MALARIA SITUATION & DRUG RESISTANCE MANAGEMENT IN CAMBODIA

AND

CONTAINMENT RESPONSE ALONG THAI-CAMBODIA BORDER AND BEYOND

ACTMalaria EB AND PARTNER MEETING
IN LAO PDR
17-18 March 2009

Dr. CHEA NGUON, Vice Director
National Center for Parasitology, Entomology&Malaria Control Cambodia
Overview of the Presentation

- Malaria disease burden in Cambodia
- Key concerns related to the disease burden
- Obstacles/challenges faced
- Strategic Directions for the period 2006-10
- Malaria Situation from 1997-2008
- Monitoring Drug Resistance- sentinel sites
- ACT treatment failure in Cambodia
- Pailin study findings
- Three phases of the response
- Containment project and Proposal Round 9
- Activities after the training/workshop
## Malaria Disease Burden in Cambodia

<table>
<thead>
<tr>
<th>Population</th>
<th>Estimated Number</th>
<th>Year of Estimate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Population of Cambodia</td>
<td>14,363,519</td>
<td>2007</td>
</tr>
<tr>
<td>Population at risk (&lt;2km from the forest)</td>
<td>2,129,396</td>
<td>2007</td>
</tr>
<tr>
<td>Estimated malaria episodes per year</td>
<td>601,583</td>
<td>2006</td>
</tr>
<tr>
<td>(Based on % going to private sector)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reported malaria episodes per year</td>
<td>58,887</td>
<td>2008</td>
</tr>
<tr>
<td>(Public Health Facilities)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Confirmed and unconfirmed)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reported malaria episodes per year</td>
<td>24,439</td>
<td>2008</td>
</tr>
<tr>
<td>(Village Malaria Worker Project)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Malaria deaths per year</td>
<td>209</td>
<td>2008</td>
</tr>
<tr>
<td>(Reported in public sector)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Key concerns related to Cambodia’s Malaria Burden

- High incidence among non-immune migrants, forest workers
- Imprecise diagnosis as poor quality microscopy persists in remote areas
- Higher case fatality rate when compared to neighbouring countries
- Abundance of improper, inadequate, expensive and ineffective treatment regimens incl. fake drugs in private sector
Obstacles/challenges faced by NMCP

- Problems of access incl. poor roads
- Increasing migration to forest areas
- Rising operational costs
- Improper health seeking behaviour
- Poor microscopy
- Improper, inadequate, expensive & ineffective treatments including fake drugs in the private sector
- Procurement delays
- Staff turnover
Strategic Directions for NMCP from 2006-2010

- Behaviour Change Communication
- Long Lasting Insecticidal Mosquito Nets
- EDAT (RDTs /Microscopy & ACTs)
- Capacity Building (HR, Procurement Mgt., M&E, OR)

Building sustainable partnerships

Mobilizing required resources

NMCP VISION & GOAL
- Malaria Mortality
- Malaria Morbidity
Malaria Disease Burden in Cambodia

Average 9.7% annual reduction of (reported) malaria cases since 2004.
Malaria confirmed cases by age groups, 2008
Cambodia (42,124 confirmed by microscope and RDT)

- 0_4Y: 17%
- 5_14Y: 7%
- 15_49M: 51%
- 15_49F: 18%
- >50M: 2%
- >50F: 5%

Total: 100%
Proportion with ACT treatment failure in Cambodia (2001-2007)

Anlong Veng

Preah Vihear

Sampovloun

Pailin

Veal Vaeng

Chum Kiri

Ratanakiri

Snoul

2003

2002 2004 2006

Coartem

Artesunate - Mefloquine
While Artesunate + Mefloquine combination therapy (ACT) efficacy remains high in most studies, prolonged parasite clearance times following treatment with some ACTs & artemisinin monotherapy have been observed along the Thai/Cambodian border.

This clinical & parasitological observation might reflect the emergence of *P. falciparum* tolerance to artemisinins, but other factors have not been ruled out.

The sensitivity of ACTs needs to be closely monitored.

Anti malarial drug treatment policy should be reviewed every two years. The next review should be done early 2009.
Trial Profile

- Wang Pha, Thailand
  - Screened (positive RDT): 343
  - Enrolled: 40
    - AS7 (2 mg/kg): 20
      - Follow-up: 9 wks: 15; 7 wks: 1; 6 wks: 1; 4 wks: 1; 2 wks: 2
    - MAS3 (4 mg/kg): 20
      - Fol-up 9wks: 18
      - Fol-up 3wks: 2

- Pailin, Cambodia
  - Screened (positive RDT): 92
  - Enrolled: 40
    - MAS3 (4 mg/kg): 20
      - Fol-up 9wks: 19
      - Fol-up 7wks: 1
    - AS7 (2 mg/kg): 20
      - Fol-up 9wks: 20

