The Global Plan for Artemisinin Resistance Containment (GPARC)

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World Health Organization

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Supported by the Bill & Melinda Gates Foundation
Global Plan for Artemisinin Resistance Containment (GPARC)

Goal: Protect ACTs as an effective treatment for falciparum malaria

- Define priorities to contain and prevent artemisinin resistance (AR)
- Motivate actions and provide clear accountabilities for key stakeholders
- Mobilize resources to fund AR containment and prevention
- Increase collaboration and coordination on AR containment activities
- Define governance mechanisms and indicators to assess progress

Developed with input from ~100 partners across RBM partnership
Supported by the Bill & Melinda Gates Foundation

GPARC action pillars

1. Stop the spread of resistant parasites
2. Increase monitoring & surveillance to evaluate the AR threat
3. Improve access to diagnostics & rational treatment with ACTs
4. Invest in artemisinin resistance-related research
5. Motivate action and mobilize resources
GPARC builds on existing control and elimination efforts, with focus on interventions unique to AR

Malaria control & elimination

Artemisinin resistance containment & prevention

Examples
• Access to ACTs, diagnostics, vector control
• Research & Development
• Education and training

Examples
• Increase monitoring and surveillance
• Mobile population strategy
• Monotherapy removal

Examples
• Vaccine R&D
• Insecticide resistance management

(Note: Not drawn to scale)

Tier 1
Areas with credible evidence of artemisinin resistance

Tier II
Areas with significant inflows of people from Tier I areas, including those immediately bordering Tier I

Tier III
Areas with no evidence of artemisinin resistance and limited contact with Tier I areas
I. Stop the spread of resistant parasite

Preventive measures to reduce transmission – current status

Use of vector control increasing, but room for improvement

- % households protected by vector control (ITN and/or IRS)
- 34 Sub-Saharan countries – 2000-2010
- 0% - 60%
- Smallest-increase scenario
- Estimated ITN coverage
- Highest-increase scenario

Reducing transmission to stop survival & spread of resistant parasite

- Contains resistant parasites where they emerge
- Prevents spread to new areas
- Reduces potential impact if resistance were to take hold
- Is especially important among mobile/migrant populations likely to transport resistant parasites

Challenges

- Lack of perfect set of tools for SEA
- Mobile and migrants don't have good access to malaria prevention/treatment services
- Behavior of mobile/migrant population not well understood to design intervention programs

Source: Saving lives with malaria control: counting down to the Millennium Development Goals, Global Malaria Programme, World Health Organization.
II. Increase monitoring and surveillance
Evaluate the artemisinin resistance threat – current status

Routine ACT therapeutic efficacy data unavailable in many endemic countries

<table>
<thead>
<tr>
<th>WHO-compliant</th>
<th>Planning to conduct studies 2010/11</th>
<th>Last studies 2005 years ago</th>
<th>Last studies 5+ years ago</th>
<th>Difficult to conduct studies</th>
<th>Virus only</th>
<th>All endemic countries</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>In compliance</td>
<td>Not in compliance</td>
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</table>

Regular drug monitoring to evaluate AR threat

- Ensures countries are using the appropriate 1st line treatment
- Provides an understanding of the extent artemisinin resistance
- Allows timely identification of new AR foci

Challenges

- Logistically difficult in some settings
- Missing tools: no in vitro test or molecular marker available
- Not feasible in areas of very low transmission
- Not always conclusive; host factors can confound results

III. Improve access to diagnostics and ACTs
Consistent and accurate diagnostic testing – current status

Increasing availability and use of RDTs

Global distribution (Million of RDTs per year)

Increased use of diagnostic testing

- Limits the use of antimalarials to treat non-malaria fevers (esp. as transmission declines) which
  - puts partner drugs at risk
  - wastes valuable ACTs
- Helps track number of malaria cases
- Enables confirmation of suspected treatment failures

Challenges

- Distribution and inventory management
- Variability in RDT quality and performance
- Many providers / patients unaware of harm of treating non-malaria cases with ACTs
- No good models for RDT use in informal private sector

Source: Geneva, World Health Organization, Global Malaria Programme data, 2010

Use in Sub-Saharan Africa (% of suspected malaria cases tested with diagnosis)
III. Improve access to diagnostics and ACTs

Access to affordable, quality-assured ACTs – current status

ACTs: 1st line treatment in most countries; but not used consistently yet

Distribution of antimalarials by type (%)

