Point-of-care testing

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Point-of-care testing

> 20 definitions (Pai 2008)
POCT
NPT near patient testing
BT bedside testing

Fast? 3 min – 30 mins

Diagnosis, monitoring...

Self-testing
PST patient self-testing

Point-of-care testing

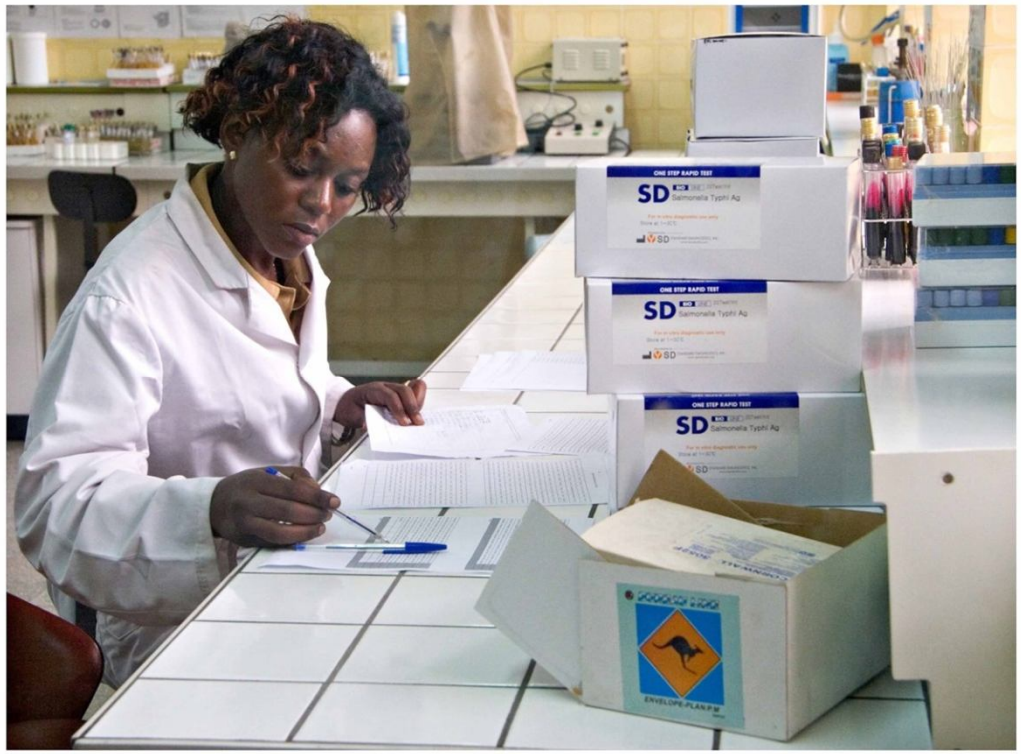
Rapid Diagnostic Test

Malaria

Low-resource setting

Central-Africa

(DR Congto)



Malaria RDTs: “role model” for other in-vitro diagnostics (IVDs)

(Platform and principle)

Production and Market mechanisms

ISO 14385 meets ISO 15189

In-vitro diagnostics: regulatory issues

Transport, shipment

Barriers

End-user friendliness

End-user errors

Experiences/lessons learned

Introduction of other RDTs

WHO prequalification & Site Inspections , Roll Back Malaria: diagnostic workstream supply

COMMODITY SPECIFIC WORKSTREAM

1 Treatment	2 Diagnosis	3 Prevention
ACTs/ Other Anti-malarials	RDTs	LLINs IRS

CROSS CUTTING WORKSTREAMS

4 Global demand forecast

5 Information and knowledge: LMIS, mHealth

6 PSM bottleneck resolution

About malaria

Endemic areas (2012)

3.400.000.000 people at risk

104 countries

207.000.000 cases/yr

627.000 deaths (< 5 years old, Africa)

Travel Medicine

10.000/yr (but may be 30.000/yr)

Case-fatality 0.6 -3.8%

60% of diagnosis > office-hours

Visiting friends and relatives, refugees

The global burden of malaria is decreasing

Endemic areas (2006)

109 countries

247.000.000 cases/yr

881.000 deaths

Control

Pre-elimination (Zanzibar, Rwanda)

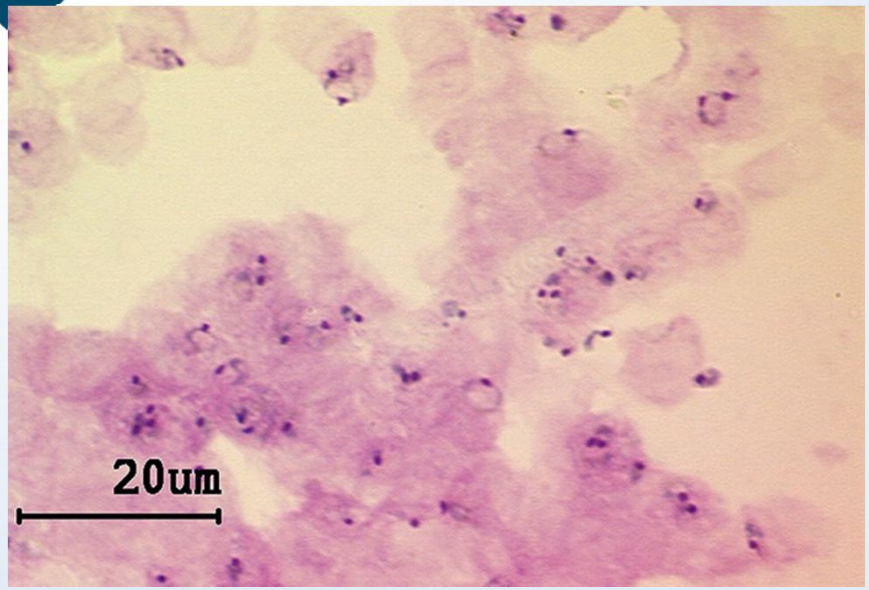
Elimination

LLIN = long lasting insecticide-treated bed nets

IRIS = indoor residual spraying

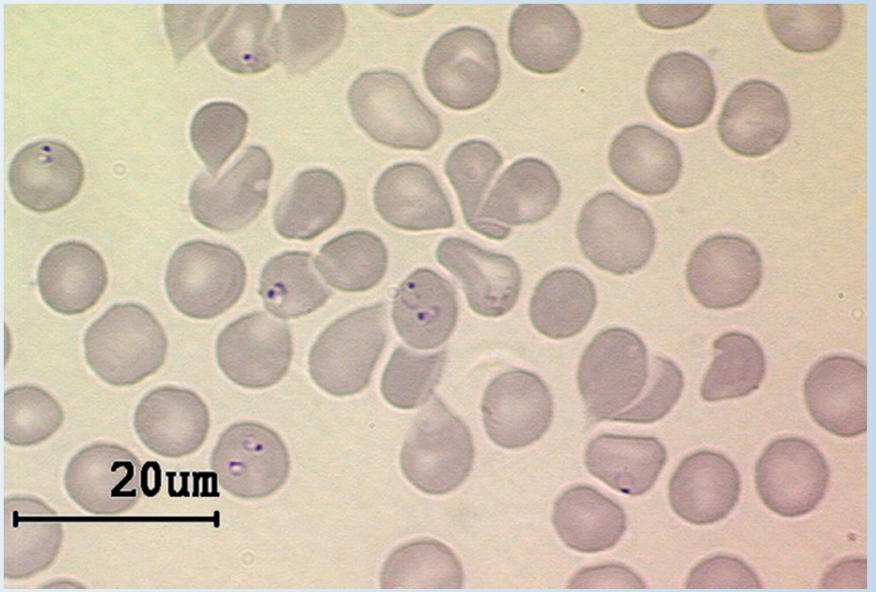
ACT = artemisimine-based comibination therapy

Thick film



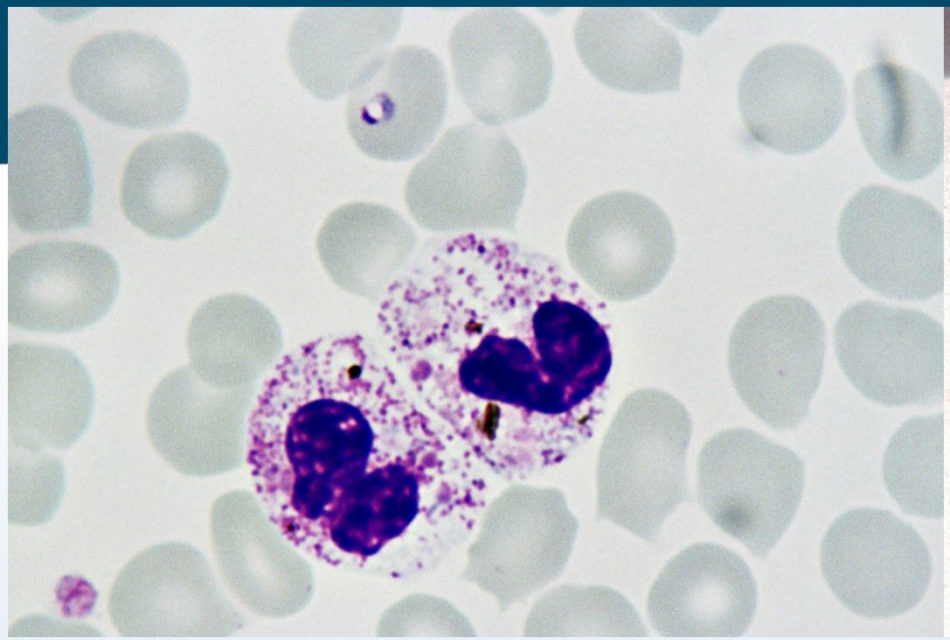
- Parasite detection.
- Quantification [parasitaemia /µl of blood].

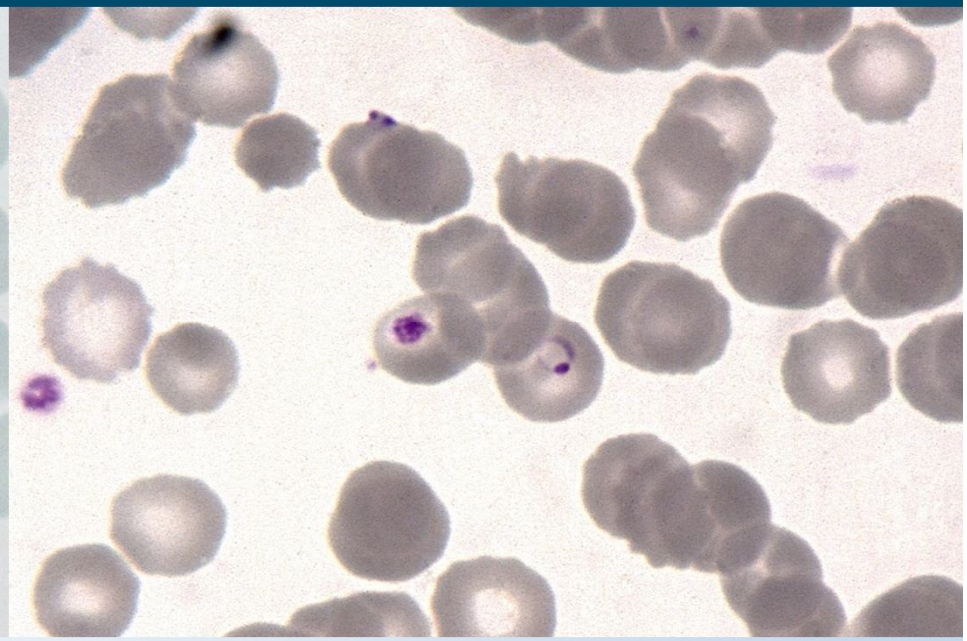
Thin film

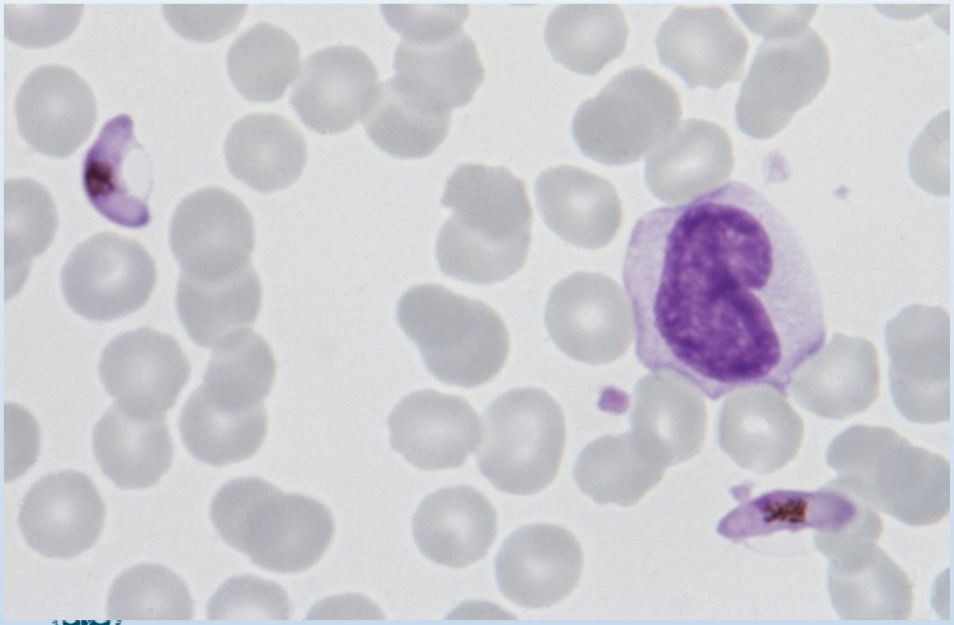


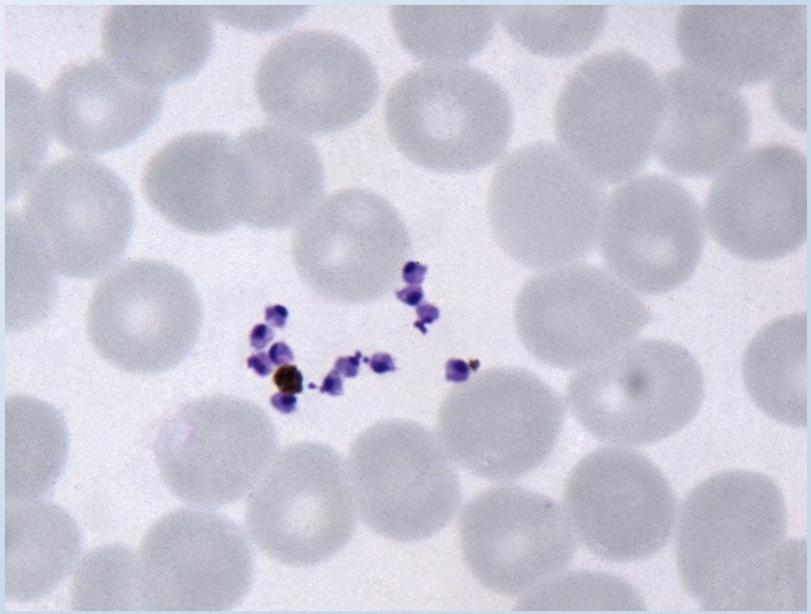
- Species/Stages
- Quantification [% infected RBC].

50.000/µl = 1% of Red Blood Cells
100/µl = 0.002% of RBC









About malaria diagnosis...

Detection limit

- Expert 50/µl
- Routine 500/µl
- Field?

Microscope

- Power?
- Dust !
- Maintenance...


ARCHIVAGE
DES
LAMES SUSPECTES
LAMES LCR ET GE
CERVEAU MENINGITE BACT)

CAAMEKI ASBL

Bâtiment Zone de santé Kisantu N° impôt A1005851 X

Tél. : 0999226791 / 0815998710 - E-mail : caameki@yahoo.fr

Compte Bancaire : -01 101-1003734-49 / USD BCDC LIMETE

FACTURE

ORIGINAL

Référence	: FC055780
Date	: 03/06/14
Mode de règlement	: Comptant
Document libellé en	: Dollar US
A payer avant le	: 03/06/14
Compte	: 411CLEXC0
Code	: CLEXC

CLIENT EXCEPTIONNEL
KINSHASA
KINSHASA
KINSHASA
Congo

Référence	Désignation	Unité	Quantité	Prix Unitaire	% Rem.	Montant H.T.
	-Bon de livraison N° BL055456 du 03/06/2014					
	-Commande client N° CC055678 du 03/06/2014					
SLAS_OILI1B1_0	Huile à immersion , 100ml, flacon, Unité	Unité	1	25.0000		25.0000
	Numéro de Lot : 1104		1			

HX895655

2014/02/20

1.09204.0502

500 ml

IMO: METHANOL SOLUTION
ICAO: METHANOL SOLUTION

IVD CE

C.I. 45380 2,4 g/l
C.I. 52015 + Azur 4,1 g/l
1 l = 0,99 kg

Lagern bei +15°C bis 25°C. Lösung stets frisch bereiten. Spezifikation auf Anfrage. Gebrauchsanweisung im Internet/auf Anfrage.

Store at +15°C to 25°C. Use only freshly prepared solution. Specification on request. Instructions for use on Internet/ on request.

Conserver de +15°C à +25°C. N'utiliser que des solutions préparées fraîchement. Spécification sur demande. Mode d'emploi sur Internet/sur demande.

Conservare tra +15°C e 25°C. Adoperare solo soluzioni preparate di fresco.

Leichtentzündlich
Highly flammable
Facilement inflammable
Facilmente infiammabile
Fácilmente inflamable

Microscopy

Giemsas Azur-Eosin-Methylenblaulösung
für die Mikroskopie
(enthält Methanol)

Giemsa's azur eosin methylene blue solution
for microscopy
(contains methanol)

Azur-éosine-bleu de méthylène selon Giemsa en solution
pour la microscopie
(contient méthanol)

Giemsa soluzione azur-eosina-blu di metilene
per microscopia
(contiene Metanolo)

Azur-eosina-azul de metileno según Giemsa en solución
para microscopia
(contiene Metanol)

4 022536 111889

MERCK

R: 11-23/24/25-39/23/24/25 S: 7-16-36/37-45

Leichtentzündlich. Giftig beim Einatmen, Verschlucken und Berührung mit der Haut. Giftig: ernste Gefahr irreversiblen Schadens durch Einatmen, Berührung mit der Haut und durch Verschlucken. * Behälter dicht geschlossen halten. Von Zündquellen fernhalten - Nicht rauchen. Bei der Arbeit geeignete Schutzhandschuhe und Schutzkleidung tragen. Bei Unfall oder Unwohlsein sofort Arzt hinzuziehen (wenn möglich dieses Etikett vorzeigen).

Highly flammable. Toxic by inhalation, in contact with skin and if swallowed. Toxic: danger of very serious irreversible effects through inhalation, in contact with skin and if swallowed. * Keep container tightly closed. Keep away from sources of ignition - No smoking. Wear suitable protective clothing and gloves. In case of accident or if you feel unwell, seek medical advice immediately (show the label where possible).

Facilement inflammable. Toxique par inhalation, par contact avec la peau et par ingestion. Toxique: danger d'effets irréversibles très graves par inhalation, par contact avec la peau et par ingestion. * Conserver le récipient bien fermé. Conserver à l'écart de toute flamme ou source d'étincelles - Ne pas fumer. Porter un vêtement de protection et des gants appropriés. En cas d'accident ou de malaise consulter immédiatement un médecin (si possible lui montrer l'étiquette).

Facilmente infiammabile. Tossico per inalazione, contatto con la pelle e per ingestione. Tossico: pericolo di effetti irreversibili molto gravi per inalazione, a contatto con la pelle e per ingestione. * Conservare il recipiente ben chiuso. Conservare lontano da fiamme e scintille - Non fumare. Usare indumenti protettivi e guanti adatti. In caso di incidente o di malessere consultare immediatamente il medico (se possibile, mostrargli l'etichetta).

Fácilmente inflamable. Tóxico por inhalación, por ingestión y en contacto con la piel. Tóxico: peligro de efectos irreversibles muy graves por inhalación, contacto con la piel e ingestión. * Manténgase el recipiente bien cerrado. Conservar alejado de toda llama o fuente de chispas - No fumar. Úsense indumentaria y guantes de protección adecuados. En caso de accidente o malestar, acúdase inmediatamente al médico (si es posible, muéstresele la etiqueta).

UN 1230

Kisantu 16/x/2011

Quality of stain

Mukadi *et al. Malaria Journal* 2011, **10**:308
http://www.malariajournal.com/content/10/1/308

MALARIA JOURNAL

RESEARCH Open Access

External quality assessment of malaria microscopy in the Democratic Republic of the Congo

Pierre Mukadi[1], Philippe Gillet[2*], Albert Lukuka[1,3], Ben Atua[3], Simelo Kahodi[4], Jean Lokombe[1,5], Jean-Jacques Muyembe[1,5] and Jan Jacobs[2,6]

Correct dimensions (> 1 cm) and thickness of the film	110 (71.0%)
Complete hemolysis of the red blood cells	118 (76.1%)
No Giemsa stain precipitates observed	60 (38.7%)
Good contrast between nucleus and cytoplasm	70 (45.1%)
Complies with all criteria mentioned above	30 (19.4%)

