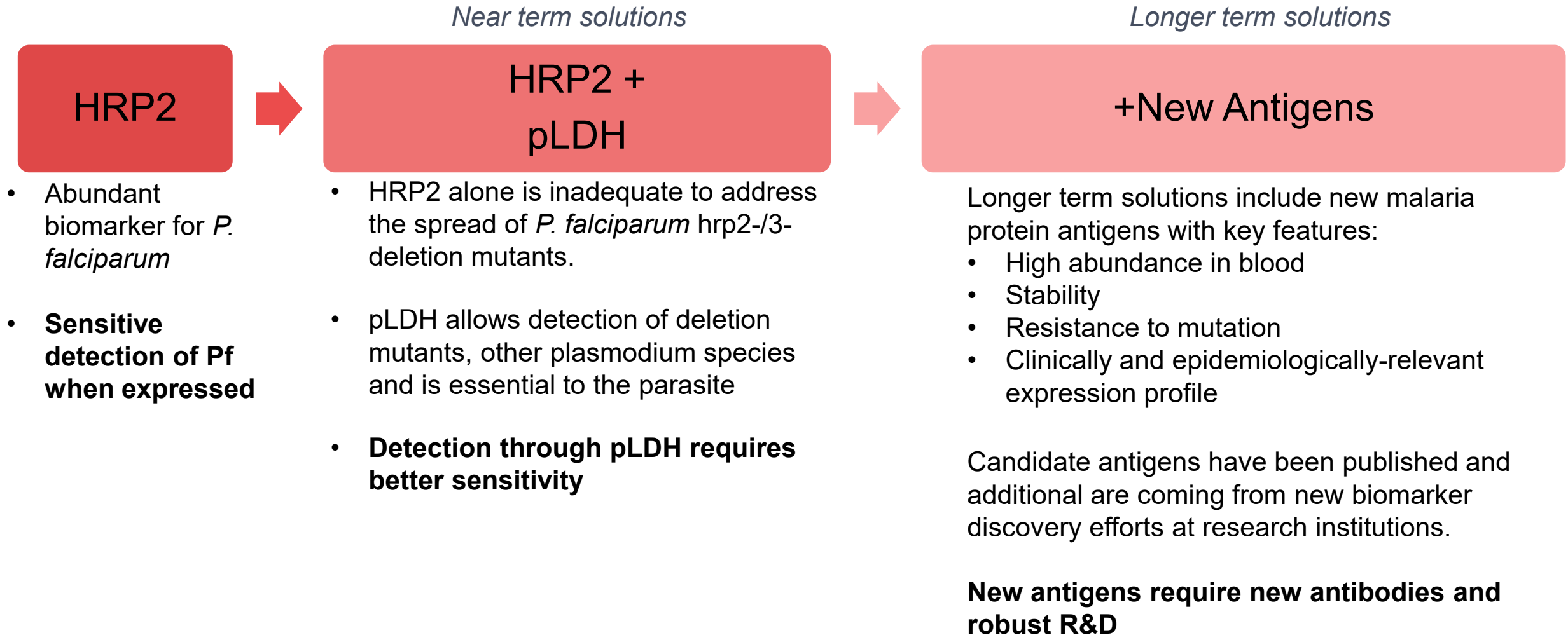


Next generation malaria rapid tests

16 May 2025

Malaria RDT Market: Disruptions and Threats

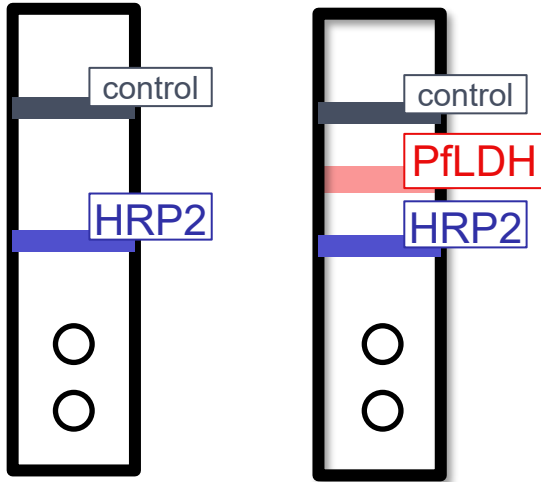
New development of rapid tests for malaria



