MALARIA ERADICATION WITHIN A GENERATION

The Lancet Commission on malaria eradication

Supporting new product availability: Early experience with tafenoquine regulation

In September 2019, the Lancet Commission on malaria eradication published the first comprehensive, peer-reviewed academic document to examine the scientific, operational, and financial challenges on the path to eradication and identify solutions that will enable us to achieve a world free of malaria within a generation. The report addresses a bold proposition: malaria, one of the most ancient and deadly diseases of humankind, can and should be eradicated by 2050. The Commission provided recommendations across ten thematic areas – ranging from improving data for decision-making to leveraging the private sector to increasing domestic financing – for countries to consider as they refine their malaria strategies and strive towards elimination.

The UCSF Secretariat of the Commission has developed a series of briefings illustrating the experiences of countries that are already successfully operationalizing the approaches recommended by the Commission, thus helping to accelerate the trajectory to malaria eradication. The briefings are intended to increase the visibility of country leadership and innovation and demonstrate practical application of the Commission's recommendations.

Introduction

The report of the *Lancet* Commission on malaria eradication (LCME) asserts that by strengthening management and operations, improving the use of existing tools, developing and deploying new tools, and spending US$ 2 billion more per year, malaria eradication can be achieved within a generation.[1] Great progress toward eradication has been made in the last two decades; since 2000, 21 countries have eliminated malaria transmission with currently available tools.[2] However, both the Commission report and the report from WHO's Strategic Advisory Group on Malaria Eradication (SAGme)[3] contend that innovative new tools and strategies will be essential for eradication, particularly in areas with the highest burdens and complex transmission dynamics. Supporting new product availability through research, development, regulatory approval, and deployment of new tools at scale requires substantial, ongoing investment in order to overcome the numerous biological challenges of malaria.[1] The reports emphasize the need for a robust research and development pipeline and the importance of bridging the regulatory gap between development and operationalization of new tools.[1,3] Focus tends to be on how global processes can improve the regulatory gap, but the role of country-level regulation is also important, often overlooked, and must be prioritized. This need is reinforced in the findings of a recent study on barriers and challenges related to introducing new tools, in which interviews with representatives from malaria-endemic countries were conducted and "interviewees recognized that regulatory processes are often slow, bureaucratic and may create bottlenecks in the timely deployment of innovations."[4] Stakeholders must consider existing policies and regulatory pathways as well as operational conditions in individual countries to ensure that new tools and products are safe, quality assured, appropriate for use, and have been approved by relevant agencies at national, regional, and/or global levels.

Support new product availability

Research, development, innovation, and the rapid deployment of new tools are essential for national and regional elimination and global eradication. Well before a new product becomes available, it is essential that countries consider the policy and operational implications, including regulatory pathways, use-scenarios, and financing options. It is also critical that drugs, insecticides, and other commodities are quality assured.

– *Lancet* Commission on malaria eradication[1]

Lengthy regulatory processes risk undermining momentum toward eradication, and speeding up the regulatory pathway while maintaining safety and quality standards is of utmost priority, especially in light of the recent stagnation in progress in high burden countries.[2,5] The LCME report recommends supporting new tool and product availability in malaria endemic countries by initiating early policy discussions, modelling, and implementation research on use case scenarios and financing; instituting expedited approval processes at regional and global levels; and matching need with innovation through the fostering of public-private partnerships.[1] In

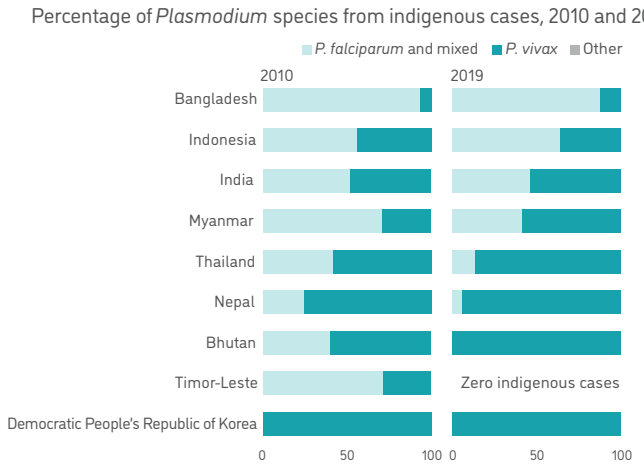
addition, the rapid development and approval of several COVID-19 vaccines in 2020-2021 demonstrate that regulatory processes can be made more efficient when there is a sense of collective urgency. Researchers are documenting the changes that have facilitated this acceleration, such as conducting different phases in parallel, using adaptive study designs, improving communication, and adopting innovative strategies for harmonization across entities globally to avoid duplication.[6] The COVID-19 vaccine experience presents an opportunity for the global regulatory community to make a seismic, systemic shift toward more coordinated international collaboration to ensure that future vaccines, drugs, and diagnostics reach populations quickly.

