



The Severe Malaria Observatory

CMWG meeting – 29th August 2017

Pierre Hugo and Kim van der Weijde

Global uptake since WHO PQ

Severe malaria:
saving more lives with injectable artesunate

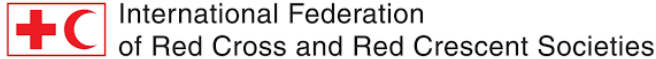


- Currently one WHO prequalified manufacturer
- 2nd manufacturer still anticipating ERP approval in 2017



The Severe Malaria Observatory: Experience. Evidence. Guidance.





Mission and Vision



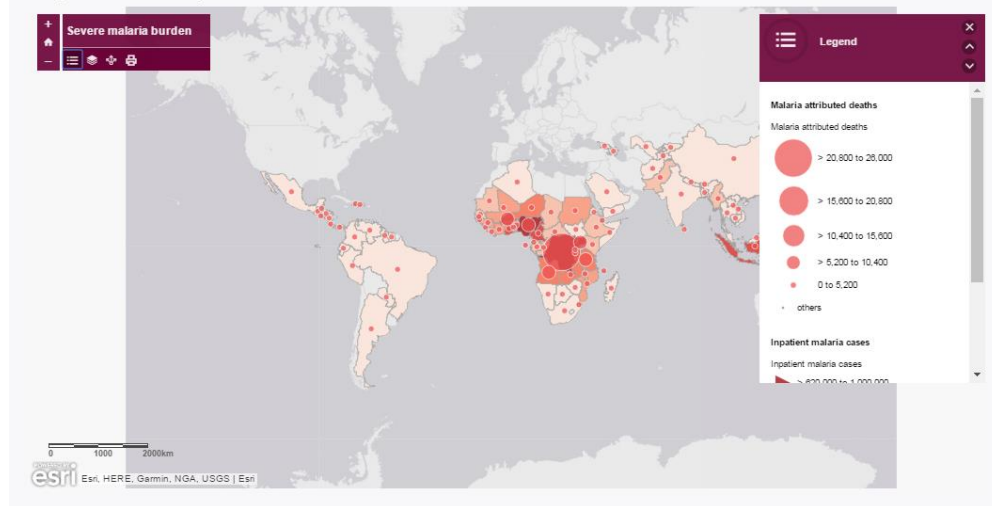
Our mission: To create an open, accessible, knowledge-sharing platform that acts as a repository of information and resources for the severe malaria community and allows the sharing of experiences and best practices in this field of work.

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

Map of malaria inpatient cases and deaths





Angola



Burkina Faso



Cameroon



Democratic Republic of Congo



Ghana



Malawi



Nigeria



Tanzania



Uganda

- Severe malaria situation and burden
- Sources of funding
- National malaria policy
- Market dynamics
- Community case management
- Health structure
- Commodities



Tool kits for severe malaria

- Quality assured products
- Dosing recommendations
- National registrations
- Volume and pricing trends
 - Injectable and suppository commodities
- Tool kits and training material

3 RECONSTITUTE

Injectable artesunate training materials and tool kit

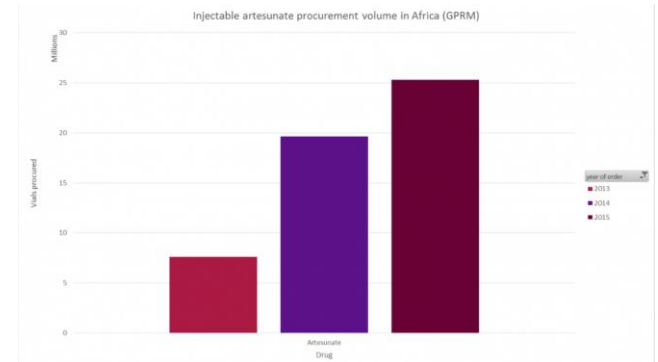
2 Remove the suppository from the wrapper

