

Meeting Report

Western Pacific Regional Consultation on the WHO Technical Brief for Control and Elimination of *Plasmodium vivax*



9 June 2014
Manila, Philippines



**WESTERN PACIFIC REGIONAL CONSULTATION ON THE WHO TECHNICAL BRIEF
ON PLASMODIUM VIVAX CONTROL AND ELIMINATION**
9 June 2014, Manila, Philippines

MEETING REPORT

**WESTERN PACIFIC REGIONAL CONSULTATION ON THE WHO TECHNICAL
BRIEF FOR CONTROL AND ELIMINATION OF PLASMODIUM VIVAX**

Convened by:

WORLD HEALTH ORGANIZATION
REGIONAL OFFICE FOR THE WESTERN PACIFIC

Manila, Philippines
9 June 2014

Not for sale

Printed and distributed by:

World Health Organization
Regional Office for the Western Pacific
Manila, Philippines

June 2015

NOTE

The views expressed in this report are those of the participants for the Western Pacific Regional Consultation on the WHO Technical Brief for Control and Elimination of *Plasmodium vivax* and do not necessarily reflect the policies of the conveners.

This report has been prepared by the World Health Organization Regional Office for the Western Pacific for Members States in the Region and for those who participated in the Western Pacific Regional Consultation on the WHO Technical Brief for Control and Elimination of *Plasmodium vivax* in Manila, Philippines, 9 June 2014.

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Keywords: Disease vectors / Malaria – prevention and control / Plasmodium vivax /
Regional health planning

1. BACKGROUND

Plasmodium vivax is responsible for 20% of current reported malaria cases in the 10 endemic countries in the Western Pacific Region. This makes the parasite, with biologically widely different strains, an important one in the Region. Effective control of *P. vivax* in the Region has been complicated due to the prevalence of G6PD deficiency and resulting safety concerns related to the use of primaquine for radical treatment.

The WHO Global Malaria Programme (GMP) is currently addressing the effective control and elimination of *P. vivax* through developing the Western Pacific Regional Consultation on the WHO Technical Brief for Control and Elimination of *Plasmodium vivax*. The document will provide an update on the biology of *P. vivax* and the epidemiological situation, summarize strategic approaches for control and elimination, and highlight additional research and development needed.

A regional consultation was conducted to review an outline of the technical briefing document.

2. PROCEEDINGS

The one-day regional consultation was held on 9 June 2014 at WHO Regional Office for the Western Pacific in Manila, Philippines. The consultation was attended by 31 participants: 11 representatives from the national malaria programmes or ministries of health of nine countries including Cambodia, China, the Lao People's Democratic Republic, Malaysia, Papua New Guinea, the Philippines, Solomon Islands, Vanuatu and Viet Nam; five temporary advisers including the chair of the *Plasmodium vivax* Technical Briefing Steering Committee, Dr Kevin Baird; an observer from the Asia Pacific Malaria Elimination Network; and 14 WHO technical staff working on malaria at headquarters, regional and country levels, including the acting director of the WHO Global Malaria Programme, Dr John Reeder (see Annex 1 for the agenda and Annex 2 for the list of participants).

The objective of the meeting was to review and provide feedback on the draft Western Pacific Regional Consultation on the WHO Technical Brief for Control and Elimination of *Plasmodium vivax*.

2.1 Setting the scene

Dr John Reeder presented the global scenario and the importance of the Western Pacific Regional Consultation on the WHO Technical Brief for Control and Elimination of *Plasmodium vivax*. He noted that *P. vivax* is more widespread globally than *P. falciparum*, with more than 2.5 billion people estimated to be at risk for vivax malaria. There are an estimated 18.9 million cases, including 200 000 in the Western Pacific Region. However, a global estimate of deaths due to *P. vivax* is currently unavailable. *P. vivax* responds more slowly to control measures and increasingly predominates as programmes move toward elimination. This is due to the multiple biological challenges that *P. vivax* presents, such as early appearance of gametocytes and the presence of hypnozoites in the liver. Dr Reeder then discussed the need for the Western Pacific Regional Consultation on the WHO Technical Brief for Control and Elimination of *Plasmodium vivax*, which will identify the challenges posed by *P. vivax* malaria, summarize existing strategies and highlight research and development needs.

Dr Kevin Baird presented an overview of the Western Pacific Regional Consultation on the WHO Technical Brief for Control and Elimination of *Plasmodium vivax* and its rationale and objectives which are: (1) highlight key issues that must be addressed to reduced and eliminate *P. vivax* infection and disease; (2) provide guidance on how to use the most appropriate tools for different settings to achieve specific goals; and (3) provide practical advice to malaria

programmes to reduce and eliminate *P. vivax*. Dr Baird then introduced the composition of the Steering Committee and the Writing Committee. He mentioned that the technical briefing will have thematic reviews on *P. vivax* biology and epidemiology, vector control considerations, diagnosis and treatment, surveillance and elimination, cost effectiveness of interventions and research priorities. Dr Baird discussed the five strategic directions of the Technical Briefing: surveillance and response; preventing cases and reducing transmission; case management; innovation and research; and advocacy and governance.

