MMV
Medicines for Malaria Venture

Request for information

Multiple first line therapies (MFTs) for malaria case management; pilot implementation approach in Sub-Saharan Africa

RFI Number: MMV-2017-MFT ACTs
Issue Date: 23rd June, 2017
Deadline for questions: 7th July, 2017
Closing date: 21st July, 2017

Background

Beginning in 2001[1] , WHO recommended the switch to artemisinin based combination therapies (ACTs) as first line treatment of uncomplicated malaria, in light of the devastating drug resistance that had rendered earlier treatments (primarily chloroquine and SP) highly ineffective at curing uncomplicated malaria infections in much of Asia, Africa and Latin America.

Artemether Lumefantrine (AL) was the first ACT available in the market as a fixed dose formulation, soon followed by other combinations, and ACTs were progressively adopted by endemic countries. WHO currently recommends 5 ACTs for use against *P. falciparum* malaria. By combining two active ingredients with different mechanisms of action, ACTs are currently considered as the most effective antimalarial medicines available. By combining two different drugs targeting the same parasite, a key biological principle for slowing down evolution and spread of novel mutant is applied by introducing drug heterogeneity into pathogen's environment. This leads to the pathogen to have to adapt to different environmental features simultaneously[2]. Therapeutic efficacy studies against local strains of *P. falciparum* malaria are regularly conducted in order to drive the choice of ACTs in a given setting.

In the process of changing their treatment strategy and adoption of ACTs, several countries initially positioned one ACT as the first line (intention) treatment and kept quinine as a second line treatment. Subsequently, with increased availability of other combinations, a second ACT was adopted as second line or alternative treatment in case of failure or contra indication to the first line drug. Currently, some countries have adopted two alternative first line treatments, allowing practitioners to prescribe from a list of up to three ACTs. In private sector practice, the choice of ACT can be determined by the preference and / or affordability of the patient.

The concept of multiple first line treatments / therapies (MFTs)

MFT is defined as a drug policy in which several therapies are made available in both the public and the private sectors, and patients and clinicians can choose which therapy to use[3]. Models have shown that MFTs reduce total clinical cases and treatment failure[4], to significantly delay resistance emergence and treatment failure, and slow resistance evolution once resistance emerges[6]. WHO has convened two Technical Expert Groups (TEGs) on Drug Efficacy and Response, which have included consideration of MFT. At the TEG meeting in December 2015, WHO concluded that while current discrepant models about the utility of MFTs are not sufficient to allow for a clear recommendation, one advantage of having MFT available is that failing therapies can be discontinued without affecting malaria treatment provision; it can also help to limit drug stock-outs. Lastly, WHO concluded that recommendations for MFT should include

[1] WHO. Antimalarial Drug Combination Therapy. Report of a WHO Technical Consultation. Geneva: World Health Organization; 2001
[2] http://www.thelancet.com/pdfs/journals/langlo/PIIS2214-109X(15)00162-X.pdf
[3] http://www.pnas.org/content/105/37/14216.full.pdf
[4] http://www.thelancet.com/pdfs/journals/langlo/PIIS2214-109X(15)00162-X.pdf

pragmatic implementation methods (e.g. using paediatric formulations in children and tablets in adults)[5]

Looking at the current settings in various African countries, there are discrepancies in terms of practice between the private and the public health sectors. Often, there are two or three ACTs recommended for the treatment of uncomplicated malaria and only one is routinely used in the public sector.In such cases, that drug is used exclusively as first line treatment and is only changed when population-level efficacy falls below the WHO threshold of 90% treatment efficacy.

An additional complexity has arisen in recent years for some NMCPs in the Sahel region of western and central Africa, with the implementation of Seasonal Malaria Chemoprevention (SMC) using SP+AQ. In areas where this drug is deployed for SMC, WHO discourages NMCPs from using ASAQ, which in many of these countries was the predominant ACT in the public sector. Thus, national malaria control/elimination programs and supply chain managers may find themselves facing split supply requirements for uncomplicated malaria treatment in the same country: ASAQ in areas where SMC is not appropriate, and an alternative ACT in areas where SMC is implemented. In such instances, learning to manage MFT is the logical solution for countries to comply with WHO guidance.

Purpose of RFI

MMV requests information from National Malaria Control Programmes (NMCPs) and/or supporting stakeholders (Implementers) interested in the introduction of MFTs to help generate information regarding the implementation and management of multiple ACTs as part of first-line therapy for the treatment of uncomplicated malaria.

In the first instance, this RFI is to help MMV obtain a better understanding of what obstacles are preventing the deployment of MFT in malaria endemic countries across Sub Saharan Africa.