Rectal artesunate training materials and tool kit

MANUEL OPÉRATIONNEL POUR LE DÉPLOIEMENT DE L'ARTESUNATE INJECTABLE

Additional resources

National malaria treatment guideline adoption of injectable artesunate





- Past (milestone) and active severe malaria projects
- Stories and films from the field
- Interviews
- FAQ



AQUAMAT



SEAQUAMAT



MATIAS



ISMO

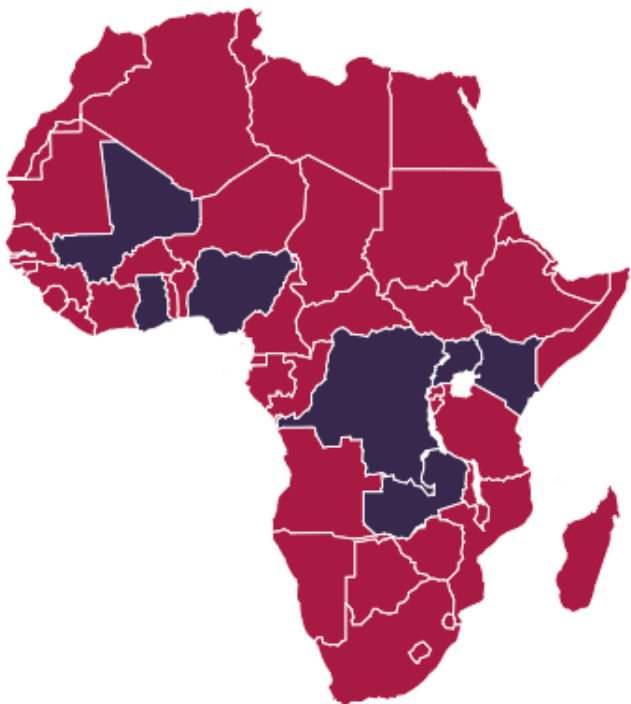


Study 13



ROSI

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

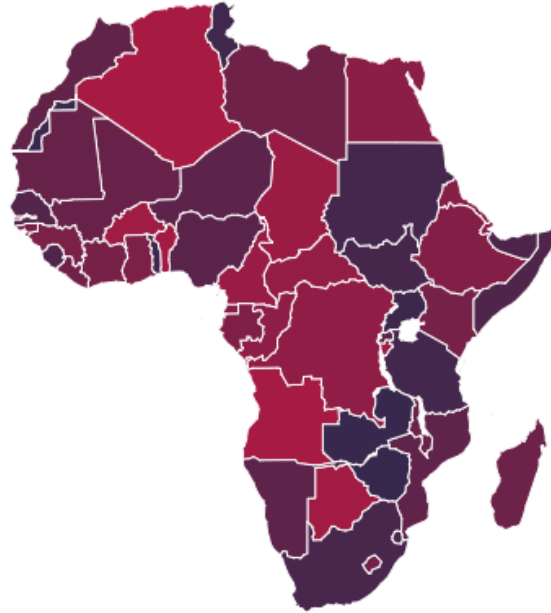


Analyzing the existing gaps in the Mopti region of Mali between WHO guidance and de facto malaria prevention and treatment practices at the community level.