Dr Eva Christophel, Team Leader of the Malaria, other Vectorborne and Parasitic Diseases unit of the WHO Regional Office for the Western Pacific, presented an overview of *P. vivax* in the Region which included the epidemiology, biology, programme aspects and challenges of *P. vivax* control. Of 2.5 million people at risk for vivax malaria worldwide, 83% live in the South-East Asia and Western Pacific Regions. A summary of the proportion of *P. vivax* among all confirmed cases was presented for 2012: in the Republic of Korea, only *P. vivax* is prevalent; all other malaria-endemic countries in the Western Pacific Region have *P. falciparum* and varying proportions of *P. vivax*, with 68% of malaria cases due to *P. vivax* in Vanuatu, and less than 50% in the other countries. In total, 23% of all confirmed reported malaria cases in 2012 were due to *P. vivax*. Country trends of malaria (*P. falciparum* and *P. vivax* cases) were also presented, with the example of Cambodia used to show that prevalence of *P. vivax* can vary significantly within a country. Dr Christophel pointed out that within the Western Pacific Region several biologically different *P. vivax* strains exist, including the tropical short incubation and fast relapsing Chesson strain and the temperate long incubation East Asia strains which have long relapse times. Programme issues especially are related to the widespread existence of G6PD deficiency in the Region, including severe variants, which affect the safety of primaquine use in the absence of G6PD testing. As a result, five out of 10 malaria endemic countries are not using primaquine systematically for the radical treatment of *P. vivax*. Additional challenges in the Region to control and elimination of *P. vivax* are:

1. adherence to the 14-day primaquine regimen which is not used by all countries;
2. limitations of diagnosis and reporting procedures, which also lead to underestimation of *P. vivax* burden and distribution;
3. reduced efficacy of chloroquine – some countries have changed to ACTs;
4. inadequate vector control coverage;
5. *P. vivax* outbreaks;
6. technical problems in therapeutic efficacy testing due to lack of parasite genotyping tools;
7. research questions not yet answered, for example, the efficacy of spring treatment and programmatic implications of the different *P. vivax* strains in the Region; and
8. *P. vivax* control receiving inadequate attention.

2.2 Vivax malaria country landscapes from the Western Pacific Region

Country landscapes were presented to highlight the diversity of *P. vivax* in the Region and programmatic challenges. Cambodia and China presented their country landscape briefs which describe *P. vivax* epidemiology, vector control data, malaria control interventions (especially *P. vivax* specific), G6PD deficiency and adverse primaquine reactions in Cambodia, drug resistance, systems of surveillance, monitoring and evaluation, analysis of patterns and changes in disease incidence/mortality, constraints to programme implementation and policy/programme guidance. Both countries highlighted the different distribution of *P. vivax* within their countries, for example, some areas in China having exclusively *P. vivax*. China highlighted the prevalence of both tropical and temperate strains and the large area where both strains are co-prevalent. Both countries also reported on the prevalence of G6PD deficiency, which in China seems to be limited to some ethnic minorities, but in Cambodia is widespread

with several different variants. Both China and the Philippines reported widespread use of primaquine without prior G6PD testing and without reported severe adverse reactions, although it was noted that reporting may be incomplete. Cambodia carried out a primaquine safety study in 2013 using the weekly regimen for *P. vivax*, which demonstrated the risk of severe hemolysis in some G6PD deficient patients. Cases of severe hemolysis attributed to the use of primaquine in patients with G6PD deficiency were also reported in Vanuatu and Solomon Islands, and since then primaquine has only been used to a very limited extent.

2.3 Review of the key elements of the WHO Technical Briefing on Plasmodium vivax Control and Elimination: Summary of comments, feedback and recommendations

Review of the Summary of *P. vivax* Strategic Directions, which had been provided by WHO GMP, involved a one hour discussion on each of the five strategic elements in plenary, after an introduction by the assigned facilitator. The results of the discussions and recommendations were captured in real time in a feedback form designed by WHO GMP. The summary of feedback is shown in Figure 1.

