Malaria Policy Advisory Committee (MPAC) Meeting

14 - 16 September 2016
Salle A, World Health Organization, Geneva, Switzerland

PROVISIONAL PROGRAMME

Wednesday, 14 September 2016			
	Session 1	**Open**	**for information**
09:00 – 09:30	Welcome for Chair, MPAC	Dr Kevin Marsh	
09:30 – 10:30	Report from the Director, GMP	Dr Pedro Alonso	
10:30 – 11:00	*Coffee break*		
	Session 2	**Open**	**for information**
11:00 – 11:45	Update on RTS, S vaccine	Dr Andrea Bosman Dr Vasee Moorthy	
11:45 – 12:30	Update on GMS malaria elimination post-ERAR	Dr Rabindra Abeyasinghe Dr Eva Christophel Dr Fred Binka	
12:30 – 13:30	*Lunch*		
	Session 3	**Open**	**for decision**
13:30 – 15:30	Review of Malaria Elimination: An operational manual	Dr Rick Steketee Dr Hoda Atta Dr Keith Carter	
15:30 – 16:00	*Coffee break*		
	Session 4	**Open**	**for decision**
16:00 – 17:30	Continued review of Malaria Elimination: An operational manual /Discussion	Dr Rick Steketee Dr Hoda Atta Dr Keith Carter	
17:30	*End of day*		
18:30	MPAC Dinner	Closed	

Report from the Global Malaria Programme

Malaria Policy Advisory Committee

Geneva, Switzerland

Dr Pedro L. Alonso, Director

14 September 2016

Global **Malaria** Programme

World Health Organization

Entomology & Vector Control updates

… above all, the spread of Zika, the resurgence of Dengue, and the emerging threat of Chikungunya are the price being payed for **a massive policy failure that dropped the ball on mosquito control in the 1970s**.

Margaret Chan
DG WHO
Opening Address
69 WHA
May 2016

Entomology & Vector Control updates

- **Global Vector Control Response**

  - A joint effort between GMP / NTD / TDR
  - Steering Committee established
  - Co chaired by Prof. Tom Scott and Dr. Ana Carolina Santelli
  - Profs. Steve Lindsay and Willem Taken
  - To be tabled at WHA 2017

Entomology & Vector Control updates

Development of the Vector Control guidelines:

- Steering group and guideline development group, external review group established
- Scope of the guideline, objectives, foreseen recommendations, existing and needed reviews, and key questions to be answered in the guideline have been drafted.
- Guideline planning proposal has been drafted and will be submitted for approval to the Guideline Review Committee

Re designing the WHO policy setting process for Vector control tools

1. VCAG EVALUATES NEW CONCEPT or PARADIGMS (NTD/GMP lead, PQ involved)

VCAG EVALUATION		OUTCOME	1 POLICY
PARADIGM ***(Product or prototype representing paradigm)***	3 step process Step 1: Concept Step 2: Proof of concept – Entomological** Step 3: Proof of concept – Public health / Disease impact	Validated paradigm & Target Product Profile. OR Interim guidance via ERG**	Step 4: WHO Policy Setting (MPAC/STAG)
	RISK ASSESSMENT (ad hoc experts)		2 **DEPLOYMENT**
	SPECIFICATIONS (JMPS or ad hoc experts)		EXPERT REVIEW GROUP (ERG) for product specific guidance
	Development of outcome criteria, testing requirements, risk assessment models and criteria for quality control and any associated guidance documents		*(**Potential short normative guidance on use, likely impact, and data requirement for definitive guidance)*

2. ONCE NEW CONCEPT or PARADIGM ESTABLISHED, PQ EVALUATES <u>ALL SUBSEQUENT PRODUCTS</u> (NTD/GMP involved)

PQ DOSSIER REVIEW (RHT)		OUTCOME	1 POLICY
PRODUCTS	Process Dossier of data according to guidelines/criteria developed during assessment of prototype (Entomological endpoints)	PQ LISTING (2017 on)	Policy for paradigm applies
	RISK ASSESSMENT (PQ)		2 **DEPLOYMENT**
	SPECIFICATIONS (JMPS or ad hoc experts)		Disease-specific programme guidance applies

Insecticide Resistance

- **Current evidence on the Public Health impact of Insecticide Resistance**

  - To be presented at ASTMH
  - 5 country study with the support of the BMGF
  - Sleeping under an Insecticide Treated bednet continues to afford protection, including in areas with high levels of pyrethroid resistance

New online mapping tool

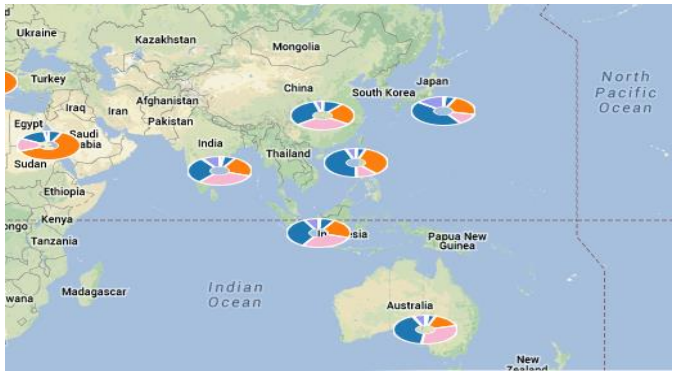
INPUTS

- Entomological database
- Antimalarial drug efficacy database
- *Pf hrp2/hrp3* deletion database

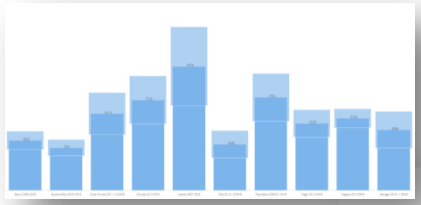
FILTERS

- Indicator
- Region
- Year
- Vector/ parasite
- Insecticide/ drug
- Mechanism / deletion

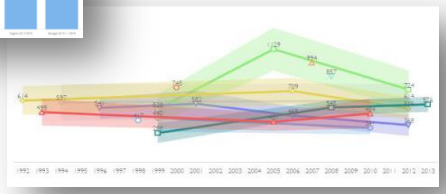
OUTPUTS



Example map symbology



Example graphical outputs



- **To be available: end December 2016**

Prevention, Diagnosis & Treatment - updates

- Diagnostics
  - HRP2 deletions
  - RDT QA and transition to the PQ department
  - NAA
  - G6PD
- Improving Access
  - IPTp
  - RAS
  - SMC
- Safety of antimalarials
- MDA
- New drugs for malaria control and elimination
- Malaria vaccines: RTS,S

Prevention, Diagnosis & Treatment - updates

Red font = in progress

Improved access to quality diagnostics

Guidance on diagnostics

- Guidance to manufacturers on RDT product labelling and instructions
- **Guidance to RDT manufacturers on transition to PQ for procurement**
- **Guidance booklet on G6PD point of care tests** (collaboration with PATH)
- Policy briefing on G6PD POCT to support anti-relapse therapy
- Road map on RDT implementation in the private sector
- Standards of practice for performing RDTs in different settings
- Printing/dissemination of QA manual for malaria microscopy (2nd Edn)
- Dissemination of SOPs for malaria microscopy

Malaria microscopy

- International system for validation of national malaria slide banks
- Center for External Competency Assessment (ECA) of malaria microscopists established @ UCAD/Senegal for Francophone countries
- Collaboration with AFRO, EMRO and WPRO to support inter-country training workshops QA of malaria microscopy and RDTs

PDT: progress over last six months

Red font = in progress

Improved access to quality diagnostics (continued)

Rapid diagnostic tests

- **Technical consultation on surveillance on *pfhrp2* gene deletions**

New system

- Continued Product Testing (PT) and Lot Testing (LT) programme (R7)
- Prepare new performance evaluation (in vitro, rec_Ags, other) for R8
- Implementing new LT methods based on rec_Ags in key national labs
- Support manufacturers in using new rec_Ags for internal quality control
- Develop web-based systems to monitor PT and LT post 2017

QA of nucleic-acid amplification based techniques

- **Develop repository for External Quality Assessment @ HTD/London**

QA of G6PD point of care tests

- **Collaboration with WHO/PQDx for laboratory assessment of G6PD POCT**

PDT: progress over last six months

Improved access to quality medicines

Red font = in progress

Guidance on antimalarial medicines

- **PPC of ivermectin for malaria transmission control**
- Dissemination and translation of WHO Treatment Guidelines
- Updating WHO Treatment Guidelines (e.g. AS-PYR, ACT in 1st trimester)
- ERG on cardiotoxicity of antimalarials
- **Operational manual on mass drug administration**
- Response plan on identified safety concerns for medicines
- Updated EOI of antimalarial medicines for WHO PQP

Supply of quality antimalarials

- Ad-hoc management of medicines donations and emergency requests

Monitoring medicines

- Monitoring sales/deliveries of prequalified ACTs from manufacturers
- Tracking WHO ban of oral artemisinin-based monotherapies AMTs

PDT: progress over last six months

Improved access to quality medicines (continued)

Red font = in progress

Intermittent preventive treatment with SP

- **Contribution to multi-Agency multi-country proposal to UNITAID for community delivery of IPTp-SP**

Management of severe malaria

- Operational research on severe malaria at hospital level (Burkina Faso)
- **Contribution to multi-Agency multi-country proposal to UNITAID for pre-referral treatment of rectal artesunate**

Improved access to quality vaccines

Support RTS,S pilot implementation in selected countries

- **Collaboration with IVR in developing a grant proposal and submission to GAVI, UNITAID and Global Fund**
- Selection of countries, briefings and preparation of MOH programs

Rapid Access Expansion 2015

- Objectives
  - 1,390,000 children aged 2-59 months living in hard-to-reach areas accessing malaria, pneumonia and diarrhea iCCM services in 5 countries by 2017
  - Stimulate policy updates in participating countries and catalyse iCCM scale-up through documentation and dissemination of best practices
- Grant Period: April 2012- March 2017
- 5 countries: Malawi, Mozambique, DRC, Niger, Nigeria (2 states)
- MoH provides leadership to the RAcE programme and iCCM is integrated with health services to facilitate sustainability
- Implemented through NGO as sub-grantees under joint guidance of MoH and WHO

RAcE Achievements

Policy-Institutional Strengthening Highlights

- Community-case management of malaria in NSP 2013-2015 of DRC and Niger
- RDTs in RAcE Districts followed by national rollout and implementation of WHO "Caring for Newborn at Home" package in RAcE district in Malawi
- Amoxicillin replaced cotrimoxizole for pneumonia in DRC and Malawi
- Ministerial decree allowing CHWs to use malaria RDTs and amoxicillin in Niger
- National iCCM Guidelines, iCCM and Supervision training tools in Nigeria

Community Health Worker Deployment

- Trained: 8295
- Active: 7271

Case Management (update: June 2016)

• Malaria Cases	2,163,402
• Pneumonia Cases	1,197,702
• Diarrhoea Cases	908,842

Sustainability Roadmap and Transition Planning

Objective:

To identify and address key determinants of sustainability to develop a national iCCM sustainability roadmap and a RAcE project transition plan in each RAcE country

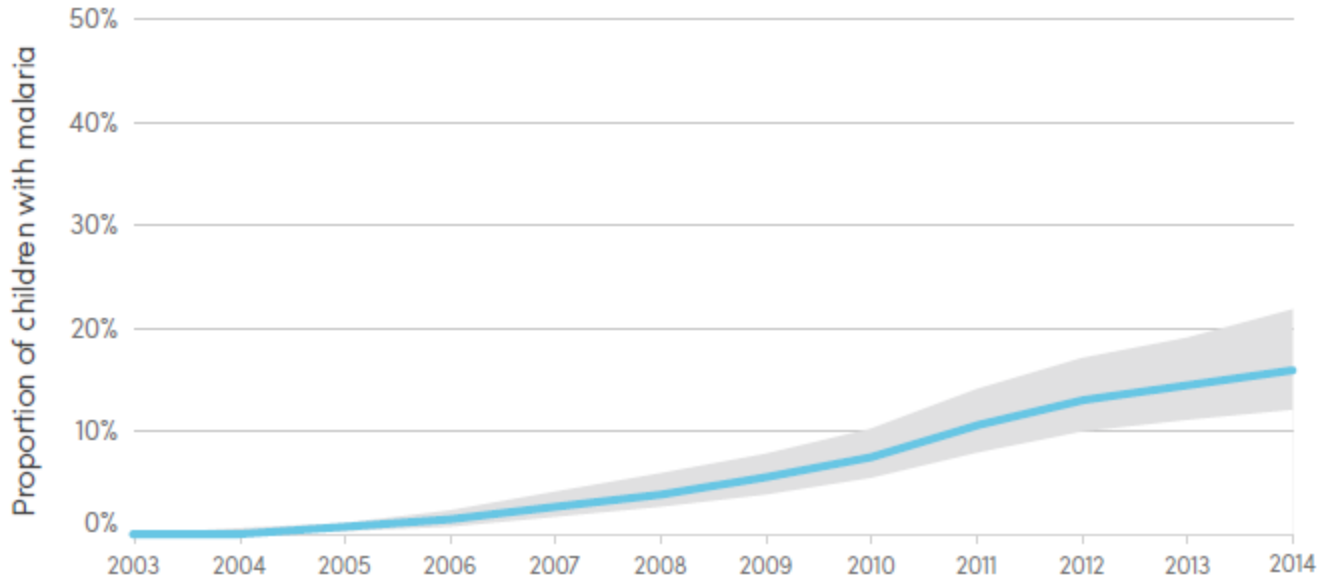
Strategy Evidence & Economics - products and activities

Core work

- World Malaria Report:
  - Summary reports of WMR 2015 released World Malaria Day (25 April 2016) in English, French and Spanish
  - *Malaria: Global progress 2000 – 2015* published in Infectious Diseases of Poverty (June 2016)
  - Online data collection for WMR 2016 launched May 2016
  - Planning meeting with regional focal points: 19-21 April, Geneva
- SME Task force:
  - Second SME Task Force meeting: 21-23 June 2016, Geneva
  - Monitoring & Evaluation framework for the GTS for malaria 2016-2030 and AIM – prepared for MPAC review
- *P. vivax*:
  - *Control and elimination of* Plasmodium vivax *malaria: the evidence base* (13 papers) in American Journal of Tropical Medicine and Hygiene – supplement in preparation.
- Support to Global Fund resource allocation, target setting and elimination scenario planning
- Support to UN for SDG indicator definitions, metadata and reporting

Access to malaria diagnostics and treatment

Figure 3.13 Estimated proportion of children aged under 5 years with confirmed *P. falciparum* malaria who received ACTs, sub-Saharan Africa, 2003–2014



Source: *Malaria treatment model from the Center for Applied Malaria Research and Evaluation (Tulane University), the Global Health Group (University of California, San Francisco) and the Malaria Atlas Project (University of Oxford).*

WORLD MALARIA REPORT 2015

Problem statement – Testing and treatment

- Great progress in extending the coverage of malaria diagnostic testing and treatment (with appropriate antimalarial medicines) between 2000 and 2015.
- Data are limited but current estimates suggest large gaps in programme coverage remain.
- A better understanding of
  - why these gaps occur,
  - who is affected by these gaps, and
  - what strategies can be used to overcome them
- … will help ensure universal access to care and enable the targets outlined in the *Global technical strategy for malaria, 2016-2030* to be attained.

WHO review and consultation

- To characterize access to and utilization of malaria diagnostic testing and treatment services, identify bottle-necks in service provision (e.g. global supply, management of supplies, access to health facilities, availability of staff and equipment etc).
- To identify particular population sub-groups or risk factors associated with gaps, and relate the results to delivery channels (public sector, private sector, community based programmes).
- To review methods to estimate access to malaria testing and treatment from routine HMIS, health facility and household surveys and provide recommendations.
- To identify strategies to increase access to, and utilization of, diagnostic testing and treatment services and elaborate a global response plan.

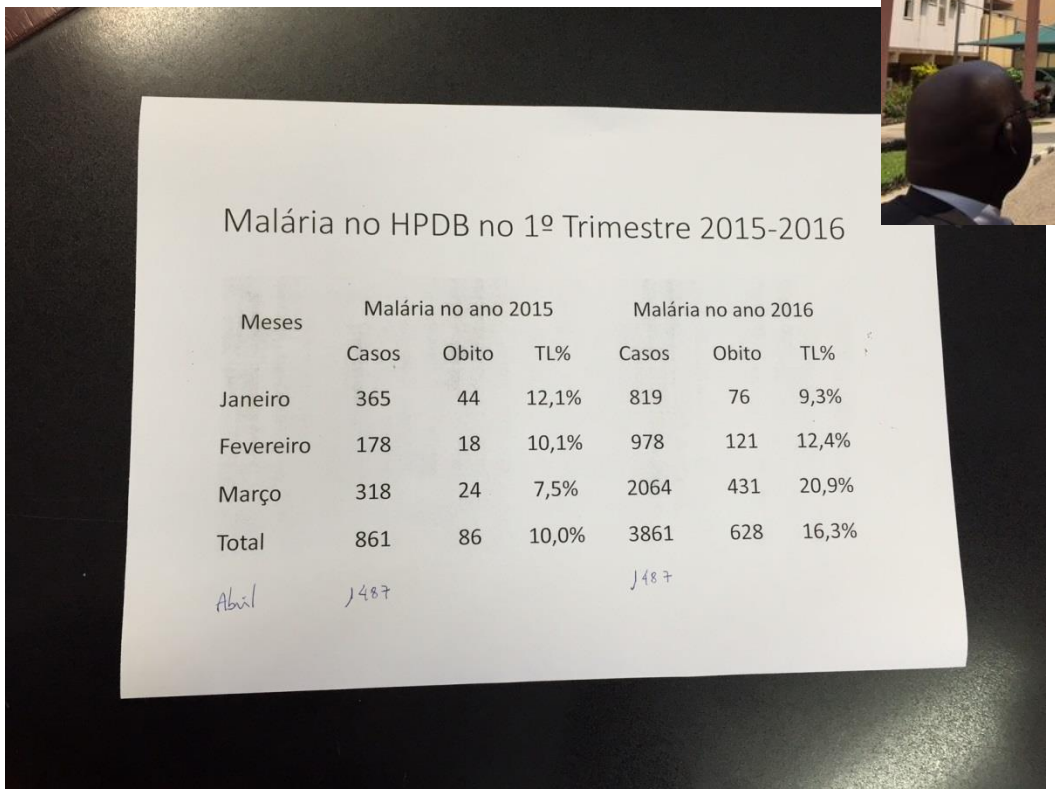
Surveillance, Monitoring & Evaluation

- Priority areas for biennium:
  - updating surveillance guidance and epidemic guidance,
  - developing an analytical report on status of surveillance systems in malaria endemic countries to define priority countries
  - Undertaking detail routine information systems assessment in selected high burden countries
  - country support and training
- GMS data hub has been established with all countries now reporting monthly sub-national data. These data were used to develop the ERAR bulletin
- Reconstitute the SME-TEG by Q4 2016