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

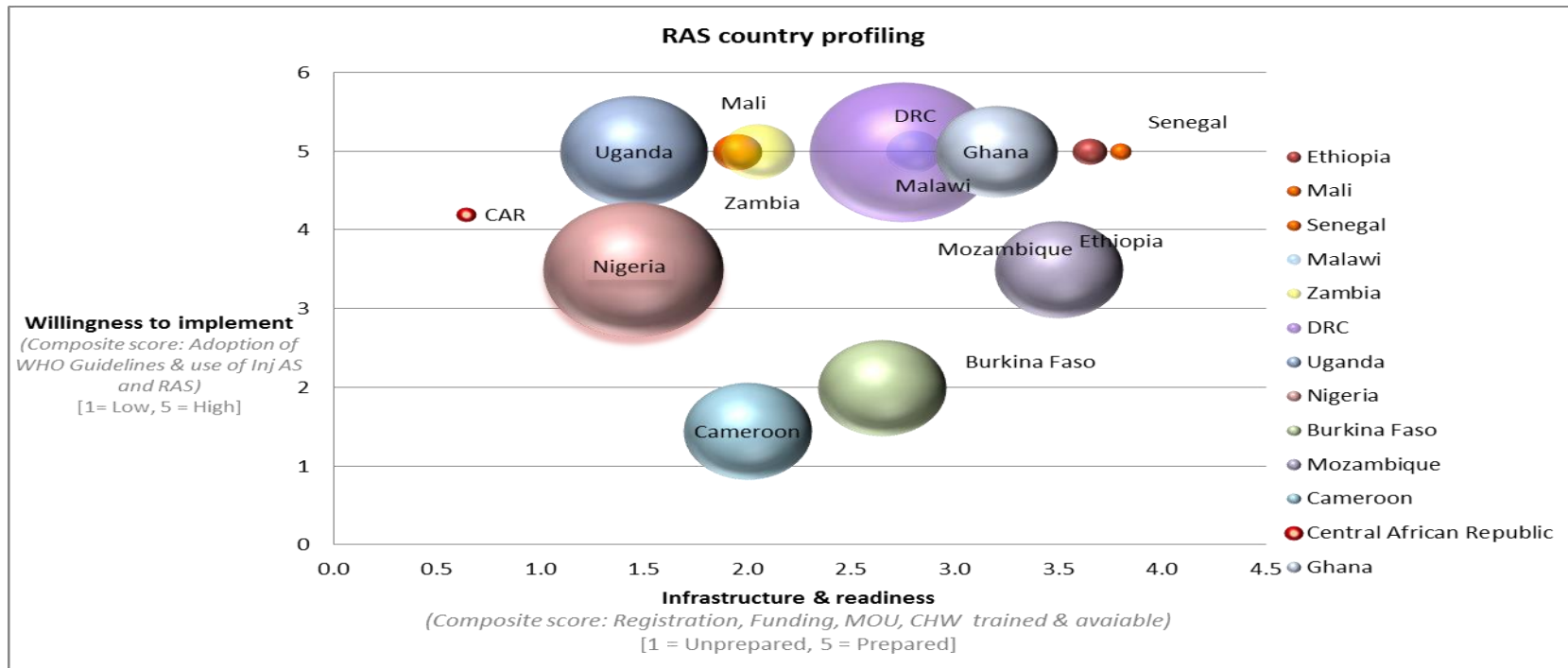
What's next?



