Stichting Kwaliteitsbewaking
Medische Laboratoriumdiagnostiek

Malaria antigeentesten

Jaap van Hellemond

Dept. Medische Microbiologie & Infectieziekten
Erasmus MC & Havenpolikliniek

Maart 2018

Resultaten 2017

2015: proef rondzending

2016-2017:

regulier onderdeel rondzending
“bloed en darmparasieten”

Ronde 1 en 3: 2 EDTA-bloed lysaten

Resultaten 2017

Rondzending “bloed en darmparasieten”
Ronde 1 en 3: 2 EDTA-bloed lysaten

Ronde 1: 69 / 83 deelnemers (83%) rapporteert resultaten
Ronde 3: 68 / 83 deelnemers (82%) rapporteert resultaten

Gebruikte antigeentesten in 2017

Ronde 1: 69 / 83 deelnemers (83%) rapporteert resultaten
Ronde 3: 68 / 83 deelnemers (82%) rapporteert resultaten

RDT	Antigenen		2016	2017
Optimal-IT	Pf-LDH	p-LDH	9	8
Binax Now	HRP-2	Alodolase	51	50
Palutop +4	HRP-2	p-LDH	2	2
SD Bioline	HRP-2	p-LDH	4	5
CareStart	HRP-2	p-LDH	1	1
Anders	?	?	1	2
Totaal			68	68

Resultaten 2016

2016.1E:	negatief	(59/59, 100% correct)
2016.1F:	positief	
	• *P. falciparum* antigeen	(58/59, 98% correct)
	• *Plasmodium* species	(57/59; 97% correct)
2016.3E:	positief	
	• *P. falciparum* antigeen	(68/68, 100% correct)
	• *Plasmodium* species	(64/68; 94% correct)
2016.3F:	positief	
	• *P. falciparum* antigeen	(58/68, 85% correct)
	• *Plasmodium* species	(6/68; 94% correct)

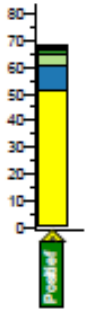
Resultaten 2016

2016.1E:	negatief	(59/59, 100% correct)
2016.1F:	positief	
	• *P. falciparum* antigeen	(58/59, 98% correct)
	• *Plasmodium* species	(57/59; 97% correct)
2016.3E:	positief	
	• *P. falciparum* antigeen	(68/68, 100% correct)
	• *Plasmodium* species	(64/68; 94% correct)
2016.3F:	positief	
	• *P. falciparum* antigeen	(58/68, 85% correct)
	• *Plasmodium* species	(6/68; 94% correct)

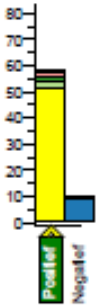
Sneltesten

P.falciparum antigeen sneltest

2016.3 E



2016.3 F

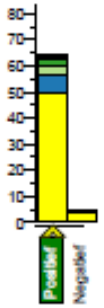


Legenda

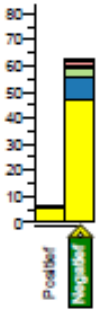
Binax Now | Optimal-IT | SD Bioline 05FK50 Malaria Ag P.f/Pan | Palutop +4 | Anders | CareStart