Technical Support and Capacity Building

- **Supported countries in accessing and in implementing GF grant**:
- **Worked with partners, including GF, in preparing proposals for catalytic funding**:
- **Supported mobilization of additional resources**
- Post-ebola follow-up actions in Guinea and Sierra Leone
- Desk review and identification and resolution of bottlenecks in 25 countries in Africa (on going)

Malaria epidemics



Malária no HPDB no 1º Trimestre 2015-2016

Meses	Malária no ano 2015			Malária no ano 2016		
	Casos	Obito	TL%	Casos	Obito	TL%
Janeiro	365	44	12,1%	819	76	9,3%
Fevereiro	178	18	10,1%	978	121	12,4%
Março	318	24	7,5%	2064	431	20,9%
Total	861	86	10,0%	3861	628	16,3%
Abril	1487			1487		

Technical Support and Capacity Building

- Malaria elimination training in Zanzibar (26 Sept – 1 Oct 2016)
- Malaria elimination training in E8 countries (Nov 2016)
- IPO/NPO training in AFRO
    - focus on WHO recommendations, GTS and its implementation in Africa, malaria program reviews, national strategy development and Global Fund concept note development (10 – 14 Oct 2016 in Ethiopia; 24 – 28 Oct in Benin)
- IPO/NPO training in PAHO
    - focus on malaria elimination (28 Nov – 2 Dec 2016)
- Establishment of a global consultant roster
    - Orientation of consultants in AFRO on WHO policies, GTS and its implementation in Africa, malaria program reviews, national strategy development and Global Fund concept note development (in Brazzaville; dates TBD)
- Malaria surveillance and data management training (AFRO; in Nov)
- Malaria program reviews (Afghanistan, Bhutan, Bangladesh, Indonesia, Mozambique, etc)


ELIMINATING
MALARIA
World Health
Organization

Country progress: 2000 - 2015

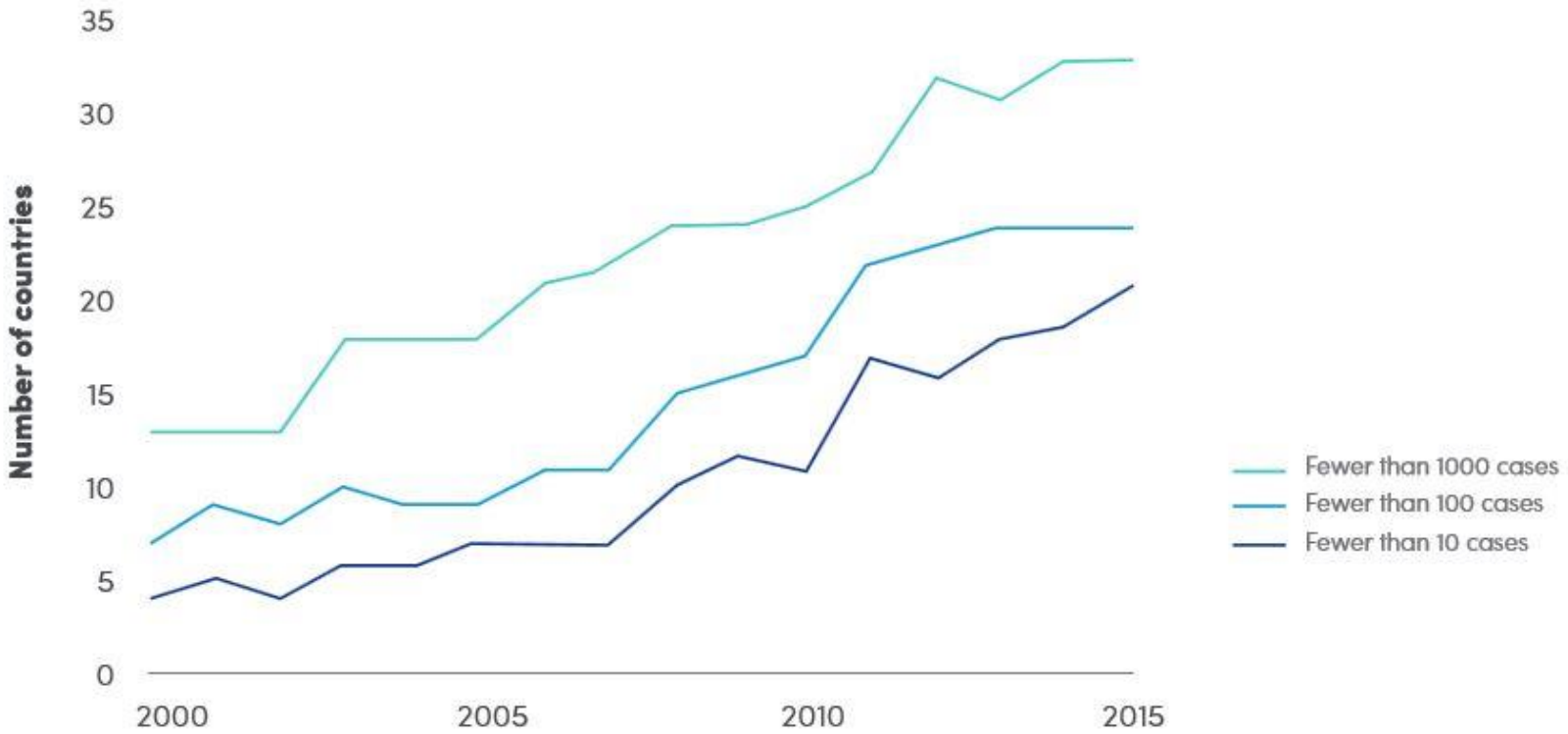
In recent years, more countries have been moving towards elimination

- In 2000, 13 countries had fewer than 1000 cases of malaria. By 2015, 33 countries had achieved this milestone.

- The number of countries with fewer than 100 cases of malaria, and with fewer than 10 cases of the disease, has also increased sharply since 2000.

Country progress: 2000 - 2015

FIGURE 2.
Country progress towards malaria elimination, 2000–2015

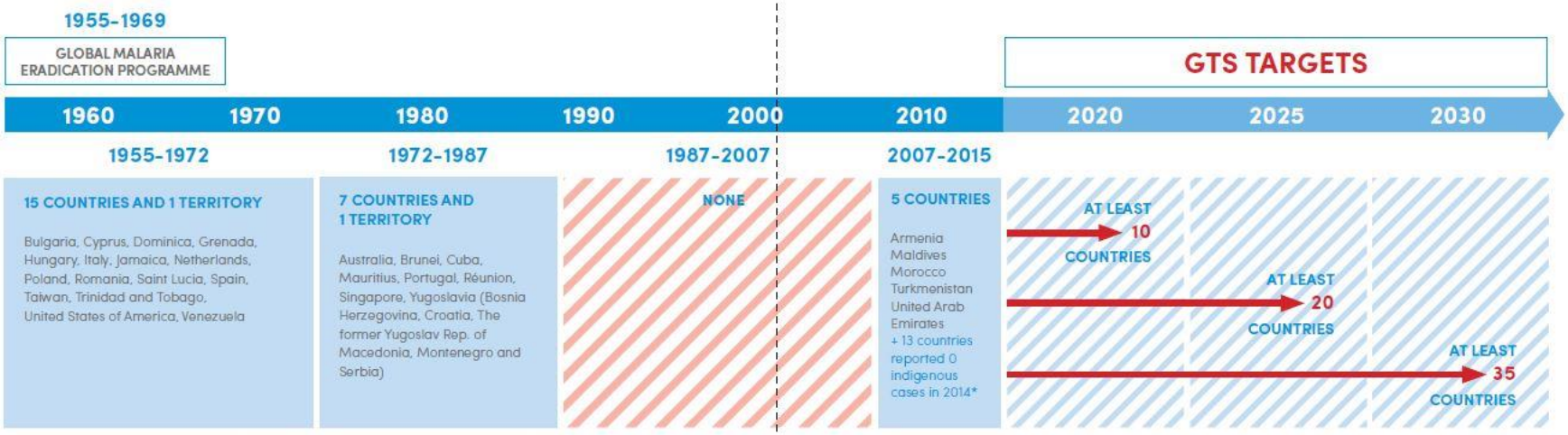


Countries certified by WHO as malaria-free

- Since the early 1960s, 33 countries and territories have been certified and entered in the WHO official register.
- The most recent additions: UAE (2007), Morocco (2010), Turkmenistan (2010), Armenia (2011).
- The Maldives was certified in 2015 but has not yet been added to the WHO official register.
- Sri Lanka was certified malaria free on 5 Sept. 2016
- Kyrgyzstan: final reported being reviewed
- Argentina: awaiting final mission

Countries certified as malaria-free and future elimination targets

TABLE 1.
Countries certified as malaria-free by WHO (1955–2015) and future elimination targets



GTS elimination targets: The Global Technical Strategy for Malaria (GTS) calls for the elimination of malaria in at least 10 countries by 2020. To meet this target, a country must achieve at least one year of zero indigenous cases by 2020. According to the WHO analysis presented in this report, 21 countries have the potential to reach this target: Algeria, Belize, Bhutan, Botswana, Cabo Verde, China, Comoros, Costa Rica, Ecuador, El Salvador, Iran (Islamic Republic of), Malaysia, Mexico, Nepal, Paraguay, Republic of Korea, Saudi Arabia, South Africa, Suriname, Swaziland and Timor-Leste.

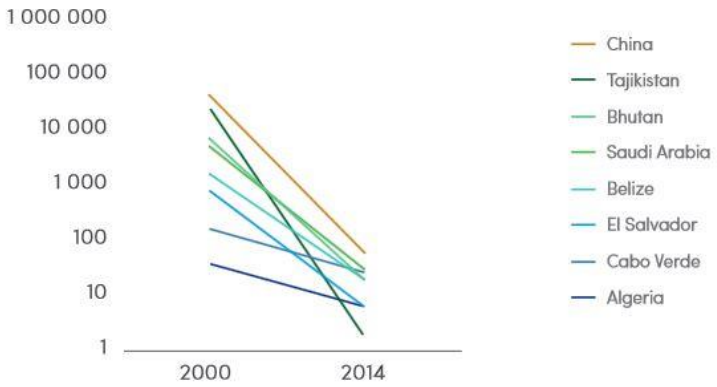
Certification of malaria elimination: Countries that achieve at least three consecutive years of zero indigenous cases are eligible to apply for a WHO certification of malaria-free status. Between 1955 and 2015, 27 countries and two territories received this WHO certification. Three countries recently started the certification process: Argentina, Kyrgyzstan and Sri Lanka.

***Zero indigenous cases:** In 2014, 13 countries reported 0 indigenous cases of malaria. They are: Argentina, Azerbaijan, Costa Rica, Georgia, Iraq, Kyrgyzstan, Oman, Paraguay, Sri Lanka, Syrian Arab Republic, Tajikistan, Turkey and Uzbekistan.

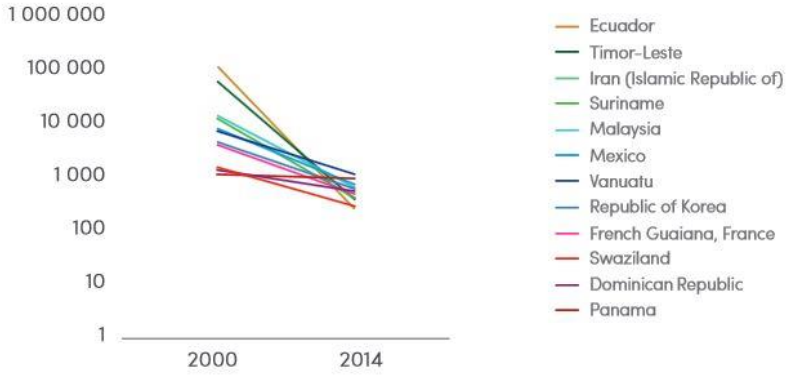
Recent trends in malaria cases

FIGURE 3.

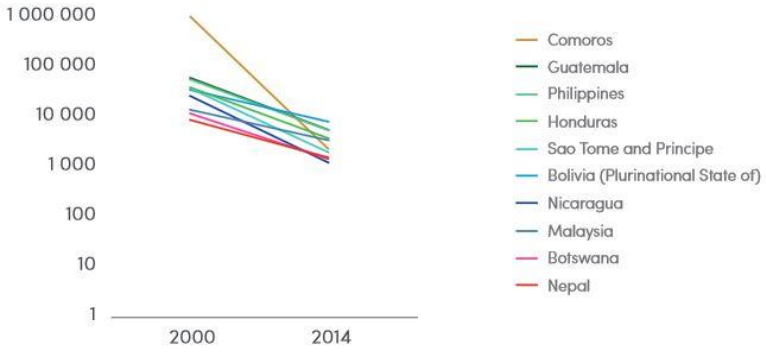
Countries with fewer than 100 indigenous malaria cases in 2014



Countries with 100 to 1000 indigenous malaria cases in 2014[10]



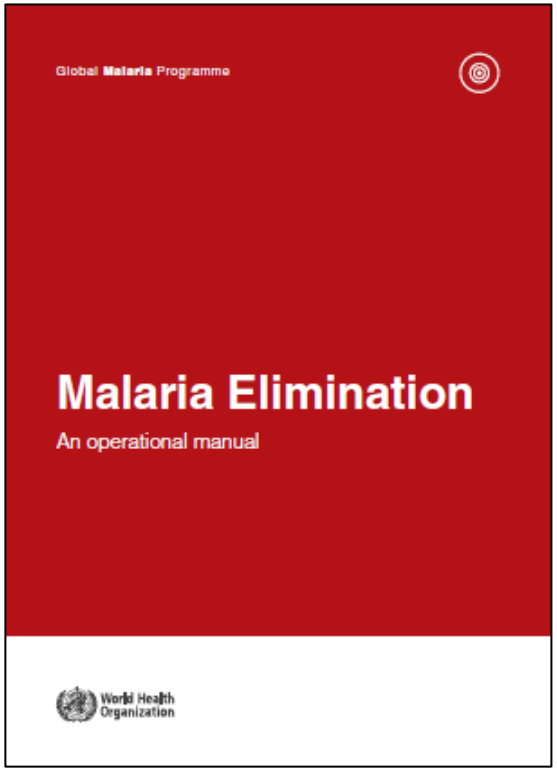
Countries with 1000 to 10 000 indigenous malaria cases in 2014



21 countries by the year 2020

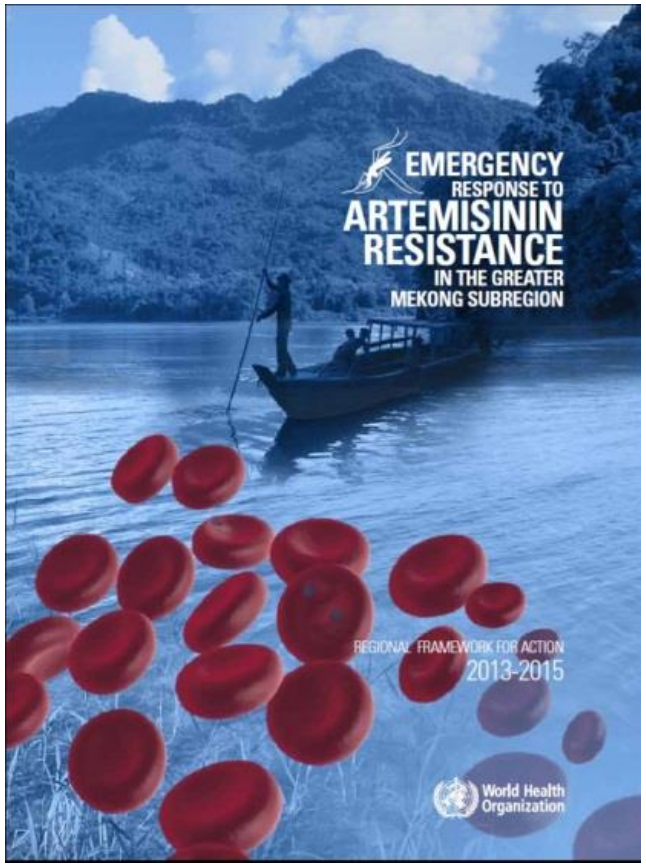
Countries with the potential to eliminate local transmission of malaria by 2020

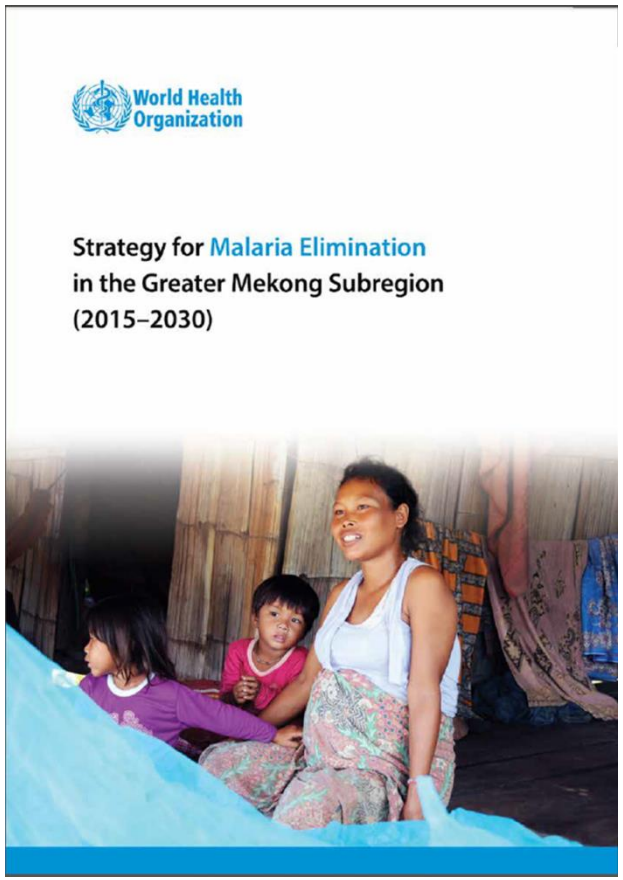
WHO Region	Country
African Region	Algeria, Cabo Verde, Comoros Botswana, South Africa, Swaziland
Region of the Americas	Belize, Costa Rica, Ecuador, El Salvador, Mexico, Paraguay, Suriname
Eastern Mediterranean Region	Iran (Islamic Republic of), Saudi Arabia
South-East Asian Region	Bhutan, Nepal, Timor-Leste
Western Pacific Region	China, Republic of Korea, Malaysia


Global Malaria Programme
Malaria Elimination
An operational manual
World Health Organization