Figure 1. Summary of comments, feedback and recommendations

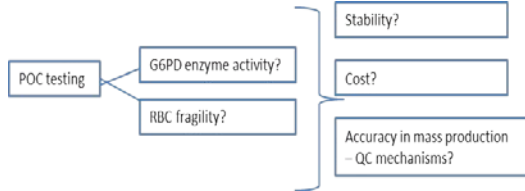
Key guidance	Regional feedback	Comments
1. Surveillance and Response		Facilitator: Dr Lasse Vestergaard
<i>P. vivax</i> in general: 1.1 Ensure accurate diagnostic testing, recording and reporting of <i>P. vivax</i> malaria in all settings where cases occur including in aggregate records.	<input type="checkbox"/> 1. Acceptable as is <input checked="" type="checkbox"/> 2. Requires modification (indicate if regional-specific_Y/√N) <input type="checkbox"/> 3. Delete	<ul style="list-style-type: none"> • There is a consensus on the statement: species differentiation information should be available throughout the country. • Elimination programmes require additional information. • There is an issue with classification of RDT non- <i>P. falciparum</i> results. • Each relapse should be counted as a single case given the difficulty to differentiate relapse from re-infection. • Need to ensure outbreak management, in general and for <i>P. vivax</i>.
Severe vivax malaria: 2.1 Record and report details for all in-patient <i>P.vivax</i> cases. 2.2 Investigate all suspected <i>P.vivax</i> deaths.	<input type="checkbox"/> 1. Acceptable as is <input checked="" type="checkbox"/> 2. Requires modification (indicate if regional-specific√Y/_N) <input type="checkbox"/> 3. Delete	<ul style="list-style-type: none"> • Severe vivax and deaths due to vivax malaria seem to lack credibility in some settings. Capacity building needed. • Cause of death reporting is weak throughout the Region. Health system strengthening is needed. • Investigation of deaths of suspected malaria at this point is not feasible in many countries. • Agreed that recording of severe vivax and death investigation should be carried out where feasible. • Define elements of investigation of suspected malaria deaths.
3.1 Screen travelers and migrants from endemic areas before entry into receptive malaria-free areas.	<input type="checkbox"/> 1. Acceptable as is <input checked="" type="checkbox"/> 2. Requires modification (indicate if regional-specific√Y/_N) <input type="checkbox"/> 3. Delete	<ul style="list-style-type: none"> • Screening of individuals from endemic areas is not feasible on a large scale at this time in most countries in the Region. But countries currently in elimination phase are considering expanding such screening. • Screening (with consideration of presumptive treatment) of certain high risk groups entering from high risk areas could be useful as a public health intervention. • Should be changed to “travelers, mobile and migrant populations”.
3.2 Sustain good surveillance even when case numbers are close to zero.	<input type="checkbox"/> 1. Acceptable as is <input checked="" type="checkbox"/> 2. Requires modification (indicate if regional-specific_Y/√N) <input type="checkbox"/> 3. Delete	<ul style="list-style-type: none"> • Sustaining surveillance after interruption of local transmission is particularly important for <i>P vivax</i>.
2. Preventing case and reducing transmission 2.1 Vector Control		<ul style="list-style-type: none"> • Facilitator: Dr Rabindra Abeyasinghe
5.1 Ensure good coverage with appropriate strategies based on epidemiology and local vector surveillance data, including the variation of vectors behaviours (e.g. outdoor/indoor biting).	<input type="checkbox"/> 1. Acceptable as is <input checked="" type="checkbox"/> 2. Requires modification (indicate if regional-specific_Y/√N) <input type="checkbox"/> 3. Delete	<ul style="list-style-type: none"> • This is universally applicable for <i>P. falciparum</i>, <i>P. vivax</i>, and others. • Human behaviour needs to be taken into account. • Good coverage should be changed to full coverage. • In elimination areas full coverage may not be needed in all places.