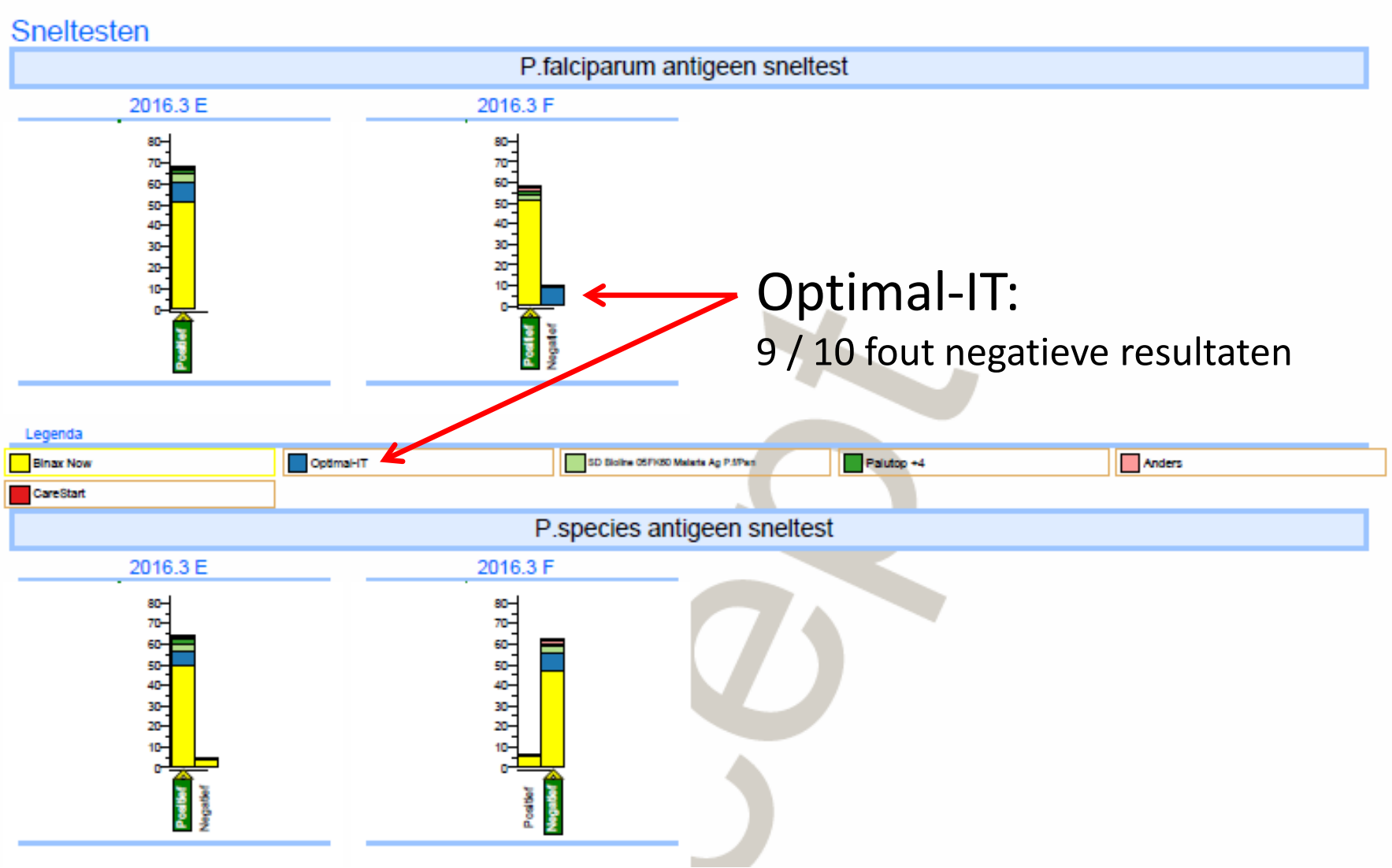
P.species antigeen sneltest

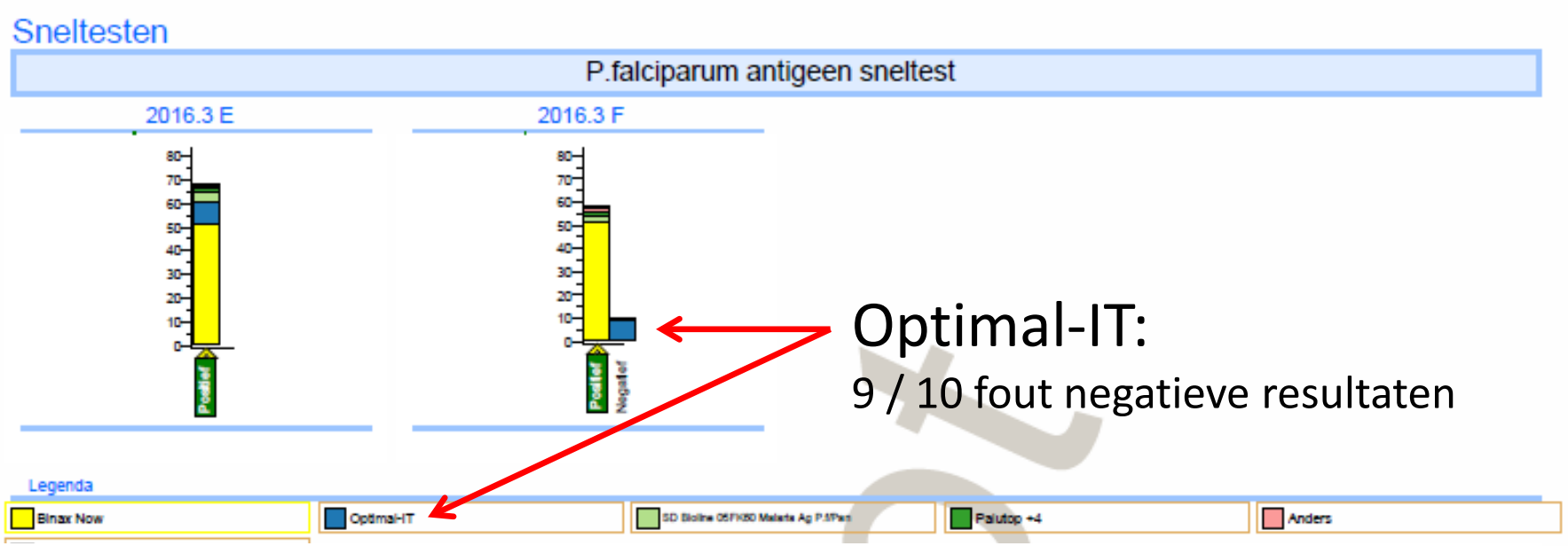
2016.3 E



2016.3 F




Sneltesten
P.falciparum antigeen sneltest
2016.3 E
2016.3 F
Positief
Negatief
Optimal-IT:
9 / 10 fout negatieve resultaten
Legenda
Binax Now
Optimal-IT
Palutop +4
Anders
CareStart
P.species antigeen sneltest