Malaria Rapid Diagnostic Tests: alternative

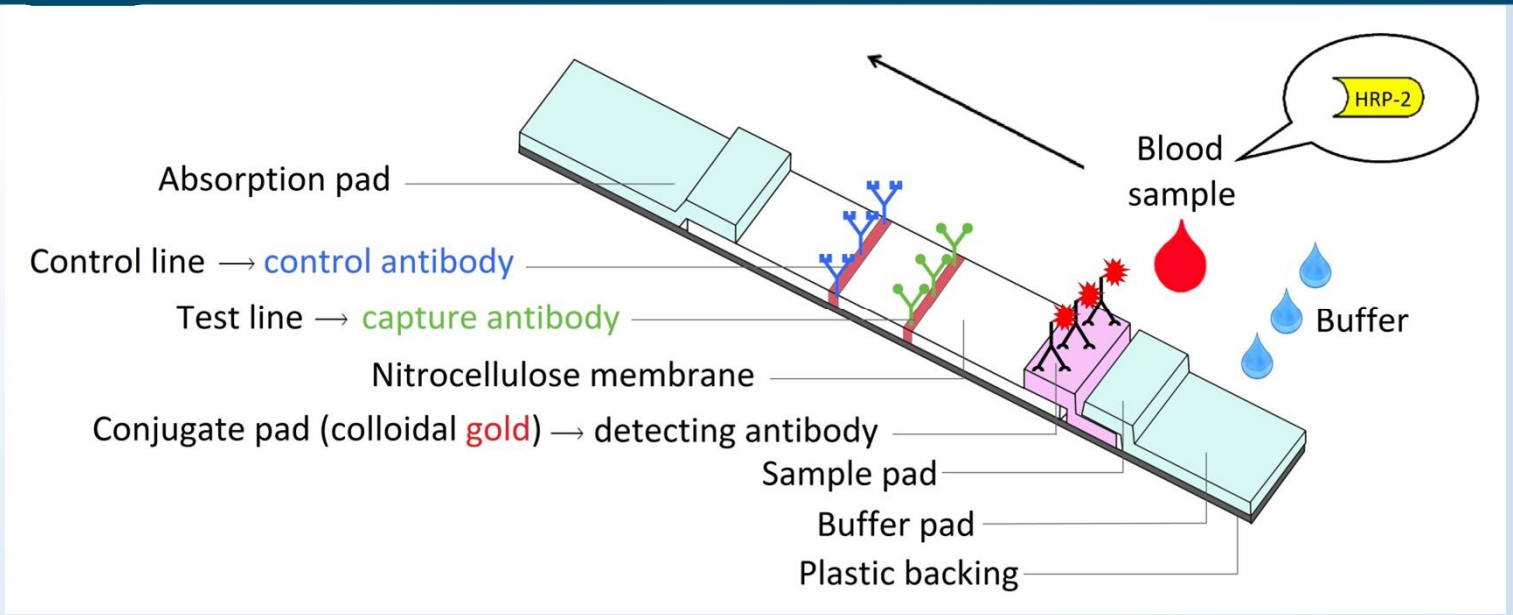
Dipstick

Card

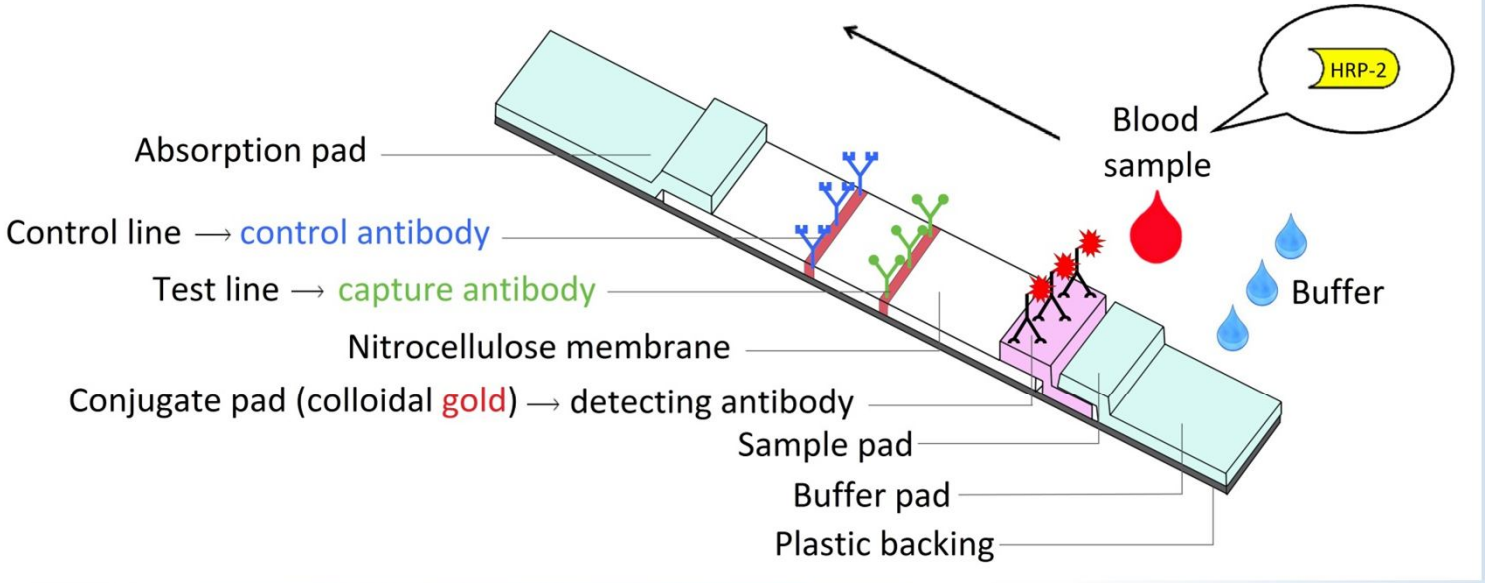
Plastic casette

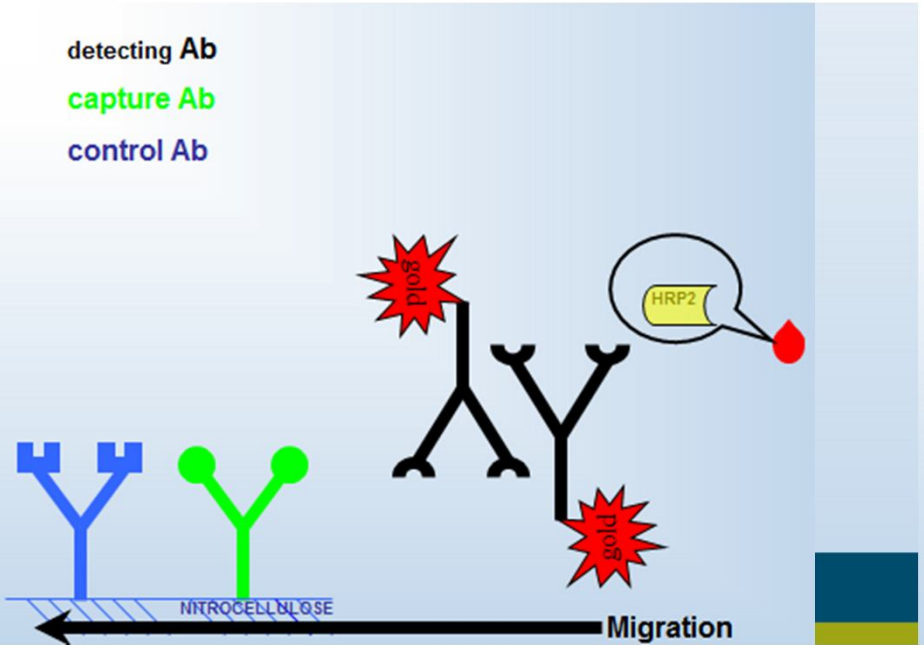
Hybrid casette-dipsticks

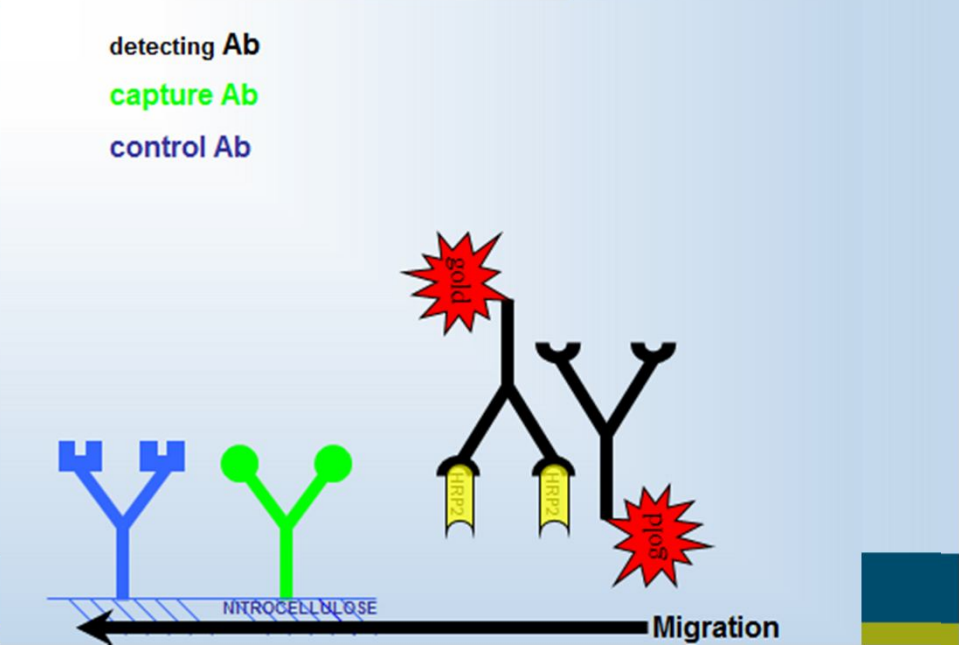
Lateral flow – principle

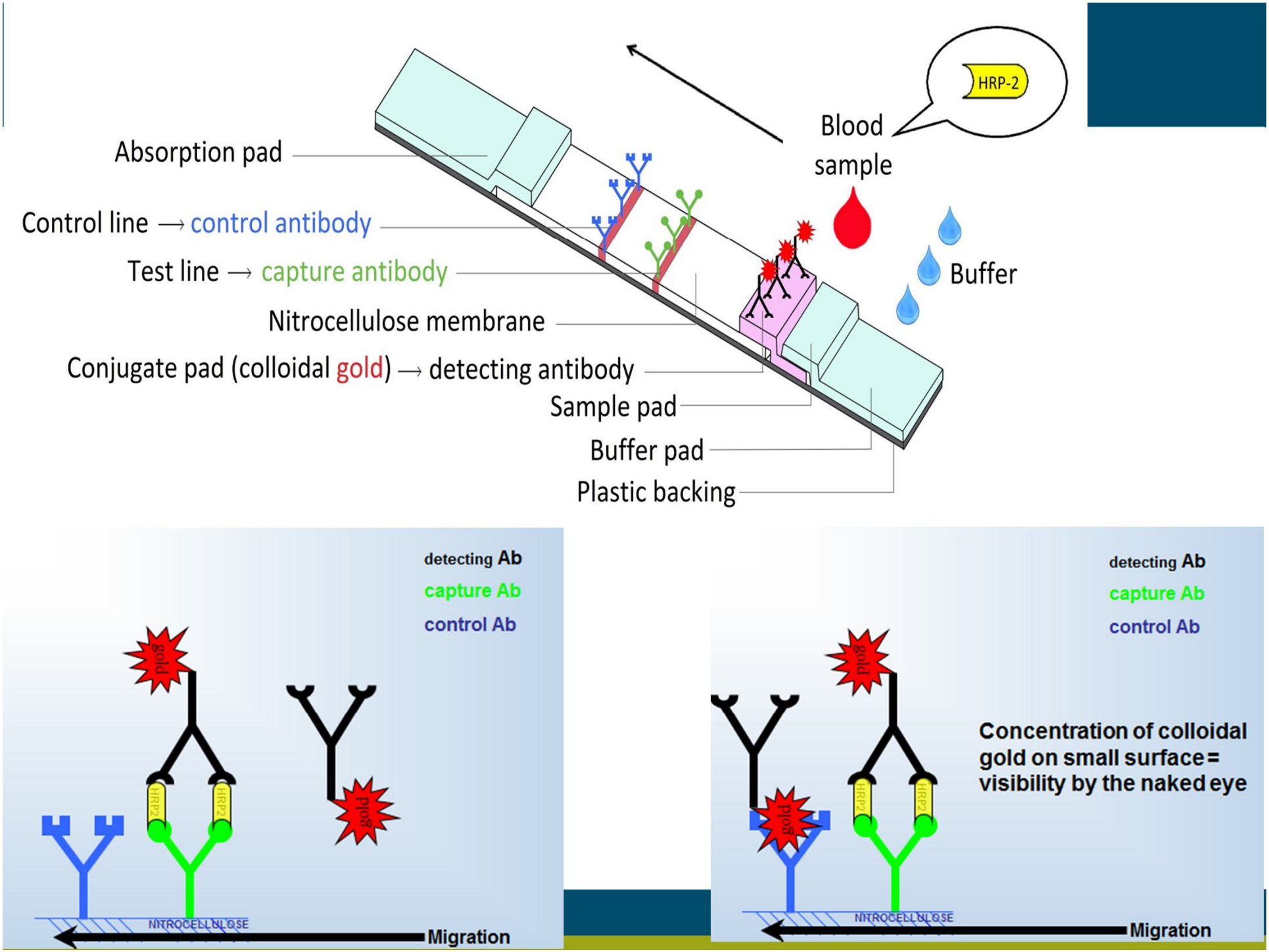


Lateral flow – principle





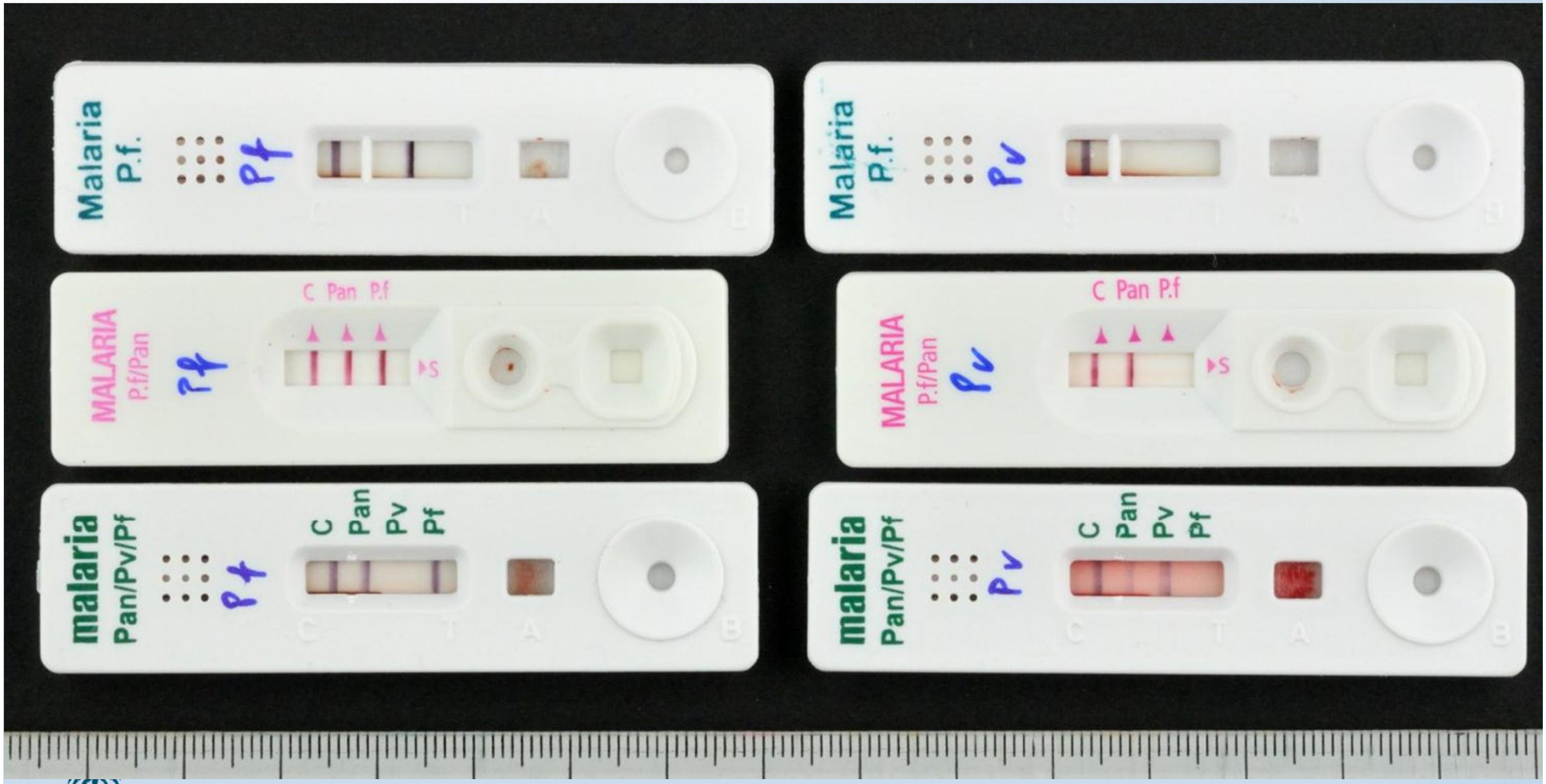



HRP-2
Blood sample
Buffer
Absorption pad
Control line ⟶ control antibody
Test line ⟶ capture antibody
Nitrocellulose membrane
Conjugate pad (colloidal gold) ⟶ detecting antibody
Sample pad
Buffer pad
Plastic backing
detecting Ab
capture Ab
control Ab
gold
HRP2
NITROCELLULOSE
Migration
detecting Ab
capture Ab
control Ab
Concentration of colloidal gold on small surface = visibility by the naked eye
gold
HRP2
NITROCELLULOSE
Migration

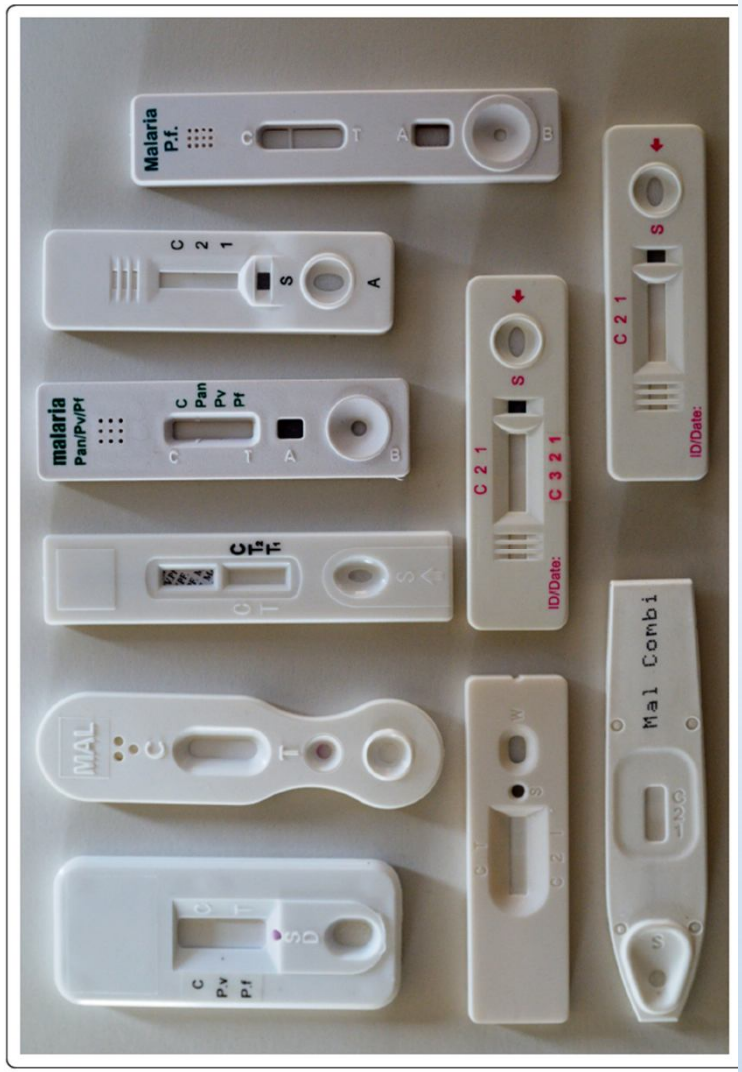
Antigens targeted by malaria RDTs

HRP-2 Histidine-rich protein-2	P. falciparum	Trophozoites + young gametocytes Persistence up to 43 days after treatment
pLDH Parasite Lactate Dehydrogenase	1. P.falciparum 2. All species (pan) 3. P.vivax	Viable trophozoites and gametocytes No persistence
Aldolase	All species	No persistence

Two-, three- and four band RDTs



POC: pursuing the ASSURED criteria



- Affordable
- Sensitive
- Specific
- User-friendly
- Robust
- Equipment-free
- Deliverable to end-user

Diagnostic characteristics of malaria RDTs

Sensitivity	***P. falciparum***	**95 – 100%**	**drops below 100/µl***
	P. vivax	**75 – 90%**	**drops below 500/µl**
	P. malariae	**10 – 50%**	
	P. ovale	**10 – 50%**	

Specificity **Rheumatoid factor and antinuclear antibodies**
Schistosomiasis, hepatitis B/C, sleeping sickness (rare)

*** Children and non-immune persons may have symptoms**

So mostly supplied all-in (“Kit” and “Single kit”)

Single kit meenemen)

… in remote settings, where no microscopy is available

RDTs perform well, equal or superior to routine microscopy

A good RDT is better than “avarage” microscopy for diagnosis of *P. falciparum* malaria

Reliable tool for parasite-based treatment (WHO)

No species determination

(though presence of P falciparum confirmed)

No treatment follow-up

No parasite density

RDTs : excellent but not fail-proof

(Design and Engineering)
Rolling out
The intended user
Production
Market
Procurement
Supply
Transport, storage
End-user errors
Harmonization

Design and Engineering I

HRP-2 deletions

Low parasite densities: detection limt
High parasite densities: prozone

HRP-2 persistence: up to 42 days
- Uncomplicated malaria: recurrence overlooked (Ayden-Schmidt 2014)
- Severe malaria: mostly recent malaria
- Travellers: recent malaria

Line intensity
- Faint test lines: low parasite densities but also product-related
- Faint test lines are disregarded as negative

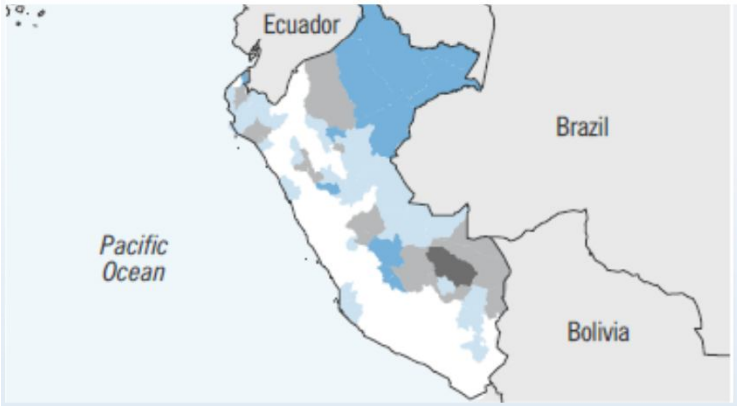
OPEN ACCESS Freely available online

PLOS ONE

Rapid Diagnostic Tests for Malaria Diagnosis in the Peruvian Amazon: Impact of *pfhrp2* Gene Deletions and Cross-Reactions

Jessica Maltha[1]*, Dionicia Gamboa[2,3], Jorge Bendezu[2], Luis Sanchez[2], Lieselotte Cnops[1], Philippe Gillet[1], Jan Jacobs[1]

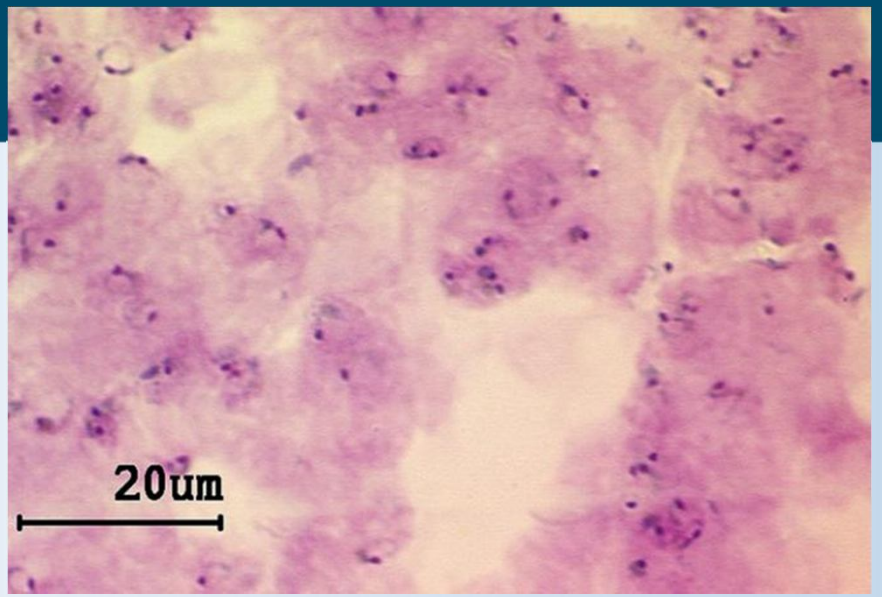
1 Department of Clinical Sciences, Institute of Tropical Medicine, Antwerp, Belgium, **2** Instituto de Medicina Tropical "Alexander von Humboldt", Universidad Peruana Cayetano Heredia, Lima, Peru, **3** Departamento de Ciencias Celulares y Moleculares, Facultad de Ciencias y Filosofia, Universidad Peruana Cayetano Heredia, Lima, Peru



Detection antigens	Nr of RDT products
PfHRP2	1
PfHRP2 & pan-pLDH	3
PfHRP2 & Pv-pLDH	5
Pf-pLDH & pan-pLDH	3
PfHRP2 & Pf-pLDH	1

Detection antigen	% Sensitivity median (range)
PfHRP2	71.6% (70.3 %– 71.6%)
Pf-pLDH	98.7% (97.3% - 98.7%)

PATIENT FROM NIGERIA

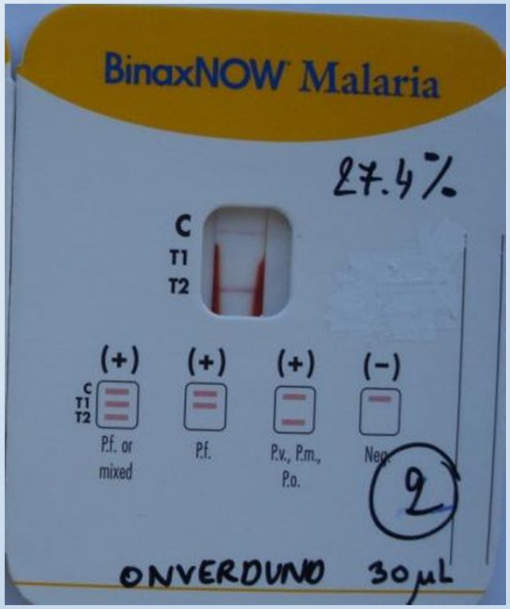


Microscopy:

- *P. falciparum*
  - **Parasitaemia : 30 %**

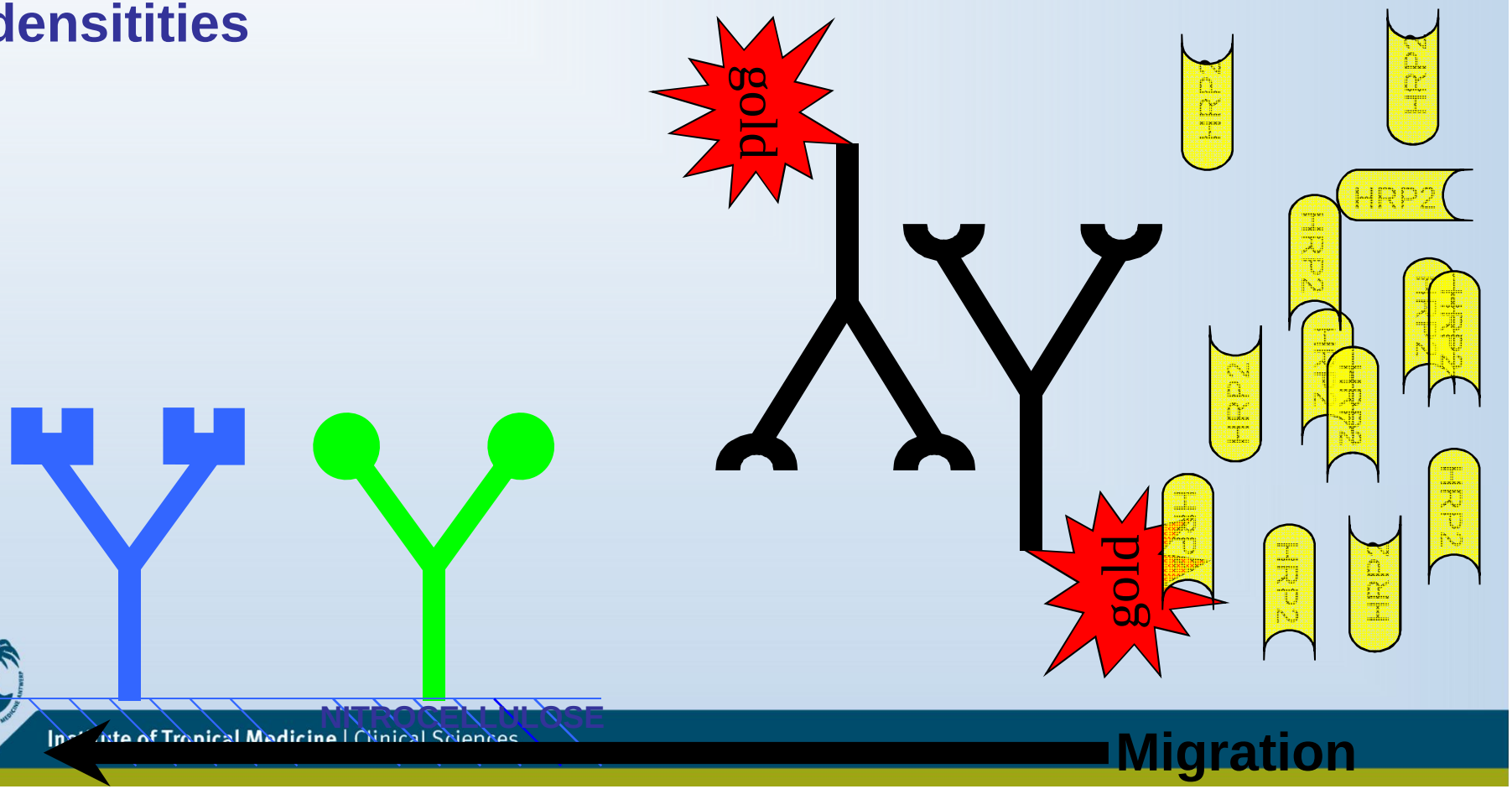
RDT:

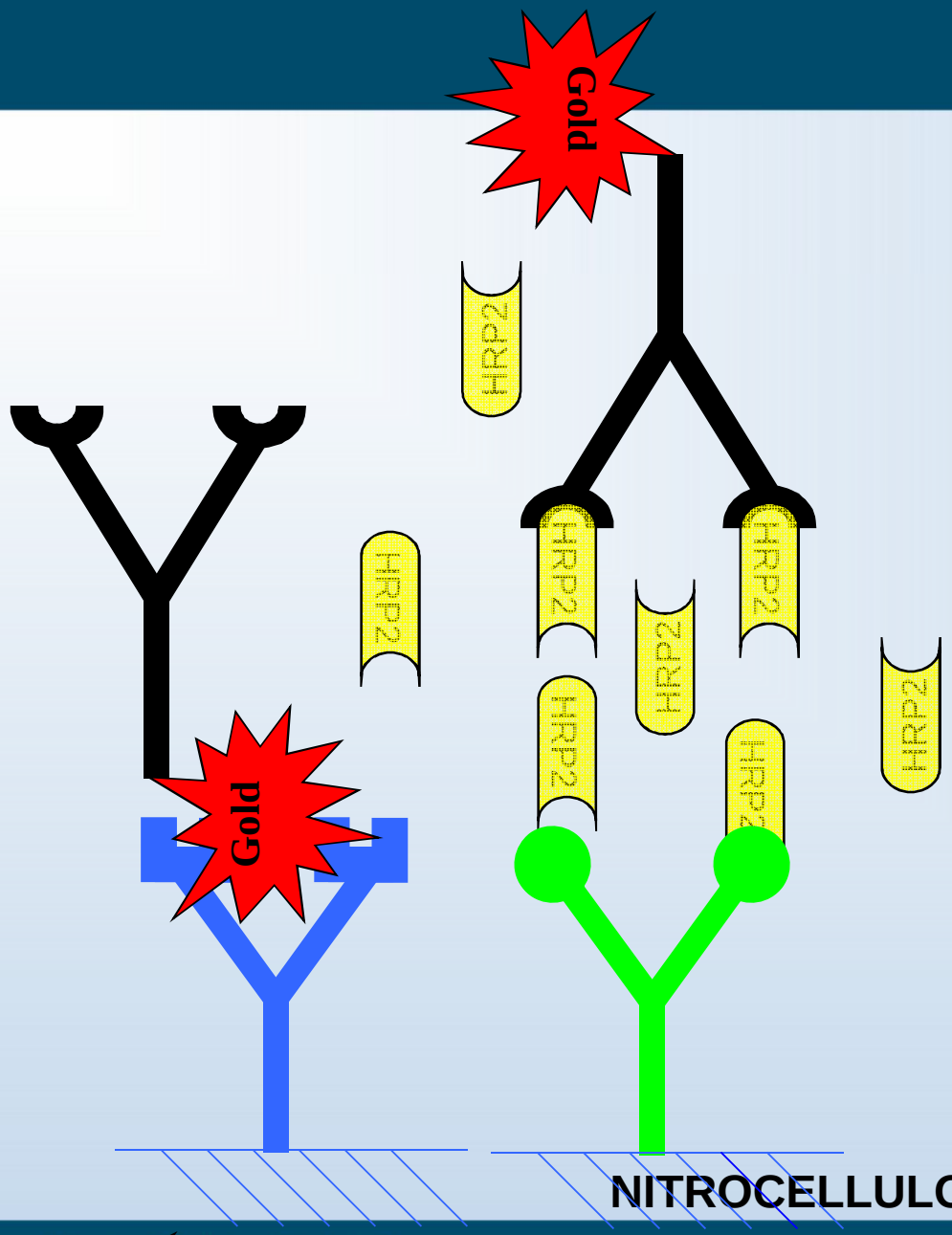
- ***Plasmodium* non *falciparum***



Prozone effect or High Dose Hook Effect”

False-negative results at high parasite densitities




Gold
HRP2
HRP2
HRP2
HRP2
HRP2
HRP2
HRP2
Gold
detecting Ab
capture Ab
control Ab
NITROCELLULOSE MEMBRANE

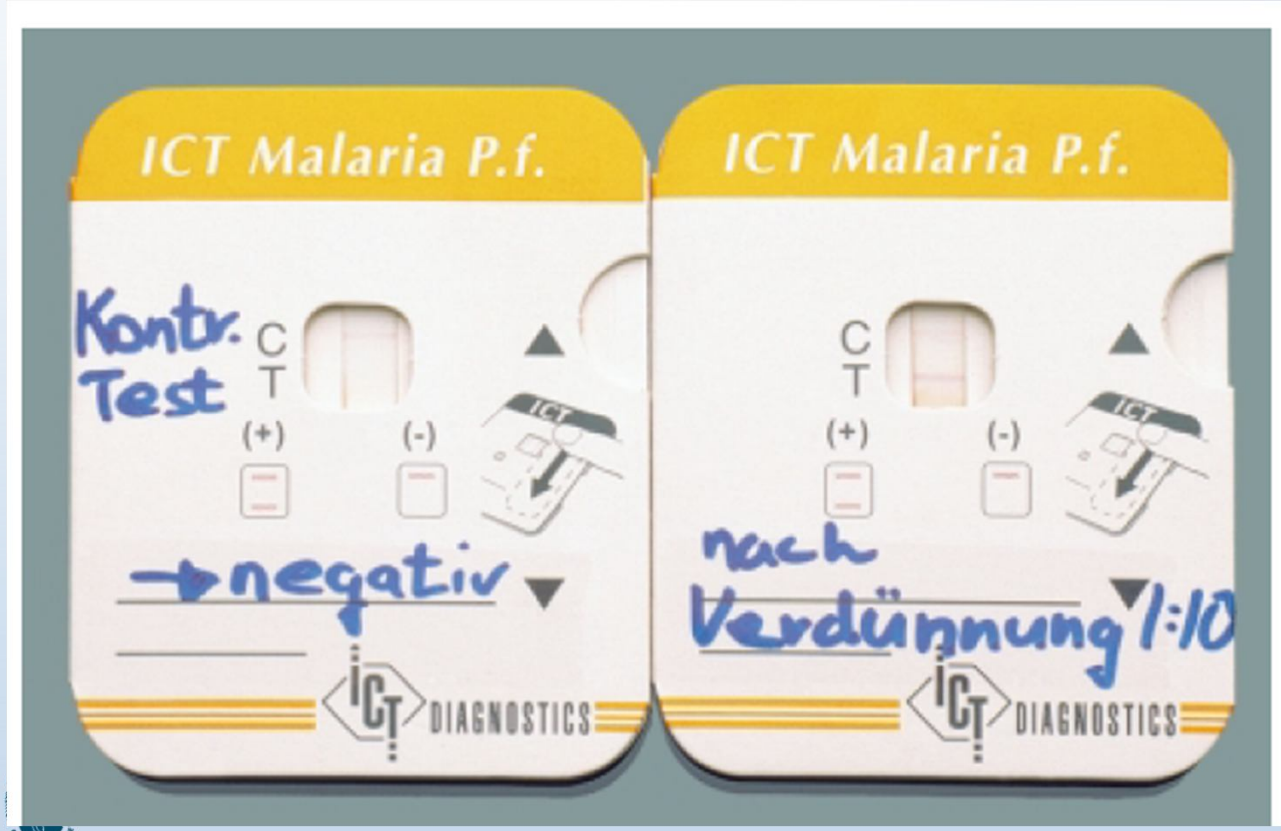
Coup d'œil

Schweiz Med Wochenschr 1999;129:1002

Falsch negativer Malaria-Schnelltest

L. Risch, M. Bader, A. R. Huber

Zentrum für Labormedizin,
Kantonsspital Aarau



Bedside diagnosis of imported malaria using the Binax Now malaria antigen detection test

LOTHAR WIESE[1], BRITA BRUUN[2], LEIF BÆK[3], ALICE FRIIS-MØLLER[4], BENTE GAHRN-HANSEN[5], JOANNA HANSEN[2], OLE HELTBERG[6], TOVE HØJBJERG[7], MAREN KATHRINE HORNSTRUP[8], BIRGIT KVINESDAL[9], GRETHE GOMME[1] & JØRGEN A. L. KURTZHALS[1]

From the [1]Centre for Medical Parasitology, Department of Clinical Microbiology, Copenhagen University Hospital (Rigshospitalet), [2]Department of Clinical Micr Clinical Microbiology, Copenhagen University Hospital (Herlev), [4]Department University Hospital (Hvidovre), [5]Department of Clinical Microbiology, Odense U Microbiology, Næstved Hospital, [7]Department of Clinical Microbiology, Aalborg [8]Department of Infectious Diseases, Odense University Hospital, and [9]Departme

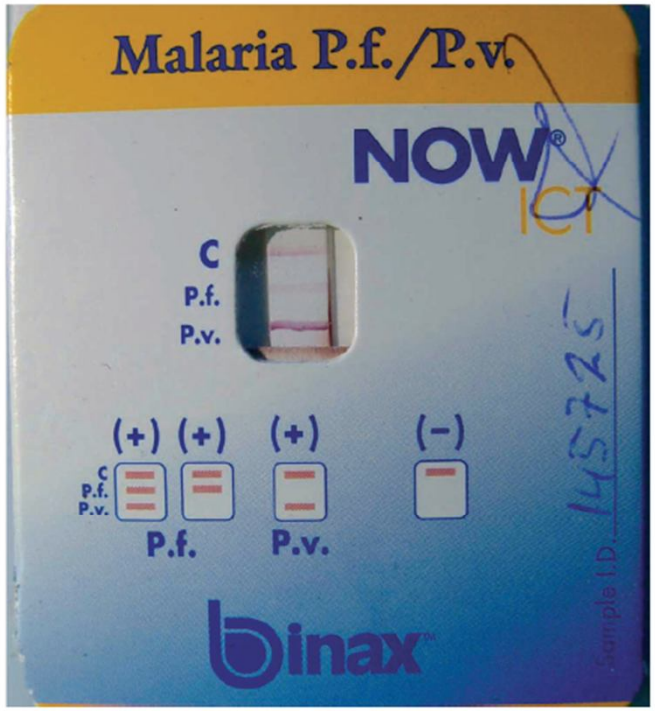


Figure 1. Test result in a 64-year old woman who had returned from The Gambia a week before hospitalization. The parasitemia detected by microscopy was 31%. The weak Plasmodium falciparum band is notable.

Example

REVIEW Open Access

Assessment of two malaria rapid diagnostic tests in children under five years of age, with follow-up of false-positive pLDH test results, in a hyperendemic falciparum malaria area, Sierra Leone

Sibylle Gerstl[1*], Sophie Dunkley[2], Ahmed Mukhtar[2], Martin De Smet[3], Samuel Baker[4], Jacob Maikere[3]

a parasitaemia of 1-2 parasites/μl. The two study persons with false negative results for Paracheck-Pf® test had a parasitaemia of 288,000 and 580,000 parasites/μl.

RESEARCH Open Access

Accuracy of a rapid diagnostic test on the diagnosis of malaria infection and of malaria - attributable fever during low and high transmission season in Burkina Faso

Zeno Bisoffi*[1,2], Sodiomon B Sirima[3], Joris Menten[4], Cristian Pattaro[5], Andrea Angheben[1], Federico Gobbi[1,2], Halidou Tinto[6], Claudia Lodesani[7], Bouma Neya[2], Maria Gobbo[1] and Jef Van den Ende[8]

ties. In one case, in the rainy season, a high parasite density (> 150,000/μl) was missed by the RDT. The patient, a six-year-old boy, was diagnosed as a case of malaria (the only symptoms were high fever and vomiting), but after the RDT result he was not given any antimalarial, but an antibiotic.

RESEARCH Open Access

Prozone in malaria rapid diagnostics tests: how many cases are missed?

Philippe Gillet[1*], Annelies Scheirlinck[1], Jocelijn Stokx[1,2], Anja De Weggheleire[1], Hélder S Chaúque[2], Oreana DJV Canhanga[2], Benvindo T Tadeu[3], Carla DD Mosse[3], Armindo Tiago[4], Samuel Mabunda[4], Cathrien Bruggeman[5], Emmanuel Bottieau[1] and Jan Jacobs[1]

Prospective field study, Mozambique

Most severely hit HRP-2 RDT: absent HRP-2 line

- **0.05% of patients suspected of malaria**
- **0.5% of *P. falciparum* samples**
- **4.4% of *P. falciparum* samples with high parasite density**

Design and Engineering I

Low parasite densities: detection limt

High parasite densities: prozone

HRP-2 persistence: up to 42 days

- Uncomplicated malaria: recurrence overlooked (Ayden-Schmidt 2014)
- Severe malaria: mostly recent malaria
- Travellers: recent malaria

Line intensity

- Faint test lines: low parasite densities but also product-related
- Faint test lines are disregarded as negative

Maltha *et al. Malaria Journal* 2014, **13**:20
http://www.malariajournal.com/content/13/1/20

MALARIA JOURNAL

RESEARCH Open Access

Accuracy of *Pf*HRP2 *versus* *Pf*-pLDH antigen detection by malaria rapid diagnostic tests in hospitalized children in a seasonal hyperendemic malaria transmission area in Burkina Faso

Jessica Maltha[1,2*], Issa Guiraud[3], Palpouguini Lompo[3], Bérenger Kaboré[3], Philippe Gillet[1], Chris Van Geet[2,4], Halidou Tinto[3] and Jan Jacobs[1]

Field – research setting

Co-infections and/or post-malaria bacterial infections

"Recent" malaria

Hospitalised children – severe malaria

SD 90 = HRP-2 and Pf-pLDH on a single RDT

Equal sensitivity (but overall lower line intensity of Pf-pLDH)
As expected, lower specificity of HRP-2

Table 3 Diagnostic accuracy of *Pf*HRP2- compared to *Pf*-pLDH-detection

	*Pf*HRP2	*Pf*-pLDH	*p*-value
RDT pos, n (%)	515 (74.2)	404 (54.2)	
SE (95% CI)	100.0 (94.7 - 100.0)	98.7 (93.5-99.9)	1.0
Sp (95% CI)	70.9 (67.4 - 70.9)	94.0 (90.6 - 94.8)	< 0.001
PPV (95% CI)	69.4 (65.7 - 69.4)	91.6 (86.8 - 92.7)	< 0.001
NPV (95% CI)	100.0 (95.1 - 100.0)	99.1 (95.5 - 100.0)	1.0

N = number, NPV = negative predictive value, *Pf*HRP2 = *P. falciparum* Histidine-rich protein-2, *Pf*-pLDH = *P. falciparum*-specific parasite lactate dehydrogenase pos = positive, PPV = positive, predictive value SE = sensitivity, Sp = specificity.

Example

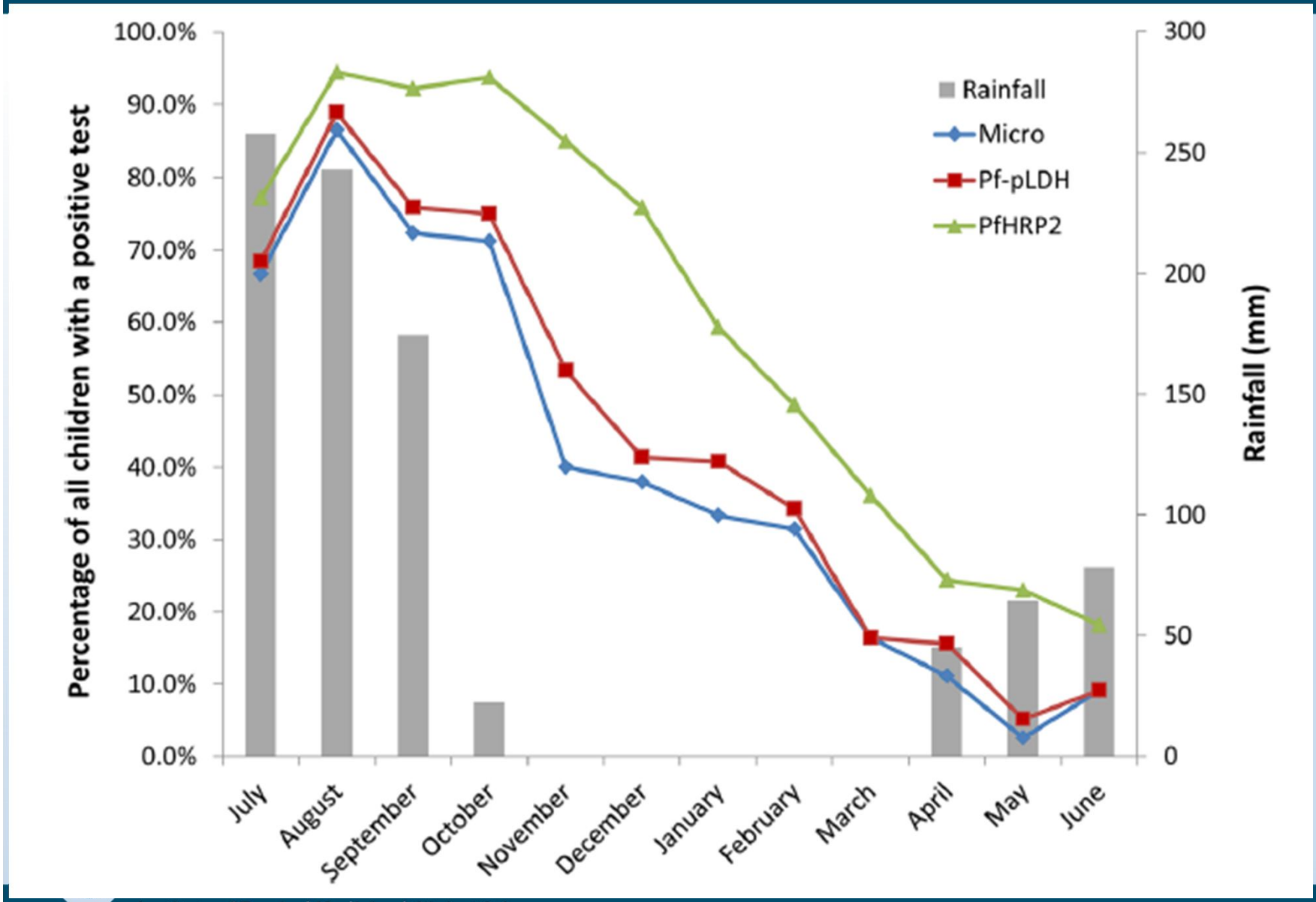
RDT line intensity

For *Pf*-pLDH, 2.4% (nine/375) of true positive test lines was of faint intensity, for *Pf*HRP2 this was 0.5% (two/376). For the *P. falciparum* positive samples, the *Pf*HRP2 test line compared to the corresponding *Pf*-pLDH test line for the same sample was of stronger and weaker intensity in 179/376 (47.6%) and 31/376 (8.2%) samples, respectively. For seven samples with high parasite density (82,080-392,535/µl) *Pf*HRP2 was of weak intensity while *Pf*-pLDH was of strong intensity. Among the false positive test lines (excluding pure gametocytaemia), two/20 (10%) *Pf*-pLDH and 67/126 (53.2%) *Pf*HRP2 lines were of medium or strong intensity.

Table 2 *Pf*HRP2 and *Pf*-pLDH results according to parasite density

Microscopy	Number	*Pf*HRP2 pos		*Pf*HRP2 neg	
		Pf-pLDH pos	*Pf*-pLDH neg	*Pf*-pLDH pos	*Pf*-pLDH neg
1 - 100	3	2	1		
101 - 1,000	25	25			
1,001 - 10,000	66	66			
10,001 - 100,000	199	199			
> 100,000	83	83			
pure gametocytemia	13	8	4	1	
Microscopy negative	303	17	110	1	175
P. ovale	2			2	
Total	694	400	115	4	175

Specificity decreases in the course of rainy season



Example

False-positive HRP-2 was associated with

- **Recently installed treatment**
- **PCR-positivity**

! Referral-track

Prior use of anti-malarial treatment (either by self-medication or prescription) reflects real-life situation in malaria-endemic settings. To know if the child is actually suffering from malaria, an ideal RDT should be able to differentiate ongoing infection from a previously currently cured episode of infection, but *Pf*HRP2 is not capable of doing so. *Pf*-pLDH RDTs seem to be more promising in that respect as they turn negative in two to seven days, but future studies should assess their evolution over time after start of treatment.

