



*RBM Case Management Working Group,
Geneva*

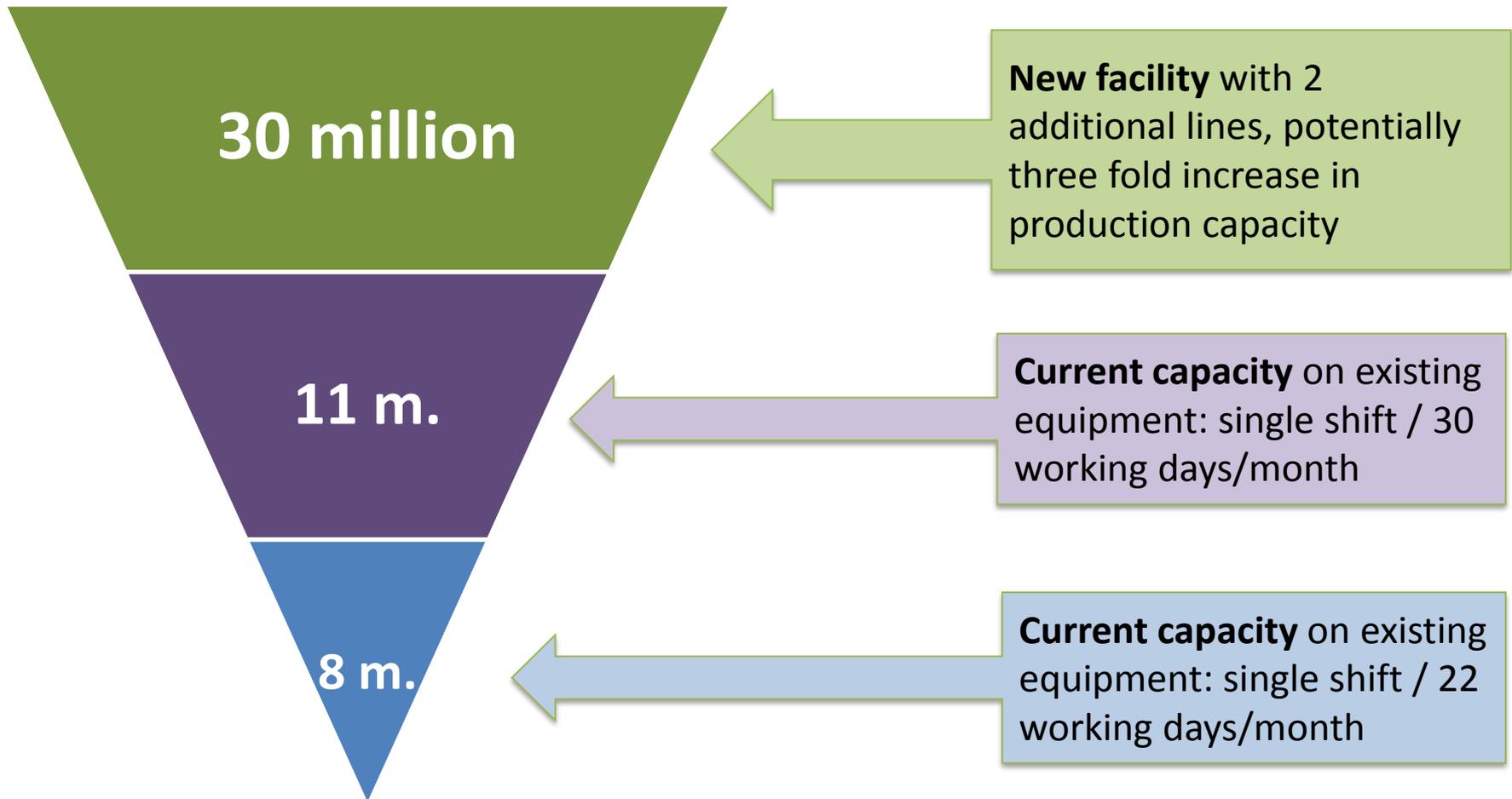
Severe Malaria: Supply and demand for injectable artesunate,

