Global uptake since WHO PQ

- Currently one WHO prequalified manufacturer
- 2nd manufacturer still anticipating ERP approval in 2017

~100 Million
Vials delivered since WHO prequalification

500,000 – 600,000
Additional lives saved in comparison to treatment with quinine
Mission and Vision

Our mission: To create an open, accessible, knowledge-sharing platform that acts as a repository of information and resources for the severe malaria community and allows the sharing of experiences and best practices in this field of work.

Our vision: A world in which severe malaria case management is significantly improved by freely available information and open access to resources so that no child has to suffer from this fatal disease.
• What is severe malaria?
• Burden
• Symptoms
• Diagnostics
• Treatment
• Groups at risk
• Severe malaria situation and burden
• Sources of funding
• National malaria policy
  o Community case management
  o Health structure
  o Commodities
- Quality assured products
- Dosing recommendations
- National registrations
- Volume and pricing trends
  - Injectable and suppository commodities
- Tool kits and training material
Past (milestone) and active severe malaria projects
Stories and films from the field
Interviews
FAQ
The opportunity

Increasing access to quality assured products for malaria chemoprevention and pre-referral treatment of severe malaria.

Monitoring Quality of Inpatient Malaria Case Management at Kenyan County Hospitals. To determine levels and trends: availability/knowledge/coverage of HCW, hospital commodities and services

Developing innovative approaches to increase rural access to commodities for the case management of severe malaria

Analyzing the existing gaps in the Mopti region of Mali between WHO guidance and de facto malaria prevention and treatment practices at the community level.

Modified Cohort Event Monitoring (CEM) to study all adverse events to Inj AS, Inj Artemether (AR) and quinine (Q) in Ghana and Uganda
What’s next?

www.severemalaria.org
Back up slides
RAS Country profiling

Review plans for roll-out (countries & timelines)

Note: Size of the bubble represents severe malaria cases as per WHO report 2015
X axis - 

Infrastructure & readiness
(Composite score: Registration, Funding, MOU, CHW trained & available)
[1 = Unprepared, 5 = Prepared]
Lessons learnt Storage and Distribution
CSD, Monitoring, Coordination at HCFs level.

- **Cost of Distribution**
  - In general it is 8% (3% for storage and 5% for distribution)
  - Required in practice by NMS in some countries for Donations
  - Should be budgeted for to guarantee distribution

- **Distribution Monitoring**
  - Crucial to inform the quantification process
  - Prevent expiries and wastage

- **Coordination within HCFs**
  - A system should be in place for **Pharmacists** to systematically inform **health workers** in charge of prescriptions.
Use of Inj AS, quinine and other antimalarials for the treatment of severe malaria over one year

Number of sites

Cameroon: 30
Ethiopia: 30
Kenya: 32
Malawi: 30
Nigeria: 90
Uganda: 30

Total: 242

% Procurement of Inj AS in the public sector vs Quinine is above 95%
<table>
<thead>
<tr>
<th>Challenges vs Opportunities</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ensuring completion of referral process</strong></td>
</tr>
<tr>
<td>• UNITAID RAS project</td>
</tr>
<tr>
<td>• RFI - Developing innovative approaches to increase rural access to commodities for the treatment and case management of severe malaria</td>
</tr>
<tr>
<td><strong>The most challenging environments: where the need is the greatest</strong></td>
</tr>
<tr>
<td>• Support for fragile/conflict states</td>
</tr>
<tr>
<td>• Offer technical support for implementing projects</td>
</tr>
<tr>
<td><strong>Misalignment of guidelines</strong></td>
</tr>
<tr>
<td>• Work with WHO, iCCM partners, MCHIP on guideline harmonization</td>
</tr>
<tr>
<td><strong>Multiple dosage availability (200mg, 100mg, 50mg)</strong></td>
</tr>
<tr>
<td>• Harmonization of recommendations</td>
</tr>
<tr>
<td>• Pharmacovigilance of field practices using various dosages</td>
</tr>
<tr>
<td><strong>Country adoption of RAS policy</strong></td>
</tr>
<tr>
<td>• Support harmonization of country guidelines with WHO</td>
</tr>
<tr>
<td>• Understand evidence/reasoning of country guidelines</td>
</tr>
<tr>
<td>• Monitoring and pharmacovigilance</td>
</tr>
<tr>
<td><strong>Adequacy of RAS training materials on the field</strong></td>
</tr>
<tr>
<td>• Assessment of RAS IEC materials in a real-life context</td>
</tr>
</tbody>
</table>
## Regulatory submission plan for Cipla and Strides