This briefing focuses on the regulatory aspects of a new product, using single-dose tafenoquine as a case study. The early rollout of tafenoquine for the radical cure of *Plasmodium vivax* malaria, the most recent malaria drug to receive approval, is an example of how to operationalize accelerated access to a new life-saving product. Although the implementation of tafenoquine is still in a nascent stage, the drug's approval processes offer potential lessons for other new and emerging malaria tools and products.

Progress toward radical cure for *P. vivax*

Some of the biggest biological challenges to eradicating malaria – containment of antimalarial drug resistance and eliminating all parasite lifecycle stages – require drug-based solutions. Several drugs and drug combinations to overcome these challenges are currently in the development pipeline. Single-dose tafenoquine (300 mg) is indicated for radical cure of *P. vivax* malaria by treating hypnozoites, the dormant liver-stage form of *P. vivax* responsible for relapsing infections. Hypnozoites evade detection with current diagnostics and are unaffected by the most commonly prescribed blood-stage antimalarials. Currently, WHO recommends a 14-day primaquine regimen with glucose-6-phosphate dehydrogenase (G6PD) testing. However, a regimen as long as 14 days often presents patient adherence challenges. A single dose of tafenoquine in combination with G6PD point-of-care screening has potential to overcome this limitation of primaquine and transform *P. vivax* case management, particularly in Asia Pacific and the Americas where *P. vivax* remains a significant challenge.[7] From 2000 to 2019, malaria cases fell by 90% in the Greater Mekong Subregion

Figure 1. P. vivax increasingly accounts for the majority of malaria cases in Asia Pacific.