Defeating Malaria Together
12th, June 2012

Adequate production capacity to support uptake of injectable artesunate

Production capacity at Guilin

Source: MMV commissioned manufacturing capacity assessment of Guilin by Quintiles (Feb 2012)



Guilin orders for 2011 = 2 m. vials

Supply of WHO PQ injectable artesunate

2 million vials* of
WHO-prequalified
artesunate injection
delivered in 2011



*510,000 treatment courses for young children

Successful collaboration around severe malaria

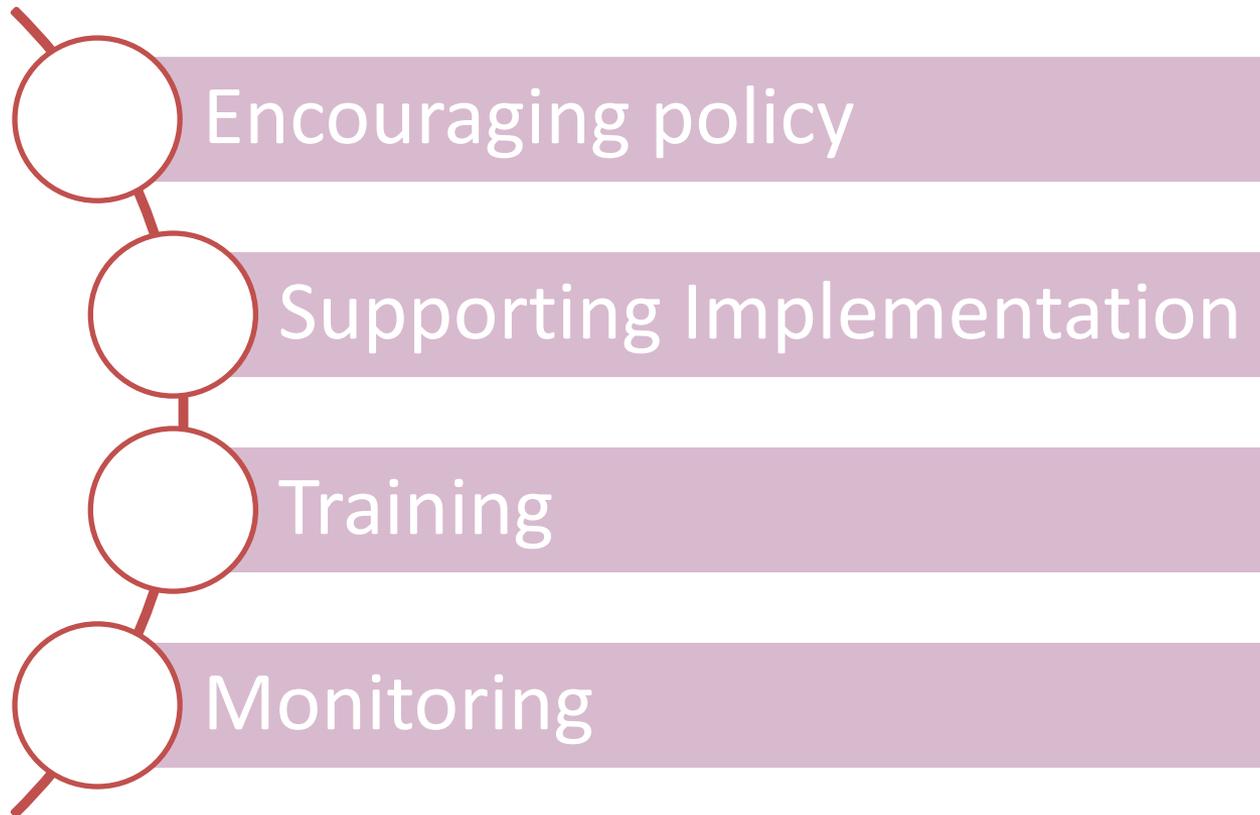
Saving more lives with artesunate injection

