirements for public health pesticides are also squeezed into the regulatory template that is more suitable for pesticides used in Agriculture.

Mandatory In-country efficacy testing:

Evaluation of pesticides proving their efficacy on the intended target pests are a mandatory part in the registration process of the product. However, there are requirements in some countries in the region to conduct efficacy testing of Public Health pesticides that have been adequately tested and proven for its efficacy either as part of WHOPES full recommendation / PQ listing or in a country in the region. There are a few countries among the focus countries such as Indonesia and Vietnam wherein local testing of product efficacy is mandatory for registration of the product in the country. In Indonesia, the testing has to be done in Government approved testing institutes. In Vietnam, the testing has to be done in NIMPE. Regional trial data are not considered for regulatory approval. In Malaysia, trial data from any region with similar climatic conditions are accepted for registration. In Myanmar, due to the lack of efficacy testing facilities, reports of trials conducted following international protocols are accepted. However, in-country chemical analysis of the end use product is mandatory in all the countries.

The mandatory testing of efficacy in the region adds to the cost of the registration and also adds to the delay of the product being approved for use in the country.

Unwarranted in-country evaluation of the efficacy of pesticidal products for use in Public Health which have already been adequately tested for their effectiveness is something that can be avoided but are still mandatory requirements in some countries in the region.

Lengthy Registration Process:

Registration timelines are the time taken from the submission of application along with dossier to the time the registration is approved leading to issuance of registration certificate. Timelines include – dossier check, review of documents, in-country efficacy testing, quality testing, chemical analysis, review of test reports, technical committee recommendation, pesticide board approval and issuance of registration certificate.

There are various processes that take time in product registration steps. The registration process in some countries such as Indonesia take a minimum of 12 – 15 months whereas in some countries such as Vietnam the process takes about 6 months. The reasons for lengthy registration processes are due to some of the following reasons: In-country trials; lower capacity with an increasing workload; complicated document requirement; less transparency in process

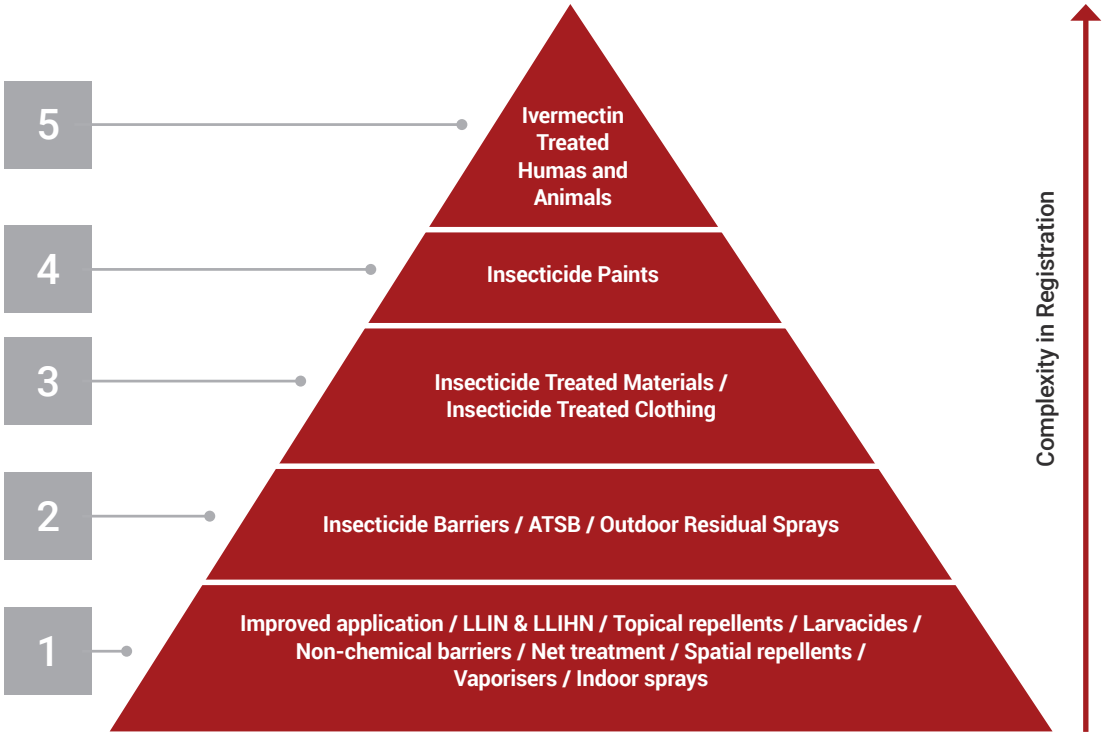
Lack of Enforcement and Implementation:

The gap between the letter of the Law and implementation of the same is very wide. There is a lack of coordination between the various ministries in the countries in the region. The regulations are by the Ministry of Agriculture predominantly but without the cooperation of the other ministries such as Ministry of Health, Ministry of Industries, Ministry of Commerce, Ministry of Environment etc. there is no proper enforcement or implementation of the legislation.

Without proper enforcement and implementation of the legislation, there are many gaps in monitoring of pesticide imports, sale of unregistered pesticides, sale of counterfeit pesticides and thereby the availability of good quality pesticide is seriously hampered. As a consequence, there is no motivation or encouragement for genuine manufacturers and suppliers and directly impedes the vector control operations in the country.

Vector Control Toolbox from Regulatory Perspective:

1. LLIN (LLIN & LLIHN)
2. Indoor Residual Sprays
3. Outdoor Residual Sprays
4. Topical Repellents
5. Forest packs
6. Space Sprays
7. Insecticide treated screens
8. Insecticide treated paints
9. ATSB (Attractive Toxic Sugar Baits)
10. Ivermectin treated Livestock
11. Ivermectin treated Humans



The bottom (1) layer of products such as LLIN / LLIHN, Topical repellents, Larvicides, Spatial repellents, Conventional net treatments, Spatial repellents, Vaporizers, IRS are all registered as recommended public Health products in the various countries in the region. There are several registered vaporizers, coils and topical repellents in the various focus countries in the region. These are registered to be sold in retail markets. Apart from these, several brands of LLINs and Chemical pesticides have been registered and approved to be used in mass distribution under various Vector borne diseases control programs.

So, these are potentially products that are available for easy adoption and induction into the public health programs appropriate for specific countries as per the need identified by technical landscape and the challenges identified in the market access profiling of the country. Based on the funding source and need suitable product mix can be picked up from the tool box and provided to the end users.

The second level (2) of products such as Insecticides Barriers i.e. materials treated with insecticides such as Insecticidal screens, Attractive Toxic Sugar Baits (ATSB), Outdoor residual sprays are some products which have not been registered. However, the complexity of registration of these products are less and can be easily considered for registration with some minimal data generated. Since Outdoor residual sprays would have to have additional environmental safety studies and stability studies done there would be some time to be factored in for the registration of this product. Insecticide barriers in the form of a net would be a label extension of indoor nets but this too would have some additional data generated.

Since, vector control success depends on integrated vector management and a steady supply of innovative intervention tools, it is important to start working on securing specifications and country specific registrations for these products. However, it is also important that the regulatory processes in the countries would create legislations to fast track certain low risk products or use extension of certain existing products.

The third level (3) of products consists of Insecticide treated clothing and Insecticide treated materials. There are no categories created for these products, but some commercial products have been tested and approved for use especially by military in some countries. These products would be of much importance for forest dwellers and migrant population – a scenario which is very common in this focus region. However, the regulatory requirements should be made less complex for these products and the regulatory authorities in the focus countries should take help from international regulatory authorities who have experience in working on such products.

Since, the regulatory authorities are mostly from Ministry of Agriculture, the onus would be with the Vector Borne Diseases Control programs under the Ministry of Health who would have to work closely with the regulators in making them understand the importance of these newer innovative products.

The fourth level (4) of product(s) are insecticide paints – this is an innovative product which would be of great help in reducing vector burden inside the houses and can be safer and aesthetic alternative for indoor residual sprays. However, the product needs extensive testing and proof of concept to be established. Nevertheless, there are specifications to be finalized and then data requirements need to be finalized.

The regulatory landscape for this product on a complexity scale would be high and the regulators need to be quick to formulate guidelines for registration.

The fifth level (5) level would probably be regulated under Animal Health Directorate or human Directorate. This is a complex level of regulation.

Pathways to the Future:

The regulatory pathways landscape has been constantly being upgraded with new legislations and making the regulations more robust and more adaptable. However, the changes have not been rapid and there is much to be changed and for these changes, the following would be pathways that can be taken into consideration.

Regional Harmonization:

There is a need to harmonize the regulatory processes in the various countries in the region. There have been many attempts and workshops on the harmonization of regulatory processes and the changes in the legislations and processes can be to some extent be attributed to these programs. However, there needs to be a systematic look at the various aspects of regulatory process in the region and the various countries in the region to bring about a homogenous harmonization.

In this direction, the ASEAN harmonization work has been initiated in the year 2018 and work is under progress to bring about harmonized regulatory processes for Pesticides used in various categories. There is also work done by programs such as VCAP (Vector Control Platform for Indo-Pacific) spear-headed by APLMA, Unitaid and APMEN in the South East Asian Region.

Standardized Guidelines:

The guidelines for various intended use of pesticides need to be streamlined and standardized. The current guidelines in some countries for pesticide registration is a standard guideline – in terms of studies required for pesticides to be registered for use in Agriculture, Public Health / Household, Veterinary, Industrial etc. Currently in some countries there is no specific guidelines and testing methods provided for specific use categories. There is no reference to WHO guidelines which have been standardized for different use categories of Public Health Pesticides. There are specifications and study guidelines including risk assessments for Mosquito coils, vaporizers, Indoor residual sprays, LLINs, spatial sprays, Larvicides, fogging etc. but these guidelines are not referred nor recommended in the guidelines for registrations of public health pesticides in many of the focus countries.

Moreover, in some countries such as Vietnam there is no guidelines for registration of microbial pesticides to be used in Public Health. This situation gives a platform for low quality microbial intervention tools to be used in the country. This situation of not having any regulation is more harmful than a situation wherein there is slack in the regulatory process.

Acceptance of Regional trials:

Some countries in the region insist on in country testing of public health pesticides and data generated in institutes approved by the regulatory authority, before registration is granted. This requirement is despite the fact that the product would already be tested adequately and listed in Pre-Qualified (PQ) list or the product has been tested in the country in the region. Only some regulatory authorities in the region accept regional trial like Malaysia, Singapore etc. whilst in some countries such as Vietnam, Indonesia insist on local bio-efficacy trials. This disparity in the regulatory requirements is to be standardized and acceptance of trials conducted in any country in the region following international or standardized trial protocols should be accepted. Moreover, when trials have been conducted on the product especially for PQ listing and the product has been comprehensively tested, the need for repetitive in-country evaluation not only increases cost but also the time to market these valuable tools for protecting human lives against deadly vector borne diseases.

Harmonization of guidelines and processes would help in regional countries accept regional trials regardless of which country the trials have been conducted.

Prioritization of Public Health Pesticides:

Many of the countries in the region do not have any specific legislation to promote the registration of pesticides used for public health by providing special categories such as reduced risk or minor use pesticides. Moreover, there are no provisions for accordance of priority for public health pesticides by taking into consideration the need of these products quickly so that their use in saving human lives could be expedited. Therefore, there should be legislations enacted in the act wherein priority in evaluation, scrutiny and approval of public health pesticides especially to be used in mass distribution under malaria elimination programs should be done. This would help manufacturers and malaria / dengue elimination / control programs to avail a fast track regulatory mechanism and thereby have newer products.

Strengthening analytical and testing facilities:

The focus countries in the region had varying capacity and capability of testing facilities in the country. Some of the countries such as Malaysia have highly evolved facilities in terms of entomological and chemical testing. Several laboratories are ISO 17025 and GLP accredited in Malaysia. In Vietnam, many ISO 17025 accredited laboratories are available but very few GLP accredited laboratories are available. In Indonesia, the testing is all to be done by government approved laboratories. However, there are several private testing laboratories which are ISO 17025 accredited. Myanmar, Cambodia and Papua New Guinea needs to have their capacity and capability improved. There is a need for improving the equipment and facilities for testing and also for upgrading the capabilities of personnel in testing and evaluation of products.

Coordination and cooperation of policy makers:

The regulatory mechanism is only effective as long as proper implementation of the regulations are enforced properly. For the implementation of the regulatory mechanism there should be proper co-operation and coordination with the different governmental department. In many countries, the ministry of Agriculture is the regulatory authority regulating pesticide registration, but the importance of other ministries such as Ministry of Health, Ministry of Commerce, Ministry of Trade, Ministry of Environment for proper implementation of the legislation in terms of testing, monitoring, surveillance, import of unregistered pesticides, manufacturing license of pesticides, selling license of pesticides, disposal and use of pesticides. These are monitored by different government entities under different ministries and only if there is seamless coordination between the ministries the legislation can be enacted properly and regulatory processes will be able to implement the intended process.

Unfortunately, this is less evolved in some countries and it has to be streamlined so that implementation could be done effectively.

Potential Advocacy Groups / Influencers:

ASEAN

The regulatory processes in the region has to be harmonized so that the guidelines, testing, review, labelling, monitoring and implementation would be uniform across the various countries whereby the registration of public health products would be seamless across boundaries making it easier for innovative vector control tools be introduced for the control of vector borne diseases.

ASEAN (Association of South East Asian Nations) is in the process of developing detailed harmonized guidelines for registration of pesticides in South East Asian Region. This would enable swifter and robust registration of pesticides for use in various fields.

Regional / Global Malaria Programs

The regulatory processes in the various countries can be bolstered by the regional and global malaria programs who could impress upon the regulatory authorities on the need for quicker approval process in the various countries. The launch of VCAP (Vector Control Platform for Indo-Pacific) is a good forum for sensitizing the regulatory authorities on the need for streamlined regional regulatory processes in the various countries in the Indo-Pacific region. This could be good platform for countries outside the ASEAN region for regulatory process upgradation and also for capacity building.

Donors

Donors can play a pivotal role in funding for effective malaria control in different countries based on the capacity of the country as well as the disease burden in the country. Donors also wield significant powers in influencing policy changes in the country especially when the need for innovative intervention tools are required.

Manufacturing companies

Due to diversity in vector population, population dynamics, resistance issues manufacturing companies should be constantly be innovating to discover newer vector control products. However, one of limiting factors to innovation is the sluggish pace at which some of the country regulations allow new innovations into the market. This discourages manufacturers from investing time and money on innovations for vector control products. Therefore, the manufacturing companies should influence policy makers to consider streamlining regulations for hastening regulatory processes for public health pesticides.

Country Level Governmental bodies

Though the regulatory processes in the country level have representations from various ministries such as Ministry of Health (MoH), Ministry of Commerce (MoC), Ministry of Environment (MoE), Ministry of Industry and Trade (MoIT) in the regulatory processes. However, the co-operation and coordination between the various ministries is very slack and needs a much better robust cooperation. If a seamless cooperation exists between the various ministries then there would better sharing of information and also coordination of the various ministries in the strengthening of the legislations as well as better implementation of the legislations.

Market Access Landscape

Regional Overview

Economic Situation

Countries in the Indo-Pacific region had a relatively high economic growth rate of 5.8% in 2017 as compared to 5.4% in 2016. About two-thirds of the regional economies, accounting for 80% of the region's GDP, achieved faster economic growth in 2017.

The recent recovery in global manufacturing, investment, and trade propelled the already steady expansion of economic output in the Indo-Pacific region. However, this upturn – the fastest global output expansion in five years – comes after an extended period of weak investment and low productivity growth. Thus, there is an element of uncertainty in terms of the continuation of these trends.

Investment expenditures and trade volumes, which have shown lukewarm growth in recent years, also showed signs of recovery in 2017. Firmer global demand and increased public infrastructure outlay supported a pickup in investments. Sustained investment recovery could be undermined by protectionist trade measures, tighter financial conditions, and uncertainty over the domestic legal and regulatory environment.

Supported by robust domestic demand and improved global economic prospects, developing Indo-Pacific economies are projected to grow by 5.5% in 2018 and 2019. In line with the region's growing purchasing power, domestic private consumption is likely to remain the major source of economic growth.

Consumer price inflation in developing countries of the Indo-Pacific region is projected to rise to 3.5% by 2019. This increase is in line with the rise in global oil prices and strong aggregate demand for oil. Inflation is likely to remain steady at low levels. Aside from country-specific factors, such as good harvests and stable food prices, there are a few global reasons relating to the energy sector, currencies, capacity utilization, and technology, which pave the way for inflation.[70]

Health Indicators

Life expectancy increased by almost 6 years since 2000, but maternal mortality is still twice the Sustainable Development Goal target in lower-middle and low-income countries in the region.

Life expectancy at birth among the lower-middle and low-income population in Indo-Pacific countries reached 70 years in 2016. The upper-middle and high-income population in Indo-Pacific countries gained – on average – 3.6 years, and OECD countries gained 3 years during the same period.

The infant mortality rate has fallen dramatically among the lower-middle and low-income population in Indo-Pacific countries since 2000, with several countries experiencing a decline greater than 50%. At an average of 30 deaths per 1,000 live births in 2016, the infant mortality rate in the lower-middle and low-income population in Indo-Pacific countries is still eight times the rate in the high-income population in Indo-Pacific countries.

Between 2000 and 2015, the average maternal mortality rate across the lower-middle and low-income population in Indo-Pacific countries decreased by more than half, but it is still high at 140 deaths per 100,000 live births, which is twice the Sustainable Development Goals (SDG) target of 70 deaths per 100,000 live births.

In the high-income populations of Indo-Pacific countries, the share of the population aged over 65 years is expected to double and reach 27.6% by 2050, whereas the share of the population aged over 80 years is expected to triple and reach 10.2% by 2025.

In upper-middle income and lower-middle income populations in Indo-Pacific countries, the share of the population aged over 65 and 80 will be two and a half and four times the current share and will reach 23.9% and 14.5% (over 65) and 7.9% and 3.5% (over 80), respectively.[71]

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[70] United Nations Economic And Social Survey of Asia And The Pacific 2018.

[71] OECD/WHO (2018), Health at a Glance: Asia/Pacific 2018.

Healthcare Structure

The national healthcare system is burdened by the recent demographic and epidemiological transitions, which are amplified by the growing demand for an increasingly educated and affluent population for high-quality healthcare. Several traditional health practices persist alongside the use of new medical technologies and pharmaceutical products, presenting regulatory problems in terms of safety and quality.

Countries in Southeast Asia and their health system reforms can thus be categorized according to the stages of development of their healthcare systems. A typology of common issues, challenges, and priorities are generated for the diverse mix of health systems at different stages of socioeconomic development.

So far, healthcare systems with dominant tax funding were fairly stable, in view of the strong role of governments and effective controls by health agencies to overcome inequity problems. However, at present, crucial issues arise that involve rising costs, future sustainability of centralized tax-financed systems, efficiency and quality of public services, and high public expectations.

With the anticipated rise in the aging population and future problems of intergenerational funding through pay-as-you-go mechanisms, there are experiments with new healthcare financing, such as compulsory medical savings and social insurance for long-term care. Some countries, such as the Philippines, Vietnam, and Indonesia, have radically decentralized their healthcare systems with the devolution of health services to local governments – a restructuring that has affected several aspects of systems performance and equity, even though the impetus for decentralization was mainly political. Consequently, to ensure increased financial coverage and affordability, several governments have passed laws to establish national health insurance systems and mandated universal coverage, although the implementation is problematic. With the existing policies of decentralization and liberalization, equity issues and poor infrastructure will continue to challenge the development of the healthcare sector.