Near term solutions for Pf detection: RDT form and pipeline

Status quo currently PQ RDTs

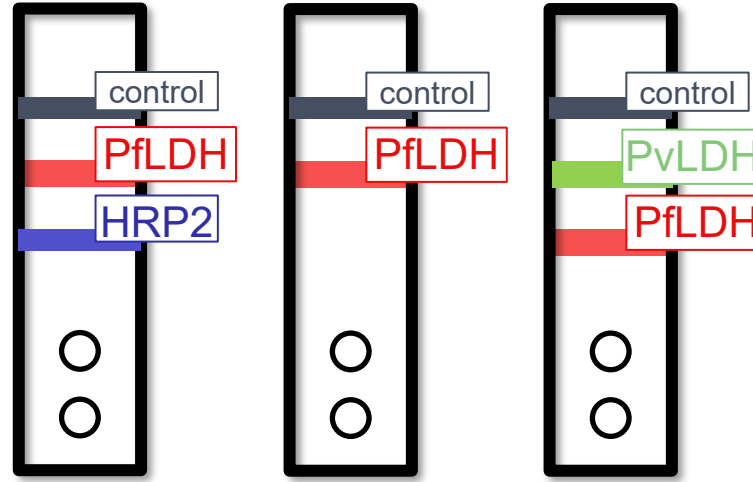
HRP2 only
PfHRP2 and PfLDH lines



- HRP2-only tests are market majority
- pLDH detection is lower sensitivity

- Multiple manufacturers and products available
- Not sustainable with increasing risk of deletions

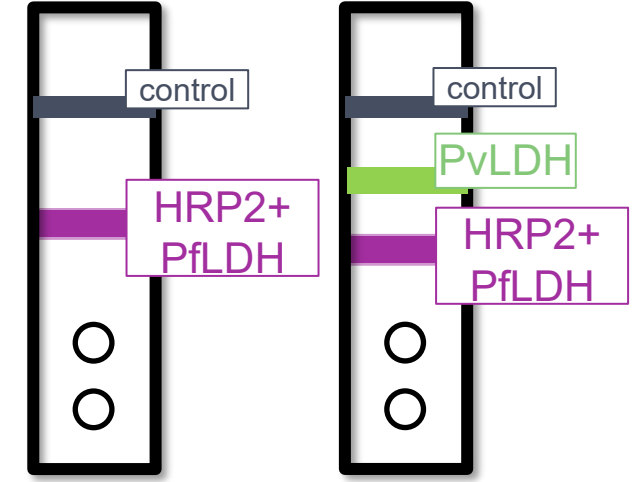
Current improved PfHRP2 and PfLDH lines



- Addresses *hrp2*-/3- risk
- Improved pLDH sensitivity
- Without HRP2, there is an overall sensitivity tradeoff even with improved pLDH sensitivity
- Coinciding improvement for PvLDH detection

ERPD approved RDTs available

Next-generation improved and combined PfHRP2+PfLDH RDTs



- Improved pLDH sensitivity combined with HRP2
- Higher usability for Pf and Pf/Pv tests

- Over 15 products in multiple stages of development.
- Expect some to enter market starting in late 2025 to 2026

Analytical performance targets for next-generation tests

Development of next-generation RDTs

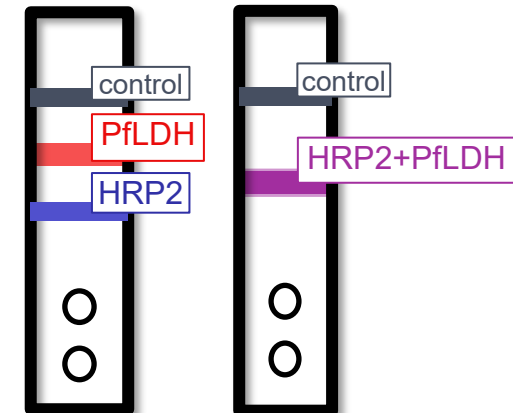
- **High quality reagents** to maximize sensitivity
- Improve usability with multi-target Pf line: **HRP2 and PfLDH combined.**
- Understanding analytical performance
 - **NIBSC International Standard**
 - Traceability for LOD reagents
- Understand test reactivity to HRP3
- Single/double hrp2 and hrp3 deletions –
 - **Confirm reactivity to PfLDH in the absence of HRP2 (and HRP3)**
- International Pf Standard detection limits:
 - Higher sensitivity tests can detect < 5 IU/mL
 - target 1 ng/mL PfLDH or lower

