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AMAZON NETWORK FOR THE SURVEILLANCE OF ANTIMALARIAL DRUG RESISTANCE (RAVREDA)

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Preliminary report on the Efficacy and safety of Artemether Combination therapy for the treatment of acute uncomplicated Plasmodium falciparum malaria infections, conducted at Malaria Clinic Georgetown Hospital, Region 4, Guyana, 2011-2012

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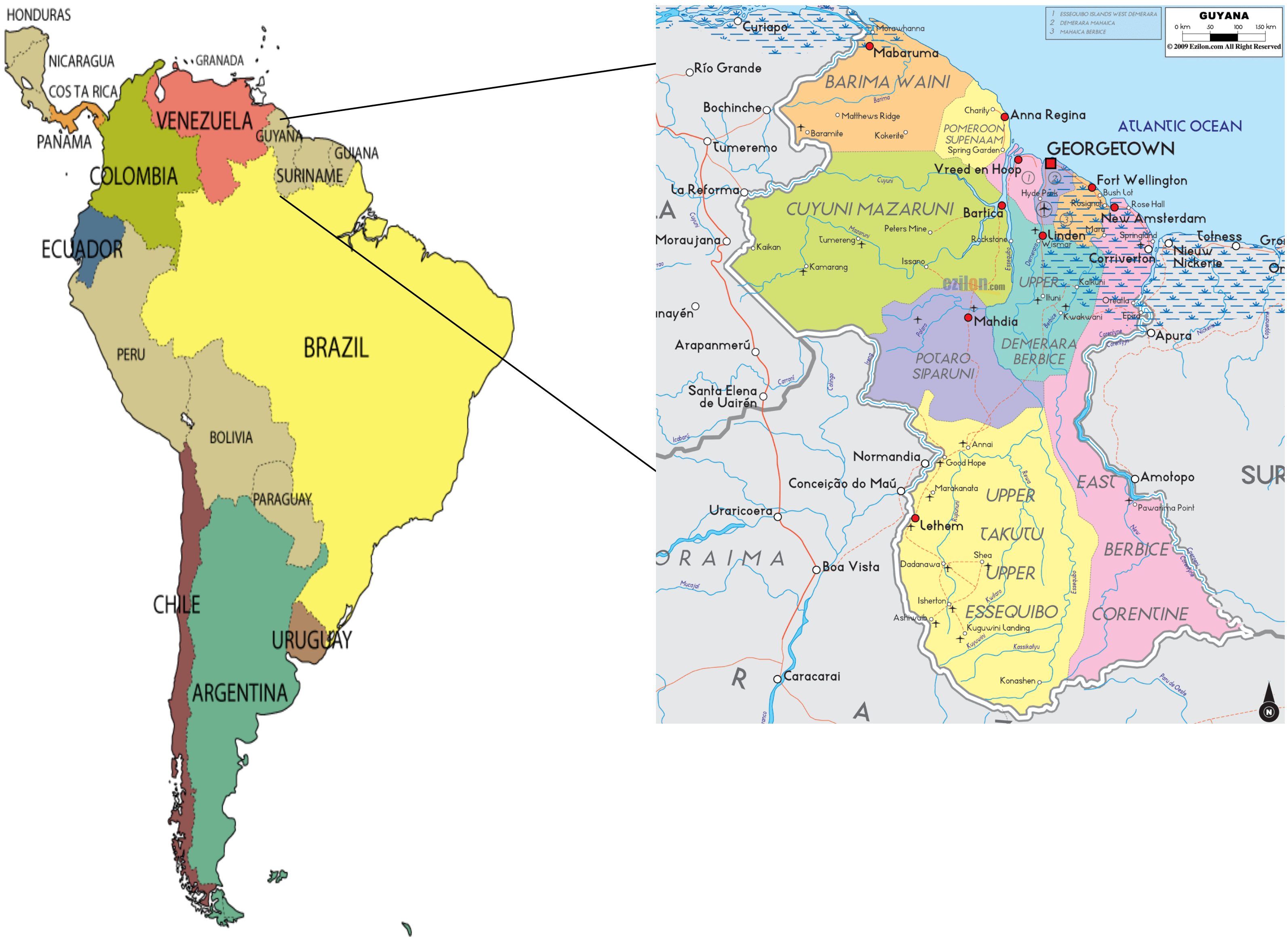

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Situation

- Malaria has spread geographically to various regions, mainly focused in the hinterland Regions 1, 7 and 8.