Healthcare Spending

Lower-middle and low-income populations in Indo-Pacific countries spend just below USD200 per person per year on health, compared to the spending of USD670 and USD3,450 by the upper-middle income and high-income population in Indo-Pacific countries, respectively. This amounts to over 4.3% of the GDP, on average, in middle and low-income Indo-Pacific countries, compared to over 7.3% of the GDP in high-income Indo-Pacific countries in 2015. On average, high-income countries reported an increase of 0.8% from 2010-2015, twice the increase reported by middle and low-income countries at 0.4%.

The share of public spending in total health spending increased in all Indo-Pacific countries from 2010 to 2015, but it is much lower in lower-middle and low-income Indo-Pacific countries compared to upper-middle and high-income Indo-Pacific countries: 41.9% compared to 62% and 72.3%, respectively.

On average, household out-of-pocket expenditure (that is, payments made directly by households for health services and goods) accounted for 48.2% of the total health expenditure in lower-middle and low-income Indo-Pacific countries in 2015, an increase of 1% from 2010, signalling significant gaps in providing health coverage in the region.

Spending on pharmaceuticals accounted for almost one-third of the total healthcare expenditure on average across lower-middle and low-income Indo-Pacific countries in 2015, whereas it accounted for 28% and 15% of health spending in upper-middle and high-income Indo-Pacific countries, respectively. Most of the spending on pharmaceuticals across the lower middle and low-income Indo-Pacific countries is incurred by households (out-of-pocket expenditure).[73]

[73] OECD/WHO (2018), Health at a Glance: Asia/Pacific 2018).

Market Overview

Vector Control Overview

As described in the Technical Landscape, vector control remains an effective and critical measure to prevent the transmission of various VBDs in Indo-Pacific countries. In the Indo-Pacific region, all 5 *Plasmodium* species are present, along with a large diversity of vector species. Transmission ranges from forest areas to international borders and densely populated urban cities in a few Asian countries. The outdoor biting nature of some species of mosquitoes in the Indo-Pacific region means that vector control measures that are only focused on domestic settings, which include the use of ITNs and IRS, may not be adequate in malaria elimination efforts. This propels the need for integrated vector control measures.

TABLE 5: COMPARING THE POTENTIAL OF VECTOR CONTROL PRODUCTS/TOOLS [74]

Market Type	**Retail Market**							**Donor-driven Market**		
Vector Control Products / Tools	Lotions, Sprays & Oils with DEET	Lotions, Sprays & Oils without DEET	Clip-on	Mosquito Coils	Citronella Candles	Mosquito Lamps	Mosquito Zappers	Mosquito Traps	Mosquito Nets	Insecticide-treated Nets
Covers 10 Foot Zone									●	●
Odorless			●			●	●		●	●
No Open Flame	●	●	●				●	●	●	●
No Skin or Clothing Contact				●	●	●	●	●	●	●
Unlimited Usage (with Refill)	●	●	●			●	●	●	●	●
Cost Efficient				●	●			●	●	●
Durable / Long Lasting						●		●	●	●
No maintenance									●	●
Small & Portable	●	●	●	●	●			●		

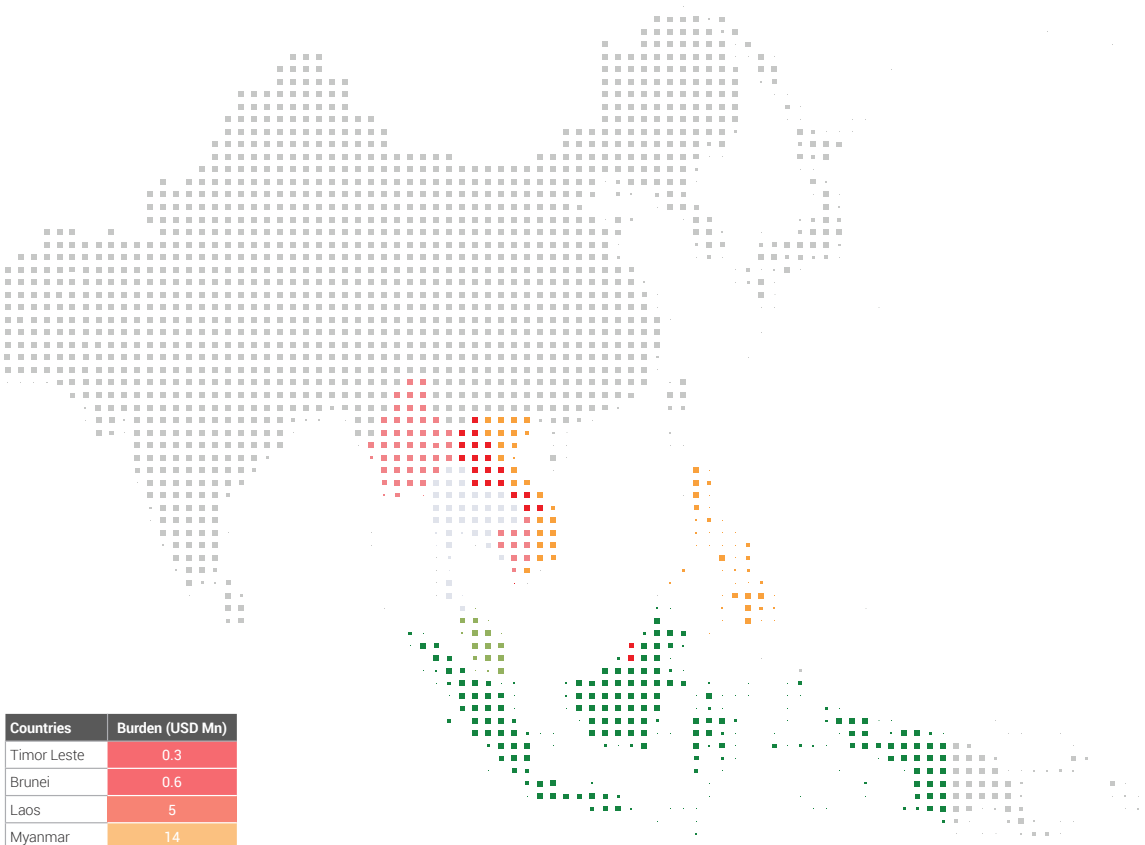
[74] Thermacell (CL: Medium).

Economic Burden of VBD

Dengue:[75]

Dengue represents a monumental burden in Southeast Asia, where it is endemic. Studies conducted between 2001 and 2005 have reported dengue-specific cases to cost Cambodia three million dollars, annually, Malaysia at 42 million dollars annually, and Thailand 53 million dollars annually. Another study estimated annual costs for Cambodia to be eight million dollars. In 2009, officially reported dengue cases were estimated to cost Malaysia 100 million dollars. The SEA estimates of burden of disease due to dengue are available only for a fraction of countries in the region. Estimates vary depending on the methodology of studies and variance in officially reported cases. Although dengue is a notifiable disease, there is a considerable amount of underreporting.

FIGURE 16: ESTIMATED ANNUAL ECONOMIC BURDEN OF DENGUE IN SOUTHEAST ASIA[17]



Countries	Burden (USD Mn)
Timor Leste	0.3
Brunei	0.6
Laos	5
Myanmar	14
Cambodia	16
Vietnam	23
Malaysia	27
Singapore	67
Philippines	80
Thailand	290
Indonesia	323

[75] Muhiuddin Haider et.al. 2015.

Cost of malaria elimination in the Indo-Pacific[76]

The Indo-Pacific region has made significant progress against malaria, reducing cases and deaths by over 50% between 2010 and 2015. These gains have been facilitated in part by a strong political and financial commitment of governments and donors. However, funding gaps and persistent health system challenges threaten further progress. Achieving the regional goal of malaria elimination by 2030 will require an intensification of efforts and a plan for sustainable financing.

The model used to estimate the cost of malaria elimination predicted that it is possible for Indo-Pacific countries to achieve the elimination of *P. falciparum* and *P. vivax* by 2030. China, the Republic of Korea, and Sri Lanka are the only countries predicted to achieve elimination without scaling-up current interventions. Elimination was predicted to be possible in Cambodia, Democratic People's Republic of Korea (DPRK), India, Lao PDR, Myanmar, Solomon Islands, and Thailand by 2030 using new tools, technological innovation, and Mass Drug Administration.

Program costs included the expenses of testing and treating malaria cases that were uncomplicated or outpatient, and severe or inpatient; vector control (i.e., LLIN distribution and IRS); supply chains; surveillance through community health workers; information, education, and communication; training; MDA; new treatments (e.g., tafenoquine for *P. vivax*); and the rollout of new LLINs. Unit costs for each activity were obtained using a combination of empirical data collected from authors, literature reviews, and proxies, when the previous options were unavailable (refer to the appendix for detailed per unit cost estimates).

The total cost to achieve malaria elimination in the Indo-Pacific between 2017 and 2030 was estimated to be USD29.024 billion (range: USD23.65–36.23 billion). The median cost in 2017 for the elimination scenario was USD1.51 billion. Cost escalation was predicted by 2020 (approximately USD4.29 billion), followed by a decline (less than USD1 billion by 2027 and less than USD450 million by 2030). Elimination may save over 400,000 lives and avert 123 million malaria cases, translating to almost USD90 billion in economic benefits. Lower costs incurred are expected to continue after the elimination date, as Prevention of Reintroduction of malaria interventions will continue. If interventions were only applied to 70% of the population at risk in the low-transmission areas (a crude proxy for the effect of improved targeting of interventions), the total cost would be about USD22.49 billion.

Discontinuing vector control interventions and reducing treatment coverage rates to 50% will reverse the gains made, resulting in an additional 845 million cases, 3.5 million deaths, and excess costs of USD7 billion.

[76] Thermacell (CL: Medium).

Market Analysis

Procurement Channels

Donors such as The Global Fund provide funds to Procurement Service Agencies (PSA) in a particular country. These agencies are responsible for procuring vector control products from manufacturers. Vector control products are further shipped from manufacturers to distributors and then to wholesalers. Further, products are distributed to end users via retailers.

In another mode of fund allocation, global donors such as The Global Fund will allocate funds to the National Government of the respective country. The National Government will procure vector control products from manufacturers, which are further distributed to the local government, then to the end user via community services or hospital/health service agencies. In some countries, NGOs play a major role in the distribution of vector control products.

Distribution Strategy

Donor Products: Distribution of vector control products happens at different levels involving stake-holders such as international organizations, national government bodies, NGOs, and community health services. Vector control products are delivered through mass distribution campaigns, antenatal care services, immunization programs, healthcare facilities, and mobile teams as part of outreach services.

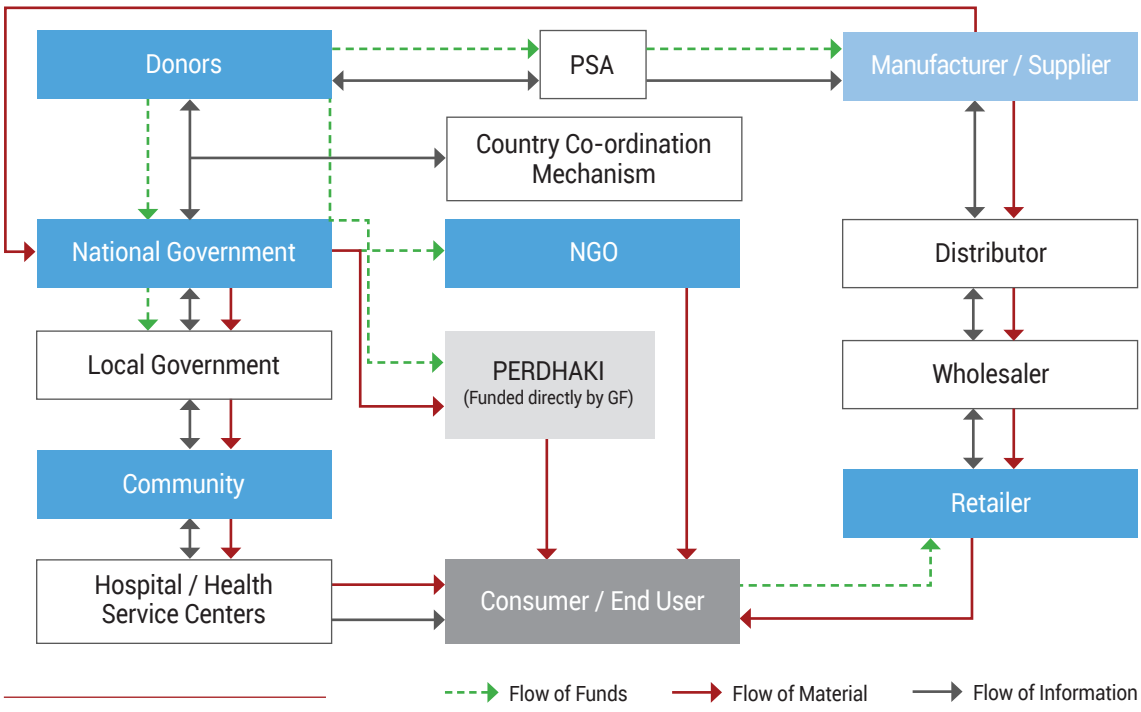
Delivery of LLINs through antenatal care is practiced or planned in two ways:

Giving a free or subsidized LLIN (i.e., direct product), or

Giving a voucher or coupon that can be exchanged for an LLIN at a distribution point, such as a commercial/retail outlet. This has been done in several African countries, but not yet introduced by programs in the Indo-Pacific.

Retail Products: The most common outlets where retail vector control products, (e.g. insecticide coils, electric insecticides, topical repellents, and aerosols/sprays) are made available include grocery stores, supermarkets, convenience stores, hypermarkets, e-commerce, general stores, and hawkers in rural areas.

FIGURE 17: APAC PROCUREMENT CHANNELS FOR VECTOR CONTROL PRODUCTS[77]



[77] FutureBridge Analysis.

Stakeholders

Key Stakeholders in the Indo-Pacific Vector Control & Prevention Market

Major funding agencies across the Indo-Pacific region are The Global Fund, UNICEF, Unitaid, USAID/CDC through the President's Malaria Initiative (PMI), The World Bank, DFAT and the Bill & Melinda Gates Foundation. These agencies provide funds as an individual entity or in collaboration with one another. Domestic donors in respective regions, such as the Ministry of Health, are also considered as a major funding agency. Other business partnerships are Business Alliance against Malaria, M2030, and ZERO by 40.

Funding

The Global Fund is a major funding body across all regions for malaria elimination activities

Founded in 2002, The Global Fund (GF) is a partnership organization designed to accelerate the end of AIDS, tuberculosis, and malaria. GF raises and invests an estimated amount of USD4 billion annually to carry out programs by local experts and communities.[78] An estimated USD3.1 billion was invested globally in malaria control and elimination efforts in 2017. The Global Fund distributed 197 million mosquito nets in 2017 for malaria prevention. Around 20% of The Global Fund is invested in Indo-Pacific, and 32% of the funds allocated to the Indo-Pacific region have been invested in malaria prevention and control activities.[79]

In the Indo-Pacific region, PMI funds are concentrated in the Greater Mekong Sub-region (GMS)

The President's Malaria Initiative (PMI) is an interagency initiative led by the U.S. Agency for International Development (USAID, implemented together with the U.S. Centre for Disease Control and Prevention (CDC) of the U.S. Department of Health and Human Services. PMI was launched in 2005 with the aim to reduce malaria-related mortality by 50% across 15 high-burden countries in sub-Saharan Africa. With the development of the U.S. Government Malaria Strategy for 2009–2014, PMI extended its operations in four new countries in Sub-Saharan Africa and conducted one regional program in the GMS. In 2017, PMI funded an amount of USD723 million to 24 PMI-focus countries. This amount was also allotted for three programs in the GMS for malaria elimination.[80] Moreover, a funding amount of USD10 million was provided to Myanmar in 2017.[22]

Unitaid and APLMA collaborate for malaria elimination in the Indo-Pacific Region

Unitaid is an international organization investing in innovations to prevent, diagnose, and treat HIV/AIDS, tuberculosis, and malaria affordably and effectively. In 2013, the leaders of Indo-Pacific countries jointly created APLMA with the aim to strengthen their anti-malaria efforts both to help protect hard-won national gains, and ultimately to defeat malaria in the region altogether. In 2018, APLMA and Unitaid launched a collaborative platform to accelerate innovative approaches to halt the spread of malaria and other vector-borne diseases in the Indo-Pacific region. Unitaid invested a sum amount of ~USD300 million in 2018 towards malaria elimination, which is twice that of 2015, and it is anticipated that Unitaid will increase its funds to USD450 million by 2020.[81]

Total Funding for Vector Control in the Indo-Pacific region

Funding for malaria control has increased intensely over the last decade. In Asia, funding has increased from USD284 million in 2011 to over USD29.024 billion (range: USD23.65 – USD36.23 billion) for the duration 2017-2030. The Global Fund continued to remain a major donor, both globally as well as in Asia. Initially, up to 2005, the total donor's share was <50% to the total available funds. The Global Fund started providing grants from 2002 onwards, and these grants were limited to a few countries in the Indo-Pacific region.[82] From 2012 to 2018, countries in the Indo-Pacific region have increased their domestic financing for malaria by 44%, and it is estimated that it will increase by an additional 40% during 2018-2020.

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78 The Global Fund

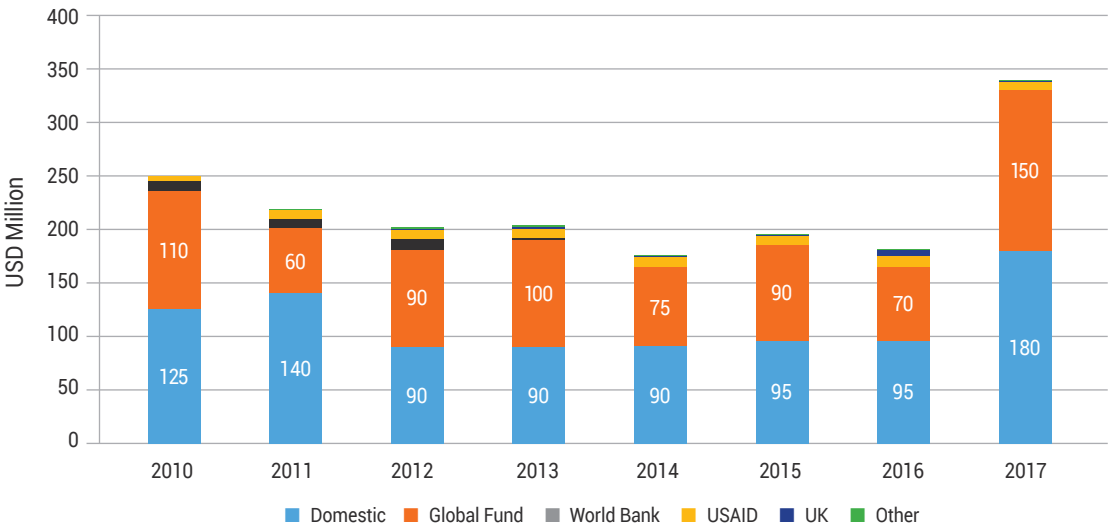
79 Procurement and Quality Assurance Updates, The Global Fund

80 PMI

81 UNITAID)

82 Rajesh Bhatia, et, al., December 2013

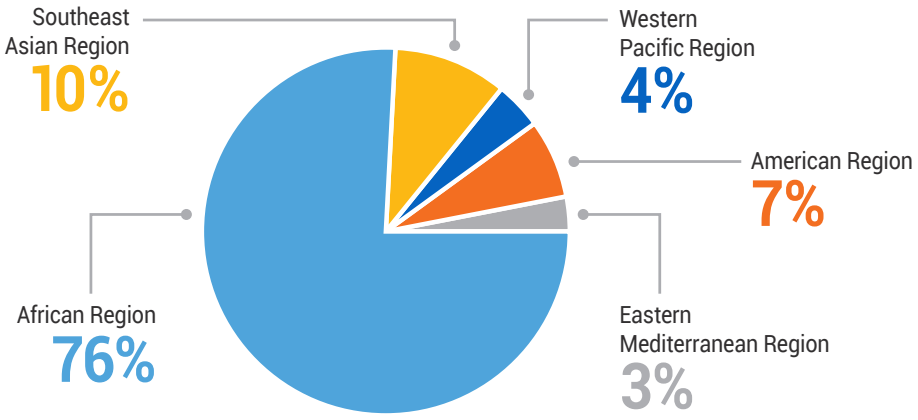
FIGURE 18: FUNDING SPLIT BY SOURCES FOR MALARIA PREVENTION & CONTROL IN INDO-PACIFIC, 2010-2017[83]



*Note: Other comprises of NGOs, regional & local bodies, and partnership funding.