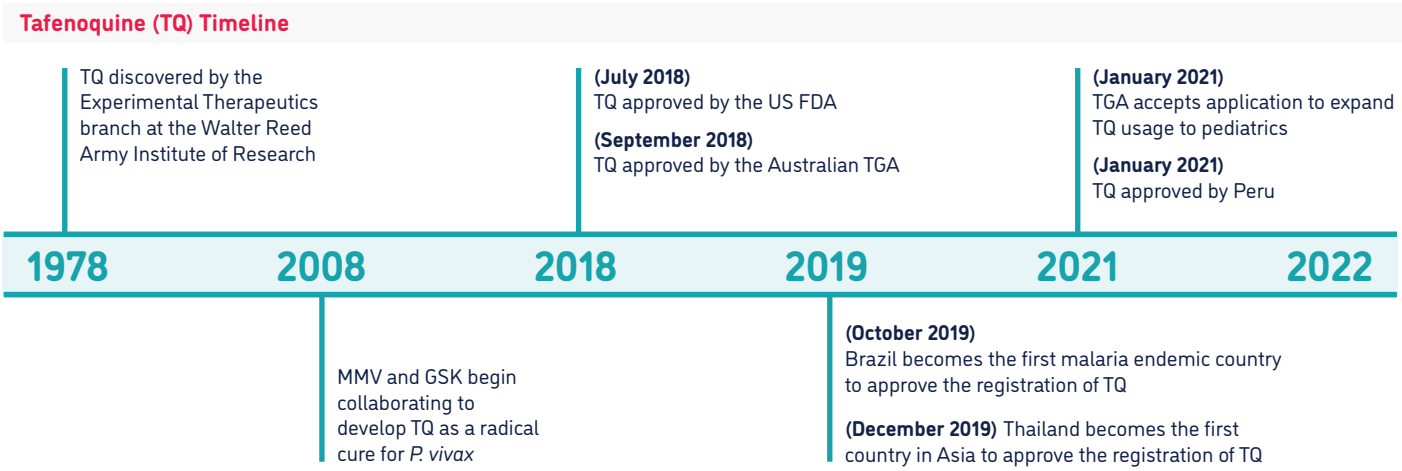


Source: World Malaria Report 2020

(GMS) and the remainder of cases are increasingly *P. vivax*, as shown in Figure 1.[2] It is estimated that 46% of malaria cases in the GMS are now *P. vivax* and in some countries, such as Thailand, *P. vivax* cases are the overwhelming majority.[2] Similarly, in Latin America, *P. vivax* is the predominant form of malaria, accounting for 76% of all cases, with the majority concentrated in Brazil, Colombia, and Venezuela.[2]

Tafenoquine was first discovered in 1978 as part of the US Army's efforts to find alternatives to chloroquine and primaquine.[32] Several entities joined the US Army, particularly the Australian military, and spent several decades researching its potential (Figure 2).[8] In 2008, Medicines for Malaria Venture (MMV) began formally collaborating with GlaxoSmithKline (GSK) to develop tafenoquine as a radical cure for *P. vivax*. Single-dose tafenoquine was granted "orphan-drug designation" and "breakthrough designation" by the US Food and Drug Administration (FDA) in 2013.[9] Orphan-drug designation means that a drug treats a condition that is rare enough that the government provides some financial incentive and breakthrough designation is granted to help expedite a drug's development and review when early clinical evidence suggests it could be a significant improvement to existing therapies.[10] In 2018, ten years after the start of GSK and MMV's collaboration, Priority Review Designation was sought for 300mg single-dose tafenoquine.[9] The designation is an indication of the profound contribution that regulators expect a drug to make, and shortens the US FDA dossier review from the typical ten months

Figure 2. Timeline of tafenoquine's development and registration approval pathway.



down to just six months. In July 2018, single-dose tafenoquine for radical cure was approved by the US FDA, making it the first new drug introduced for *P. vivax* treatment in over six decades – a significant milestone.[11,12] The Australian Therapeutic Goods Administration (TGA) approved single-dose tafenoquine shortly after, in September 2018.[13] Because of the stringent criteria of the US FDA and Australian TGA, these consecutive approvals served as an important endorsement of the drug for regulatory agencies in malaria endemic countries. Increased attention was placed on securing tafenoquine's registration in malaria endemic countries and supporting expedited processes while maintaining safety and quality standards. In October 2019, Brazil became the first malaria endemic country to approve the registration of tafenoquine,[14] followed shortly thereafter by Thailand in December 2019[15,26] and Peru in January 2021.[16] Tafenoquine Marketing Authorization Applications are under review in a number of other endemic countries to bring the drug to market.

Despite the potential impact of single-dose tafenoquine on *P. vivax* elimination, noteworthy challenges remain ahead of implementation. Like primaquine, tafenoquine is an 8-aminoquinoline class drug and poses a risk of hemolysis in individuals with G6PD deficiency, the most common enzyme deficiency worldwide.[17] An estimated 400 million people have G6PD deficiency, often unbeknownst to them, and both prevalence and severity vary by region, ethnic group, and sex.[18-20] Thus the recommended standard of care prior to administration of an 8-aminoquinoline class drug is a G6PD test. For tafenoquine in particular, this will be a requirement, so point-of-care G6PD testing is key to the successful deployment of tafenoquine. Enormous strides have been made on this front recently, with a semi-quantitative point-of-care G6PD analyzer recently approved by the Australian TGA in May 2021. However, the complexity of this diagnostic device, its cost, and integration as an additional step in the patient pathway means careful consideration is needed to determine how to ensure its access where patient caseloads are highest. A number of partners are working on this, including MMV which recently began a Unitaid-funded project that plan to involve feasibility studies of semi-quantitative point-of-care G6PD testing in Ethiopia, India, Indonesia, Myanmar, Papua New Guinea, and Peru to inform primaquine and tafenoquine regimens. It is expected that the project will lead to an additional 1.1 million patients receiving optimized radical cure by 2029 as well as new insights on feasibility.[23]