- In Guyana more than 200,000 people live in areas considered at high and medium risk for malaria.

Source: Annual Country Reports to PAHO/WHO

Prevalence species: *P. falciparum and P. vivax*

- In recent years an increase in the proportion of *P. falciparum* among the two predominant species was observed.

- *P. falciparum* and mixed infections increased from 39% in 2007 to 69% in 2011.

Source: Annual Country Reports to PAHO/WHO

Conclusions of Quality of anti-malarials collected in the private and informal sectors in Guyana and Suriname

The Guyana results illustrate the persistent problem of poor quality medicines and other aspects of irrational use of anti-malarial medicines in countries, especially if the malaria-endemic regions are remote or difficult to access.
As illustrated by the Guyana test results in particular, there is a greater chance of buying non-registered and/or poor quality products in private establishments than in informal ones.

Findings from these studies are similar to those that investigated the quality of medicines in the private and informal sectors in Africa and Southeast Asia, where there was also high incidence of poor quality anti-malarials [28-30]. Coupled with the ease with which the artemisinin-based products can be acquired and the availability of clinically inappropriate artemisinin-based monotherapy, these are a major cause for worry.

Together, they not only risk patient safety but also present serious implications for the development of drug-resistant strains of the *Plasmodium* parasite. A novel treatment is not foreseeable in the near future, thus placing malaria treatment at risk globally.

http://www.malariajournal.com/content/11/1/202

Monitoring the therapeutic efficacy of Antimalarial drugs in Guyana

Artemether - Lumefantrine	(P.falciparum) 2004 - 2005
Artesunate - Mefloquine	(P.falciparum) 2004 -2005
Mefloquine	(P.falciparum) 2004 - 2005
Artemether - Lumefantrine	(P.falciparum) 2007- 2008
Artemether - Lumefantrine + Primaquine	(P.vivax) 2009-2010
Artemether-Lumefantrine	(P.falciparum) 2011- 2012

Source: Annual Country Reports to PAHO/WHO

In vivo 2007-2008 Parasite density and Quality control				
Results	Guyana		Control OMAN	
Day	# Pos	%	# Pos	%
2	28	43.1	36	55.4
3	15	23.1	11	16.9
7	0	0.0	2	3.1
14	2	3.1	1	1.5
21	1	1.5	0	0.0
28	1	1.5	0	0.0
	47		50	

Source: Ministry of Health & PAHO/WHO, Guyana

Efficacy and safety of Artemeter Combination therapy-2011-2012

In vivo anti-malarial drug efficacy of Artemether-Lumefantrine Combination therapy (ACT) at the Malaria Clinic & Tropical Diseases Laboratory, Georgetown Public Hospital Corporation (GPHC), Region 4, Guyana.

- Subjects $\geq$ 10 Kg of a body-weight with parasitological-confirmed, acute uncomplicated *P. falciparum* infections

- Assigned treatment with (6-dose regimen) to Assess the efficacy and safety of ACT therapy for the treatment of *P. falciparum* infections (with follow up as per PAHO/WHO guidelines)

Source: Ministry of Health, Guyana & PAHO/WHO

Objectives

General objective: Assess the therapeutic efficacy and safety of Artemether – lumefantrine Co-artem® for the treatment of uncomplicated *P. falciparum* malaria in Georgetown hospital Region 4, Guyana.

Specific objectives:

• to measure the clinical and parasitological response to Artemether – lumefantrine (Co-artem®) among patients between 6 months to 69 years age suffering from uncomplicated *P. falciparum* malaria

• to differentiate recrudescence from new infection by polymerase chain reaction (PCR) analysis;

To formulate recommendations and to enable the Ministry of Health to make informed decisions about whether the current national antimalarial treatment guidelines should be updated

Source: Ministry of Health, Guyana & PAHO/WHO

Methods

This study was a one-arm prospective survey of clinical and parasitological responses to directly observe treatment for uncomplicated malaria.