The figure above provides a detailed split of funds for malaria prevention and control in the Indo-Pacific region from 2010 to 2017. Other than domestic funding, The Global Fund, the World Bank, USAID, and other organizations, contribute funds for malaria control and prevention activities. The Global Fund and domestic funding are the major sources of funds in the Indo-Pacific region, and their share increased between 2010 and 2017.

FIGURE 19: GLOBAL FUNDING FOR MALARIA CONTROL, 2017 [84]



[83] World Malaria Report 2018

[84] WHO, World Malaria Report 2018

In 2017, USD3.1 billion were disbursed globally for malaria prevention activities. Malaria financing increased by 7% between 2016 and 2017. Of USD3.1 billion invested, USD2.2 billion was allocated to the African region, followed by USD0.3 billion to the Southeast Asian region. A sum of USD0.2 billion was offered to the Americas, and USD0.1 billion each to the Western Pacific region and the Eastern Mediterranean region.[23]

Various partnerships are launched to fight against malaria in the Asian region. For instance, in September 2018, the Indo-Pacific Leaders Malaria Alliance (APLMA), announced support for two new initiatives: Blended Finance for Impact and M2030 to accelerate the elimination of malaria and improve health outcomes. Blended Finance for Impact is a partnership of the Asian Development Bank (ADB), The Global Fund to Fight AIDS, Tuberculosis, and Malaria, and APLMA to enable and increase long-term integrated financing for health, including malaria. M2030 aims to bring together some of the most influential businesses in Asia to raise funds, engage consumers as agents of change, and sustain political support for malaria elimination.[85] Similarly, the Australian and Japanese governments have provided a majority of bilateral funding for malaria elimination activities in the Indo-Pacific region, since 2007.

TABLE 6: NON-PMI FUNDING LANDSCAPE IN GREATER MEKONG SUB-REGION, 2017 [86]

Funding	Total Budget in USD (Funds Disbursed)	Duration	Key Implementing Partners	Key Activities
BMGF	29,000,000	NA	CHAI	Malaria elimination efforts in Southern Africa and the GMS
DFID	19,400,000	2014 - 2017	ADB (Secretariat)	Regional malaria and other communicable disease threats trust fund
DFAT	16,300,000			
Global Fund RAI (ICC)	15,000,000	2014 - 2016	SMRU, MAM, CPI	Cross-border; inter-country coordination; mass drug administration pilots; and establishing malaria posts in Myanmar
BMGF	10,000,000	2013 - 2015	WHO	WHO regional Emergency Response to Artemisinin Resistance (ERAR) hub
DFAT	5,000,000			
ADB	4,500,000	October 2015 - June 2017	MOH/CDC of Cambodia, Laos, and Myanmar	Malaria and communicable diseases control in the GMS focused on malaria surveillance and diagnostic quality assurance, mobile and migrant populations (Myanmar, Cambodia, and Laos), and regional coordination

*Note: **ADB:** Asian Development Bank; **BMGF:** Bill & Melinda Gates Foundation; **CDC**: Communicable Diseases Control; **DFAT**: Department of Foreign Affairs and Trade; **DFID**: Department for International Development; **ERAR**: Emergency Response for Artemisinin Resistance; **GMS**: Greater Mekong Subregion; **RAI**: Regional Artemisinin Resistance; **ICC:** Inter-Country Component; **SMRU**: Shoklo Malaria Research Unit; **MAM**: Medical Action Myanmar; **CPI**: Community Partners International; **CHAI**: Clinton Health Access Initiative; **MOH**: Ministry of Health.

[85] World Economic Forum

[86] PMI Greater Mekong Sub-region Malaria Operational Plan 2017

The table above elaborates the list of donors in the Greater Mekong Sub-region other than PMI and The Global Fund. Donors collaborate with other agencies, such as CDC or WHO or the Ministry of Health, for proper utilization of funds. Besides PMI, there are other international bodies that provide funds for malaria control and prevention activities in the Indo-Pacific region. The Bill and Melinda Gates Foundation, along with the Clinton Health Access Initiative, invested USD29 million in 2017 for malaria elimination efforts in Southern Africa and the Greater Mekong Sub-region. DFID and DFAT, along with ADB, invested USD19.4 million and USD16.3 million regional trust fund for malaria and other communicable disease threats. The Global Fund invested USD15 million, along with SMRU, MAM, and CPI, for cross-border, inter-country coordination, mass drug administration pilots, and establishment of malaria posts in Myanmar. The Bill and Melinda Gates Foundation and DFAT, along with WHO, invested USD10 million and USD5 million respectively, in WHO Regional Emergency Response to Artemisinin Resistance (ERAR) hub. The Asian Development Bank and MoH/CDC of Cambodia, Laos, and Myanmar funded USD4.5 million during October 2015-June 2017 for malaria and communicable diseases control in the Greater Mekong Sub-region.

RAI2E – Towards Elimination of Malaria[87]

Growing resistance to Artemisinin in the Greater Mekong Subregion is a serious threat to global malaria control and elimination efforts. In order to overcome this, there was a need for an accelerated and well-coordinated regional approach for this emergency, which would also follow the lead of other partner efforts in the region (including the Emergency Response to Artemisinin Resistance framework developed by WHO). The Global Fund allocated USD115 million for the Regional Artemisinin-resistance Initiative (RAI) grant during 2014-2017, which would cover 5 GMS countries.

The second phase of the RAI program is RAI2-Elimination (RAI2E), for which The Global Fund has granted USD243 million for the period of 2018-2020. RAI2E will accelerate the elimination of *P. falciparum* malaria in the Greater Mekong Sub-region for a three-year period.

RAI2E will increase the malaria service coverage for remote populations situated in border areas and other at-risk populations. It will also assist in case management through health volunteers and strengthen the national surveillance system. UNOPS is the Regional Principal Recipient for RAI2E, implemented in collaboration with the existing partners of The Global Fund at country level and under the strategic oversight of the RAI Regional Steering Committee.

Funding Gap

In 2017, the global funding need for malaria control was estimated to be USD4.4 billion, but the total fund allocated was USD3.1 billion. Hence, there was a shortfall of USD1.3 billion. The funding gap increased by USD0.3 billion in 2017 as compared to 2016. This funding gap affects all areas (such as research & development of new products and procurement and distribution of vector control products) where the international response could be of necessary assistance.

According to the 'Malaria Elimination Transmission and Costing in the Indo-Pacific: Developing an Investment Case' study, an amount of USD3 billion is required to achieve malaria elimination during 2018-2020 in Indo-Pacific. The funding gap is projected to be USD0.5 billion in the region during 2018-2020. Therefore, the anticipated financing gap is likely to be 80% during the period 2018-2020.[88]

[87] UNOPS.

[88] Shretta R et al., (2019).

Market Description and Analysis

Retail Market

The Indo-Pacific vector control retail market is growing at an exponential rate as compared to the African retail market. Retail vector control products such as insecticide coils, insecticide sprays or aerosols, household insect repellents, electric insecticides, moth proofers, and others are used extensively in the Indo-Pacific region. While LLINs have replaced ITNs in most countries worldwide, ITNs are still available in certain retail markets, particularly in Asia. Donors focus exclusively on funding LLINs over ITNs.[89]

The retail market in the Indo-Pacific region is highly fragmented, and sales are dependent on weather conditions. Retail products such as coils, repellents, and mats are mostly preferred over LLINs, as they do not hinder daily activities.

As the population in most of the Indo-Pacific countries has a low-income level and low purchasing power, insecticide coils are preferred over vector control products due to their affordable cost. In 2018, the market for insecticide coils generated a value of USD 1.3-1.4 billion, with a sales value of approximately 2.1 billion. However, owing to factors such as health concerns with the use of coils, sprays and aerosols are likely to project growth and replace coils in the coming years.

Leading companies in the retail market for vector control products in the Indo-Pacific region are SC Johnson & Son Inc., Earth Chemical Co. Ltd., Godrej Group, ST Corp, and Henkel AG & Co. KGaA, among others. Leading brands in the retail market are Good Knight, Baygon, Hit, Earth, Ridsect, Jumbo, Odomos, and others.

Donor Market

The vector control and prevention market in the Indo-Pacific region is largely funded by The Global Fund. Other funding agencies in this region are governments of endemic countries, World Bank, UNICEF, USAID, CDC, WHO, the Bill & Melinda Gates Foundation, and Unitaid.

Funds received from The Global Fund in the Indo-Pacific region for vector control programs are widely used for awareness campaigns, distribution of LLINs, and provision of other medical treatment for malaria, dengue, and other VBDs.

TABLE7: CHARACTERISTICS OF DONOR-DRIVEN AND RETAIL MARKET PRODUCTS [90,91]

Parameter	Donor-driven	Retail Market
Products	LLINs, IRS, fumigation, and biological prevention	Coils, insecticide sprays, lotions, and electric bats
End-user	Primarily focused on covering all epidemic areas and vulnerable population, but may not necessarily cover the most vulnerable or the poorest populations	Frequently focused on urban rather than rural settings
Availability	Depends on funds from donors and usually available in epidemic areas, or natural calamity affected areas; LLINs are available at health units or through distribution campaigns	Products are available at nearest pharmacies or general stores
Price	Mostly free of cost or sold at a subsidized price	Cost may vary from product to product
Efficacy	The effectiveness of products is for a longer duration, as they target the root cause (e.g., LLINs can be used for ~3 years)	Most products have a temporary effect, as they do not aim to eliminate the vector, but instead drive it away from homes
Off-Label Use	LLINs are used as fishing nets; nets are also used to protect seedlings, and as goods sacks	No off-label use as products are purchased for their intended use
Education and Awareness	Dedicated campaigns to provide education and awareness regarding the use of donor-driven products	No training or education required

[89] Malaria Vector Control Commodities Landscape.

[90] Brieger WR 2017).

[91] George S, et. al., Malaria Consortium Learning Paper Series 2014.

TABLE 8: VOLUME AND SALES OF VECTOR CONTROL PRODUCTS IN INDO-PACIFIC [23]

Product Class	Indo-Pacific						
	Volumes 2016 (Million)	Volumes 2017 (Million)	Volumes 2018 (Million)	Average Unit Price (USD)	Value 2016 (USD Million)	Value 2017 (USD Million)	Value 2018 (USD Million)
Insecticide Coils	1,833	1,967	2,083	0.6	1,000 - 1100	1,100 - 1,250	1,250 - 1,350
LLINs	21.05	35.93	47.36	2.25	47.36	80.84	NA
Electric Insecticides	464	524	595	2.1	950 - 1,000	1,050 - 1,150	1,200 - 1,300
Sprays / Aerosols	344	371	417	4.8	1,500 - 1,700	1,600 - 1,800	1,900 - 2,100
Insecticide Bait	NA	NA	NA	NA	200 - 225	200 - 225	200 - 225
Other Home Insecticides	NA	NA	NA	NA	700 - 750	750 - 850	750 - 850
Leading Brands	• Good Knight • Baygon • Hit • Earth				• Ridsect • Jumbo • Odomos		
Leading Companies	• SC Johnson & Son, Inc. • Earth Chemical Co. Ltd. • Godrej Group				• ST Corp • Henkel AG & Co. KGaA		

FIGURE 29: KEY PLAYERS AND BRANDS IN THE REGION [92]

Global Brand Owner	Electric Insecticides	Coils	Aerosols
Godrej	Good Knight Hit 	Good Knight Hit 	Hit 
SC Johnson & Son Inc	All Out Raid Baygon 	Raid 	Raid Baygon 
Fumakilla Ltd	Vape 	Fumakilla 	Fumakilla 
Henkel AG & Co KGaA	Bloom 		Combat 

[92] FutureBridge Analysis.

Challenges

Although overall gains in malaria elimination have been impressive, several countries still face serious challenges:

The most pressing technical challenge is **multi-drug resistance**. In 2006, Artemisinin-resistant *P. falciparum* malaria was first reported in eastern Cambodia, and by 2013, confirmed or suspected Artemisinin resistance had been identified in another four countries of the Greater Mekong Sub-region. By 2015, the resistance of *P. falciparum* to several antimalarial medicines reached worrying levels in Thailand, and there were concerns that in the area straddling the Cambodia-Thailand border, *P. falciparum* malaria might become untreatable within a few years. In response to the worsening situation, the WHO led the development of the *Strategy for Malaria Elimination in the Greater Mekong Sub-region (2015-2030)*.

A lack of diagnostic tools for P. vivax hypnozoites and of a fully effective test for diagnosing glucose-6-phosphate dehydrogenase (G6PD) deficiency (which undermines the use of 8-aminoquinolones needed to effect a radical cure of P. vivax infections) are both huge challenges, which disproportionately affect operations in Southeast Asia, considering that the region accounts for more than half of the global burden of vivax malaria.

Insecticide resistance is also a concern, as it could reduce the effectiveness of insecticide-treated bed nets and IRS operations. There is widespread dichlorodiphenyltrichloroethane (DDT) and pyrethroid resistance as well as carbamate and organophosphate (Malathion) resistance in some areas of the Southeast Asian region. Increased use of pyrethroids in agriculture is likely to exert selective pressure for resistance and may prove to be an important risk factor.

Limitations in financing, following the global economic downturn, threaten to slow elimination efforts in some countries. Funding for malaria control in the Indo-Pacific region increased from USD125 million in 2005 to USD240 million in 2010; however, it witnessed a decline and reached USD189 million in 2016. Per capita funding is the lowest in countries with the largest populations at risk, including India and Indonesia. Most countries will need to identify additional sources of domestic funding and increase efficiencies within their healthcare systems if elimination efforts are to succeed.

Access is another key issue affecting malaria control and elimination efforts as well as progress towards Universal Health Coverage. Mobile populations, migrants (both within and between countries), and tribal and other populations in remote areas or areas affected by political instability are often underserved by routine malaria prevention and case management services. Humanitarian and environmental crises may also compromise access to healthcare.

Key health systems issues undermining progress in some countries include: limited human resources; incomplete integration of malaria services with primary and preventive care; and multiple weaknesses in technical capacity, commodity procurement systems, supply chain management, and External Quality Assessment of laboratory diagnosis for malaria as well as surveillance, monitoring, and evaluation.

Governmental regulations and procedures in certain instances adversely affect the capacity of programs to absorb grant funding. Addressing weaknesses in surveillance is a key priority, given its pivotal role in malaria elimination.[93]

[93] WHO South-East Asia Regional Action Plan 2017-2030

INSIGHTS FROM PRIMARY RESEARCH:[94, 95]

> " Gap in evidence based decision making process and focus on larval control and reducing the adult population."

> " Virtually no research scholars, either from government or WHO or NGO are conducting studies for evidence generation."

> " Funding is mostly based on vaccine development. Lack of fund for surveillance and monitoring."

Market Dynamics

Market Trends

Increasing the use of the digital platform to spread awareness

The upsurge in the use of digital media across Indo-Pacific countries has helped spread awareness regarding various approaches used for control and prevention of vector-borne diseases. In Malaysia, digital programs such as 360° Vector Control and the Mosquito Learning Lab are used to spread awareness as well as monitor the success against the disease. Cambodia uses digital tools such as MIS to focus on malaria control and elimination activities in endemic areas. In Indonesia, digital tools such as the Bayer Mosquito Learning Lab, LaCak Malaria, and Pokentik help create awareness, track down disease cases, and monitor the behaviour of clean living.

Active research for new ingredients in bed nets

Continuous research and development have propelled new and upcoming technology or products for fast and effective VBD prevention. Active research for new ingredients in bed nets and IRS is conducted to prevent insecticide resistance. New tools for outdoor residual transmission are in the developmental stage and are being field-tested. Moreover, genetic modification of the mosquito population is being explored to control all vector-borne diseases, including malaria, dengue, and Zika.

Shift in usage pattern towards consumer products

A huge part of the population in the Indo-Pacific region, especially in the rural areas, believes that killing mosquitoes will prevent vector-borne diseases, such as malaria and dengue. Thus, instead of using LLINs that only prevent mosquitoes from biting, they prefer using retail vector control products (such as aerosols or sprays) to kill mosquitoes. This will cause a shift from the donor market to the retail market in the near future.

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[94] Primary Research and FutureBridge Analysis

[95] Primary Research and FutureBridge Analysis

Market Drivers

Enhancement of cross-border and regional collaborations to the prevent spread of malaria

There is an uncontrolled cross-border migration between malaria-endemic countries and receptive areas, thereby increasing the risk for the spread of malaria. Meaningful inter-country coordination and cooperation are necessary to overcome this risk. Factors to be considered to achieve inter-country coordination include the regular exchange of all malaria-related information, prompt information of unusual malaria situations across borders, promotion of regular border meetings at district as well as national level, mapping of malaria-relevant cross-border migrants, and development of joint special evidence-based interventions at the high-risk, cross-border areas. Increasing cross-border coordination will encourage the effective use and allocation of vector control and preventive measures, thereby preventing VBDs.

Strategic partnership across all sectors will encourage smooth functioning of vector control and prevention activities

Malaria elimination can be effectively achieved by coordination between government bodies and society. As malaria-endemic areas share borders, the success of malaria programs largely depends on regional collaborations and coordination. This has further led to collaboration with government sectors, such as finance, agriculture, and defence, as well as with private sectors, such as private health facilities and the tourism industry. Collaboration with the agricultural sector will help recognize the migrant population, which, in turn, could assist in identifying and preventing breeding sites for mosquitoes. Community engagement programs play a key role in successful malaria elimination. Hence, strategic partnership programs enhance the success and optimum utilization of vector control methods.

Partnerships and Collaborations

Effective prevention, control, and elimination of VBDs requires a multi-level partnership, coordination, and collaboration. Partnerships may be inter-sectoral; public and private; government and non-governmental; and national and international. Prevention and control programs across the Indo-Pacific region would be more effective by sharing data, knowledge, and experience as well as coordinating activities and collaborating on research agendas.

1. The Asia-Pacific Malaria Elimination Network (APMEN), Unitaid, and Indo-Pacific Leaders Malaria Alliance (APLMA) joined forces for vector control and malaria elimination in the region[96,97]

In January 2018, representatives from the ministries of health of various countries, development organizations, and industry and research centers, met to explore challenges and opportunities for strengthening vector control measures in the Indo-Pacific region. The inaugural policy dialogue was co-hosted by Unitaid and APLMA. The collaboration builds on the work of the APMEN vector control working group, which helps scientists, industry representatives, as well as government representatives, address priority policy challenges for vector control in the region.

[96] Unitaid.

[97] APLMA.

Participants identified some of the key challenges to innovation and access, including specificities of vector behaviour in the Indo-Pacific region and the **time-consuming registration processes** for new tools. They also discussed the possibility of **joint registration processes for WHO pre-qualified products**, as well as opportunities to generate interest around innovative products among national regulatory agencies. Participants agreed that an ongoing, **coordinated, and cross-sectoral approach is essential** to improving access and innovation of vector control tools in support of both malaria elimination and promoting overall health security for the Indo-Pacific region.