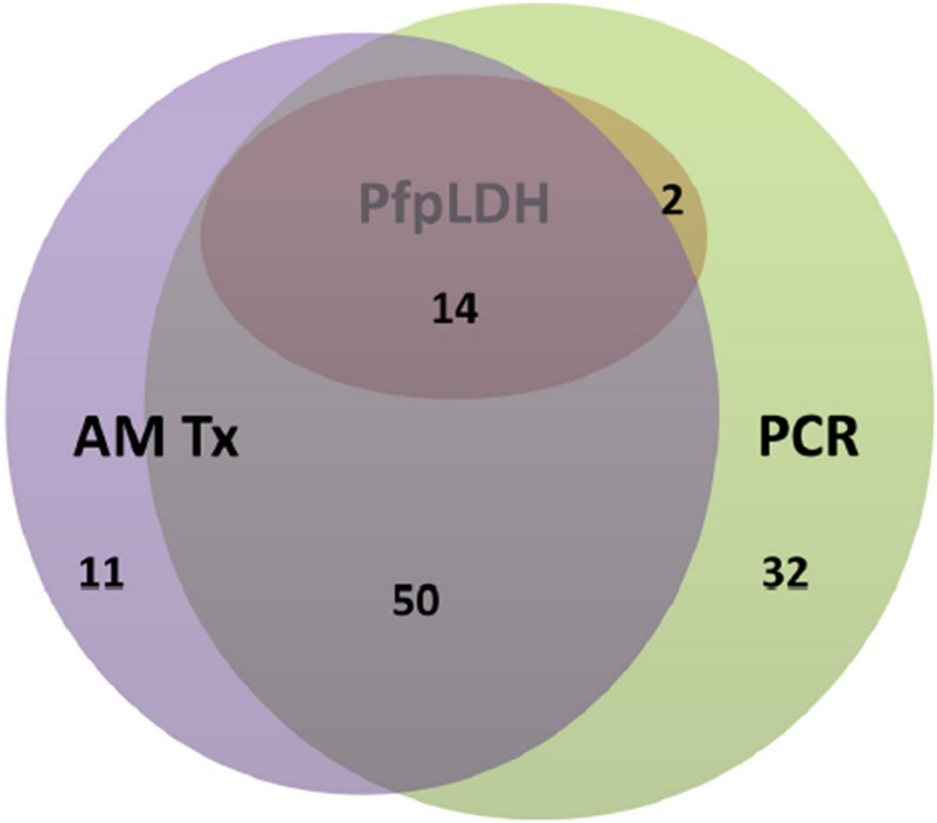


Figure 3 Positive polymerase chain reaction and *Pf*-pLDH results and report of previous anti-malarial treatment for false-positive *Pf*HRP2 samples. *Only those samples with false positive PfHRP2 for which PCR was performed are displayed (n = 114). AM Tx = previous anti-malarial treatment, PfpLDH = positive Pf-pLDH test line, PCR = positive PCR result. For five children none of the aforementioned was positive.*

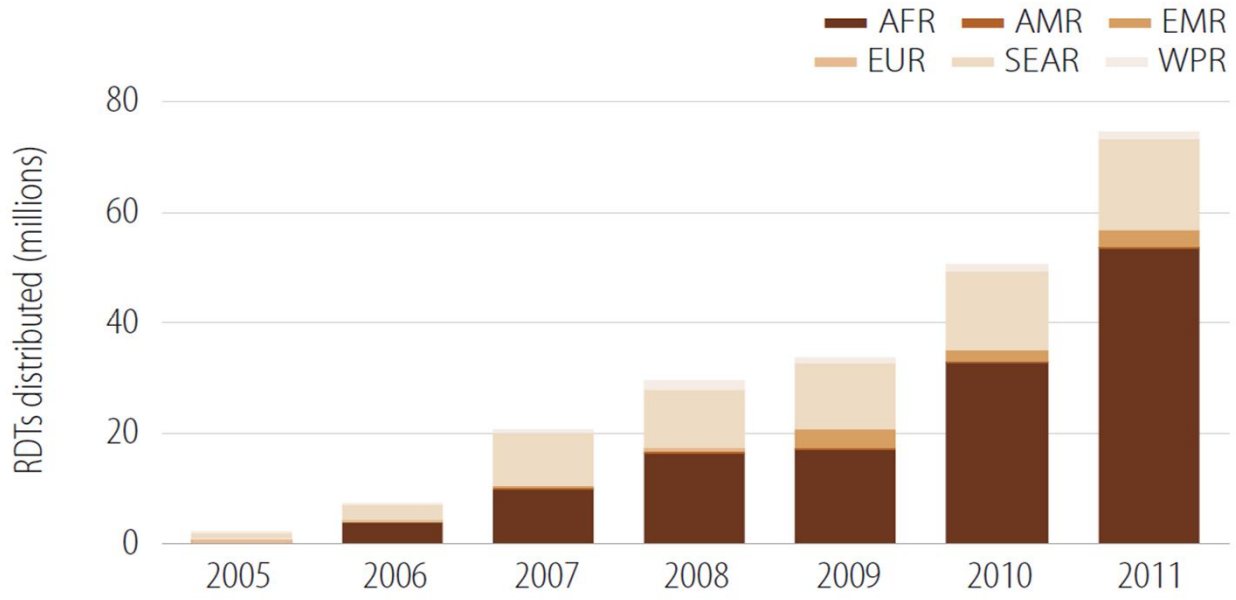
WHO 2010: no treatment without diagnosis (Test, Treat, Track)

Market of Scale

200.000 tests in 2005

220.000.000 tests in 2013

Figure 6.4 RDTs distributed by NMCPs, by WHO Region, 2005–2011



Source: NMCP reports
RDTs distributed in Europe and Americas are a very small fraction of the number distributed in other WHO Regions

The end-user: from laboratory to decentral testing

- Travel medicine
- Reference laboratory
- Health center
- Health post
- Community health worker
- Private sector
- Retail outlets & Shops
- Home testing
- Self testing

Professional use versus Self-testing

Non-endemic settings (Europe):

Diagnostic Laboratories ISO 15189

Point-of-Care ISO 22870

Endemic setting:

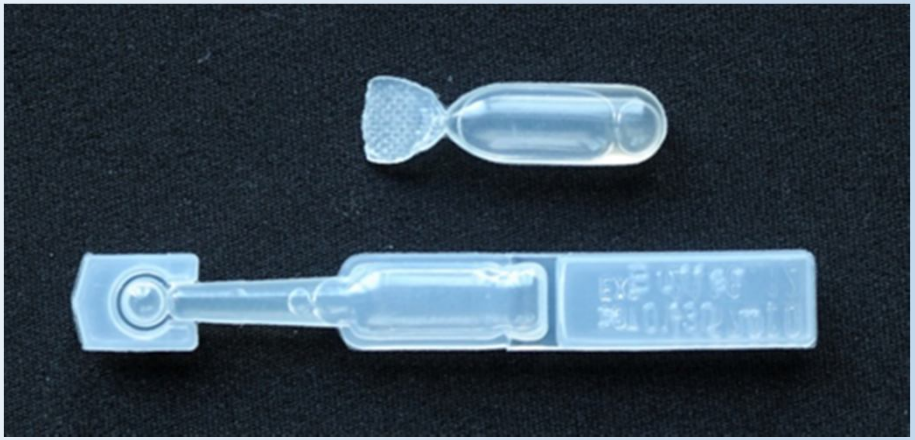
"Intended for professional use"

ISO 18113: professional user =
"qualified to perform IVD testing through special education and training":
leaves room for community health worker and private sector.

ISO 18113: self-testing = lay-person =
"no formal training in a relevant medical field or discipline"

Long-term and expatriates

“Single packs” but no formal (CE) approval for Self-testing



Market of Scale

200.000 tests in 2005

220.000.000 tests in 2013

Pressure on Prices

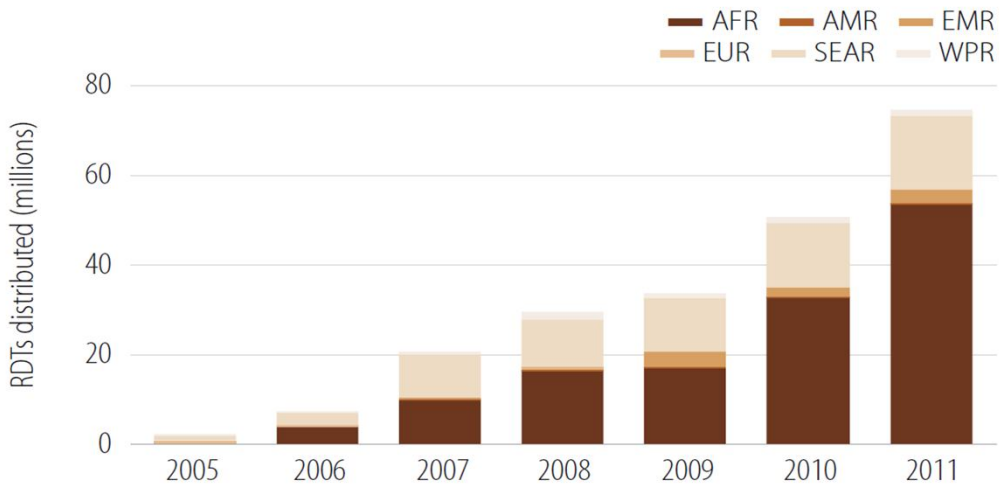
Pressure on Lead times

Pressure on Manufacturing

Pressure on Cost-savings

Pressure on R & D

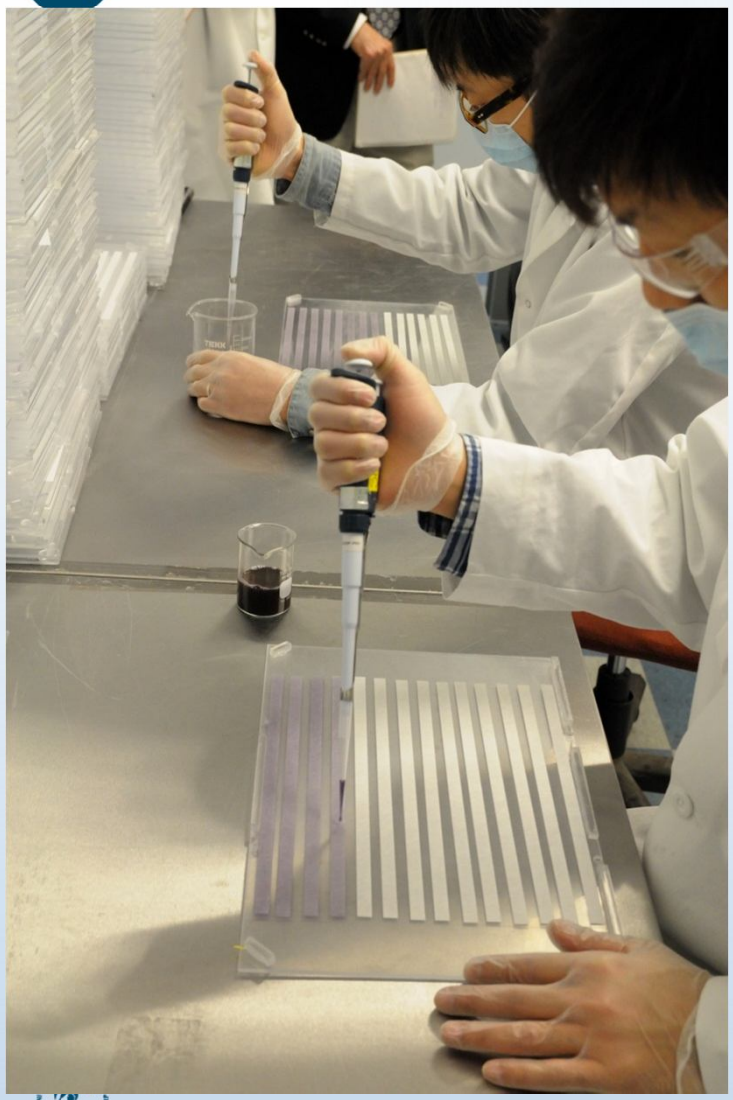
Figure 6.4 RDTs distributed by NMCPs, by WHO Region, 2005–2011



Source: NMCP reports
RDTs distributed in Europe and Americas are a very small fraction of the number distributed in other WHO Regions

Scaling up of production….
Skills – Human Resources

Production = still manual work



Pressure on cost/No standards

Barbé *et al. Malaria Journal* 2012, **11**:326
http://www.malariajournal.com/content/11/1/326

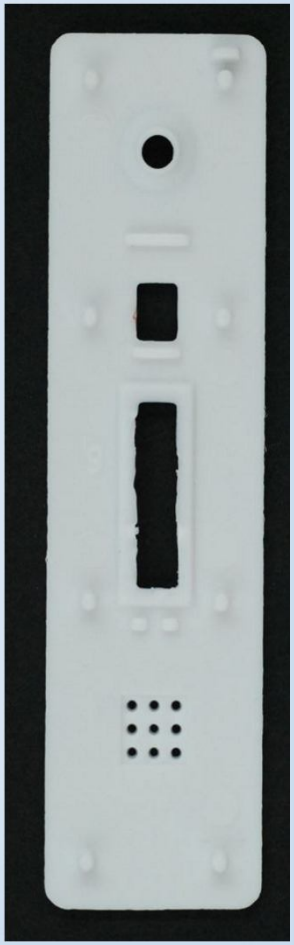
MALARIA JOURNAL

RESEARCH Open Access

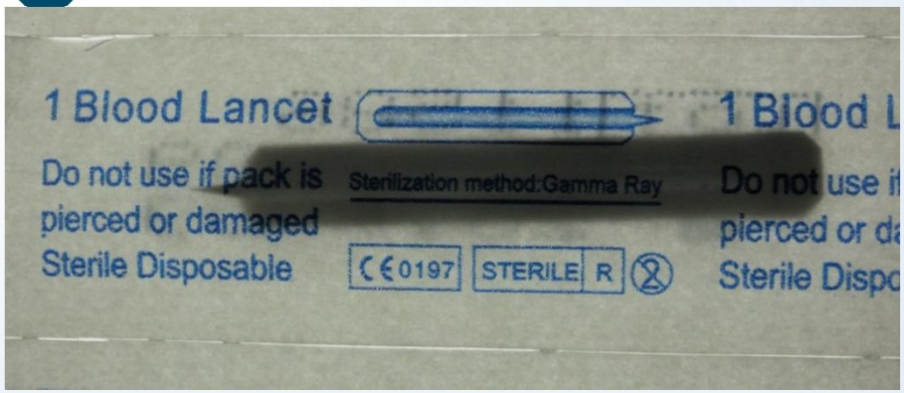
Assessment of desiccants and their instructions for use in rapid diagnostic tests

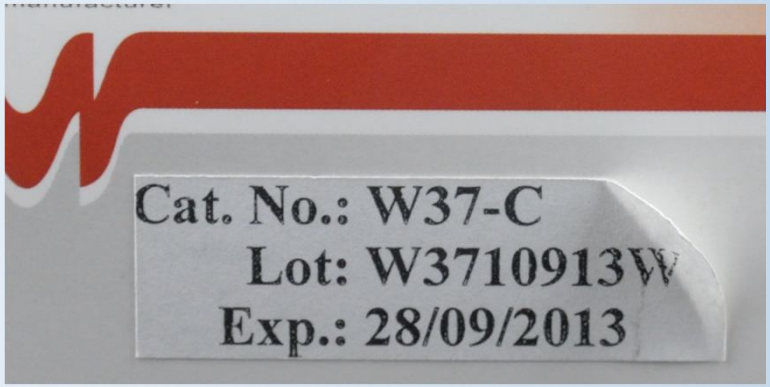
Barbara Barbé[1], Philippe Gillet[1], Greet Beelaert[2], Katrien Fransen[2] and Jan Jacobs[1*]

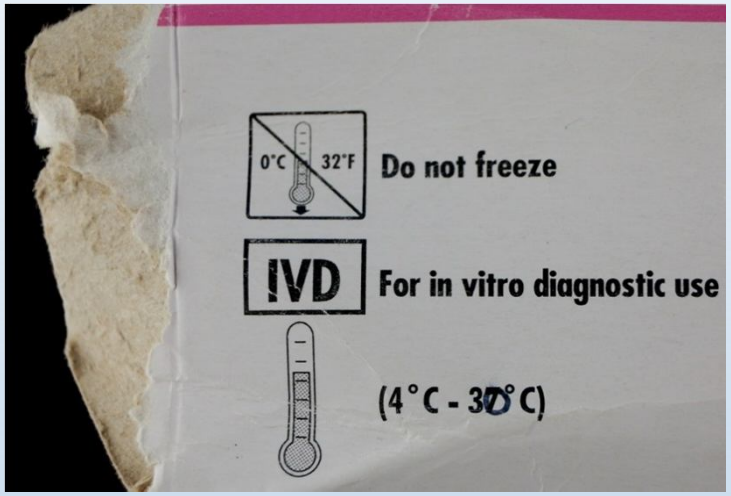
Pressure on cost/No standards

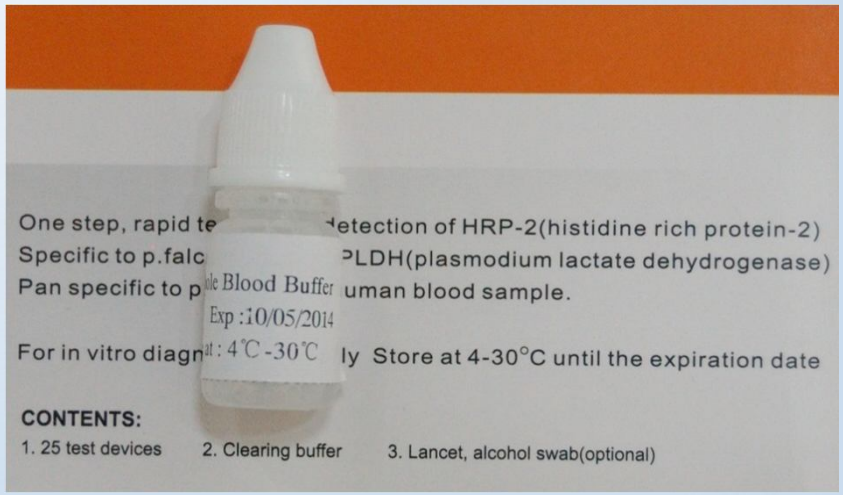


Pressure on quality









Procurement/supply pipeline National Malaria Control Programme

Select type of RDT

Estimate needs

Budget (donors)

Technical “specs”

Diagnostic performance

Manufacturer

Lot-testing

Bidding proces

Custom clearance

Shipment and Distribution

Batch traceability

Global Fund GF
Presidents’ malaria initiative PMI
World Bank
NGOs

WHO Global Malaria Programme
Foundation for Innovative New Diagnostics

WHO Prequalification

Guidance

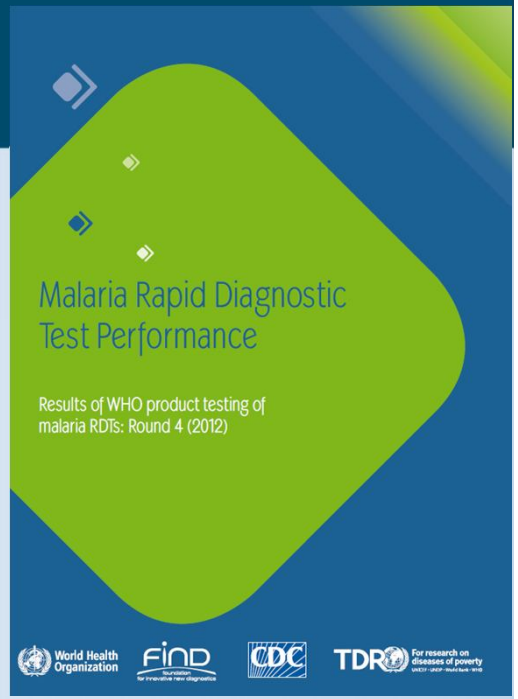
WHO Global Malaria Program

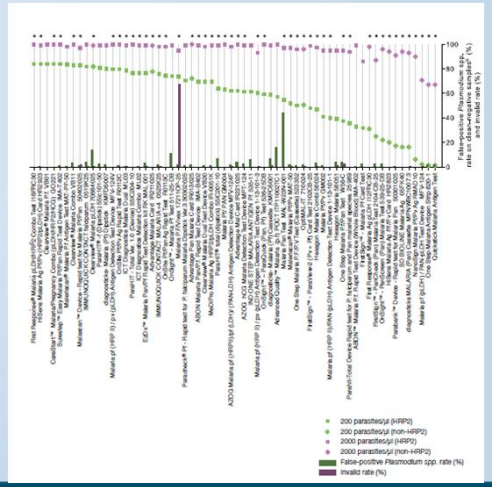
Foundation for Innovative New Diagnostics

- Side-to-side testing
- Lot testing

WHO prequalifcation

- ISO 13485
- audits and post-marketing surveillance





Stock management... Example time and quantity of ordering

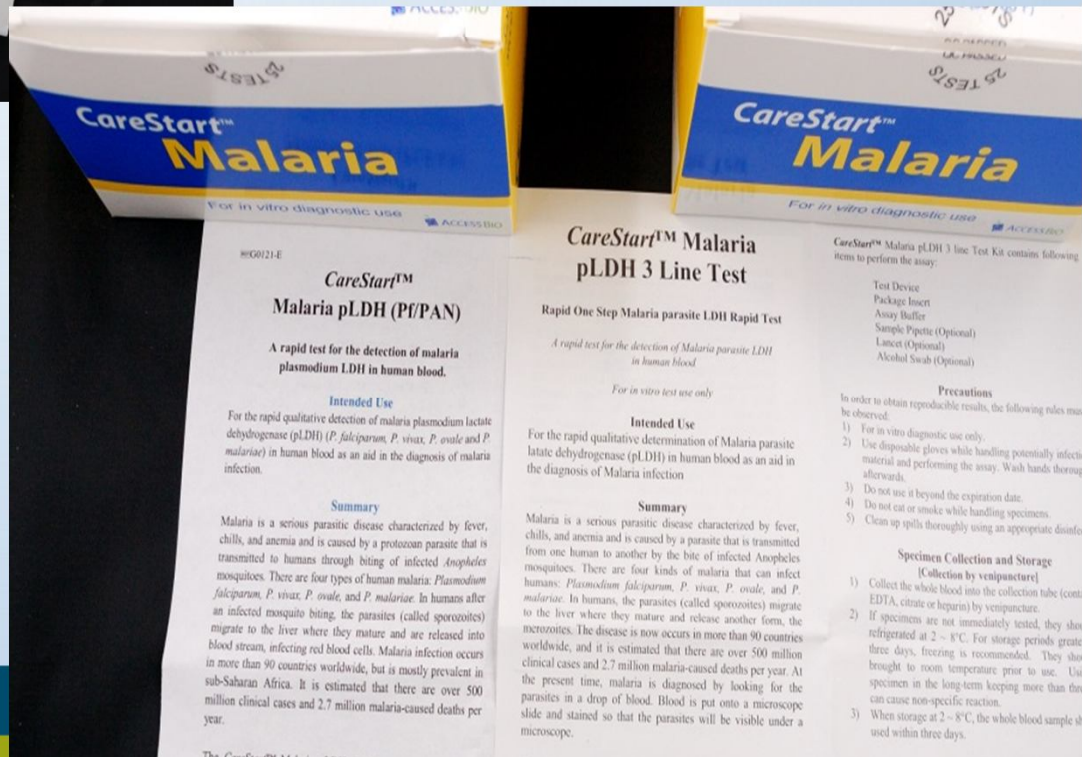
$$Qo = Ca \times (LT + PP) + SS - (Si + So)$$

- **Qo** is the quantity of RDTs to be re-ordered in the next procurement period
- **Ca** is the average monthly consumption, adjusted for stock-outs
- **LT** is the lead time (expressed in months)
- **PP** is the procurement period (expressed in months)
- **SS** is the safety stock
- **Si** is the stock in inventory (on hand)
- **So** is the stock on order but not yet received

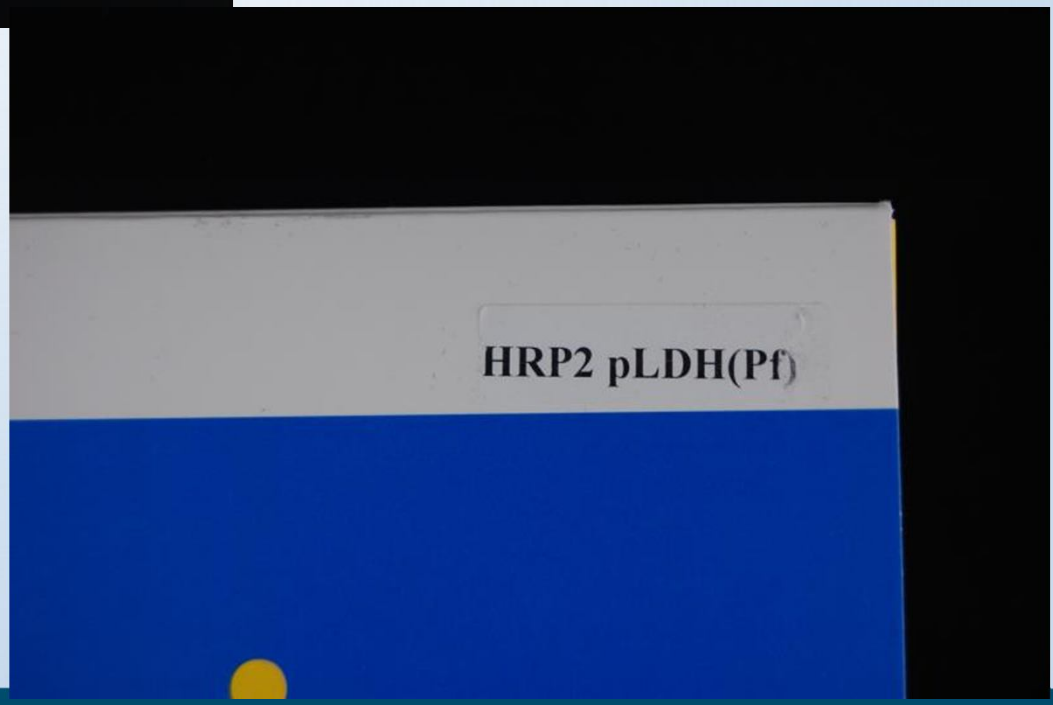
Procurement and supply

- Unequivocal product name
- Unequivocal product code
- Meaningful name
- Clear labeling
- Commercial pressure?


