Malaria Vector Control: Proposed and Potential Advisory Mechanisms for Policy Setting

September 2012

1. Background and Introduction

During the past decade, unprecedented progress has been achieved in controlling malaria, much of it attributable to successful vector control. However, reports of insecticide resistance in a number of countries especially from sub-Saharan Africa, threaten these fragile gains. Long-lasting insecticidal nets (LLINs) and indoor residual spraying are the central pillars for malaria vector control; fortunately, they remain highly effective in most settings.

Urgent action to prevent resistance from emerging at new sites, and to maintain the effectiveness of vector control interventions in the short, medium and long-term have been clearly articulated out in the Global Plan for Insecticide Resistance Management in malaria vectors (GPIRM) – http://www.who.int/malaria/vector_control/ivm/gpirm/en/index.html – developed by the WHO Global Malaria Programme (GMP) in consultation with a wide range of Roll Back Malaria partners and other stakeholders.

The GPIRM consists of five major activities (pillars) which include the planning and implementation of insecticide resistance management in malaria endemic countries; ensuring proper, timely entomological monitoring and effective data management; developing new and innovative vector control tools; filling the gaps in knowledge on mechanisms of resistance and impact; and ensuring that enabling mechanisms (advocacy, human and financial resources) are in place.

Whereas the first two pillars are country-driven, the development of innovative vector control tools requires working closely with industry among other partners. This is not only key to finding alternative products to manage insecticide resistance but also to ensure that vector control interventions are scaled up and control gains are sustained.
2. Vector Control Advisory Group (VCAG) on new forms of vector control

The need for new forms and new tools for vector control broadly, and the lack of a comprehensive process to assess new tools, technologies and approaches for vector control, led WHO (GMP together with the Neglected Tropical Diseases department, where WHOPES is housed) to see the need to establish a Vector Control Advisory Group (VCAG) for new forms of vector control. To date, the process to generate public health norms, standards and policy recommendations has been primarily focused on new products within existing categories of technology (e.g. long-lasting insecticidal nets) – with no defined "entry point" or process for new forms or "paradigms" of vector control.

Stakeholders have indicated that the absence of a defined process has, in the past, delayed the adoption and implementation of new forms of vector control. VCAG is intended to fill this gap, and to provide a predictable and clear process by which new forms of vector control can gain an initial "proof of principle" recommendation. The process of developing the VCAG was begun approximately 2 years ago; funding for the process was secured in August 2012, and the VCAG is now in the process of being constituted.

In summary, VCAG has the potential to benefit to vector-borne disease control by:

- Providing a predictable and defined process by which new forms of vector control can be introduced into public health practice
- Reducing uncertainty for innovators through this clarification
- Accelerating the process of public health implementation of new forms of vector control
- Providing a forum for dialogue and guidance to innovators on evidence requirements early in the process to reduce risks; and
- Providing WHO GMP and NTD departments, with evidence-based advice on the epidemiological mode of action\(^1\) and the public health value of new forms of vector control, and, through the NTD STAG and the GMP Malaria Policy Advisory Committee, provide such advice to national vector-borne disease control programmes and other stakeholders.

VCAG will act as a standing group with dual reporting to MPAC and STAG (see Figure 1). For vector control topics outside of VCAG’s scope (e.g. recommendations on the appropriate mix of existing vector control interventions in different settings), temporary Evidence Review Groups, Expert Committee Meetings or Working Groups may be convened by MPAC or STAG as appropriate.

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\(^1\) The Epidemiological Mode of Action of an intervention describes how the effect of the intervention on mosquitoes and mosquito populations lead to epidemiological benefits for populations at risk, e.g. in the case of ITNs, the relative importance of personal protection and the "mass effect" (see Lengeler et al: “Net Gain: A New Method for Preventing Malaria Deaths”, Chapter 2)
3. Detailed VCAG activities in relation to MPAC

In order to illustrate the gap that VCAG is intended to fill, it is helpful to consider the process of introducing a new form of vector control. For candidate new vector control technologies, the process of obtaining a recommendation from WHO will in most cases begin with an assessment by VCAG of “proof of principle”, in other words, whether the evidence about the intervention is sufficient to justify its potential application for some public health purpose in one or more specific settings. The assessment will ensure that the evidence generated is relevant for obtaining a public health policy recommendation. The activities performed by VCAG depend on where the proposed new form of vector control stands in the innovation process. There are three major steps of the innovation process in which VCAG can play an essential role, and a fourth step in which its input would be required (see Figure 2).
Figure 2: Three major steps where VCAG has a role to play