- Declined consent: 2
  - Low parasitemia: 23
  - High parasitemia: 4
  - Mixed infection: 5
  - P. vivax infection: 4
  - Neg. microscopy: 9
  - Severity criteria: 3
  - Pre-treatment: 2
Parasite & Fever Clearance, ETF, Gametocytemia

<table>
<thead>
<tr>
<th></th>
<th>Wang Pha</th>
<th>Pailin</th>
<th>Wang Pha v Pailin</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>AS7</td>
<td>MAS3</td>
<td>AS7</td>
</tr>
<tr>
<td>Time to clearance</td>
<td>54</td>
<td>48</td>
<td>83</td>
</tr>
<tr>
<td>(IQR, hrs)</td>
<td>(42, 72)</td>
<td>(30, 54)</td>
<td>(54, 96)</td>
</tr>
<tr>
<td>No. early treatment</td>
<td>0</td>
<td>0</td>
<td>7</td>
</tr>
<tr>
<td>failure, (%)</td>
<td>(0)</td>
<td>(0)</td>
<td>(35)</td>
</tr>
<tr>
<td>Gametocyte duration,</td>
<td>19</td>
<td>13</td>
<td>10</td>
</tr>
<tr>
<td>days</td>
<td>(7, 19)</td>
<td>(1, 19)</td>
<td>(7, 19)</td>
</tr>
<tr>
<td>Gametocytemia*</td>
<td>0.058</td>
<td>0.070</td>
<td></td>
</tr>
<tr>
<td>person weeks</td>
<td>(0.047, 0.070)</td>
<td>(0.059, 0.082)</td>
<td></td>
</tr>
<tr>
<td>FCT-A (IQR), days</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>(1, 2)</td>
<td>(1, 2)</td>
<td>(1, 2)</td>
</tr>
</tbody>
</table>

Values are median (range), except * is geometric mean (95% CI)
Three Phases of the Response

Phase 1: January to December 2008
Phase 2: January 2009 to December 2010
Phase 3: January 2011 to December 2015
January 2007, Phnom Penh: WHO Informal Consultation on Containment of Malaria Multi-Drug Resistance on the Cambodia-Thailand Border


9-10 February 2008, Bangkok: ARC3 Clinical Trials Meeting

13-14 February 2008, Bangkok: WHO MMP Informal consultation to define a strategy to contain/eliminate Plasmodium falciparum parasites with altered response to artemisinins


August 2008: Submitted 2-year, multi-country proposal to the Bill and Melinda Gates’ Foundation.

September 2008: Clarification of BMGF comments including the adjustment of budget and resubmitted on 16th September
Preparatory work

(October-December 2008)

- Held stakeholders’ meetings to discuss medium term containment strategy as well as national private sector strategy for malaria control in October 2008.

- Preparatory work for conducting feasibility study of MSAT in containment zone 1.

- Start preparation for implementation of Phase 2 (write SOPs, recruit new staff, meet with partners) which is expected to commence in January 2009.

- Mobilize other potential donors to address the financial gap for 2009 and 2010.

- Prepare medium to long term plan to submit through GFATM Round 9.
Project Goal: To prevent the spread of artemisinin-tolerant Plasmodium falciparum parasites by removing selection pressure and ultimately eliminating falciparum malaria.

Strategic approach

- Ensure early and effective cure of all symptomatic infections by passive and active case detection, including eliminating infective stages of the parasite.
- Detection and complete treatment of asymptomatic parasite/gametocyte carriers by mass screening and DOTs.
- Focussing on P. falciparum but taking P. vivax into account.
Objective 1: To eliminate tolerant/resistant parasites by detecting the majority of malaria cases in target areas and ensuring effective treatment and gametocyte clearance.

Objective 2: To prevent use of artemisinin-based monotherapy (AMT), fake drugs and inappropriate treatment in the private sector.

Objective 3: To prevent transmission of tolerant/resistant parasites by mosquito control and personal protection.

Objective 4: To limit the spread of tolerant/resistant parasites by mobile populations.

Objective 5: To support containment of tolerant/resistant parasites through comprehensive BCC, community mobilization, advocacy.

Objective 6: To undertake implementation and operational research to ensure strategies apply are evidence-based.

Objective 7: To apply an effective management and information system to enable rapid and high quality implementation of the strategy.