Industry and other research and development representative participants include Sumitomo Chemical, Bayer Crop., Syngenta, WellTech Healthcare, BASF, Vestergaard, the National Center for Genetic Engineering and Biotechnology, and Mahidol University.

2. Unitaid partners with APLMA to drive malaria elimination in Indo-Pacific[98]

In July 2018, APLMA and Unitaid launched a collaborative platform to accelerate access to innovations and eliminating the spread of malaria and other mosquito-borne diseases in the Indo-Pacific region. The new platform, known as the Vector Control Platform for the Asia-Pacific (VCAP), links national regulators, policy-makers, industries, academicians, and the global health community to boost the development and use of antimalarial tools, such as mosquito nets and insecticides. The knowledge-sharing platform is one of the first initiatives under a new Unitaid/APLMA collaboration aimed at driving regional progress towards malaria elimination. The objective of the partnership is to associate the two organizations with other malaria control stakeholders, through co-hosting specific events and identifying opportunities to support governments, donors, and other partners.

[98] APLMA and Unitaid partnership.

3. Blended Finance for Impact: Partnership between the ADB, GFATM, and APLMA[99,100]

In December 2017, a health financing Memorandum of Understanding (MOU) was signed between The Global Fund to Fight AIDS, Tuberculosis, and Malaria (GFATM) and the Asian Development Bank (ADB). The MOU lays out a framework for countries that currently receive Global Fund grants to leverage additional funding from the ADB, create clear and transparent financing frameworks, and move towards a more sustainable funding system. Presently, the two funding flows (national and international) are separate but can be 'blended' to achieve more impact and efficiency.

'Blended Finance for Impact' is a partnership among the ADB, GFATM, and APLMA to enable long-term integrated financing for healthcare initiatives, including malaria prevention. In September 2018, ADB announced the establishment of a new Regional Health Fund (RHF). The fund addresses the increasing demand from governments for new forms of health financing, particularly financial modalities that blend grants and loans to tackle the most pressing health challenges in Indo-Pacific countries.

4. Dentsu Aegis Network and APLMA[101]

APLMA teamed up with the region's innovative digital marketing and communications firm, Dentsu Aegis Network. As part of the creative partnership, Dentsu Aegis Network became one of the main corporate partners in the APLMA-led 'M2030 - Defeating Malaria Together'. Dentsu Aegis' media agency, Vizeum, assumed the role of a creative partner to lead the conceptual execution, strategy, and brand development for M2030.

99 ADB and GFATM sign MOU.

100 World Economic Forum.

101 APLMA.

5. The Business Alliance Against Malaria (BAAM)[102]

The alliance was formerly known as the Private Sector Malaria Coalition (PSMC). Its objective is to catalyse action, promote innovations that support treatment and prevention, and provide a reputational platform for its members. The alliance has worked closely with leading malaria organizations, such as the RBM Partnership to End Malaria, The Global Fund, and WHO. BAAM serves as the only platform that unites companies across industries and continents to bring multi-sectoral expertise and strategic partnership to the fight against malaria.

Member companies of the alliance include major pharmaceutical groups, companies specialized in vector control tools, and firms involved in consumer / staff malaria initiatives, such as Nando's.

Current Members include:

6. M2030[103]

M2030, incorporated in Singapore, was launched by APLMA and private sector partners in April 2018. M2030 is a platform for cause-based corporate engagement that takes a novel approach to eliminate malaria by 2030. It brings together international health organizations, Asian corporations, and consumers so that a small part of everyday purchases or actions can contribute to fighting the disease, thereby allowing stakeholders in each part of the retail process to be a part of a larger cause.

M2030 marks the first time that influential Asianled businesses have united under the same brand to collaborate and champion the fight against malaria. The DT Families Foundation, represented at the event by Dr. Wit Sootaranun, is a key partner in M2030. Current M2030 partners include the Tahir Foundation (Indonesia), DT Families Foundation (Thailand), Dentsu Aegis Network, Outdoor Channel Asia, Shopee, Yoma Strategic Holdings, WaveMoney, Pun Hlaing Siloam Hospitals, and The Global Fund to Fight AIDS, Tuberculosis, and Malaria.

[103] World Economic Forum.

Product Effectiveness Criteria

The WHO issued detailed guidelines for monitoring the durability of long-lasting insecticidal mosquito nets (LLINs) under operational conditions. The information derived by monitoring is useful in planning the replacement of worn-out nets under the LLIN program. It also helps make decisions to procure the most suitable LLINs for various settings and understand the factors associated with the durability of LLIN products.

Listed below are the elements to measure the durability of LLINs:[104]

Survivorship is the proportion of distributed nets still available for use as intended in the households to which they were given after a defined period, e.g., 1, 2, 3, or more years.

Attrition (opposite of survivorship) is the proportion of nets no longer in use, as intended after a defined period, post their distribution to the households. Attrition can be categorized by main reasons, namely, decay (e.g., destroyed, so torn and worn out that it is considered useless for protection against mosquitoes), absence (e.g., stolen, given away, moved), or used for other purposes.

Physical or fabric integrity reflects the number, location, and size of holes in each net. When possible, the assessment can also be categorized by the type of hole (burn, tear, seam failure, nibbled, or chewed by animals). The physical or fabric integrity of surviving nets can be assessed as a function of the length of use until deterioration leads to the net being discarded or used for another purpose.

Insecticidal activity (bio-efficacy): It is the degree of knock-down, mortality, or inhibition of blood-feeding induced in susceptible mosquitoes, as determined by standard WHO test procedures and criteria (i.e., cone bioassay, tunnel test). Insecticidal activity is associated with the type and content or availability of insecticide. The insecticide content is expressed as g/kg or mg/m2 of the LN and is determined by the method outlined in WHO specifications for LNs1. This information is of value in interpreting data on bio-efficacy. The insecticidal activity can be assessed as a function of the length of use.

Follow-ups are required to measure the above elements. Below are the outcomes that are used for the measurement of the efficacy of LLINs:

Net survivorship and attrition: Households should be visited and the physical presence of the LLIN should be recorded to measure survivorship. If the net is still present in the household, the investigator should record whether the net is being used for its intended purpose. Nets that have never been used should also be recorded, but excluded from the analysis. If the net is no longer in the house, the investigator should determine the reason for its loss.

Fabric integrity: Fabric integrity is assessed from the questionnaire by counting the number of holes (including tears in the netting and split seams) by their location on the net and their size. Holes can be classified into the following categories:

- Smaller than a thumb (0.5-2 cm)
- Larger than a thumb but smaller than a fist (2-10 cm)
- Larger than a fist but smaller than a head (10-25 cm)
- Larger than a head (> 25 cm)
- Holes less than 0.5 cm can be ignored; evidence of repairs to the net fabric and the type of repair should also be recorded on the form

Insecticidal activity: Recommended tests for bio-efficacy are the WHO cone test and tunnel test. These tests are direct measures of the amount of insecticide available to contact and kill mosquitoes. Chemical assays of the insecticide content of nets provide useful supporting information, but the results may be misleading by themselves, particularly for nets with incorporated insecticide, in which much of the insecticide is inside the fibres and not available to contact and kill mosquitoes.

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[104] World Economic Forum.

Scientific literature comparing the effectiveness of vector control product

Investigation of mosquito net durability for malaria control in Tanzania:[105]

A scientific study conducted in 2014, in collaboration with the National Malaria Control Program (NMCP), was carried out in Tanzania to assess the mosquito net durability.

Three LLINs, namely, **Olyset, PermaNet 2.0**, and **Netprotect**, were being tested as per recommendation from the WHO Pesticide Evaluation Scheme.

A two-stage approach was being used: First, LLINs from recent national net campaigns were evaluated retrospectively in 3,420 households. Those households received one of three leading LLIN products at random (Olyset, PermaNet 2.0, or Netprotect) and were followed up for three years in a prospective study to compare their performance under operational conditions.

LLIN durability was evaluated by measuring attrition (the rate at which nets are discarded by house-holds), bio-efficacy (the insecticidal efficacy of the nets measured by knock-down and mortality of mosquitoes), chemical content (g/kg of insecticide available in net fibres), and physical degradation (size and location of holes).

This data was of importance to policymakers and vector control specialists, both in Tanzania and the Sub-Saharan Africa region. It helped ensure cost-effective coverage and maximize current health gains in malaria control.

A meta-regression analysis of the effectiveness of mosquito nets for malaria control[106]

LLINs have been widely used as an effective alternative to conventional ITNs for over a decade.

A systematic review of over 2,000 scholarly articles published since the year 2000 was performed. The final dataset included 26 articles for meta-regression analysis, with a sample size of 154 sub-group observations.

The study found that the overall Odds Ratio (OR) for reducing malaria by LLIN use was 0.44 indicating a **risk reduction of 56%**, while **ITNs were slightly less effective** with an OR of 0.59.

The meta-regression model carried out in this study confirmed that **LLINs are statistically more effective than ITNs** in preventing malaria. These findings support the importance of treated nets and their use in malaria control.

The study results suggest that **nets are less effective in protecting children** under the age of five, which may be due to differences in child behaviour or inadequate coverage.

Effectiveness of long-lasting Piperonyl Butoxide-treated insecticidal net and indoor spray interventions[107]

The study evaluated the effectiveness of Piperonyl Butoxide (PBO) long lasting insecticidal nets versus standard LLINs, as single interventions and in combination with the indoor residual spraying of pirimiphos-methyl.

The study interpreted that PBO LLINs and non-pyrethroid IRS interventions showed **improved control** of malaria transmission as compared with standard LLINs where pyrethroid resistance is prevalent, and either intervention could be deployed to good effect.

As a result, the WHO recommended increasing the coverage of PBO long lasting insecticidal nets. **Combining IRS with pirimiphos-methyl and PBO LLINs** provided **no additional benefit** as compared with PBO long-lasting insecticidal nets alone or standard long-lasting insecticidal nets, along with indoor residual spraying.

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[105] Lena M Lorenz et.al. 2014 (CL: High).

[106] Gi-geun Yang et.al. 2018 (CL: High).

[107] Natacha Protopopoff et.al. 2018 (CL: High).

The efficacy of topical mosquito repellent (picaridin) and LLINs versus LLINs alone.[108]

A randomized controlled trial to study the efficacy of topical mosquito repellent (picardin), along with LLINs versus LLINs alone was performed in 117 endemic villages in the Ratanakiri province in Cambodia.

Although effective topical repellents provide personal protection against malaria, whether the mass use of topical repellents in addition to long lasting insecticidal nets can contribute to a further decline of malaria was not known, particularly in areas where outdoor transmission occurs.

The trial concluded that there were **no post-intervention differences** for *Plasmodium falciparum* or *Plasmodium vivax* malaria among treatment groups.

Daily compliance and appropriate use of repellents, achieved under optimum trial conditions with sufficient resources to promote and distribute the repellent product, remained the main obstacle.

Mass distribution of highly effective topical repellents in addition to impregnated bed nets **did not contribute** to a further decline in malaria endemicity in a pre-elimination setting in Cambodia.

Strengthening LLIN effectiveness monitoring using retrospective analysis across Sub-Saharan Africa.[109]

Bed nets averted 68% of malaria cases in Africa between 2000 and 2015. However, concerns over insecticide resistance remain. A population-based, cross-sectional study using data from 162,963 children younger than 5 years of age participating in 33 Demographic and Health and Malaria Indicator Surveys was conducted in 21 countries between 2009 and 2016. This study aimed to address the effectiveness of LLINs against malaria.

A Bayesian logistic regression model was used to determine patterns of associations among the age of LLINs, insecticide type, and malaria. Children sleeping under LLINs experienced **21% lower odds of malaria infection** than children who did not.

Nets less than one year of age exhibited the **strongest protective effect** and protection weakened as the net age increased.

LLINs containing different insecticides exhibited similar protection.

Freely-available, population-based surveys can enhance and guide current entomological monitoring amid concerns of insecticide resistance and bed net durability. These surveys can be used with locally-collected data to **support decisions on LLIN redistribution** campaign timing and provide information on insecticides suitable for use.

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[108] Sluydts V, et.al. 2016.

[109] Mark Janko et.al. 2018.

Comparison of focus Countries

Asia ranks second to Africa in terms of malaria burden. Most cases of malaria in 2017 were reported in the African region (200 million or 92%), followed by the Southeast Asian region (5%), and the Eastern Mediterranean region (2%).[110]

The prevalence of vector-borne diseases is closely linked to the physical environment of the country/region. In most Southeast Asian countries, the majority of the high-risk category population are farmers or forest workers, ethnic minorities, refugees, displaced persons, tourists, and pilgrims. Moreover, island countries such as Indonesia and Papua New Guinea (PNG) have high malaria burden due to their geographical challenges and difficulty to reach population at-risk, owing to the inconvenient logistics of vector control products.

Globally, significant progress has been made in reducing morbidity and mortality due to vector-borne diseases. However, there are numerous key challenges that need to be addressed to sustain the gains and eliminate malaria in most parts of Asia. Some of these challenges are controlling the spread of resistance in *Plasmodium falciparum* to Artemisinin, limiting outdoor transmission, controlling the spread of vivax malaria, and ensuring universal coverage of key interventions.

Six focus countries (Vietnam, Indonesia, PNG, Malaysia, Cambodia, and Myanmar) have varied geographical challenges and a high burden of VBDs among other Asian countries. Listed below are a few key data pointers for the in-focus countries:

TABLE 9: COUNTRY COMPARISON ON FUNDING, LLINS, MARKET SIZE [111]

Parameter	Indonesia	PNG	Malaysia	Myanmar	Cambodia	Vietnam
Population at Risk (2017)	●	●	●	●	●	●
Incidence of Malaria (2017)	●	●	●	●	●	●
Number of LLINs distributed (2017)	●	●	●	●	●	●
Public Funding (2017-18)	●	●	●	●	●	●
Public Fund (D) / Person at Risk	●	●	●	●	●	●
Retail Market (2018)	●	●	●	●	●	●
Est. Funding for LLINs (% of Public Fund)	●	●	●	●	●	●

Note: High ● Medium ● Low ●

[110] World Malaria Report 2018.

[111] FutureBridge Analysis..

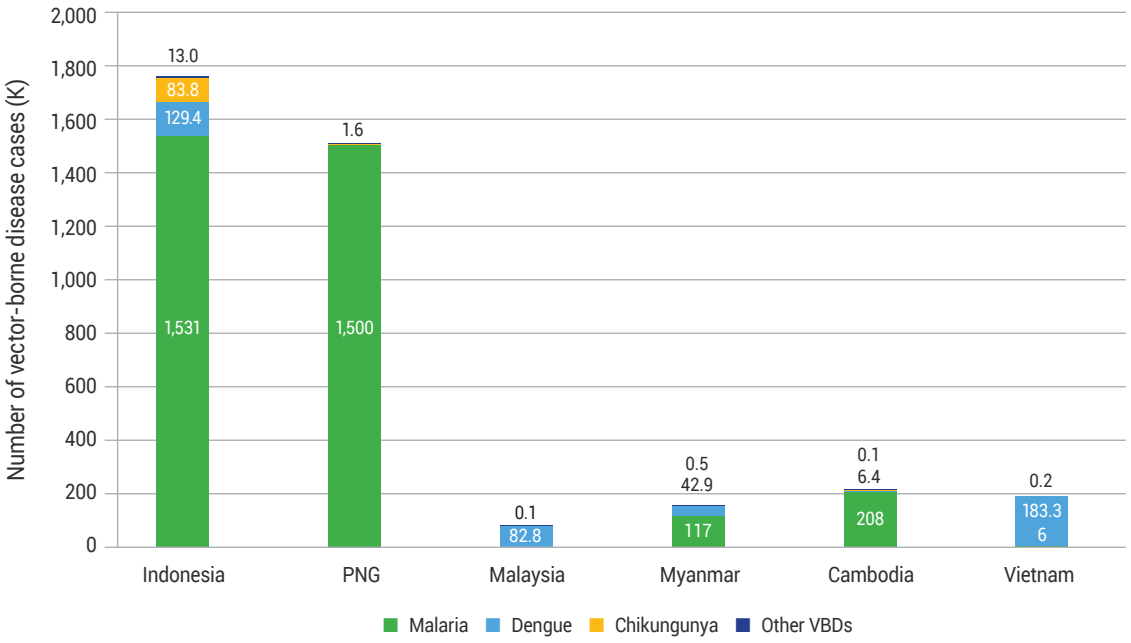
TABLE 10: MALARIA BURDEN, FUNDING & LLINS DISTRIBUTED (2017-2018)

Country	Population at Risk 2017 (Millions)	Incidence of Malaria (Cases/1000)	Funding 2017-18 Total in USD Million (USD/Person at Risk)	LLINs Distributed 2017 (Millions)	Estimated % funding for LLINs **
Indonesia	263	5.8	38.3 *(0.5)*	4.4	26%
PNG	8.3	189	13.4 (1.6)	1.7	28%
Malaysia	1.26	0.003	48.8 (38.7)	0.3	1.4%
Myanmar	31.7	2.1	58.8 (1.9)	5.8	22%
Cambodia	8.6	13	29.4 (2.6)	2.0 + 0.6* = 2.6	20%
Vietnam	70.4	0.06	19.2 (0.3)	0.8	9%

Note: *Approximately 0.6 million hammock nets have been distributed in Cambodia during 2016-17. ** The cost of a net is assumed to be USD2.25.

The burden of malaria in Asia is high and varies from country to country. In several countries, it has been observed that increased malaria incidence rates were mostly concentrated along the border areas with high population mobility and low population density.

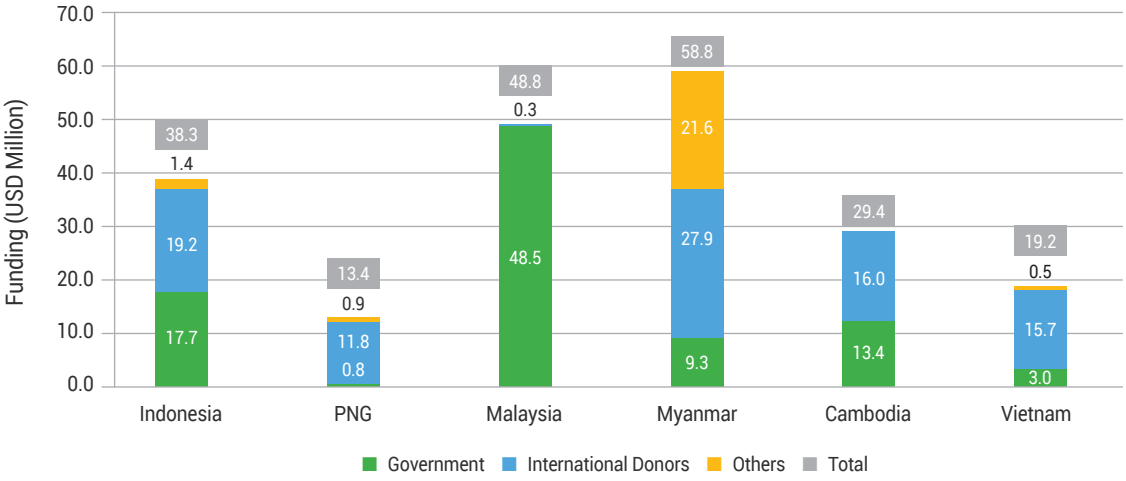
FIGURE 19: REPORTED BURDEN OF VECTOR-BORNE DISEASES (2017)



In 2017, Indonesia accounted for the highest number of VBD cases among other in-focus countries. Additionally, the country has also reported the highest number of malaria cases compared to other countries. Indonesia accounts for 8% of the total vivax malaria cases in 2017 (Source: World Malaria Report 2018).