Roadmap for the regulatory approval and introduction of Tafenoquine in Thailand

Thailand is a leading example of how a country prepares for the adoption of new tools such as tafenoquine. Recognizing the catalytic potential of tafenoquine in its mission to eliminate malaria by 2024, Thailand leveraged the Indo-Pacific Regulatory Strengthening Program to initiate collaboration between the Thai FDA and the Australian TGA to expedite the regulatory review process of tafenoquine.[15] Assistance from technical experts and assessment reports from the TGA supported the Thai FDA's evaluation of the submitted evidence and enabled a fast-tracked review.[24] The Regulatory Strengthening Partnership for Malaria Elimination, led in 2018 by the Asia Pacific Leaders Malaria Alliance (APLMA) and other partners, helped facilitate this partnership between Thailand and Australia.[15]

While the Thai FDA reviewed the tafenoquine dossier, the Thailand Ministry of Public Health organized an orientation to sensitize health care workers to new products, including single-dose tafenoquine and also began exploring an update to the malaria treatment guidelines.[15,25] The registration approval of tafenoquine by the Thai FDA in December 2019 enabled the Division of Vector-Borne Diseases to plan a study on the feasibility of administering tafenoquine in tandem with G6PD point-of-care testing.[15,24,26] The study has been delayed due to the COVID-19 pandemic, but is anticipated to start in October 2021.[26] As the first country in Asia Pacific to assess the feasibility of tafenoquine implementation throughout the health system, Thailand is leading the way in positioning the region for adoption of radical cure for *P. vivax*.

Regional partners are ensuring that best practices on expediting the regulatory approval and adoption of new tools are shared widely with other countries. In collaboration with the Thailand Ministry of Public Health and other partners, APLMA published a roadmap for introducing radical cure for *P. vivax*[24] accompanied by an access tracker (Figure 3) that illustrates key milestones for accelerating access, although some milestones may require adjustment in light of the COVID-19 pandemic. Creating an enabling environment for adoption of new tools, like tafenoquine, requires resource mobilization, development of standard operating procedures, and other key steps, necessitating strong political will and the participation of many government agencies. The access tracker delineates the multisectoral, coordinated approach needed to ensure continued pre-positioning for the successful roll-out and scaling of tafenoquine in Thailand.

Thailand's commitment to an accelerated timetable for registration of tafenoquine aims to close the gap between licensure of tafenoquine, routine use, and scale-up. Other countries can learn from Thailand's efficient approach with tafenoquine to ensure new drugs, diagnostics, vaccines, and vector control tools are suitable for the context, delivered appropriately, and operationalized expediently.

Examining the feasibility of Tafenoquine in Latin America

The Brazilian Health Regulatory Agency gave marketing authorization approval of tafenoquine in October 2019, making it the first malaria endemic country worldwide, and the first country in Latin America, to register tafenoquine.[14,27] In partnership with MMV, Brazil's Ministry of Health is planning a feasibility study known as the Tafenoquine Roll-oUt STudy (TRuST) to start in 2021.[26] Similar to work underway in Thailand, the goal of TRuST is to better understand the feasibility of providing appropriate radical cure (tafenoquine or primaquine) based on results of point-of-care G6PD testing to inform the inclusion of tafenoquine within Brazil's Unified Health System. Implemented in the municipalities of Manaus and Porto Velho, the outcomes of TRuST will guide the Ministry of Health in developing treatment guidelines for tafenoquine in *P. vivax*-endemic areas.[14,27] Additionally, Brazil is conducting cost-effective studies, expected to be completed in November 2021 and has also modelled the potential impact of integrating tafenoquine into malaria case management protocols.[28,29]

The study outcomes in Brazil will likely also help inform regulatory and deployment processes in other countries in the region. The Peruvian regulatory authority granted approval of tafenoquine for radical cure in early 2021, becoming the second country in Latin America to do so, and along with Brazil and Thailand, Peru took

Figure 3. A tracker developed by the Ministry of Public Health in Thailand and its partners to illustrate the key milestones for meeting Thailand's elimination goal of 2024.