Multi drug resistance

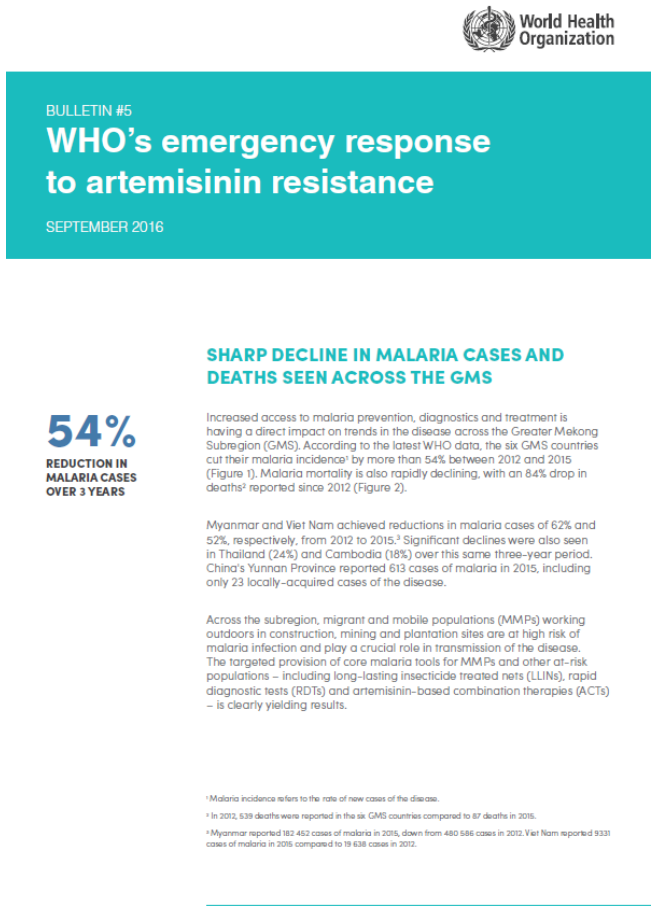
P. falciparum resistance to artemisinins has been detected in five countries in the Greater Mekong subregion. Chloroquine resistance in *P. vivax* has been confirmed in 10 countries





From the ERAR framework to the Mekong Malaria Elimination Project

- Bulletin 5 on WHO's emergency response to artemisinin resistance released September 2016
  - 6 GMS countries have cut malaria incidence by more than 54% between 2012 and 2015
  - 84% drop in deaths reported since 2012
- Partners Forum – 21-22 November in Phnom Penh, Cambodia



World Health Organization

BULLETIN #5

WHO's emergency response to artemisinin resistance

SEPTEMBER 2016

54%

REDUCTION IN MALARIA CASES OVER 3 YEARS

SHARP DECLINE IN MALARIA CASES AND DEATHS SEEN ACROSS THE GMS

Increased access to malaria prevention, diagnostics and treatment is having a direct impact on trends in the disease across the Greater Mekong Subregion (GMS). According to the latest WHO data, the six GMS countries cut their malaria incidence[1] by more than 54% between 2012 and 2015 (Figure 1). Malaria mortality is also rapidly declining, with an 84% drop in deaths[2] reported since 2012 (Figure 2).

Myanmar and Viet Nam achieved reductions in malaria cases of 62% and 52%, respectively, from 2012 to 2015.[3] Significant declines were also seen in Thailand (24%) and Cambodia (18%) over this same three-year period. China's Yunnan Province reported 613 cases of malaria in 2015, including only 23 locally-acquired cases of the disease.

Across the subregion, migrant and mobile populations (MMPs) working outdoors in construction, mining and plantation sites are at high risk of malaria infection and play a crucial role in transmission of the disease. The targeted provision of core malaria tools for MMPs and other at-risk populations – including long-lasting insecticide treated nets (LLINs), rapid diagnostic tests (RDTs) and artemisinin-based combination therapies (ACTs) – is clearly yielding results.

[1] Malaria incidence refers to the rate of new cases of the disease.

[2] In 2012, 539 deaths were reported in the six GMS countries compared to 87 deaths in 2015.

[3] Myanmar reported 182 452 cases of malaria in 2015, down from 480 586 cases in 2012. Viet Nam reported 9331 cases of malaria in 2015 compared to 19 638 cases in 2012.

Strategic Advisory Group on Malaria Eradication

News recruits to the WHO Malaria Team

Dr Gawrie Galapaththy - Technical Officer
Elimination Unit

Prof. Fred Binka - Coordinator
Mekong Malaria Elimination Project

Prof. David Schellenberg
Scientific Advisor

Prof. Abdisalan Noor - Team Leader
Surveillance, Monitoring & Evaluation unit

Update from WHO on RTS,S/AS01

Vasee Moorthy and Andrea Bosman

Malaria Policy Advisory Committee (MPAC) Meeting
14 - 16 September 2016
Salle A, World Health Organization, Geneva, Switzerland

World Health Organization

Advisory Group Established with SAGE/ MPAC representation

- The RTS,S pilot implementation programme is a WHO joint project between the WHO Global Malaria Programme and the Immunization and Vaccines Department, developed in collaboration with PATH and GSK
- Design based on WHO technical consultation held in on 19 January 2016
- Further developed into full technical proposal for submission to funding agencies

RTS,S Malaria Vaccine:
Public call for Expression of Interest from MoH
10 countries expressed interest

World Health Organization

CALL FOR EXPRESSIONS OF INTEREST

Date of this EOI: 18 December 2015

Closing date for receipt of EOI: 15 January 2016

OVERVIEW

WHO is looking for national ministries of health to collaborate on pilot implementation projects of Mosquirix (RTS,S/AS01), the malaria vaccine.

Country selection criteria

- Ministry of Health engagement
- Potential size of the surviving infant cohort for pilots
- Malaria transmission/disease burden
- All-cause mortality in the relevant age group
- Immunization and malaria programme functionality
- Prior participation in Phase 3 programme
- Pharmacovigilance perspectives (meningitis, cerebral malaria)
- Agreement to proceed with randomised design

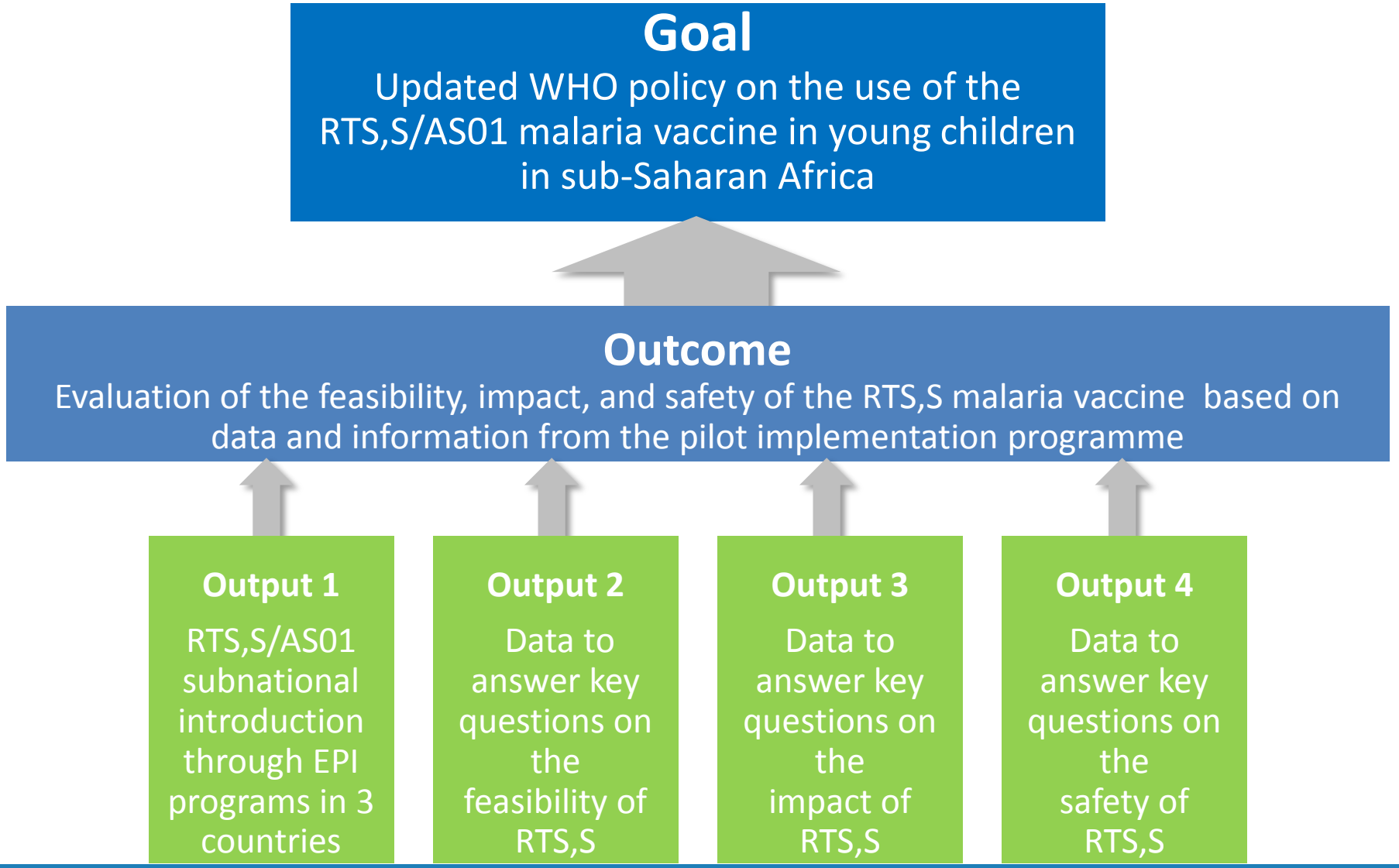
Prerequisites for pilots

- Selection of up to 3 countries, based on above listed selection criteria, following on open call for expressions of interest.
  - Ten countries submitted an expression of interest for participation in the pilots.
  - Prioritisation based on criteria above

Prerequisites for pilots (continued)

- Registration by GSK of RTS,S by national regulatory authorities
- Mobilisation of financial resources to support implementation of sound project proposal
- Review and approval of project proposal by national ethical review bodies and WHO ERC
- Coordination of safety monitoring component of pilot implementation with GSK Phase IV study in same countries

Goal, expected outcome and outputs



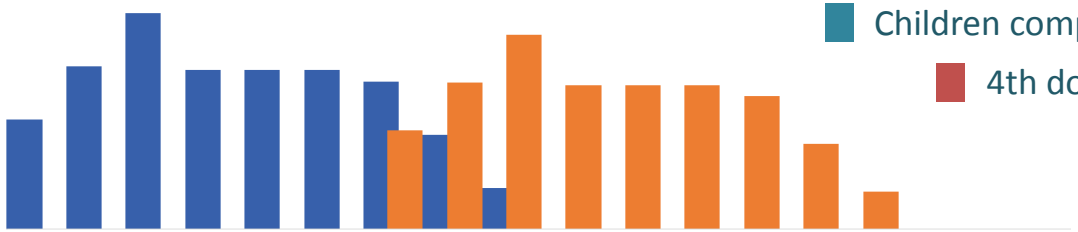
World Health Organization

Phase I: 2017-2020

Phase II: 2021-2022

2016 2017 2018 2019 2020 2021 2022

Pilot progress



Scientific review

Feasibility, safety & impact data collected through end 2019

March/April 2020
MPAC/SAGE review of interim data and decision on continuation

End 2022
MPAC/SAGE review of final data and recommend ation

World Health Organization

Summary of interactions with GSK

Close engagement with GSK, with formal collaboration agreement under development between legal departments of WHO, PATH and GSK

In discussions with GSK to proceed working closely with WHO and PATH, and with good alignment of GSK Phase 4 studies within larger pilot programme

Summary of Gavi process

- Submission by WHO of WHO/PATH joint proposal in April 2016
- Gavi technical committee review in May 2016 – proposed that Board is requested to support 50% of pilot budget (up to $27.5 million for the first 4 years)
- Gavi Board endorsed support of up to $27.5 million for the 2017 to 2020 period (Phase I) **contingent on matching funds**

- Strong support from African representation on Board

Summary of UNITAID process

- Submission by WHO of WHO/PATH joint proposal in April 2016
- UNITAID Board agreed that malaria vaccine could be a strategic fit with UNITAIDs mandate in June 2016
- UNITAID technical committee review in July 2016
- Board decided to commit up to $9.6 million to support research components for 2017-2020 (Phase I) in August 2016

Summary of Global Fund status

- Proposal submitted to catalytic fund for $ 5.4 million
- Proposal will be reviewed by the Global Fund Strategy Committee on 13 September
- Global Fund Board decision expected in November 2016

Concluding remark

The consequences of not proceeding with the pilots after EMA positive opinion and WHO recommendation will be very serious for malaria vaccine development to meet public health needs in low income countries

More in general: the situation highlights a critical gap in the funding landscape: implementation research of new products solely intended for low income countries

What modifications to the pilots can be considered?

- WHO is actively following several leads to fill the financial gap and proceed with 3 countries to evaluate the feasibility of implementation, safety and impact against all-cause mortality
- It may help if MPAC could make a statement about the imperative for the pilots to go ahead from the malaria programme perspective

Conclusion

SAGE and MPAC were unequivocal on the need to determine the public health role of this vaccine

After Gavi and UNITAID Board decisions there is $19.2 million secured leaving a large financial gap of approximately $15.4 million

WHO hopes to be able to fill the gap in the coming months

Backup

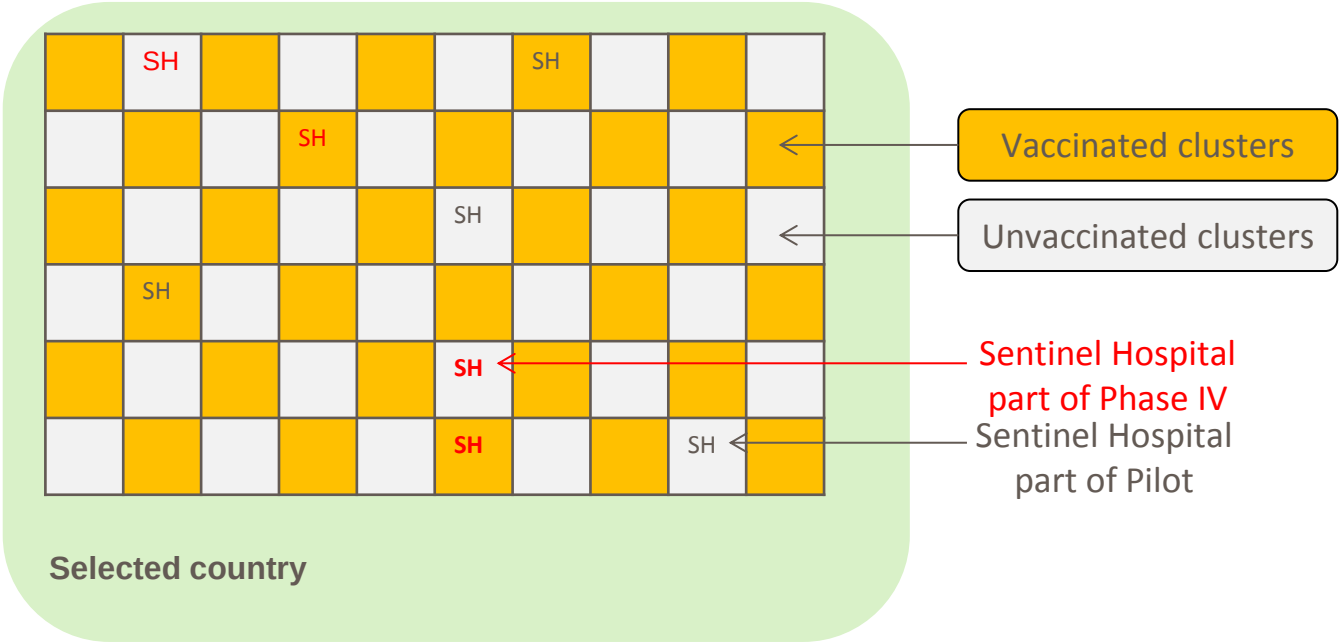
Prerequisites for pilots

- Selection of up to 3 countries, based on above listed selection criteria, following on open call for expressions of interest.
  - Ten countries submitted an expression of interest for participation in the pilots.
  - Prioritisation based on sub-national data on the parasite prevalence in children (from most recent MIS or DHS surveys), insecticide-treated bednet ownership at household level, DTP3 and MCV1 vaccine coverage, under-5 mortality (less neonatal mortality), the population of surviving infants, capacity to assess meningitis and cerebral malaria, and participation in the RTS,S Phase 3 trials

GSK Phase IV and WHO Pilot

Per country:

- 30 clusters / arm (120,000 subjects / arm)
- 4 clusters / arm with sentinel hospital (SH*) (16,000 subjects / arm); 2 (50%) of them are included in the Phase IV studies



45,000 subjects in GSK Phase IV (22,500 in exposed and 22,500 in unexposed clusters)

720,000 subjects in pilots (360,000 in exposed clusters: 360,000 in unexposed)

* A study population of 4 sentinel hospital is the minimum number; it may be that greater numbers will be included in the pilot safety evaluation if further hospitals can be identified in the pilot region to contribute to the randomized safety analyses

World Health Organization

Progress of Malaria Elimination Efforts in the Greater Mekong Subregion 2016

WHO MPAC BRIEFING

GENEVA 14th September 2016

Dr Fred Binka/ ERAR, Dr M Aregawi/ERAR,
Dr EM Christophel/SEARO, Dr R Abeyasinghe/WPRO