CareStart™
Malaria
For in vitro diagnostic use
Store at 4°-30°C (39°-86°F)
ACCESSBIO
pLDH 3 lines (PAN/Pf)
CareStart™
Malaria
For in vitro diagnostic use
Store at 4°-30°C (39°-86°F)
25 TESTS
ACCESSBIO
CareStart™
Malaria pLDH (Pf/PAN)
A rapid test for the detection of malaria plasmodium LDH in human blood.
Intended Use
Summary
CareStart™ Malaria
pLDH 3 Line Test
Rapid One Step Malaria parasite LDH Rapid Test
A rapid test for the detection of Malaria parasite LDH in human blood
For in vitro test use only
Intended Use
Summary


CareStart™
Malaria
For in vitro diagnostic use
ACCESSBIO
25 TESTS
CareStart™
Malaria
For in vitro diagnostic use
ACCESSBIO
25 TESTS
CareStart™
Malaria pLDH (Pf/PAN)
A rapid test for the detection of malaria plasmodium LDH in human blood.
Intended Use
For the rapid qualitative detection of malaria plasmodium lactate dehydrogenase (pLDH) (P. falciparum, P. vivax, P. ovale and P. malariae) in human blood as an aid in the diagnosis of malaria infection.
Summary
Malaria is a serious parasitic disease characterized by fever, chills, and anemia and is caused by a protozoan parasite that is transmitted to humans through biting of infected Anopheles mosquitoes. There are four types of human malaria: Plasmodium falciparum, P. vivax, P. ovale, and P. malariae. In humans after an infected mosquito biting, the parasites (called sporozoites) migrate to the liver where they mature and are released into blood stream, infecting red blood cells. Malaria infection occurs in more than 90 countries worldwide, but is mostly prevalent in sub-Saharan Africa. It is estimated that there are over 500 million clinical cases and 2.7 million malaria-caused deaths per year.
CareStart™ Malaria
pLDH 3 Line Test
Rapid One Step Malaria parasite LDH Rapid Test
A rapid test for the detection of Malaria parasite LDH in human blood
For in vitro test use only
Intended Use
For the rapid qualitative determination of Malaria parasite latate dehydrogenase (pLDH) in human blood as an aid in the diagnosis of Malaria infection
Summary
Malaria is a serious parasitic disease characterized by fever, chills, and anemia and is caused by a parasite that is transmitted from one human to another by the bite of infected Anopheles mosquitoes. There are four kinds of malaria that can infect humans: Plasmodium falciparum, P. vivax, P. ovale, and P. malariae. In humans, the parasites (called sporozoites) migrate to the liver where they mature and release another form, the merozoites. The disease is now occurs in more than 90 countries worldwide, and it is estimated that there are over 500 million clinical cases and 2.7 million malaria-caused deaths per year. At the present time, malaria is diagnosed by looking for the parasites in a drop of blood. Blood is put onto a microscope slide and stained so that the parasites will be visible under a microscope.
CareStart™ Malaria pLDH 3 line Test Kit contains following items to perform the assay:
Test Device
Package Insert
Assay Buffer
Sample Pipette (Optional)
Lancet (Optional)
Alcohol Swab (Optional)
Precautions
1) For in vitro diagnostic use only.
2) Use disposable gloves while handling potentially infecti material and performing the assay. Wash hands thorou afterwards.
3) Do not use it beyond the expiration date.
4) Do not eat or smoke while handling specimens.
5) Clean up spills thoroughly using an appropriate disinfe
Specimen Collection and Storage
[Collection by venipuncture]
1) Collect the whole blood into the collection tube (cont EDTA, citrate or heparin) by venipuncture.
2) If specimens are not immediately tested, they shou refrigerated at 2 ~ 8°C. For storage periods greate three days, freezing is recommended. They shou brought to room temperature prior to use. Us specimen in the long-term keeping more than thr can cause non-specific reaction.
3) When storage at 2 ~ 8°C, the whole blood sample sh used within three days.

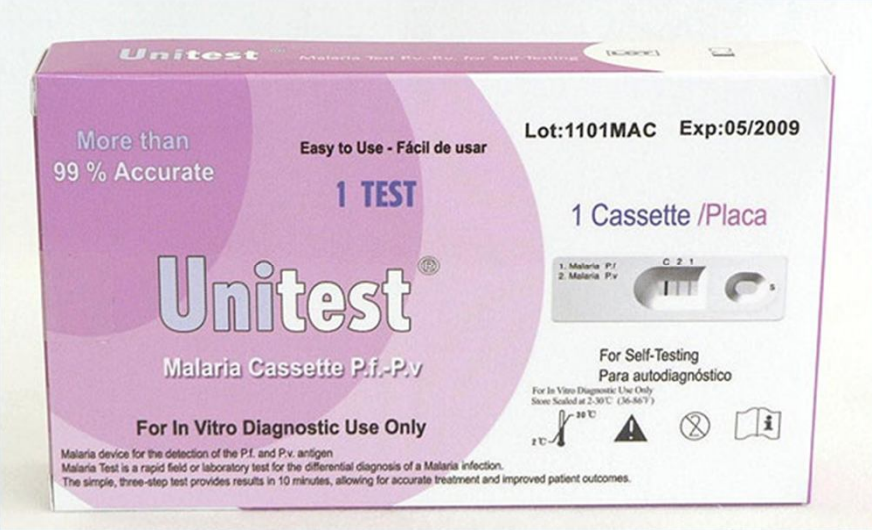
One box is used for all types of malaria RDTs – local distributor added label with the targeted antigens

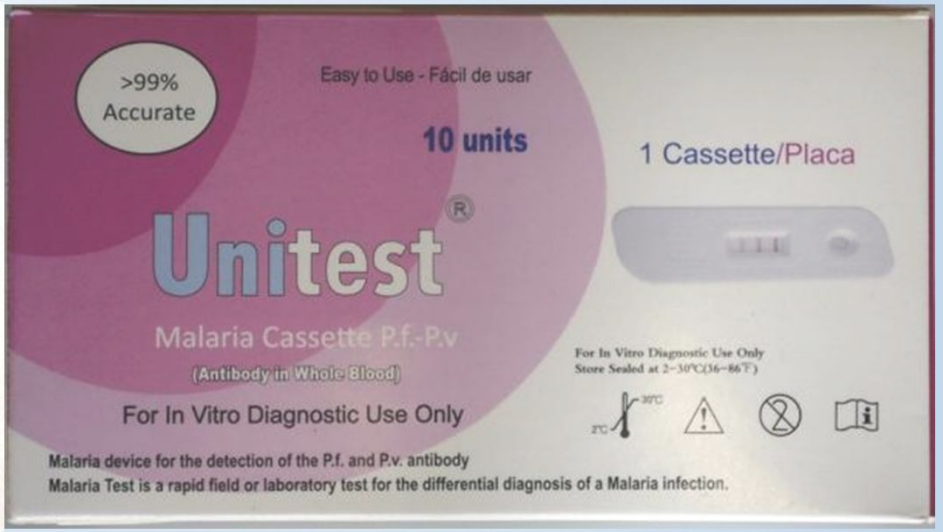


1 label for buffer bottles of all RDT products of 1 company

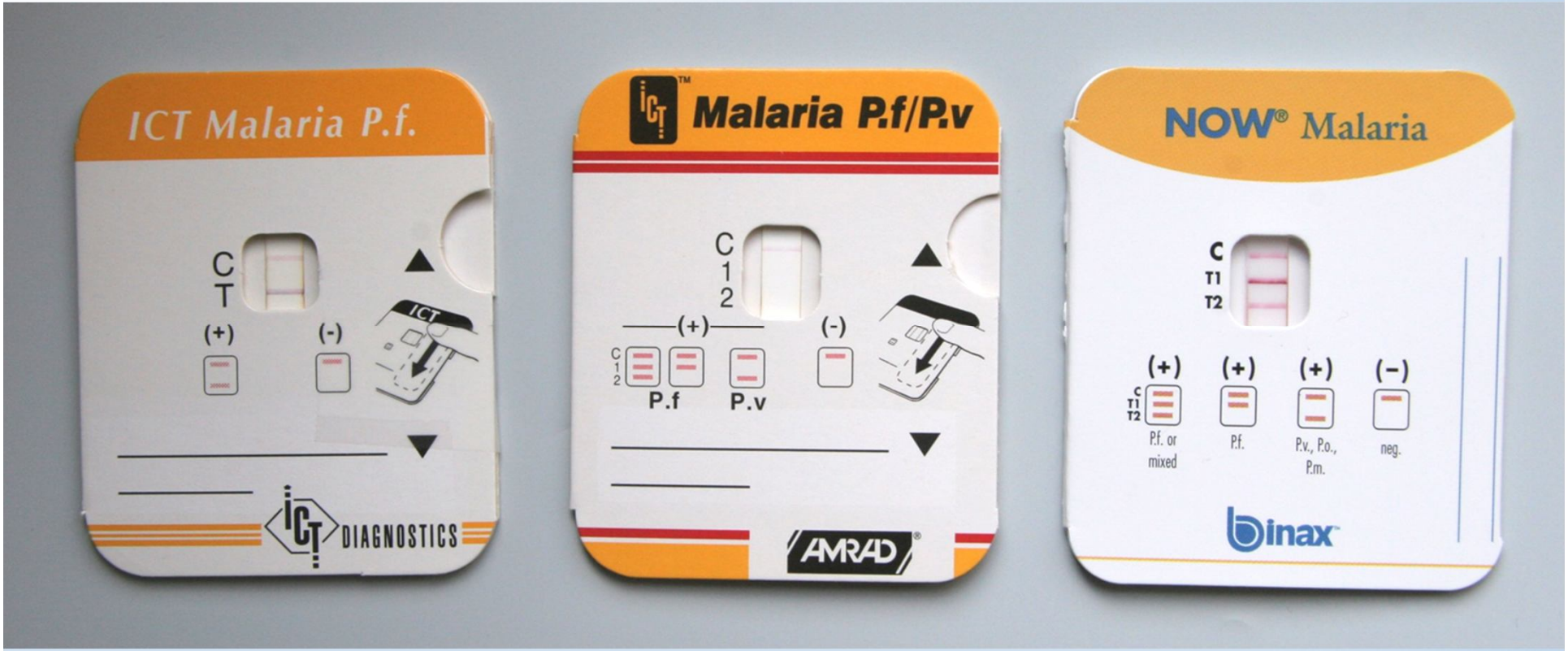
Internet Sales (Peeling2011, Maltha2013)

Upon ordering a malaria RDT, we received...





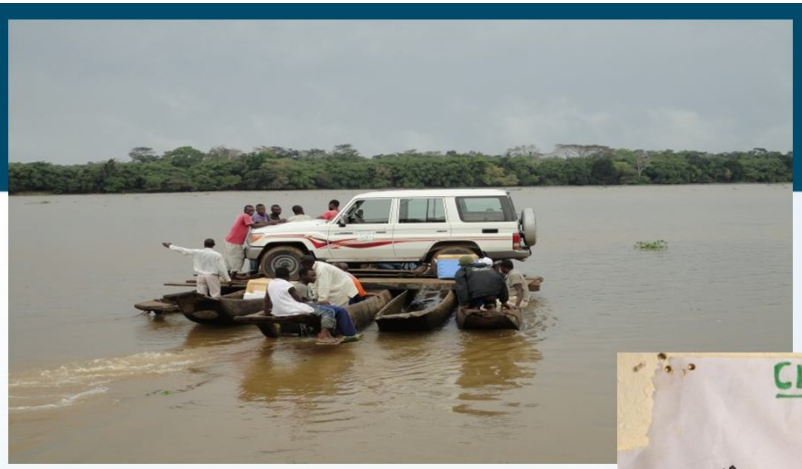
1996 1999 2000

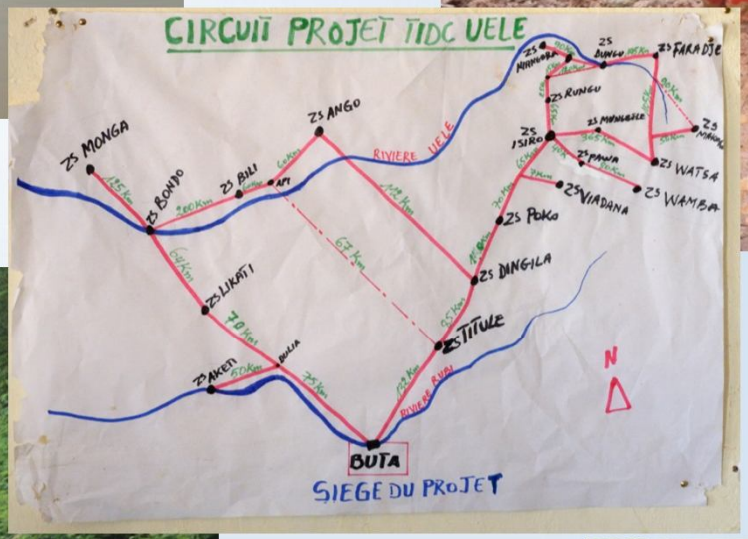



Visual OnSite Care Diagnostics (VOCD)
23336
OnSight
STAT Test
ParaQuick
Rapid Test for Malaria (Pan/Pf)
DEVICE
25 Tests
Visual OnSite Care Diagnostics (VOCD)
OnSight
STAT Test
25 Tests
AMGENIX
PRODUCT RELEASE PROTOCOL
SR.No. 006
DATE 09/07/2007
PRODUCT OnSight - ParaQuick (Device)
Rapid Test for Malaria - Pan + Pf
LOT.No. A101006(s)
MFG. DT. 06/2007
EXP.DT. 05/2009
PACK 25 TESTS
SPECIFICITY AND SENSITIVITY TEST
SR. No. | SAMPLE / STANDARD | RESULTS AT 15 MINUTES TEST BAND PAN | PF | CONTROL BAND C
MALARIA NEGATIVE PANEL
1 WHOLE BLOOD SAMPLE -1 0 0 4+
2 WHOLE BLOOD SAMPLE -2 0 0 4+
3 WHOLE BLOOD SAMPLE -3 0 0 4+
4 WHOLE BLOOD SAMPLE -4 0 0 4+
5 WHOLE BLOOD SAMPLE -5 0 0 4+
P.vivax POSITIVE PANEL
1 WHOLE BLOOD SAMPLE -1 4+ 0 4+
2 WHOLE BLOOD SAMPLE -2 3+ 0 4+
3 WHOLE BLOOD SAMPLE -3 2+ 0 4+
4 WHOLE BLOOD SAMPLE -4 1+ 0 4+
5 WHOLE BLOOD SAMPLE -5 1w 0 4+
P.falciparum POSITIVE PANEL
1 WHOLE BLOOD SAMPLE -1 4+ 4+ 4+
2 WHOLE BLOOD SAMPLE -2 3+ 3+ 4+
3 WHOLE BLOOD SAMPLE -3 2+ 2+ 4+
4 WHOLE BLOOD SAMPLE -4 1+ 1+ 4+
5 WHOLE BLOOD SAMPLE -5 1w 1w 4+
NOTE : The intensity of control band 'C' is taken as 4+. The nos. 1 to 4 are assigned to the intensity of test band at regions 'Pan' / 'Pf ' as compared to control band.A weak but clearly visible band is taken as 1w. No band is defined as 0.
MANUFACTURING RECORDS ARE VERIFIED, CHECKED AND PRODUCT IS MANUFACTURED AS PER THE MASTER FORMULA, SAMPLES TESTED AND LOT IS RELEASED FOR SALE.
MANUFACTURING
QUALITY ASSURANCE
DO NOT SWALLOW DRYING AGENT
OnSight ParaQuick
Pan
Pf
C
Visual OnSite Care Diagnostics (VOCD)
OnSight
STAT Test
ParaQuick
Rapid Test for Malaria (Pan/Pf)
CARD
25 Tests
Rapid Diagnostics for Decision Point
Unimed
First Sign
ParaView
Rapid Test for Malaria (Pan+Pf) Card Test
CLKB 23946
PRODUCT RELEASE PROTOCOL
Unimed
SR.No. 001
DATE 28/06/2007
PRODUCT First Sign - ParaView (Device)
Rapid Test for Malaria - Pan + Pf
LOT.No. U101001(s)
MFG. DT. 06/2007
EXP.DT. 05/2009
PACK 25 TESTS
SPECIFICITY AND SENSITIVITY TEST
SR. No. | SAMPLE / STANDARD | RESULTS AT 15 MINUTES TEST BAND PAN | PF | CONTROL BAND C
MALARIA NEGATIVE PANEL
1 WHOLE BLOOD SAMPLE -1 0 0 4+
2 WHOLE BLOOD SAMPLE -2 0 0 4+
3 WHOLE BLOOD SAMPLE -3 0 0 4+
4 WHOLE BLOOD SAMPLE -4 0 0 4+
5 WHOLE BLOOD SAMPLE -5 0 0 4+
P.vivax POSITIVE PANEL
1 WHOLE BLOOD SAMPLE -1 4+ 0 4+
2 WHOLE BLOOD SAMPLE -2 3+ 0 4+
3 WHOLE BLOOD SAMPLE -3 2+ 0 4+
4 WHOLE BLOOD SAMPLE -4 1+ 0 4+
5 WHOLE BLOOD SAMPLE -5 1w 0 4+
P.falciparum POSITIVE PANEL
1 WHOLE BLOOD SAMPLE -1 4+ 4+ 4+
2 WHOLE BLOOD SAMPLE -2 3+ 3+ 4+
3 WHOLE BLOOD SAMPLE -3 2+ 2+ 4+
4 WHOLE BLOOD SAMPLE -4 1+ 1+ 4+
5 WHOLE BLOOD SAMPLE -5 1w 1w 4+
NOTE : The intensity of control band 'C' is taken as 4+. The nos. 1 to 4 are assigned to the intensity of test band at regions 'Pan' / 'Pf ' as compared to control band.A weak but clearly visible band is taken as 1w. No band is defined as 0.
MANUFACTURING RECORDS ARE VERIFIED, CHECKED AND PRODUCT IS MANUFACTURED AS PER THE MASTER FORMULA, SAMPLES TESTED AND LOT IS RELEASED FOR SALE.
MANUFACTURING
QUALITY ASSURANCE
DO NOT SWALLOW
First Sign ParaView
Pan
Pf
C
Registered Office : 3, Sh
Goa Office : Unit No. 501
(W), Mumbai - 400 050, INDIA.
Plaza, Panaji, Goa - 403 001, INDIA.
783139.
First Sign
ParaView
Rapid Test for Malaria (Pan/Pf) Card Test
One Card Test

Manufacturer Supplier Distributor Rebrander

Manufacturer name	Probably the same tests
AZOG	Carestart, First Response
Biotec	Core, Visitect, Paramax-3
Carestart	AZOG, First Response
Core	Biotec, Visitect, Paramax-3
Nova Century Scientific	Paracheck
First Response	AZOG, Carestart
ICT	Vision
Paramax-3	Biotec, Core, Visitect
SD Bioline	Cypress
Vision	ICT
Visitect	Biotec, Core, Paramax-3
Cypress diagnostics,	ICT
Cypress diagnostics	SD bioline 60
Carestart	Permier Medical Cooperation
Span diagnostic	Omega pharma
Dialab	Humanis




CIRCUIT PROJET TIDC UELE
ZS MONGA
ZS BONDO
ZS BILI
ZS ANGO
RIVIERE UELE
ZS LIKATI
ZS AKEN
BUTA
ZS TITULE
ZS DINGILA
ZS POKO
ZS VIADANA
ZS ISIRO
ZS RUNGU
ZS BUNGU
ZS FARADJE
ZS WATSA
ZS WAMBA
N
SIEGE DU PROJET

Transport and Shipment

35°C stability

Humidity proof packaging

Stress shipments

Long shelf-life

So there we go...

Transport by road…

RSS | Alertes mail & podcast / Jeudi, Septembre 05 2013

Chercher sur le site... GO

RADIO OKAPI
MONUSCO FONDATION HIRONDELLE

FM: Kinshasa 103.5 | Bunia 104.9 | Bukavu 95.3
Goma 105.2 | Kindu 103.0 | Kisangani 94.8
Lubumbashi 95.8 | Matadi 102.0 | Mbandaka 103.0
Mbuji-mayi 93.8

ACCUEIL ACTUALITÉ SOCIÉTÉ CULTURE SPORT ÉCONOMIE POLITIQUE ENVIRONNEMENT ÉLECTIONS OFFRES D'EMPLOI

Province Orientale: plus de 30 véhicules bloqués sur l'axe Niania – Bafwasende

juin 25, 2013, | Denière mise à jour le 25 juin, 2013 à 4:55 | sous Actualité, Province Orientale. Mots clés: police, Traccasseries

Camions au poste frontalier Kasumbalesa, Katanga, RD Congo

Plus trente véhicules sont bloqués, [illegible] sur la route nationale [illegible] entre Niania et Bafwasende dans la Province Orientale. La plateforme des transporteurs du Congo accuse la police de circulation routière de Bafwasende d'imposer des taxes illégales à ces véhicules. La police de son côté affirme prélever une «taxe de défaut de surchargement».

La plateforme des transporteurs indique qu'il s'agit véhicules provenant de Beni, Butembo et Bunia en direction de Kisangani. Ils transportent des produits vivriers et diverses marchandises.

Le président des transporteurs, Modeste Pili Pili, accuse la Police de circulation

engage
déplacés
occupe
de perm

Cet eng[illegible] rétablir la sécurité dans cette zone
Cet engagement ne ramènera pas la sécurité dans cette région
Les deux parties devraient ouvrir une zone de libre passage

Votez
Voir les résultats

PUBLICITÉ

Blocked for 4 months now
Temp 40°C
Humidity 70%
15$/day

Appropriate space and room for storage

DECLARATION DU CAMBRIOLAGE

Par la présente, le Département Pédiatrique des Cliniques Universitaire déclare le cambriolage de son Laboratoire dans la nuit du 5 au 6 juin, ces inciviques avaient forcés la porte et avaient réussi emporter les articles ci-dessous :

- Un Imprimante HP 1006
- Ordinateur marque Deel
- Un stabilisateur 2000W
- Une cafetière
- Un carton de 300 pipettes de transferts stérile de 1ml

OPEN ACCESS Freely available online

PLOS | ONE

External Quality Assessment of Reading and Interpretation of Malaria Rapid Diagnostic Tests among 1849 End-Users in the Democratic Republic of the Congo through Short Message Service (SMS)

Pierre Mukadi[1,2], Philippe Gillet[3], Albert Lukuka[1,4], Joël Mbats
Jacques Muyembe[1,7], Jozefien Buyze[3], Jan Jacobs[3], Veerle Lej

Figure 2. Location of 1849 eligible MCQ answers (MCQ) and of 680 health facilities (HF) participating in the EQA.
doi:10.1371/journal.pone.0071442.g002

Table 15: Stock of malaria RDT available in health facilities at the time of survey (n= 902) (1)

Type de Structure	stock				Total
	0 to < 25	25 to 100	100 to 250	> 250	
Referral Hospital	65	26	22	32	145
Referral Health Center	50	26	25	6	107
Health Center	230	151	100	47	528
Health Post	39	10	50	1	100
Other	12	4	3	3	22
Total	396	217	200	89	902
%	43.9	24.1	22.2	9.9	100.0

*: Including 1 Provincial laboratory

Table 16: Stock out of malaria RDT reported by health facilities during 1 year (July 2012 to October 2013). Eligible answers: 873 (1)

Type de Structure	Stock out		Total
	Yes	No	
Referral Hospital	95 (69.3%)	42 (30.7%)	137
Referral Health Centre	75 (72.1%)	29 (27.9%)	104
Health Center	364 (71.1%)	148 (28.9%)	512
Health Post	30 (30.3%)	69 (69.7%)	99
Other	16 (76.2%)	5 (23.8%)	21
Total	580	293	873
%	66.4	33.6	100.0

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External Quality Assessment of Reading and Interpretation of Malaria Rapid Diagnostic Tests among 1849 End-Users in the Democratic Republic of the Congo through Short Message Service (SMS)

Pierre Mukadi[1,2], Philippe Gillet[3], Albert Lukuka[1,4], Joël Mbats
Jacques Muyembe[1,7], Jozefien Buyze[3], Jan Jacobs[3], Veerle Lej

Four different malaria RDT brands were used (not sp
11.5% of health facilities): (i) Paracheck Pf-Rapid Tes
Biomedical Systems, Goa, India, 77/680, 11.3%); (ii) Sl
Ag Pf/Pan (394/680, 57.9%) which is the RDT
recommended by the PNLP; (iii) SD Malaria antig
(Standard Diagnostics, Inc., Kyonggi-do, Korea, 99/68
and; (iv) SD Malaria antigen Pf (32/680, 4.7%). SI
antigen Pf/Pv exclusively circulated in Kasai Occidenta
Kivu where it was used in half of the participating healt
(respectively 62/126 and 37/71), while in Manie
Paracheck Pf-Rapid Test was used (22/24).

