

Box 1a: Symbol key

Symbol	Explanation	Symbol	Explanation
	<i>In vitro</i> diagnostic medical device		Product code
	Content sufficient for < n > tests		Consult instructions for use
	Lot number		Use by YYYY-MM-(DD)
	Date of manufacture YYYY-MM-(DD)		Manufacturer
	Do not reuse		Do not use if packaging is damaged
	Temperature limitation		Lower limit of temperature
	Sterile		Upper limit of temperature
	Irritant		Biological risk
	Keep away from sunlight		Keep dry
	Authorized representative in the European Community		European Health & Safety Product Label

Box 1b: Globally harmonized system of classification and labeling of chemicals (hazard pictograms):

<i>New CLP symbols:</i>			
	(very) Toxic		Dangerous for the environment
	Oxidizing		Highly or extremely flammable
	Corrosive		Explosive
	Replaces the harmful symbol:  Refers to less serious health hazards such as skin irritancy / sensitisation		NEW: Reflects serious longer term health hazards such as carcinogenicity and respiratory sensitisation

Box 2: Labeling legibility for *in-vitro* diagnostics

RDT box labeling:

[A] MINIMUM STANDARD:

Based on *EC guidelines for readability of labeling*¹ (i.e. Characters of at least 7 points, or of a size where the lower case “x” is at least 1.4mm in height // space between lines of at least 3mm):

This is an example of the minimum acceptable text size and spacing
for labeling of medicinal products according to EC guidelines
(to evaluate Malaria RDT box labeling)

[B] RECOMMENDED STANDARDS:

Example 1 (font and size) → Based on the *US FDA guidelines*² (e.g. ‘Serif’ font – 12 points):

This is the recommendation of FDA for text font and size
of medical device labeling aimed at patients and lay caregivers
(to evaluate Malaria RDT box labeling)

Example 2 (size) → Based on *HarT guidelines* (e.g. font size equivalent to Myriad bold 10):

**This is an example of recommended text size
mentioned in the HarT guidelines
(to evaluate Malaria RDT box labeling)**

IFU:

MINIMUM STANDARD:

Based on *EC guidelines for readability of package leaflet*¹ (i.e. At least type size of 9 points -as measured in font ‘Times New Roman’, not narrowed - with a space between lines of at least 3 mm):

This is an example of the minimum acceptable text size and spacing
for package leaflets according to EC guidelines
(to evaluate Malaria RDT IFU readability)

NOTE: It is important to choose a font in which similar letters/numbers, such as “i”, “l” and “1” can be easily distinguished from each other.

Figure 1: Convention of terms for the front-view of a malaria RDT box.

¹ http://ec.europa.eu/health/files/eudralex/vol2/c/2009_01_12_readability_guideline_final_en.pdf

² <http://www.fda.gov/RegulatoryInformation/Guidances/ucm070782.htm#c>

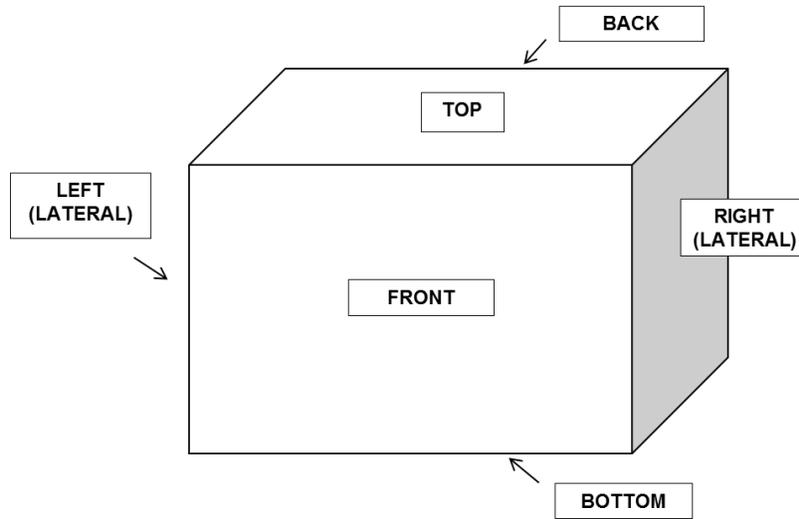


Figure 2 - Example label on the top of the RDT box

    			
Commercial name, Malaria Antigen Pf/Pan (HRP2 / pLDH) RDT			
	xxxxxxxxxxxx		XX
Rapid test for the antigen detection of malaria (<i>Plasmodium x</i>)			
Test rapide de détection d'antigène du paludisme (<i>Plasmodium x</i>)			
Prueba rápida para detección de antígeno de malaria (<i>Plasmodium x</i>)			
Teste rápido para detecção de antígeno da malária (<i>Plasmodium x</i>)			
	Professional-use only		xxxxxxxx
			YYYY-MM
	 Name and physical address of legal manufacturer. Website and/or telephone and/or fax number.		