EMERGENCY RESPONSE TO ARTEMISININ RESISTANCE IN THE GREATER MEKONG SUBREGION

World Health Organization

Outline

Summary Outcomes

Strategy

Regional Coordination

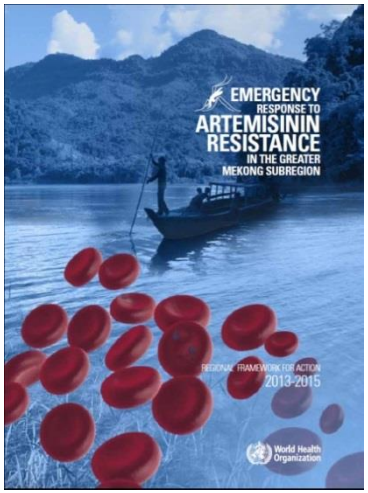
Country Progress

Challenges

Transition

World Health Organization

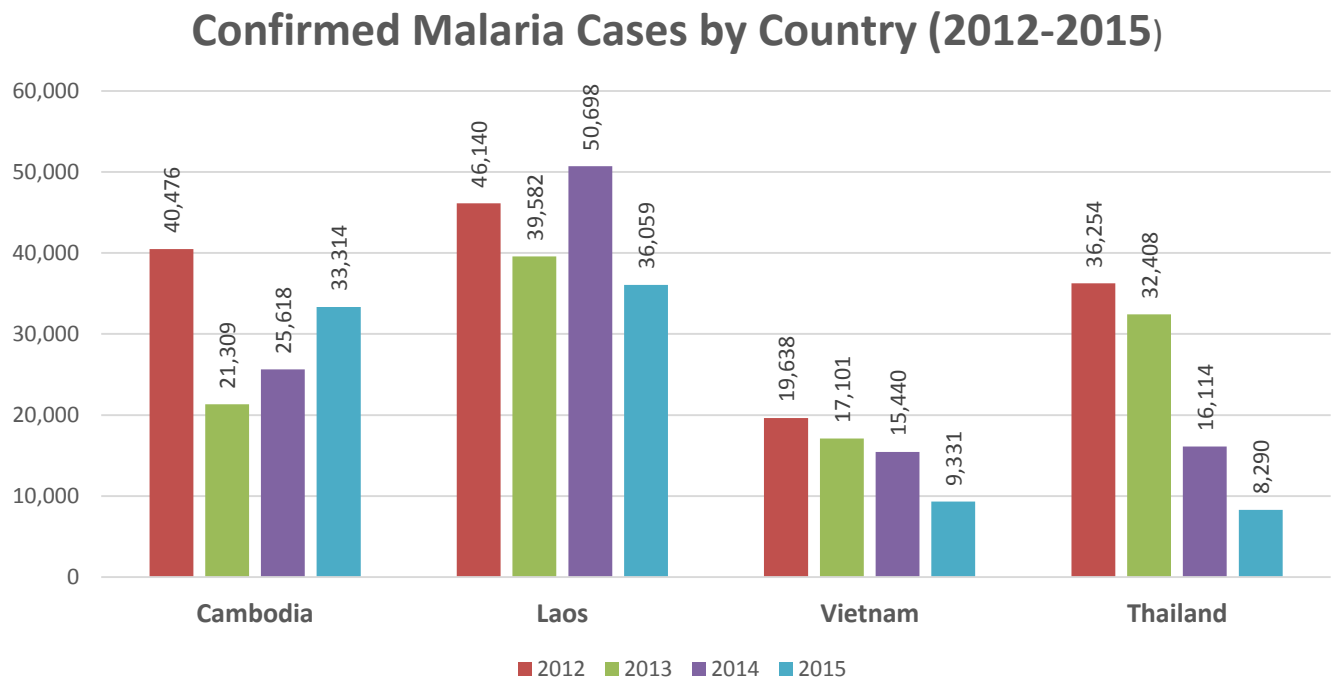
ERAR Framework transition to Elimination Strategy

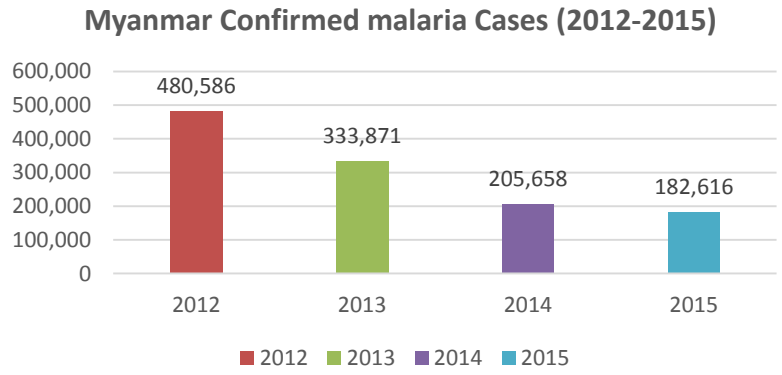


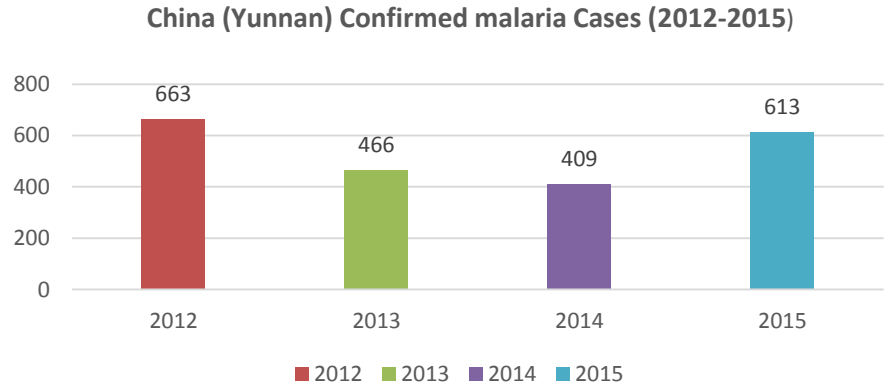
- Since 2008: Artemisinin resistance containment and elimination
  - Thailand and Cambodia border
- April 2013: WHO launched ERAR framework for GMS
  - To contain artemisinin resistance in the GMS
  - ERAR established as regional hub to coordinate containment strategies
- MPAC, Sep 2014: Elimination of *P. falciparum* in the GMS by 2030
- WHA, 2015: Strategy for malaria elimination in the GMS (2015–2030)
- 2016: Transitional year for the ERAR hub
  - Support national strategic plans to accelerate towards elimination
- 2017 onwards: ERAR hub will evolve into GMS Malaria Elimination hub
  - With strong national and leaner regional presence

World Health Organization

Malaria Case Reporting in GMS [2012-15].







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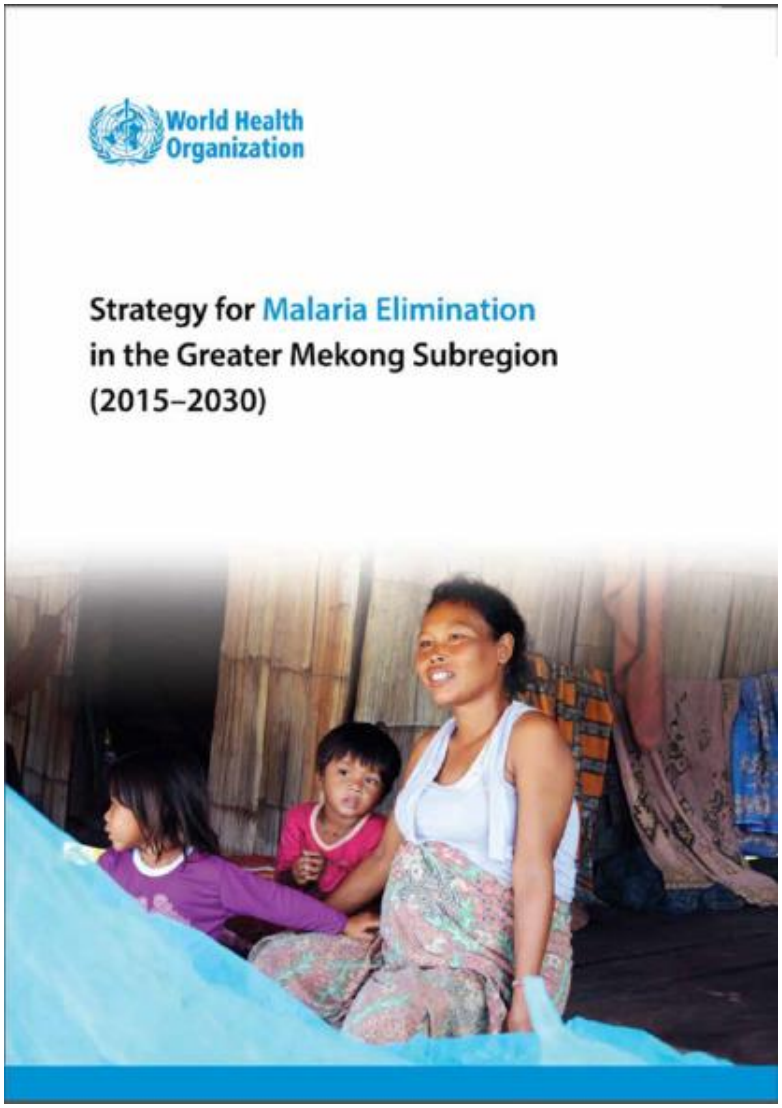
GMS Strategy overview



Goals

- To eliminate malaria by **2030 in GMS**
  - eliminate *P. falciparum* malaria by **2025 (**considering the urgency of multidrug resistance)
- To maintain malaria-free status and prevent reintroduction (where transmission has been interrupted)

Objectives

1. Interrupt transmission of *P. falciparum* in areas of multidrug resistance by **2020**, and in all areas of the GMS by **2025**.
2. Reduce malaria burden in high-transmission areas (<1 /1000 pop) and initiate elimination by **2020**
3. Prevent malaria reintroduction where interrupted.

World Health Organization

GMS Strategy overview - Prioritization

Regional level priorities

- Interrupt transmission in areas with multidrug resistance in the border (Cambodia and Thailand);
- Reduce burden in high transmission areas (Myanmar)
- Control malaria in areas of resurgence.

Country level priorities

- Eliminate malaria in areas of multidrug resistance;
- Reducing burden in areas of transmission;
- Local analysis and better targeting of measures to high risk groups (MMP)

World Health Organization

GMS Strategy 2015-2030: Milestones and targets

Malaria elimination policies/ NSPs developed/updated

Low transmission:
- surveillance for elimination

High transmission:
- Universal coverage
- systems strengthening (case & ento. surv.)

- Elimination of P.f. malaria in all GMS countries;
- Malaria eliminated in Cambodia and Thailand

2015 → 2016 → 2017 → 2020 → 2025 → 2030

Malaria transmission interrupted in 60% of districts in Thailand

- P.f. transmission interrupted in all areas of MDR
- P.f malaria eliminated in Cambodia;
- Malaria eliminated in Yunnan;
- All 1st level subnational areas in GMS in elimination mode

Malaria eliminated in all GMS

World Health Organization

GMS Strategy overview - Key interventions

Case detection and management

- Universal access to quality diagnosis (public, private sector and community)
- Treatment with ACTs, primaquine for both *P. falciparum* (single dose) and *P. vivax* (anti-relapse therapy)
- Management of severe cases and imported cases to prevent deaths

Disease prevention in transmission areas

- Vector control
- Drug based approaches

Malaria case and entomological surveillance

- Mandatory notification
- Case based malaria surveillance
- Case, foci investigation and response
- Entomological surveillance
- Outbreak detection and response
- Vigilance

Supporting elements

- Innovation and research
- Enabling environment, including HSS, multi sector engagement and governance

World Health Organization

Status of national malaria elimination planning, 2016

Country	Status	Period	Cost (USD)	Gap (USD)	Comm.
Cambodia	Completed	2016-2020	**141 351 385**	**36 700 000**	Launched in 1/2016
Yunnan Province/ China	Completed	2015-2020	**7 936 507**	**0**	Yunnan plan only
Lao PDR	Completed	2016-2020	**97 591 611**	**62 814 002**	Submitted to MOH; Launch planned
Myanmar	Completed	2016-2020	**461 751 565**	**163 812 596**	Launch TBD
Thailand	Completed	2017-2026	**97 030 000**	**61 270 000**	Launched 25 Apr 2016
Viet Nam	Completed	2016-2020	**147 434 138**	**82 114 620**	Approved

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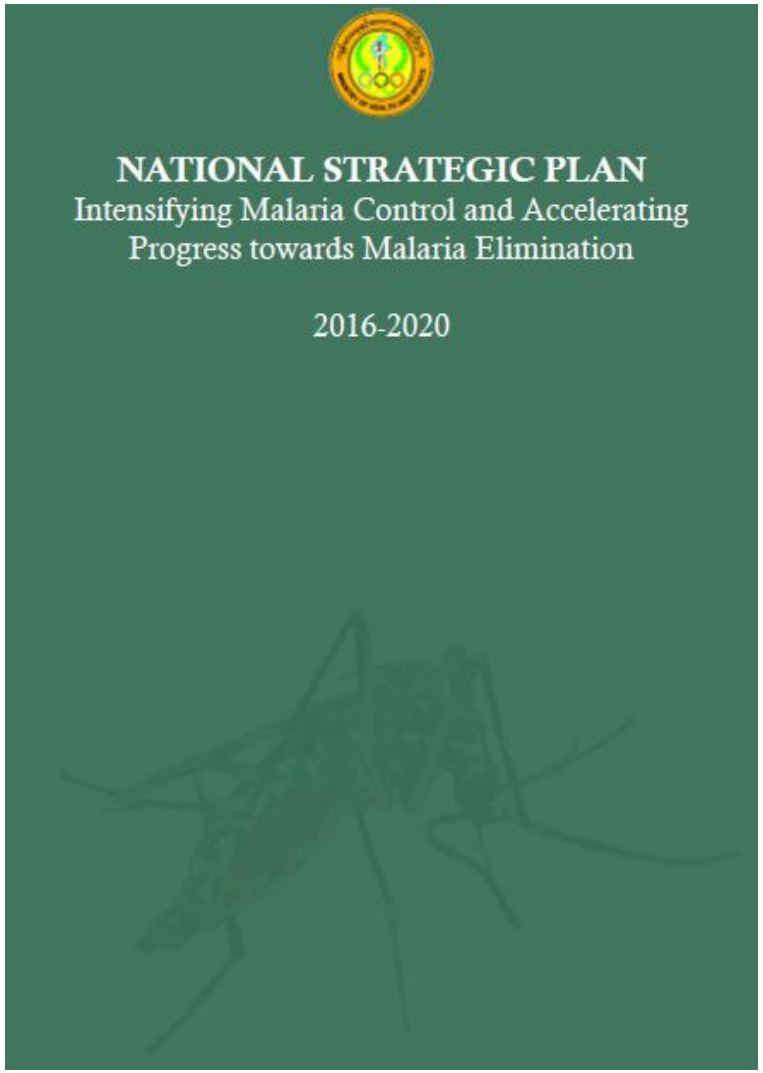
Source: GMS national malaria programs

MYANMAR National Strategic Plan



STRATEGY AT A GLANCE

VISION

A Malaria Free Myanmar by 2030

GOAL

- **Five year strategy to reduce malaria morbidity and mortality by 85%, and 75% respectively by 2020 relative to 2015 baseline figures.**
- **Maintain malaria free status and prevent re-establishment of local transmission in States/Regions where transmission has been interrupted.**
- **Eliminate *Plasmodium falciparum* malaria by 2025 and ALL malaria from Myanmar by 2030.**

World Health Organization

Regional coordination: Tracking progress, surveillance

- Data elements and indicators agreed
  - Burden reduction and elimination phases
  - New additions: elimination, cross-border, migrant and mobile populations, private sector, gender and community
- Regional Hub Database- DHIS2
  - Burden reduction-elimination
  - Replicate same to all countries
  - Monthly and subnational data sharing
  - Bulletin and reports
  - Mapping
- Country level:
  - Malaria elimination database and Case-based surveillance
    - Cambodia – starting in one out of 18 OD
    - Myanmar- 52/284 township (MS Access, others- Excel➔ DHIS2)
- Data managers being recruited in countries
  - Cam, Lao, MMR,
- Collaboration with Global Fund – RAI

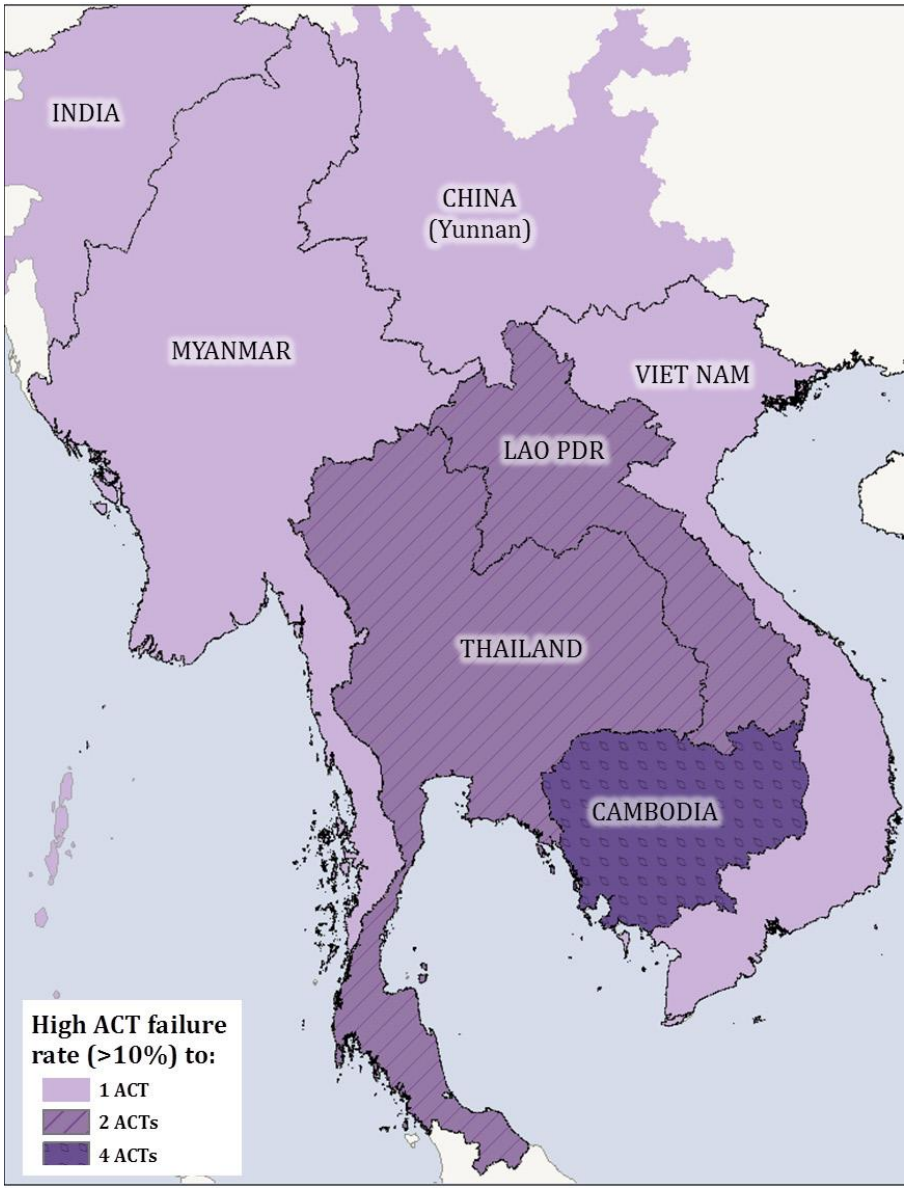
World Health Organization

Tracking historical data: monthly, subnational

Country	2010	2011	2012	2013	2014	2015	2016	Data Level	Period	Validation	Comment
Cambodia	✓	✓	✓	✓	✓	✓	Jan-Jun	District	Monthly	Yes	1. 2010-2013 Yearly data by district
Laos	✓	✓	✓	✓	✓	✓	Jan-Jun	District	Monthly	Yes	
Thailand	✓	✓	✓	✓	✓	✓	Jan-Aug	District	Monthly	Yes	1. No tested cases in 2010-2014 data 2. 2010-2014 data is yearly not monthly data
Vietnam	✓	✓	✓	✓	✓	✓	Jan-Aug	Province	Monthly	Yes	
Myanmar				✓	✓	✓	Jan-Jun	Township	Monthly	Yes	1. In process of requesting for 2010-2012 monthly data by township 2. 2013 data is yearly data
Yunnan (China)	✓	✓	✓	✓	✓	✓	Jan-Jul	District	Monthly	Yes	1. 2010-2013 data has no Tested Case

World Health Organization

Situation of ACT failures in the Greater Mekong subregion



There are currently five ACTs recommended by WHO: AL, ASAQ, AS-MEF, ASSP and DHA-PIP. A sixth ACT, artesunate-pyronaridine, was given a positive scientific opinion by the European Medicines Agency (EMA) under article 58 and is being considered for recommendation by WHO.
By default, artesunate-sulfadoxine-pyrimethamine (ASSP) is considered having a high failure rate in the region as quadruple and quintuple dhfr and dhps mutations are fixed.

http://www.who.int/malaria/areas/drug_resistance/en/index.html

World Health Organization

SUMMARY of Therapeutic Efficacy Studies 2010-16

- TES results provided evidence for the revision of national malaria treatment guidelines in Cambodia and Thailand.
- Informed the operational response for prioritization of malaria elimination efforts in areas of multi-drug resistance including ACT resistance.
- Falciparum malaria in the GMS is becoming increasingly resistant to antimalarial medicines (decreasing to <90% cure rates to AL, AS-MEF and DHA-PIP in southern Lao PDR, Thailand and Cambodia, respectively, in the last 6 years)
- Piperaquine resistance (DHA-PIP treatment failures ranging from 10% to 65%) has emerged in Western Cambodia and expanded considerably in proportion of strains affected as well as in geographical area;
- limited treatment options in Cambodia; ASAQ is currently being tested and Pyramax™ needs to be tested in eastern Cambodia.