NIBSC Pf Ag 16/376							
Base d on diluti on: IU/m L	Quansys* measure d pg/mL		Current PQ RDTs		More sensitiv e PLDH detectio n RDTs		Next -gen RDT s
	HRP2	PfLDH	HRP2	PfLDH	HRP2	PfLDH	HRP2+ PfLDH
200	20454	45433					
100	10550	26060					
50	4637	11223					
30	2866	6165					
20	1304	2990					
15	981	2931					
10	700	1871					
8	510	1350					
5	351	873					
3	183	502					
1.5	108	239					

3BD5 culture** (hrp2-/hrp3-)							
Pa ra/ μL	Quansys* measured pg/mL		Current PQ RDTs		More sensitive PLDH detectio n RDTs		Next -gen RDT s
	HRP2	PfLDH	HRP2	PfLDH	HRP2	PfLDH	HRP2+ PfLDH
4500	4	24934					
2250	4	12639					
1125	3	5718					
563	2	2753					
338	2	1783					
225	1	1129					
113	2	604					
56	1	301					



Majority replicates detected by test line



*Quantification at PATH conducted using Quansys Qplex
<https://www.quansysbio.com/products-and-services/multiplex-assays/human-malaria-5-plex/>

**3BD5 strain donated to PATH by NIAID

Clinical performance depends on: limit of detection AND the distribution of antigen

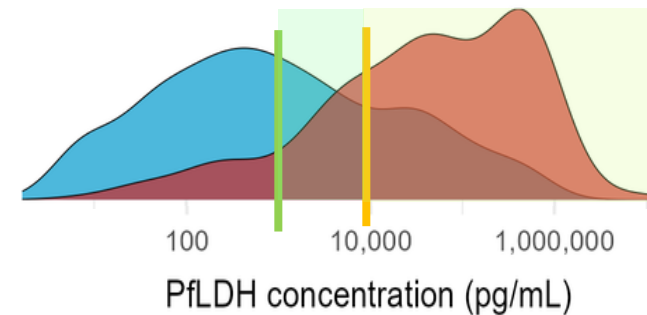
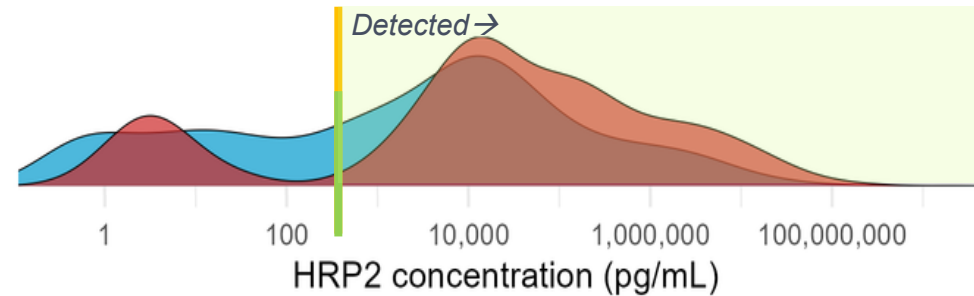
NIBSC Pf Ag							
Based on dilution: IU/mL	Quansys measured pg/mL		Current PQ RDTs		More sensitive PLDH detection RDTs		Next-gen RDTs
	HRP2	PfLDH	HRP2	PfLDH	HRP2	PfLDH	HRP2+ PfLDH
200	20454	45433					
100	10550	26060					
50	4637	11223					
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20	1304	2990					
15	981	2931					
10	700	1871					
8	510	1350					
5	351	873					
3	183	502					
1.5	108	239					
0.75	50	107					



LODs can be compared to clinical antigen distributions

RDTs with improved PfLDH sensitivity may detect more febrile and asymptomatic cases

Distributions adapted from Ref. 2



Febrile
Asymptomatic

Correlation of analytical sensitivity to clinical performance

1. Analytical Sensitivity Analysis and Clinical Impact Modeling of Rapigen Rapid Diagnostic Tests for Malaria <https://doi.org/10.4269/ajtmh.24-0003>
2. Performance and usability evaluation of three LDH-based malaria rapid diagnostic tests in Kédougou, Senegal <https://doi.org/10.1101/2024.12.12.24318945>
3. Performance of a novel *P. falciparum* rapid diagnostic test in areas of widespread *hrp2/3* gene deletion <https://doi.org/10.1093/cid/ciaf212>



Harvard dataverse: antigen concentrations and reference data on clinical samples

<https://dataverse.harvard.edu/dataverse/PATHMalariaDx>

Reagents and Resources

- Antibodies for malaria antigen targets
- Recombinant antigens
- International standards
- Culture strains and clinical specimens
 - PATH is planning to establish a biorepository of specimens (mid-2026).
- Evaluation Panels
 - PATH is working to provide benchmarking panels accessible to manufacturers (late 2025)
- Independent Evaluation
 - Analytical benchmarking: PATH can conduct testing using panels developed from the reagent resources (cost-recovery fee)
 - In addition to BEI-sourced single and double-deletion Pf strains, PATH cultures Pf strain 3BD5 (hrp2-/3-) and *P. knowlesi* for benchmarking**.