2016.3 E
2016.3 F
Positief
Negatief



N=	Sneltest	Antigenen	
9	Optimal-IT	Pf-LDH	p-LDH
51	Binax Now	HRP-2	Alodolase
2	Palutop +4	HRP-2	p-LDH
4	SD Bioline 05FK60 Malaria Ag P.f/Pan	HRP-2	p-LDH
1	Carestart	HRP-2	p-LDH
1	Anders		

Analyse oorzaak verschillende resultaten

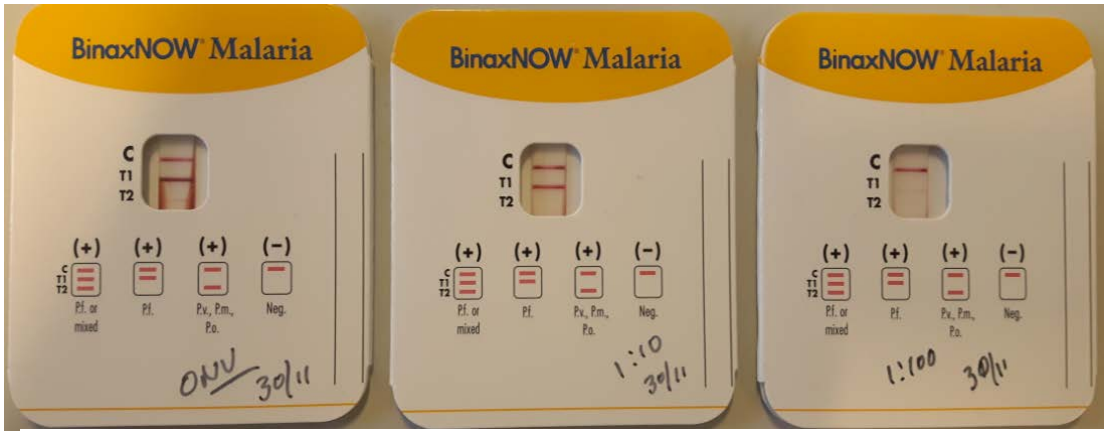
Verschil in sensitiviteit ?