World Health Organization

Summary Results and challenges

- molecular studies with Kelch 13 have confirmed that artemisinin resistance has emerged **independently** in all countries of the GMS.
  - with several variants from the eastern and western parts of the region;
- Majority of cases in the GMS who have delayed parasite clearance still clear their infections provided that the ACT partner drug remains effective even in area of high prevalence of K13 mutants (i.e. China, Myanmar),
  - except in the presence of concomitant resistance to the partner drugs (i.e., PIP in Cambodia *and southern Viet Nam*, MEF in Thailand).
- Declining number of cases in some study sites, hence longer study period to meet required sample size,
  - expand to more remote sites, and more
  - logistical and HR constraints, also affecting
  - WHO logistic and administrative approvals

World Health Organization

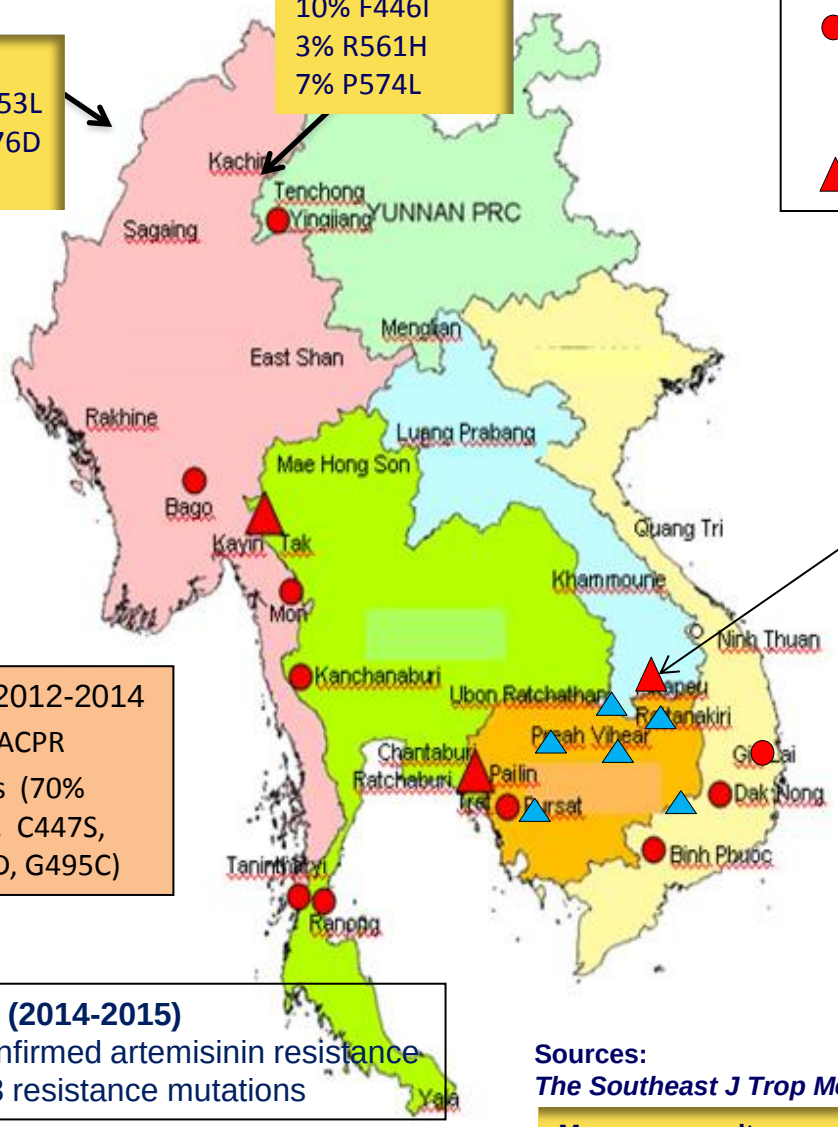
Status of artemisinin resistance in the GMS, 2008 - 2015

NE MMR, 2012
10% F446I
3% R561H
7% P574L

NW MMR, 2012
24% F446I, 1% P553L
1% P574L, 1% A676D
<5% D3+

GMS, 2008 - 2012

- Areas of suspected resistance to artemisinins (where >10% of enrolled patients still have parasites 72 hours after start of treatment)
- Areas of confirmed resistance to artemisinins



GMS, 2012 - 2015

Champassak, Laos, 2014
- 22% D3(+), 90% ACPR
- 54% C580Y, 23% R539T

Yunnan (China), 2012-2014
- <5% day 3+, >95% ACPR
- 64% K13 mutations (70% F446I and 4% C458Y, C447S, P574L, F483S, A676D, G495C)

Viet Nam, 2014
- Binh Phuoc: 30% D3+, 64% mutations
- DakNong: 29% D3+, 74% K13
- Gia Lai: 23% D3+, 46% K13 mutations

Note: all 3 sites had 100% ACPR

Binh Phuoc, 2015:
50% D3+, 65% ACPR; 76% mutations

Cambodia (2014-2015)
Areas of confirmed artemisinin resistance with validated K13 resistance mutations

Sources:
The Southeast J Trop Med and Public Health; Volume 44 (Supplement 1): 2013.

Myanmar results as reported from the TEG, May 2014

Country NMCP - WHO TES, 2012 – Jun 2016

World Health Organization

Malaria Vectors and Entomology Priorities


An dirus

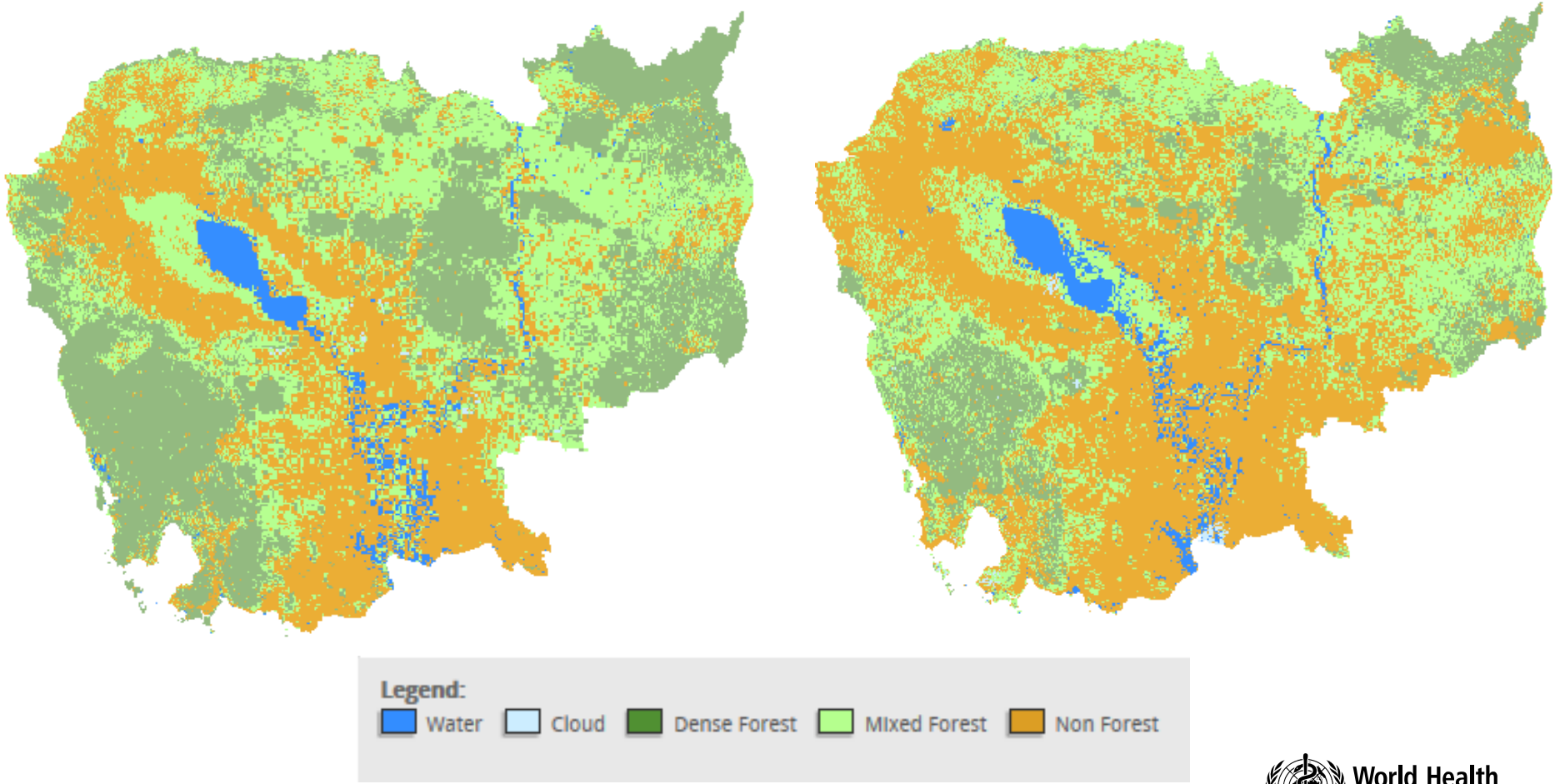

An minimus

Rapidly changing ecology and transmission risk areas

Cambodia forest cover

2000

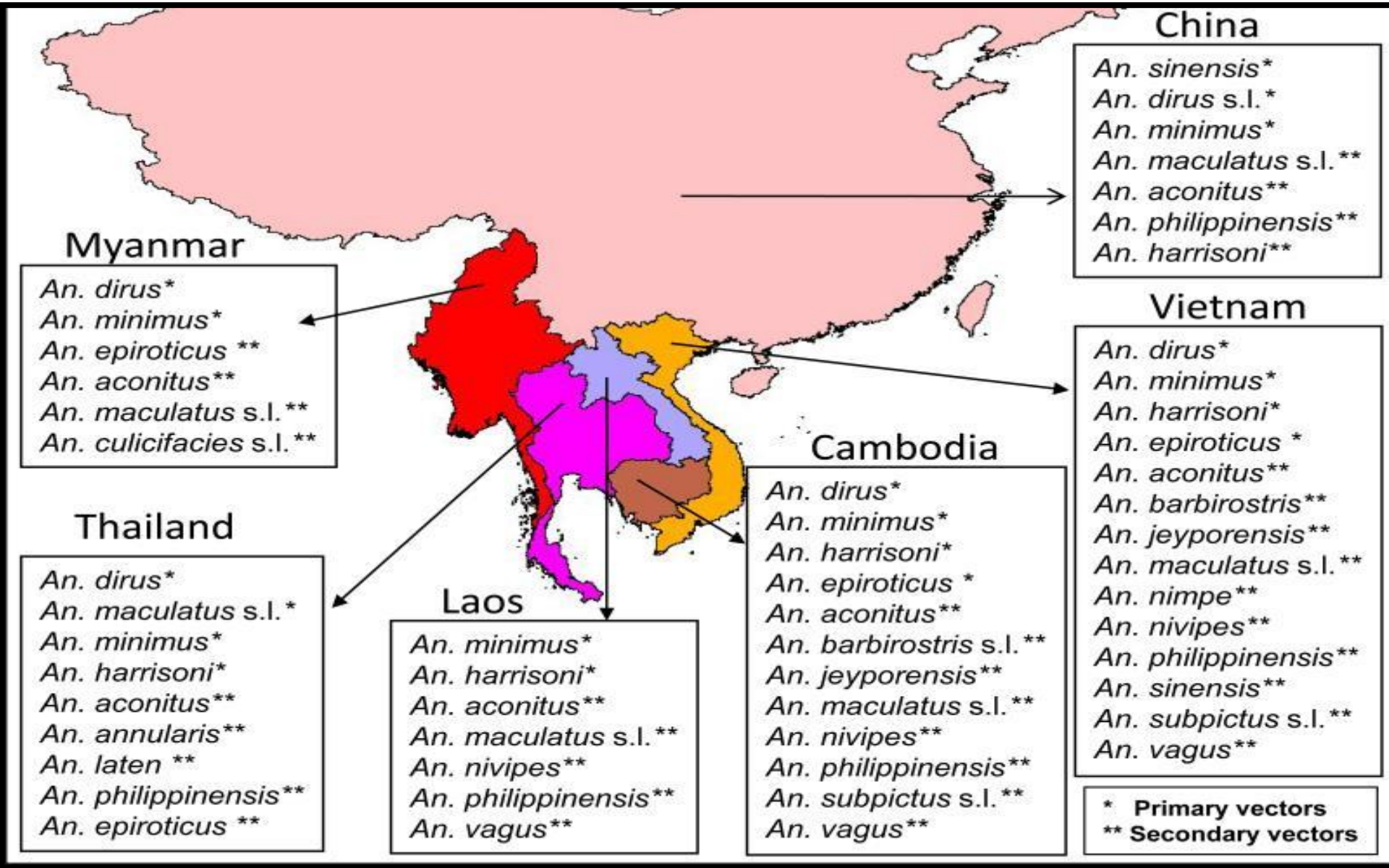
2014



Source: Open-development Cambodia https://opendevelopmentcambodia.net/

World Health Organization

Efficient primary vectors; numerous secondary vectors



Insecticide Resistance Monitoring

No evidence of resistance in *An dirus* throughout GMS

Lao PDR: *An. minimus* and *An. maculatus, An. philippinensis* sensitive to deltamethrin and permethrin; resistant to DDT.

Vietnam: possible *An. minimus* pyrethroid resistance on China border; *An. epiroticus* high pyrethroid resistance in southern delta.

Cambodia: only *An. barbirostris* with pyrethroid resistance.

Myanmar and Thailand: no evidence of vector resistance

World Health Organization

Entomology Priorities:

- Vector identification and mapping with rapidly changing ecology

- Facilitate development of personal protection for outdoor transmission.

- Systems Strengthening: posts, training, career opportunities and support for field staff

Regional coordination

Domain	Status
Capacity building & technical collaboration	• GMS elimination and surveillance training (Thailand, China) • Elimination operation manual (draft) • Expert consultation (New Delhi)
Cross border collaboration	• Cross-border initiatives: Lao-Thailand, Cambodia-Thailand, China-Myanmar, Myanmar-India/Bangladesh • MMP strategy and toolkit developed, in country MMP pilots
Product quality	• WHO Collaborative registration procedure and workshop on WHO Prequalification Programme conducted • Medicines quality issues have been discussed at the ASEAN • Improved collaboration between national stakeholders • Country workplans developed, incl oAMT elimination and surveys
Priority research	• Priority GMS research agenda defined (2013), update in progress • Support of several ongoing research projects • Regional Research Coordination group established (11/2014)
Surveillance, M& E	• Regional data sharing platform (DHIS2)-pilot launched and rollout to countries ongoing • Case-based surveillance using DHIS 2 being field-tested (in Cambodia) • Intense TES monitoring through networks (GMS and beyond) • Monitoring of mosquito vectors—Networks developed-ongoing
Coordination and governance	• Leading and supporting GMS strategy and NSP developments • Coordination of Containment to **Elimination efforts in GMS** • Facilitate regional and partner coordination (annual forum) • Tracking/engaging in resource mobilization • Advocacy & communication (website, newsletter)