Figure 2. Location of 1849 eligible MCQ answers (MCQ) and of 680 health facilities (HF) participating in the EQA.
doi:10.1371/journal.pone.0071442.g002

End-user errors

Community Health Workers

Laboratory Staff

Clinical staff

Travellers

TABLE 2. Errors committed by RDT end-users in malaria endemic settings. Study subjects were village or community health workers (Cambodia, Lao PDR, Mali, The Philippines and Zambia), staff of peripheral health centres (Malawi, Sudan and Uganda) and hospital laboratory staff (Mozambique and DR Congo). All subjects had been trained in RDT use and performance

Errors ranked according to chronology of test procedure	Effects/Comments	Countries	References
Not checking expiration date of the device	Confusion may arise from the way of displaying the expiry date [70]	Lao PDR, The Philippines, Uganda, Zambia	[21,70,73,74]
Not checking the humidity indicator of the desiccant	Humidity weakens the bonds between antibodies and nitrocellulose strip and delays particle re-solubilization [72]	Laos PDR, The Philippines, Zambia	[73,74]
Not using gloves	Gloves protect from blood-borne infection	Zambia	[21,73]
Reusing the same gloves for different patients		Uganda, Zambia	[21,70]
Not identifying the cassette with the patients' name or laboratory number	Risk of inversion of results between patients	Zambia	[21,73]
Not cleaning/disinfecting the finger before pricking		Lao PDR, The Philippines, Uganda, Zambia	[21,70,73,74]
Not allowing the finger to dry after cleaning and before pricking	Antiseptic needs enough action time	Lao PDR, The Philippines, Zambia	[21,73,74]
Reusing a lancet for a next patient		Zambia	[21]
Desterilizing the lancet before use (by touching the bench or hands)		Zambia	[21]
Pricking the wrong place on the finger (palmar instead of lateral side)	Pricking the palmar side of the finger is more painful than pricking at the side	Zambia	[21]
Not throwing the lancet in a sharps container		Zambia	[21,73]
Dispensing the wrong volume of blood or not completely transferring the blood to the sample well (leaving blood on the wall of the well)	1 Insufficient volume of blood may cause false-negative results 2 Too much blood may increase the risk or the intensity of a prozone effect [56] 3 Too much blood will cause decreased clearance of the strip	Malawi, Sudan, Uganda, Zambia	[21,70,73,106,107]
Distributing blood into the buffer well and/or buffer into the sample well	Sample and buffer well are not always unequivocally labelled [68]	Laos PDR, The Philippines	[74]
Substituting the buffer by another liquid (e.g. distilled water)	Use of any other liquid than the buffer provided in the RDT's kit may cause false-positive results [95]	Mali, Mozambique	[108]
Dispensing the wrong volume of buffer	1 Insufficient volume of buffer will impede clearance of the strip and/or slow down migration with failure to generate a control line (invalid test results) [109] 2 Too high volume of buffer may cause false-positive results due to non-specific bindings	Lao PDR, Sudan, The Philippines, Uganda, Zambia	[21,70,73,74,106]
Not using a levelled surface to place the cassette	Decreasing of the migration time may cause false-negative results[110]	DR Congo, Lao PDR, Sudan, The Philippines, Zambia	[21,74,106]
Not discarding the used materials correctly		Lao PDR, The Philippines, Zambia	[21,73,74]
Not respecting the correct reading time	1 Reading too early may cause false-negative results 2 Reading too late may cause false-positive results due to a backflow phenomenon [111]	Lao PDR, Malawi, Sudan, The Philippines, Uganda, Zambia	[21,70,73,74,106,107]
Disregarding faint or weak test lines as negative	Faint test lines may be difficult to see, particularly in unfavourable light conditions (night shifts) and by elderly readers [55,70]	DR Congo[a], Lao PDR, The Philippines, Zambia	[21,73,74]
Not recognizing invalid test results		DR Congo[a], Zambia	[73]
Interpreting line intensities as indicative of disease severity (and installing treatment accordingly)	Line intensity is not related to severity	Lao PDR, The Philippines, Uganda,	[70,74]
Not interpreting correctly a three- band RDT	Difficulties in defining the species involved based on the test line results	DR Congo[a], Sudan	[106]

[a]Pierre Mukadi et al., Challenges in Malaria Research: Progress Towards Elimination, Switzerland, 10–12 October 2012.

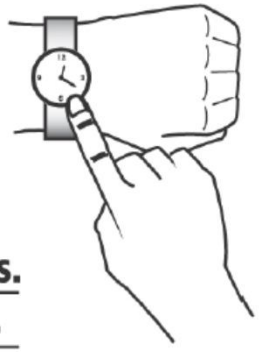
End-user's errors

1. Reading beyond the recommended time
2. Application of too much volume
3. Disregarding faint lines as positive
4. Problems with species identification
5. Failure to recognize invalid results
6. Buffer replacement or exchange

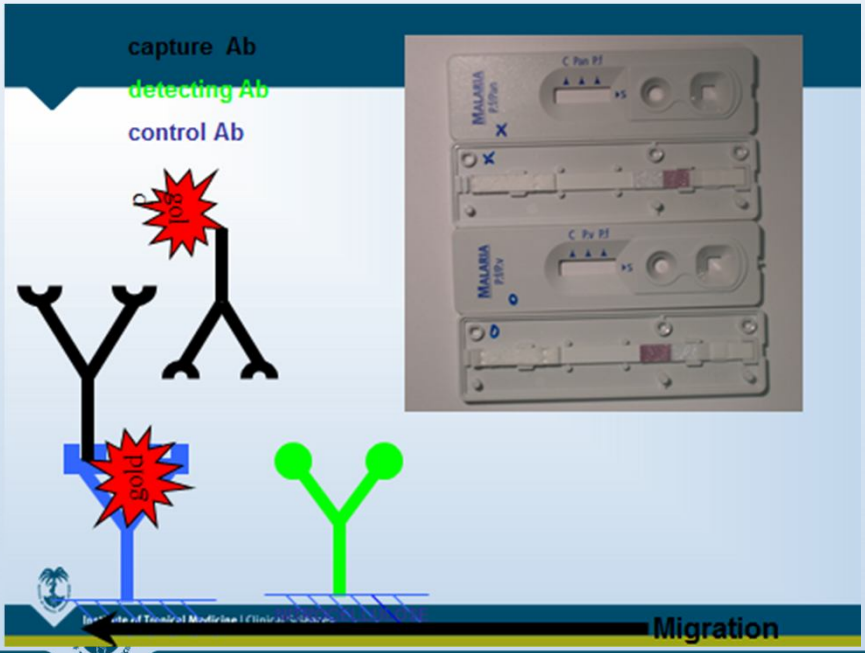
Delayed Reading (Backflow)

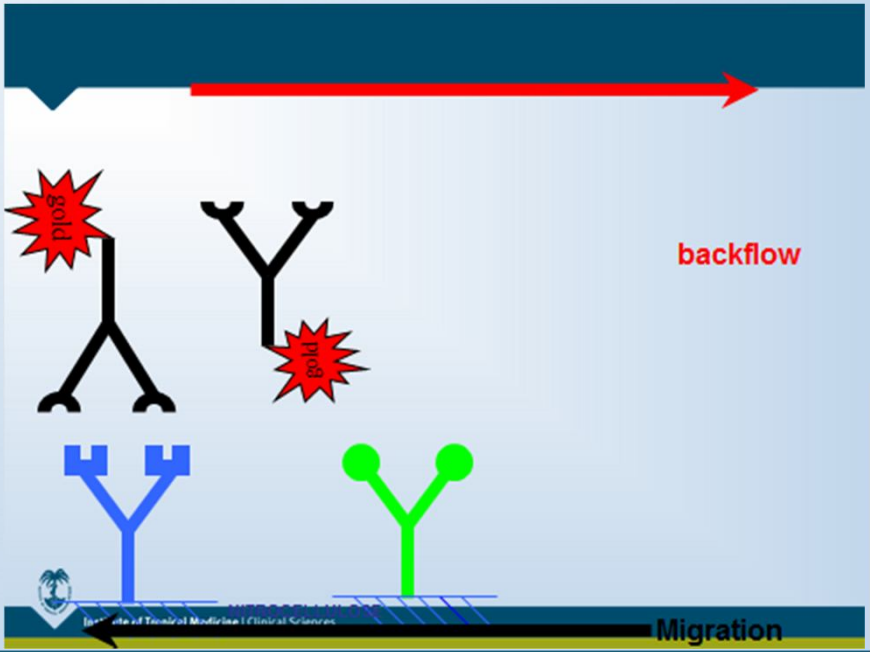
Interpret test results in 20~30 minutes.

20~30 mins

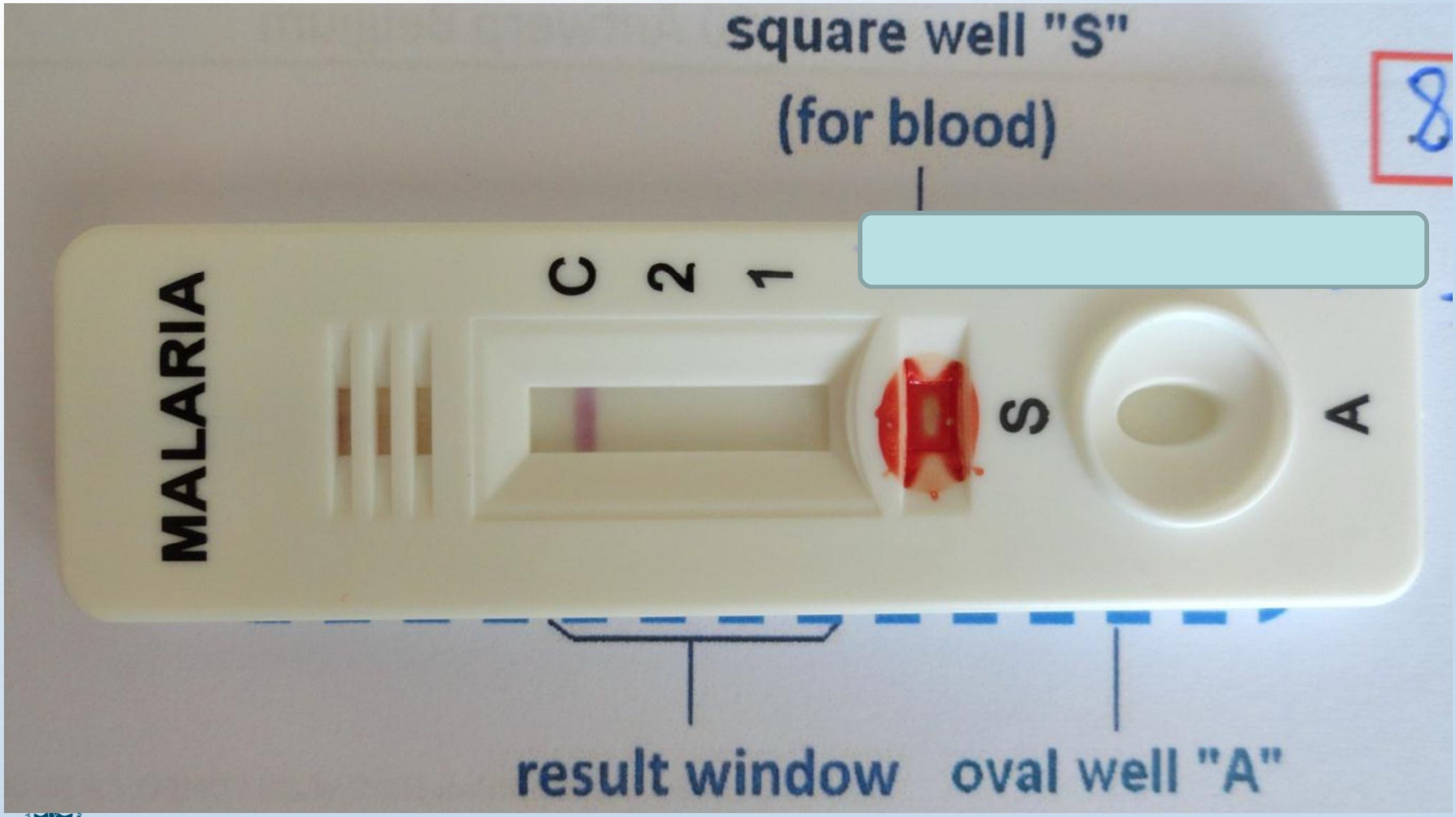


Caution :
Don't read test results after 30 minutes.
Reading too late can give false results.

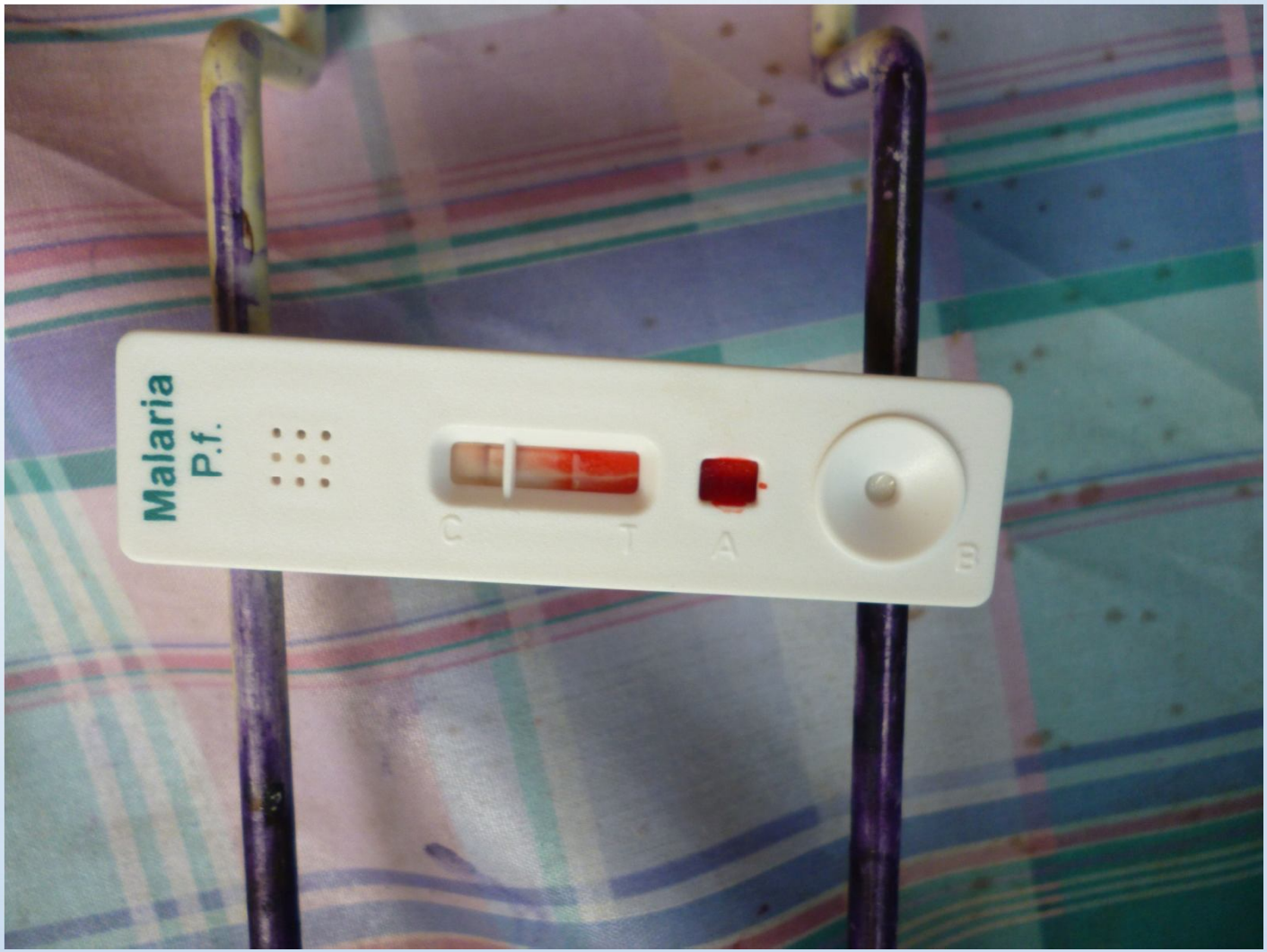




Application of too much blood…



and again...



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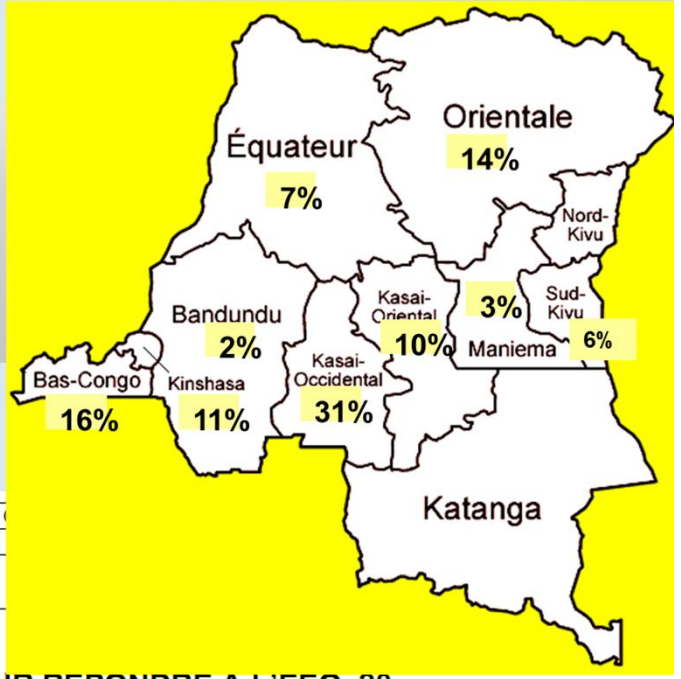
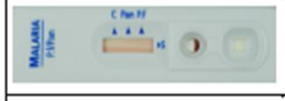
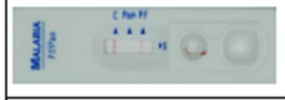
External Quality Assessment of Reading and Interpretation of Malaria Rapid Diagnostic Tests among 1849 End-Users in the Democratic Republic of the Congo through Short Message Service (SMS)

Pierre Mukadi[1,2], Philippe Gillet[3], Albert Lukuka[1,4], Joël Mbatshi[5], John Otshudiema[6], Jean-Jacques Muyembe[1,7], Jozefien Buyze[3], Jan Jacobs[3], Veerle Lejon[3,8]*

Reading and interpretation



Test de Diagnostic Rapide (TDR) du paludisme, SD BIOLINE, MALARIA Ag P.f/Pan (FK60)

A		1 Invalide, test à refaire 2 Négatif 3 Positif *Plasmodium falciparum* 4 Positif *Plasmodium falciparum*, infection mixte possible 5 Positif *Plasmodium non-falciparum* 6 Positif *Plasmodium* mais je ne sais pas quelle sorte
B		1 Invalide, test à refaire 2 Négatif 3 Positif *Plasmodium falciparum* 4 Positif *Plasmodium falciparum*, infection mixte possible 5 Positif *Plasmodium non-falciparum* 6 Positif *Plasmodium* mais je ne sais pas quelle sorte
C		1 Invalide, test à refaire 2 Négatif 3 Positif *Plasmodium falciparum* 4 Positif *Plasmodium falciparum*, infection mixte possible 5 Positif *Plasmodium non-falciparum* 6 Positif *Plasmodium* mais je ne sais pas quelle sorte
D		1 Invalide, test à refaire 2 Négatif 3 Positif *Plasmodium falciparum* 4 Positif *Plasmodium falciparum*, infection mixte possible 5 Positif *Plasmodium non-falciparum* 6 Positif *Plasmodium* mais je ne sais pas quelle sort
E		1 Invalide, test à refaire 2 Négatif 3 Positif *Plasmodium falciparum* 4 Positif *Plasmodium falciparum*, infection mixte p 5 Positif *Plasmodium non-falciparum* 6 Positif *Plasmodium* mais je ne sais pas quelle sort
F		1 Invalide, test à refaire 2 Négatif 3 Positif *Plasmodium falciparum* 4 Positif *Plasmodium falciparum*, infection mixte p 5 Positif *Plasmodium non-falciparum* 6 Positif *Plasmodium* mais je ne sais pas quelle sort
G		1 Invalide, test à refaire 2 Négatif 3 Positif *Plasmodium falciparum* 4 Positif *Plasmodium falciparum*, infection mixte p 5 Positif *Plasmodium non-falciparum* 6 Positif *Plasmodium* mais je ne sais pas quelle sort
H		1 Invalide, test à refaire 2 Négatif 3 Positif *Plasmodium falciparum* 4 Positif *Plasmodium falciparum*, infection mixte p 5 Positif *Plasmodium non-falciparum* 6 Positif *Plasmodium* mais je ne sais pas quelle sort
I		1 Invalide, test à refaire 2 Négatif 3 Positif *Plasmodium falciparum* 4 Positif *Plasmodium falciparum*, infection mixte p 5 Positif *Plasmodium non-falciparum* 6 Positif *Plasmodium* mais je ne sais pas quelle sort
J		1 Invalide, test à refaire 2 Négatif 3 Positif *Plasmodium falciparum* 4 Positif *Plasmodium falciparum*, infection mixte p 5 Positif *Plasmodium non-falciparum* 6 Positif *Plasmodium* mais je ne sais pas quelle sort

Gardez cette page pour comparer vos résultats avec les résultats corrects qui vous seront envoyés à la fin de l'

	Comité de Pilotage Assurance
	Titre: Evaluation Externe de la
	Ecrit par : MUKADI Pierre
	Revue par : Gillet P., Lejon V.