	Binax NOW				Optimal-IT			
	23-11-2016		30-11-2016		23-11-2016		30-11-2016	
	HRP-2	Aldolase	HRP-2	Aldolase	PF-LDH	Pan-LDH	PF-LDH	Pan-LDH
onverdund	3+	1+			2+	1+		
1:10	2+	neg			neg	neg		
1:100	1+	neg			neg	neg		

Sensitiviteit van Optimal-IT voor *P. falciparum* antigeen is lager dan die van Binax NOW !

Analyse oorzaak verschillende resultaten

Verschil stabiliteit HRP-2 & PfLDH antigenen in EDTA lysaat?



	Binax NOW				Optimal-IT			
	23-11-2016		30-11-2016		23-11-2016		30-11-2016	
	HRP-2	Aldolase	HRP-2	Aldolase	PF-LDH	Pan-LDH	PF-LDH	Pan-LDH
onverdund	3+	1+	3+	1+	2+	1+	2+	2+
1:10	2+	neg	2+	neg	neg	neg	zwak	zwak
1:100	1+	neg	1+	neg	neg	neg	neg	neg

Resultaat gelijk aan start situatie:

PfLDH en HRP-2 zijn stabiele antigenen in EDTA-bloed lysaat

Conclusies

1) Sensitiviteit van Optimal-IT voor *P. falciparum* antigeen is lager dan die van Binax NOW !

2) PfLDH en HRP-2 zijn stabiele antigenen in EDTA-bloed lysaat

Literatuur

OPEN ACCESS Freely available online

PLOS ONE 2013

Performance of Rapid Diagnostic Tests for Imported Malaria in Clinical Practice: Results of a National Multicenter Study

Sandrine Houzé[1,2,3*], Isabelle Boutron[4,5], Anne Marmorat[1], Marie Dalichampt[4,5], Christophe Choquet[6], Isabelle Poilane[7], Nadine Godineau[8], Anne-Sophie Le Guern[9], Marc Thellier[10], Hélène Broutier[11], Odile Fenneteau[12], Pascal Millet[13,14], Stéphanie Dulucq[15], Véronique Hubert[1], Pascal Houzé[16], Florence Tubach[17,18,19], Jacques Le Bras[1,2], Sophie Matheron[18,20]

Abstract

We compared the performance of four rapid diagnostic tests (RDTs) for imported malaria, and particularly *Plasmodium falciparum* infection, using thick and thin blood smears as the gold standard. All the tests are designed to detect at least one protein specific to *P. falciparum* (*Plasmodium* histidine-rich protein 2 (PfHRP2) or *Plasmodium* LDH (PfLDH)) and one pan-*Plasmodium* protein (aldolase or Plasmodium LDH (pLDH)). 1,311 consecutive patients presenting to 9 French hospitals with suspected malaria were included in this prospective study between April 2006 and September 2008. Blood smears revealed malaria parasites in 374 cases (29%). For the diagnosis of *P. falciparum* infection, the three tests detecting PfHRP2 showed high and similar sensitivity (96%), positive predictive value (PPV) (90%) and negative predictive value (NPV) (98%). The PfLDH test showed lower sensitivity (83%) and NPV (80%), despite good PPV (98%). For the diagnosis of non-*falciparum* species, the PPV and NPV of tests targeting pLDH or aldolase were 94–99% and 52–64%, respectively. PfHRP2-based RDTs are thus an acceptable alternative to routine microscopy for diagnosing *P. falciparum* malaria. However, as malaria may be misdiagnosed with RDTs, all negative results must be confirmed by the reference diagnostic method when clinical, biological or other factors are highly suggestive of malaria.

