

# Monitoring resistance of antimalarial drugs in Brazil

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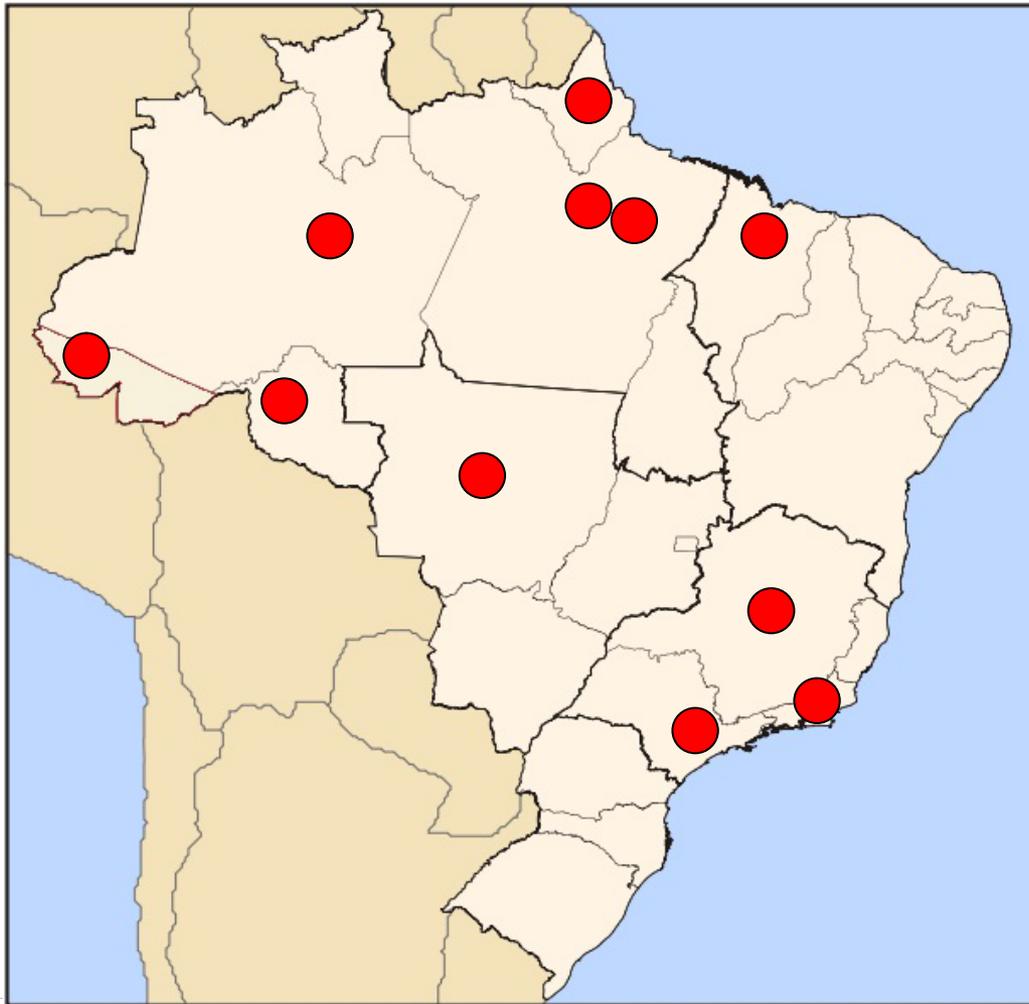
[www.saude.gov.br/malaria](http://www.saude.gov.br/malaria)



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# Collaboration Centers for RAVREDA