Access Tracker: Milestones for Accelerating Access to Vivax Radical Cure in Thailand

The purpose of the tracker tool is to highlight key milestones required to ensure universal access to appropriate radical cure for vivax in Thailand, considering the country's goal of eliminating all strains of malaria by 2024. The Tracker is designed to be used together with the Access Roadmap by APLMA and other stakeholders to advocate with senior officials within and beyond the Ministry of Health to address possible roadblocks to achieving these milestones in order to achieve elimination by 2024.

Milestones		2020				2021				2022				2023				2024			
		Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
Elimination targets	Universal access to radical cure achieved with multiple options including TQ & quantitative G6PD																				
	Malaria eliminated																				
Approvals	Tafenoquine approved by Thai FDA (Dossier submitted March 2019.)																				
	Ethics approval for feasibility studies (MMV & UCSF supported)																				
Feasibility (All planned feasibility studies will include specific focus on pharmacovigilance)	Assess feasibility of TQ & quantitative G6PD at multiple levels of the health system (Yala province) w/ MMV																				
	Assess PQ14 with quantitative G6PD at community level in 5 provinces (West & East, not Yala), with UCSF funded by RAI2																				
	Assess feasibility of PQ7 with quantitative G6PD assessed at all levels including community (with support from RAI3 tentatively)																				
Guidelines & Strategy	Evidence review to interpret feasibility findings and inform possible guideline updates																				
	National treatment guidelines updated consistent with WHO guidance & feasibility study findings																				
	Model/s of radical cure selected for all levels of health system consistent with feasibility learnings; quantification of TQ & QN G6PD product needed																				
Safe Scaling of Appropriate Radical Cure (consistent with feasibility findings)	SOPs developed including user & provider materials (adapt study tools)																				
	Health provider cascade training and post-training quality assurance support																				
	Assess and address community health facility capacity to respond to AHA																				
	Pharmacovigilance plan rolled out with Health Products Vigilance Center/Thai FDA (higher level health facilities) and DVBD (malaria clinics only), technical support from GSK: AEs routinely reported.																				
	Shift to prevention of reestablishment: quantify need in receptive and vulnerable areas and adjust service delivery accordingly																				
Surveillance	Surveillance (online) forms/system reviewed and revised if needed based on feasibility findings: particularly for follow-up forms & G6PD testing																				
Financing	Proportion of total annual malaria program costs (including vivax radical cure) covered by national budget support monitored																				
	Secure RAI3 support for radical cure and elimination activities																				
	Explore PMI funding opportunities in collaboration with research agencies																				

part in clinical studies of tafenoquine. The Peru Ministry of Health continues to collaborate with the Universidad Peruana Cayetano Heredia to assess the operationalization of tafenoquine at various levels of the Peruvian health system.[16]

Partnerships to accelerate innovation and access of new tools

As the LCME report notes, close collaborations within and between the public and private sectors are essential to ensure that scientific progress is harnessed as an aid to innovation and access. MMV and GSK have exemplified this in their partnership on single-dose tafenoquine. Additionally, MMV has taken their support one step further by collaborating with PATH on VivAccess, the main goal of which is to accelerate operational research, implementation research, and subsequent introduction and scale-up of well-tolerated radical cure of *P. vivax* malaria.[30] In October 2020, VivAccess helped host a virtual gathering of researchers and policymakers across Brazil, Colombia, and Peru to facilitate a collaborative approach to exploring new tools, including tafenoquine, to achieve regional elimination goals.[31] The work of VivAccess in ensuring that countries are supported in the uptake and implementation of existing tools and new ones, such as tafenoquine, embodies the LCME report recommendations. By providing market analytics, technical expertise, support for in-country research studies, and product delivery coordination, VivAccess is engaging strategically with partners to increase emphasis on high quality vivax case management, and working nationally to pave the way for a smooth and quick uptake of new tools as they are approved and recommended by WHO.[30]

Conclusion

The LCME report highlights the numerous regulatory obstacles that products in the development pipeline must overcome before they become available for widespread use. As seen in the case of single-dose tafenoquine, there are examples of regulatory processes becoming more synergistic and efficient, but most remain country-specific, lengthy, and uncoordinated, thus posing a barrier for public access to life-saving products. However, a new precedent has been set with the COVID-19 pandemic and emergency approvals for vaccines. The speed with which several new vaccines have been approved and deployed globally during the COVID-19 pandemic demonstrates what is achievable when stakeholders collectively prioritize access to new lifesaving tools. Re-examination of national regulatory approval processes, with an emphasis on regional streamlining can provide an opportunity for the countries of Asia Pacific and Latin America to reach national and regional malaria elimination goals, setting the stage for a malaria-free world.

