PvB2: Population screening for *Plasmodium vivax* infection surveillance

Defining the next generation of *Plasmodium vivax* diagnostic tests for control and elimination: Target product profiles

Xavier C. Ding, Maria Paz Ade, J. Kevin Baird, Qin Cheng, Jane Cunningham, Mehul Dhorda, Chris Drakeley, Ingrid Felger, Dionicia Gamboa, Matthias Harbers, Socrates Herrera, Naomi Lucchi, Alfredo Mayor, Ivo Mueller, Jetsumon Sattabongkot, Arsène Ratsimbason, Jack Richards, Marcel Tanner, Iveth J. González

S4 Table. TPP PvB2: Population screening for *Plasmodium vivax* infection surveillance

Type	Characteristic	Minimal (M) / Description	Optimal (O)	Comment
Scope	Intended use	The test goal is to provide indication of current or recent *P. vivax* infection for epidemiological surveys and surveillance activities not necessarily linked with a direct treatment of positive cases. Therefore, the test needs to accurately detect biomarkers of recent infection or low density erythrocytic forms of *P. vivax* with a high throughput and analytical sensitivity.		
	Test outcome	Inform monitoring efforts to guide response interventions		
	Target population	The target population is any individual susceptible to suffer from a latent infection from *P. vivax*, including children, and pregnant women.		
	Target users	The target users are laboratory operators with a substantial proficiency in laboratory work.		
	Implementation level	The target implementation levels are district hospital as well as reference laboratories [5].		
Performance	Analytical sensitivity	Limit of detection for target analyte corresponding to a peripheral parasitaemia of 0.1 p/µL	Limit of detection for target analyte corresponding to a peripheral parasitaemia of 0.01 p/µL	"O" corresponds to a two-fold improvement compared to current state-of-the art technologies [15,16]. For indirect tests (*e.g.* serology), the analytical sensitivity might not directly relate to parasitaemia.
	Analytical specificity	Discriminate between *P. vivax* and other *Plasmodium spp*. Do not cross-react with any other pathogen infecting humans	Identify all *Plasmodium spp.* and discriminate species. Do not cross-react with any other pathogen infecting humans	A high level of specificity and information content is expected from a specialized laboratory assay.
	Diagnostic outcome	Test-dependant	Test-dependant	A quantitative outcome (parasitaemia level) would be nice-to-have for tests detecting current infections. For indirect test (*e.g.* serology), the outcome might be associated with probability of past infection.
	Diagnostic sensitivity	> 95% as compared to a validated standard with an analytical sensitivity at least equal to the index test	≥ 99% as compared to a validated standard with an analytical sensitivity at least equal to the index test	In line with malERA recommendations (but comparator not specified) [1]. Comparator might need to be adapted for indirect tests (*e.g.* based on serology).

Type	Characteristic	Minimal (M) / Description	Optimal (O)	Comment
	Diagnostic specificity	> 90% as compared to a validated standard with an analytical sensitivity at least equal to the index test	≥ 95% as compared to a validated standard with an analytical sensitivity at least equal to the index test	Comparator might need to be adapted for indirect tests (*e.g.* based on serology).
	Repeatability (inter-operators)	*Kappa* > 0.8	*Kappa* > 0.9	Kappa statistic can be used to evaluate binary outcomes agreement. Suggested values are arbitrary.
	Reproducibility (inter-laboratories)	*Kappa* > 0.7	*Kappa* > 0.9	See *Repeatability*
Operational aspects	Assay format	96-well format assay	384-well format assay or higher	
	Assay throughput	Batch testing in line with assay format	Batch testing in line with assay format	
	Assay packaging	Package of assay-specific components and user manual	Package of all assay components and user manual	
	Operation conditions	15°C – 30°C Up to 60% relative humidity (RH)	15°C – 35°C Up to 90% RH	"M" and "O" reflect expected controlled laboratory conditions in endemic countries [10].
	Transportation and storage stability	≥ 6 months at ≤4°C and 60% RH, transport at ≤4°C acceptable	≥ 12 months at 30°C and 90% RH with transport stress (3 days at 60 °C), no cold chain needed	"M" reflects laboratory conditions that can be relatively easily achieved in endemic countries.
	In use stability	> 30 minutes	> 1 hour	For batch testing, this characteristics is likely to impact the assay throughput.
	Reagents reconstitution	Reconstitution of reagent acceptable	All reagents provided and ready to use.	
	Equipment	Transportable (≤ 20 kg)	Portable (≤ 5 kg)	

Type	Characteristic	Minimal (M) / Description	Optimal (O)	Comment
	Power requirement	Power supply, if needed, adapted for the voltage type found in *P. vivax* endemic countries	Battery operated with ≥ 24 hours testing autonomy	
	Maintenance	≤ once per year	None	
	Sample type	Capillary blood	Capillary blood or any less invasive validated sample	Sample types less invasive than capillary blood include saliva, urine, breath or transdermal detection [11].
	Sample volume	≤ 200 µL of capillary blood	≤ 100 µL of capillary blood	The analytical sensitivity is directly linked with the total volume of sample assessed. Volumes might vary for other sample types than capillary blood.
	Sample preparation	≤ 5 steps	None	Complex sample preparation is acceptable if it does not impact the overall assay throughput.
	Overall test preparation	≤ 20 steps, of which ≤ 5 are timed	≤ 10 steps, of which ≤ 2 are timed	Complex assay procedure is acceptable if it does not impact the overall assay throughput.
	Time-to-result	≤ 1 month	≤ 7 days	
	Internal control	Included	Included	
	External control	Available	Included	
	Assay interpretation	Unequivocal, recorded electronically	Identical to "M"	
	Data capture	Electronic, automated	Identical to "M"	
	Data transfer	Manual by operator	Automated via internet or GSM connectivity	
	Training	≤ 2 weeks for health worker with a substantial proficiency in laboratory work	≤ 1 week for health worker with a substantial proficiency in laboratory work	Include plan for quality control and proficiency monitoring.

Type	Characteristic	Minimal (M) / Description	Optimal (O)	Comment
	Biosafety	No reagent associated with acute toxicity hazards	No reagent associated with health hazards	According to the Globally Harmonized System of Classification and Labelling of Chemicals (GHS).
	Language	English, Spanish and Portuguese	Local languages	
Cost	End user price per test	≤1.0 USD	≤ 0.1 USD	The high throughput batch testing should facilitate a low test price.
	Cost of diagnosis	≤ 1.2 USD	≤ 0.5 USD	See End user price per test.

Supplementary References

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