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 -



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**

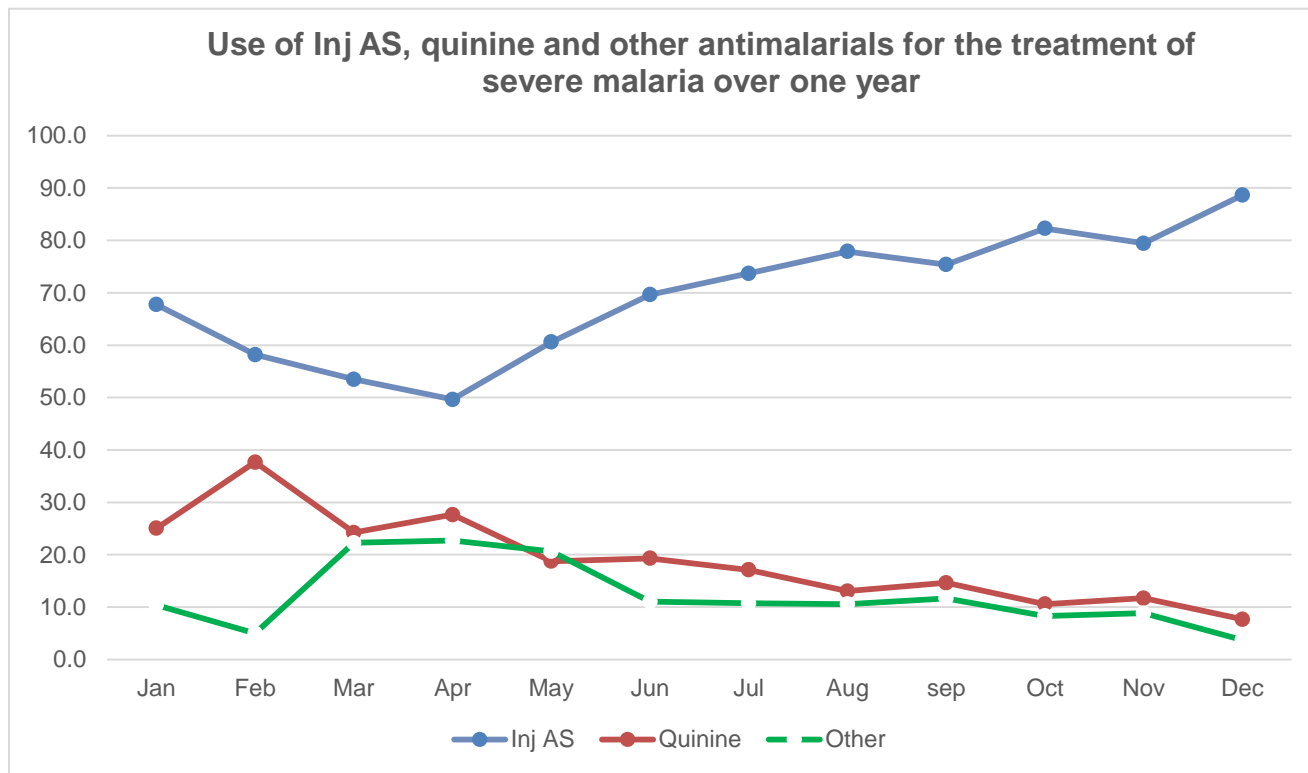
- *A system should be in place for **Pharmacists** to systematically inform **health workers** in charge of prescriptions.*

ISMO project - Proportion of severe malaria treated with Inj AS

M&E report January-December 2015.

Number of sites

Cameroon:	30
Ethiopia:	30
Kenya:	32
Malawi:	30
Nigeria:	90
Uganda:	30
Total:	242



Challenges vs Opportunities

Ensuring completion of referral process

- UNITAID RAS project
- RFI - Developing innovative approaches to increase rural access to commodities for the treatment and case management of severe malaria

The most challenging environments: where the need is the greatest

- Support for fragile/conflict states
- Offer technical support for implementing projects

Misalignment of guidelines

- Work with WHO, iCCM partners, MCHIP on guideline harmonization

Multiple dosage availability (200mg, 100mg, 50mg)

- Harmonization of recommendations
- Pharmacovigilance of field practices using various dosages
- Support harmonization of country guidelines with WHO