Injectable Artesunate Stakeholders' Meeting Report
Geneva, 11 November 2011



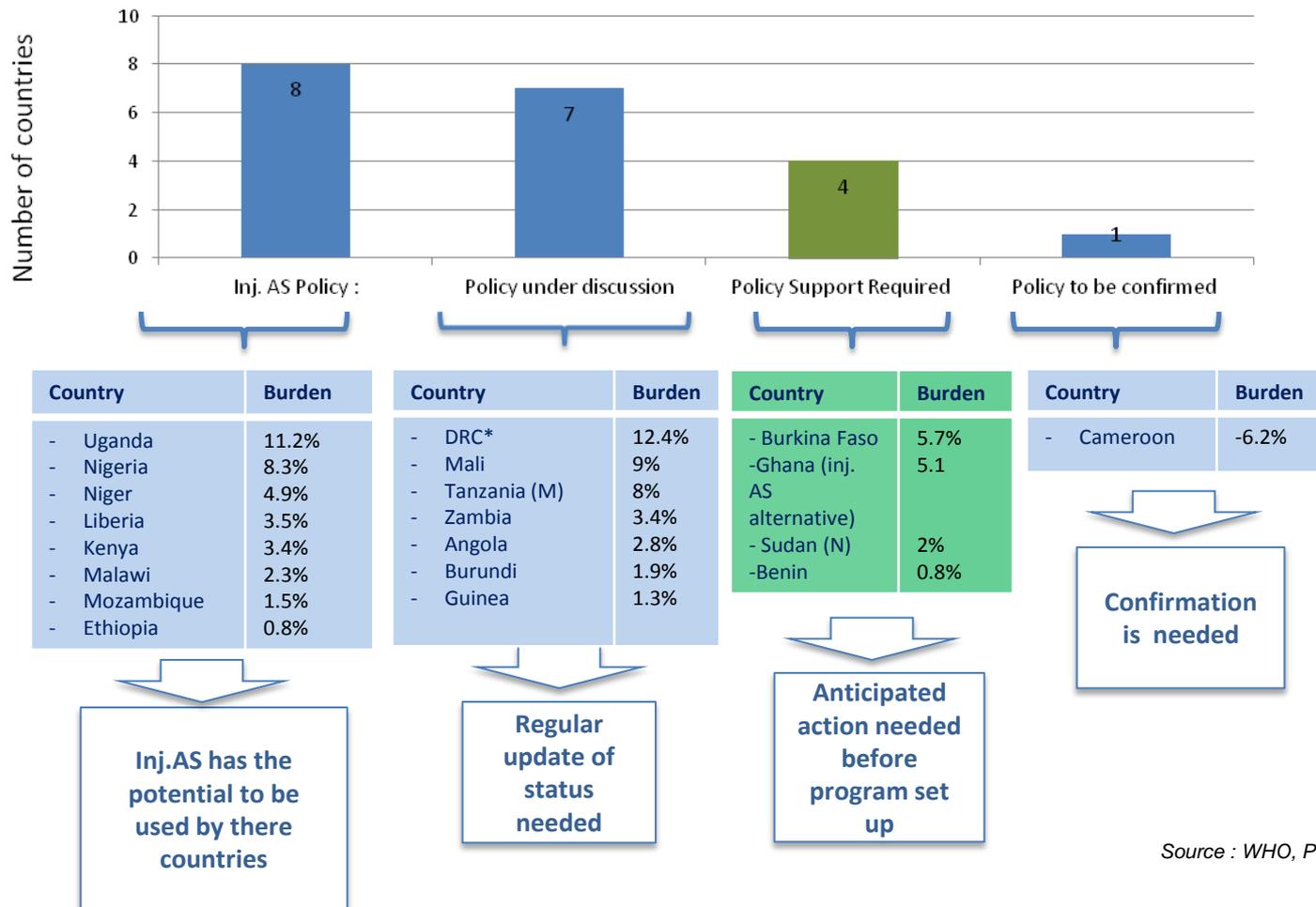
- **Work closely with**
 - WHO
 - NMCPs
 - MSF
 - CHAI
 - Swiss TPH
 - Mahidol-Oxford University
- **Stakeholders meeting in Geneva**

Areas of implementation focus and geographical coverage – Severe malaria



Encouraging policy change: Situation analysis

- Injectable artesunate is on the severe malaria guidelines in 7 of the 20 top burden countries



Source : WHO, PMI, GF and MMV

*DRC guidelines drafted

Development of tools to facilitate roll-out

- **Advocacy document**

ADVANTAGES OF INJECTABLE ARTESUNATE FOR SEVERE MALARIA WHO RECOMMENDED TREATMENT

Severe malaria is a medical emergency and is fatal if untreated. Every year an estimated 655,000 people die of malaria, 86% of whom are children under the age of 5. As death from severe malaria often occurs within hours of diagnosis at a hospital or clinic, it is essential that patients receive effective treatment as soon as possible. The WHO strongly recommends injectable artesunate over quinine for the treatment of severe *P. falciparum* malaria in both children and adults.