Persons with uncomplicated malaria who met the study inclusion criteria were invited to participate, enrolled, treated on site with Artemether – Lumefantrine Co-artem® Batch No. X1489 **and monitored for 28 days.**

The follow-up consisted of a fixed schedule of check-up visits and corresponding clinical and laboratory examinations as per PAHO/WHO guidelines.

Source: Ministry of Health, Guyana & PAHO/WHO

Screening and Follow Up

- 32976 slides examined
- 5119 diagnosed *P. falciparum*
- *2468 screened*
- *92 recruited*
- *68 followed up for 28 days*

Source: Ministry of Health, Guyana & PAHO/WHO

Reason for not enrolment

Reason for not enrolment	*#*	*%*
Not available for the study	1832	77.13
Living too far	495	20.84
Took antimalarial drugs	5	0.21
Severe Vomiting	6	0.25
Not return for results	10	0.42
Pregnancy	22	0.92
Low HB	2	0.08
Refused to participate	3	0.10
Very ill	1	0.040
Total	2376	100

Source: Ministry of Health, Guyana & PAHO/WHO

Age Group and Gender

Age group and gender

	Gender		
Age	F	M	**Grand T..**
5-14		1	1
15-45	8	72	80
46-+		11	11
Grand Total	8	84	92

Source: Ministry of Health, Guyana & PAHO/WHO

Occupation

Occupation In vivo Study 2011—2012 Guyana		
Occupation	Frequency	Percent
Agricultural	1	1.09 %
Housewife	2	2.17%
Miner	59	64.13%
Other	26	28.0%
Student	4	4.35%
Total	92	98.65%

Source: Ministry of Health, Guyana & PAHO/WHO

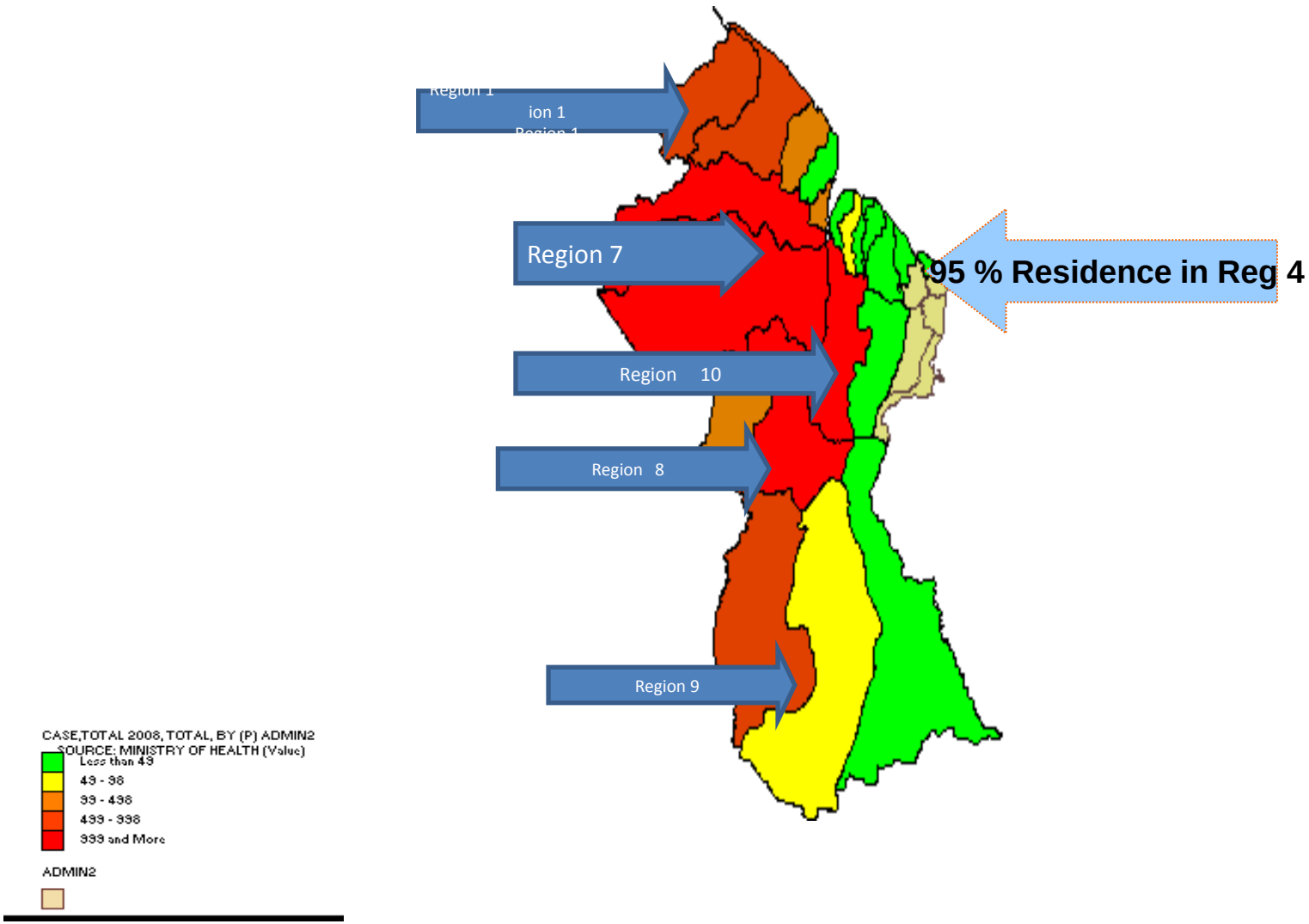
Residence – within miles of clinic, permitted follow up