- Cambodia: 94%
- Malaysia: 80%
- Zambia: 88%
- Benin: 88%
- Congo: 6%
- Other antimalarials: 12%

ACTs reduce the risk of AR development

- Mutual protection provided by two drugs reduces risk of AR
- Full course of ACT leads to:
  - Rapid clearance of parasites
  - Resolution of symptoms
  - Reduction of gametocyte carriage to limit transmission

Challenges

- Access in public sector: recurrent stockouts, limited geographic access to public health facilities, etc.
- Access in private sector: high price of ACTs, poor regulation and enforcement mechanisms, etc.

III. Improve access to diagnostics and ACTs

Removal of oral artemisinin-based monotherapies – current status

28 countries still allow marketing of monotherapies... and 39 companies still known to produce monotherapies

Countries providing marketing authorization¹ (as of Sept 2010)

- 28 allow marketing
- 34 withdrew marketing authorization
- 16 never registered

Oral artemisinin-based monotherapies believed to contribute to AR development and spread

III. Improve access to diagnostics and ACTs

Removal of substandard and counterfeit drugs – current status

Prevalence of substandard and counterfeit drugs in endemic countries

<table>
<thead>
<tr>
<th>Country</th>
<th>Substandard and counterfeit antimalarials</th>
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<tbody>
<tr>
<td>Greater Mekong Subregion</td>
<td>50%</td>
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<tr>
<td>Senegal</td>
<td>44%</td>
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<tr>
<td>Uganda</td>
<td>30%</td>
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<tr>
<td>Madagascar</td>
<td>26%</td>
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</tbody>
</table>

(Note: multiple data sources)

Use of poor-quality drugs may contribute to resistance

- Drugs with insufficient levels of artemisinin derivates may allow resistant parasites to survive and multiply

Challenges

- Limited data on prevalence of poor-quality drugs in endemic countries
- Difficult to track origin or sources
- Variety of causes, each needing different response (negligence, insufficient human / financial resources, deliberate action)
- Hard to verify ACT quality and authenticity at provider or retailer level

IV. Invest in AR-related research

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<thead>
<tr>
<th>Category</th>
<th>GPARC priority</th>
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<tbody>
<tr>
<td>Laboratory research</td>
<td>Enable faster detection of resistance, e.g.</td>
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<td>• Molecular basis of AR</td>
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<td>• Associated genotypes and phenotypes</td>
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<tr>
<td>Research &amp; Development</td>
<td>Ensure availability of new treatments, e.g.</td>
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<td>• New antimalarials</td>
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<td>• New transmission blocking formulations</td>
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<td>Applied &amp; field research</td>
<td>Determine if new or existing tools applied in novel ways can help manage AR, e.g.</td>
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<tr>
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<td>• Epidemiological and transmission reduction tools</td>
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<td>• Effectiveness of multiple 1st line therapies to delay resistance</td>
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<td>Operational research</td>
<td>Improve effectiveness of tools and programs in the field, e.g.</td>
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<td>• Scalable models for reaching mobile and migrant populations</td>
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<td>• Behavioral patterns explaining consumption of monotherapy</td>
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<td>Mathematical modeling</td>
<td>Predict the spread and impact of artemisinin resistance, including the impact of interventions intended to manage it</td>
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V. Motivate action and mobilize resources

GPARC success requires the support of many stakeholders.

**GPARC: rallying cry for all members of Roll Back Malaria Partnership**

- Malaria-Endemic Countries
- NGOs and implementation partners (International & local NGOs, CBOs)
- Funding agencies and bi-laterals
- Research and academia

**Multilaterals**

- WHO - GMP
- WHO, Regional & Country offices

**Private sector**

- International & local NGOs, CBOs
- Clinton Foundation
- Funding agencies and bi-laterals

- **World Health Organization**

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V. Motivate action and mobilize resources

Proposed areas of involvement by constituency

<table>
<thead>
<tr>
<th>Constituency</th>
<th>Global policy &amp; norms</th>
<th>Surveillance &amp; reporting</th>
<th>Contain, &amp; implement</th>
<th>Resource mobilization</th>
<th>Advocacy &amp; political engagement</th>
<th>Research</th>
<th>Local policy &amp; regulation</th>
<th>Emergency response</th>
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Primary ✓ Secondary ✓