SEVENTH MEETING
OF THE
VECTOR CONTROL ADVISORY GROUP

GENEVA, SWITZERLAND
24–26 OCTOBER 2017

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Report of the 7th meeting of the WHO Vector Control Advisory Group

Geneva, 24–26 October 2017

Background

The WHO's Vector Control Advisory Group (VCAG) serves as an advisory body to WHO on new tools, technologies and approaches for the control of vectors of malaria and of other vector-borne diseases. VCAG is jointly managed by the WHO Global Malaria Programme (GMP) and the Department of Control of Neglected Tropical Diseases (NTD), and fully involves the WHO Prequalification Team (PQT) for vector control products. To assist WHO in developing public health policy on new tools, VCAG assesses new interventions and provides guidance on developing evidence. VCAG assesses this evidence once it is generated and provides recommendations to WHO on the public health value of new tools. To date, VCAG has reviewed 17 new tools, comprising 14 new potential product classes. For most of these new tools, technologies and approaches, developers are planning or conducting epidemiological trials to generate evidence to assess their public health value.

VCAG experts and stakeholders convened in Geneva on 24–26 October 2017 for the 7th VCAG meeting. The open session was attended by members of VCAG, applicants and product developers, WHO staff from GMP, NTD and PQT, and other stakeholders, including representatives of donor and procurement agencies. The closed meeting was attended by VCAG members, the WHO Secretariat and the relevant parties only.

General VCAG objectives

1. To assess the public health value of new vector control tools, technologies and approaches submitted to WHO for evaluation.
2. To provide guidance to product developers on data requirements and study designs to generate the evidence required for a VCAG assessment.
3. To provide guidance to WHO and its policy advisory groups, the Malaria Policy Advisory Committee (MPAC) and the Strategic Technical Advisory Committee (STAG) for GMP and NTD, respectively, on the public health value of new tools, technologies and approaches, including updates on evidence gaps that preclude such assessment.

Introductory orientation closed session with VCAG – for information

Five new members were appointed to VCAG in September 2017: Salim Abdulla, Fabrice Chandre, Audrey Lenhart, Hilary Ranson and Robert Reiner. The chair of VCAG, Thomas Scott, introduced the new members present at the meeting and described the functions of the group. He then reviewed the WHO evaluation and policy development pathways for vector control tools, technologies and approaches in the VCAG portfolio.

Conclusions and recommendations – general topics from open session

Updates from WHO

Raman Velayudhan, Coordinator of the NTD's Vector Ecology and Management (VEM), briefed the open session on the functions and activities of VCAG and on WHO's leadership role in policy development for new tools, technologies and approaches for vector control.

Marion Law, Group Lead, Prequalification Team – Vector Control Group (PQT-VC), summarized the activities of PQT-VC to support assessment of safe, efficacious and good-quality products. PQT-VC will initiate manufacturing site inspections and has undertaken co-leadership in the Joint Meeting on Pesticide Specifications (JMPS) of the Food and Agriculture Organization of the United Nations (FAO) and WHO, integrated prequalification of vector control products into the meeting on prequalification (Copenhagen, 17–22 September 2017), and recruited experts for vector control product assessment. The PQT-VC team includes a team leader, a programme manager, an inspection focal point and consultants.

Jan Kolaczinski, Coordinator of the GMP's, Entomology and Vector Control (EVC), reported on two evidence review groups (ERGs): one on comparative effectiveness that reviewed data requirements for new product classes, and another on pyrethroid-PBO (piperonyl butoxide) nets that reviewed new data from one epidemiological study. Detailed outcomes of these ERGs are available on the WHO website.[1] He also provided an update on the topics discussed at MPAC, including malaria threat maps,[2] guidelines on universal coverage of long-lasting insecticidal net (LLINs)[3] and the VCAG update to MPAC. Critical feedback relevant to VCAG concerned the need to review definitions for new product classes and clarify the criteria for assigning the pathway for evaluation of new vector control product submissions. Detailed recommendations are captured in the MPAC meeting report.[4]

Conclusion

- **As per MPAC's request, WHO will work with VCAG to review definitions of new tools and product classes, and update documentation on the product evaluation process.**

Modelling entomological surrogates for epidemiological outcomes

Steve Lindsay and Thomas Scott summarized VCAG's work and recommendations related to entomological surrogates for epidemiological outcomes. A "surrogate" here refers to a biomarker intended to substitute for a clinical end-point. Tom Smith reviewed the possible uses and limitations of entomological surrogates in evaluating vector control interventions. Tom Churcher reported the preliminary results of a meta-analysis based on data generated from experimental hut trials and randomized control trials (RCTs) investigating the impact of indoor adulticidal mosquito control interventions against malaria. The analysis tested the ability of transmission dynamic models, parameterized with entomological data from experimental hut trials, to predict RCT outcomes in different epidemiological settings.