## *Research institutes and Universities*

### *In vivo efficacy studies*

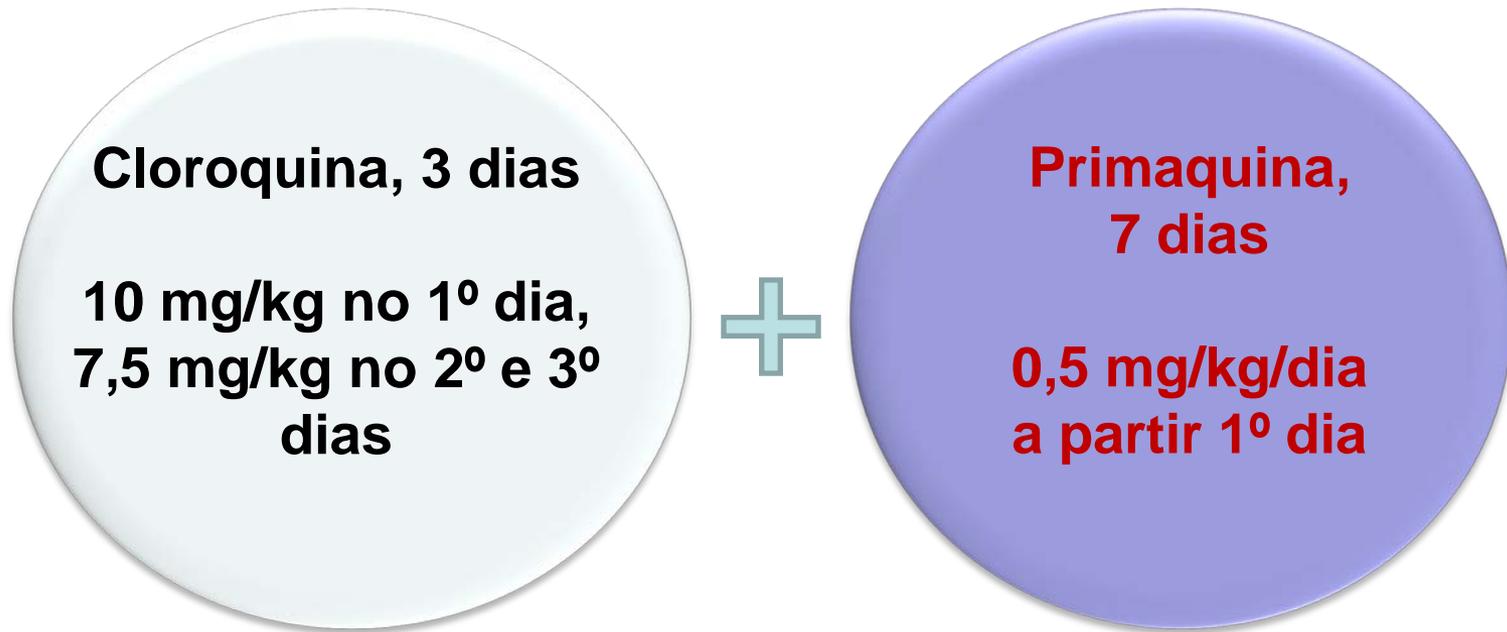
- Standard protocols
- Antimalarial blood levels
- Quality assurance (antimalarials, diagnosis)
- Genotyping
- Supervision