<p>5.2 Provide full coverage for vulnerable populations or those untreatable with primaquine (pregnant/lactating mothers and infants) with long-lasting insecticidal bed nets (LLINs) and indoor residual spraying (IRS).</p>	<p><input type="checkbox"/> 1. Acceptable as is <input checked="" type="checkbox"/> 2. Requires modification (indicate if regional-specific <u>_Y/√N</u>) <input type="checkbox"/> 3. Delete</p>	<ul style="list-style-type: none"> • Add “or those who cannot use primaquine for whatever reason”. • Full coverage for vulnerable populations should be provided, especially in countries with high G6PD deficiency prevalence. • Add “and effective tools against outdoor biting to prevent transmission of vivax” (e.g. repellents or larval source management).
<p>2. Preventing case and reducing transmission 2.2 Preventive Chemotherapy and Travelers</p>		
<p>Chemoprophylactic approaches may include: 6.1 Travelers taking primaquine throughout the duration of their stay in an endemic area and one week after return (causal prophylaxis).</p>	<p><input type="checkbox"/> 1. Acceptable as is <input checked="" type="checkbox"/> 2. Requires modification (indicate if regional-specific <u>_Y/√N</u>) <input type="checkbox"/> 3. Delete</p>	<ul style="list-style-type: none"> • Target population needs to be better defined. Implementation will depend on country dynamics. • Primaquine not registered for use as causal prophylaxis. The indication should be revisited. • G6PD problem in the Region should be taken into account.
<p>Chemoprophylactic approaches may include: 6.2 Presumptive anti-relapse therapy (PART) in travelers returning from endemic areas.</p>	<p><input type="checkbox"/> 1. Acceptable as is <input checked="" type="checkbox"/> 2. Requires modification (indicate if regional-specific <u>_Y/√N</u>) <input type="checkbox"/> 3. Delete</p>	<ul style="list-style-type: none"> • Move to Strategic Direction 3: Case Management (section 11). • More evidence is required. • G6PD problem in the Region should be taken into account.
<p>6.3 Intermittent treatment strategies, including ‘spring treatment’ (treatment at the beginning of transmission seasons in sub-tropical/temperate zones).</p>	<p><input type="checkbox"/> 1. Acceptable as is <input checked="" type="checkbox"/> 2. Requires modification (indicate if regional-specific <u>√Y/_N</u>) <input type="checkbox"/> 3. Delete</p>	<ul style="list-style-type: none"> • Has been used in the some parts of the Region for many years (China). • More evidence needed for effectiveness of spring treatment. Move to Strategic Direction 4: Research. •
<p>6.4 MDA, including a full therapeutic dose of anti-relapse therapy (in certain very high risk and accessible populations).</p>	<p><input type="checkbox"/> 1. Acceptable as is <input checked="" type="checkbox"/> 2. Requires modification (indicate if regional-specific <u>√Y/_N</u>) <input type="checkbox"/> 3. Delete</p>	<ul style="list-style-type: none"> • This is a research issue. Move to Strategic Direction 4: Research. • G6PD problem in the Region should be taken into account.
<p>3. Case management 3.1 Diagnosis</p>		
<p>7.1 Provide good quality microscopy at facilities that provide microscopy services especially to identify low parasitaemias and mixed infections.</p>	<p><input type="checkbox"/> 1. Acceptable as is <input checked="" type="checkbox"/> 2. Requires modification (indicate if regional-specific <u>_Y/√N</u>) <input type="checkbox"/> 3. Delete</p>	<p>Facilitator: Dr Kevin Baird</p> <ul style="list-style-type: none"> • Good quality microscopy includes good quality equipment and supplies, as well as maintenance. • Quality of microscopists should be maintained through an ongoing QA system, especially as motivation and quality of microscopists is deteriorating. • Proper initial microscopy training and regular refresher training is essential to allow good quality microscopy.

<p>7.2 Deploy approved* bivalent RDTs at clinic and community level to improve access to timely diagnosis and treatment.</p>	<p><input type="checkbox"/> 1. Acceptable as is <input checked="" type="checkbox"/> 2. Requires modification (indicate if regional-specific <u>_Y/√N</u>) <input type="checkbox"/> 3. Delete</p>	<ul style="list-style-type: none"> • Replace “approved” with “quality assured”. • There is a need for highly sensitive RDTs to detect low levels of <i>P. vivax</i> parasitemia. • Note that the level of parasitemia is lower in <i>P. vivax</i> therefore a high sensitivity of the test is important. • Procurement decisions for programmes should select product-tested RDTs that are highly sensitive for vivax.
<p>8.1 Maintain diagnostic capabilities even when malaria is eliminated or close to elimination.</p>	<p><input type="checkbox"/> 1. Acceptable as is <input checked="" type="checkbox"/> 2. Requires modification (indicate if regional-specific <u>_Y/√N</u>) <input type="checkbox"/> 3. Delete</p>	<ul style="list-style-type: none"> • “Effective” diagnostic capabilities should be maintained. • Possible redundancy with 3.2.
<p>9.1 Ensure good quality PCR or other high sensitivity tools to provide reference services for the identification of asymptomatic and sub-patent infections.</p>	<p><input type="checkbox"/> 1. Acceptable as is <input checked="" type="checkbox"/> 2. Requires modification (indicate if regional-specific <u>_Y/√N</u>) <input type="checkbox"/> 3. Delete</p>	<ul style="list-style-type: none"> • Aimed at programmes in elimination or pre-elimination phase; not relevant in control situations. • Make reference to the MPAC recommendations on malaria diagnostics in low transmission settings (March 2014).
<p>10.1 Provide G6PD testing facilities within existing health services (possibly with referral from lower to higher level health facilities).</p>	<p><input type="checkbox"/> 1. Acceptable as is <input checked="" type="checkbox"/> 2. Requires modification (indicate if regional-specific <u>√Y/_N</u>) <input type="checkbox"/> 3. Delete</p>	<ul style="list-style-type: none"> • G6PD is a huge problem in the Region, with high diversity of variants including severe ones. • Some countries are screening newborns for G6PD deficiency (Malaysia, the Philippines). At least one country tests each patient for G6PD before PQ treatment, and hospitalizes patients during PQ treatment for <i>P. vivax</i> (Malaysia). In many countries G6PD testing can only be carried out at hospital level. • Further evaluation of point-of-care G6PD deficiency rapid tests is needed. • Specify for delivery of radical cure in the context of G6PD testing. • On what to do regarding G6PD+ patients see 5.2. • PQ should not be used for <i>P. vivax</i> radical cure without G6PD testing in areas with severe forms or high prevalence of G6PD deficiency.
<p>3. Case management 3.2 Treatment - Radical therapy</p>		
<p>In low transmission settings, where primaquine therapy is already recommended: 11.1 Ensure timely access to treatment to achieve clinical cure and prevent progression to severe disease.</p>	<p><input type="checkbox"/> 1. Acceptable as is <input checked="" type="checkbox"/> 2. Requires modification (indicate if regional-specific <u>_Y/√N</u>) <input type="checkbox"/> 3. Delete</p>	<ul style="list-style-type: none"> • Change to: “Ensure timely access and adherence to achieve radical cure and prevent relapses, possible progression to severe disease and onward transmission”. •
<p>In low transmission settings, where primaquine therapy is already recommended:</p>	<p><input type="checkbox"/> 1. Acceptable as is <input type="checkbox"/> 2. Requires modification (indicate if regional-specific</p>	<ul style="list-style-type: none"> • Redundant with 11.1