MMV believes that one major obstacle to recommendation and implementation of MFT is the logistic hurdle for NMCPs and central medical stores to manage multiple first-line drugs simultaneously, with differential targeting of each drug to different sub-groups, but always for the same indication (treatment of uncomplicated malaria.) In keeping with WHO's recommendation from its 2015 TEG, it will be useful to help countries begin to develop pragmatic implementation methods that will:

(a) Minimize additional burdens on program management
(b) Optimize supply chain systems
(c) Improve training requirements for clinicians (particularly frontline health workers)

The second part of this RFI focuses on implementation; MMV would like to hear more from National Malaria Control Programmes (NMCPs) and/or supporting stakeholders (Implementers)

[5] Minutes of the Technical Expert Group (TEG) on Drug Efficacy and Response – 10–11 December 2015

on how the obstacles can be removed, by proposing an effective MFT implementation plan. This may include the following (but please feel free to supplement with specific insights and experience):

- Solutions that are permitting the introduction of different ACTs as a replacement for ASAQ in areas where SMC is currently deployed
- Approaches that target differentiated use of ACTs for distinct sub-segments of the population (e.g. deployment of different ACTs according to age group, or to risk-profiles of specific vulnerable sub-populations, etc.)
- Consideration of a minimum of 3 ACTs to be managed by the health care providers in the selected health district and be used for the various population segments
- Approaches to address logistical, training and supply chain requirements of MFT implementation, including quantification requirements
- Assessment measures to determine success of the MFT implementation in terms of logistics and supply chain performance, stock availability, and health worker and population acceptability

Budget

An initial budget (seed funding) will be available to support a **pilot project** to generate "proof of concept" data which can then be used to support the intervention to be taken to scale by the country. Additional funding may be sought to complement the available seed funding if needed.

RFI Response (Guidance)

RFI responses for the pilot project are expected to be at the concept stage (i.e. no prior experimental work is required) and work needs to be completed within 2 year time period. Selection will be made based on: 1) partner's ability to collaborate, 2) disease-endemic countries interest in piloting the project, 3) ability for co-funding the pilot project, 4) integration with current systems (National or otherwise), scalability and sustainability, 5) ease of implementation and risk mitigation 6) overall impact of the pilot MFT implementation plan.

Sustainability

The purpose of this pilot project is to test the proof of concept for the potential expansion into the rest of the country and to share key learnings with other countries. Organizations should take this into consideration, ensuring sustainability beyond the pilot. We strongly encourage integration with the local supply chain and health system, as well as leveraging local contacts such as with the NMCP and MoH. Utilizing and expanding upon existing structures within the local supply chain generally offers a more sustainable and scalable approach, and should be strongly considered in the RFI responses. Furthermore, the necessary commodities, resources, and infrastructure should be able to support the activities of the project beyond the scope of the project.

Pilot Implementation Plan Outline

Please propose activities (what, by who and how) that will contribute to achieving the above mentioned outcomes of the project, expected results and measurement. In addition it would be good to understand in which areas or districts will the pilot project be implemented along with why they were selected (including but not limited to malaria disease burden; need for support; capacity to absorb activities and/or presence of staff of partners. Please list the individuals that will be supporting this project and their role. Finally please provide information on how the plan ensures that the necessary ACTs will be available at the public healthcare facilities. This may include but is not limited to management of stock-out, use of local supply chain and procurement of commodities not currently available.

About MMV

MMV is a not-for-profit public-private partnership and was established as a foundation in Switzerland in 1999. MMV's mission is to reduce the burden of malaria in disease-endemic countries by discovering, developing and facilitating the delivery of new, effective and affordable antimalarial medicines. MMV's vision is a world in which these innovative medicines will cure and protect the vulnerable and under-served populations at risk of malaria and help to ultimately eradicate this terrible disease. In partnership with pharmaceutical companies and research institutions worldwide, MMV has supported the development, approval and uptake of 8 new treatments for malaria, and has over fifty other drug discovery and development projects. MMV works closely with its partners and provides disease-specific and development expertise in addition to financial support in return for certain commitments such as pricing and supply of product in the public sector.

Instructions to interested parties

Submission of RFI responses

a) All RFI responses, should be submitted in English and in the format of a PDF or WORD document

b) RFI responses should be submitted via e-mail with the subject line *Request for information (RFI) - MMV-2017-ACT-MFT* to Sandra Johnson at johnsons@mmv.org

c) RFI responses received after the stipulated closing date of 21st July 2017 shall be invalid

Questions and answers

a) Questions should be addressed in writing to Sandra Johnson at johnsons@mmv.org by the stipulated deadline for questions (July 7th 2017)

b) Answers will be posted on the MMV internet

c) Telephone requests cannot be honored

Eligibility

This RFI process is open to organizations which design operational research and implement public health programs or other entities acceptable to MMV

Costs of preparing documents

All costs associated with preparing and submitting a response to this RFI will be borne by the Responder

Confidentiality

Information which the Responder considers to be proprietary should be clearly marked as such. All such information will be treated as confidential and used for MMV internal purposes only.

Disclosure

Information relating to the examination, clarification, and evaluation of responses shall not be disclosed to Responders or any other persons not officially concerned with such process.

Minimum information requirements for response

Responders should provide the following information at a minimum:

a) Written proposal detailing:

   1) current obstacles being faced by proposed country (ies) (1500 words)

   2) current thoughts on how to implement an effective MFT pilot project which can then be expanded countrywide (1500 words)

b) Organization information: biographies of key staff

c) Additional information about your current and past level of activity, interest and expertise in the development and implementation of similar public health programs

d) Ball park estimate for delivery pilot project

MMV will review RFIs with the goal of assessing whether it may be able to play a larger supporting role in helping deploy winning strategies that can deliver effective MFT strategies on a cost-effective basis. To that end, by 25th August 2017, MMV will notify respondents to the RFI if a subsequent RFP will be issued to respond to a specific set of proposal requirements which will have been designed and communicated at that time.