References

1. Feachem RGA, Chen I, Akbari O, et al. Malaria eradication within a generation: ambitious, achievable, and necessary. *Lancet* 2019; 394: 1056–112.
2. WHO Global Malaria Programme. World Malaria Report 2020: 20 years of global progress and challenges. Geneva: World Health Organization, 2020 https://www.who.int/publications/i/item/9789240015791 (accessed December 2020).
3. WHO Strategic Advisory Group on Malaria Eradication. Malaria eradication: benefits, future scenarios & feasibility. Geneva: World Health Organization, 2020 https://www.who.int/publications-detail/malaria-eradication-benefits-future-scenarios-feasibility (accessed April 2020).
4. RBM. Innovation and Access in Malaria Programmes: A Snapshot of Perspectives from Malaria Affected Countries. Roll Back Malaria, 2021 https://endmalaria.org/related-material/innovation-and-access-malaria-programmes-snapshot-perspectives-malaria-affected (accessed March 2021).
5. PATH. Bridging the gaps in malaria R&D: An analysis of funding-from basic research and product development to research for implementation. Seattle: PATH; 2018 https://www.malariavaccine.org/resources/reports/investigating-second-valley-of-death-malaria-rd (accessed March 2021).
6. Defendi HGT, da Silva Madeira L, Borschiver S. Analysis of the COVID-19 vaccine development process: an exploratory study of accelerating factors and innovative environments. *J Pharm Innov* 2021; 1-17.
7. Campo B, Vandal O, Wesche DL, Burrows JN. Killing the hypnozoite – drug discovery approaches to prevent relapse in *Plasmodium vivax*. *Pathog Glob Health* 2015; 109(3): 107-122.
8. Soares JM. USAMMDA Celebrates FDA Approval of Antimalarial Drug Tafenoquine. October 26th, 2018.https://www.army.mil/article/212996/usammda_celebrates_fda_approval_of_antimalarial_drug_tafenoquine (accessed May 2021).
9. Center for Drug Evaluation and Research. NDA 210-795: Tafenoquine for the prevention of relapse (radical cure) of *P. vivax* malaria. January 19th, 2018. https://www.accessdata.fda.gov/drugsatfda_docs/nda/2018/210795Orig1s000TherR.pdf (accessed May 2021).
10. US Food and Drug Administration. Breakthrough Therapy, January 4th, 2018. https://www.fda.gov/patients/fast-track-breakthrough-therapy-accelerated-approval-priority-review/breakthrough-therapy (accessed May 2021).
11. MMV. Press release: US FDA approves Krintafel (tafenoquine) for the radical cure of *P. vivax* malaria. July 20th, 2018. https://www.mmv.org/newsroom/press-releases/us-fda-approves-krintafel-tafenoquine-radical-cure-p-vivax-malaria (accessed May 2021).
12. US Food and Drug Administration. Drug Approval Package: KRINTAFEL (tafenoquine). 20 July 2018. https://www.accessdata.fda.gov/drugsatfda_docs/nda/2018/210795Orig1s000TOC.cfm (accessed May 2021).

13. GSK. Press release: Kozenis (tafenoquine) approved by the Australian Therapeutic Goods Administration for the radical cure of *P. vivax* malaria. September 21st, 2018. https://www.gsk.com/en-gb/media/press-releases/kozenis-tafenoquine-approved-by-the-australian-therapeutic-goods-administration-for-the-radical-cure-of-p-vivax-malaria/ (accessed May 2021).

14. da Silva Júnior JG. Article: Malaria treatment will have a new drug in Brazil. December 12th, 2019. https://portal.fiocruz.br/en/news/malaria-treatment-will-have-new-drug-brazil (accessed May 2021).