11.2 Ensure availability and adherence (providers and patients) to radical therapy.	<input type="checkbox"/> _Y/_N) <input checked="" type="checkbox"/> 3. Delete	
12.1 Consider providing radical cure under all transmission settings.	<input checked="" type="checkbox"/> 1. Acceptable as is <input type="checkbox"/> 2. Requires modification (indicate if regional-specific _Y/_N) <input type="checkbox"/> 3. Delete	<ul style="list-style-type: none"> Will require availability of G6PD testing.
3. Case management 3.2 Treatment - Monitoring drug efficacy		
13.1 Conduct TES to monitor the efficacy of chloroquine against <i>P.vivax</i> according to standard procedures as laid out in the <i>WHO Methods for Surveillance of Antimalarial Drug Efficacy (2009)</i> .	<input type="checkbox"/> 1. Acceptable as is <input checked="" type="checkbox"/> 2. Requires modification (indicate if regional-specific _Y/ <input checked="" type="checkbox"/> N) <input type="checkbox"/> 3. Delete	<ul style="list-style-type: none"> There are two drug monitoring efficacy networks in place in the Region (Mekong and Pacific networks). <i>P. vivax</i> TES are part of the workplans of the countries, and chloroquine and ACT testing is done. However, there are problems with the current TES protocol, as recrudescence cannot be differentiated from relapses or reinfections; likely relapses within 28 or 42 days are called 'treatment failures'.
13.2 Ensure the inclusion of a measurement of chloroquine content in blood and report parasite clearance time.	<input checked="" type="checkbox"/> 1. Acceptable as is <input type="checkbox"/> 2. Requires modification (indicate if regional-specific _Y/_N) <input type="checkbox"/> 3. Delete	<ul style="list-style-type: none"> In countries where ACTs are used for <i>P. vivax</i> treatment, blood level measurement of the ACTs is not feasible.
14.1 Demonstrate and monitor primaquine safety and efficacy to prevent relapse when combined with schizontocides other than chloroquine.	<input type="checkbox"/> 1. Acceptable as is <input checked="" type="checkbox"/> 2. Requires modification (indicate if regional-specific _Y/ <input checked="" type="checkbox"/> N) <input type="checkbox"/> 3. Delete	<ul style="list-style-type: none"> Move to Strategic Direction 4: Innovation and Research. Functional pharmacovigilance is needed to capture severe adverse events due to PQ.
4. Innovation and Research		<ul style="list-style-type: none"> Facilitator: Dr David Bell
15. Research priorities:		<ul style="list-style-type: none"> Identify gaps and prioritize. Emphasize operational research issues to guide programmes e.g. safe PQ use; importation of <i>P. vivax</i> malaria; develop and validate new measures and tools to prevent transmission of <i>P. vivax</i>. In general, it was felt that the list of research priorities was too generic, and needed refining and then prioritization, to make the best use of the limited research funding available. Please see below points/issues to be considered for each of the suggested research priorities:
a. Develop higher sensitivity diagnostic tools that can better detect sub-patent, latent, and asymptomatic infections and are applicable in the field.	<input type="checkbox"/> 1. Acceptable as is <input checked="" type="checkbox"/> 2. Requires modification (indicate if regional-specific _Y/ <input checked="" type="checkbox"/> N) <input type="checkbox"/> 3. Delete	<ul style="list-style-type: none"> Sub-patent <u>symptomatic</u> infection (below RDT and microscopy density). Information is needed on frequency, and on variation between countries (geographic strains) 'improved' RDTs, +/- introducing e-reader technology, would help to address this problem. A cost-benefit analysis of e-reader introduction should be performed when suitable