- **Injectable artesunate can save more lives than quinine**
Clinical studies from two tropical, multi-ethnic trials in South East Asia (SEAQUAMAT) and Africa (AQUAMAT) showed a reduction in the risk of death when artesunate compared to quinine. In fact throughout Africa, injectable artesunate could have up to an additional 165,000 lives saved.
- **Artesunate substantially reduces mortality from severe malaria compared to quinine**
A bar chart comparing mortality rates: Artesunate 14.7% vs Quinine 22.2% (SEAQUAMAT) and Artesunate 15.9% vs Quinine 25.5% (AQUAMAT).
- **Injectable artesunate can save more lives than quinine**
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- **Treatment with artesunate is cost-effective**
Although the average cost of injectable artesunate is currently higher than quinine (\$3 vs. \$1), several costs are found to be discounted. Cost models from the trials and others show that if total costs are considered in particular the cost of administering the drugs and management of side effects, artesunate is found to be cost-effective.
- **For over a century, quinine administered by injection has been the best treatment available for treating severe malaria, but thanks to the development of the artesunate components, we now have a safer and much more effective treatment?**
- **Case study**
The comparative benefits of injectable artesunate relative to quinine for the treatment of severe malaria was significant. A case study was presented based on a hypothetical country with an average of 450,000 cases of severe malaria treated each year in health facilities, among which half are children under 5 years of age. The estimated total cost of treatment would be \$200,480. The clinical studies showed that the expected mortality rate would be 25.7% higher with quinine compared to injectable artesunate. Therefore, artesunate can save 10,454 additional lives, among which half are children (5,227) of the total population.

Supporting governments in the use of injectable artesunate

Job-Aid
MMV, with its partners, has developed a poster for health workers to facilitate the preparation and administration of the treatment. This material is available at www.mmv.org/pubs-library.

User-friendly pack
In parallel, only injectable artesunate being less than 100mg/ml, it is essential to be able to inject it in a more comfortable way. MMV is currently working on a new formulation pack including a sterile vial and a syringe for use on the patient's feet/shoulder/rectum/ear.

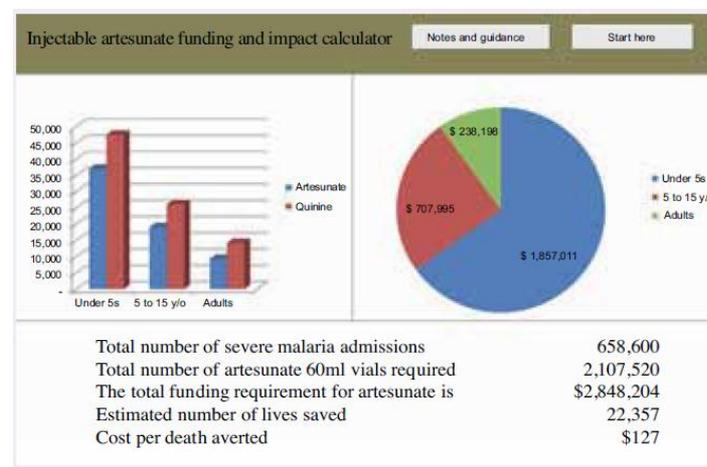
Artisanal production for severe malaria
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Funding calculator
MMV and Malaria Clinical Tropical Medicine Research Unit have developed a calculator to estimate funding requirements and health impact in terms of estimated number of lives saved from injectable artesunate. This Excel-based calculator is available at www.mmv.org/pubs-library. The calculator is easy to use and allows country stakeholders to update the model with individual country data.