**Step 1: Early notification:**

At the very early stages of innovation, product developers can notify new ideas (and interventions concepts being drafted) to VCAG. The secretariat will log these notifications in a confidential list which will be regularly shared with VCAG members, so that VCAG can comprehend future requirements (e.g. expertise needed for future assessments and potential issues to consider). The VCAG secretariat will also be available to respond to any general inquiries about the review process (e.g. nature of assessment and timelines)

*Output(s) of this step: VCAG secretariat runs a list of projects notified by product developers and communicates it on a regular basis to VCAG members.*

**Step 2: Initial interaction on data needs:**

If the product developers wish, VCAG can provide advice on the type and depth of evidence that will likely be used for the assessment, providing an opportunity for product developers to align with VCAG on overall evidence requirements before the launch of resource-intensive activities such as large-scale epidemiological trials.

The advice will be provided in individual discussions between the product developers and the Group at the VCAG meeting. It may cover, for instance, the needs concerning evidence of epidemiological and entomological outcomes, epidemiological mode of action, economic feasibility or user acceptability. To support its deliberations, VCAG may consider the initial results of tests and studies carried out by the product developers.

*Output(s) of this step: VCAG provides advice to innovators on the type of evidence that will likely be used in the review in step 3 to help them strengthen their dossier. VCAG reports to*
Step 3: Review and assessment of public health value:

Once a relevant body of evidence has been presented to VCAG, which contains at least some indication of the epidemiological outcome of the new form of vector control, VCAG will review all available evidence (which may include other available sources than the data presented by the product developers).

Based on this review, VCAG evaluates the public health value of the new intervention, by answering a question of this form: "Is this new intervention efficacious, for some defined public health purpose and in some defined circumstances, and will it be useful to and feasible for its intended users?". The answer might in some instances request additional evidence.

As soon as VCAG decides that the answer to this question is "yes", and that proof of principle has indeed been established for the new form of vector control, responsibility within WHO for further assessment will pass: (a) to the advisory bodies (MPAC and STAG) of the technical department(s) (WHO GMP and NTD) responsible for the particular vector-borne disease(s) against which the new intervention is considered likely to be useful; and (b) to WHOPES.

Hence, after validating the value of the new form of vector control, VCAG will present its results to MPAC and STAG in their respective meetings, expressing its opinion on the usefulness of the new intervention. In particular, VCAG will detail the epidemiological mode of action and value of the new paradigm in a given setting.

In the case of establishment of a proof of principle, VCAG may submit a technical data package to MPAC, STAG and WHOPES for further use in policy and product standard setting. In parallel, product developers are informed of VCAG's opinion of the technology reviewed.

Output(s) of this step: VCAG prepares a report including its assessment of the public health value of the new form of vector control. It may advise product developers on need for additional evidence in some instances. VCAG presents to MPAC and STAG its findings, through the expression of its recommendation ("yes", "no", "yes but" and describing the specific considerations to take into account). A technical data package is also transmitted to MPAC, STAG and WHOPES if relevant.

Step 4: Policy development and product evaluation: [In this step, VCAG mainly provides input]

Once VCAG has presented its findings at the MPAC and STAG meetings, the task of defining what public health roles and functions are appropriate for the new form of vector control in the context of the disease will devolve to these committees. In particular, they will establish the role of the new intervention for a specific disease and eco-epidemiological setting,
and in relation to other disease control interventions. While VCAG will concentrate on the characteristics of the intervention itself and whether it is technically efficacious, MPAC and STAG work at a higher strategic level on the role of the intervention vis-à-vis other interventions within specific disease control programmes, i.e. when, where and how the intervention should be deployed.

Figure 3: Illustrative options of how the articulation between VCAG and MPAC/STAG could work

[Initial propositions for consideration by MPAC and STAG; may require adaptation]

Option 0: Additional evidence required
- Direct deliberations on data needs by MPAC/STAG and write-up of needs/pilots following VCAG’s presentation

Option 1: Low complexity and/or narrow application
- Direct deliberations and a policy statement write-up by the committee following VCAG’s presentation

Option 2: Some complexity or broader application
- Policy statement prepared overnight by “drafting committee”, deliberations on next day

Option 3: Complex issue and/or broad application
- MPAC/STAG secretariat asked to prepare draft statement, to be circulated post-meeting to committee members

Option 4: Highly complex issue and broad application
- MPAC/STAG requests an Evidence Review Group, Expert Committee or Working Group to prepare a policy statement to be submitted at next meeting

In parallel to the VCAG review, WHOPES will need to develop standard definitions, testing/assessment methods (efficacy and safety) and quality control criteria adapted to the pesticide product, so that other commercial products using the same technology can be assessed using a common set of criteria, and appropriate recommendations can be given to prospective purchasers.