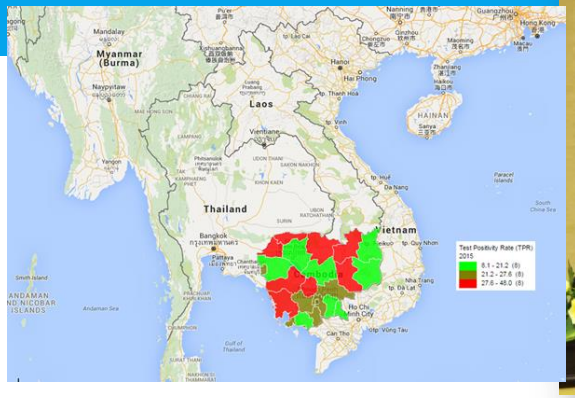
World Health Organization

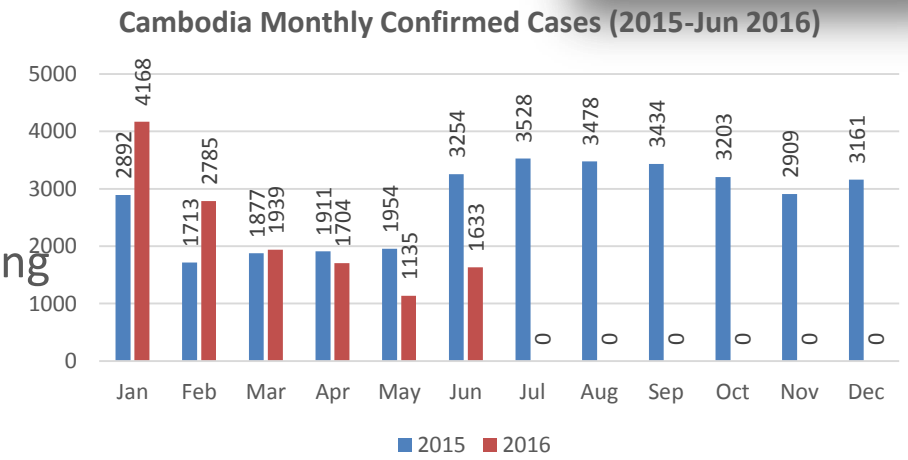
COUNTRY PROGRESS REPORTS

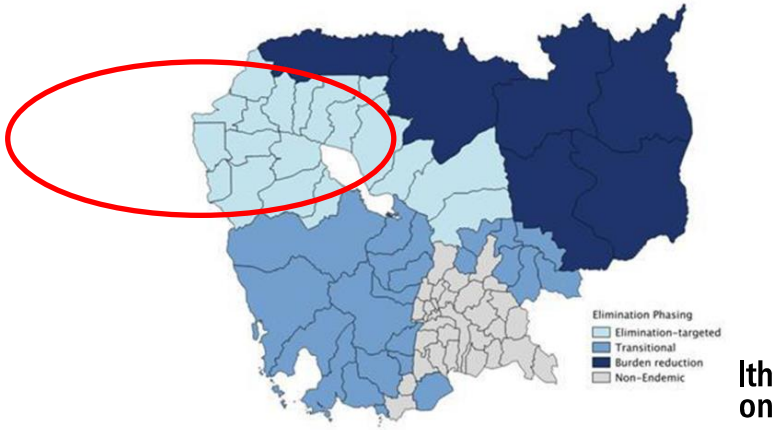
World Health Organization

Country updates: **Cambodia**

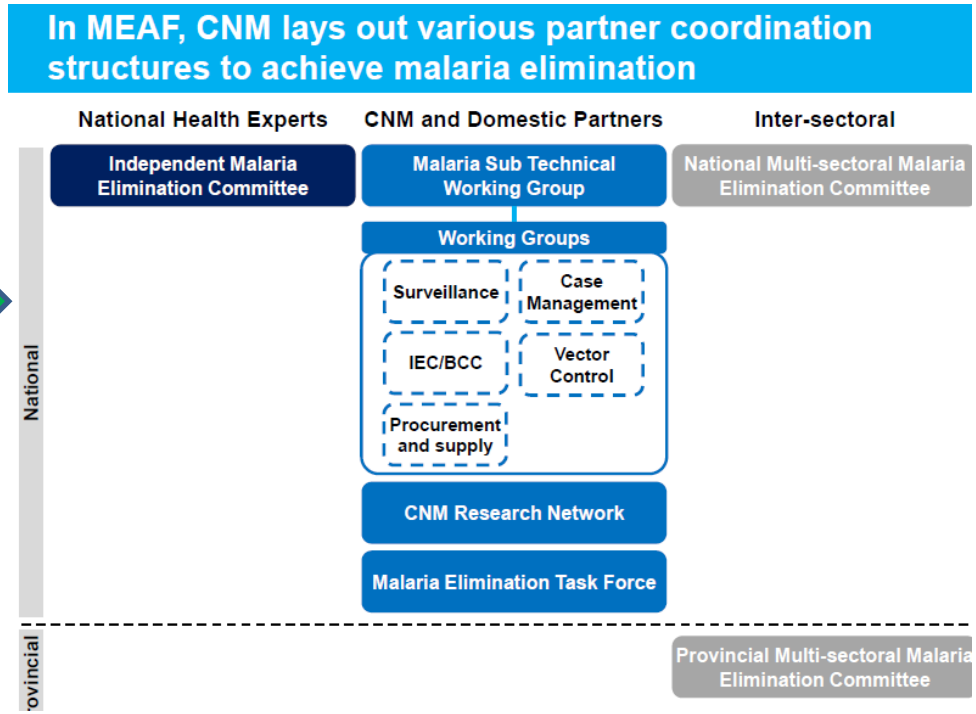
- NSP: MEAF 2016 – 2020 launched
  - Cost $143.2m 2016-2017 is $49m
- Study: low dose primaquine
- Technical support: forecasting, registration, procurement and management of antimalarials
- TES:
  - DHA-PPQ: >60% failure in Siem Reap,
  - 30-40% in Oddar Meanchey, Stung Treng and Battambang provinces
- Elimination in 18 Ods
- Case-based surveillance being field tested (initiated)
- limited entomology capacity at sub-national level







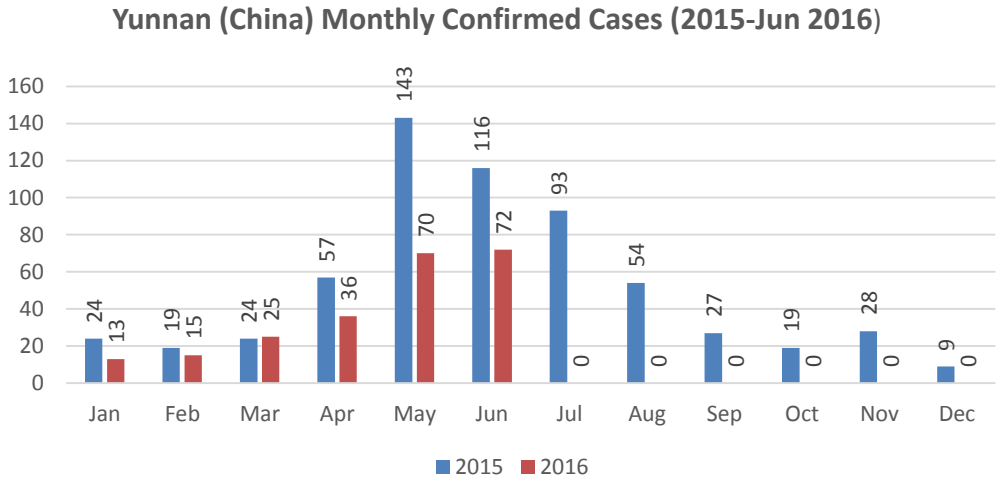
Country updates: **Cambodia** – CNM and Partners

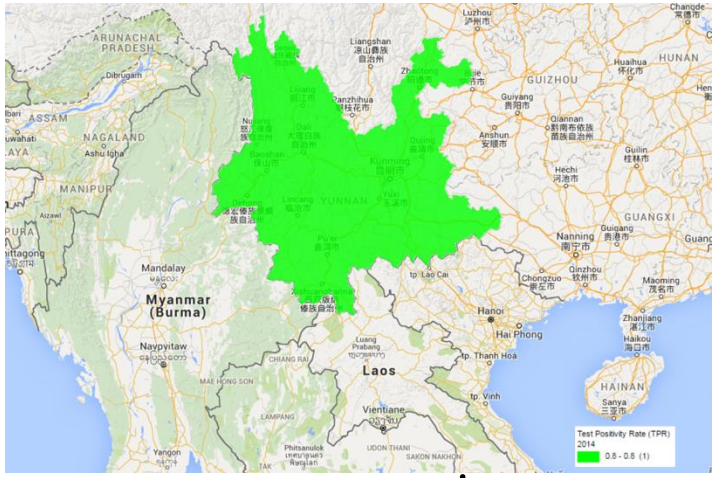


World Health Organization

Country updates: **China**

- **39 local cases nationwide, Yunnan, 23 indigenous cases in 2015**
- Preparing for certification
- Updated national elimination strategy & Yunnan elimination strategy (2015)
- Yunnan surveillance training
  - Conducts international trainings
- Cross border collaboration meeting between Myanmar and China, 3/2016
- Evaluation of border malaria ports planned





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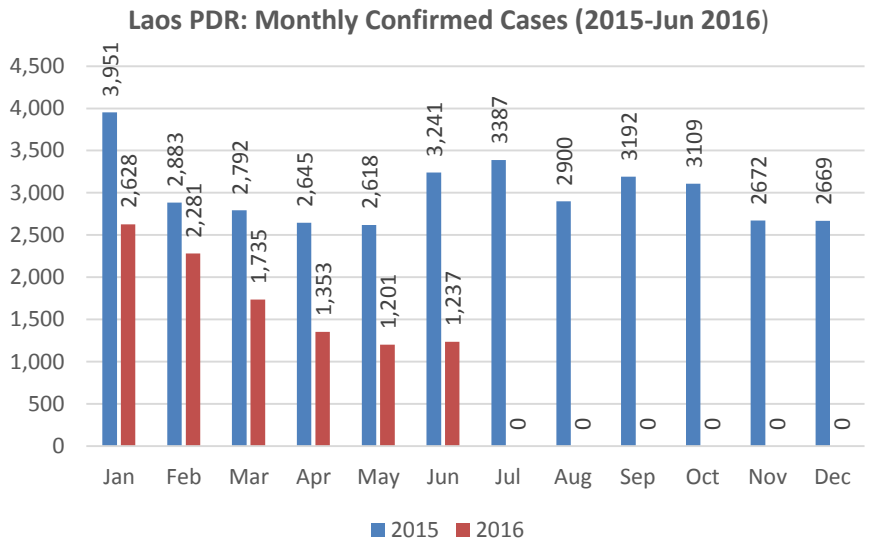
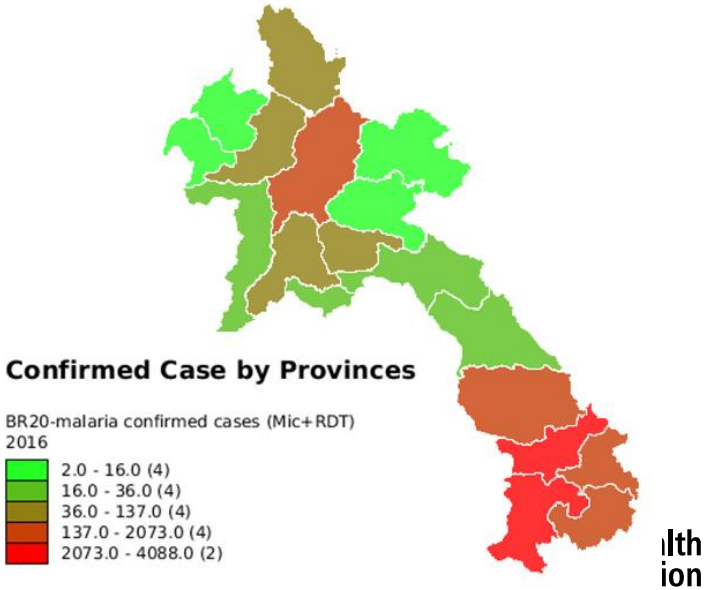
Country updates: **Lao People's Democratic Republic**

- No. of malaria cases reversing rapidly from the outbreak years (2012-2014)
- NSP 2016 – 2020 completed, planned launch, October 2016;
- Interventions for MMPs started
- Expand work with private sector
- Integration of malaria data into DHIS2
  - Training rolled out in 5 Southern Provinces
- National slide bank established (Mic)
- TES completed in Sekong (ACPR 86%) and Champasak (ACPR 90%) provinces.
- No significant resistance to pyrethroids, some to DDT in secondary vectors





Country updates: **Myanmar**

- Decrease in incidence
  - 2013 vs 2014: Cases-38%, Deaths 68%
  - 2014 vs 2015: Cases 41%, (<180,000)
- Increased testing with RDT
  - Malaria Programme Review completed
  - NSP and costing Completed
  - Concept Note GF (NFM, RAI), June 2016
  - Cross border meetings: China and SEA countries
  - Mapping of complex partners (>25) and interventions coverage completed
  - Surveillance: (>70 additional M&E staff), MIS and DHIS ongoing
  - Primary Vectors still susceptible to Pyrethroids
  - Strengthen coordination (6 TSG meetings in 2015)

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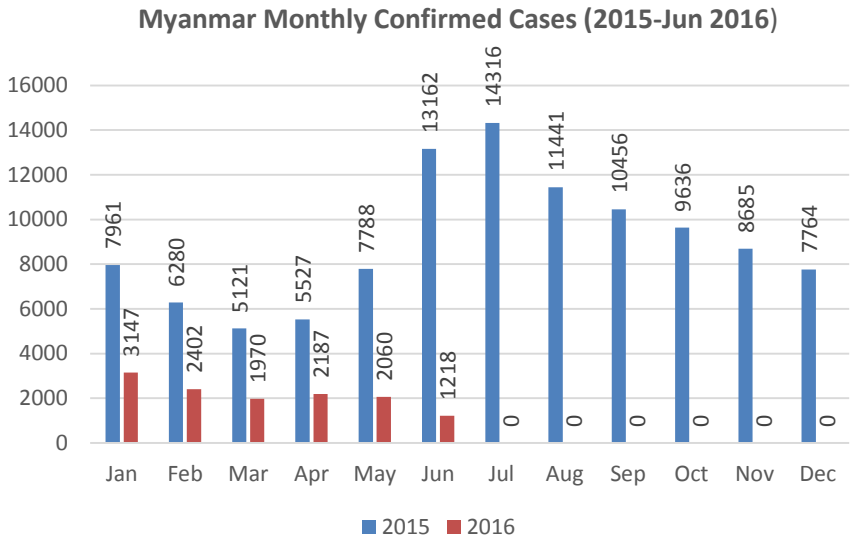
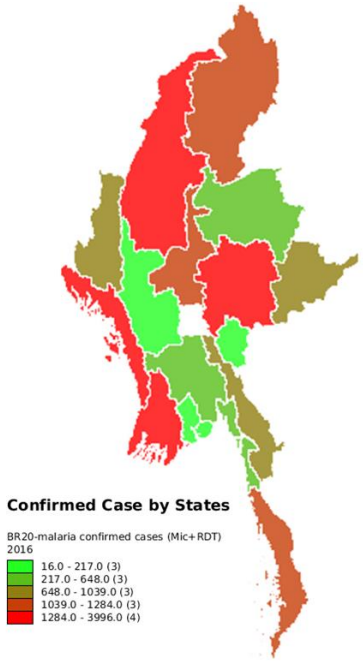
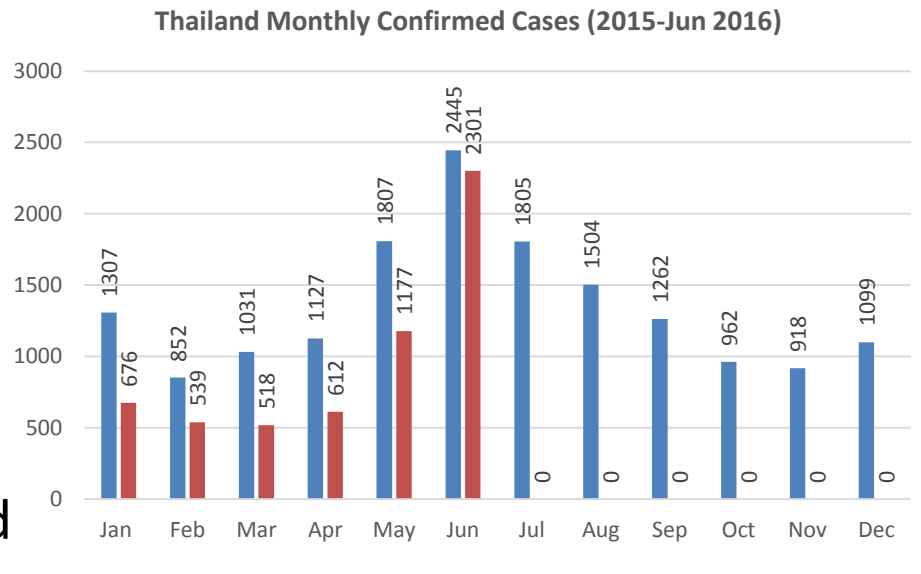


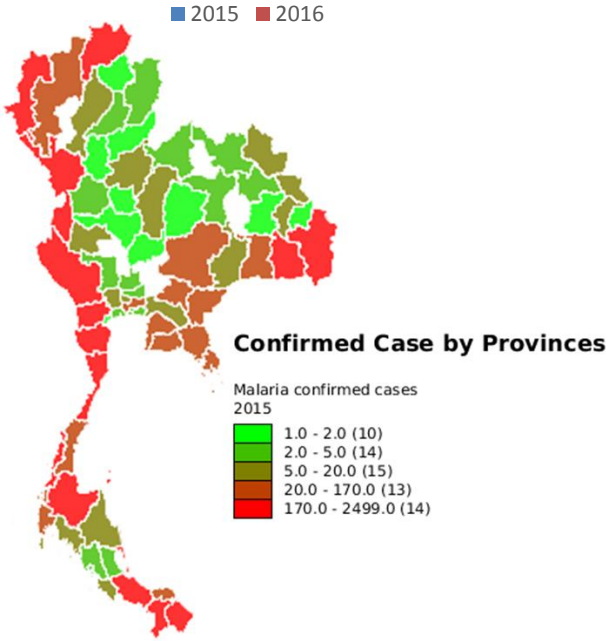


World Health Organization

Country updates: **Thailand**

- NSP for malaria elimination (2017-2026), launched, 25 April 2016
- Drug policy changed in Q2/2015 to DHA-PIP, rollout in 2016
- Premaquine roll out
- P.f API= 0.02/1000 pop
- Strengthening of microscopy QA
- Surveillance Web-based established Business Intelligence (BI)
- Shortfall of malaria staff
  - requires integration into general service
- Evaluation of DOTs ongoing
- Strong system of entomology at central and provincial level as well as in university. Strong OR on outdoor transmission



