Vector Control Advisory Group

MEETING REPORT
4–6 October 2021

Fifteenth meeting of the WHO Vector Control Advisory Group

World Health Organization

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ISBN 978-92-4-004085-4 (electronic version)
ISBN 978-92-4-004086-1 (print version)

Suggested citation. Fifteenth meeting of the Vector Control Advisory Group. Geneva: World Health Organization; 2021. Licence: CC BY-NC-SA 3.0 IGO.

Cataloguing-in-Publication (CIP) data. CIP data are available at http://apps.who.int/iris.

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1. BACKGROUND

The Vector Control Advisory Group (VCAG) of the World Health Organization (WHO) serves as an advisory body to WHO on new interventions for the control of vector-borne diseases. These interventions include novel tools, technologies and approaches. VCAG is jointly coordinated by the WHO Global Malaria Programme, the WHO Department of Control of Neglected Tropical Diseases and the WHO Prequalification Team for Vector Control Products. Specific functions of the advisory group are:

- to provide guidance to product developers, innovators and researchers on the generation of epidemiological data and study designs to enable assessment of the public health value of new vector control interventions;
- to assess the public health value of new vector control interventions submitted to WHO; and
- to provide advice to WHO, for submission to the Malaria Policy Advisory Group and the Strategic and Technical Advisory Group for Neglected Tropical Diseases, on the public health value of new interventions.

The 15th VCAG meeting was convened on 4–6 October 2021. This report details the proceedings and outcomes of the meeting, which was held virtually due to the ongoing COVID-19 pandemic. VCAG provided feedback and recommendations to applicants who had made submissions under the following intervention classes:.

- insecticide-treated nets (ITNs) designed to kill host-seeking insecticide-resistant mosquitoes;
- ITNs designed to sterilize and/or reduce the fecundity of host-seeking insecticide-resistant mosquitoes;
- lethal house lures.

The meeting was co-chaired by Heather Ferguson and Salim Abdulla. All 15 VCAG members were in attendance, along with two temporary advisors, applicants (including product developers, innovators and researchers) and observers. Members of the Malaria Vector Control Guidelines Development Group participated as observers in the two sessions of the meeting in which ITN trial results were presented.

Before the meeting, all VCAG members and invited experts completed Declaration of Interest forms for WHO experts. The declared interests and how they were managed by the WHO VCAG Secretariat are summarized in Annex 1.

The agenda is reproduced in Annex 2, and the participants are listed in Annex 3. There was no publicly open session held during this 15th meeting.

2. WELCOME AND OPENING REMARKS

VCAG members were officially welcomed by Dr Daniel Dagne, Unit Head of the Prevention, Care and Treatment Unit within the Department of Control of Neglected Tropical Diseases, on behalf of its Director, Dr Mwelecele Malecela. Dr Dagne noted the importance of VCAG's review of the first epidemiological trials assessing two dual active ingredient ITNs. These dual active ingredient nets could provide considerable additional benefit over the current standard of care for malaria, which is an ITN with a single active ingredient.

Dr Dagne also mentioned the forthcoming scheduled rotation of VCAG co-chairs. Chairs have been serving parallel terms within VCAG, but the group is transitioning to staggered co-chair terms. Dr Salim Abdulla, who is completing his term, was thanked for his contributions and leadership as co-chair over the last three years. Dr Audrey Lenhart has accepted the invitation to take on the role of co-chair from the 16th VCAG meeting. During this transitional period, Dr Heather Ferguson will be staying on as co-chair until the end of her membership term in early 2023. Dr Kalpana Baruah was also thanked for her contributions, having completed her term as a VCAG member.

3. SUBMISSIONS

VCAG received three submissions from applicants, representing three different intervention classes. All submissions were reviewed during the meeting.

3.1. Intervention class: ITNs designed to kill host-seeking insecticide-resistant mosquitoes

Nets in this intervention class are designed to provide superior protection over and above the standard pyrethroid-only nets due to the addition of a second, non-pyrethroid active ingredient. Interventions in this class are anticipated to be effective against mosquitoes that are resistant to pyrethroid, carbamate and organophosphate insecticides.

3.1.1. Intervention: Interceptor G2®

Applicant: BASF

Interceptor G2 nets are treated with a pyrethroid insecticide combined with chlorfenapyr, which has a mode of action (inhibition of oxidative phosphorylation) distinct from that of pyrethroids. Interceptor G2 is the first-in-class product being evaluated for this intervention class.