In order to minimize the time of developing these guidelines, WHOPES will be in close contact with the VCAG secretariat and participate in VCAG meetings/communications throughout the VCAG process. This will enable WHOPES to develop draft guidelines (with relevant experts) in parallel with the VCAG review, using VCAG’s on-going assessment as primary input for defining relevant indicators and guidelines. Once the VCAG review is finalized establishing public health value of a new tool, technology or approach, WHOPES will then proceed to a larger consultation of the draft guidelines for finalization and publication.
Although VCAG reviews classes of technology, some evidence considered by VCAG may refer to a "first-in-class" commercial product. If this product is also submitted to WHOPES, WHOPES will build on VCAG's work, taking all the already existing evidence fully into account to avoid duplication of efforts.

*Output(s) of this step: GMP and NTD publish policy recommendations, based on the advice of their respective policy committees MPAC and STAG. WHOPES publishes product category testing/assessment guidelines and product recommendations for specific products.*

4. **Membership of VCAG**

Members of VCAG will be expected to provide GMP and NTD with high quality, well considered advice on matters related to new methods of vector control and the factors that determine their efficacy, and to contribute to the role and reputation of VCAG as a useful and internationally-recognized advisory group in the field of vector control. The provisional plan is that VCAG will comprise up to 11 members, who will serve in their personal capacity and will represent a wide range of expertise relevant to practical vector control, including vector biology, ecology and management, insecticides and insecticide resistance, epidemiology of vector-borne diseases, study design and statistics as well as operational research. The panel will include a broad range of opinion, with the capacity to challenge assumptions, as well as direct experience in the design and management of vector control programmes. As far as possible, members will be selected on the basis of the principles of equitable geographical representation from developed and developing countries and gender balance.

An open call for inviting submissions and/or nomination of experts to serve on VCAG will be posted on WHO web site and sent out through other appropriate channels. VCAG members, including the Chairperson, will be appointed by a panel composed of the Directors of NTD and GMP, a regional WHO vector advisor and the STAG and MPAC Chairpersons, upon the proposal of the Coordinators of VCU and VEM. The panel may also consult with other relevant WHO departments. Members of VCAG, including the Chairperson, will be appointed to serve for an initial term of two years. The two-year terms can be renewed, but as a general rule, members, including the chairperson, will be expected to serve for no more than four years out of any six, although exceptions may be made at the discretion of the appointment panel. The Chairperson of VCAG will be invited as a resource person to all MPAC and STAG meetings at which vector control issues are being discussed.

Membership of VCAG may be terminated for any of the following reasons:

- failure to attend two consecutive VCAG meetings;
- change in affiliation resulting in a conflict of interest; and
- lack of professionalism involving, for example, a breach of confidentiality.
WHO Regional Offices and other WHO departments, including Special Programme for Training and Research in Tropical Diseases (TDR), will be invited as members of the Secretariat to participate in VCAG meetings and deliberations.

Additional experts will be invited to participate in meetings, as appropriate, to ensure that a sufficiently broad base of expertise is available for the specific agenda items at each meeting.

5. VCAG Operating Procedures

VCAG will meet at least once a year in open and closed meetings. For the four year period of the project, five meetings are planned, including four yearly meetings and one addition ad hoc meeting that could be set up if needed depending on the number of new vector control tools that are submitted for review. Open meetings can be attended by anyone interested in vector-borne diseases and are intended for discussion of new tools, technologies and approaches and issues related to the agenda item(s) of the closed meeting. Closed meetings will follow the open meetings and will be restricted to VCAG members and the other independent experts to be invited by GMP and NTD. Depending on the needs and requests received to assess new products, additional ad-hoc VCAG meetings could be proposed by GMP and NTD.

A web page will be established for VCAG. Initially, draft procedural guidelines for VCAG will be published on the website, and comments and suggestions will be invited on VCAG working procedures through the website and by direct contact with a selected set of stakeholders. Later, the website will be used to allow access to supporting documentation and the agenda of VCAG, to solicit further items for the agenda, and to disseminate the recommendations and meeting reports of VCAG.

