

S1 Table. Summary of existing malaria diagnostic TPPs

Four TPPs for malaria diagnostics have been made publicly available from various organizations over the past 5 years. Two TPPs, for case management and screening and surveillance were published by the The Malaria Eradication Research Agenda (malERA) initiative [1]. Preferred characteristics for new technologies are presented in the meeting report of WHO Evidence Review Group on Malaria Diagnosis in Low Transmission Settings [2]. Finally PATH published a draft TPP for active case detection of sub-patent and asymptomatic malaria infections within the frame of the DIAMETER project [3]. The malERA and WHO TPPs are relevant for both *P. falciparum* and *P. vivax* while the PATH DIAMETER TPP is specifically designed for *P. falciparum*.

In addition to these four TPPs, recommendations for new *P. vivax* diagnostics are briefly discussed in the recently released WHO technical brief on the Control and Elimination of *Plasmodium Vivax* Malaria [4]. These are for diagnostic methods that more readily detect parasites in a clinical setting with a sensitivity of 25 p/μL for blood stage *P. vivax* infections as well as diagnostic methods that can detect hypnozoite (liver stage *P. vivax* infections).

	malERA: Diagnoses and Diagnostics (January 2011) [1]		MPAC Session 10 (March 2014) [2]	DIAMETER Project (March 2014) [3]
Intended use	Case Management in Elimination Settings	Screening/Surveillance (District Level or Below)	Detection of parasites in low transmission settings	« Active infection detection interventions aimed at low-density and subclinical infection detection. »
Target analyte	<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	M ^a : HRP2 O ^a : HRP2, one other <i>P. falciparum</i> specific antigen, plus a Pan or <i>Plasmodium vivax</i> antigen
Analytical sensitivity	M: ≤ 200 p/μL O: < 5 p/μL	M ≤ 20 p/μL O: ≤ 5 p/μL	≤ 2 p/μL	M: ≤ 10 p/μL O: ≤ 5 p/μL
Analytical specificity	M: <i>P. falciparum</i> O: <i>P. falciparum</i> / Pan Negative for all pathogens and common blood disorders	M: <i>P. falciparum</i> O: Discriminate all human infection <i>Plasmodium</i> spp., identify hypnozoite and optionally gametocyte Negative for all pathogens and common blood disorders	Detection at genus level with subsequent species differentiation	M: <i>P. falciparum</i> O: <i>P. falciparum</i> / <i>P. vivax</i> / <i>Plasmodium spp.</i>

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Diagnostic sensitivity	M: > 95% O: ≥ 99%	M: > 95% O: ≥ 99%	≥ 95% for <i>Plasmodium</i> genus	M: ≥ 97% O: ≥ 99%
Diagnostic specificity	M: > 90% O: > 95%	M: > 95% O: > 99%	<i>n/a</i>	M: ≥ 90% O: ≥ 99%
Repeatability (inter-operators)	Kappa > 0.9	Kappa > 0.9	<i>n/a</i>	<i>n/a</i>
Operating conditions	<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	M: 20 to 35°C O: 10 to 40°C
Sample type and volume	M: capillary blood from finger prick O: non-invasive	M: capillary blood from finger prick O: non-invasive	≤ 50 µL of blood	M: ≤ 50 µL of capillary blood from finger prick O: ≤ 25 µL of less invasive sample
Assay throughput	<i>n/a</i>	<i>n/a</i>	48 samples / person / platform / day	M: 7 samples / person / platform / hour O: >10 samples / person / platform / hour
Time-to-result	M: > 30 minutes O: > 15 minutes	M: > 2 days O: > half-day	M: > 24 hours O: > 16 hours	M: > 30 minutes O: > 15 minutes
Assay format	Usable at community level Simple, few steps	Usable by medical technician	Automated end-point format, instrument independent Objective reading, easy to interpret Minimum number of steps	Lateral-flow immunochromatographic strip in cassette format. High-contrast, clear results for naked-eye Two (M) or no (O) timed step
Packaging	Individual, moisture-proof, with all required consumable included and temperature violation detection	Moisture-proof, with all required consumable included and temperature violation detection	<i>n/a</i>	O: temperature violation detection
Reagents	All necessary reagent provided	All necessary reagent provided	<i>n/a</i>	All necessary reagent provided
Equipment	All necessary equipment provided	<i>n/a</i>	Portable	Highly portable Battery-powered reader if required No water need
Power requirement	No external power source	<i>n/a</i>	<i>n/a</i>	No external power source

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Transport and storage stability	M: stable at > 35°C for 2 years (incl. 18 months in country) O: stable at > 45°C for 36 months	M: stable at ≤ 30°C for 1 year (incl. 6 months in country) O: stable at ≤ 30°C for 2 years (incl. short period at 45°C)	No transport required below 4°C Stable at 4°C for > 1 year, at RT for > 6 months	M: stable at 2 - 30 °C for 18 months (+ 2 weeks at 40 °C) O: stable at 2 - 40 °C for 36 months (+ 2 weeks at 50 °C)
Control	<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	Internal control line Compatible with positive control well
Connectivity	<i>n/a</i>	<i>n/a</i>	Desirable network connectivity for data transfer	O: Cloud-based, real-time data handling
Training	Half day for community health worker	≤ 1 week for pretrained medical technician	≤ 1 week	M: < 1 day O: < half-day
Biosafety	High blood safety Non-toxic reagents	High blood safety Non-toxic reagents	Low contamination risk No hazardous waste	High blood safety No hazardous waste
Cost	≤ 1 USD / test	≤ 1 USD / test	Affordable	M: ≤ 2 USD / test, no capital cost except for reader O: ≤ 1 USD / test, no capital cost
Comments	“The sensitivity required for <i>P. vivax</i> is generally at least that required for <i>P. falciparum</i> , and the parameters here should be applied to both.”		Analytical sensitivity setting based on one log improvement over expert microscopy to be a "significant improvement"	

^aM: minimal, O: optimal

Supplementary References

1. The malERA Consultative Group on Diagnoses and Diagnostics. A Research Agenda for Malaria Eradication: Diagnoses and Diagnostics. *PLoS Med.* 2011;8: e1000396. doi:10.1371/journal.pmed.1000396.t001
2. World Health Organization. WHO Evidence Review Group on Malaria Diagnosis in Low Transmission Settings [Internet]. 21 Mar 2014 [cited 11 Oct 2015] pp. 1–33. Available: http://www.who.int/malaria/mpac/mpac_mar2014_diagnosis_low_transmission_settings_report.pdf
3. PATH. Target Product Profile: Point-of-Care Malaria Infection Detection Test. In: sites.path.org [Internet]. [cited 25 Jun 2016]. Available: http://sites.path.org/dx/files/2012/11/DIAMETER_IDT_TPP_FINAL_forwebsite.pdf
4. World Health Organization. Control and Elimination of Plasmodium Vivax Malaria. 2015.