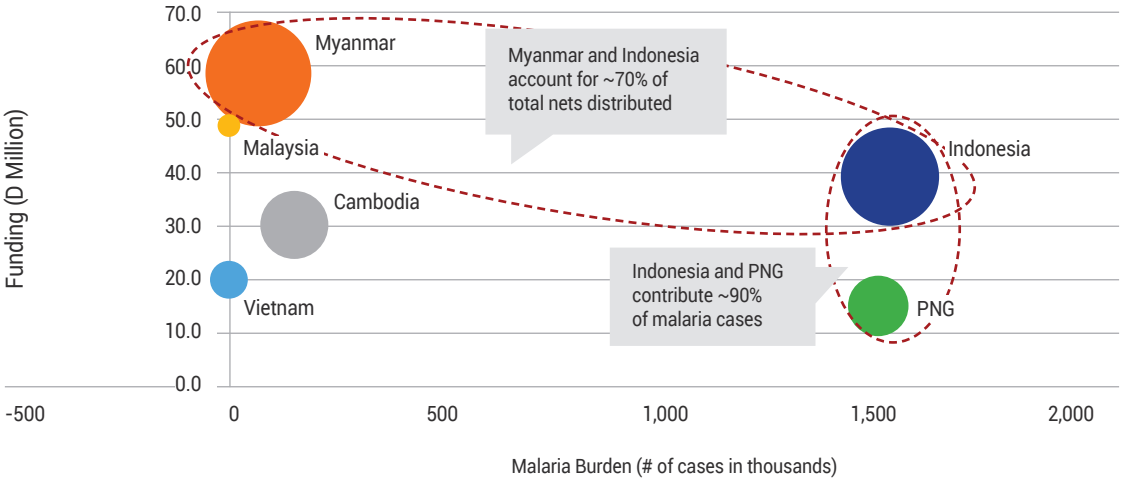
Fighting malaria is one of the key concerns of the 21st century. Domestic funding and various international organizations such as The Global Fund, The President's Malaria Initiative (PMI), the Bill & Melinda Gates Foundation, and the WHO, among others, are focused on contributing towards the fight against malaria in the Indo-Pacific region.

FIGURE 4: MALARIA CONTROL PUBLIC FUNDING (2017-2018)



Among the in-focus countries, Myanmar received the highest international funding of USD ~59 million between 2017 and 2018 for malaria control. In contrast, Malaysia uses only domestic funds for malaria control activities.

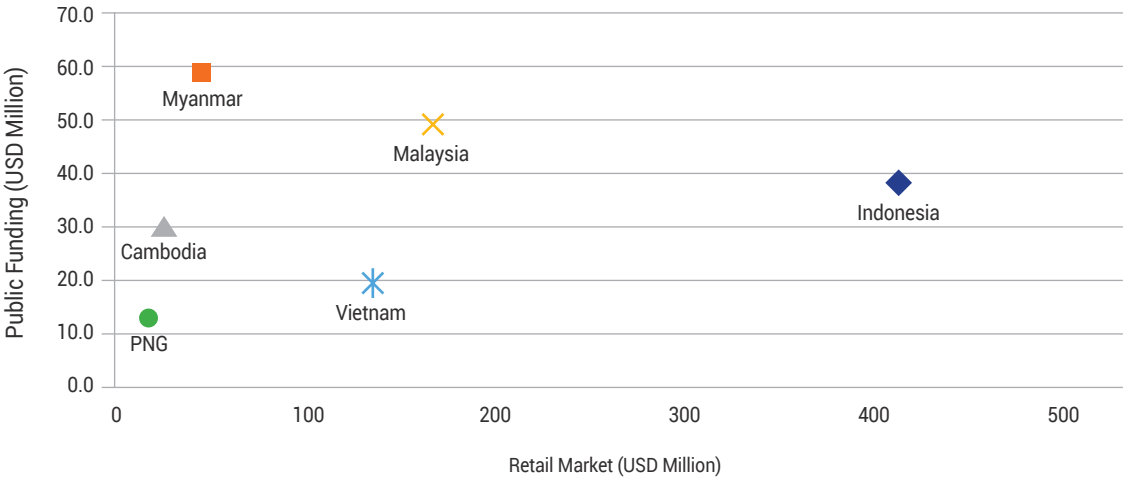
FIGURE 5: MALARIA BURDEN VS. FUNDING (2017-2018)



Note: *Bubble size indicates the number of nets distributed.

- Myanmar and Indonesia invest more than 20% of their funding in the procurement of nets.
- PNG receives the lowest fund of ~USD13.5 million among other in-focus countries; of which 28% is used for the distribution of ITNs.
- Malaysia distributes the highest number of nets per person (lowest incidence country), whereas it is the lowest in Vietnam.

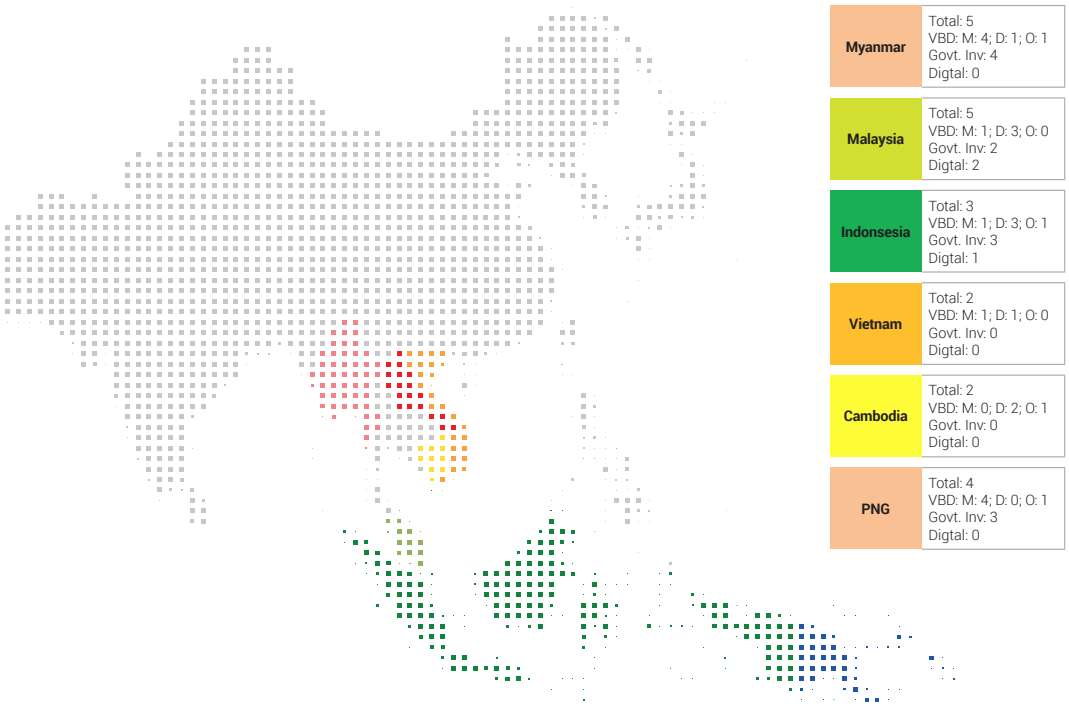
FIGURE 20: PUBLIC FUNDING VS. RETAIL MARKET (USD MILLION), 2017-2018



Note: *The retail market comprises insecticide coils, sprays/aerosols, and electric insecticides.

- In terms of the overall retail market size, Indonesia ranks the highest with the estimated market size of ~USD410 million in 2018.
- Malaysia also has a significant retail market that is estimated to be ~USD170 million.
- The retail market for vector control products in Vietnam is estimated to be ~USD140 million.
- The retail market in Indonesia and Vietnam comprises ~90% of the overall spending on vector control activities.

FIGURE 21: AWARENESS CAMPAIGNS ACROSS COUNTRIES



Total: Number of awareness campaigns identified; **VBD:** Vector-borne Diseases; **M:** Malaria; **D:** Dengue; **O:** Other VBD.

Govt. Inv.: Number of campaigns with government involvement; **Digital:** Number of digital awareness campaigns.

- Myanmar witnessed the maximum number of awareness campaigns, followed by Malaysia and PNG.
- The duration of the campaigns ranged from one month to one year.
- Malaysia and Indonesia are the only countries wherein innovative digital campaigns have been launched.
- Indonesian government spending on Information, Education, and Communication (IEC) activities for malaria control was USD0.8 million in 2018.[112]

Examples of Campaigns:

A. 1 Rumah 1 Jumantik/3M Plus-

This activity involved the elimination of mosquito habitats in **Indonesia** in **2015**

Result: All houses in South Tangerang city were found **larva-free**

[112] The Global Fund Indonesia, 2018.

B. Jumat Keliling (Jumling) – Clean Friday Movement

Spreading awareness to eradicate mosquito larvae from **Jakarta (Indonesia)** region in **2018**

Result: **Only one case** reported in April 2018

C. No larvae – No mosquito – No dengue

Malaria Consortium, with PHD and NDCP, launched the 1st dengue campaign in **Pailin, Cambodia** in **2015**

Result: Trained target audience to keep surroundings clean, employ larviciding and seek proper treatment for dengue

D. MosquitoZone International Malaria Prevention Campaign

The campaign focused on onshore pipeline construction, airport, and gas conditioning plant construction workers (~6,000) in PNG from 2005-2010

Result: Malaria incidence reduced by 83%

E. Program Meso-Vietnam

Implemented in northern and central Vietnam targeting ~380K people between October 2007 and December 2010

Result: No new cases of dengue were registered after similar interventions

F. Strive for Dengue – Free Malaysia (MerdekaTanpaDenggi)

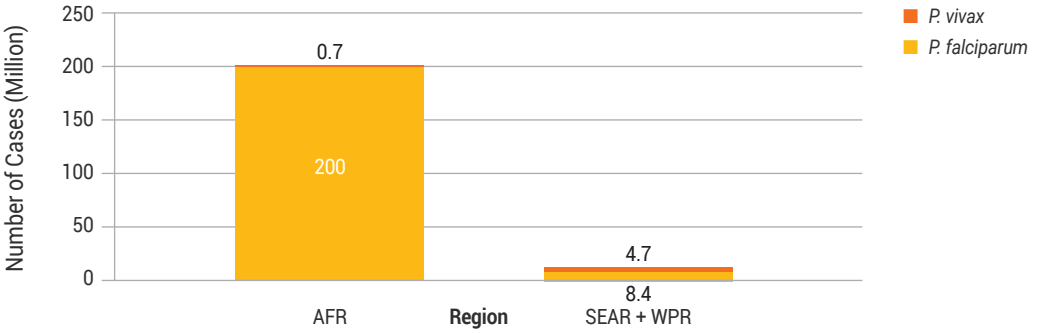
The initiative by **Sanofi Malaysia** in **July 2014** was undertaken to create awareness among the people of Malaysia for the prevention of dengue

Comparison with Africa

The World Malaria Report 2018 estimates that there were 219 million cases of malaria in 2017 worldwide.[113] African countries witnessed an estimated 3.5 million more cases of malaria in 2017 as compared to the previous year. Malaria continues to claim the lives of more than 435,000 people each year, largely in Africa. Children under the age of 5 are especially vulnerable; the fact that every two minutes a child dies from this preventable and curable disease is unacceptable.[114]

Fifteen countries carried the heaviest malaria burden in 2016, together accounting for 80% of all global malaria cases and deaths. In the Southeast Asian region 1.24 million confirmed malaria cases were identified in 2017.

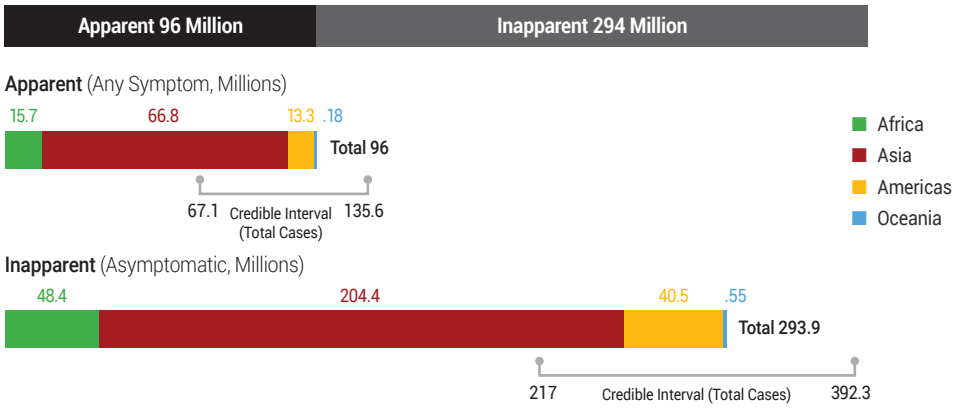
FIGURE 6: ESTIMATED MALARIA CASES 2017 [115]



SOUTHEAST ASIA AND WESTERN PACIFIC REGION MALARIA BURDEN OF DISEASE REPRESENT 6.5% OF THE AFRICAN MALARIA BURDEN.

Dengue is also a major concern across the globe. Major factors contributing to dengue proliferation include worldwide rapid population expansion, urbanization, and globalization of markets. These factors, coupled with new modes of human transportation, have facilitated the dissemination of both people and disease. Moreover, rapid urbanization and development of Asian cities have a drastic effect on the transmission of infectious diseases. Currently, millions of people inhabit several cities in Asia; coupled with a lack of wastewater infrastructure, insufficient housing, and unhygienic societal conditions, this promotes the propagation of dengue infection. These factors are some of the major contributors to the proliferation of dengue in Asia.[116]

FIGURE 7: APPARENT AND IN-APPARENT DENGUE BURDEN



USD10.1 billion are needed to implement malaria national strategic plans in 30 African countries over the next three years (2018- 2020) and achieve the WHO Global Technical Strategy targets. Of these total requirements, USD4.7 billion is not yet financed, including USD1.3 billion for essential commodities.

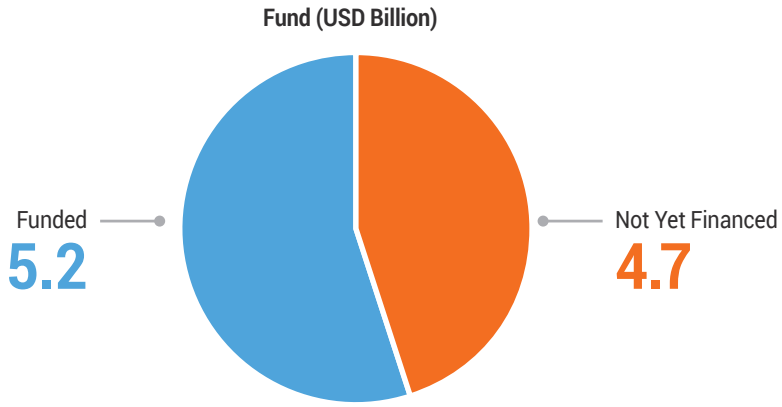
[113] WHO Malaria Report.

[114] World Malaria report 2018.

[115] WHO, World Malaria Report 2018.

[116] Haider H., et, al., June 2015.

FIGURE 8: TOTAL GLOBAL FINANCIAL REQUIREMENT FOR MALARIA STRATEGIC PLANS IMPLEMENTATION IN 30 AFRICAN COUNTRIES IN 2018-2020[117]



Out of the funds not yet financed, USD1.3 billion are allocated for essential commodities.

In Africa, 22 out of 30 countries are facing gaps in financing essential commodities, which include LLINs or IRS for vector control; RDTs for diagnosis; and Artemisinin Combination Therapy (ACTs) for treatment. However, additional commodity needs such as microscopy equipment and drugs for intermittent preventive therapy in pregnancy and for seasonal malaria chemoprevention are not included in these essential commodity gaps.

- Six countries are facing a combined gap in ACTs, amounting to 280 million treatment doses
- An extra 136 million LLINs need to be funded in 15 countries
- 7 countries that have been implementing IRS have a financial gap of USD163 million
- 4 countries are facing a gap in malaria RDTs

Alone with international funding, national/domestic funding plays an important role in malaria elimination.

[117] RBM Partnership.

FIGURE 27: HIV DOMESTIC FINANCING, 2021-2023 (TOTAL USD 24.4 BILLION)

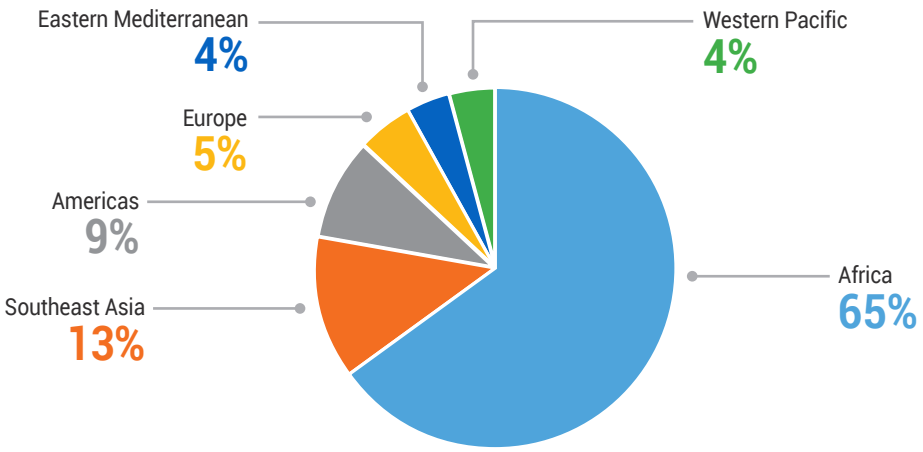
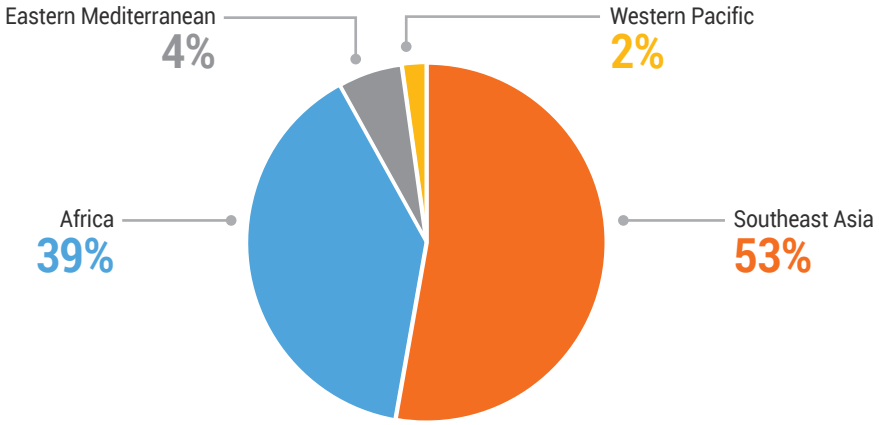


FIGURE 28: MALARIA DOMESTIC FINANCING, 2021-2023 (TOTAL USD 8.5 BILLION)

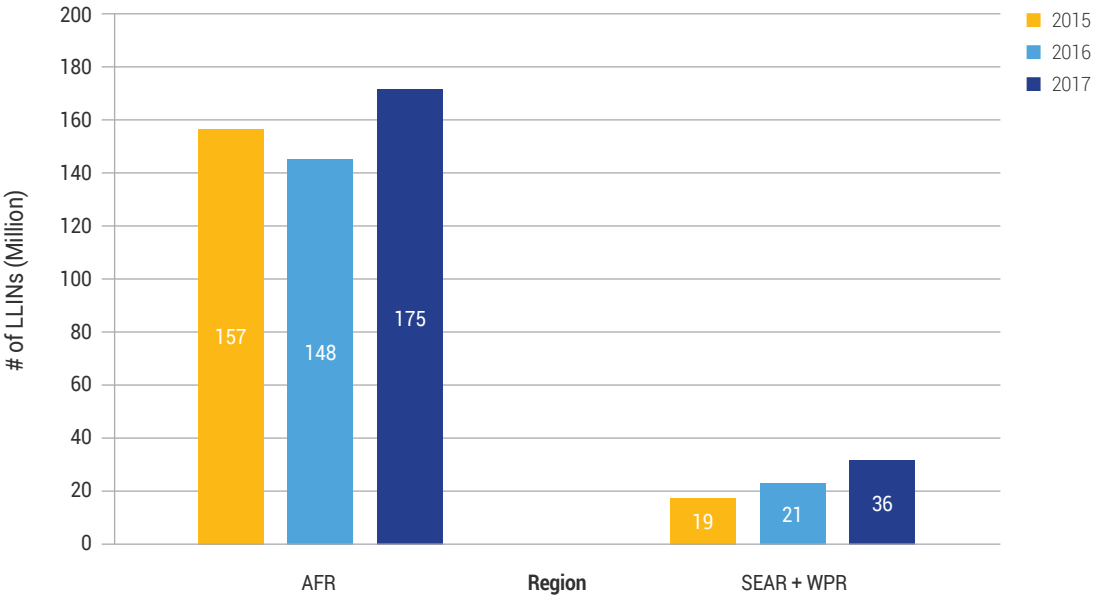


The above figure clearly indicates that domestic funding in Africa is focusing on HIV control (65%) rather than malaria (39%). On the other hand, Southeast Asia is concentrating on malaria control (53%) rather than HIV (13%).[118]

ITNs/LLINs were introduced in the African region as an effective means of preventing mosquito bites and malaria transmission, following the meeting of African Heads of States in Abuja, Nigeria in 2000. Pregnant women and children aged 0-5 years were the main target population, as they are the most affected by the malaria scourge. Among the available malaria interventions, the use of ITNs/LLINs has become the major intervention to limit malaria incidence in localities. The availability of ITNs/LLINs was scaled up by their free distribution, achieving near 100% coverage of the population at risk of contracting malaria. The distribution of free ITNs/LLINs in Africa was meant to support the WHO's recommendation for universal access to ITNs/LLINs, especially among people living in malaria-affected areas.