Country adoption of RAS policy

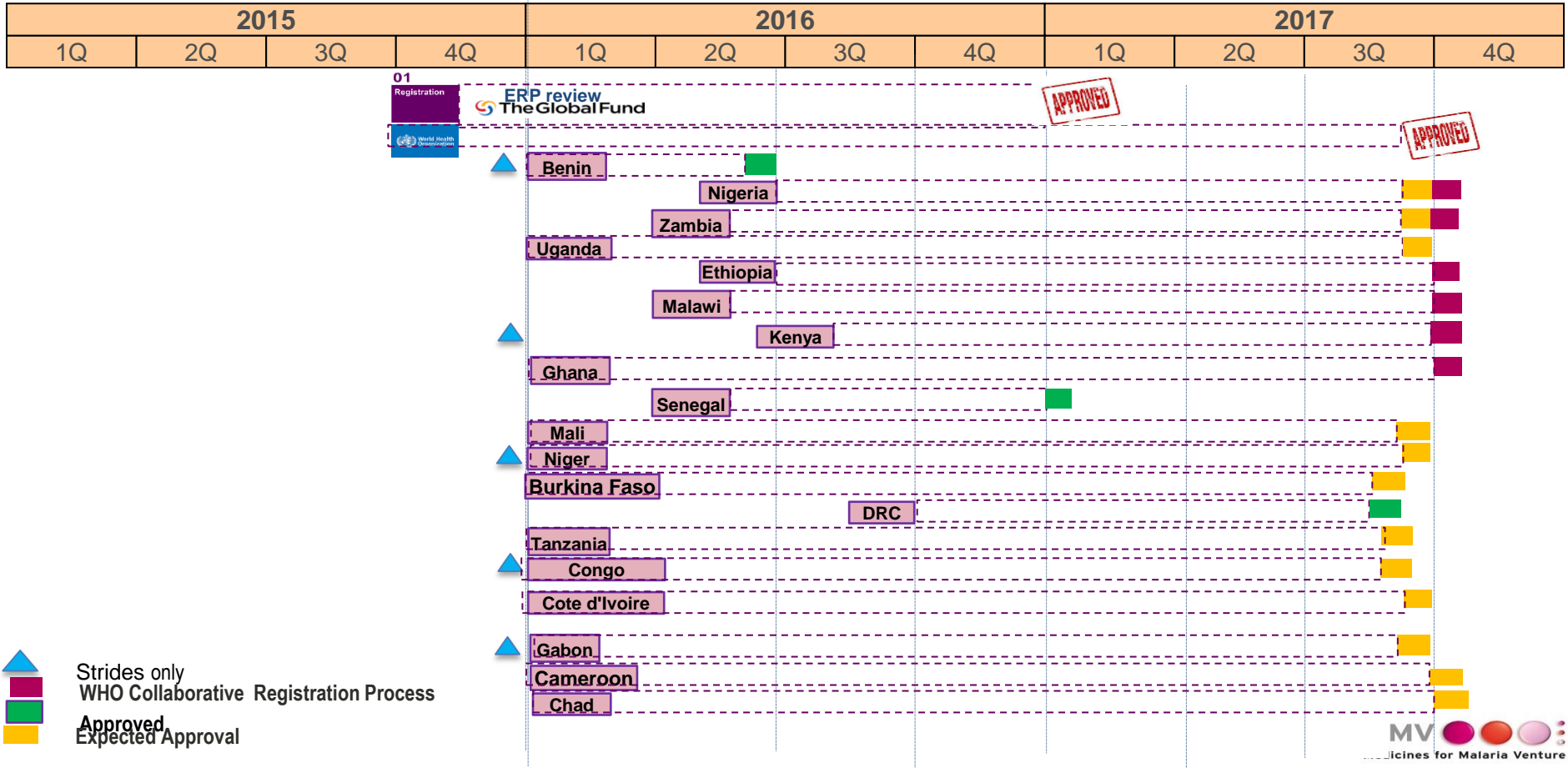
- Understand evidence/reasoning of country guidelines
- Monitoring and pharmacovigilance

Adequacy of RAS training materials on the field

- Assessment of RAS IEC materials in a real-life context

Regulatory submission plan for Cipla and Strides

Submitted in 19 countries



▲ 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.

Fever of 37.5°C or more



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

Weigh the child or get an approximate weight



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

Age	From 6 months to less than 3 years	From 3 years to less than 6 years
Weight range	From 5kg to less than 14kg	From 14kg to 19kg
Dose 10 mg/kg	1 suppository (1 x 100mg)	2 suppositories (2 x 100mg)

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 bursts or is melted, insert a fresh one.



If the suppository slips out:

- if it is still intact, reinsert the same one.
- if it has burst or partially melted, reinsert a new one.

3 Refer

to the nearest hospital or health care facility where the child will receive a full course of treatment. Rectal artesunate is only the first step in treatment.

Complete the referral form



Where to refer ?