[1] http://www.who.int/malaria/mpac/policyrecommendations/en
[2] http://apps.who.int/malaria/maps/threats/
[2] http://apps.who.int/malaria/maps/threats/
[3] http://apps.who.int/iris/bitstream/10665/259478/1/WHO-HTM-GMP-2017.20-eng.pdf
[4] http://www.who.int/malaria/publications/atoz/mpac-report-october-2017/en/

Conclusions

- **An extensive review of the data was not conducted by this committee. Rather, the two presentations explored the use of entomological surrogates and transmission dynamic models for predicting public health outcomes for specific purposes.**
- **One presentation highlighted that, for some vector-borne diseases (e.g. dengue and other *Aedes*-borne viral diseases), few epidemiologically relevant entomological surrogates have been identified and, for other diseases, surrogates that may be informative require considerable effort to collect (e.g. the entomological inoculation rate for malaria vectors).**
- **For interventions that target malaria vectors inside houses, a modelling study indicated that there is a positive correlation between model predictions based on data generated from experimental hut trials (i.e. WHO Pesticide Evaluation Scheme [WHOPES] Phase II for LLINs) and the observed epidemiological impact measured in an RCT. More data are needed to better understand the relationship between entomological data and epidemiological outcomes, and to use that information to predict the effectiveness of vector interventions.**
- **Modelling can help in trial design and in predicting how a new intervention will function; however, modelling based on entomological surrogates is not currently recommended as a replacement for epidemiological RCT data, and should not be used as the primary evidence supporting decisions on the efficacy to public health of new product classes.**

Recommendation

- **When further evidence is available, VCAG should review the utility of modelling based on entomological surrogates in supporting the formulation of specific WHO recommendations. At present, it is recognized that epidemiological data are key for policy development associated with new product classes.**

Integrating entomological and epidemiological trial designs for LLINs

Some new LLINs under development will contain non-pyrethroid active ingredients, alone or in combination with pyrethroids. For pyrethroid-only nets or for nets where the active ingredient is fast acting, current entomological testing guidelines[1] can be used to generate entomological evidence to demonstrate efficacy, although an update of these guidelines is required to ensure that data requirements associated with the revised evaluation process for vector control tools are being met. For new LLINs that include a novel insecticide or a novel claim, VCAG requires both epidemiological and entomological data to assess the net's potential public health value. Studies on LLIN durability (i.e. WHOPES Phase III) will still need to be conducted. To investigate how to collect these data alongside RCTs, VCAG is developing guidance for an RCT protocol design that includes entomological data requirements relevant to LLIN durability. A sample protocol will be finalized in early 2018 (Q1/Q2) and will be made available for reference. VCAG will review and provide feedback on the protocol for integrating WHOPES Phase III evaluation into epidemiological trials as it is developed.

[1] Guidelines for laboratory and field testing of long-lasting insecticidal nets. Geneva: World Health Organization; 2013 (WHO/HTM/NTD/WHOPES/2013.1, http://www.who.int/whopes/resources/9789241505277/en/).

Open discussion on VCAG processes and policy development for new vector control tools

The following topics were raised for discussion with stakeholders during the open session: improved communication with stakeholders; clarity in WHO pathways for assessment and policy development for new vector control tools; addressing the cost and disadvantages of first-in-class products; funding for epidemiological trials; and encouraging the development of effective new products which may cost more than current tools.

Conclusions

- **WHO policy recommendations need to be evidence based. VCAG is charged with reviewing evidence, but is sometimes criticized for causing delays in the deployment of innovations due to rigorous data requirements. VCAG's role to support WHO recommendations on public health policy for new products is critical for countries where vector-borne diseases are endemic and where lack of capacity and financial support in public sectors makes it more difficult to generate necessary evidence and to evaluate new products.**
- **Policy recommendations for all public health interventions, including vector control, require a well-developed evidence base and should not be based on minimal datasets. For all new public health products, including medicines and vaccines, the cost and time needed to generate evidence to support public health use is a challenge. For medicines and vaccines, however, evidence reviews are undertaken by national regulatory authorities that are highly advanced in many countries. Such reviews are generally not undertaken for vector control products.**
- **The absence of a comparable rigorous assessment process of efficacy, safety and quality of vector control tools caused Member States to request that WHO provides these independent assessments to provide an evidence base for policy development. Currently, Member States endemic for vector-borne diseases rely heavily on the evaluation of efficacy, safety and quality conducted by WHO (VCAG and PQT-VC).**
- **Manufacturers should justify to their leadership the cost and timelines for development of new vector control tools, and ensure that they have the capacity – just as manufacturers of drugs and vaccines do – to support the development of protocols and oversee evaluations in line with VCAG guidance. Manufacturers need to have adequate technical expertise or collaborate with partners that have the appropriate expertise to carry out independent RCTs under the new evaluation process.**
- **Clear evaluation criteria for new first-in-class products will assist manufacturers to plan for the**

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