		<p>readers (providing a significant drop in limit of detection) are available.</p> <ul style="list-style-type: none"> • Good quality studies of current RDTs across a range of geographic locations are important to quantify the need for more sensitive tests. <p><u>Asymptomatic</u> low-density blood-stage infection:</p> <ul style="list-style-type: none"> • How significant is this clinically (does recrudescence occur)? • How significant is it to transmission (infectivity to mosquitoes)? • What level of detection is needed? (trade-off between sensitivity versus cost and ease-of-use – cost-benefit analysis is needed when suitable tools are available). <p>Latent (liver-stage) infection.</p> <ul style="list-style-type: none"> • Management options depend partly on relapse frequency (need to know this). • Suitable direct biomarkers are not available, and may not be present in sufficient concentration. • It may be feasible to use indirect biomarkers such as antibodies related to vivax infection. A better understanding is needed of the specificity of such biomarkers (e.g. serology) and candidate diagnostic platforms to support them. <ul style="list-style-type: none"> • There is a need for field tests that differentiate between relapse and re-infection. Such tests will be vital for understanding how interventions are impacting on vivax transmission.
<p>b. Develop better drugs, shorter dosing regimens, and accurate point-of-care G6PD testing for targeting hypnozoites.</p>	<p><input type="checkbox"/> 1. Acceptable as is</p> <p><input checked="" type="checkbox"/> 2. Requires modification (indicate if regional-specific <u>_Y/√N</u>)</p> <p><input type="checkbox"/> 3. Delete</p>	<p>More information is needed on the use of current drugs including:</p> <ul style="list-style-type: none"> • CQ resistance • efficacy/safety profiles of ACT alone, and in combination with • PQ regimens: <ul style="list-style-type: none"> • comparison of dose and timing regimens (efficacy and adherence); and • geographical variation of parasite susceptibility to the major dosing regimens (<i>P. vivax</i> variants).
<p>c. Validate ACT co-administered with primaquine therapeutic options for radical therapy.</p>	<p><input type="checkbox"/> 1. Acceptable as is</p> <p><input checked="" type="checkbox"/> 2. Requires modification (indicate if regional-specific <u>_Y/√N</u>)</p> <p><input type="checkbox"/> 3. Delete</p>	<p>New drugs:</p> <ul style="list-style-type: none"> • cost-benefit of tafenoquine introduction; • a target product profile for what an ideal anti-vivax drug would look like; and • blood and liver stage, short course, etc. <p>Management of severe vivax:</p> <ul style="list-style-type: none"> • drug management • fluid management • supportive care etc. <p>Drug safety - G6PD</p> <p>A review and cost-benefit analysis of various testing/management options would be useful to</p>

		<p>guide future policy:</p> <ul style="list-style-type: none"> • point of care (POC) testing • centralized (one-off) testing and recall of data • mapping of variants and regionally-specific regimens (PQ or no PQ) • combinations of above.  <p>Modeling questions: Cost-benefits of various options, which will vary with population frequency of G6PD deficiency.</p>
<p>d. Determine appropriate IPT approaches for pregnant women and infants.</p>	<p><input type="checkbox"/> 1. Acceptable as is</p> <p><input checked="" type="checkbox"/> 2. Requires modification (indicate if regional-specific <u>Y/√N</u>)</p> <p><input type="checkbox"/> 3. Delete</p>	<p>Impact of symptomatic and sub-patent infection in pregnancy is unclear. More data would guide decisions on IPT_p, IPT_i regimens:</p> <ul style="list-style-type: none"> • impact (recrudescence, relapse) • safety feasibility
<p>e. Develop improved drug screening assays.</p>	<p><input type="checkbox"/> 1. Acceptable as is</p> <p><input checked="" type="checkbox"/> 2. Requires modification (indicate if regional-specific <u>Y/√N</u>)</p> <p><input type="checkbox"/> 3. Delete</p>	<p>Drug screening is limited by an inability to maintain <i>P. vivax</i> in prolonged culture. Clarity is needed on priorities: should investment be in new technologies (e.g. culture – expensive and high risk), or in better strategies for use of in-vivo monitoring and trials? Guidance on health system responses to evidence of resistance could also be clearer.</p>
<p>f. Develop continuous in vitro cultivation of <i>P. vivax</i> blood and liver stages.</p>	<p><input type="checkbox"/> 1. Acceptable as is</p> <p><input checked="" type="checkbox"/> 2. Requires modification (indicate if regional-specific <u>Y/√N</u>)</p> <p><input type="checkbox"/> 3. Delete</p>	<p>This would enable development of improved drug screening, diagnostics development, and pathophysiological understanding.</p> <p>The feasibility and potential costs versus resource use elsewhere need to be understood before this is prioritized.</p>
<p>g. Define site-specific role of vector species and behavioural traits.</p>	<p><input type="checkbox"/> 1. Acceptable as is</p> <p><input checked="" type="checkbox"/> 2. Requires modification (indicate if regional-specific <u>Y/√N</u>)</p> <p><input type="checkbox"/> 3. Delete</p>	<p>Need to define what further knowledge is required on the main vector species. Priorities include:</p> <ul style="list-style-type: none"> • changes in distribution associated with ecological changes (forest loss etc.) • indoor / outdoor biting • insecticide resistance. <p>This should include evaluation of the effectiveness of interventions</p>
<p>h. Increase <i>P. vivax</i> epidemiological studies to obtain accurate data on its presence and distribution of strains with different relapse rates.</p>	<p><input type="checkbox"/> 1. Acceptable as is</p> <p><input checked="" type="checkbox"/> 2. Requires modification (indicate if regional-specific <u>√Y/_N</u>)</p> <p><input type="checkbox"/> 3. Delete</p>	<p>Main priorities are:</p> <ul style="list-style-type: none"> • Relapse rates and incubation periods versus strain/geography <ul style="list-style-type: none"> • Proportion of infections due to relapse versus re-infection? • Relative transmissibility of each? <p>Implication of different <i>P. vivax</i> strains for control and elimination programmes.</p>