BASF, the manufacturer of Interceptor G2, has been engaging with VCAG since 2014. BASF has been collaborating with the London School of Hygiene & Tropical Medicine (LSHTM) to conduct the two required cluster-randomized trials with epidemiological end-points. A second intervention, Royal Guard®, manufactured by Disease Control Technologies (DCT), is being tested in these same trials (see Section 3.2.1 of this meeting report). The trials evaluating Interceptor G2 and Royal Guard are being conducted in Benin and the United Republic of Tanzania. VCAG reviewed the Tanzanian protocol at the seventh and ninth VCAG meetings *(1, 2)*; the Beninese protocol was reviewed at the ninth meeting *(2)*.

The trial in the United Republic of Tanzania has four arms: three intervention arms (Royal Guard, Interceptor G2 and Olyset® Plus) and a control arm deploying a standard pyrethroid (alpha-cypermethrin) net. Baseline data for this trial were collected in 2018, with the intervention being evaluated over a total intervention period of 24 months. Data collection for the primary end-point in this trial has been completed. Final assessments of net durability and sustainability of efficacy are due to be completed in January 2022, amounting to a total trial duration of three years.

The trial in Benin has two intervention arms (Royal Guard and Interceptor G2) and one control arm (Interceptor®, an alpha-cypermethrin treated net). This trial started one year after the trial in the United Republic of Tanzania. Results after two years of intervention are anticipated to be available for WHO review in mid-2022.

Updates

During the 15th VCAG meeting, BASF and its collaborators from LSHTM presented results for the primary end-point of their epidemiological trial in the United Republic of Tanzania, which compared Interceptor G2 to Interceptor over a 24-month period. The

applicants requested VCAG's assessment of the results in relation to demonstration of public health value.

The applicants also summarized progress with regulatory submissions and approvals of the Interceptor G2 nets in different countries. Despite delays, lockdowns and logistical constraints related to the COVID-19 pandemic, the product has now been registered in 14 African countries. Dossiers are under review in three countries, and submissions are being prepared for an additional seven. The applicants were successful in delivering 4 million nets in 2019 and 11 million in 2020. During the first half of 2021, 6.5 million nets were delivered to malaria-endemic countries.

Summary of discussions

The key finding of the trial in the United Republic of Tanzania was that areas with Interceptor G2 had significantly lower parasite prevalence in children 6 months to 10 years of age at both 12 and 24 months post-ITN distribution, compared to Interceptor. A mixed effects logistic regression model estimated a 55% reduction in the odds of malaria prevalence (odds ratio: 0.45; 95% CI: 0.30–0.67, $p = 0.0001$) at 24 months, relative to Interceptor. Protection against malaria infection provided by Interceptor G2 at 12 months after distribution was similar to the 24-month observation; however, no statistically significant difference was observed between arms at the 18-month timepoint. Interceptor G2 net usage in the wider community dropped from 68% at three months after distribution to 46% at 24 months, while usage of Interceptor nets dropped from 77% to 50% over the same period. Within the actual cohort enrolled in the study, net usage remained high – over 85% for both years one and two.

There was significantly lower cumulative incidence of malaria in the cohort of children who received Interceptor G2 nets than in the Interceptor control group. The mixed effects Poisson regression model showed an overall 44% reduction in malaria incidence in the Interceptor G2 treatment arm, compared to the Interceptor arm (rate ratio: 0.56; 95% CI: 0.37–0.86, $p = 0.0072$). Efficacy was higher in the first year than in the second year. There was evidence of reductions in both vector densities (*Anopheles gambiae* and *An. funestus*) and entomological inoculation rates (EIRs) observed over the two years. The applicants concluded that Interceptor G2 was more effective than the standard net, with the effect being stronger in the first year of the trial.

Fewer adverse events were reported in the Interceptor G2 trial arm compared to the standard Interceptor trial arm. Most of the reported adverse events occurred in the first three months and were related to skin irritation (60%), presumably due to alpha-cypermethrin. The concentration of chlorfenapyr in the Interceptor G2 nets declined to 18% after 24 months of use.

The applicants also presented modelling data on incremental costs and cost-effectiveness to highlight their conclusion that Interceptor G2 is a cost-effective ITN.

Initial discussion focused on clarification of the data collection period for the primary results. The applicants clarified that prevalence of infection at 24 months' follow-up was the primary trial end-point, rather than incidence of clinical malaria, which constituted the secondary end-point. Net usage, durability and prevalence are being monitored through 36 months.