PROCÉDURE POUR REPONDRE A L'EEQ_20

1. **Notez les résultats de votre interprétation pour chaque test (voir photos des TDRs) dans la grille « Code résultats » en mettant le numéro de la réponse correcte sous la lettre de la photo.**

	A	B	C	D	E	F	G	H	I	J
Code résultat:										

Exemple : *Vous pensez que la bonne réponse pour Photo A est la réponse 6.*

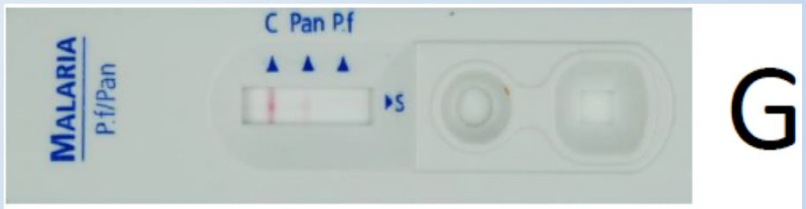
A

1 Invalide
2 Négatif
3 Positif *Plasmodium falciparum*
4 Positif *Plasmodium falciparum*, infection mixte possible
5 Positif *Plasmodium* non-*falciparum*
(6) Positif *Plasmodium* mais je ne connais pas l'espèce

(i) Overlooking faint/weak test lines as negative results (A, D, G, H) : 1.5 to 29.1%

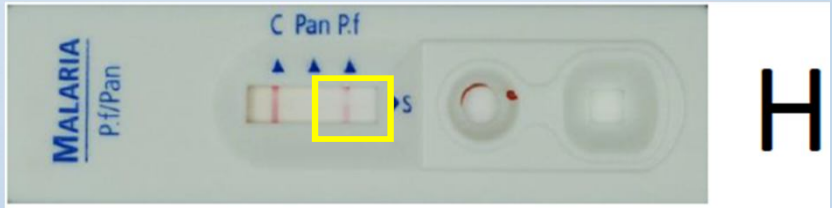
Photograph	Reported result (%) N= 2344					
	Invalid	Negative	*P. falciparum*	*P. falciparum*, mixed infection possible	P. non-*falciparum*	Positive, but species not known
A	6.9	29.1	54.8	3.0	1.7	4.5
D	5.1	1.5	24.3	65.7	1.3	2.1
G	6.4	7.2	6.1	4.7	70.7	4.9
H (weak)	3.5	1.5	85.9	4.4	2.9	1.8

A



G

D



H

Faint test lines

Night shifts

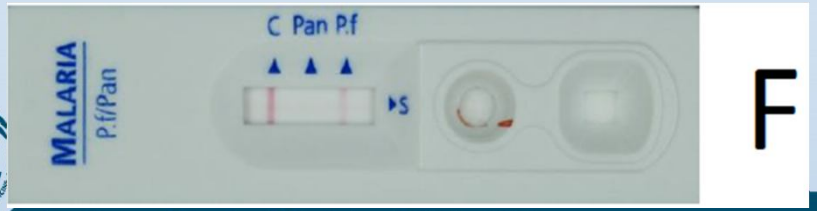
+ 38

(ii) Failure to distinguish the correct *Plasmodium* species (D, F, H, I) : 3.4 to 7.0%

Photograph	Reported result (%) N= 2344					
	Invalid	Negative	*P. falciparum*	*P. falciparum*, mixed infection possible	P. non-*falciparum*	Positive, but species not known
D	5.1	1.5	24.3	65.7	1.3	2.1
F	3.9	3.3	82.8	3.0	3.2	3.8
H	3.5	1.5	85.9	4.4	2.9	1.8
I	2.0	0.6	4.1	89.9	1.1	2.3

D

H

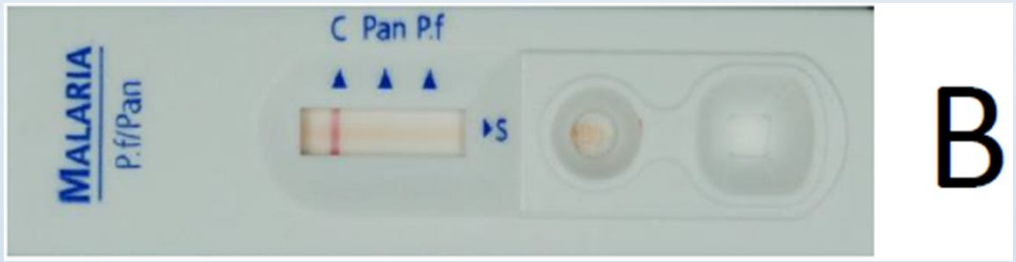


F

I

iii) Overlooking negative test (B, E): 10.0 & 12.4%

Photograph	Reported result (%) N= 2344					
	Invalid	Negative	*P. falciparum*	*P. falciparum*, mixed infection possible	P. non-*falciparum*	Positive, but species not known
B	5.2	90.0	2.6	0.4	0.7	1.0
E	6.5	87.6	2.1	1.8	1.0	1.0



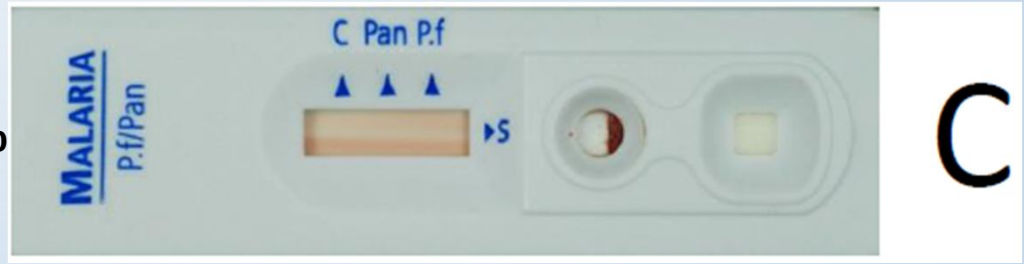
B

E

iv) Not detecting Invalid test (C, J): 8.4 & 23.6%

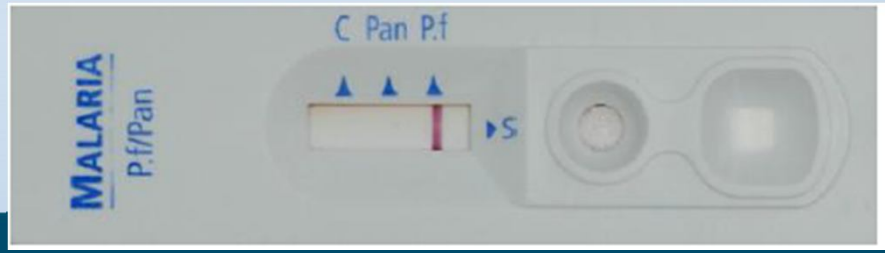
Photograph	Reported result (%) N= 2344					
	Invalid	Negative	*P. falciparum*	*P. falciparum*, mixed infection possible	P. non-*falciparum*	Positive, but species not known
C	91.6	6.1	0.9	0.6	0.3	0.4
J	76.4	6.6	7.4	1.0	1.0	7.6

- No control line, no test line: 8.4%



C

- No control line, presence of test line: 23.6%



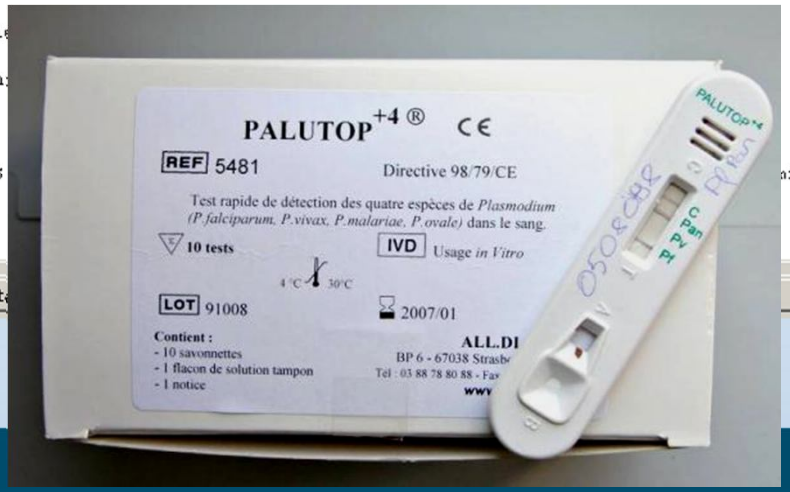
J

METHODOLOGY **Open Access**

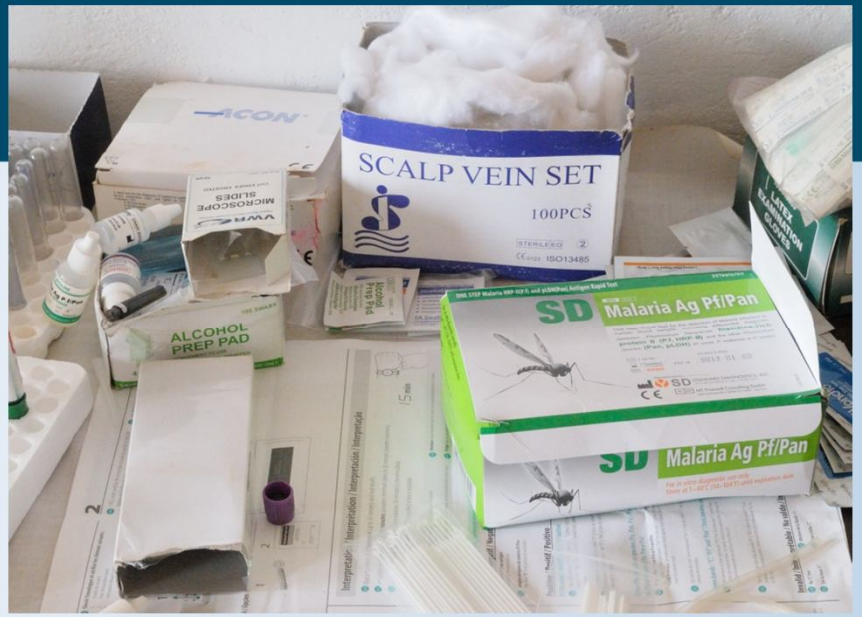
Buffer substitution in malaria rapid diagnostic tests causes false-positive results

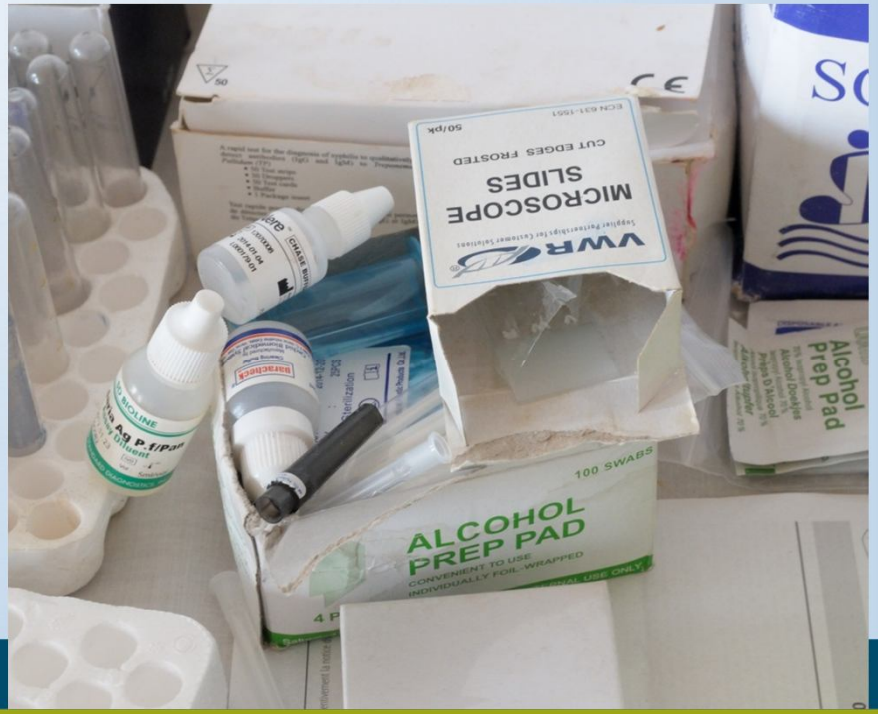
Philippe Gillet[1*], Marcella Mori[1], Jef Van den Ende[1], Jan Jacobs[1,2]

Can we use water when we are running out of buffer?




SCALP VEIN SET
100PCS
SD
Malaria Ag Pf/Pan


SCALP VEIN SET
100PCS
ALCOHOL
PREP PAD
SD
Malaria Ag Pf/Pan
SD
Malaria Ag Pf/Pan


MICROSCOPE
SLIDES
CUT EDGES FROSTED
VWR
100 SWABS
ALCOHOL
PREP PAD
CONVENIENT TO USE
INDIVIDUALLY FOIL-WRAPPED
Alcohol
Prep Pad

Compliance with results: the clinician

Disregarding negative RDT result (17% – 50%)

More prescription of antibiotics

Anecdotal failures or perceived errors may erode confidence (prozone, HRP-2 deletions...)

Clinical algorithms – mixed malaria/bacterial infections

Diagnostic tools for non-malaria febrile illness are required to increase compliance

Patient and Public perception

Patient looks “over the shoulder”
(at the cost of the doctor’s clinical eye)

Patient wants to be taken seriously
- antibiotic prescribing?

The expanded market : need for harmonization

Expansion of RDT market = unprecedented

200 RDT products, 60 manufacturers

Diversity of products and issue of quality

shape, transfer device device

volume specimen numbers of drops, reading time...

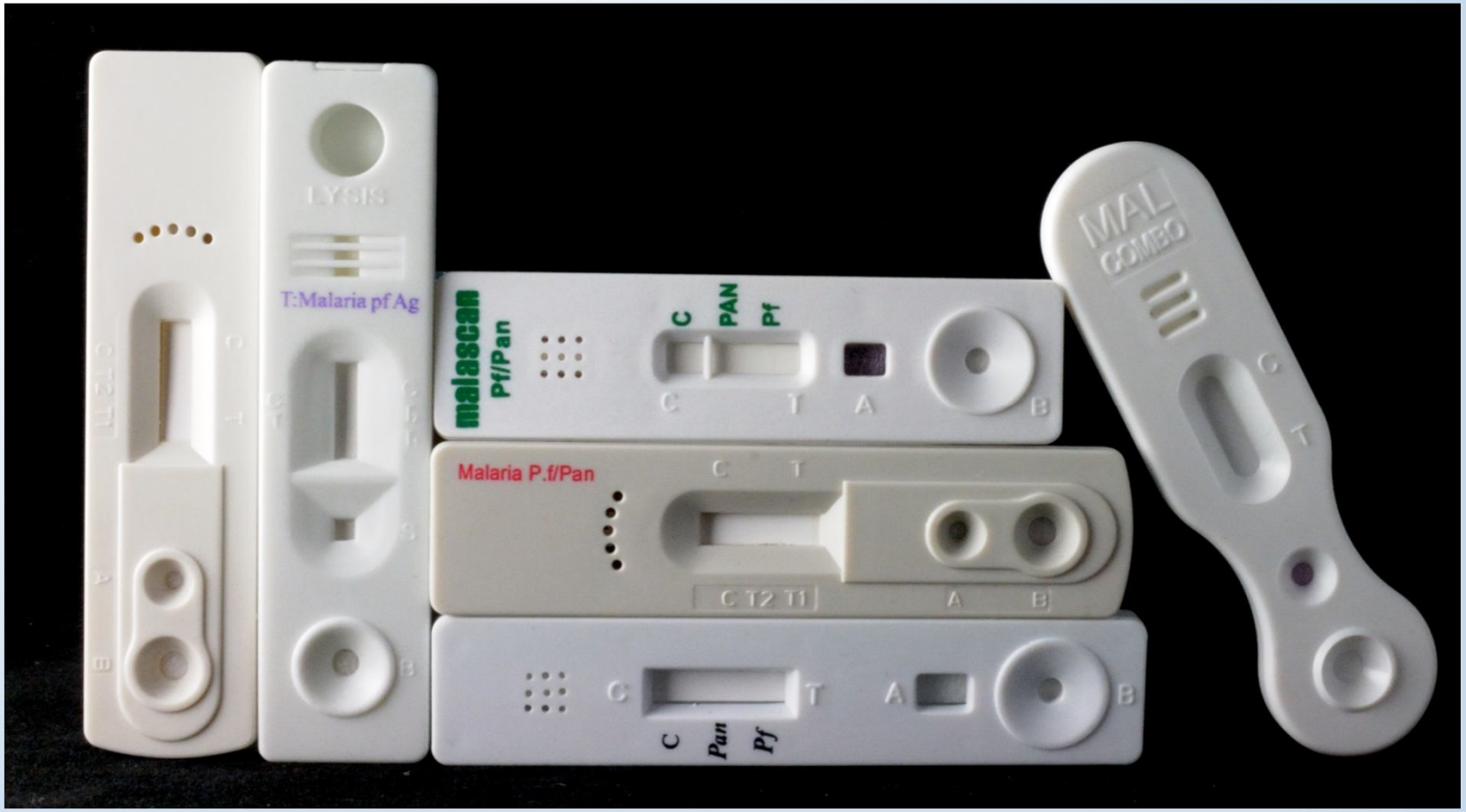
ASSURED

Training

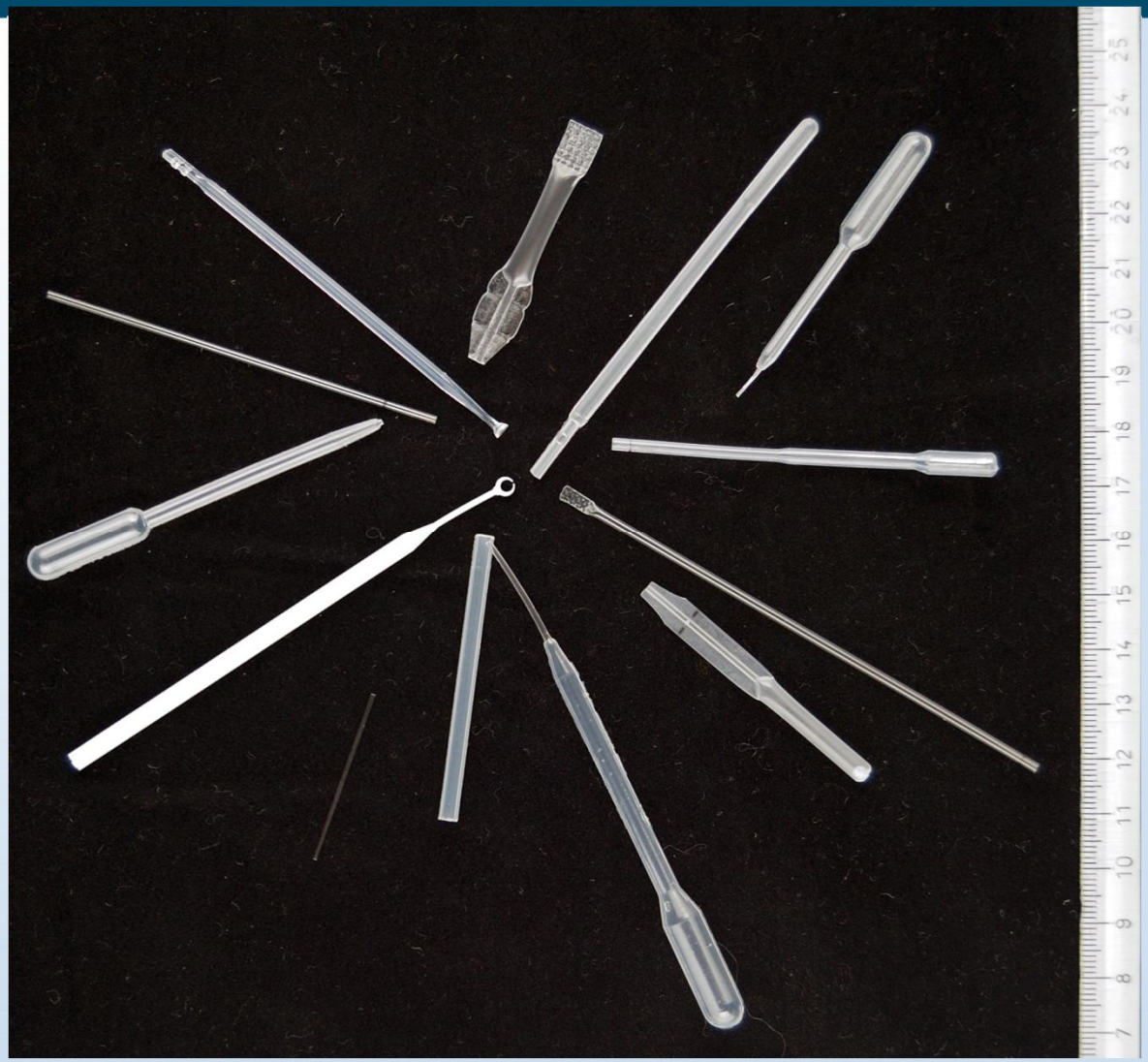
Procurement and Supply

Switching from one product to another (market strategy)