[118] The Global Fund.

FIGURE 29: NUMBER OF LLINS SOLD OR DELIVERED, 2015-2017[119]



LLINs sold or delivered in South East Asia and the Western Pacific regions represent 15.8% of LLINs sold or delivered in Africa.

The success of malaria control with ITNs/LLINs has been challenged by issues related to delivery, distribution, usage, and acceptability of these products in Africa. Public awareness and acceptance of ITNs vary from community to community in countries where this method of malaria control has been adopted. As a result of poor acceptability of ITNs/LLINs, it is important that both the government and health workers in various African countries undertake steps to increase the level of awareness regarding vector control methods through health education. It is also necessary to ensure easy access to ITNs/LLINs through mass importation, so as to motivate more people to use these products.[120]

Various campaigns are undertaken in the African region to control and eliminate VBDs. These include:

The sterile insect technique: This technique involves a genetic birth control method in which laboratory mass-produced sterile male insects are released into the wild at a ratio that effectively inundates a target population. This forces most females to mate with sterile males, substantially reducing their fecundity, and resulting in population suppression. The sterile insect technique has been piloted against mosquito vectors of Zika, yellow fever, chikungunya, and dengue viruses, but has never been used for malaria control efforts. The South African sterile insect technique initiative, together with a similar trial in Sudan, is a first for African malaria vectors.[121]

Zero Malaria Starts with Me (ZMSWM) Campaign: This continent-wide campaign seeks to revive national and regional progress against malaria. The African Union Commission, ALMA, and the RBM Partnership to End Malaria developed a campaign toolkit to assist countries with the rollout. As ZMSWM is implemented across Africa, the ALMA Scorecard for Accountability & Action, which is produced quarterly, will remain an important tool that countries use to track performance against key indicators in malaria-endemic countries.[122]

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[119] WHO, World Malaria Report 2018.

[120] Sina O J (2018).

[121] Conversation.com.

[122] Endmalaria.org.

Market Access Conclusion

Indo-Pacific is the major contributor for vector-borne diseases

Indo-Pacific carries the second-largest burden for malaria, followed by Africa with approximately 28 million cases and 45,000 deaths each year. Along with malaria, other vector-borne diseases such as dengue, Japanese encephalitis, Zika, and filariasis are also prevalent across the Indo-Pacific region. Globally, there are 2.5 billion people at risk for dengue, out of which 70% are found in the Indo-Pacific region. Monkey malaria is highly prevalent around the forest area in Malaysia. Increasing incidence of vector-borne diseases has a significant impact on the economic status of several countries in the Indo-Pacific region, especially the rural areas of countries such as Myanmar, PNG, and Cambodia where the purchasing capacity of vector control products serves to be the biggest challenge. Hence, these areas are highly endemic for vector-borne diseases.

An increase in the use of the digital platform to spread awareness, monitoring and surveillance of vector control activities, extensive research to find new tools for outdoor residual transmission, new ingredients in bed nets, and change in consumer preference from donor to retail products are considered to be the key market trends. Financial partnership, cross-border collaborations, and strategic partnership among sectors such as finance, agriculture, and defence are factors expected to drive the Indo-Pacific vector control market.

Vector Control and Prevention Activities

Integrated Vector Management (IVM) consists of a portfolio of operational actions and priorities for the control of vector-borne parasites, that are tailored to different epidemiological and entomological risk scenarios. IVM activities for vector control should include awareness campaigns and mass distribution of LLINs.

The Global Fund and PMI are the major funders for vector control and prevention activities in Indo-Pacific

The successful completion of vector control programs is backed by funds received from international organizations, such as The Global Fund, PMI, Unitaid, UNOPS, APLMA, APMEN, WHO, and UNICEF, among others. Most of the funds from donors are concentrated on malaria control activities, owing to the increasing incidence of vector-borne diseases. Domestic funding is less than 50% in majority of the Indo-Pacific countries, and thus, it is essential to address the funding gap.

Inter-and intra-sectoral collaborations and strategic partnerships will increase the penetration of vector control activities.

Several organizations work in collaboration/partnership with one another to increase the availability, accessibility, and affordability of vector control products. Intra- and inter-sectoral collaboration among government bodies, such as finance, agriculture, and defence will help control the spread of vector-borne diseases across borders. Partnerships between NGOs, local government bodies, and health ministries of respective countries will also accelerate vector control activities.

The retail market is highly fragmented; however, it is growing due to the acceptability of retail products.

LLINs are essential donor products in the Indo-Pacific region; however, LLINs are not preferred as they are considered to be bulky for mobile and migrant populations, are difficult to carry and can accommodate only two persons. Hence, there is growing acceptability of retail products such as insecticide coils, electric insecticides, and aerosols/sprays, owing to their small size, easy availability, and effectiveness in eliminating mosquitoes at site.

The increase in the number of the migrant populations is the biggest challenge for the judicious implementation of vector control and prevention activities.

Resistance to key insecticides, including pyrethroids and DDT, which are used in ITNs and LLINs, are a major of concern in various malaria-affected countries. In several Indo-Pacific countries, unstable healthcare systems and lack of skilled human capacity are factors that act as key challenges impacting malaria control goals and targets. The lack of well-functioning health information and surveillance systems will hamper evidence-based programming decisions. The increasing numbers of the migrant population makes it difficult to monitor vector control and prevention activities, thereby becoming another significant challenge to the market.

Indo-Pacific has more than half of the market share for mosquito repellents[123]

Indo-Pacific has the highest market share for mosquito repellents worldwide. It has held a market share of ~55% as of 2016; this share continues to increase due to varied climate conditions and improper waste management. An increase in awareness and affordability of vector control products in this region are major contributors to the growth of the vector control market.

The vector control market in the Indo-Pacific region can be divided into 3 types:

- Household Insect Repellents
- Outdoor Insect Repellents
- Body-worn Insect Repellents

Apart from LLINs and IRS, the household insect repellents can be divided into:

Coils, Vaporizers, Mats, Aerosols, and Creams

Major players in household insecticides

Behavioural factors affecting the Indo-Pacific vector control market

- **Climate change:** Climatic conditions and ineffective waste management in the Indo-Pacific region are conducive to insect and rodent breeding. With global warming, the temperature in the tropical region is on the rise, and simultaneously, the number of mosquitoes is also increasing.
- **Increasing population at risk:** The Indo-Pacific region includes ~2 billion people who are at risk of developing vector-borne diseases. The population at risk includes mobile populations and migrants, static villagers, and forested workers/rubber tappers.
- **High species variation:** In the Indo-Pacific region, all 5 Plasmodium species are present, along with a large number of vector species, making malaria epidemiology complex.
- **Resistance to insecticides:** The Indo-Pacific region is an epicentre for Artemisinin and pyrethroid resistance.

[123] FutureBridge Analysis.

Annex

Technical

Disease statistics by country

Reported disease statistics by country, ranked from **highest to lowest burden** or **risk per disease** (top three highest burden countries by disease highlighted in red).

Country	Malaria API (2016)	Country	Malaria cases (2017)	Country	Dengue cases (2017)	Country	Chikungunya cases*	Country	Zika risk (last update Mar 2018)	Country	Pop covered by LF MDA*	Country	Japanese encephalitis (2017)
Papua New Guinea	181.9	India	9,590,000	Sri Lanka	185,000	Indonesia	83,756	Samoa	Cat 1	India	419,112,086	India	2,043
Solomon Islands	171.0	Indonesia	1,530,566	Vietnam	183,287	Sri Lanka	37,000	Solomon Islands	Cat 1	Indonesia	50,785,500	China	1,147
Cambodia	18.4	Papua New Guinea	1,500,657	India	157,000	India	30,121	Bangladesh	Cat 2	Myanmar	34,016,081	Myanmar	442
Vanuatu	8.2	Pakistan	956,280	Indonesia*	129,435	Bangladesh	14,160	Cambodia	Cat 2	Nepal	11,207,367	Philippines	361
India	7.7	Cambodia	208,273	Pakistan	125,000	Pakistan	8,387	Fiji	Cat 2	Philippines	7,000,897	Indonesia	281
Lao PDR	5.8	Myanmar	116,772	Philippines	117,654	Lao PDR	4,638	India	Cat 2	Papua New Guinea	5,602,188	Vietnam	200
Indonesia	5.8	Solomon Islands	103,482	Malaysia	82,840	Samoa	2,500	Indonesia	Cat 2	Timor Leste	1,279,948	Nepal	63
Pakistan	4.9	Bangladesh	32,924	Myanmar*	42,913	Papua New Guinea	1590	Lao PDR	Cat 2	Lao PDR	149801	Thailand	28
Myanmar	3.7	Lao PDR	20,712	Thailand*	26,616	Cambodia	1,500	Malaysia	Cat 2	Fiji	78,862	Sri Lanka	23
Bangladesh	1.9	Philippines	15,253	Lao PDR	11,039	Thailand	453	Myanmar	Cat 2	Samoa	61325	Malaysia	20
Thailand	0.8	Thailand	11,043	Cambodia	6372	Philippines	282	Papua New Guinea	Cat 2	Malaysia	30642	Bangladesh	19
Nepal	0.5	Vietnam	5,481	China	5900	China	173	Philippines	Cat 2	Bangladesh	0	Lao PDR	9
Philippines	0.3	Nepal	3,829	Bhutan*	4700	Bhutan	68	Thailand	Cat 2	Bhutan	0	Timor-Leste	7
Timor Leste	0.2	Vanuatu	2,270	Vanuatu	3,000	Malaysia	30	Vietnam	Cat 2	Cambodia	0	Cambodia	5
Vietnam	0.1	Malaysia	85	Samoa	2,466	Nepal	3	Vanuatu	Cat 3	China	0	Bhutan	3
Malaysia	0.1	Timor Leste	36	Fiji	2200	Fiji	1	Bhutan	Cat 4	Pakistan	0	Papua New Guinea	1
Bhutan	0.02	Bhutan	11	Solomon Islands*	1,212	Myanmar	0	Nepal	Cat 4	Solomon Islands	0	Pakistan	0
China	0	China	0	Bangladesh	876	Solomon Islands	0	Sri Lanka	Cat 4	Sri Lanka	0	Samoa	0
Fiji	0	Fiji	0	Timor Leste*	278	Timor Leste	0	Timor Leste	Cat 4	Thailand	0	Fiji	Not available
Samoa	0	Samoa	0	Nepal*	183	Vanuatu	0	China	Not available	Vanuatu	0	Solomon Islands	Not available
Sri Lanka	0	Sri Lanka	0	Papua New Guinea**	0	Vietnam	0	Pakistan	Not available	Vietnam	0	Vanuatu	Not available
Source: WHO WMR 2017.		Source: WHO WMR 2018. Estimated cases (point value).		*Data from other years (preceding 2017). Sources: ECDC, WHO, MOH. ** DENV cases in PNG rarely reported, but study published by Senn et al (2011) indicates a seroprevalence of 8% amongst patients presenting to Madang clinics with acute febrile illness. According to Luang-Sarkia et al (2018), DENV surveillance not undertaken, patients with acute febrile illness not regularly tested.		*Various years. Sources: ECDC, MOH, WHO, peer-reviewed literature.		Sources: WHO, CDC, ECDC. Cat 1: Area with new introduction or re-introduction with ongoing transmission. Cat 2: Areas with virus transmission following previous virus circulation. Cat 3: Areas with interrupted transmission and with potential for future transmission. Cat 4: Area with established competent vector but no known documented past or current transmission.		*Various years; proxy for populations at risk for F. Sources: Graves et al (2013), MOH, WHO.		ource: WHO Global Data Observatory.	

Regulatory Pathways

Regulatory pathways summary by country

Vietnam / Indonesia / Myanmar / Malaysia / Cambodia / Papua New Guinea

Registration Requirement / Process

S.No.	Parameters	Vietnam	Indonesia	Myanmar	Malaysia	Cambodia	Papua New Guinea
1.	Registration Requirement [Whether registration in country is mandatory or not]	Mandatory for Household use pesticides under MoH and Agricultural Pesticides under MoA. Microbial Pesticides are not regulated under MoH. Reg. validity – 5 years – Renewable	Registration for Pesticides for household use / vector control is regulated under MoA. Biological Pesticides are also regulated under the MoA. Reg. Validity – 5 years – Renewable	Registration for pesticides for household use / vector control is regulated under MoA. Reg. Validity – 10 years – Renewable	Registration for all household pesticides and public health use pesticides are under MoA. Registration validity – 5 years. Renewable	There are no requirements for registration of pesticides for public health use. Allows import of products recommended by WHO / PQ listed	The Environmental contaminants Act governs pesticide usage. Need to obtain a permit for pesticides being imported into the country. Validity of Permit – 1 year. Renewable.
2.	Ease of Regulatory Process [How stringent are the regulatory processes in country] (Scale 1 – 10*) *Scale given below the table	Dossier requirement is simple. In-country trials are mandatory. Scale: 5	Lengthy registration process with long delays in securing registration. Scale: 8	Process can be very long since registration committee doesn't meet regularly. New Products process can be very lengthy Scale: 6	Systems for registration are place. Guidelines are available. Justifications are acceptable. Scale: 4	No specific requirement for registration of pesticides to be used in Public Health. Rating given on import permit instead of registration Scale: 2	Simple process to obtain permit. Requirements are minimal. Rating is given on import permit Scale: 2
3.	Regulatory authority [Name and address of the regulatory authority regulating VCP]	HEMA (Health & Environmental Management Agency) Ministry of Health – MoH	Ministry of Agriculture - MoA	Plant Registration Board (PRB) under the Plant Protection Department (PPD) under the Ministry of Agriculture (MoA)	Pesticide Board under the Ministry of Agriculture (MoA)	Pesticides are regulated by Ministry of Agricultural, Forestry and Fisheries (MAFF) for Ag. Use.	Ministry of Environment (MoE)
4.	Timeline for approval [How long does regulatory process take for placing product in market]	6 – 12 months depending on the product i.e. for Mosquito coils, vaporizers the registration timeline would be around 5 – 7 months and the rest would be 8 – 12 months.	18 – 24 months depending on the product and the complexity of the registration	6 – 8 months Process can become very long if it is an innovative product	8 – 12 months	No regulatory process. Hence no timelines	Securing a permit to import pesticide is about 1 – 2 months
5.	Registration Holder [Is registration given to foreign entity or for local entity only]	Local Representative / Local Entity	Local company or a local agent for a foreign company.	Local distributor or legal entity	Local legal entity or distributor should be the registrant	Any entity or individual interested in importing can import the product	Any local entity or supplier of pesticide can apply for permit
6.	Data Requirement [Broad requirement of data for VCP registration in country]	Standard data required – Company registration certificate, LoA, LoS, Physicochemical, Bio-efficacy, Toxicological and Labelling.	Standard data required – Company registration, trademark registration, LoA, LoS, Physicochemical, Efficacy, Toxicological and Labelling.	Standard data required. Local distributor Company certificate	Standard physicochemical, Toxicological, packaging and labeling is required. Efficacy trials from region is acceptable.	None	Environmental risk assessment, labels, SDS and other country registration certificates.
7.	Harmonization of Process [Is there any regional harmonization of regulatory process]	No harmonization of data or regulatory process	No harmonization of data or regulatory process	No harmonization of data or regulatory process	No harmonization of data or regulatory process	No harmonization of data or regulatory process	No harmonization of data or regulatory process
8.	Online Process [Is there provision for online processing of VCP registration]	Online submission of various applications – Registration & Licensing is available	Online submission of registration available in the regulatory system.	No provision for online submission	Yes, online submission provision is available	No online process is available	No online process is available
9.	Registration Fees [What is the total cost of registration including trial cost]	Cost of Registration – 450 USD Cost of trials – 10000 – 15000 USD Additionally, for PH Programs studies are to be done in North, Central and South Provinces	Cost of Registration 600 USD Cost of Trials - ~15000 – 20000 USD	Chemical analysis – 200 USD / unit Cost of Registration – 3200 USD for Full registration and 1300 USD for Provisional Reg. EUP – 650 USD	Cost of registration – 750 USD	None	Cost of Permit – 40 USD