There was discussion around why Interceptor G2 was associated with reduced prevalence at 12 and 24 months, but had no clear impact at 18 months. The applicants proposed that this may be due to high variability and differences in the burden of disease at the 18-month time point, which occurred in July/August (during the long dry season following the main transmission season). By contrast, the 12- and 24-month assessments were performed after the low transmission season.

The applicants provided clarification on the apparent differences between the comparator arms in terms of the entomological parameters at baseline. Estimates of baseline vector density and EIR appeared to be considerably lower in the intervention arm, giving the impression of an underlying difference. However, the applicants

clarified that this apparent difference in the point estimates was based on very small sample sizes (as collections were performed in the dry season) and that the 95% confidence intervals around these estimates overlapped between the arms. Substantial heterogeneity in entomological characteristics, such as species composition and abundance, was noted throughout the study area.

The applicants confirmed that the baseline entomological parameters were not used during cluster randomization or included as covariates in the modelling of the primary and secondary outcomes. Instead, habitat suitability for each species (*An. gambiae* and *An. funestus*) was estimated from an ecological niche model. VCAG raised concerns mostly about the appropriateness of using habitat suitability in this way. The applicants agreed to provide further information on the habitat suitability index at baseline and a sensitivity analysis to assess the extent to which use of the index influenced results.

Conclusions

VCAG congratulated the applicants on successful completion of the 24-month follow-up of the trial in the United Republic of Tanzania. VCAG appreciated the clear presentation and productive discussion. Next year, VCAG looks forward to reviewing data from the ongoing follow-up of the third year of the trial, as well as the results from the trial in Benin.

VCAG reviewed the information on the modelling approach used to address variability in baseline species composition (provided in the supplemental files submitted to the Secretariat); VCAG felt that the information lacked sufficient detail to enable assessment of the validity of the approach for capturing the underlying heterogeneity. Further clarification will be sought, aiming to enable fuller interpretation of the study results. VCAG also considered the ecological context of the results in terms of whether the setting was characterized by high/moderate/low outdoor biting and how EIR was impacted.

Overall, the data presented from the trial in the United Republic of Tanzania showed a significant impact of Interceptor G2 on malaria prevalence compared to a pyrethroid-only ITN. VCAG awaits the completion of the second trial in Benin. A significant impact in the second trial should enable full assessment of the potential public health value of Interceptor G2 and the intervention class under which it falls.

Recommendations

VCAG requests some additional information to ensure that the overall characterization of the trial outcome is clear and transparent.

- VCAG requests additional information and clarification on the ecological context of the trial and the niche modelling approach used to characterize the variation in entomological characteristics in order to assist interpretation of the epidemiological results. More specifically, the following information would be valuable: EIR over time, including variability of the time-specific and overall estimates; data on the proportion of outdoor biting over time; and resistance phenotypes over the course of the trial.
- VCAG recommends that the applicants conduct additional exploratory analyses to help rule out the possibility that temporary changes in the protocol during COVID-19 restrictions may have affected the outcome measures. For example, participant characteristics evaluated under the baseline and temporary protocols could be compared.
- VCAG also recommends that the statistical analysis plan (SAP) be updated to provide more detail on the nature of the statistical models to ensure a clear record of the specific analyses undertaken. For example, it would be useful to summarize exactly how the variables used to constrain the randomization were included as covariates in the analysis (e.g. as mean values or categories and, if the latter, then how these were defined). The subgroup analyses described in Section 5.2.1 of the SAP should be explained in more detail and justified.

3.2. Intervention class: ITNs designed to sterilize and/or reduce the fecundity of host-seeking insecticide-resistant mosquitoes

ITNs in this intervention class are those treated with an active ingredient in addition to the standard pyrethroid in order to cause mosquito sterility or reduced fecundity following exposure to the net. Interventions in this class are anticipated to kill pyrethroid-susceptible mosquitoes and sterilize or reduce the fecundity of mosquitoes resistant to the pyrethroid, thereby depressing the vector population. It is assumed that this entomological mode of action would then translate into improved efficacy in terms of malaria control compared to the deployment of pyrethroid-only nets.

3.2.1. Intervention: Royal Guard®

Applicant: Disease Control Technologies

The Royal Guard® net is treated with alpha-cypermethrin, a pyrethroid that acts as a neurotoxicant, and pyriproxyfen, which acts as an insect growth regulator *(3)*. Exposure of mosquitos resting on the net to pyriproxyfen is expected to sterilize males and reduce oviposition in any females that survive pyrethroid exposure due to resistance.