Submitted in 19 countries

<table>
<thead>
<tr>
<th>2015</th>
<th>2016</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>1Q</td>
<td>1Q</td>
<td>1Q</td>
</tr>
<tr>
<td>2Q</td>
<td>2Q</td>
<td>2Q</td>
</tr>
<tr>
<td>3Q</td>
<td>3Q</td>
<td>3Q</td>
</tr>
<tr>
<td>4Q</td>
<td>4Q</td>
<td>4Q</td>
</tr>
</tbody>
</table>

**Countries:**
- Benin
- Nigeria
- Uganda
- Zambia
- Ethiopia
- Malawi
- Ghana
- Senegal
- Mali
- Niger
- Burkina Faso
- DRC
- Tanzania
- Cameroon
- Chad
- Gabon
- Congo
- Cote d'Ivoire
- Tanzania
- Ghana
- Uganda
- Ethiopia
- Malawi
- Zambia
- Benin
- Nigeria
- Burkina Faso
- DRC
- Congo
- Cote d'Ivoire
- Cameroon
- Chad
- Gabon
- Mali
- Niger
- Senegal
- Guinea
- Sierra Leone
- Liberia
- Ghana
- Benin
- Nigeria
- Burkina Faso
- DRC
- Cote d'Ivoire
- Cameroon
- Chad
- Gabon
- Mali
- Niger
- Senegal
- Guinea
- Sierra Leone
- Liberia

**Status:**
- Strides only
- WHO Collaborative Registration Process
- Approved
- Expected Approval
RAS poster and job aid developed by MMV

Administer rectal artesunate and refer

**Age**
For children between 6 months to less than 6 years old

**Danger signs requiring rectal artesunate**
If in addition to fever or history of fever, you notice one or more of these danger signs, administer rectal artesunate.

- LETHARGY / UNCONSCIOUSNESS
- REFUSAL TO FEED
- CONVULSIONS
- REPEATED VOMITING

**Step 1: Administer rectal artesunate**

**Step 2: Refer**
After receiving rectal artesunate suppository the child must be referred immediately to the nearest hospital or health care facility where the full required treatment for severe malaria can be provided.

Administer rectal artesunate for severe malaria: 4 steps

1. **Prepare**
   - Wash your hands
   - Put on a pair of disposable gloves
   - Place the child in lateral position

2. **Administer**
   - Remove the packaging and insert the suppository
   - 1–2 minutes

3. **Refer**
   - Complete the referral form
   - Where to refer?
   - Urgent transport

4. **Follow up**
   - Follow-up within a few hours and ensure that the caregiver has indeed travelled to the nearest hospital or health care facility with the child. Once the child has returned, be sure to follow up at least once per week for up to one month until the child has fully recovered.

**Check the dosage relative to the child’s age and weight**

<table>
<thead>
<tr>
<th>Age</th>
<th>From 6 months to less than 3 years</th>
<th>From 3 years to less than 6 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight range</td>
<td>From 5kg to less than 14kg</td>
<td>From 14kg to 19kg</td>
</tr>
<tr>
<td>Dose</td>
<td>1 suppository (1 x 100mg)</td>
<td>2 suppositories (2 x 100mg)</td>
</tr>
</tbody>
</table>

**Trouble shooting:**
- If the suppository breaks or is melted, insert a fresh one.
- If the suppository slips out: reinsert the same suppository that has been or partially melted, insert a new one.
Speed up new product introduction post-ERP approval

• Collaboration with TGF on innovative projects that may speed new product introduction post-ERP approval, e.g. through collaborative fast-track registration procedures.