Resultaat invoer in Qbase 2017

2 antigeentesten

- *P. falciparum* antigeen negatief/positief
- *Plasmodium* species antigeen negatief/positief

4 conclusie mogelijkheden:

Resultaat invoer in QBase

2 antigeentesten

- *P. falciparum* antigeen negatief/positief
- *Plasmodium* species antigeen negatief/positief

4 conclusie mogelijkheden

P. falciparum	*P.* species	Conclusie
negatief	negatief	Geen *Plasmodium* infectie
positief	negatief	*P. falciparum* infectie
positief	positief	*P. falciparum* ± *P.* species infectie
negatief	positief	Non falciparum *Plasmodium* infectie

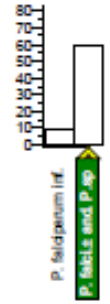
Performance score 2917 obv interpretatie

Kwalitatieve scores

Bepaling	Deze ronde				Cumulatief			
	juist	onjuist	totaal	pictogram	juist	onjuist	totaal	pictogram
Sneltesten								
Conclusie malaria antigeentest	1	0	1		1	0	1	

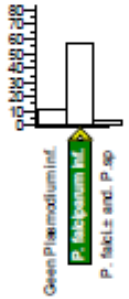
Conclusie malaria antigeentest

2016.3 E



score : 2

2016.3 F



Resultaten 2017

2017.1E: *Plasmodium* species (62/69, 90% correct)
5x fout NEG, 2x fout POS Pf

2017.1F: *P. falciparum* ± P. species
- *P. falciparum* antigeen (69/69, 100% correct)
- *Plasmodium* species (66/69; 96% correct)

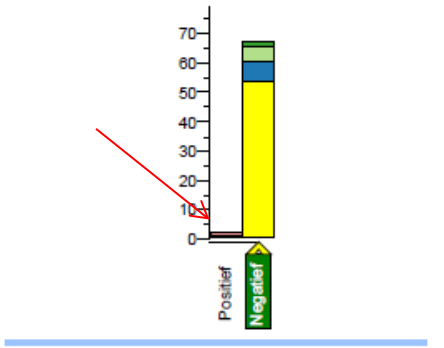
2017.3E: *P. falciparum* (± P. species)
- *P. falciparum* antigeen (67/68, 99% correct)
- *Plasmodium* species (17/68 positief)

2017.3F: *P. falciparum* ± P. species
- *P. falciparum* antigeen (68/68, 100% correct)
- *Plasmodium* species (65/68; 96% correct)

