Request for proposal (RFP)
Field testing of Tafenoquine paediatric (user-friendly) packaging in malaria endemic countries

Contents
1. Introduction to Medicines for Malaria Venture (MMV) and its work
2. The P. vivax challenge and (the) Tafenoquine (proposition)
3. Rationale for user-friendly packaging
4. Compliance-enhancing packaging for TQ paediatric
5. Project description and scope of work
6. Required experience/expertise
7. RFP Timelines and submission requirements

1. Introduction to Medicines for Malaria Venture (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. MMV and partners manage a portfolio of 65 projects, the largest portfolio of antimalarial R&D and access projects ever assembled. The portfolio includes nine new drugs in clinical development addressing unmet medical needs in malaria, including medicines for children, pregnant women and relapsing malaria, and drugs that could support the elimination/eradication agenda.

2. The Plasmodium Vivax challenge (source: Global launch strategy) and (the) Tafenoquine (TQ) (proposition)

P. vivax is the most widespread species of malaria and accounts for nearly half of the total number of malaria cases outside Africa. It contributes significantly to the national burden of malaria, particularly in Asia and Latin America. A distinctive feature of the disease is the
dormant hypnozoites in liver cells that can cause multiple relapses and are undetectable by the available diagnostic methods. The current standard of care for *P. vivax* relies on a dual approach, comprising a 3-day treatment phase for the blood-stage infection, with either chloroquine (CQ) or artemisinin-based combination therapy (ACTs), followed by a 14-day treatment for the liver-stage (hypnozoite) infection with primaquine (PQ).

PQ is an 8-aminoquinoline treatment, a category of medicines associated with the development of haemolysis in individuals with G6PD deficiency; therefore, World Health Organization (WHO) recommends G6PD testing prior to PQ use as best practice in order to determine the appropriate treatment regimen. The 14-day dosing required for successful radical cure with PQ leads to poor compliance resulting in incomplete cure of liver stage infections. Therefore, the elimination of *P. vivax* will be difficult, if not impossible, without an improved, simplified treatment option for radical cure.

Data from Phase III studies conducted by GSK and MMV have demonstrated that TQ is a viable single-dose option for the radical cure of liver-stage *P. vivax* infections. TQ reduced the risk of relapse at any given time by 70% compared to CQ only, and the safety profile of TQ was consistent with its known safety profile when administered with CQ in the Phase III studies. Like PQ, TQ is an 8-aminoquinoline treatment and therefore poses a risk when given to G6PD deficient individuals. TQ must only be administered to individuals with levels of G6PD enzymatic activity that are at least 70% of normal. To ensure the safe use of TQ, the Program for Appropriate Technology in Health (PATH) is leading diagnostic development that will support the introduction of a quantitative point-of-care G6PD diagnostic.

TQ has the potential to enhance the clinical management and operational feasibility of deploying routine radical cure of this disease, with simplified single-dosing leading to improved compliance and superior risk management through G6PD testing. It will also be an additional tool for *P. vivax* elimination. Closely aligned partnerships with the malaria community will facilitate the affordable, timely and eventually widespread adoption of the TQ Proposition in order to accelerate its public health impact.

### 3. Rationale for pre-packaged medicine
A literature review suggests that adherence is improved when:
1) treatments are effective; and
2) interventions focus on provider knowledge and behavior, packaging and provision of correct dosages¹.

According to the WHO (2004)², pre-packaged treatment (PPT) improves compliance because clear instructions tend to facilitate patient recall and can enhance product acceptability among both staff and patients. The WHO report also highlights that “PPT with instructions is empowering... consumers like pre-packaging with instructions... as they do not need someone to read for them”.

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Packaging design has attracted interest not only because it can ensure that patients are provided with the right drug dose, but because it also has the capacity to enhance adherence to treatment through well designed communications messages. Color coding, pictures, and diagrams can communicate key messages to caregivers. Also packaging can serve as a mode of communication between providers and clients particularly where medicines are distributed by those with little medical knowledge. This requires that the key information about the drug is presented in a way that enhances understanding. For patients with lower literacy skills, combining easy-to-read written messages with culturally sensitive graphics, complemented with oral instructions from a health provider has been found to improve compliance.

4. Compliance-enhancing packaging for TQ paediatric

Tafenoquine paediatric will be provided in blister packs of 3 tablets and patients will be given the correct number of tablets in line with their weight. This is major change from the current norm of providing antimalarials in weight-specific blister pack. This will simplify quantification as it will eliminate the need to quantify the treatment needed by weight band. The challenge however will be to ensure that health care providers and care givers (e.g. parents) fully understand the dosing instructions. Two different approaches using user-friendly pictograms and messages have been developed to illustrate the weight bands and dosing instructions.

Tafenoquine paediatric will be administered by health workers after conducting a G6PD test to ensure that the patient has adequate levels of G6PD enzyme activity. Patients will be given a 3-day blood stage treatment and TQ as a single dose. The TQ dose may be taken in front of the health worker or at home, depending on the organization of the health services. The tablet(s) will need to be dispersed in a little water and taken all at once. (SEE ANNEX 1 – Patient journey)

A user-friendly leaflet for providers and patients will be developed with visual aids with information about the dosing schedule and correct use of treatment. – This will serve as a reminder for the caregiver in case they do not fully recall the oral instructions from the health worker.

Remarks: detailed information on the packaging design as well as the administration process will be shared once non-disclosure agreement signed with the selected research entity.

5. Project description and scope of work

MMV is seeking a partner (a consultant /agency) who will:

(1) Conduct an assessment of the packaging in order to evaluate the best option out of the 2 options in terms of attractiveness and understanding of key information.