6. Malaria vector control policy setting beyond the VCAG

The relevant issues in malaria vector control that may require WHO to provide policy recommendations are summarized in Table 1. These issues appear to fall into three classes, needing potentially different skill sets: new vector control technologies, insecticide resistance management, and implementation of malaria vector control programmes. Of these, the functions needed for new technologies and insecticide resistance have already been given some attention through previous discussions about VCAG and through the recommendations articulated in the Global Plan for Insecticide Resistance Management; hence, the issues of general programme management are listed in more detail. It may be noted that, according to the RBM Harmonisation Working Group, the issues that are most likely to cause failure of Global Fund proposals are related to this latter category: stratification, quantification, cost-effectiveness, IEC, monitoring and evaluation.
In recent years, the RBM Vector Control Working Group (VCWG) has become a vibrant and active forum for global discussion around issues related to malaria vector control. The group, which generally meets annually, has often attracted more than 100 participants from the global malaria community for its meetings. There has been some degree of confusion around the role of this group, with some members appearing to view the VCWG as a policy setting body. This is not the case, as RBM’s core roles are advocacy, partner harmonization, and resource mobilization. The RBM partnership secretariat and its mechanisms do not have a policy setting mandate. This is particularly important given that groups such as the VCWG are self-selected, and include partners with a financial stake in the interventions being discussed.

In part, the current situation has arisen because of the absence of a clear policy setting mechanism at WHO with regard to malaria generally, and malaria vector control more specifically. The creation and implementation of the MPAC offers an opportunity to rectify this situation.

It is not possible to merge the issues related to practical malaria vector control implementation with the role of the VCAG (or vice versa). One reason is that the VCAG is not a malaria-specific body: it deals with all forms of vector control, e.g. for leishmaniasis, trypanosomiasis, dengue, tick-borne diseases, etc. The main point, however, is that different skills are needed. The VCAG will mainly assess whether new technologies do or do not have the desired effect on the vectors, and for this upstream proof-of-principle decision-making, deep expertise in public health management is not needed, while knowledge of technology, chemistry, biology, and product development is essential. The downstream issues are malaria-specific, and directly connected to practical programme management at country-level, e.g.: the role of IRS in malaria epidemics; how to combine alternative LLIN distribution systems; and LLIN procurement quantification that takes into account expected lifespan of LLINs. For these decisions, it is critical to have specialised malariologists with public health training and experience.

Thus, there is a need for the MPAC to decide how it wishes to address malaria vector control issues that are not covered under the VCAG. Broadly, there are two options.

The first is for the MPAC to create a Technical Expert Group (TEG) for malaria vector control. This TEG could include task forces on issues of perennial importance, such as insecticide resistance. The potential advantages of convening such a group are: 1) there would be a standing group that could respond quickly to the needs of the MPAC as new issues arise that require policy recommendations; 2) an overarching group such as a TEG would allow for a synthetic view of the vector control issues requiring policy recommendations. The potential disadvantages are: 1) the original conception of the MPAC was to largely rely on time-limited
ERGs and to avoid the creation of too many standing TEGs; 2) the malaria vector control issues that require policy recommendations are highly heterogeneous, and may require highly specialized experts. Given this, a standing TEG on malaria vector control might still need to convene ERGs to review specific issues, adding a third layer into the policy setting process, which would not be desirable from a perspective of efficiency or timeliness.

The second is for the MPAC to convene time-limited ERGs to address specific malaria vector control issues as the need arises. The potential advantages of such a system are: 1) being nimbly responsive to policy requirements without creating further fixed architectural components for malaria policy setting; 2) being able to convene highly specialized groups of experts capable of making recommendations directly to the MPAC. Potential disadvantages include: 1) The ERGs might consider a single vector control policy recommendation without taking other vector control issues into context (although presumably the MPAC would be charged with that synthetic function); 2) there are so many vector control issues pending that there will be a continuous convening and disbanding of ERGs that could be time consuming and inefficient.

In either case, the VCAG would remain a distinct and smaller entity, convened jointly by GMP and NTD, focussed on upstream decisions about candidate technologies and reporting to the MPAC either directly or through a malaria vector control TEG if the MPAC were to convene such a group.