Design and labeling of cassettes

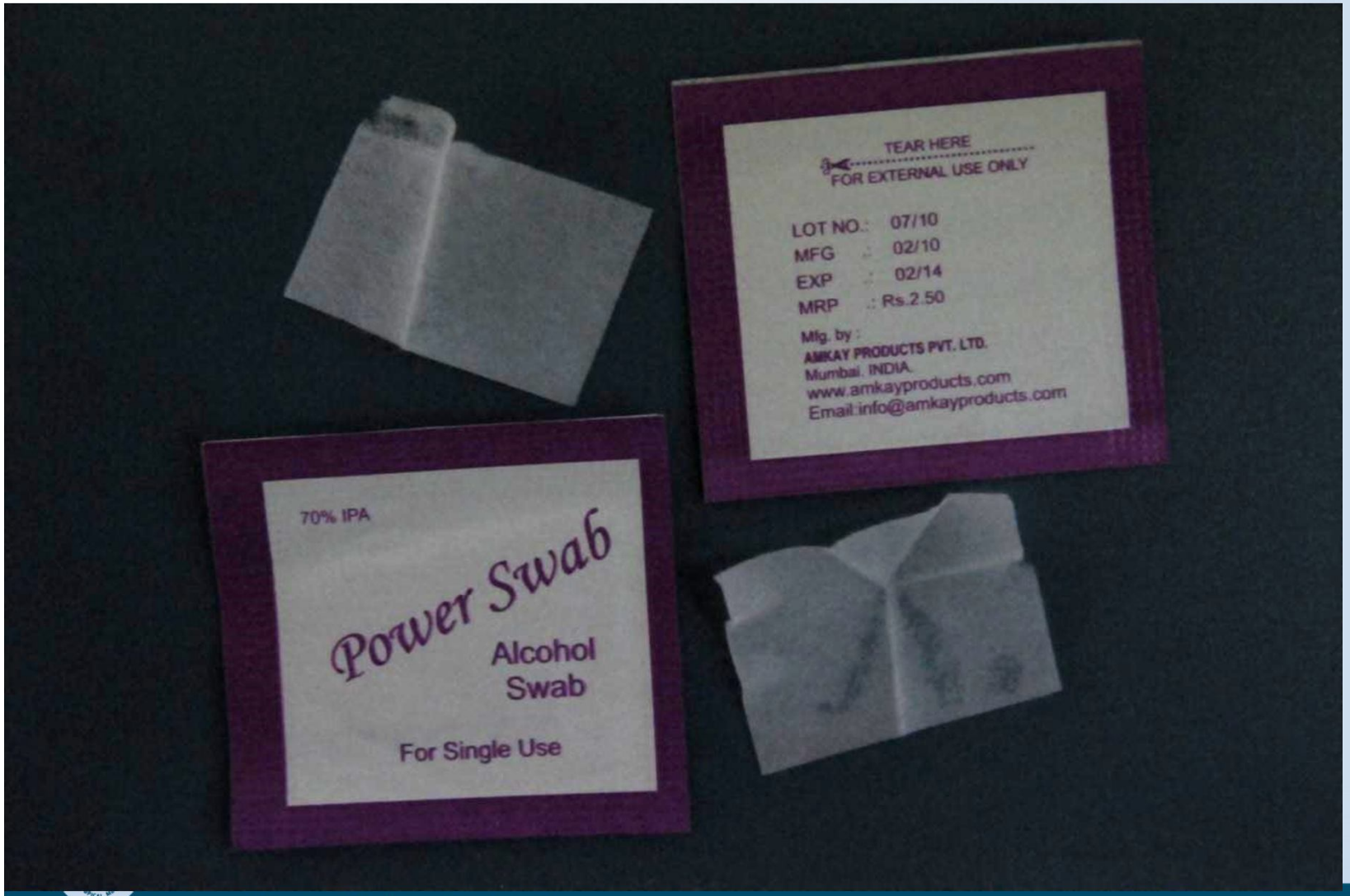


Accessories



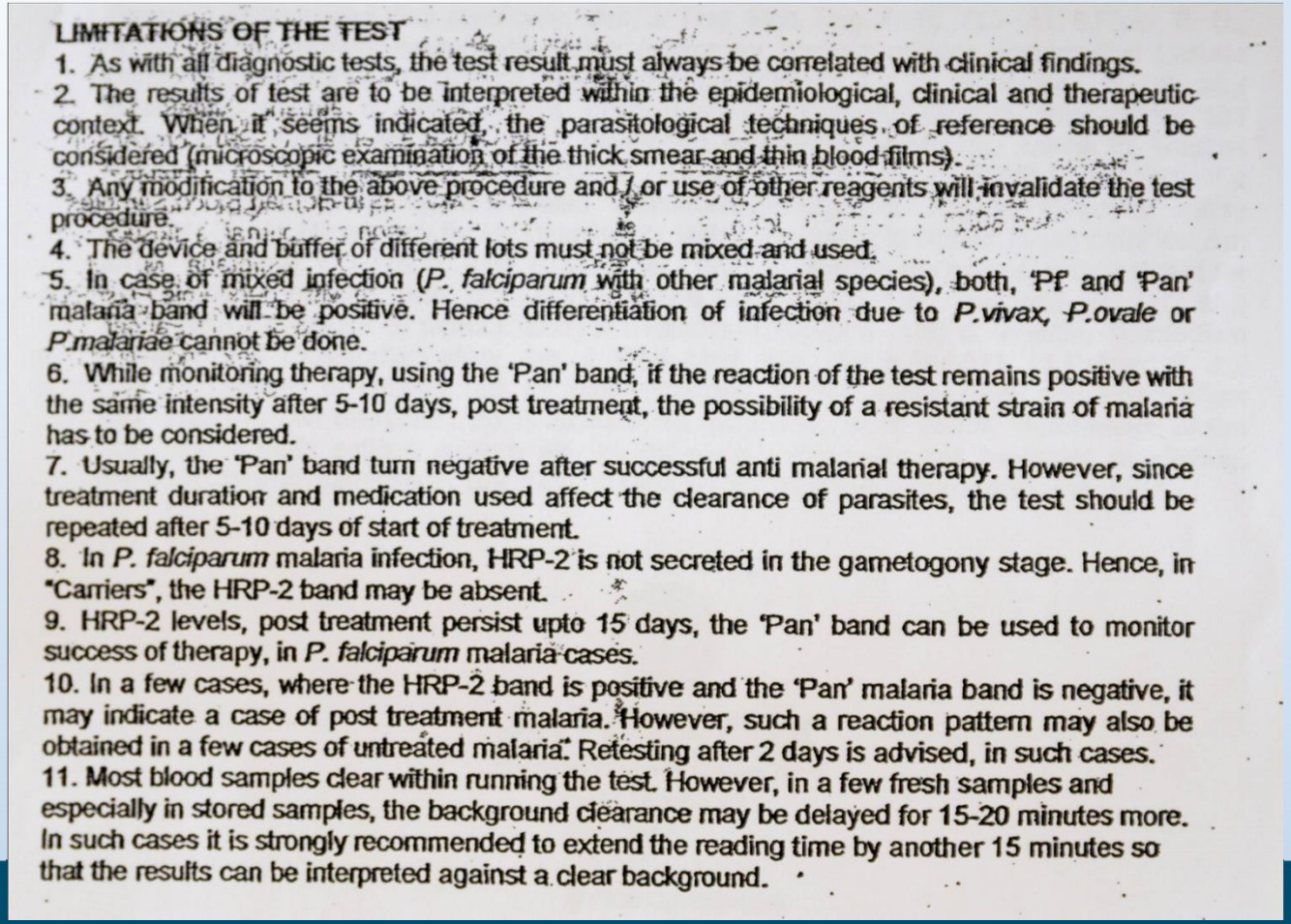
Accessories

Accessories



Instructions for use: readability

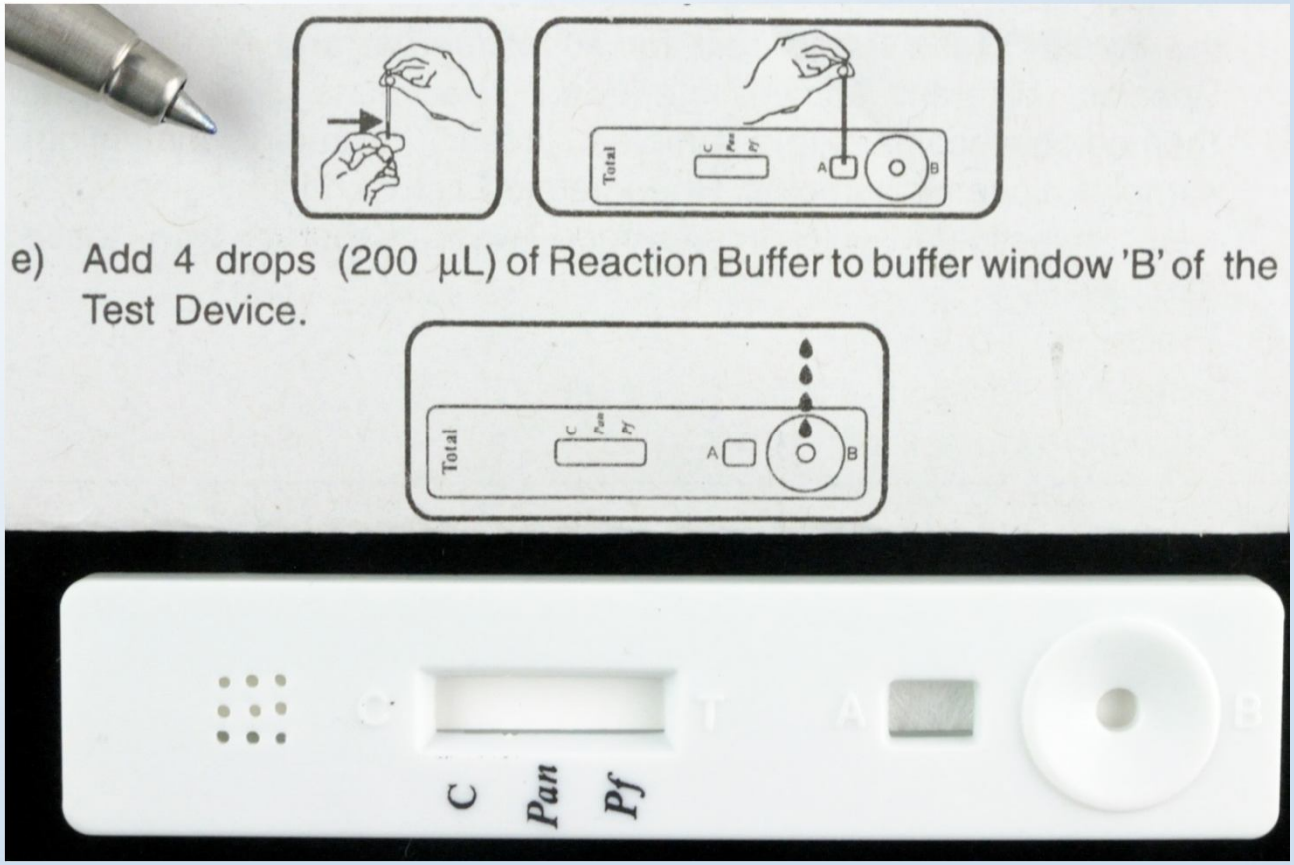
- Too high readability level (>9 years of education needed)
- User-unfriendly typography
- Poor printing/paper quality



LIMITATIONS OF THE TEST

1. As with all diagnostic tests, the test result must always be correlated with clinical findings.
2. The results of test are to be interpreted within the epidemiological, clinical and therapeutic context. When it seems indicated, the parasitological techniques of reference should be considered (microscopic examination of the thick smear and thin blood films).
3. Any modification to the above procedure and / or use of other reagents will invalidate the test procedure.
4. The device and buffer of different lots must not be mixed and used.
5. In case of mixed infection (*P. falciparum* with other malarial species), both, 'Pf' and 'Pan' malaria band will be positive. Hence differentiation of infection due to *P.vivax*, *P.ovale* or *P.malariae* cannot be done.
6. While monitoring therapy, using the 'Pan' band, if the reaction of the test remains positive with the same intensity after 5-10 days, post treatment, the possibility of a resistant strain of malaria has to be considered.
7. Usually, the 'Pan' band turn negative after successful anti malarial therapy. However, since treatment duration and medication used affect the clearance of parasites, the test should be repeated after 5-10 days of start of treatment.
8. In *P. falciparum* malaria infection, HRP-2 is not secreted in the gametogony stage. Hence, in "Carriers", the HRP-2 band may be absent.
9. HRP-2 levels, post treatment persist upto 15 days, the 'Pan' band can be used to monitor success of therapy, in *P. falciparum* malaria cases.
10. In a few cases, where the HRP-2 band is positive and the 'Pan' malaria band is negative, it may indicate a case of post treatment malaria. However, such a reaction pattern may also be obtained in a few cases of untreated malaria. Retesting after 2 days is advised, in such cases.
11. Most blood samples clear within running the test. However, in a few fresh samples and especially in stored samples, the background clearance may be delayed for 15-20 minutes more. In such cases it is strongly recommended to extend the reading time by another 15 minutes so that the results can be interpreted against a clear background.

Point-of-care testing



ASSAY PROCEDURE

1. Dispense 1 drop (10µl) of whole blood to the "S" we
   the plastic dropper provided according to the figure.
2. Add three drops of Sample Diluent to the "D" well afte
3. Interpret test results at 15 minutes.

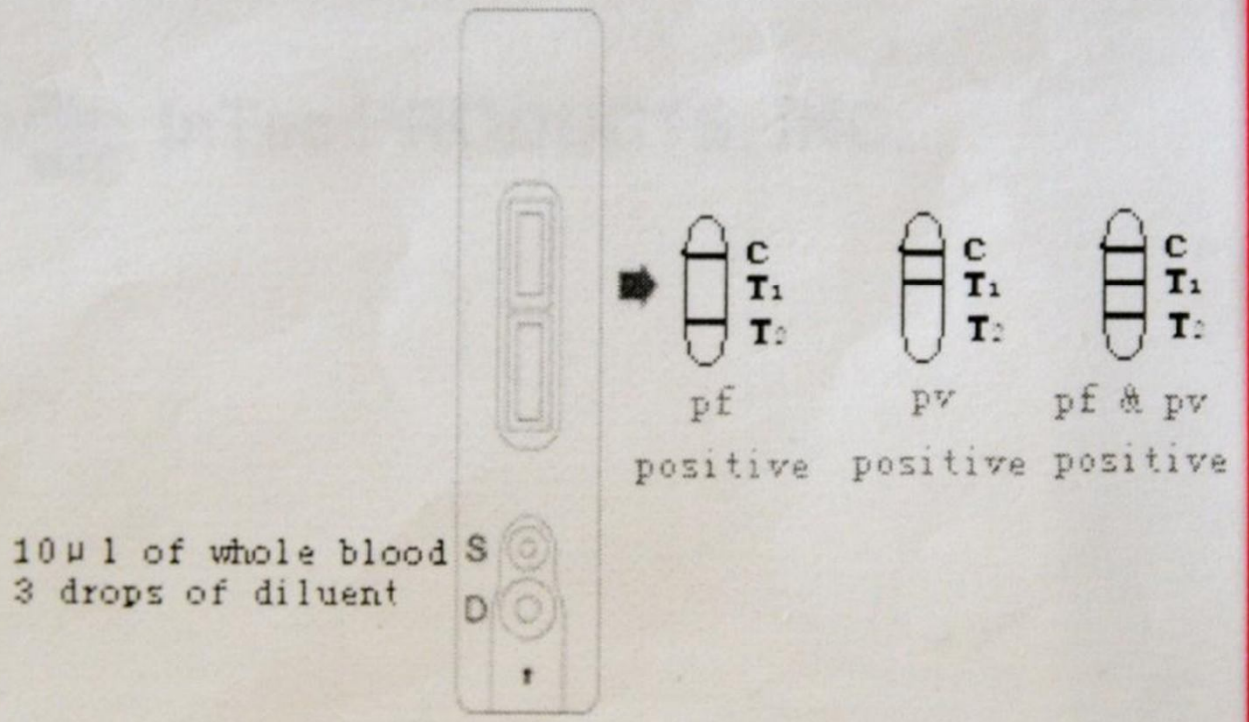
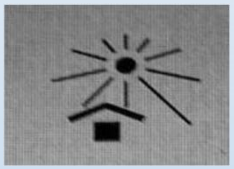


Figure 4.















Malaria Journal

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Assessment of the knowledge of graphical symbols labelled on malaria rapid diagnostic tests in four international settings

Malaria Journal 2011, **10**:331 doi:10.1186/1475-2875-10-331

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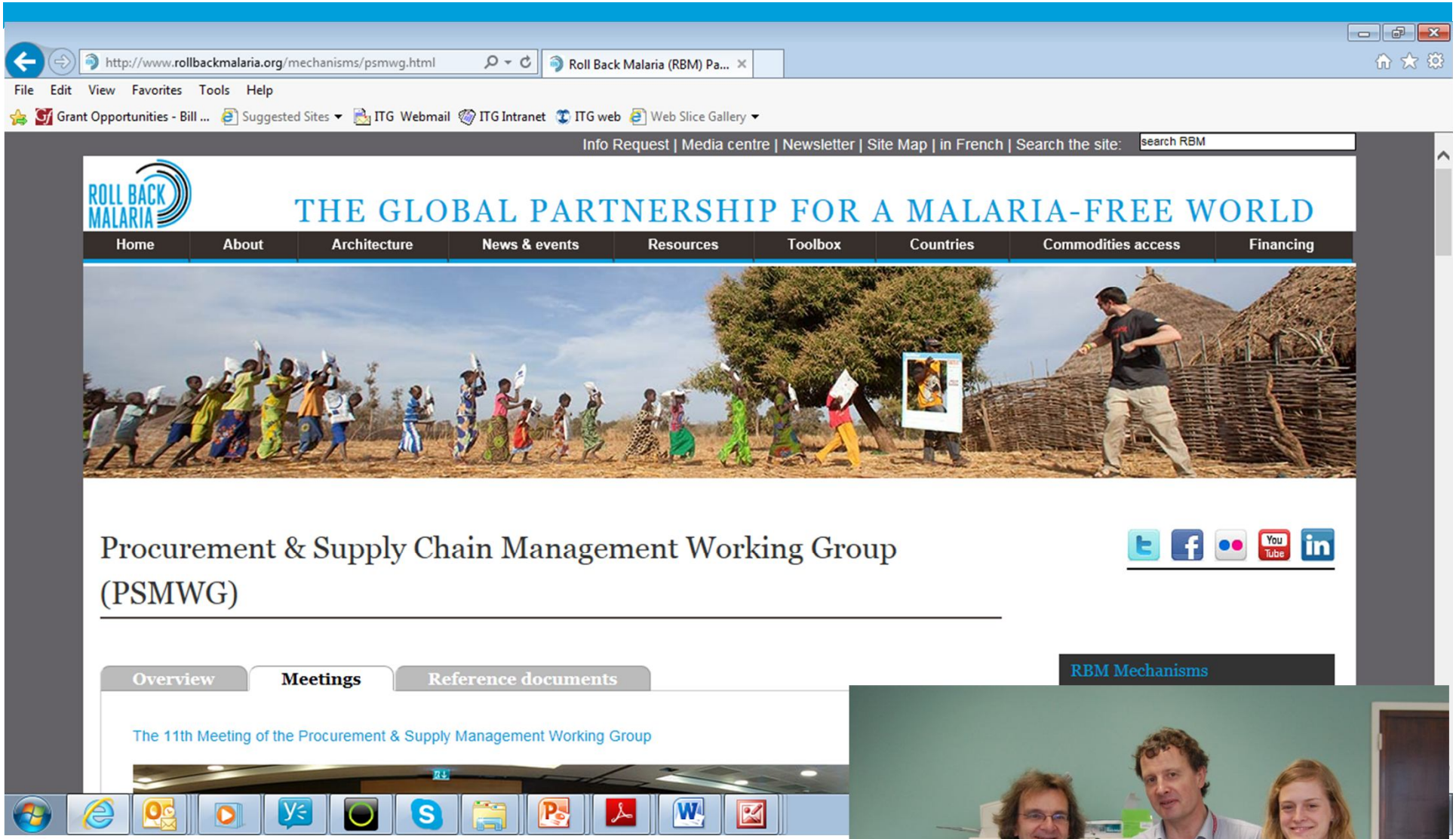

Compilation of “best practices”

Harmonization Task Force

HarT members & ITM team

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ITM Team
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Philippe Gillet

Procurers
Implementers NMCP
NGOs
Regulatory experts
Funding agencies
WHO
Regulatory experts

In-vitro diagnostics: risk management, labeling

IVDs are part of Medical Devices
(tongue depressors to pacemakers)

Labeling = labels + instructions for use

Regulation of IVDs targets = based on risk assessment.
Risks of IVDs are minimized by design, construction and manufacturing .
Communication of any residual risk = provided by labeling.

Labeling should target the user's profile
= explicit regulatory responsibility of the manufacturer

Guidelines for lay-out and readability are not easy to compile

International Medical Device Regulators Forum (IMDRF) (http://www.imdrf.org/)

Australia, Brazil, Canada, the European Union, Japan, nited States of America, China and the Russian Federation

WHO is observer

Guidance documents but non-binding

Open-access, no restrictions on reproduction and diffusion

"Label and Instructions for Use for Medical Devices" (GHTF/SG1/N70:2011)

International Organization for Standardization (ISO) (http://www.iso.org/iso/home.html)

Federation of national standard bodies

ISO 18113 "In vitro diagnostic medical devices - Information supplied by the manufacturer (labelling)"

ISO 15223 "Medical devices-Symbols to be used with medical device labels, labelling and information to be supplied"

ISO documents are copyrighted

European Union (EU) : IVDD 98/79/EC

Regulatory framework = EU Directive

"In Vitro Diagnostic Medical Device Directive (IVDD 98/79/EC)"

- currently under revision

- to be adopted by each of the member countries

CEN-documents: The European Committee for Standardization (CEN) works out the Directives

- European Standard EN 980 "Symbols for Use in the Labeling of Medical Devices".

- ISO and CEN have close interaction EN980 = ISO 15223 standard

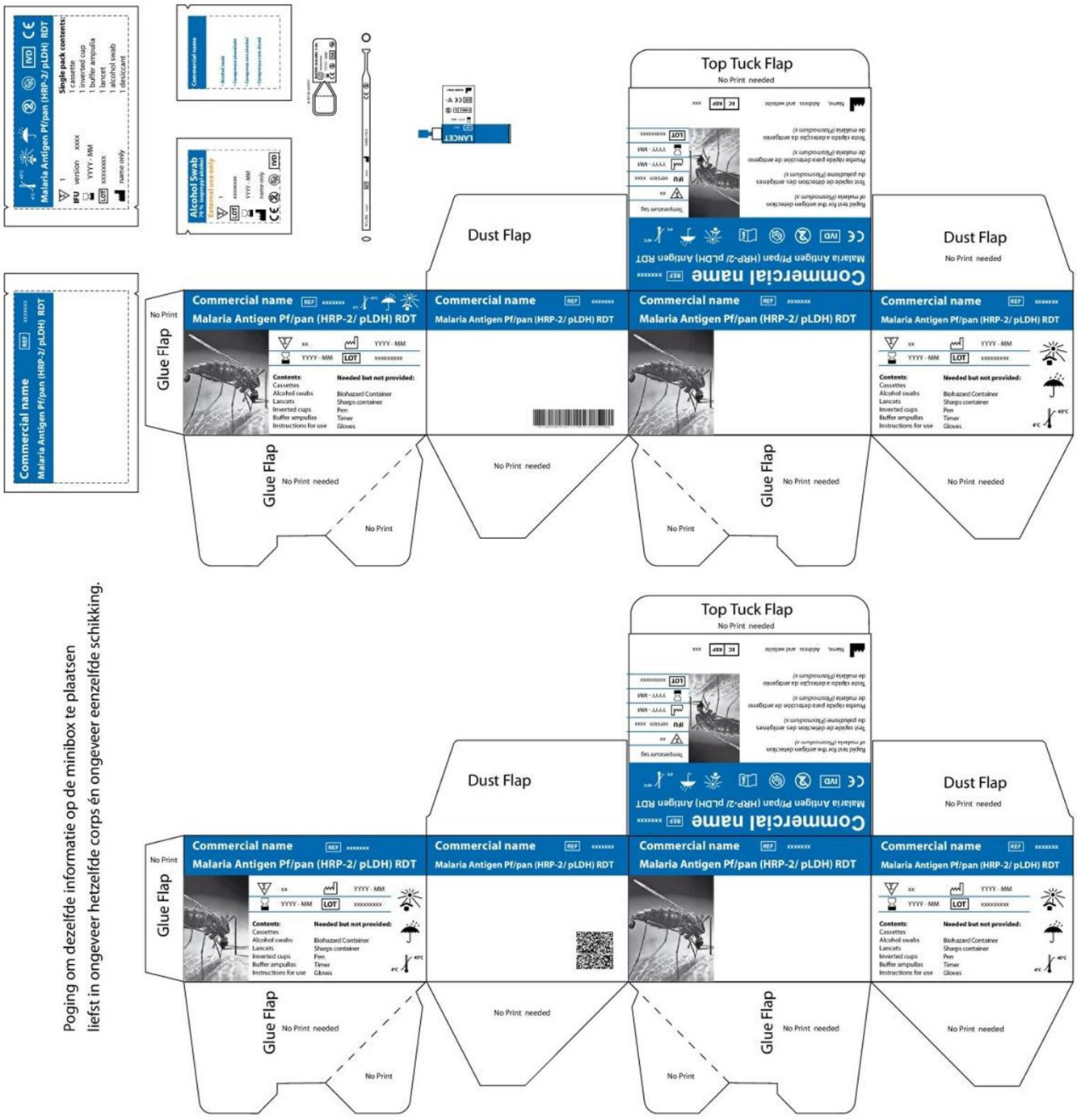
MEDDEVs = guidelines produced by experts

MEDDEV.2.14/3 rev.1 "IVD GUIDANCES: Supply of Instructions for Use (IFU) and other information for In-vitro Diagnostic (IVD) Medical Devices"

USA Food and Drug Administration (FDA) (http://www.fda.gov/)

Title 21 of the Code of Federal Regulations, Part 809 (21 CFR 809.10)

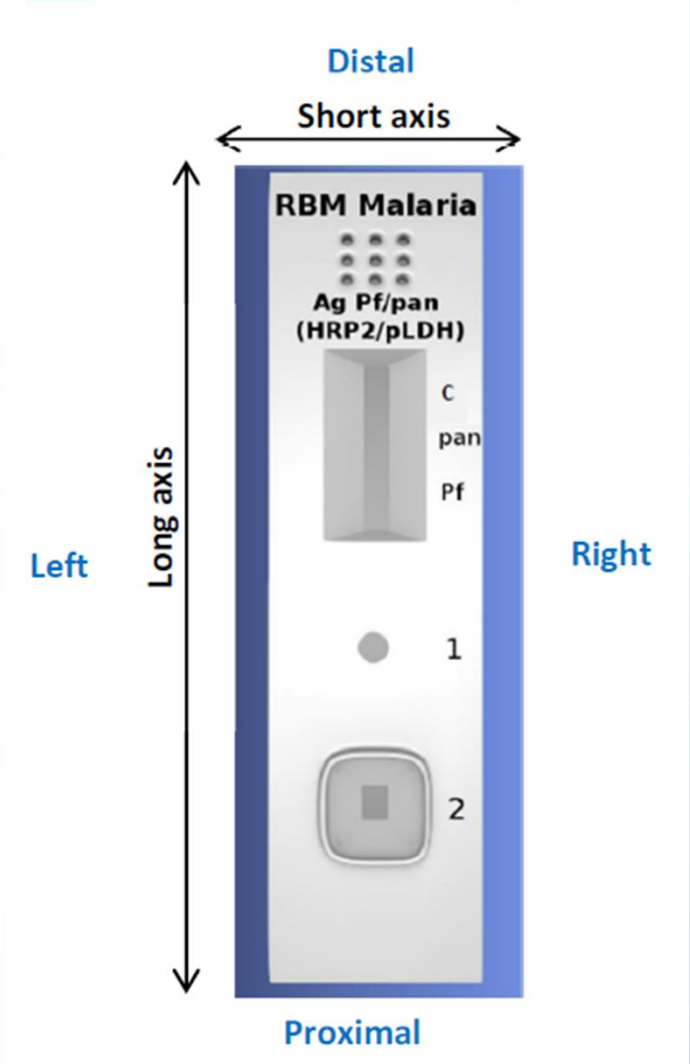
Requirements are in line with those described in IMDRF guidelines and ISO/CEN standards



Poging om dezelfde informatie op de minibox te plaatsen
liefst in ongeveer hetzelfde corps én ongeveer eenzelfde schikking.

Harmonization/Standardization & User friendliness
“Bluebox” = labeling, instructions

Harmonization of RDTs “Blue Box”



Additional file 1. Suggested terms and abbreviations related to malaria RDTs

1. Recommended terms

Preferred Term	Description	Comments/synonyms (not suggested term)
Accessories	Articles intended explicitly by its manufacturer to be used together with the RDT to achieve its intended purpose (*i.e.* specimen transfer device, lancet, alcohol swab).	Synonym: "ancillary items"
Alcohol swab	Gauze pad that is saturated with alcohol and used to clean and/or disinfect skin.	Synonym : "alcohol pad, alcohol wipe, alcohol pre pad"
Auto-transfer cassette	Cassette presenting with an opening which allows direct sampling of the blood on the nitrocellulose strip.	

Generic Instructions for Use

2. Check the expiration date of the test.
   If expired, do not use it but take another test from an unexpired kit.
3. Check that the cassette packaging is not damaged.
   If damaged, discard the cassette packaging and use another test.
4. Open the cassette packaging and check the desiccant.
   If there is a humidity indicator and it shows saturation (color changed from orange to green), throw away the cassette and take another cassette packaging.
   If the color of the desiccant does not show a change, you can use the test.
   Throw away the desiccant in the non-sharps disposal container.
5. Take the cassette and place it on a horizontal surface.
   You see:
   - a result window (marked with C, pan, Pf)
   - a circle well marked "1" (for specimen)
   - a square well "2" (for buffer)
6. Write the patient name or patient identifier on the cassette.
7. Put on gloves. Use new gloves for each patient.
8. *Add if needed additional instructions on how to open the buffer bottle correctly – for instance, how to pierce the nozzle.*

! Perform the test immediately after opening of the cassette packaging.

! Do not re-use the test.

Take home messages

To design an excellent POC/RDT is one thing, to make it properly work at the point of care is another one...

To implement an excellent RDT is challenging

- production
- quality
- regulations
- transport, shipment
- user
- clinicians and patients

To be taken into account when developing new targets (AB resistance!)

Thanks to ITM-team and Partners

Pierre Mukadi

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Marjan Van Esbroeck

Barbara Barbé

Lieselotte Cnops

Peter Konings

Agnes D'Hondt