<p>i. Perform robust estimates of morbidity and mortality burdens from key endemic zones.</p>	<p><input type="checkbox"/> 1. Acceptable as is <input checked="" type="checkbox"/> 2. Requires modification (indicate if regional-specific _Y/<input checked="" type="checkbox"/>N) <input type="checkbox"/> 3. Delete</p>	<p>This should involve both health system strengthening (presorting) and specific studies, including morbidity /mortality and:</p> <ul style="list-style-type: none"> • Geographical variation • Impact of co-morbidities • Management of severe vivax disease <ul style="list-style-type: none"> • Drug therapy • Fluid management etc.
<p>j. Conduct research to better understand <i>P. vivax</i> pathophysiology.</p>	<p><input type="checkbox"/> 1. Acceptable as is <input checked="" type="checkbox"/> 2. Requires modification (indicate if regional-specific _Y/<input checked="" type="checkbox"/>N) <input type="checkbox"/> 3. Delete</p>	
<p>k. Perform operational research on combinations of interventions to be used in different settings and how they should be delivered.</p>	<p><input type="checkbox"/> 1. Acceptable as is <input checked="" type="checkbox"/> 2. Requires modification (indicate if regional-specific <input checked="" type="checkbox"/>Y/_N) <input type="checkbox"/> 3. Delete</p>	<p>Operational research, where needed, supplemented by modeling, e.g.</p> <ul style="list-style-type: none"> • G6PD variants and actual risk (real or perceived?). • Strategies for seasonal MDA with radical cure. • Implications of different <i>P. vivax</i> strains for control and elimination strategies. • Cost versus impact: adherence to current PQ regimens versus costs of PQ and G6PD. • How to improve patient adherence to primaquine, and how to implement directly observed treatment (DOT). <p>Current course of declining transmission (slow decline in comparison to <i>P. falciparum</i>). Is reported decline in vivax incidence slowed by relapse, but destined to go the same way with maintenance of current interventions?</p>
		<p>Others: What would a vivax vaccine look like?</p> <ul style="list-style-type: none"> • Not getting on the board of current priorities. Culture likely to be essential first?
<p>5. Advocacy and Government</p>		<p>Facilitator: Ms Cecilia Hugo</p> <p>Change “government” to “governance”</p>
<p>16.1 Increase the visibility of policy and practice of <i>P. vivax</i> control as a key component of overall malaria control and elimination strategic plan.</p>	<p><input type="checkbox"/> 1. Acceptable as is <input checked="" type="checkbox"/> 2. Requires modification (indicate if regional-specific _Y/<input checked="" type="checkbox"/>N) <input type="checkbox"/> 3. Delete</p>	<ul style="list-style-type: none"> • Adequately include <i>P. vivax</i> in the national strategic plans • Should include partnerships with private sectors and public health legislation (under existing legal frameworks). • Official statement on <i>P. vivax</i> needed from the Region for political support. • Include <i>P. vivax</i> relapse in advocacy messages, or elimination plans. • Separate technical and non-technical issues for advocacy. • Ensure adequate inclusion of <i>P. vivax</i> in GTS and GMAP2. <p>Building business case for <i>P. vivax</i> is needed especially in the context of elimination.</p>