The MPAC is asked to consider the needs of the global malaria community with regard to policy advice on vector control, and recommend to WHO whether to establish a standing TEG for malaria vector control, or whether to convene time-limited ERGs on particular malaria vector control issues as the need for policy decisions or recommendations arises.
Table 1: A summary of issues in malaria vector control and proposed mechanisms for policy decisions

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<th>Mechanisms</th>
<th>GMP and NTD</th>
<th>GMP: Management of Malaria Vector Control in Public Health</th>
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<td>VCAG (not only malaria)</td>
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**Skills**

Technological: vector control engineers: entomology, biology, basic epidemiology, insecticides, product development, testing methods etc. Note the need for broad skills across all vectors (not just malaria).

Insecticides and insecticide resistance: genetics and population genetics (including ‘80s modelling work), operational vector control, malaria programme planning and management.

Technical implementation of malaria vector control programmes (entomologists), including logistics and operational planning, public health epidemiology, and economics including cost-effectiveness, social science

**Potential Questions**

New methods of vector control (not only malaria):

(a) proof of principle (not only malaria)

(b) epidemiological mode of action i.e. the causal chain from the intervention’s direct entomological effects on insects, through to epidemiological benefits for people – e.g. repellency vs killing; mass effect vs personal protection. (This is needed in order to develop standard tests and to generalise from trial data to a wide range of other settings).

Managing insecticide resistance:

1) Regular (at least annual) reviews of new data, and at sub-regional level:
   a) interpretation of those data,
   b) making recommendations on technical developments, tactics and trends e.g. “spraying programmes in the east of the region should be preparing for a switch away from insecticide x and towards either insecticide y or z. LLIN programmes should be closely monitoring insecticide z.”

2) Strategic support for the decision-matrix initially presented in the GPIRM:
   a) Technical guidance on implementation
   b) Keep the matrix up-to-date and be responsive to the rapid appearance of new data on the evolution of resistance, its impact on control, and methods for resistance management.

1) Stratification for choice of vector control methods:
   a) Where to use LLINs alone
   b) Use of IRS as
      i) Sole method of VC
      ii) supplement to LLINs
      iii) epidemic prevention and control – highland, arid
      iv) urban fringe
      v) diverse settings in Asia and Latin America
      vi) cordon sanitaire (barrier spraying)

2) Where and when to use a niche-specific form of vector control:
   i) Environmental engineering for source reduction
   ii) Larviciding
   iii) Outdoor transmission
   iv) Housing modifications etc.

3) Management of IRS vs LLINs: Where and when to choose one or the other or some combination of both? How to manage the delivery of both (logistics, training, capacity, procurement etc).

4) Managing LLIN delivery systems so as to sustain universal coverage efficiently, especially:
   a) combining routine continuous distribution with campaigns: e.g.
we tell programmes to “regard the campaign as day 1 of the routine service, plan for both together!” but there is no-one to tell them how to do this, e.g. the practicalities of procurement and quantification for the combination
b) proposed “push-pull” systems
c) the HWG’s 8:20:50 rule for allowing for existing nets
d) what to do when there is enough donor funding for some nets but not for all (Free Universal Coverage is not affordable)
e) is the WHO’s “1 for 1.8” rule working?
f) manage end-of-life of nets
g) define the mechanism by which donors can allow countries to procure the locally-most-durable brand of LLIN
h) manage pressures from donors for increased standardisation in net size...and the contrary pressures from social scientists and local activists for less standardisation in net size and shape, more adjustment to local user-preferences
i) role of social marketing (for some donors this is still an attractive option)
j) net usage: some promotion of usage is needed, but how much is too much? Need rules of thumb for what is cost-effective, and what is not?

4) General vector control capacity building:
i) by defining a core curriculum which builds on Garrett-Jones course from the 60’s
ii) especially capacity on entomological monitoring – is this not collected because no-one has the skill (or field allowances) to collect good data? Or because no-one has the skill to use the data well for programme management?
iii) linking entomological monitoring with all the “which VC where” questions listed above

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<th>Potential Outputs</th>
<th>1) Proof of Principle recommendations (not just malaria)</th>
<th>Annual report on new developments in:</th>
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<td>2) Interim findings on ‘epidemiological mode of action’</td>
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<td>Occasional papers on specific policy issues – e.g. “maintaining universal coverage with LLINs that wear out gradually over a long period” (i.e. how to combine campaigns with routine LLIN delivery systems)</td>
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