Antibodies

Antibody Supplier name	Location	Antibodies to malaria proteins offered	Website
Fapon	Dongguan, China and MA state, USA	HRP2, PfLDH, PvLDH, PanLDH	https://en.faponbiotech.com/
Vista	WA state, USA	HRP2, PfLDH, PvLDH, PanLDH, PoLDH	https://vistalaboratoryservices.com/
Arista	PA state, USA	HRP2, PfLDH, PvLDH, PanLDH	https://www.fortislife.com/arista-biologicals/
Bio Matrix Research Inc.	Japan	HRP2, PfLDH, PvLDH, PanLDH	http://www.biomatrix.co.jp/en/product.html
NBI	Pinetown, South Africa	HRP2, aldolase	https://nbisa.org.za/

Many suppliers have additional antibodies in development or available – ask about new part numbers available

Target Line	Reactivity Towards LDH from:					
	P. falciparum LDH	P. vivax LDH	P. malariae LDH	P. ovale LDH (curtisi & wallikeri)	P. Knowlesi LDH	Human LDH
P. falciparum LDH	O	X	1	2	1	X
P. vivax LDH	X	O	2	1	2	X
Pan LDH	O	O	O	O	O	X

X	Not acceptable - should not react with high concentration non-target
O	Target affinity – should be highly reactive
1	Acceptable cross reactivity based on treatment decisions
2	Acceptable but not preferred cross-reactivity based on treatment decisions

Antigens and International Standards

Antigen Supplier	Species + protein	Website
CTK Biotech	Pf (LDH), PvLDH, HRP2, aldolase	https://ctkbiotech.com/
MyBioSource	PfLDH, PvLDH, HRP2	https://www.mybiosource.com/
University of Queensland Protein Expression Facility UQ PEF	Pf (LDH), PvLDH, HuLDH, PmLDH, PoLDH (<i>curtisi</i>) PoLDH (<i>wallikeri</i>) and PkLDH coming soon.	https://pef.facility.uq.edu.au/research-services/malaria-proteins-pef-and-path
Span Diagnostics S.A.R.L	Pf (HRP2 type B), A, C PfLDH, PvLDH, PmLDH, PoLDH (w), PoLDH (c), PkLDH, aldolase	https://span-diagnostics.com/products/antigens/
Fapon Biotech	pLDH and Pf HRP2	https://en.faponbiotech.com/

Many suppliers have additional antigens in development or available – ask about new part numbers available

Supplier	Part Number	Description	Website
National Institute for Biological Standards and Control (NIBSC)	16/376	<i>Plasmodium falciparum</i> antigens (1st International Standard) 16/376	https://nibsc.org/products/brm_product_catalogue/detail_page.aspx?catid=16%2f376
National Institute for Biological Standards and Control (NIBSC)	19/116	1st WHO <i>Plasmodium</i> <i>vivax</i> antigen (LDH) 19/116	https://nibsc.org/products/brm_product_catalogue/detail_page.aspx?CatId=19/116

Culture strains and clinical specimens

Parasite	Source	Part number
ITG, Culture <i>P. falciparum</i>	BEI Resources	MRA-326
Dd2 (<i>hrp2</i> -/ <i>hrp3</i> +) Culture <i>P. falciparum</i>	BEI Resources	MRA-150
HB3 (<i>hrp2</i> +/ <i>hrp3</i> -) Culture <i>P. falciparum</i>	BEI Resources	MRA-155
LA476-1 (<i>hrp2</i> -/ <i>hrp3</i> -) Culture <i>P. falciparum</i>	BEI Resources	MRA-1332

Other strains available

BEI Resources :

<https://www.beiresources.org/Home.aspx>

Sample types	Source	notes
Pf- and Pv-positive clinical samples (febrile).	Discovery Life Sciences: https://dls.com/biospecimens/	May require additional confirmation by PCR.
Pf- and Pv-positive clinical samples	PATH Biorepository, in collaboration with clinical partners	Planning for availability in 2026

PATH
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