Blue color indicates RDT product specific items.
 Exception: custom/variable prints (e.g. lot number, expiration date) can be printed only in one side.

Commercial name, Malaria Antigen Pf/Pan (HRP2 / pLDH) RDT			
<div style="border: 1px solid black; padding: 2px; display: inline-block;">REF</div> xxxxxxxxxxxx			
Content:	Cassettes (XX) Specimen transfer devices (XX) Alcohol swabs (XX) Lancets (XX) Buffer bottle (XX) Instructions for use (XX)	 <div style="border: 1px solid black; padding: 2px; display: inline-block;">LOT</div> <div style="border: 1px solid black; padding: 2px; display: inline-block; margin-right: 5px;">STERILE</div> <input type="checkbox"/>	(XX) xxxxxxxx <i>[indicate symbol for method of sterilization]</i>
Required but not provided:	Gloves Biosafety sharps container Biohazard waste container Timer Pencil / pen		YYY-MM
			xx °C

(XX) indicates Quantities: Number of items or Number of pouches (and what each pouch contains)

Blue color indicates RDT product specific items.

Exception: custom/variable prints (e.g. lot number, expiration date) can be printed only in one side.

Figure 4 – Example labeling of the cassette primary packaging

SIDE A

	
<p>Commercial name, Malaria Antigen Pf/Pan (HRP2 / pLDH) RDT</p> <p>For product code: XXXXXXX</p>	
	<p>xx</p>
Content:	<ul style="list-style-type: none"> - 1 cassette - 1 desiccant - 1 specimen transfer device
	<p>Manufacturer Name or logo</p>



SIDE B

	<p>XXXXXXX</p>
	<p>YYYY-MM</p>

Blue color indicates RDT product specific items.

Figure 5 – Conventions for terms of the cassette

Distal

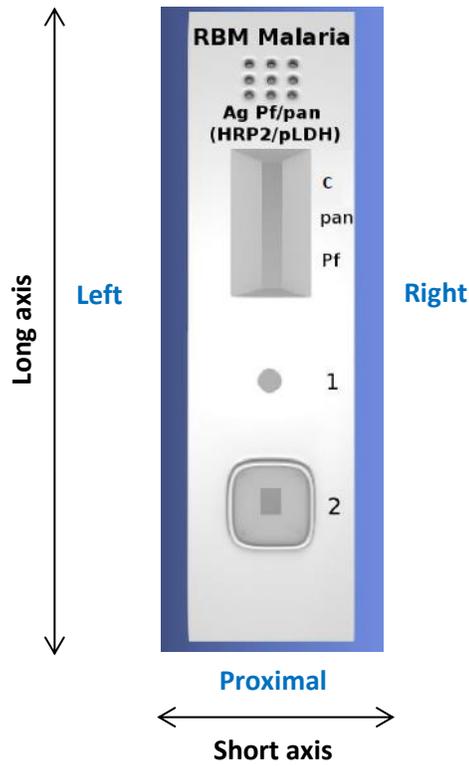


Figure 6 – Proposal for printing relevant information on the buffer bottle

<p>Commercial name, Malaria Antigen Pf/Pan (HRP2/ pLDH) RDT For product code: XXXXXX</p>	
<p>Contents : Buffer</p>	
	<p>XXXXXXXX</p>
	<p>YYYY-MM</p>
	<p>Manufacturer Name (or logo)</p>
<p>XX ml or XX number of examinations</p>	

Box 3: Test Principle (IFU)

The cassette contains a test strip pre-coated with capture antibodies. The sequence of events is as follows:

- (1) Whole blood is applied to the specimen well (labelled well 1).
- (2) Next, buffer is applied to the buffer well (labelled well 2).
- (3) Migration of the blood specimen/buffer mixture starts, towards the other end of the cassette.
- (4) The blood specimen-buffer mixture passes the conjugate pad, which contains detection antibodies targeting Pf-HRP2, Pf-pLDH, Pv-pLDH, pan-pLDH and/or aldolase antigens. These detection antibodies are conjugated to colloidal gold. If present in the specimen, Plasmodium target antigens bind to this detection antibody-conjugate.
- (5) The antigen-antibody-conjugate complex migrates further and binds to the capture Plasmodium-specific antibodies present on the test line. These capture antibodies bind to another site (epitope) of the Plasmodium target antigens.
- (6) The capture antibodies are applied on a narrow section of the test strip: as a result, the antibody-conjugate with the colloidal gold will be concentrated and become visible as a red colored line.
- (7) The excess of the detection antibody-conjugate that was not bound by the Plasmodium target antigens and the capture antibodies moves further until it binds to a goat anti-mouse control antibody. There, the colloidal gold will create a red colored control line. The visualization of the control line indicates that the migration was successful. It does not confirm the presence of specimen.

Table 1: Description of different result possibilities

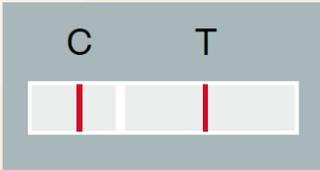
Lines that you see	Record the following result	Picture/Drawing
NO line at 'C' (= control)	INVALID -Take a new cassette packaging and repeat the test!	All possible line combinations*
Line at 'C' and NO other line	NEGATIVE	All possible line combinations*
Line at 'C' AND at 'Pf'	POSITIVE for <i>Plasmodium falciparum</i>	All possible line combinations*
Line at 'C', at 'Pf' AND at 'pan'	POSITIVE for <i>Plasmodium falciparum</i> (or rarely, a mixed infection with <i>P. vivax</i> , <i>P. ovale</i> and/or <i>P. malariae</i>)	All possible line combinations*
Line at 'C' AND at 'pan'	POSITIVE for non- <i>falciparum</i> malaria: <i>P. vivax</i> , <i>P. ovale</i> or <i>P. malariae</i> (or, rarely, a mixed infection with these species)	All possible line combinations*
Other line combinations	Write down the result	All possible line combinations*

*See below examples for a 2-band, 3-band and 4-band test. A full 'Guide to interpretation of results' for all RDT types is available in Annex 2 of WHO-FIND Product Testing reports:

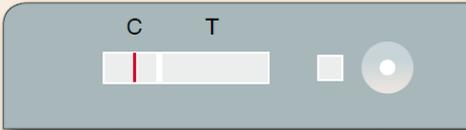
<http://www.who.int/malaria/publications/atoz/9789241510035/en/>

Guide to results of generic Pf malaria RDT:

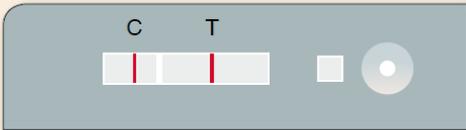
Results window: C=control line; T=test line with bound HRP2 or Pf-specific pLDH antibody.



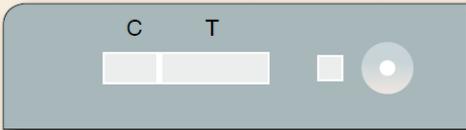
Negative results: One line 'C' appears in the results window.



Positive results: *P. falciparum* infection. Two lines 'C' and 'T' appear in the results window. Test is positive even if the test line is faint.

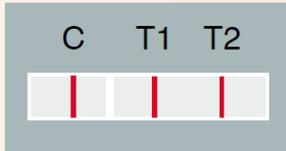


Invalid results: No 'C' line appears in the results window. Repeat the test with a new RDT if no control line appears.

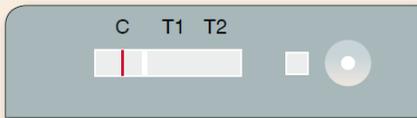


Guide to results of generic pan – Pf malaria RDT:

Results window: C=control line; T1=test line with bound pLDH or aldolase antibody; T2=test line with bound HRP2 and/or Pf-specific pLDH antibody.