Defeating Malaria Together **MMV Medicines for Malaria Venture**

- **Funding calculator**

- Co-developed with MORU
- Estimate funding required and number of additional lives saved



Training materials to facilitate correct use

WHO
RECOMMENDED
TREATMENT

ARTESUNATE INJECTION FOR SEVERE MALARIA



PRODUCT DESCRIPTION

Artesunate powder: 60mg + 1 ampoule sodium bicarbonate + 1 ampoule saline solution.

Dose: 2.4 mg/kg

Can be given by intravenous route (IV) or intramuscular route (IM)

1 WEIGH THE PATIENT AND CHECK VIALS NEEDED

| Weight | 5 kg-25 kg | 26-50 kg | 51-75 kg | 76-100 kg |
|------------|------------|----------|----------|-----------|
| 60 mg vial | 1 | 2 | 3 | 4 |

4 ADMINISTER

Withdraw the required dose in ml according route of administration:

| For intravenous route (IV) | For intramuscular route (IM) |
|--|--|
| 2.4 mg x body weight (kg) IV artesunate solution concentration 10 mg/ml | 2.4 mg x body weight (kg) IM artesunate solution concentration 20 mg/ml |
| Round up to the next whole number | Round up to the next whole number |

| Example: | Example: |
|---|--|
| Dose needed (ml) for 8 kg child: $\frac{2.4 \times 8}{10} = 1.92\text{ml}$ Round up to 2 ml | Dose needed (ml) for 8 kg child: $\frac{2.4 \times 8}{20} = 0.96\text{ ml}$ Round up to 1 ml |

Inject slowly

IV: Slow injection 3-4 ml per minute.



IM: Inject in an appropriate site. Use a different site for dose greater than 3-5 ml.



2 RECONSTITUTE

Artesunate powder + bicarbonate ampoule immediately before use.

1. Artesunate powder + bicarbonate ampoule
2. Inject full contents of bicarbonate ampoule into artesunate vial.
3. Shake approximately 2 minutes until dissolved. Solution will be cloudy.
4. The reconstituted solution will clear in about 1 min. Discard if not clear.

3 DILUTE

Reconstituted artesunate + saline solution (or dextrose 5%)

5. Artesunate reconstituted + saline solution
6. Insert needle to remove air.
7. Inject required volume of saline into the reconstituted solution.
8. Artesunate solution is now ready for use.

| Concentration | IV | IM |
|-----------------------------|-------------|-------------|
| Bicarbonate solution volume | 1 ml | 1 ml |
| Saline solution volume | 5 ml | 2 ml |
| Total volume | 6 ml | 3 ml |

Artesunate 60mg solution concentration: 10 mg/ml, 20 mg/ml

5 DOSING SCHEDULE

IMPORTANT

Give a **minimum 3 parenteral doses** even if the patient can take oral medication:

- Dose 1: on admission
- Dose 2: 12 hours later
- Dose 3: 24 hours after first dose

- Prepare a fresh solution for each administration.
- Discard any unused solution after use.

After 3 parenteral doses:

- If patient cannot take oral medication, continue with parenteral treatment every 24hrs, for a maximum of 7 days, until oral medication can be given.
- If patient can take oral medication, prescribe a full 3-day course of oral Artemisinin Combination Therapy (ACT).

Evaluate the patient's progress regularly.

- Developed by MMV in collaboration with WHO GMP, Mahidol-Oxford University, NMCP (Kenya and Uganda), MSF, CHAI, and Guilin
- Tested in Kenya and Uganda
- Dosing chart still not finalized



MMV Inj-AS country projects to support policy change & implementation



Nigeria

DRC

Objectives:

accelerate the adoption and uptake of injectable artesunate

Area:

- 6 states (ca. 25% of national population)

- 3 health zones

Partners:

- Ministry of Health (Federal and states), CHAI

- Ministry of Health, Swiss TPH, MSF, SANRU

Key activities:

- Advocacy and implementation support
- M&E to inform scale-up

- Update policy
- Implementation pilots to assess feasibility and inform national roll-out

Status:

- MoUs signed with 6 states;
- Taskforce, AdBoard set-up, Lagos state procuring

- NMCP severe draft guidelines updated to include Inj-AS