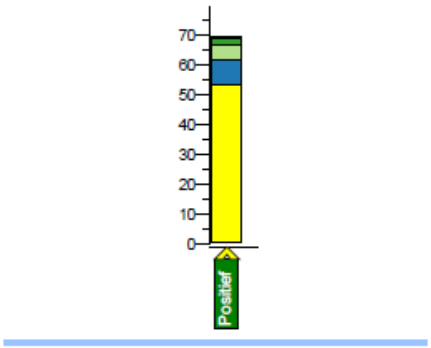
Sneltesten

P.falciparum antigeen sneltest

2017.1 E



2017.1 F



Legenda

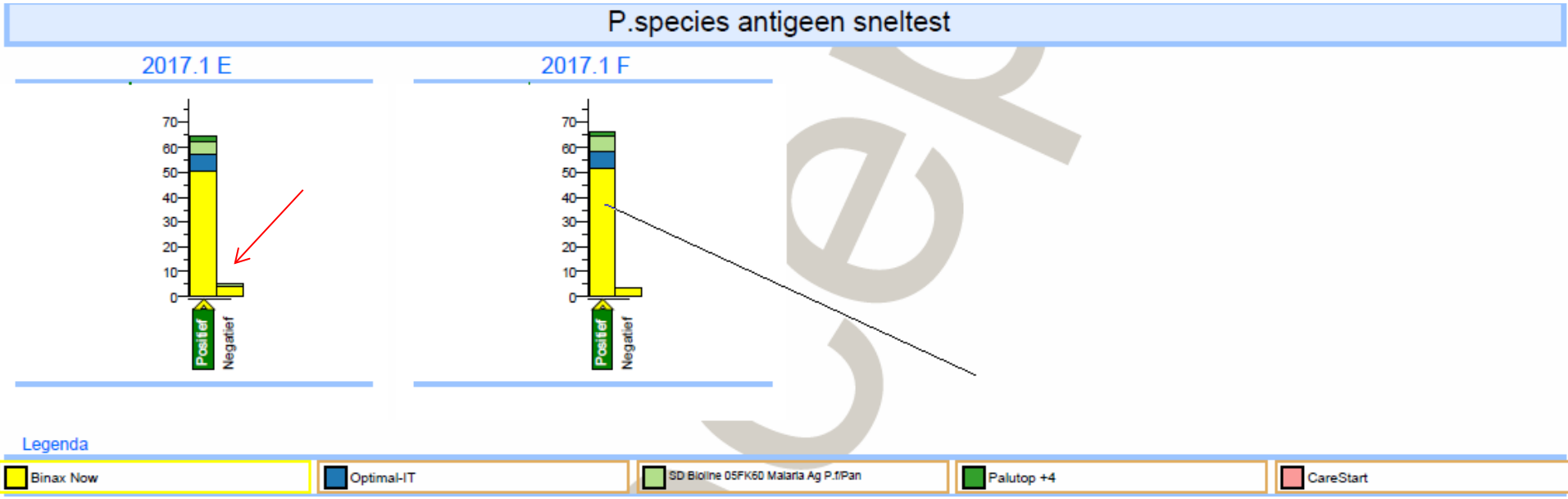
Binax Now | Optimal-IT | SD Bioline 05FK60 Malaria Ag P.f/Pan | Palutop +4 | CareStart

Fout positief *P. falciparum*:

1x Optimal-IT
1x CareStart

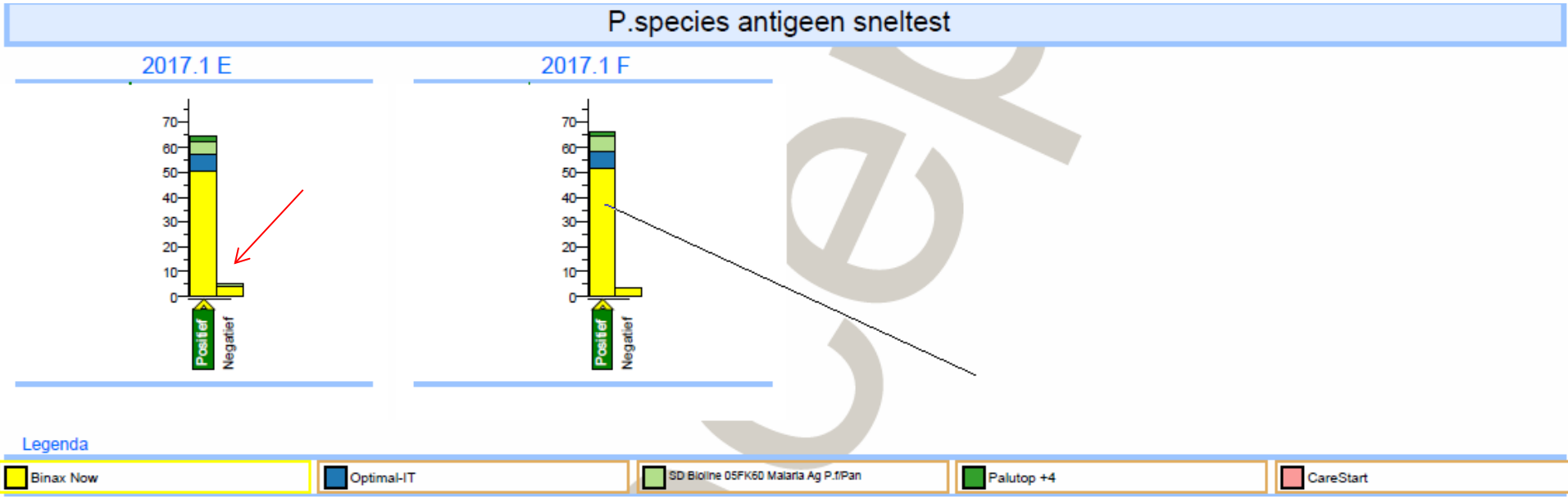
Oorzaak ?