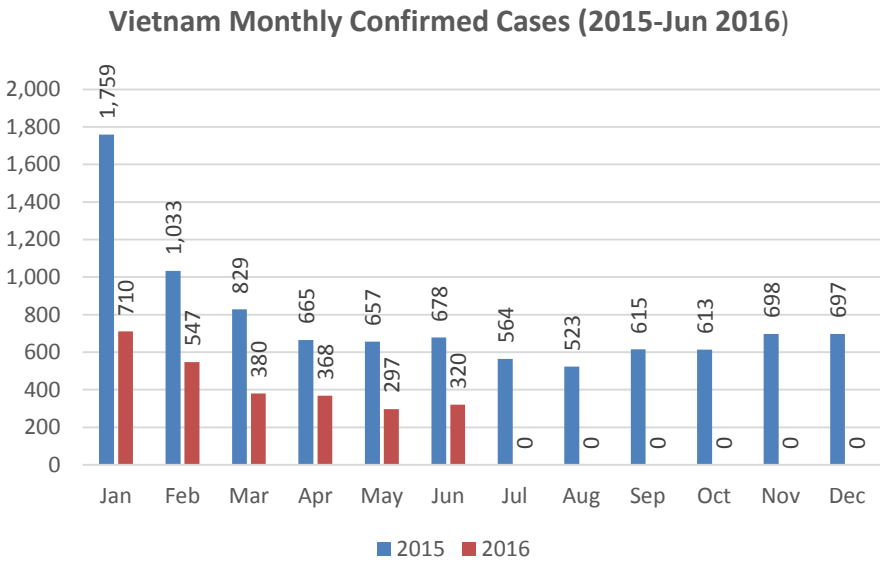


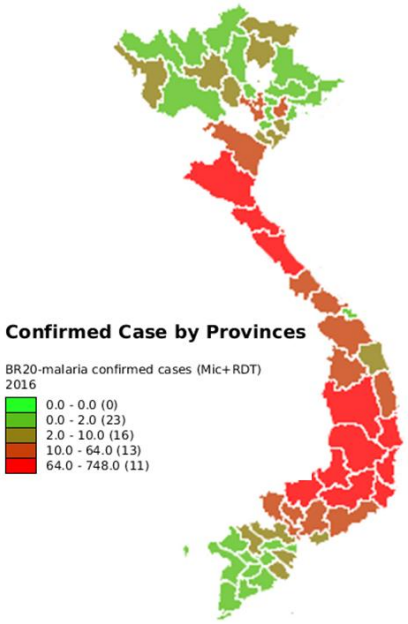
Country updates: **Viet Nam**

- Cases reduced significantly
  - 2013 vs 2015: 46% (17 123 to 9331)
- Premaquine
  - Single dose-ongoing
  - Radical cure-compliance
- 21% of pharmacies still selling oAMT
  - 94/445 pharmacies (survey, 5 provinces, 2014)
- Costed NSP developed
- Mapping of MMPs completed in 1 province
- Expansion of malaria posts (access for MMPs) - RAI
  - 140 posts already established.
- Expanding resistance to ACT (PPQ)- revise guide line

Retreatment of conventional nets from market with ICON 2.5CS

High national entomology capacity for national institutes





World Health Organization

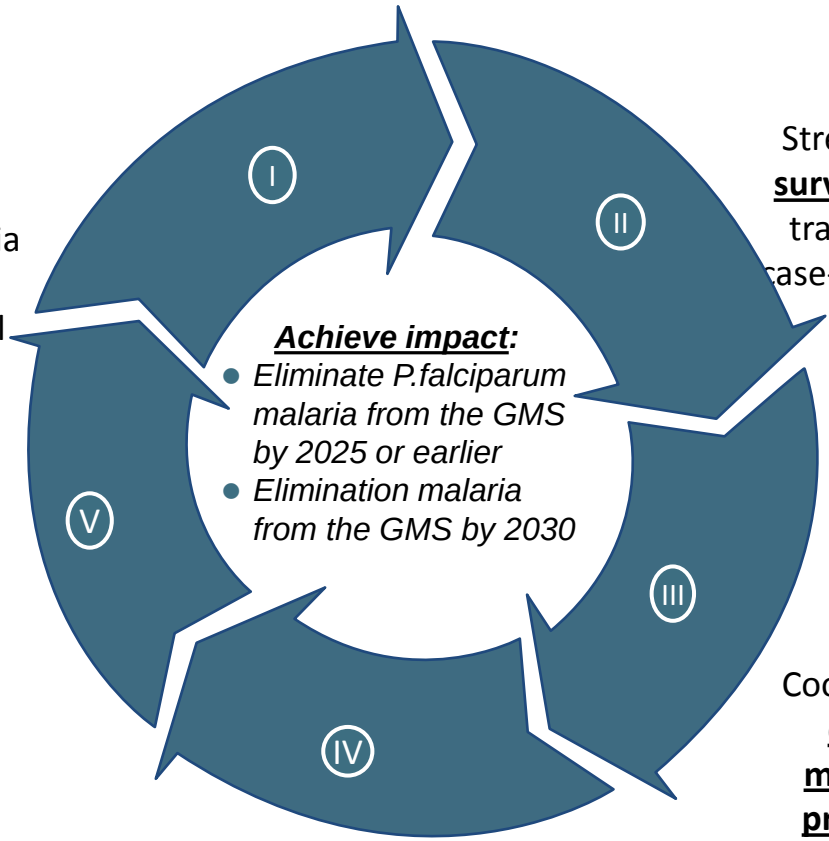
Policy and Implementation Challenges

- Country ownership
- Interventions in hard to reach populations
  - Measuring the magnitude
  - Accessing the risk groups
- Cross border collaboration
  - Definition of the focus
  - Joint work plans
  - Tracking and documentation
- Complex partners landscape
  - Fragmentation and stakeholder coordination
- Expanding drug resistance
- Delays in rollout of policies and guidance
  - Drug policy change (ACT rotation, primaquine, etc.)
  - Choice/targeting of VC interventions
- Elimination- largely new concept
  - implications on HR, structures
  - re-orientation, change mind-set
  - more domestic funding & commitment
- Weaknesses of health systems
  - leadership & governance, HR, HIS, health financing, PSM, health technologies incl mic)

World Health Organization

Way forward

Reorient the Regional Hub from containment to elimination



I

Promote high level and **multi stakeholder engagement** to keep malaria elimination high on the agenda and ensure mutual accountability

II

Strengthen existing malaria **surveillance** systems in their transition towards malaria case-based and entomological surveillance as core intervention

III

Coordinate and synergize **case detection and management, disease prevention and vector control interventions** in-country and across programs and sectors

IV

Plan and implement **capacity strengthening** activities (training, mentoring and supervision)

V

Keep an **independent score** of sub regional progress in malaria elimination, including **drug & insecticide resistance and cross border collaboration**

World Health Organization

THANK YOU

A field visit in Sanya to investigate a malaria case

World Health Organization

Evidence Review Group (ERG) on malaria elimination

Dr Richard Steketee, ERG chair

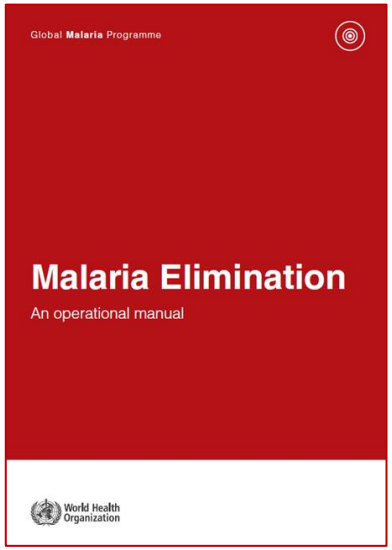
MPAC meeting - Geneva, 14 September 2016

Global **Malaria** Programme

World Health Organization

Rationale for an ERG on malaria elimination

- **The malaria landscape has changed dramatically since 2007**
  - Increased funding for malaria programme activities
  - Large-scale implementation of malaria interventions
  - Impressive reductions in malaria burden
  - Increasing number of countries eliminating or considering elimination of malaria
  - Changes in policy recommendations and available tools
  - Development of new Global Technical Strategy for Malaria 2016-2030 (3 pillars incl. elimination, 2 supporting elements) – all countries to accelerate towards malaria elimination



"Malaria elimination: An operational manual" for release in Q4, 2016

ERG on malaria elimination - membership

- 13 members with expertise and experience across relevant disciplines:

  - Dr Rick Steketee, PATH-MACEPA *(ERG Chair)*
  - Dr Majed Al-Zadjali, Department of malaria, MoH, Oman
  - Dr Graham Brown, Nossal Institute for Global Health
  - Dr Tom Burkot, James Cook University
  - Dr Justin Cohen, Clinton Health Access Initiative (CHAI)
  - Dr Mikhail Ejov, independent consultant
  - Dr Rossitza Mintcheva-Kurdova, independent consultant
  - Dr Bruno Moonen, Bill & Melinda Gates Foundation
  - Dr Gao Qi, Jiangsu Institute of Parasitic Diseases
  - Dr Frank Richards, The Carter Center
  - Dr Christophe Rogier, French Military Medical Service
  - Dr Allan Schapira, independent consultant
  - Dr Robert Snow, KEMRI Wellcome Trust Research Programme

ERG on elimination: 1st reporting to MPAC - Sept 2015

- **1st ERG meeting** in New Delhi (9/13 experts attending), July-August 2015 : deep dive into the current manual (2007), with identification of gaps/new content and needed changes for the new guidance
  - Title: "Malaria elimination: An operational manual"
  - Audience: all, but primarily National Malaria Control Programme managers
  - Scope : all epidemiological settings as opposed to countries nearing elimination only
  - Focus: progression of all malaria-endemic countries towards elimination in accord with the GTS, moving away from the previous multi-staged / compartmented process from control to elimination
  - Steps A to E to progress towards elimination with package of interventions – link with GTS pillars and SEs
- **New content identified**
  - Chapter "Innovation and research"
  - Section on Subnational verification of malaria elimination
  - Glossary to be aligned with the WHO malaria terminology work underway at that time (released in June 2016, available at http://apps.who.int/iris/bitstream/10665/208815/1/WHO_HTM_GMP_2016.6_eng.pdf)
- **First outline drafted** with writing/peer-review assignments among experts for 1st draft to be developed by November 2015

ERG on elimination: 2nd reporting to MPAC - March 2016

- Development and consolidation of **first draft** of the new Malaria elimination: An operational manual (134 pages)

- **2nd ERG meeting** in Montreux (11/13 experts attending), December 2016: comprehensive analysis and review of the draft. Decision points:
  - Rewriting work/synthesis to be done jointly by WHO-MACEPA staff based on a **final and detailed outline (for review during 3rd and final ERG meeting)**
  - Further components to be developed
    - section on surveillance
    - annex on diagnostic tools
    - details on the biology of malaria
    - clarification of re-introduction vs re-establishment throughout the manual
    - more details on case/focus classification

ERG on elimination: 3rd reporting to MPAC - Sept 2016

- January through May 2016: Malaria elimination operational manual revised by PATH-MACEPA and WHO staff based on inputs from the Montreux meeting – document made more concise.
- 2-3 June 2016: 2nd draft reviewed during a **3rd and final ERG meeting** (11/13 experts attending) held in Shanghai where a final outline was approved with further writing assignments for ERG experts and WHO programme staff due within 10 days.
- Consolidation by PATH-MACEPA.
- Consultation process over July/August 2016
  - Review and final suggestions by all ERG members, WHO regional advisors and GMP Director, Coordinators & Team leaders
  - Field testing of the document at malaria elimination training workshops held end of June/beginning of July (Bhutan and Philippines, respectively under SEARO and WPRO)
  - Comments received from malaria managers and experts in other WHO regions: WHO NPOs (AFRO), MoH and NMCP staff (Botswana, Brazil, Myanmar, South Africa and Suriname).
- Consolidation of most inputs into the document presented for MPAC review. Relevance of other inputs (received or to be received) still to be examined, also in light of MPAC feedback.

Overview of where we are and next steps

- Review of the draft guidance
- Clear and detailed outline set

- Deep dive into the manual
- Consensus on the gaps and suggested changes
- Outline of new guidance and each chapter
- Focal point to coordinate the process of collecting revised sections and compilation of inputs

Experts to develop working papers, conduct in-depth search or review papers/collect historical experience

Prep. work

1st ERG meeting New Delhi

2nd ERG meeting Montreux

July-Aug 2015

Dec 2015

Consultative process

- Discussion at regional meetings
- ITWs with programme managers

Feedback consolidation work

Final review

Write, synthesize and rearticulate

(WHO-PATH/MACEPA)

3rd ERG meeting China

March 2016

May 2016

2-3 June 2016

- **Incorporation of inputs from MPAC**
- Review of other feedback (from regions and countries)

MPAC presentation

14 Sept 2016

Production & publishing

Nov 2016

Launch in Cairo (TBC)

Regular teleconferences as needed

Ongoing interactions with GMP coordinators

Global **Malaria** Programme

World Health Organization

What's new in the manual?

- **All** malaria-endemic countries are addressed as opposed to moderate and low endemic ones previously
- Programme actions are highlighted across the continuum of transmission, **from high to very low/zero**
- Notion of feasibility of elimination is replaced by **critical requirements** to achieve and maintain elimination
- Emphasis on the critical role of **information systems** and **surveillance as an intervention**
- Emphasis on systems required for appropriate documentation of **certification** of elimination (national level) , on the role of **verification** of elimination (subnational level), and on the role of **celebrating incremental progress** in reducing incidence, illness, severe disease and mortality
- Acceleration and the speed of change are quicker than anticipated, **planning** for next step has to be done early
- **RDTs** and **light microscopy** are both recommended for malaria diagnosis
- **Focus classification has been simplified** : 3 instead of 7 types of foci with an emphasis on defined, but adaptable intervention packages for each focus type
- **Updated strategies** are recommended for different transmission intensities (e.g. MDA)
- Proposed **simplified process for certification of malaria elimination** with key role by a WHO malaria Certification Elimination Panel (CEP), recommendation by the MPAC and decision by the WHO DG (following request of the MPAC in September 2015)
- Careful national investigation and consultation with WHO will be required before a country's malaria-free certification is lost. A **minimum threshold for possible re-establishment of transmission** would be the occurrence of ≥3 indigenous malaria cases per year in the same focus for 3 consecutive years irrespective of the malaria species.

Outline of the manual for MPAC review (1)

Glossary – aligned with WHO terminology, some revisions for discussion

"What's new"

Introduction (malaria biology, recent progress, GTS, malaria elimination, challenges and opportunities, regional initiatives)

1. Principles and practices of malaria elimination (to include all countries and settings): Understanding transmission intensity and country stratification; Accelerating to elimination: aligning field actions with the *GTS for malaria 2016-2030;* illustrative spectrum of transmission intensity and intervention package; "Documenting malaria elimination" box

2. Strategies and interventions for elimination (*the "What"*)

- 2.1 Introduction
- 2.2 Local stratification according to receptivity and transmission intensity
- 2.3 Vector control for malaria elimination: core interventions; supplemental strategies; vector control in active transmission foci; vector control after elimination/prevention of re-establishment; M&E of vector control)
- 2.4 Enhancing and optimizing case detection and case management: case detection (passive and active); parasitological diagnosis; treatment incl. asymptomatic infections; role of QA and reference laboratories in malaria elimination
- 2.5 Surveillance: increasing sensitivity of surveillance systems; surveillance as an intervention; case characterization, classification and investigation; focus identification, characterization, classification and investigation; special surveys; data management, analysis, feedback and decision-making)
- 2.6 Accelerating efforts to elimination: population-wide medicine-based strategies; additional interventions to accelerate malaria elimination

3. Management and planning (*the "How"*)

- 3.1 Planning process: strategic and operational planning; resource mobilization
- 3.2 Data for decision-making: monitoring and evaluation; data quality; data management
- 3.3 Programme structure and management: programme management; programme staffing; training and retaining staff

Outline of the manual for MPAC review (2)

- 3.4 Supply chain systems
- 3.5 Independent national malaria elimination advisory committee
- 3.6 Creating an enabling environment: political commitment; necessary legislation; strategic partnerships across sectors (other government sectors, private sector); community engagement

4. Prevention of the re-establishment of malaria

- 4.1 What are the risks of malaria re-establishment: how to measure receptivity/vulnerability; how to manage these risks, i.e. lower and mitigate receptivity and vulnerability
- 4.2 Maintaining a strong health system
- 4.3 Integrating malaria activities into general health services

5. Certification and verification of malaria elimination

- 5.1 WHO certification of malaria elimination - general
- 5.2 WHO certification of malaria elimination – procedure (with “New steps for the certification process” box): national elimination report, activities of the malaria CEP; field visit
- 5.3 Follow-up of WHO certification
- 5.4 Subnational verification of malaria elimination: general principles and suggested process for interested countries

6. Innovation and research for malaria elimination

- 6.1 R&D for malaria elimination and eradication: medicines; diagnostics; vector control; vaccines
- 6.2 Operational research
- 6.3 Regulatory environment for malaria elimination

Outline of the manual for MPAC review (3)

Annexes

- 1. Biology of malaria: parasitological and entomological aspects (includes malaria transmission cycle)
- 2. Diagnosis and treatment of *P. f.* vs *P. v.* malaria
- 3. Monitoring and evaluation indicators for different interventions in an elimination programme
- 4. Terms of reference for the WHO malaria Certification Elimination Panel (CEP) – *drawn from the presentation made at the MPAC in September 2015*
- 5. Key documents of the elimination database to be prepared by the national government for the CEP
- 6. Outline of the content of the national elimination report
- 7. Sample of a national malaria case register
- 8. Sample malaria case investigation record form
- 9. Sample malaria focus investigation record form
- 10. Information to be included in the annual report for follow-up of WHO certification

Thank you

Evidence Review Group (ERG) on malaria elimination

Dr Richard Steketee, ERG chair

Dr Hoda Atta, WHO malaria advisor for EMRO

MPAC meeting - Geneva, 14 September 2016

Global **Malaria** Programme

World Health Organization

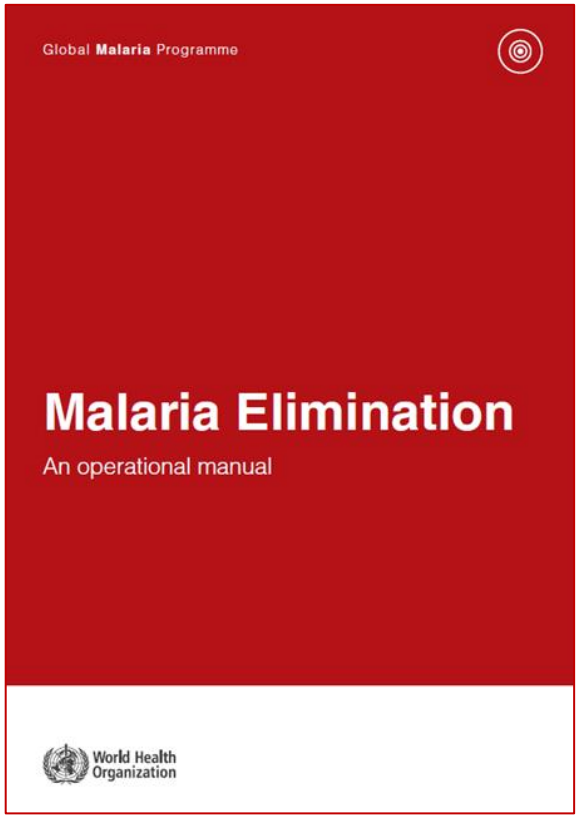
Objectives of the session

- The revised manual introduces new concepts and includes key changes from the "*Malaria Elimination – A field manual for low and moderate endemic countries*" (2007)
- The guidance submitted for review is the result of ~15 months of collaborative work, incl. 3 meetings, between experts across disciplines and includes perspectives from the malaria field (consultation process)

It is now time to solicit feedback from the MPAC. Proposed process is the following:

- Overall judgment, e.g. are we on the right track?
- Consideration of the following specific issues / changes (13 slides overall) – for endorsement and/or MPAC consensus
- Beyond previous clarification questions, and issues discussed and agreed upon, are there other elements that need addressing, then that require content changes?