Example: Establish comprehensive malaria surveillance information and management system.
Containment Zones

Zone 1 (Pink) = Evidence of tolerant parasites
Zone 2 (Green) = Buffer zone
The containment implementation area includes 10 provinces in Cambodia along the border with Thailand.
## Zone 1 - Target area and population

<table>
<thead>
<tr>
<th>Provinces</th>
<th>ODs</th>
<th>ADs</th>
<th>HC/HP</th>
<th>Villages</th>
<th>Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Battambang</td>
<td>Sampov Loun</td>
<td>Sampov Loun</td>
<td>2</td>
<td>27</td>
<td>24470</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Phnom Prek</td>
<td>3</td>
<td>40</td>
<td>46945</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Kam Reang</td>
<td>3</td>
<td>48</td>
<td>39528</td>
</tr>
<tr>
<td>Battambang</td>
<td>Samlot</td>
<td>Samlot</td>
<td>4</td>
<td>56</td>
<td>32254</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>4</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>171</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>143197</td>
</tr>
<tr>
<td>Pailin</td>
<td>Pailin</td>
<td>Pailin</td>
<td>2</td>
<td>51</td>
<td>31959</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Sala Krao</td>
<td>3</td>
<td>60</td>
<td>26253</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Sala Krao</td>
<td>2</td>
<td>5</td>
<td>111</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>58212</td>
</tr>
<tr>
<td>Pursat</td>
<td>Sampov Meas</td>
<td>Veal Veng</td>
<td>2</td>
<td>23</td>
<td>10769</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1</td>
<td>2</td>
<td>23</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>10769</td>
</tr>
<tr>
<td>Kampot</td>
<td>Chhouk</td>
<td>Chum Kiri</td>
<td>4</td>
<td>49</td>
<td>55570</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1</td>
<td>4</td>
<td>49</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>55570</td>
</tr>
<tr>
<td>Total: 4</td>
<td></td>
<td></td>
<td>5</td>
<td>8</td>
<td>23</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>354</td>
<td>26,7748</td>
</tr>
</tbody>
</table>
## Zone 2-Target area and population

<table>
<thead>
<tr>
<th></th>
<th>ODs Total</th>
<th>ADs Total</th>
<th>HC/HP</th>
<th>Population Total</th>
<th>Population (&lt; 2km of forest)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Battambang</td>
<td>5</td>
<td>12</td>
<td>74</td>
<td>754,248</td>
<td>150,258</td>
</tr>
<tr>
<td>Banthey Mean Chey</td>
<td>4</td>
<td>8</td>
<td>53</td>
<td>650,812</td>
<td>74,113</td>
</tr>
<tr>
<td>Pursat</td>
<td>2</td>
<td>6</td>
<td>31</td>
<td>417,932</td>
<td>77,884</td>
</tr>
<tr>
<td>Oddor Mean Chey</td>
<td>1</td>
<td>5</td>
<td>14</td>
<td>126,015</td>
<td>117,105</td>
</tr>
<tr>
<td>Preah Vihear</td>
<td>1</td>
<td>7</td>
<td>13</td>
<td>130,902</td>
<td>126,871</td>
</tr>
<tr>
<td>Koh Kong</td>
<td>2</td>
<td>8</td>
<td>14</td>
<td>132,106</td>
<td>93,380</td>
</tr>
<tr>
<td>Kampot</td>
<td>4</td>
<td>8</td>
<td>47</td>
<td>418,515</td>
<td>132,365</td>
</tr>
<tr>
<td>Kampong Speu</td>
<td>3</td>
<td>7</td>
<td>50</td>
<td>576,538</td>
<td>105,344</td>
</tr>
<tr>
<td>Siem Reap</td>
<td>4</td>
<td>13</td>
<td>43</td>
<td>816,173</td>
<td>138,696</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>26</strong></td>
<td><strong>74</strong></td>
<td><strong>339</strong></td>
<td><strong>4,023,241</strong></td>
<td><strong>1,016,016</strong></td>
</tr>
</tbody>
</table>
Border collaboration with Vietnam

- Anthropology study
- The project supported by ITM, Belgium
- Project site in Rattanakiri
Activities after the ACTMalaria Training Courses

Malaria Microscopy and QA

✓ Provided training on basic laboratory and quality control for lab technician from HCs and hospitals in Pailin and Oddar Meachey provinces.

✓ Carried out the laboratory monitoring as well as on-the-job training in 17 laboratories of public health facilities at four target provinces. Monitoring checklists were used for the follow up.

✓ Cross check 263 blood slides were collected from 17 lab facilities for quality control.

✓ Conduct assessment on:
  - General lab and supplies managementent
  - Lab capacity staff checking
  - Malaria quality control by QC cross-checking in 17 laboratories
  - Lab materials & equipment availability and supply
Activities after the ACTMalaria Training/workshop

Pharmaceutical Management of Malaria

✓ Established the drug coordinators in all levels for an effective drug delivery system, especially for the containment project by collaboration with DDF&CMS.
✓ Organized Drug management training for provincial, OD and HC
✓ Conduct the drug supply chain assessment with expert from Clinton Foundation.
✓ Consultative meetings for partners for the drug supply chain management.
✓ Developed the new format for the drug distribution to community through VMWs.
✓ Monitored and assessed the drug management in the public health facilities and collected the drug sample from the private outlet.
Activities after the ACTMalaria Training Courses

**Vector Control Management**

- Provide the coordination to the provincial staff
- Set up the provincial network for the future pilot integration of VIM.
- Training on entomology basic skill to provincial staff.
- Entomological survey
- Insecticide monitoring.
- In the field and insectary.
- Trap evaluation.