- Geen materiaal verwisseling



Fout negatief *Plasmodium* species

4x Binax NOW
1x SD Bioline

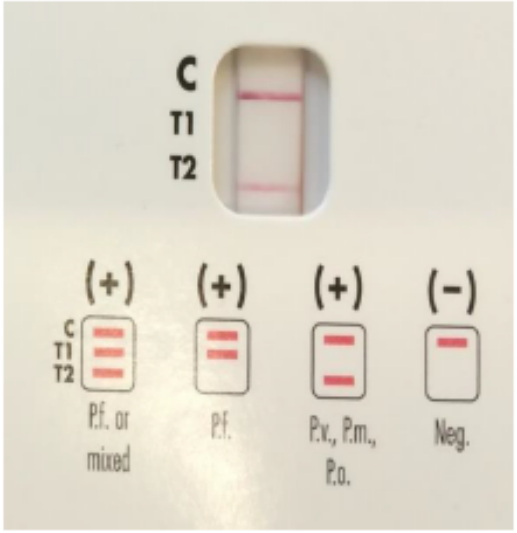


Fout negatief *Plasmodium* species

4x Binax NOW
1x SD Bioline

- Fout negatieve malaria antigeentest resultaten voor non-falciparum *Plasmodium* infecties komen geregeld voor !!!
- Met name voor *P. malariae* (lage parasitaemie) en *P. ovale*

Imported malaria from Africa with false negative rapid diagnostic test for *P. falciparum* due to deletion of the histidine-rich protein 2 gene



