



# Test characteristics of the CareStart™ HRP2/LDH Combo rapid diagnostic test for the diagnosis of malaria in returned travellers

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## Introduction

Malaria Rapid Diagnostic Tests (MRDT) are widely used for diagnosing malaria. The present laboratory study evaluated the CareStart™ Malaria HRP2/pLDH Combo Test targeting the *Plasmodium falciparum* specific antigen Histidine rich protein (HRP-2) and the pan-*Plasmodium* antigen lactate dehydrogenase (pLDH) in a reference setting.

## Material and Methods

- Collection of samples (n = 495) obtained in returned international travellers:
  - P. falciparum* (n = 320), *P. vivax* (n = 76), *P. ovale* (n = 76), *P. malariae* (n = 23),
- Microscopy corrected by PCR was used as the reference method
- Tests were read by three blinded observers and test line intensities were scored (N = negative, F = faint, W = weak, M = medium, S = strong)
- End points were - sensitivity and specificity
  - inter-observer agreement and reproducibility for test results and line intensity readings
  - evaluation of the ease of use



**Table 1: Test characteristics of the SD FK70 matched with species identification and parasite density**

Species and parasite density (asexual parasites/μl)	Nrs tested	Correctly identified by CareStart™	Sensitivity % (95% CI)
<i>P. falciparum</i> , all samples combined	320	284	88.8 (84.8-92.0)
<i>P. falciparum</i> , 0-100 / μl	56	39	70.6 (44.0-89.7)
<i>P. falciparum</i> , > 100 / μl	247	233	94.3 (90.7-96.9)
<i>P. falciparum</i> , > 1000 / μl	133	132	99.3 (95.9-100)
All non- <i>falciparum</i> species combined	175	80	45.7 (38.2-53.4)
<i>P. vivax</i>	76	59	77.6 (66.6-86.4)
<i>P. ovale</i>	76	14	18.4 (10.5-29.0)
<i>P. malariae</i>	23	7	30.4 (13.2-52.9)
Total	495		

## Results

- Table 1**
- Overall sensitivity for *P. falciparum* was 88.8 % and for non-*falciparum* species 45.7 %
  - Sensitivity increased at higher parasite densities
  - Sensitivities for *P. malariae* and *P. ovale* were poor
  - 8 *P. falciparum* samples only showed a visible pan-pLDH test line

- Table 2**
- 205 of 284 (72.2%) positive *P. falciparum* samples showed medium or strong line intensities
  - There was a correlation between test line intensity and parasite density
  - The false positive results for non-*falciparum* samples showed faint or weak line intensities

- Table 3**
- *P. ovale* samples only generated faint or weak test lines
  - For *P. falciparum* samples, a strong pLDH line was indicative for parasite density > 1000 / μl

- Overall**
- none of the *Plasmodium* negative samples showed a positive test line
  - inter-observer agreement was good en test results were reproducible
  - the test was scored as practical in use and easy to read

**Table 2: CareStart HRP-2 test line intensity for the different parasite densities.**

N=negative, F=faint, W=weak, M=medium, S=strong

Species	Consensus readings					
	N	F	W	M	S	Total
<i>P. falciparum</i> , all	36	13	66	66	139	320
<i>P. falciparum</i> , 0-100 / μl	17	5	19	8	7	56
<i>P. falciparum</i> >100 / μl	14	5	44	56	128	247
<i>P. falciparum</i> >1000 / μl	1		20	29	83	133
<i>P. vivax</i>	74	1	1			76
<i>P. ovale</i>	75	1				76
<i>P. malariae</i>	23					23

**Table 3: CareStart pan-pLDH test line intensity for the different parasite densities.**

N=negative, F=faint, W=weak, M=medium, S=strong

Species	Consensus readings					
	N	F	W	M	S	Total
<i>P. falciparum</i> , all	69	60	62	12	117	320
<i>P. falciparum</i> 0-100 / μl	36	17	3			56
<i>P. falciparum</i> > 100 / μl	25	41	55	12	114	247
<i>P. falciparum</i> > 1000 / μl	1		11	8	113	133
<i>P. vivax</i>	15	7	24	11	19	76
<i>P. ovale</i>	62	11	3			76
<i>P. malariae</i>	16	2	2	3		23

## Discussion

- The test characteristics of the CareStart™ were good for detection of *P. falciparum* and *P. vivax*, and results were in line with findings in previous studies
- The low sensitivities for *P. malariae* and *P. ovale* are of note, though a similar two-band CareStart™ pLDH detected all 6 *P. malariae* infections
- The single pan-pLDH lines occurring in eight *P. falciparum* samples are of concern
- Faint and weak test line intensities may cause problems while reading results and the LDH test line intensity should be adapted

## References

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## Conclusion

The CareStart™ performed well for the detection of *P. falciparum* and *P. vivax*, but sensitivities for *P. ovale* and *P. malariae* were poor. The CareStart™ is an valuable adjunct to microscopy in the diagnosis of *P. falciparum* or *P. vivax*.