16.2 Recognize that in areas currently in the malaria pre-elimination and elimination phases, <i>P. vivax</i> is often the predominant malaria species; therefore the need to continue financing.	<input type="checkbox"/> 1. Acceptable as is <input checked="" type="checkbox"/> 2. Requires modification (indicate if regional-specific <input checked="" type="checkbox"/> Y/ <input type="checkbox"/> N) <input type="checkbox"/> 3. Delete	<ul style="list-style-type: none"> Financing is needed not just for elimination but also in control and pre-elimination phases (e.g. financing of G6PD tests). Tools required to support building a business case (e.g. cost-benefit analysis, cost per death averted).
Does the guidance document reflect the <i>P. vivax</i> priority issues of the Region?	Subject to the clauses highlighted above.	
16.3 Invest in research, development and implementation of <i>P. vivax</i> -specific interventions.	<input checked="" type="checkbox"/> 1. Acceptable as is <input type="checkbox"/> 2. Requires modification (indicate if regional-specific <input type="checkbox"/> Y/ <input checked="" type="checkbox"/> N) <input type="checkbox"/> 3. Delete	

Additional guidance not captured by the *P. vivax* document:

Community advocacy	(indicate if regional specific <input type="checkbox"/> Y/ <input checked="" type="checkbox"/> N)	Reasons: Sustaining community support for achieving elimination and preventing re-introduction and resurgence.
Health systems issues	(indicate if regional specific <input type="checkbox"/> Y/ <input checked="" type="checkbox"/> N)	Reasons: While health system issues are important for malaria overall, there are specific issues with management of primaquine adherence and laboratory testing for <i>P. vivax</i> and G6PD deficiency.

3. CONCLUSIONS AND RECOMMENDATIONS

P. vivax has long been an important parasite in the Western Pacific Region, with major unresolved issues affecting *P. vivax* control and elimination, especially regarding the non-use of primaquine in half of the affected countries due to G6PD deficiency issues. In addition, there are number of different *P. vivax* strains with very different incubation periods and relapse behavior which requires different programmatic approaches.

Development of the WHO Technical Briefing on *P. vivax* is a timely and important initiative for the Region. Regional specificities should be highlighted in the document. Of particular importance, this document fulfills an important advocacy function for *P. vivax* and should also clearly list the research priorities to achieve control and elimination of *P. vivax*.

Annex 1. Agenda

Western Pacific Regional Consultation on the WHO Technical Briefing on *Plasmodium vivax* Control and Elimination

Room 210, WHO Regional Office for the Western Pacific, Manila, Philippines
9 June 2014

AGENDA

Meeting objective: review and provide feedback on the draft WHO Technical Briefing on *Plasmodium vivax* Control and Elimination.

08:00 – 08:30	Registration	
08:30 – 08:50	Opening session	Dr Shin Young-soo, WHO Regional Director for the Western Pacific
	Setting the scene	
08:50 – 09:00	Global scenario and importance of the vivax malaria technical briefing	Dr John Reeder, Acting Director GMP/WHO
09:00 – 09:10	Overview of the WHO Technical Briefing on <i>Plasmodium vivax</i> Control and Elimination	Dr. Kevin Baird, Chair of the Vivax Malaria Steering Committee
09:10 – 09:20	Overview of <i>Plasmodium vivax</i> in the Western Pacific Region	Dr. Eva Christophel, MVP unit WHO Western Pacific Regional Office
09:20 – 09:30	Discussion	
09:30 – 10:00	<i>Group photo</i> <i>Coffee/tea break</i>	
	Vivax malaria country landscapes from the Western Pacific Region	
10.00 – 10.05	Introduction to country landscapes	Dr Gao Qi
10:05 – 10:15	Cambodia	National Programme
10:15 – 10:25	China	National Programme
10:25 – 11:00	Discussion	Moderator: Dr Gao Qi

**Review of the key elements of the WHO
Technical Briefing on *Plasmodium vivax*
Control and Elimination** (plenary
discussion, with on screen summary of key
points)

11:00 – 11:05	Introduction to the review session	Dr Eva Christophel
11:05 – 12:30	Strategic Element 1: Surveillance and Response	Facilitator: Dr Lasse Vestergaard
12:30 – 13:30	<i>Lunch Break</i>	
13:30 – 14:15	Strategic Element 2: Preventing Cases and Reducing Transmission	Facilitator: Dr Rabindra Abeyasinghe
14:15 – 15:00	Strategic Element 3: Case Management	Facilitator: Dr Kevin Baird
15:00 – 15:30	<i>Coffee/ tea break</i>	
15:30 – 16:15	Strategic Element 4: Innovation and Research	Facilitator: Dr David Bell
16:15 – 17:00	Strategic Element 5: Advocacy and Governance	Facilitator: Ms Cecilia Hugo
17:00 – 17:15	Summary of key regional inputs and way forward	Dr Eva Christophel, MVP WHO Western Pacific Regional Office
17:15 – 17:30	Closing session	Dr John Reeder, GMP

Annex 2. List of participants

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