### **Training**

- Good practices in clinical trials

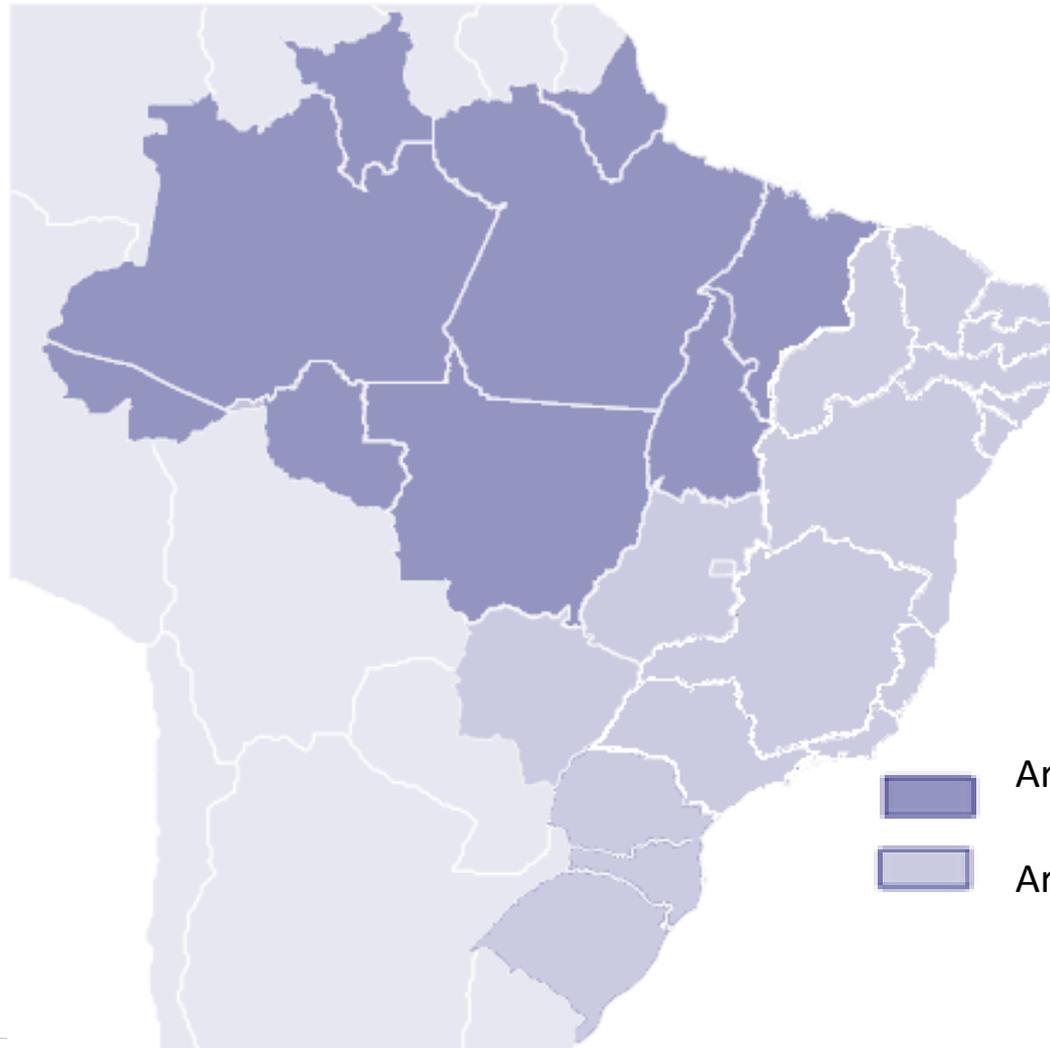
# Treatment Schemes for Malaria

## Uncomplicated vivax malaria



PQ dose adjusted according to patient weight

# Falciparum Malaria Treatment



Artemether + Lumefantrine and  
Primaquine



Artesunate + Mefloquine and  
Primaquine

# Amapá State



**LACEN (Central Laboratory of Public Health in Amapa)**

- **Site:** Oiapoque
- ***P. vivax*:** Chloroquine and Primaquine (finished)
- ***P. falciparum*:** Artemether + Lumefantrine (to start 2<sup>nd</sup> semester 2014)

# *P. vivax* in Amapá

- Chloroquine and primaquine
- Patients enrolled: 103
- Special attention:
  - Primaquine dose according to patient weight
  - Good microscopy
  - Quality of antimalarials
- Analysis
  - Slide review and PCR confirmation for enrollment samples
  - CQ blood levels
  - Antimalarials quality
    - Pill weight
    - Active ingredient analysis
  - Parasite clearance time

# *P. vivax* in Amapá

- 95 (92%) of 103
- Demographics
  - 30% gold miners in illegal areas
  - 32% overweight patients (PQ adjusted)
- Analysis of antimalarials quality with good results
  - Release of Active pharmaceuticals ingredients (API dissolution)
  - API quantification
- ~95% low parasitemia
- ACPR: 94 (99%)

# Amazonas



- **FMT-HVD**
- ***In vivo* efficacy studies**
  - *P. falciparum*: AL (stopped)
  - *P. vivax*: DHA (ongoing)
  - *P. vivax*: CQ and PQ
- ***In vitro* studies**
  - Mef, CQ and DHA (preliminary results)

# Amazonas State

## Artemether + Lumefantrine for *Pf*

- Manaus
- Start in 2010, stop due to fail to enroll
- 25 patients enrolled
  - D3 11/24 (46%) positive for asexual forms
  - D7 1/23 (4%) positive for asexual forms
  - D28 0/22 (0%) positive for asexual forms
  - Previous results considered sexual forms

# Amazonas – Coari e Manaus

## Chloroquine and Primaquine

- Comparison between primaquine dose (CDC and MoH) and administration period.
- 240 patients followed until D180
  - MS group: 253 patients (123 followed until D180)
  - CDC group: 170 patients (117 followed until D180)

## – Failure, MoH group

D 60 – 11%

D 90 – 19.5%

D180 – 30%

## – Failure, CDC group

D 60 – 11.1%

D 90 – 18.2%

D 180 – 37.5%

# Amazonas – Coari e Manaus

- In vitro for *P. vivax*
- Chloroquine, Primaquine and Dihydroartemisinin
- Manaus
  - CQ 11,6%
  - Mefloquine: 7,4%
  - DHA 0%
- Coari
  - CQ 5,5%
  - Mefloquine: 5,5%
  - DHA 0%

# Rondônia



## Cepem/FarManguinhos

- Porto Velho (RO)

## *In vivo* efficacy studies

- ACT for *P. vivax* (temporarily suspended)
- Coblister CQ + PQ

## Fiocruz/RO

## *In vivo* efficacy studies

- Candeias (RO)
- CQ+PQ for *P. vivax*

# Rondônia - Candeias

## CQ and PQ (“intermittent” treatment)

- Evaluation of intermittent treatment to prevent vivax relapses
- Patient enrollment starting March, 2014
- \* Intermittent treatment here should be understood as an weekly chloroquine treatment for 12 weeks, starting right after the 7 days CQ +PQ treatment.