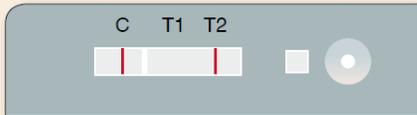


Negative results: Only one line 'C' appears in the results window.

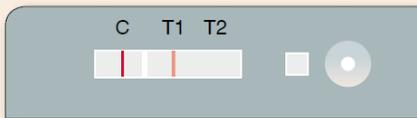


Positive results:

P. falciparum: Two lines 'C' and 'T2' appear in the results window.



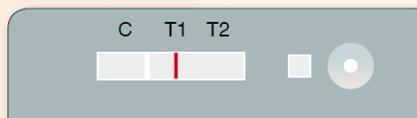
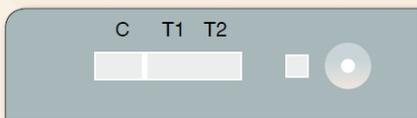
Non-*falciparum* infection (*P. vivax*, *P. ovale*, *P. malariae*) or mixed infection: Two lines 'C' and 'T1' appear in the results window.



P. falciparum or mixed infection. Three lines 'C', 'T1' and 'T2' appear in the results window.

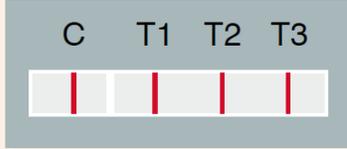


Invalid results: No 'C' line appears in the results window. Repeat the test with a new RDT if no control line appears.

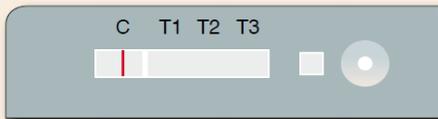


Guide to results of generic pan – Pv – Pf malaria RDT (I):

Results window: C=control line; T1=test line with bound pLDH or aldolase antibody; T2=test line with bound *P. vivax*-specific pLDH; T3=test line with bound HRP2 or Pf-specific pLDH antibody

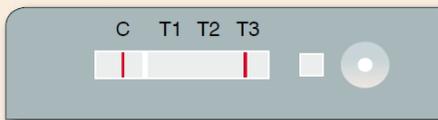


Negative results: Only one line 'C' appears in the results window.

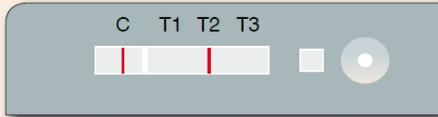


Positive results:

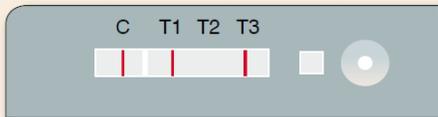
P. falciparum infection. Two lines 'C' and 'T3' appear in the results window.



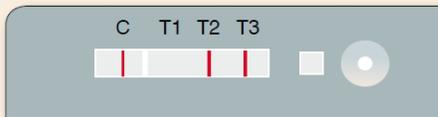
P. vivax infection. Two lines 'C' and 'T2' appear in the results window.



P. falciparum with or without mixed infection with *P. ovale* or *P. malariae*. Three lines 'C', 'T1' and 'T3' appear in the results window.



P. falciparum and *P. vivax* mixed infection. Three lines 'C', 'T2' and 'T3' appear in the results window.

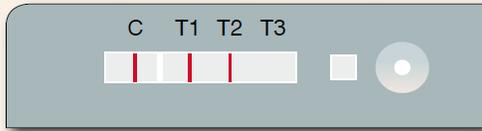


P. falciparum and *P. vivax* mixed infection with or without *P. ovale* and/or *P. malariae* infection. Four lines 'C', 'T1', 'T2' and 'T3' appear in the results window.

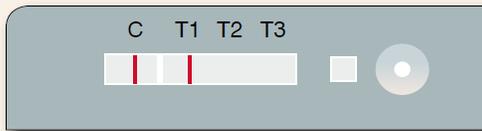


Guide to results of generic pan – Pv – Pf malaria RDT (II):

P. vivax with or without *P. ovale* and/or *P. malariae* infection. Three lines 'C', 'T1' and 'T2' appear in the results window.



P. malariae with or without *P. ovale* and/or *P. vivax* infection. Two lines 'C' and 'T1' appear in the results window.



Invalid results: No 'C' line appears in the results window. Repeat the test with a new RDT if no control line appears.