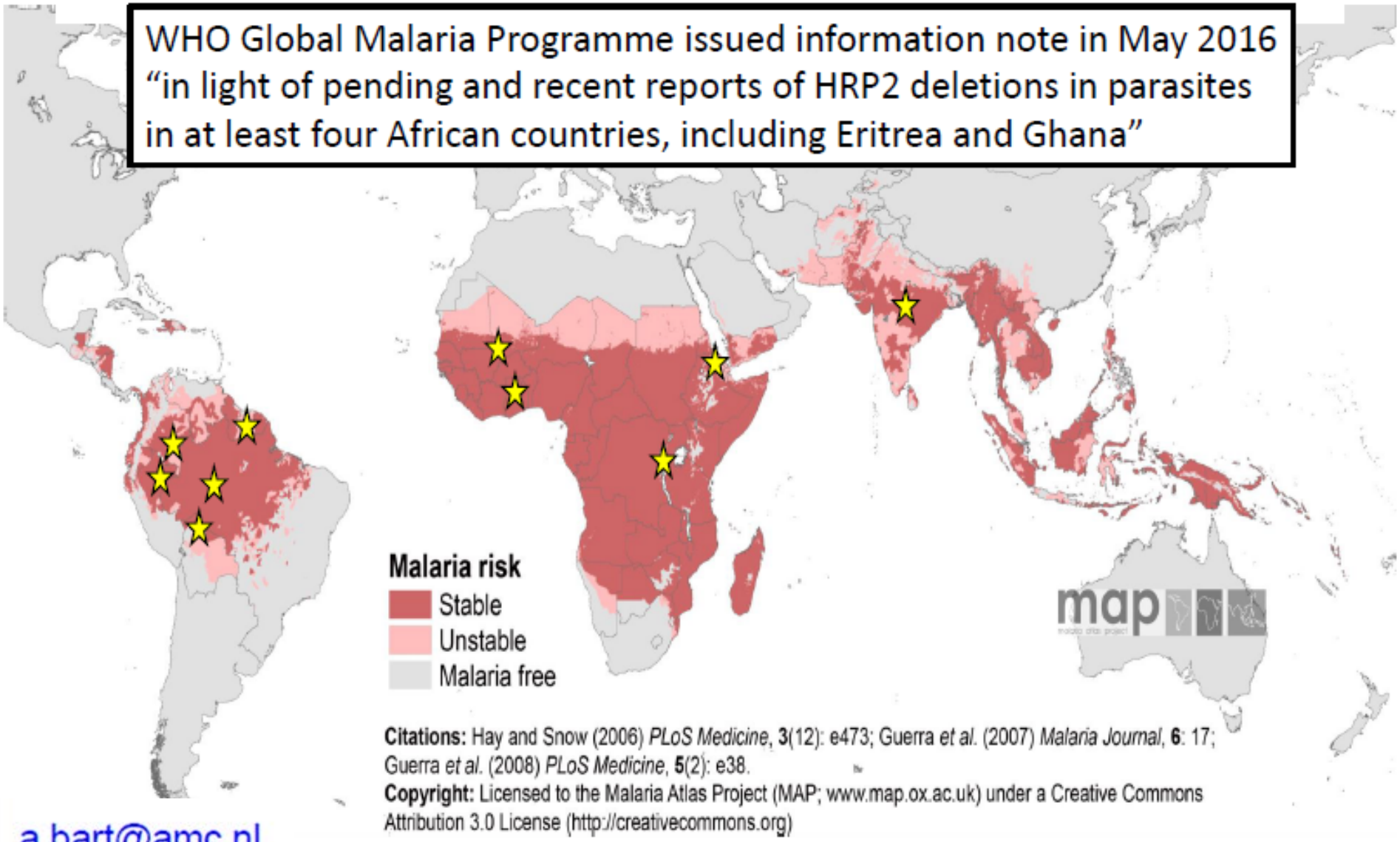
Aldert Bart[1], Nienke Verhaar[1], Jarne van Hattem[1], Michèle van Vugt[2], Godelieve de Bree[2], Tom van Gool[1]

[1]Department of Medical Microbiology and [2]Department of Internal Medicine, Academic Medical Center, Amsterdam, The Netherlands

a.bart@amc.nl
@AldertBart

Countries where HRP2 negative *P. falciparum* were reported

WHO Global Malaria Programme issued information note in May 2016 "in light of pending and recent reports of HRP2 deletions in parasites in at least four African countries, including Eritrea and Ghana"



Citations: Hay and Snow (2006) *PLoS Medicine*, **3**(12): e473; Guerra *et al.* (2007) *Malaria Journal*, **6**: 17; Guerra *et al.* (2008) *PLoS Medicine*, **5**(2): e38.

☆ HRP2 negative *P. falciparum* reported, prevalence up to 40%

a.bart@amc.nl
@AldertBart

Conclusion and Discussion

- HRP2 negative *P. falciparum* are no longer confined to South America.
- Do not rely on HRP2 reactivity alone for *P. falciparum* detection in imported cases, keep confirming negative RDT results by microscopy or other sensitive tests (e.g. Illumigene)

a.bart@amc.nl
@AldertBart

Dankwoord

Aldert Bart	AMC
Rob Koelewijn	Erasmus MC
Nicolette van der Ham	Erasmus MC