1. Overall judgement



- Is the guidance relevant, are we on the right track?
- General comments and discussion > decision points

2. Specific issues for endorsement/consensus

Changes in WHO Malaria Terminology? (1/3)

- **Malaria elimination**: interruption of local transmission (reduction to zero incidence) of a specified malaria parasite in a defined geographic area as a result of deliberate efforts. Continued measures to prevent re-establishment of transmission are required.

- One or more defined malaria species?
- One or more human malarias?
- In the manual, do we adequately deal with the *P. knowlesi* description and the approach that does not include it for elimination?
- Can/Should we provide more information regarding our interest and ability to eliminate *P. f.* only or *P. f./P. v.* while *P. m.* or *P. o.* is still there?
- Should we provide more detail differentiating between malaria elimination (of one or more defined species) and certification of elimination (all human malarias, without *P. knowlesi* for now)? If we do, where does it fit best (Annex 1 or Annex 2 where we do not have a focus on the other species)?

Changes in WHO Malaria Terminology? (2/3)

- **Malaria focus**: A defined and circumscribed area situated in a currently or formerly malarious area that contains the epidemiologic and ecological factors necessary for malaria transmission.

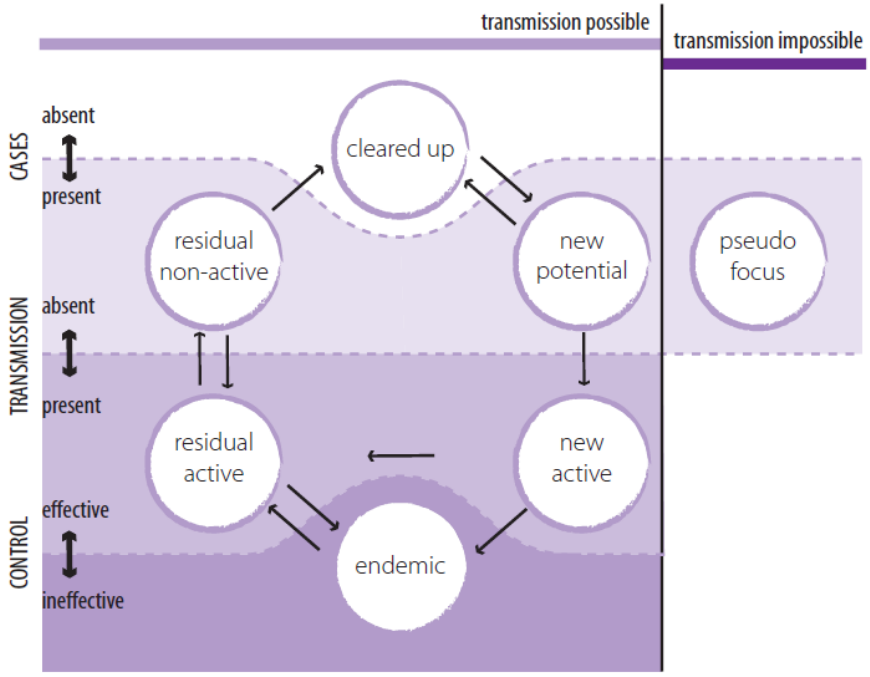
  Note: Foci can be classified as **endemic**, **residual active**, **residual non-active**, **cleared up**, **new potential**, **new active** or **pseudo**.

Foci can be classified as **active**, **non-active residual** and **cleared**.

Changes in WHO Malaria Terminology? (2/3, cont'd)

2007 manual

Figure 4. Transition of functional status of a malaria focus depending on the situation



[a] Adapted from *Guidelines on the elimination of residual foci of malaria transmission* (2).

2.5.4.2. Classification of foci (*page 56*)

Table 6. Types of malaria foci with operational criteria and recommended minimum standards of response

Classification		
Type of Focus	**Definition**	**Operational criteria**
Active	A focus with ongoing transmission	Locally acquired case(s) have been detected within the current transmission season.
Non-active residual	Transmission interrupted recently (1-3 years ago)	The last locally acquired case(s) was detected in the previous transmission season/calendar year or up to 3 years earlier.
Cleared	A focus with previous cases, but no current transmission or within the last three years.	Only imported, induced or relapsing/old cases detected in current calendar year or transmission season. No locally-acquired case(s) detected up to 3 years earlier.

Changes in WHO Malaria Terminology? (3/3)

- **Transmission, re-establishment of**: Renewed presence of a measurable incidence of locally acquired malaria infection due to repeated cycles of mosquito-borne infections in an area in which the transmission had been interrupted.

Note: A minimum indication of possible re-establishment of transmission would be the occurrence of three or more introduced and/or indigenous malaria infections in the same focus, for 2 consecutive years for *P. falciparum* and for 3 consecutive years for *P. vivax*.

A minimum threshold for possible re-establishment of transmission would be the occurrence of three or more indigenous malaria cases per year in the same focus for three consecutive years irrespective of the malaria species.

Key concepts (#1)

- Manual addresses
  all epidemiological settings / the whole continuum
  (high to very low/zero transmission)

even if <u>focus is on low to zero transmission</u>.

Chapter 1 discusses inclusivity and provides some welcoming of **<u>all</u>** malaria-endemic countries into the realm of ultimately planning for and considering sequential progress toward elimination

From Chapter 2 on

Key concepts (#1, continued)

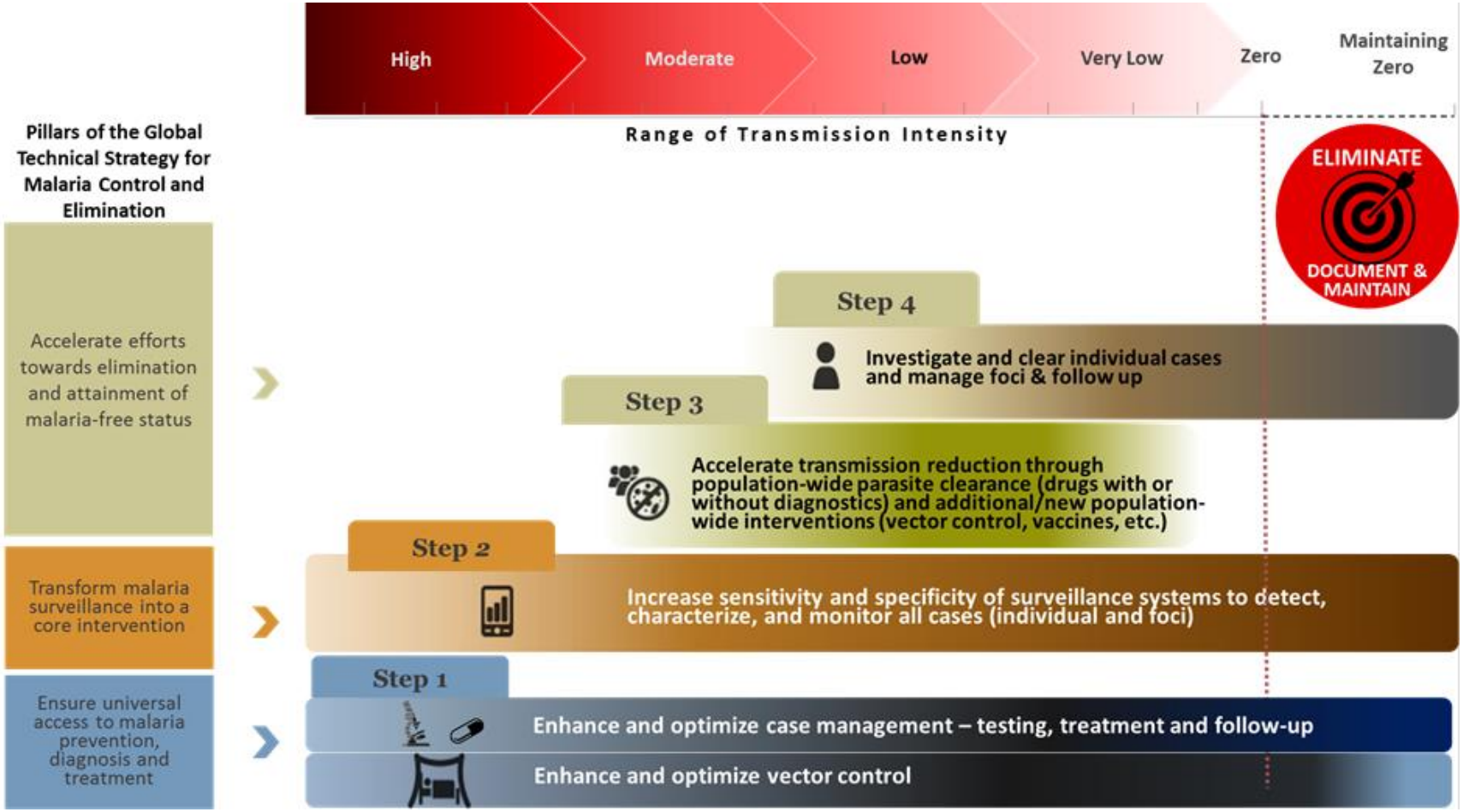
Table 2 (page 22): Illustrative spectrum of transmission intensity: cases per catchment area as they relate to annual parasite incidence and parasite prevalence

Range of transmission intensity					
Measure	High	Medium	Low	Very low	Zero
Annual parasite incidence (API) (range)	≥500	350 (250-420)	175 (130-240)	20 (<5-30)	0
P. falciparum or *vivax* prevalence rate (Pf/vPR) (% range)	≥35	20% (7-27)	10% (1-12)	≤1% (0.3-3)	0
Cases per health facility per week (range)	≥30	15 (10-20)	8 (5-10)	≤1 (0.3-3)	0
Entomological inoculation rate (EIR)	≥10	1	0.1	0.01	0

Is it of relevance to be explicit in a table of different transmission intensities with indicators (API, prevalence, cases per week, EIR)?

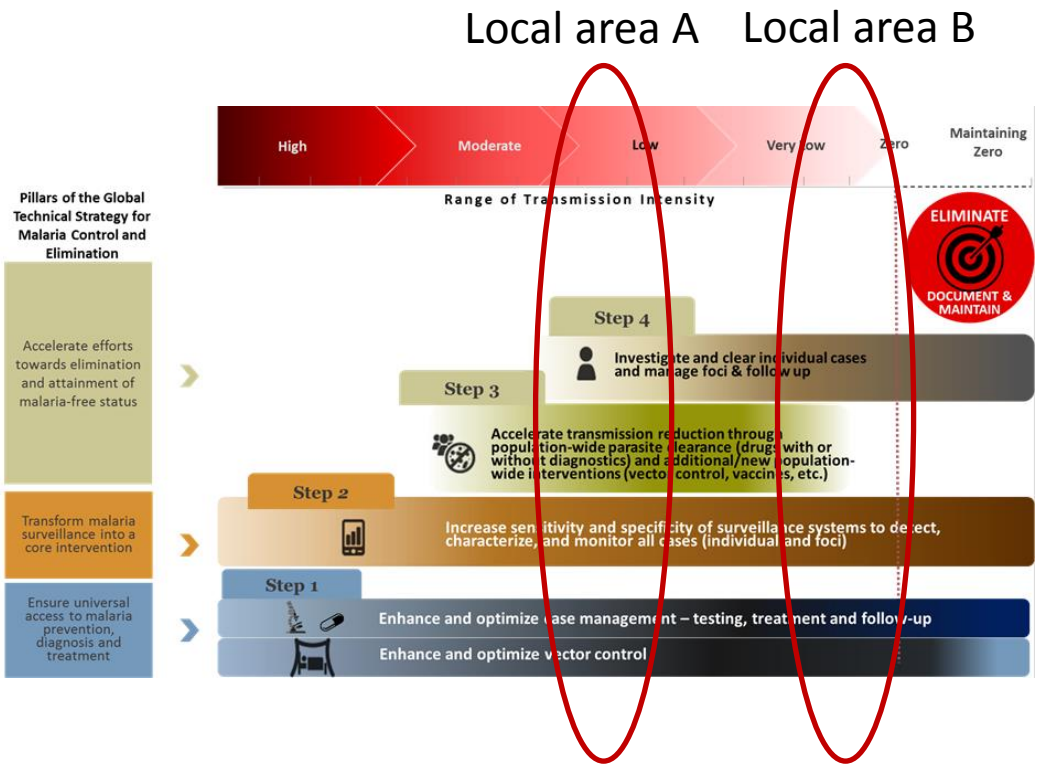
Key concepts (#1, continued)

Figure 3 (page 25): *is the illustrative intervention package useful? Is it clear in the surrounding texts that it can be adapted? That step 3 is a potential time-limited tool, hence can be discarded?*



Key concepts (#1, continued)

- **Need to adapt and tailor interventions to specific geographical areas within the same country – notion of stratification**



"There is no one-size-fits-all package of interventions suitable for all areas with malaria transmission or transmission risk. Epidemiologic, ecologic, and/or societal features that determine stratification permit national malaria programmes to assign intervention package choices and application methods."

Key concepts (#2)

- **Diagnostic testing in elimination settings**: norm remains RDT or light microscopy (without finer/molecular testing techniques).

- (page 43) “The detection of malaria infection among symptomatic cases is primarily based on blood examination by RDTs or microscopy”

- (page 44) “more sensitive methods …. are not recommended for routine case management and surveillance”.

  - Review “Quality and performance of surveillance” indicators in Annex 3 (“% of RDT results with microscopy results” relevant?, inclusion of RDT/slides cross-checked by national reference laboratory?)
  - Sensitivity of diagnosis: if a country has achieved malaria-free status using microscopy and RDT, but later on uses PCR and detects new cases, how should this be addressed? Recommendations? (*practical case in Yunnan province*)

Key concepts (#3)

Updated strategies are recommended (2007 vs 2016 elimination guidance)

- MDA is now a recognized strategy that can be considered for accelerating the time to elimination; it may be needed only in some settings
- Revised malaria treatment guidelines
- *P. vivax* strategy
- Diagnostic testing: TDR or microscopy

Revised WHO certification process (#4)

- **Differences between existing process (WER, 2014 No. 29) and revised one:**

a) The country, after reporting ~~(zero locally acquired)~~ **zero indigenous malaria cases** for the last 3 years at least **through a sensitive and robust national surveillance system**, can submit an official request for certification to WHO.
b) WHO and the country formulate a plan of action and timeline for the certification process during a WHO assessment mission.
c) The country finalizes the required national ~~certification documentation~~ **elimination report** and submits it to WHO.

- A team of the independent **Malaria Certification Elimination Panel (CEP), established by WHO**, i) reviews the national elimination report and other key documents indicated in Annex 5, ii) conducts field visits to verify its findings, and iii) develops a final evaluation report.
- The final evaluation report is **reviewed and finalized by the CEP and submitted to the WHO Malaria Policy Advisory Committee (MPAC) with a recommendation** to certify malaria elimination or to postpone certification with details on the extra evidence required to demonstrate that malaria elimination has been achieved.
- The **WHO MPAC makes a final recommendation** on granting malaria-free status and provides a summary of the final evaluation report to the WHO Director General.

Then, the WHO Director General makes the final decision and officially informs the national government.

National verification (#5) of elimination

- Option for large countries that have achieved interruption of local transmission within certain parts of their territories & useful tool for countries that have geographically isolated territories, e.g. islands.
- Documenting elimination of local malaria transmission at subnational level should be as rigorous as the national certification process, but is country-owned.
- Assessment of malaria elimination in subnational areas is at the country's discretion.
- Process and criteria for subnational verification should emulate the WHO national-level certification scheme; same criteria and assessment procedures for subnational verification as for WHO certification.
- National authorities verify, subnational areas/local authorities are the subjects of verification.

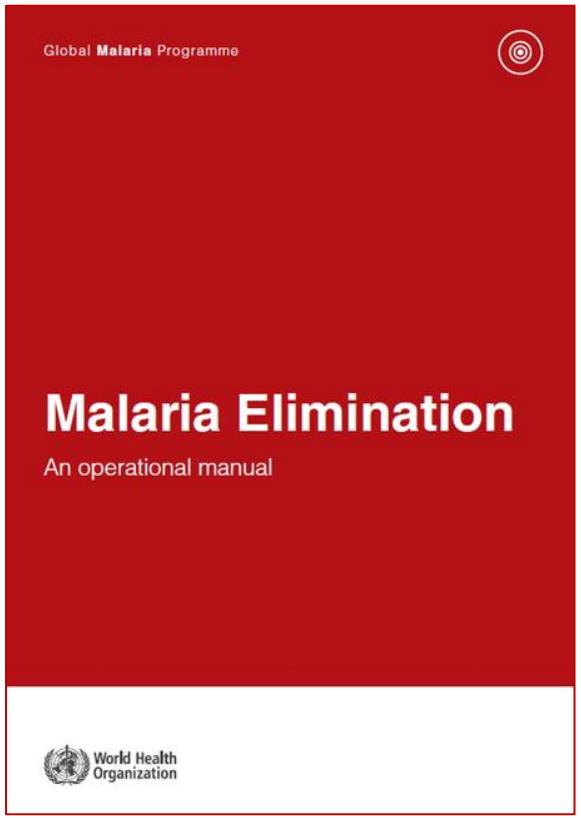
Suggested process

- Achieving subnational verification subject to official regulations and/or administrative orders
- Higher-level experienced and independent National Commission for Malaria Elimination (NCME) should be established to i) monitor and verify the work of the programme, ii) help document it and iii) paly a national political and advocacy role for continued efforts
- Evaluations by independent national teams, incl. international experts
- Review of documentation and validation of locally-transmitted cases for 3 consecutive years
- Status of subnational verification of malaria elimination to be withdrawn in the event of re-establishment of local transmission, i.e. three or more indigenous malaria infections linked in space and time to each other by local mosquito-borne transmission in the same geographical focus **in the same year** (*different from indication of re-establishment at national level: for three consecutive years*)

Annexes (#6)

- **Annex 1**: Consensus on the critical observable interval "Typical duration of untreated infection" for *P. falciparum* and *P. vivax*
- **Annex 3**: Discussion on relevance of M&E indicators (impact, quality and performance of surveillance, case management, vector control and programme milestones) in an elimination programme in particular in light of the M&E framework for the GTS/AIM
- **Annex 7** "Sample of a national malaria case register" and **Annex 8** "Sample malaria case investigation record form" to assemble so case characterization, categorization and investigation are considered within one annex?
- **Annex 9** "Sample malaria focus investigation record form" to adapt to Annex 7 (categories of characterizing, categorizing and investigating)?

3. Other changes needed



- Further points for consideration?
- Consensus on way forward

Thank you