S.No.	Parameters	Vietnam	Indonesia	Myanmar	Malaysia	Cambodia	Papua New Guinea
10.	Technical (active substance) Reg. [Should active substance be registered before VCP is registered]	The regulatory authority does not register Technical (a.s.) material. They have a list of approved Technical substances and VCPs are to be from these active substances.	Information on Technical (a.s.) material needs to be submitted along with the dossier for formulated product. Technical product registration is available.	Technical (a.i.) material registration process is not a capability under the registration department.	Yes, Technical (a.i.) material registration is required.	None	There is no requirement for Technical (active substance) registration required.
11.	Technical Equivalence (a.s.) [Is there a provision to have equivalence for technical material]	No Technical equivalence provision available.	No Technical Equivalence procedure available	No Technical equivalence provision is available.	Technical equivalence provision is available in for comparative Technical grade	No Technical equivalence provision is available.	No Technical equivalence provision is available.
12.	'Me Too' / Identical Registration [Can a registration be obtained for already approved VCP]	No identical or 'me too' registration provision.	No identical or me-too registration provision	No identical or 'me-too' registration provision	Identical registration process is not available in the country.	No identical or 'me-too' registration provision	No identical or 'me-too' registration provision
13.	Country Specific Labelling [Is there a country specific labelling for VCP products]	The requirement for the labelling is not specific but reference is made to GHS. Preferred language on the label is Vietnamese. If main label is in foreign language then secondary label should be in Vietnamese.	The labelling requirements to be followed are provided in the Pesticide Act. Labelling generally follows the GHS or FAO guideline. Indonesian language required.	Nothing specific but standard labelling requirement. FAO labelling guidelines referred to. Language required is Burmese.	Yes, labelling requirement are clearly defined by regulatory authority. GHS labeling guidelines are followed. Labels should have 3 languages describing safety procedures	Labelling required for pesticides used in agriculture. Since no registration of PHP labelling not required.	No country specific labeling is required.
14.	VCP approved [What are the broad categories of VCP approved in-country] The approved lists of each country are annexed in Appendix	There is no specific list of approved VCPs available. There is however, a list of banned and prohibited list of pesticides available.	There is specific list of pesticides with trade name of the product, company name available.	List of approved pesticides available which includes Public Health Use pesticides.	Vector control products are registered under Household pesticides category and is separately listed in registered products list	For Public Health Programs all PQ listed products are allowed.	No specific list of pesticides used for Public Health use.
15.	VCP in Public Health Programs [What are the VCPs in Public Health Programs in the country]	PH programs pesticides should be PQ listed.	Yes, a list of pesticides in PH programs is also available.	Public Health Pesticides are listed in the list of approved public Health pesticides	Yes, PH pesticides are listed as PCO or Household pesticides	All PQ listed products are allowed in Public Health Programs.	None
16.	Biological Vector Control Products [Are Biological VCPs to be registered in the country]	Registration not required for Biological VCP. Hence there is no list.	Registration is required for Biological products too and this is also listed in the list of registered pesticides	Yes, Biological Vector Control Products are also registered under the regulatory department.	Microbial pesticides are registered under the same regulatory authority.	No specific guidelines or registration requirement for Biological Vector Control Products.	No specific guidelines for Biological Vector Control products
17.	Emergency Situations [Are unregistered products or are registrations fast tracked during exigencies]	There is no provision for Emergency regulatory approval process under the regulatory authority.	There are no provisions for an emergency approval process.	No specific provisions for emergency use registration	There are no specific provisions for unregistered pesticides to be approved for emergency.	No specific guidelines.	No specific guidelines.
18.	Retail Markets [Are approved VCPs allowed to be sold in retail markets?]	All registered products have a default permission to be sold in retail market. A retail permit must be obtained.	Specific licensing to be obtained for retailing pesticides. Retail license to be obtained from DoH and is valid for 4 years.	Retail permit to be obtained as a separate license to sell pesticides in retail shops	Retail permit / licensing is mandatory for placing pesticides in retail markets.	No specific requirement for getting retail permit for public health products	No specific requirement for retail permit for public health pesticides
19.	Insecticides Banned [Are any VCP banned or not registered in-country due to restrictive processes]	All Class 1a and 1b pesticides as per the WHO toxicological classification are banned and cannot be registered.	All Class 1a and Ib pesticides as per the WHO toxicological classification are banned and cannot be registered.	All Class 1a and Ib pesticides as per the WHO toxicological classification are banned and cannot be registered. (POP & PIC List Pesticides)	Highly hazardous pesticides are also registered. Commodity & Proprietary pesticides. Different costs for registration of different toxicity class	All Class 1a and Ib pesticides as per the WHO toxicological classification are banned and cannot be registered.	No specific list of banned pesticides.

*Scale 1 – 10 with 1 – very easy / no regulations & 10 – very strict; The ease is measured cumulatively based on time taken, data required, processes involved etc.

Source: http://www.pertanian.go.id/ - INDONESIA ; http://vihema.gov.vn/ - VIETNAM ; http://ppdmyanmar.org/ - MYANMAR; http://www.doa.gov.my/index.php/pages/view/302?mid=141 – MALAYSIA; http://web.maff.gov.kh/contactus?lang=en – CAMBODIA; http://www.pngcepa.com/ - PA-PUA NEW GUINEA

Local trials / Local Testing capabilities

S.No.	Parameters	Vietnam	Indonesia	Myanmar	Malaysia	Cambodia	Papua New Guinea
20.	Are Local trials required? [Are local trials required for in-country regulatory approval]	Yes, both chemical and efficacy trials are to be conducted in country as part of registration process	Yes, both chemical and efficacy trials are to be conducted in country as part of registration process	In country chemical analysis is required. Efficacy trials are not mandatory. Country capacity to conduct trials limited.	Bio-efficacy trials are required as part of registration but in country trials are not mandatory. Regional trials are accepted	No local trial is required for public health products.	No local trial data is required.
21.	Is GLP data mandatory? [Should data be generated in facilities with GLP accreditation]	No, GLP is not mandatory but study on efficacy as well as chemical content must be done under ISO 17025 accredited labs.	GLP data not required for physicochemical or efficacy data. But Toxicological data is to be conducted in GLP accredited labs	GLP data not mandatory.	Yes, toxicological data and physicochemical data are to be done in GLP certified labs	Not applicable	No specific requirement is given
22.	Testing facilities capability [Are there any international or GLP accredited facilities in country]	There are several ISO 17025 labs accredited to conduct chemical content. However, ISO 17025 labs conducting efficacy are limited.	MoA has a list of approved labs for conducting efficacy trials. The country also has several GLP and ISO accredited labs.	Limited testing capability	There are many testing facilities for efficacy, chemical analysis and toxicological studies. WHO collaborating center is also available	In country testing is severely limited. No efficacy testing facility. Chemical analysis facility available.	Limited testing capability
23.	Cost of Local trials [What is the cost of conducting local trials]	~10000 – 15000 USD	~15000 – 20000 USD	200 - 300 USD (Analytical studies)	Regional trial data is acceptable Local trial cost would be around 10000 USD	No local testing	No local testing
24.	Institutes approved for Local trials [What institutes in country are approved for local trials]	NIMPE – National Institute for Malariology, Parasitology and Entomology IMPE	A list of approved institutes by the MoA	National Agricultural Laboratory (NAL)	Regional trial data is acceptable. In country testing facility such as USM is readily acceptable.	No testing capacity or capability	No testing capacity or capability

Source: Regional Regulatory Authorities, Pesticide Manufacturers, WHO – https://www.who.int/whopes/resources/by_year/en/; https://www.who.int/pq-vector-control/en/

Regional / International Advocacy

S.No.	Parameters	Vietnam	Indonesia	Myanmar	Malaysia	Cambodia	Papua New Guinea
25.	FAO-WHO JMPS Specification [Is it mandatory or a requirement for Technical (a.i.) to have JMPS specs]	It is not mandatory for the technical to have FAO-WHO specification to be considered for registration under household use category or for PH programs	FAO specifications is referred but is not a mandatory requirement.	FAO specifications are preferred but not mandatory.	FAO / WHO specifications are recommended for PHP products. However, it is not mandatory for registration.	WHO approved products are permitted for import into the country for public health programs.	FAO / WHO specification is not referred.
26.	Stringent Regulatory Authority [Would stringent regulatory authority registration waive in country registration]	SRA registration does not expedite nor waive registration requirement	SRA registration does not expedite nor waive registration requirement	SRA registration does not expedite nor waive registration requirement.	SRA registration does not expedite nor waive registration requirement	SRA registration has no bearing on regulatory processes. There are no registrations for PHPs	SRA registration has no bearing on regulatory processes. Only permits are required.
27.	WHOPES / PQ Recommendation [Is there waiver of regulatory process if VCP is WHOPES / PQ recommended]	WHOPES or PQ listing does not waive registration requirement.	No waiver or fast tracking of registration	No waiver or fast track registration process	No waiver or fast track registration process	No registration of PH pesticides.	Not applicable
28.	WHOPES / PQ mandatory [Is WHOPES / PQ listing mandatory for approval of VCP]	For country registration of VCP WHOPES recommendation / PQ listing is not mandatory. Registration is done despite PQ status. Public Health Programs consider only PQ listed products	Not mandatory for registration Public Health Programs consider only PQ listed products	Not mandatory for registration Public Health Programs consider only PQ listed products	Not mandatory for registration Public Health Programs consider only PQ listed products	Public Health Programs consider only WHOPES/PQ listed products	Public Health Programs consider only WHOPES/PQ listed products
29.	Regional Influencers [Any regional influencers on in-country registration process]	A registration with a regional regulatory authority does not influence the registration process in the country.	No regional influencer or registration scheme that can influence registration process. Registration in the region can be favorable	No regional influencer or registration scheme that can influence registration process. Registration in the region can be favorable.	No regional influencer of registration scheme	No regional influencer – No regulatory requirement	Registration under APVMA (Australian Reg. Authority) would hasten the process.
30.	Collaborative Registration [Does the country RA collaborate with any other Registration Authority]	There is no collaborative registration process under which the regulatory authority is part off.	No collaborative registration process	No collaborative registration process	No collaborative registration process	No collaborative registration process	No collaborative registration process

Manufacturing / Licenses

S.No.	Parameters	Vietnam	Indonesia	Myanmar	Malaysia	Cambodia	Papua New Guinea
31.	In-Country Manufacturing [Is there manufacturing of VCP's in the country]	In country manufacturing of household pesticides such as LLINs and other retail products are predominant	Pesticide re-packaging is done extensively. Mosquito coils, vaporizers are manufactured but no capability to manufacture LLINs or other chemical pesticides	No manufacturing capability. Pesticides are all imported into the country.	Yes, capacity if there for formulation. No manufacturing of LLINs.	No manufacturing capability. Pesticides are all imported into the country.	No manufacturing capability. Pesticides are all imported into the country.
32.	Manufacturing Licenses [Is there a need for obtaining manufacturing license to manufacturing VCPs]	Manufacturing license is to be obtained prior to manufacturing of formulations, repackaging of pesticides.	Manufacturing license is to be obtained for formulation, repackaging of pesticides	Manufacturing license to be obtained if formulation or repackaging of pesticides is to be done	Yes, manufacturing license is to be obtained if any formulating or repackaging is done	No manufacturing capacity	No manufacturing capacity
33.	Marketing Licenses [Is there a need to obtain marketing licenses in different states or provinces in-country]	Marketing licenses are not required. Registration certificate is enough for marketing.	Selling and Storage License needs to be obtained. Public Health Pesticides have to obtain permit from Department of Health, MoH	Selling and Storage License to be obtained prior to stocking and selling of pesticides in shops	Yes, selling and storage license is to be obtained prior to stocking and selling of pesticides.	No specific marketing license required	No specific marketing license required
34.	Pre / Post Shipment Inspection [Is pre-or post-shipment inspection of VCPs mandatory by 3rd party accreditations req,]	Not a requirement for registration. But donors and or implementing agencies in country would insist on 3rd party inspections	Not a requirement for registration. But donors and or implementing agencies in country would insist on 3rd party inspections	Not a requirement for registration. But donors and or implementing agencies in country would insist on 3rd party inspections	No specific requirement. But donors and implementing agencies might insist on inspection	Donors and implementing agencies might insist on inspection	Donors and implementing agencies might insist on inspection
35.	Certifications / PCO [Any other in-country certifications to be obtained for VCPs]	Licensing of Pest Control Operators are limited. PCOs have to apply for a license. Restricted pesticides application can be done by licensed applicators.	No quality certification program for registered pesticides. Licensing not very structured. PCOs have to obtain license before undertaking any pesticide application	Certified licensed applicator is the one responsible for PCO work Applicator training certificate and First aid training license essential.	Robust certifying process exists in the country.	Semi regulated and not proper	No specific process or regulatory requirement.

Source: http://www.pertanian.go.id/ - INDONESIA ; http://vihema.gov.vn/ - VIETNAM ; http://ppdmyanmar.org/ - MYANMAR; http://www.doa.gov.my/index.php/pages/view/302?mid=141 – MALAYSIA; http://web.maff.gov.kh/contactus?lang=en – CAMBODIA; http://www.pngcepa.com/ - PA-PUA NEW GUINEA

Procurement

S.No.	Parameters	Vietnam	Indonesia	Myanmar	Malaysia	Cambodia	Papua New Guinea
36.	In-Country Manufacturing [Is there manufacturing of VCP's in the country]	Ministry of Health	Directorate General for Communicable Diseases and Environmental Health, the Directorate for Vector Borne and Zoonotic Diseases, and the Sub-directorate for Vector Control, MoH	Vector Borne Diseases Control under Department of Public Health under Ministry of Health	Vector Borne diseases control under Ministry of Health	CNM – Cambodia National Malaria program	National Malaria Program
37.	National Guidance Document [Is there a National Guidance document to procure VCPs]	National Malaria Control Program National Dengue Control Program (The National Strategy for Malaria Control and Elimination)	National Malaria Elimination Action Plan Procurement is done by Malaria Sub Directorate.	National Malaria Control Program (National Plan for Malaria Elimination in Myanmar 2016-2030)	National Vector Borne Diseases Control Program monitors all vector borne diseases	Yes, National malaria elimination Policy document exists	National Malaria Program governs all policies regarding malaria control.
38.	Global Donors [Which are the Global Donors active in the country]	Global Fund PMI	Global Fund Government funding	Global Fund – UNOPS being the principal recipient of the fund. PMI, Save the Children, JICA	Exclusively country funding only.	Global Fund, PMI, Country funding	International Donor funding is limited despite high disease burden.
39.	Guidance document on disposal [Is there a guidance document on the disposal of used VCPs]	No clear guidance document existing on the disposal of VCPs.	Disposal document is provided as part of the MoA legislation on Pesticide registration.	No specific guidance on disposal of Vector Control Products.	No detailed guidance document available on disposal. Standard disposal methods defined.	No specific guidance on disposal of vector control products	No specific guidance on disposal of vector control products

Source: http://www.searo.who.int/entity/malaria/data/en/

Country Policies

S.No.	Parameters	Vietnam	Indonesia	Myanmar	Malaysia	Cambodia	Papua New Guinea
40.	Resistance Status [What is the resistance status of mosquito vectors]	Pyrethroids resistance observed.	Pyrethroids and Carbamates resistance observed	Pyrethroids, OPs and OCs Resistance observed	Resistance to Pyrethroids is prevalent.	Pyrethroids, OPs and OCs Resistance observed	Pyrethroids resistance observed.
41.	IRM Policies [Are there any active Insecticide Resistance Management policies in-country]	NIMPE & IMPE do annual resistance monitoring in 3 sites (Northern, Central and Southern provinces) For inclusion in PHP programs, trials have to be done in North, Central and South provinces)	No routine surveillance IRM Policy on monitoring and reporting.	No annual country IRM Policy on monitoring and reporting. National Malaria Control Program has stressed the importance of IRM. However segmented monitoring is followed.	Country wide resistance monitoring is structured and actively	No resistance monitoring system in the country. Capacity is missing.	No resistance monitoring system in the country. Capacity is missing.
42.	IVM Policies [Are there any Integrated Vector Management policies in-country]	No country IVM Policy. MoH and MoA are planning to implement guidelines for correct use of PHPs. This is yet to be put in place.	No country IVM Policy as part of the Vector control program.	IVM is not formally a part of National Malaria Elimination Program. No country IVM Policy. National Malaria Control Program has stressed the importance of IVM	IVM policy is adequately incorporated in the Vector Borne diseases program.	No structured country IVM policy.	No structured IVM policy in the malaria program.

Source: http://www.searo.who.int/entity/malaria/data/en/ ; http://www.searo.who.int/entity/malaria/documents/myanmar_mpr/en/

Comparison with African Regulations

S.No.	Parameters	Vietnam	Indonesia	Myanmar	Malaysia	Cambodia	Papua New Guinea
43.	Comparative VCP Regulations [What is the comparison / differences in the regulatory process in Africa vs Asia]	The regulatory process is under the MoH and this is similar to the regulatory mechanisms followed in some West African countries by the Ministry of Health.	Regulatory process in MoA can be considered similar to East African Regulatory bodies – SEARCH Countries	Regulatory systems are evolving in Myanmar. There are guidance documents on the regulatory processes for Agrochemicals. The system can be on par to some evolving regulations in Africa.	Regulatory processes are well structured with robust guidelines and legislations.	Many African countries depend upon WHO / PQ listing for permitting Public Health pesticides. The regulations in Cambodia are similar to that.	The regulatory requirements are similar to the countries wherein WHOPES / PQ listing is acceptable.

Source: JVP analysis

Gaps

S.No.	Parameters	Vietnam	Indonesia	Myanmar	Malaysia	Cambodia	Papua New Guinea
44.	Gaps in Regulatory Process [What are the gaps / barriers in the regulatory processes that delay or hinder registration of new products]	Regulatory system is under the Ministry of Health with limited inputs from Ministry of Agriculture. No specific regulatory requirement for various categories of VCPs. Biological VCPs are not regulated. In country efficacy testing is mandatory making registration process quite long. WHO Guidelines not implemented for regulating VCPs Additional trials required for inclusion into PH Programs Harmonization lacking	Lengthy registration process In country efficacy testing is mandatory. No specific guidelines for different types of Public health pesticides. No priority accorded for Public Health Pesticides No expedited registra-tion process for Public health pesticides WHO Guidelines not implemented for regulating VCPs	Lacks specific guidance documents to be followed. Lacks quality control processes No in-country testing facilities IVM Policies are lacking. FAO / WHO guidelines not utilized Limited cooperation between ministries	Lack of Prioritization PHP registration	No regulations / registration process for Public Health Pesticides. Limited Capacity for quality control and testing Enforcement / Monitoring of illegal pesticide trade very scarce.	No percepti-ble regulatory system exists. Guidelines very vague. Legislation does not exist for pesticides.

Advocacy

S.No.	Parameters	Vietnam	Indonesia	Myanmar	Malaysia	Cambodia	Papua New Guinea
45.	Advocacy [Who / Which groups or agencies that can potentially do advocacy in the region]	WHO / FAO Donor agencies Regional Disease Control partnership – APLMA, APMEN, MHDC Manufacturers and Suppliers of VCPs ASEAN & ADB					

Dossier Requirements

Legal:

Indonesia:

1. Requires Free Sales Certificate (Registration in the country of Origin)
2. Requires registration of trademark in trademark registry

Vietnam:

1. Requires Free Sales Certificate (Registration in the country of Origin) – Legalized in the Vietnamese embassy in the country of origin.
2. All documents should be translated into Vietnamese

Physical and Chemical:

Myanmar:

1. Requires payment of analytical test fees and this should be attached along with the application form with samples for the application to be accepted.