• In line with current global objecting of GF to increase access to innovative health technologies

• Providing information in advance to country regulators on ERP approved products will have a significant impact on the approval date /marketing authorization
RAS Age in Guidelines
RAS poster and job aid developed by MMV

Administer rectal artesunate and refer

**Step 1: Administer rectal artesunate**

**Step 2: Refer**

Danger signs requiring rectal artesunate

If in addition to fever or history of fever, you notice one or more of these danger signs, administer rectal artesunate.

**LETHARGY / UNCONSCIOUSNESS**

**REFUSAL TO FEED**

**CONVULSIONS**

**REPEATED VOMITING**

For children between 6 months to less than 6 years old

Age

Check the dosage relative to the child’s age and weight

<table>
<thead>
<tr>
<th>Age</th>
<th>Weight range</th>
<th>Dose 10 mg/kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>From 6 months to less than 3 years</td>
<td>From 5kg to less than 14kg</td>
<td>1 suppository (1 x 100mg)</td>
</tr>
<tr>
<td>From 3 years to less than 6 years</td>
<td>From 14kg to 19kg</td>
<td>2 suppositories (2 x 100mg)</td>
</tr>
</tbody>
</table>

Check the dosage relative to the child’s age and weight

1. **Prepare**
   - Weigh the child or get an approximate weight
   - Wash your hands
   - Put on a pair of disposable gloves
   - Place the child in lateral position

2. **Administer**
   - Remove the packaging and insert the suppository
   - Insert the suppository
   - Cover the buttocks

1-2 minutes

Trouble shooting:

- If the suppository breaks or is melted, insert a fresh one.
- If the suppository slips out, it is still intact: insert the same one. If it has been or partially melted, insert a new one.

3. **Refer**
   - Complete the referral form
   - Where to refer?
   - Urgent transport

Follow up

- Follow up within a few hours and ensure that the caregiver has indeed travelled to the nearest hospital or health care facility with the child. Once the child has returned, be sure to follow up at least once per week for up to one month until the child has fully recovered.
- Check if the child is anemic, feverish, has appetite and general condition.

RAS poster and job aid developed by MMV
WHO-TDR vs. Test Capsules

• Cipla, Strides and WHO-TDR capsules are qualitatively similar; they are NOT identical
• Neither the Cipla nor Strides capsules are lubricant coated
  - Data obtained to date show no adverse impact on stability
  - Uncoated capsules give the advantage of a solvent-free process
• Both companies have had sight of the WHO-TDR analytical methods, but have chosen to use their own
  - Analysis of test and comparator capsules by both companies with TDR and in-house assays gives equivalent results
• Both Cipla and Strides have been able to tighten the related substance and dissolution acceptance criteria for both release and shelf-life compared to the WHO-TDR specification
SPC and Dosing Instructions

• The recommended dose (WHO guidelines) is 10mg/kg

• The single 100mg capsule dose used in WHO-TDR Study 13, led to a tendency to under dose older, heavier children

• WHO-TDR data show that age rather than weight is likely to be the primary criterion used for determining dose

• Based on Study 13 data, WHO-TDR revised their SPC in 2014, such that older children would be dosed with 2x 100mg capsules

• This was discussed with the WHO-PQ and a revised age/weight dosing regimen was agreed. This has been adopted by both Strides and Cipla

<table>
<thead>
<tr>
<th>Age</th>
<th>Weight</th>
<th>Rectal artesunate (10mg/kg body weight dose)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 months to ≤3 years</td>
<td>5kg to ≤14kg</td>
<td>1 x 100mg suppository</td>
</tr>
<tr>
<td>&gt;3 to 6 years</td>
<td>&gt;14kg to 20kg</td>
<td>2 x 100mg suppositories</td>
</tr>
</tbody>
</table>