Place of Residence

	Gender		
Place of resi..	F	M	**Grand T..**
E.B.D		8	8
E.C. D	4	42	46
G / Town	4	30	34
W.B.D		3	3
W.C.D		1	1
Grand Total	8	84	92

Source: Ministry of Health, Guyana & PAHO/WHO

Place of residence and Region visited before the diagnosis

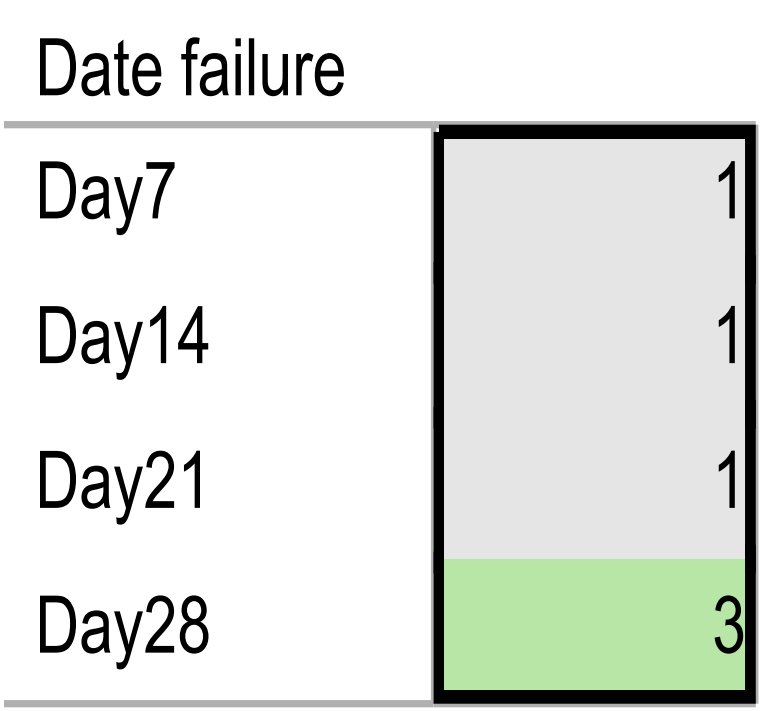


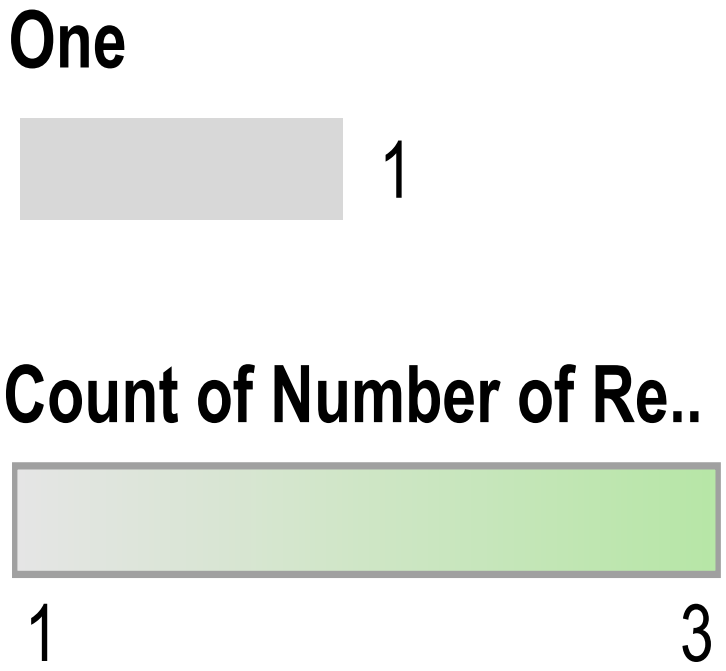
Source: Ministry of Health, Guyana & PAHO/WHO

Initial Diagnosis In vivo study, Guyana 2011-2012			
Diagnosis(Thick)		Frequency	%
+	1 parasite per field	5	5,43 %
++	2-20 parasites per field	63	68,47 %
+++	>20 parasites per field	19	20,65 %
> + 1/2	40-60 parasites in 100 fields	5	5,43 %
Total		92	99.98

Source: Vector Control Service, Ministry of Health, Guyana

Day of failure





Source: Ministry of Health, Guyana & PAHO/WHO

Conclusions

• This In-vivo study was conducted between May 2011 to July 2012.

• A total of 2468 patients were screened for possible enrolment into the study, only a total of 92 patients were enrolled; 2376 not enrolled

• From the 92 patients recruited, only 68 patients continued follow up for the total period of 28 days.

•86.95 % were between 15-49 years old,

• Occupation 64 % miners and 35 % other activity.

• Gender, 91.30 % male, and 8.6 % female**,**

• Ethnic group 70 % Afro-Guyanese, and 17.39 % Mixed,

• The regions visited before the diagnosis: 57 % from region 7, 25 % from region 8, 9.78 % from region 1, region 9 an region 10, 1.09 % each.

• The report of this study shows that Artemether-lumefantrine has a cure rate of 91.10 %, however there was a significant decrease in efficacy in relation to the evaluations conducted in 2004 and 2008 which was 100 and 98.5 % efficacy respectively.

• There were 62/89 positive on D 3 (68%)

• There were 6/68 treatment failures (8.9%)

• Treatment failures were on D 7, 14, 21, (1 case each) and 3 on D 28

Source: Ministry of Health, Guyana & PAHO/WHO

• Cases with gametocytes on D1 present, majority with values in the range of 1-99 (GD). Decreased until day 14 and 21 but cleared on day 28.

• The clinical and parasitological efficacy of Artemether–Lumefantrine in patients aged between 6 months to 69 years with uncomplicated falciparum malaria, resulted in adequate clinical and parasitological response 91.10 %; early treatment failure of 0%, late clinical and parasitological failure was probably an indicator of decreasing efficacy of this combination therapy.

• To confirm that, and to differentiate recrudescence from new infection (PCR) method; slide samples were sent to CDC for external quality control validation.

• Malaria Laboratory Guyana D3: 62/89 (68% positive)

•Comparative slide and PCR results from CDC not yet available

Source: Ministry of Health, Guyana & PAHO/WHO