Indonesia:

1. Analytical test report should be from GLP accredited test lab.

Vietnam:

1. Analytical test report should be from an ISO 17025 accredited lab

Bio-efficacy:

Malaysia:

1. Regional test reports are accepted – if done following internationally accepted test protocols
2. Regional testing should be done in countries which have similar pest profile and climatic conditions

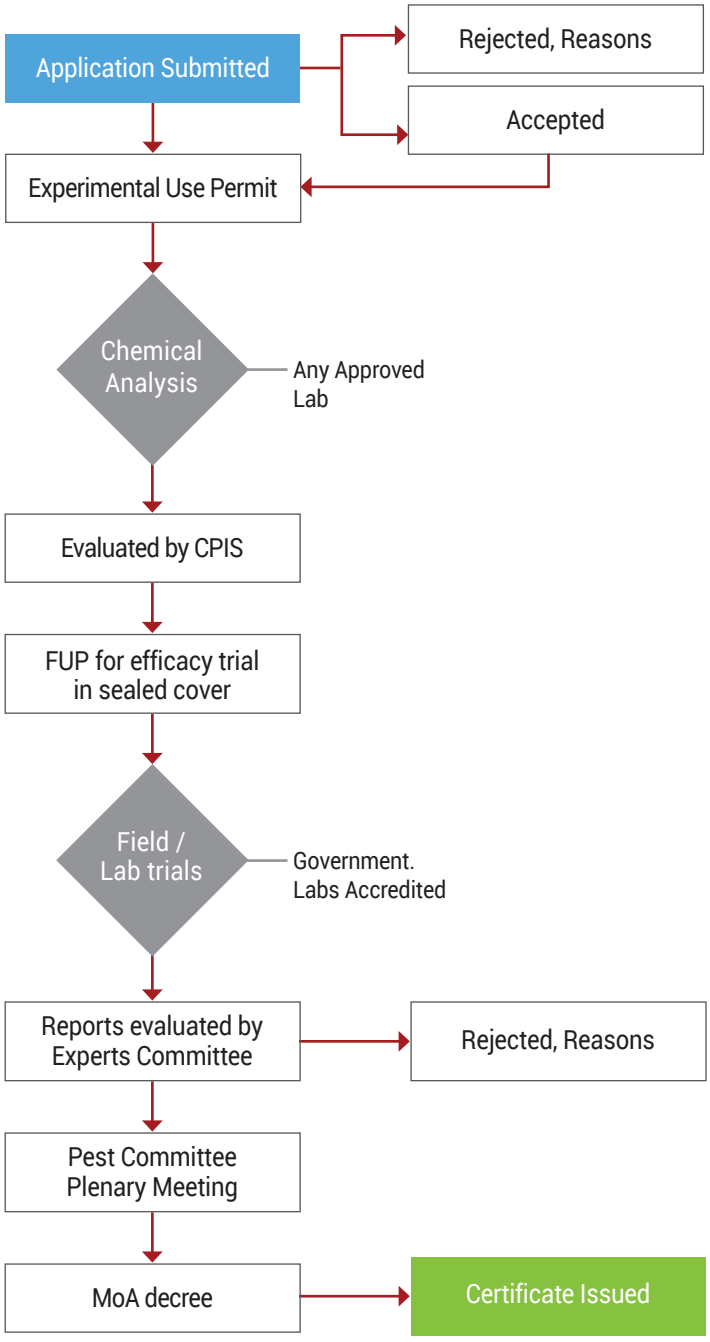
Indonesia:

1. In country testing is mandatory. Other country data is not acceptable and the need for in country trials is not waived off.
2. Trials need to be done in one of the trial institutes approved by the Ministry of Agriculture to conduct efficacy testing of Public Health Pesticides

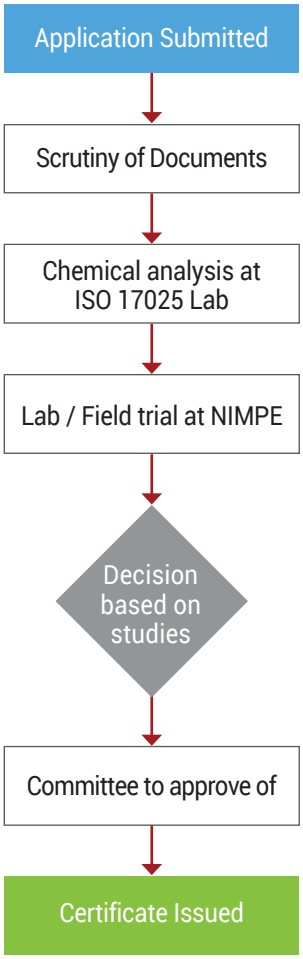
Vietnam:

1. In country evaluation of public Health pesticides is mandatory
2. Testing has to be done in ISO 17025 accredited labs and that too from NIMPE (National Institute for Malariology, Parasitology and Epidemiology)

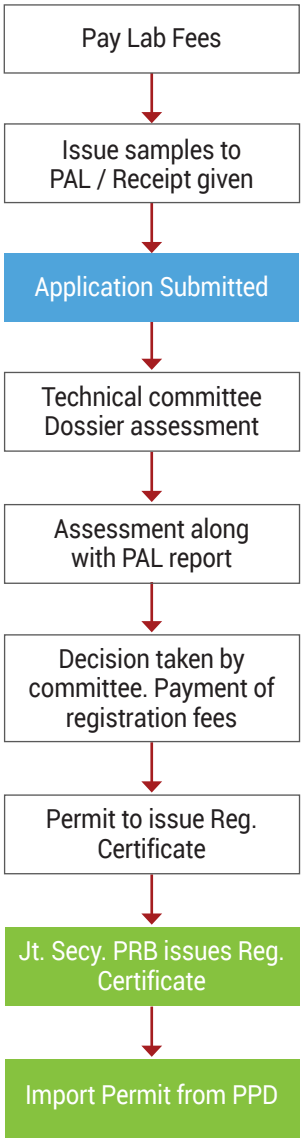
Flow Chart of Registration Process in focus countries:



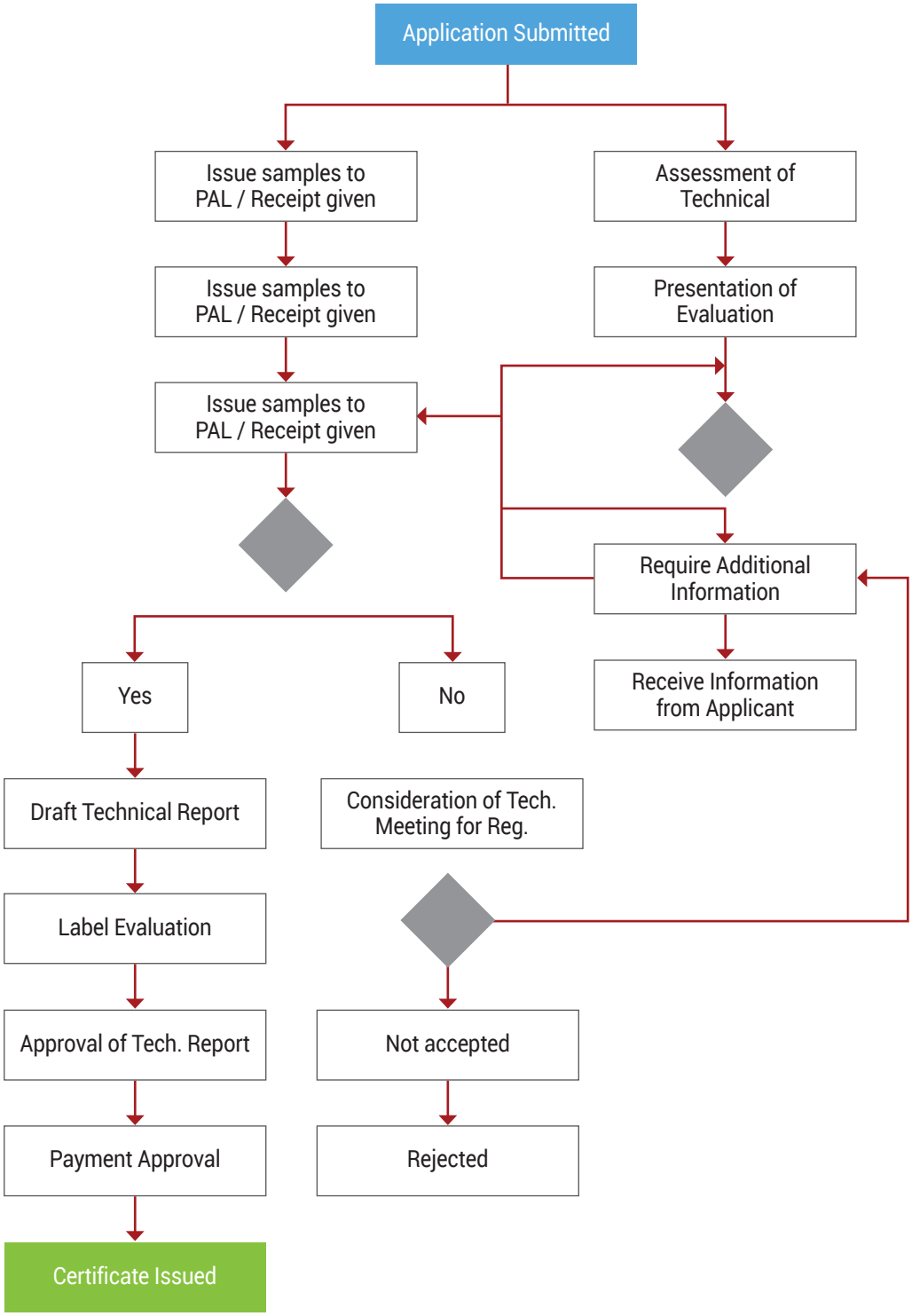
Indonesia



Vietnam



Myanmar


Application Submitted
Issue samples to PAL / Receipt given
Assessment of Technical
Issue samples to PAL / Receipt given
Presentation of Evaluation
Issue samples to PAL / Receipt given
Require Additional Information
Yes
No
Receive Information from Applicant
Draft Technical Report
Consideration of Tech. Meeting for Reg.
Label Evaluation
Approval of Tech. Report
Not accepted
Payment Approval
Rejected
Certificate Issued

Experimental Use Permit:

MALAYSIA

Need Experimental Use Permit?	Yes, Experimental Use Permit is mandatory for import of unregistered pesticides for conducting trials leading to the registration of the product or for research purposes
Application Form?	Form A
Procedure for obtaining?	Application form in prescribed form be submitted to the Pesticides Board along with prescribed fees. Board, if satisfied, will lay some conditions such as import quantity, disposal process and then permit for a limited one-time import for the requested use only – such as research, trials for registration etc. A permit issued under Section 14 of Pesticides Act, 1974 cannot be breached of its conditions.
Timeline for securing permit?	1 – 2 months
Penalties?	1. If a pesticide is imported under this permit and is used for any other purpose other than educational or research purpose is liable for prosecution with imprisonment for three (3) years or fine of fifty thousand (50,000) Ringgit. 2. If unregistered pesticide is imported into the country without an experimental use permit, the person is liable for imprisonment for six (6) years or a fine of fifty thousand (50,000) Ringgit.

MYANMAR

Need Experimental Use Permit?	Yes, Experimental Use Permit is mandatory for import of unregistered pesticides for conducting trials leading to the registration of the product or for research purposes
Application Form?	No prescribed form but a list of required data to accompany the application is prescribed
Procedure for obtaining?	Application with the following information on the pesticide need to be submitted for review by the Pesticide Registration Board (PRB)… 1. Trade Name 2. Physical Chemical Properties 3. Information on Technical Substance 4. Efficacy study reports – Laboratory 5. Specification 6. Toxicological Reports – Acute / WHO toxicity reports 7. Disposal guidelines
Timeline for securing permit?	2 months (longer if it is a new product)
Fee?	1000000 (MMK) = 656 USD
Validity of Permit	2 years
Penalties?	1. If a pesticide is imported without a permit, then for first offence a minimum of 1000 MMK = 0.66 USD to up to 5000 MMK = 4 USD 2. For second offence then the penalty will be 10000 MMK = 8 USD

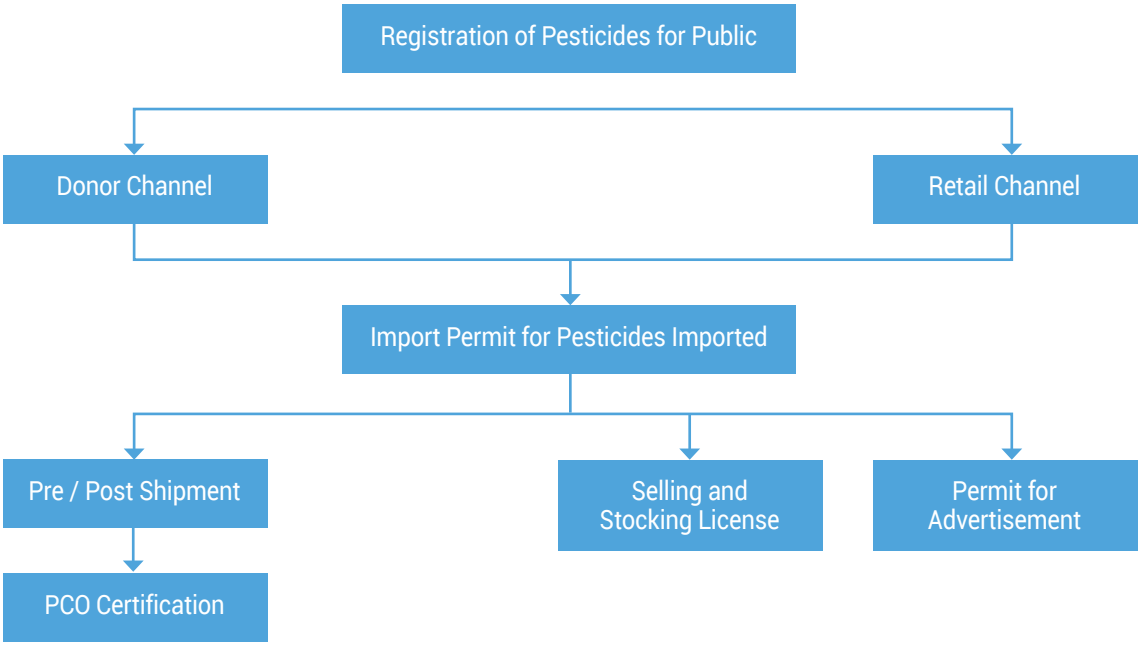
INDONESIA

Need Experimental Use Permit?	Yes, Experimental Use Permit is mandatory for import of unregistered pesticides for conducting trials leading to the registration of the product or for research purposes
Application Form?	No prescribed form but a list of required data to accompany the application is prescribed
Procedure for obtaining?	Application with the following information on the pesticide need to be submitted for review by the Pesticide Registration Board (PRB)… 1. Business Trade License 2. Company Affidavits 3. Trade Name as in Trademark Registry 4. Letter of Supply (LoS) from the Technical Substance supplier 5. Letter of Access (LoA) for technical information 6. Information on Technical Substance 7. Certificate of Analysis (CoA) 8. Analytical Methods 9. Certificate of Composition 10. Completed Registration Form – FORM 5
Timeline for securing permit?	20 – 30 working days
Fee?	200 USD
Validity of Permit	Initially granted for a period of 1 year. This can be extended for up to 2 times (each 1 year)
Penalties?	

Trial Institutes

S. No.	Country	Trial Institutes
1.	Indonesia	Directorate General of Disease Control & Env. Health, MoH, Indonesia Institute of Science (LIPI), Faculty of Veterinary Medicine, Ag. University, Bogor, Parasitology Division, Faculty of Medicine, Gadjah Mada University, Yogyakarta Division of Entomology of Tropical Medicine, Gadjah Mada University, Yogyakarta Faculty of Agriculture, Bogor Ag. University, Bogor
2.	Vietnam	National Institute of Malariology, Parasitology and Epidemiology (NIM-PE)
3.	Malaysia	Ministry of Health University of Malaya, Sabah Universiti Sains Malaysia (USM), Penang
4.	Myanmar	National Agricultural Laboratory (NAL)
5.	Cambodia	No registration for Public Health Pesticides hence no requirement for testing. However, Testing facilities such USF, MSF available.
6.	Papua New Guinea	No government facility available for testing public health pesticides

Registration Process for Pesticides – Donor Channel vis-à-vis Retail Channel



The pesticide registration process is the same regardless of whether the pesticide is for donor channel or for retail channel. The requirements for registration are the same for pesticides used in Donor and Retail channels. However, there are some differences in the requirements in a few countries in the pre-registration processes in some countries the requirements vary post registration.

Registration	In Vietnam, public health pesticides imported for distribution under donor funded programs do not need registration. Only an import permit is required. All other countries registration is mandatory and import permit is also mandatory.
Import Permit	Import permit is mandatory for import of pesticides for use in Public Health in all focus countries.
Pre/ Post Shipment Inspection	Post shipment inspection of LLINs is mandatory in Indonesia. But in other countries pre or post shipment inspection is mandatory for pesticides imported or supplied under donor funded projects. The inspection is insisted by donors or implementing agencies. Inspections are done by third party certifying bodies e.g. SGS, Intertek, Bureau Veritas, COTECNA, TUV etc.
Selling and Stocking License	Selling and Stocking license is mandatory for pesticides that need to be stocked and sold through retail channels. Technically, even pesticides procured for mass distribution and needs.
Permit to Advertise	Some countries have stringent rules on advertisement of pesticides and this includes pesticides used in public health especially through the retail channel. Countries such as Malaysia, Myanmar and Indonesia have requirements to obtain permission to advertise prior to airing advertisements of the products in media or publications.
Pest Control Operators Certification	PCO certification is part of the donor channel insecticide delivery. A trained and certified PCO is essential in effective vector control operation in public health programs.

Market Access

Malaria Burden Funding, Retail Market – Data

Parameter	Indonesia	PNG	Malaysia	Myanmar	Cambodia	Vietnam
Population at Risk 2017	263	8.2	1.26	31.7	11.3	70.4
Incidence of Malaria (2017)	5.8	189	0.003	2.1	13	0.06
No. of LLINs distributed (2017)	4.4	0.3	1.7	5.8	2.6	0.8
Public Funding (2017-18)	38.3	13.4	48.8	58.8	29.4	19.2
Public Fund (D)/person at risk	D0.5	D1.6	D38.7	D1.9	D2.6	D0.3
Retail Market (2018)	412	18	167	45	25.2	136
Retail Spending (D)/person at risk	1.6	2.2	132.5	1.4	2.2	1.9
Est. funding for LLINs (% of Public Fund)	26%	5%	8%	22%	20%	9%

Cost estimations used by the study (Shretta R, et. al., May 2019) for calculating total elimination cost

Intervention	Cambodia	Indonesia	Malaysia	Myanmar	PNG	Vietnam
Cost of pp protected by IRS	4.24	3.88	4.27	4.24	0	1.17
Cost of pp protected by LLINs	2.51	2.5	6.87	3.17	3.05	2.51
Cost of falciparum antimalarial (outpatient)	2.2	2.2	0.93	2.2	0.93	2.2
Cost of treatment as outpatient	1.82	13.43	15.3	1.3	2.92	2.43
Cost of vivax antimalarial	0.54	0.54	0.29	0.29	1.16	0.29
Cost of G6PD testing	7	7	7	7	7	7
Cost of antimalarial (inpatient)	14.46	25.89	14.46	25.89	7.19	14.46
Cost of treatment as inpatient	38.33	159.6	593.62	22.22	293.48	152.46
Cost of RDT	1.08	0.4	3.88	0.4	0.67	1.2
Cost of slide	0.86	0.86	0.86	0.86	0.86	0.86
Cost of surveillance pp	0.44	0.23	0.36	0.36	0.36	0.36
Cost of training pp	0.15	0.03	0.02	0.02	0.02	0.02
Cost of IEC pp	0.1	0.04	0.06	0.06	0.06	0.06
OOP expenditures	21.84	36.36	21.84	21.84	9.08	21.84
Artesunate injection	11.57	11.57	11.57	11.57	11.57	11.57
Cost of new vivax treatment	0.5	0.5	0.5	0.5	0.5	0.5
Cost of new falciparum treatment	2.5	2.5	2.5	2.5	2.5	2.5
Cost of new LLIN	6	6	6	6	6	6
Cost of MDA pp	13	13	13	13	13	13
Cost per CHW	1726	1726	1726	1726	1726	1726
GDP per capita (USD)	1,158.69	3,347	9768.33	1161.49	2,336.52	2111.14
GDP per capita per day (USD)	4.45	12.87	37.57	4.47	7.49	8.12
Coefficient for VLY calculation	2.2	2.2	2.2	2.2	2.2	2.2
Discount rate (%)	3	3	3	3	3	3
Mortality	33.66	33.55	36.5	32.86	29.36	39.35
Life expectancy at 40 (years)	33.66	33.55	36.5	32.86	29.36	39.35
Length of OP malaria case (days)	4.82	9.3	4.82	4.82	4.82	4.82
Duration of illness IP (days)	8.75	9.3	8.75	8.75	8.75	8.75
Length of IP malaria hospitalization	5	3.65	5	5	5	5