Urgent transport



4 Follow up

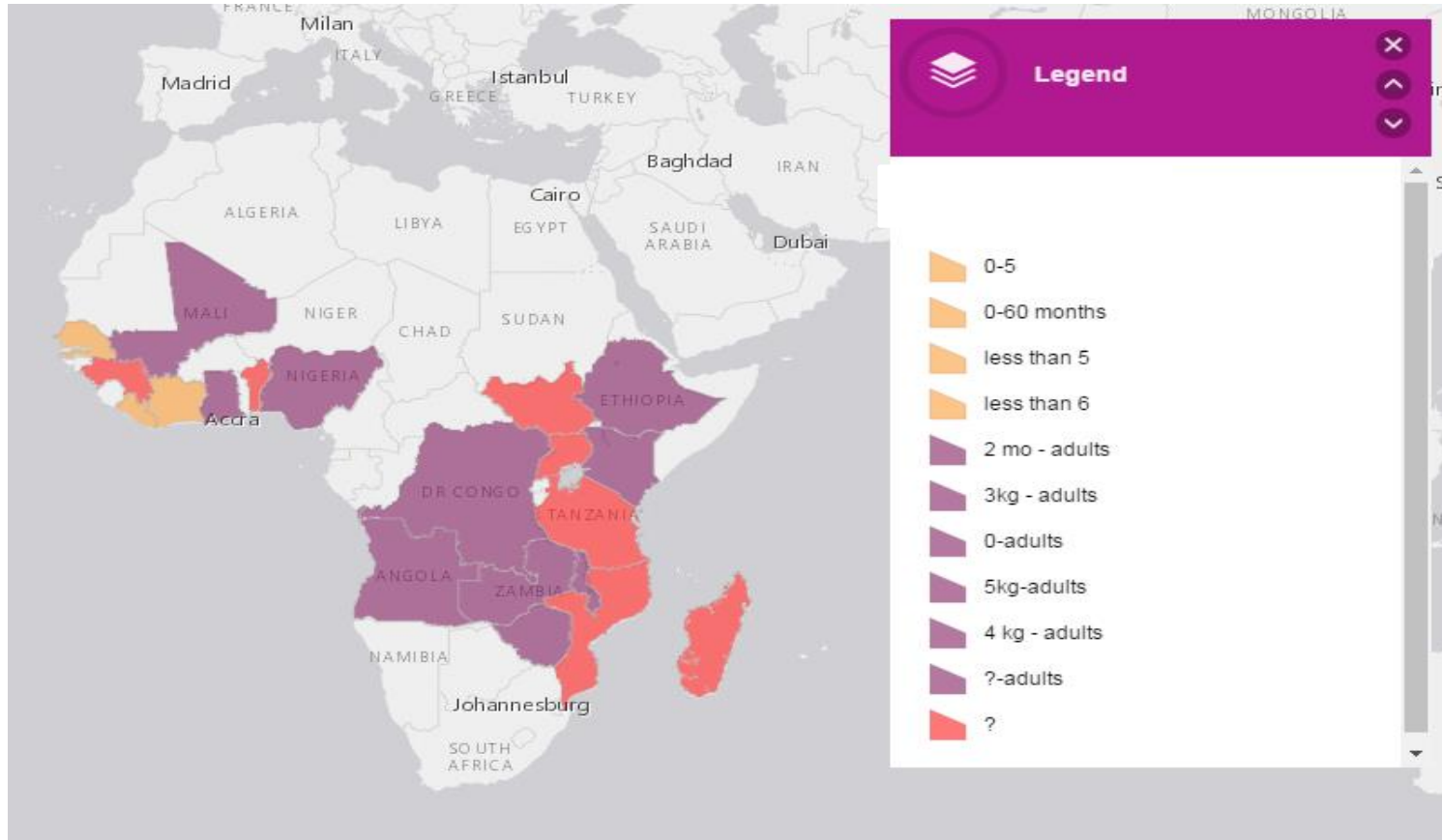
Follow up within a few hours and ensure that the caregiver has indeed travelled to the nearest hospital or health care facility with the child. Once the child has returned, be sure to follow up at least once per week for up to one month until the child has fully recovered. Check if the child is anemic,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



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



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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

Age	Weight	Rectal artesunate (10mg/kg body weight dose)
6 months to ≤ 3 years	5kg to ≤ 14 kg	1 x 100mg suppository
> 3 to 6 years	> 14 kg to 20kg	2 x 100mg suppositories