(2) Field test information on mock-ups of the packaging prototypes content (primary, secondary packs and patient /caregiver leaflet). The field test should provide consolidated feedback to help refine the materials so that critical information is presented in a manner that is easily understood by the end-user and will thus facilitate the correct dispensing and use of the medicine.

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(3) Field test the understanding of the preparation and administrations steps by the health workers
(4) Assess the use of the primary packaging by healthcare workers; split blisters for different prescriptions/number of tablets on each side of the blister, store remaining blisters & stock control.
(5) Assess the proposal for number of leaflets & blisters in a bulk pack, fit for purpose & sufficient leaflets to supply one leaflet for at home-administration performed by a non-healthcare worker.

The findings will inform any modification of the designs in an iterative process so ensure full comprehension and thus facilitate the correct use of the product.

Target groups:
- Health staff involved in treating *P. vivax* patients
- Community health workers?
- Care givers (e.g. parents)

Geographical focus: malaria endemic countries
- 2 countries: Brazil and Thailand
- Remark: the Ethical Review process in Thailand could take up to 6 months therefore India or Vietnam are considered as alternative countries in Asia.

**a. Research questions**

**The aim of the field testing is to assess acceptability, appropriateness and comprehension by the target groups and to identify preferred graphical options.**

The field-testing is critical to ensure correct understanding, interpretation and acceptability of the packaging and communication materials across countries with *P. vivax* malaria.

Key insights will be drawn from these questions:
- Are the key messages on the packaging and leaflet clearly understood by both target groups (health workers and care givers)? Are these key messages available at time of need (in the right place)?
- To what extend do the messages on the packaging convince the end-user to undertake the desired behaviour?
- Are the images on the packaging socially and culturally acceptable by end users?

In particular, the field-testing will assess the target group’:
- comprehension of instructions / pictograms about key information:
  - the fact that this is an antimalarial treatment
  - dosing regimen for different weight bands
  - the need for G6PD testing
  - the minimum G6PD enzyme activity before providing TQ
how to prepare the dispersible solution and need to provide food with the treatment the sequence of events (i.e. vivax diagnosed; G6PD test done; TQ to be given on 1st and 2nd day of treatment with chloroquine)

- perception of overall attractiveness, cultural acceptability / appropriateness of the illustrations

b. Scope of work
- Development of field-testing research design/method / data collection tools.
- Preparation and submission of the study protocol to research country ethical review boards.
- Coordination of data collection in countries
- Research analysis
- Recommendations / report in English
- Presentation of the results
- *Publication of the research findings in a peer review journal (TBD)*

6. Required experience / expertise
- Sound and relevant experience of qualitative research for health information/products in developing countries
- Good network in malaria-endemic countries with a preference for Latin America and South East Asia.
- Strong experience with pharmaceutical packaging design would be an asset.

7. RFP Timelines and submission requirements

- **RFP timelines**

<table>
<thead>
<tr>
<th>Event</th>
<th>Date</th>
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<tbody>
<tr>
<td>RFP Published:</td>
<td>May 3rd, 2018</td>
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<tr>
<td>Deadline for submission of RFP.</td>
<td>May 25th, 2018</td>
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<tr>
<td>RFP should be submitted to Sandra Johnson:</td>
<td><a href="mailto:johnsons@mmv.org">johnsons@mmv.org</a> copy: <a href="mailto:majeresm@mmv.org">majeresm@mmv.org</a></td>
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<tr>
<td>Review of RFPs</td>
<td>May 28th - June 8th</td>
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<tr>
<td>Contract negotiation</td>
<td>June 11th - July 13th, 2018</td>
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<tr>
<td>Project starts</td>
<td>July 16th, 2018</td>
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- **Submission requirements**

Responses to the RFP must address all questions in the required format. Documents to submit include:

1. **Project Proposal** based on provided outline in PDF format.
2. **Financial Proposal** budget sheet (in USD) in excel format and **Budget Narrative** in PDF format.
RFP should be submitted in full by the time and date indicated above, in pdf form. Please submit 3 separate files with your response, 1 x Technical Proposal, 1 x Financial Proposal and 1 x Budget Narrative with files clearly labeled as follows:

II. [Respondent Organization name RFP MMV-TQpaed Financial Proposal.xls]; and
III. [Respondent Organization name RFP MMV-TQpaed Budget Narrative.pdf]

MMV reserves the right to change or cancel the requirement at any time during the RFP and/or solicitation process. MMV also reserves the right to require compliance with additional conditions in the next round.
ANNEX 1 – Patient journey

Tafenoquine Pediatric Patient Treatment Journey

Day 1
- Malaria diagnosis and treatment
- CQ dose 1
- Weight and Child
- GPDP test

Day 2
- TQ dose 2
- Preferred route of administration
- TQ dose 3

Day 3
- CQ dose 3
- TQ dose 3
- TQ dose 3

Treatment to WHO malaria treatment guidelines

Key:
- TQ: Tafenoquine 50mg/500mg tablet
- CQ: Chloroquine 15mg/kg tablet
- GPDP: Glucose-6-phosphate dehydrogenase
- WHO: World Health Organization
- P: Parent Assessment
- Q: Health Care Professional Assessment
- T: Treatment
- H: Hospitalization
- C: Fever
- P: Paediatrics
- A: Adult
- P: Pregnancy
- R: Rural
- S: Semi-urban
- U: Urban

General trial factor assessment: CQ treatment 70% without

Note: Dates and geographical location.

Design: DPBD G6 March 2018