15. APLMA. Blog: A big step towards malaria elimination: Thailand approves new radical cure for vivax malaria. April 28th, 2020. https://www.aplma.org/blogs/a-big-step-towards-malaria-elimination-thailand-approves-new-radical-cure-for-vivax-malaria (accessed May 2021).

16. *P. vivax* information hub. Article: New single-dose medicine to prevent relapse of *P. vivax* malaria just approved in Peru. January 18th, 2021. https://www.vivaxmalaria.org/news/new-single-dose-medicine-to-prevent-relapse-of-p-vivax-malaria-just-approved-in-peru (accessed May 2021).

17. Dean L, Kane M. Tafenoquine Therapy and G6PD Genotype. 2020 Oct 13. In: Pratt VM, Scott SA, Pirmohamed M, et al., editors. Medical Genetics Summaries [Internet]. Bethesda (MD): National Center for Biotechnology Information (US); 2012-. https://www.ncbi.nlm.nih.gov/books/NBK562890/ (accessed May 2021)

18. Howes RE, Piel FB, Patil AP, et al. G6PD deficiency prevalence and estimates of affected populations in malaria endemic countries: a geostatistical model-based map. *PLoS Med* 2012; 9(11): e1001339.

19. Sathupak S, Leecharoenkiat K, Kampuansai J. Prevalence and molecular characterization of glucose-6-phosphate dehydrogenase deficiency in the Lue ethnic group of northern Thailand. *Sci Rep* 2021; 11(1): 1-9.

20. Ruwende C, Khoo SC, Snow RW, et al. Natural selection of hemi- and heterozygotes for G6PD deficiency in Africa by resistance to severe malaria. *Nature* 1995; 376(6537): 246-249.

21. Domingo GJ, Advani N, Satyagraha AW, et al. Addressing the gender-knowledge gap in glucose-6-phosphate dehydrogenase deficiency: challenges and opportunities. *Int Health* 2019; 11(1): 7-14.

22. Anderle A, Bancone G, Domingo GJ, et al. Point-of-care testing for G6PD deficiency: opportunities for screening. *Int J Neonatal Screen* 2018; 4(4): 34.

23. Unitaid. Better tools for the diagnosis and treatment of *Plasmodium vivax* malaria. https://unitaid.org/project/better-tools-for-the-diagnosis-and-treatment-of-plasmodium-vivax-malaria/#en (accessed May 2021).

24. APLMA. Roadmap to accelerating radical cure for vivax malaria in Thailand. https://aplma.s3.ap-southeast1.amazonaws.com/aplma/assets/65te5n3J/thailand_policy_roadmap_accelerating_access_to_radical_for_p-_vivax.pdf (accessed May 2021).

25. Email correspondence with APLMA on May 19th, 2021.

26. Email correspondence with MMV on May 17th, 2021.

27. MMV. Press release: Brazil becomes first malaria-endemic country to approve single-dose tafenoquine (Kozenis) for radical cure of *P. vivax* malaria October 30th, 2019. https://www.mmv.org/newsroom/press-releases/brazil-becomes-first-malaria-endemic-country-approve-single-dose-tafenoquine (accessed May 2021).

28. MMV. Improving access to tafenoquine, a single-dose treatment of *P. vivax* malaria. February 2021. https://www.mmv.org/access/products-projects/improving-access-tafenoquine-single-dose-treatment-pvivax-malaria (accessed May 2021).

29. Nekkab N, Lana R, Lacerda M, et al. Estimated impact of tafenoquine for *Plasmodium vivax* control and elimination in Brazil: a modelling study. *PLoS Med* 2021; 18(4): e1003535.

30. Health Policy Watch. Article: PATH and MMV launch 5-year global initiative to support elimination of relapsing malaria. April 23rd, 2019. https://www.healthpolicy-watch.org/path-and-mmv-launch-5-year-global-initiative-to-support-elimination-of-relapsing-malaria/ (accessed May 2021).

31. PATH. South American countries meet to discuss rollout of new innovations for malaria elimination. October 30th, 2020. https://www.path.org/media-center/south-american-countries-meet-discuss-rollout-new-innovations-malaria-elimination/ (accessed May 2021).

32. Peters W. The evolution of tafenoquine--antimalarial for a new millennium?. *J R Soc Med* 1999; 92(7): 345-352.

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