# Acre State



Cruzeiro do Sul

SesAcre/ Fiocruz-RJ

- **Artesunate+  
mefloquine for *Pf***
- 2011 – 2012

SesAcre/ CDC/ IEC

- **CQ + PQ for *Pv***
- Started Feb/2014*

# Acre – Cruzeiro do Sul

## Artesunate+ mefloquine for *Pf*

- 180 patients enrolled
  - 160 followed until D42
  - No treatment failure
  - D3 data – under revision

## CQ + PQ for *Pv*

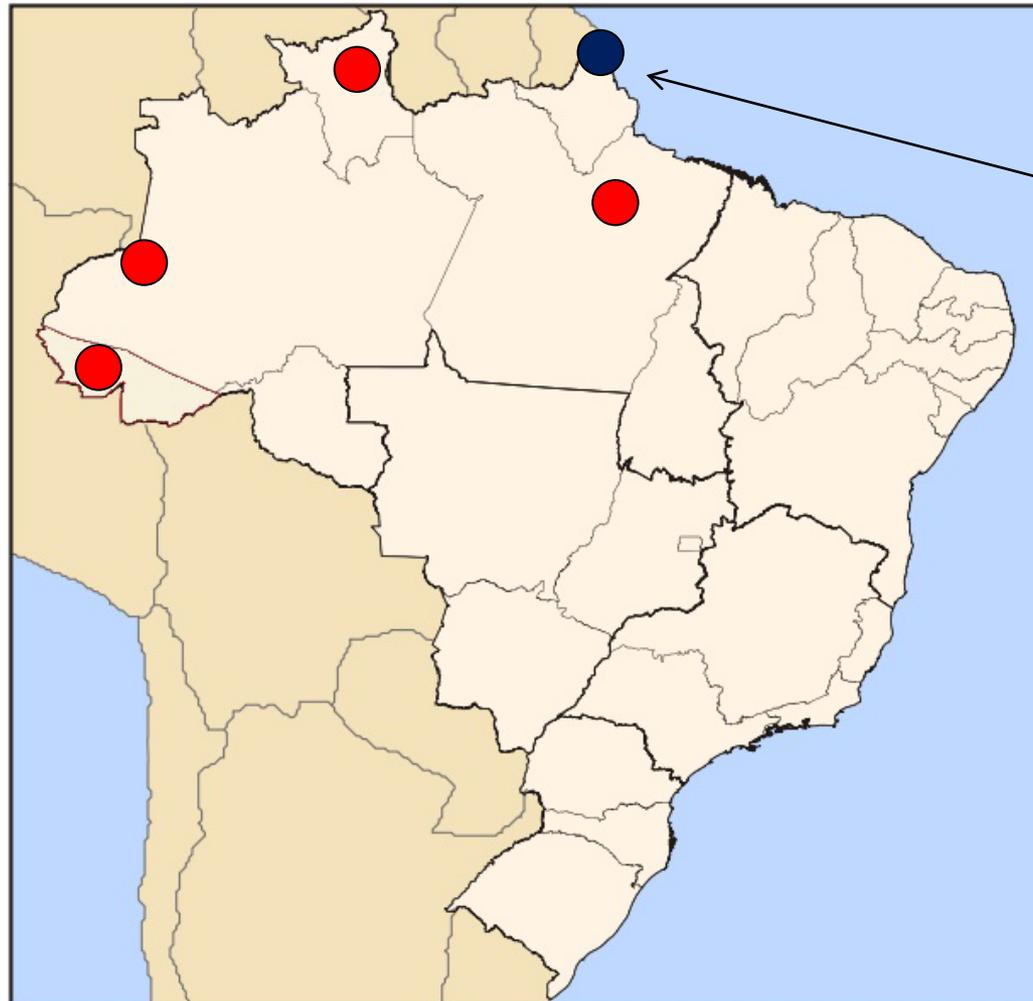
- Feb – Nov 2014
- Diagnostic: thick smear
- G6PD analysis
- D28 – clinical and parasitological evaluation
- Blood levels on D7 and FT (until D28)
- D 168 of total follow up
- ‘Experimental’ genotyping

# Supervision of efficacy studies

- Contract for planning and supervision of the efficacy studies in loco by a specialized consultant .
- Technical visits, coordinated along with PAHO and NMCP.
- Efforts to have researches according to defined protocols.

# D3 Surveillance – Sentinel Sites

- Routine surveillance;
- No observed treatment



9 enrolled  
D3+ 5/9

● 2013  
● 2014

# Obrigada

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