As Royal Guard is the first-in-class product in this intervention class, the manufacturer, Disease Control Technologies (DCT), is generating evidence on public health value in two trials with epidemiological end-points. As described above, DCT is also collaborating with LSHTM to perform the required trials. VCAG first reviewed the protocol for the trial in the United Republic of Tanzania including Royal Guard in an off-cycle review, captured in the ninth meeting report (November 2018) *(2)*. In that same meeting, the protocol for the Benin trial was also reviewed by VCAG. An update on both trials was provided to VCAG at the 12th meeting in June 2020 *(4)*.

Updates

At the current meeting, DCT and its collaborators from LSHTM presented the final results (24-month data) of the trial that was completed in the United Republic of Tanzania and sought VCAG's assessment of the results. The submission also included the current protocol (version 4) and SAP used to analyse the data.

The applicants also shared with VCAG entomological data on bio-efficacy, including measures of both the 24-hour mortality of mosquitoes and abnormal mosquito ovary development. There was also a presentation on entomological outcomes from experimental hut studies conducted in Côte d'Ivoire.

Summary of discussions

The main finding of the trial in the United Republic of Tanzania was that, at 24 months, there was no difference in the impact of the Royal Guard net on disease control compared to the standard pyrethroid-only net. The odds ratio for malaria prevalence in the Royal Guard arm was 0.79 (95% CI: 0.54–1.17, $p = 0.235$) relative to the standard net. The applicants confirmed that malaria prevalence at 24 months is the primary end-point intended to demonstrate public health value, although the overall trial duration is 36 months. There were high levels of net usage in the trial cohort of children, although usage declined over time in the wider population.

Seeking to understand the lack of strong evidence in favour of the intervention, there was discussion about the parameters used for the power calculation, with reference to the observed values. Comparing the published study protocol *(3)* to the values obtained in the study itself, the relative reduction in prevalence was 22%, as opposed to the 28% originally estimated. In addition, the observed absolute prevalence values were closer to 50% (in the control arm, 40% had been assumed, but 45.8% was observed), which reduced the power due to greater binomial variance. In terms of cluster-level variation, the value for inter-cluster correlation used in the power analysis (0.03) was also lower than that found during the trial (0.05).

There was discussion of the potential for imbalance in entomological variables (vector density, species composition and EIR) between control and intervention arms at baseline. Indeed, the control arm had three times the EIR value of the Royal Guard intervention arm. The applicants clarified that the confidence intervals around the baseline values for entomological variables were wide and overlapping. In terms of the EIR, the applicants explained that a high degree of variation had been observed over the duration of the trial, including during the low transmission season (September to December); this could potentially explain the wide confidence intervals.

Baseline entomological results were not used to constrain the randomization because these results were not available at the time clusters were assigned. Therefore, these baseline results were not included as covariates in the statistical models for estimating epidemiological outcomes. There was some discussion of the details and appropriateness of this approach, with VCAG requesting further information to aid interpretation.

The applicants highlighted the low bio-efficacy of pyriproxyfen, possibly related to the reduced retention of pyriproxyfen on the nets over time; at 24 months, the net concentration had declined to 28% of the initial level. The manufacturer noted, however, that it remains unclear how much of the pyriproxyfen is on the surface of the net fibres and hence bioavailable. While it is possible that pyriproxyfen-resistant *An. funestus* and *An. gambiae* could have contributed to the low bio-efficacy, it was noted that the discriminating dose of 100 µg/mL used in their bottle assay may not be optimal for this compound.

VCAG noted that at least some of the subgroup analyses specified in section 5.2.1 of the SAP could be carried out within an analysis of the complete dataset. For example, the possibility that effectiveness differs by age could be explored by including the corresponding interactions in the model.

Conclusions

VCAG congratulated the applicants on successful conclusion of the trial, despite the impact of the COVID-19 pandemic. VCAG agreed with the applicants in terms of the main conclusion, i.e. that the Royal Guard net did not demonstrate higher disease impact compared to the control net. VCAG also agreed with the approach described for determining the reasons (e.g. retention, discriminating dose) for the bio-efficacy results.

VCAG found that the information on the modelling approach to address the variability in baseline entomological characteristics lacked some detail and did not enable adequate assessment of the validity of this approach for capturing underlying heterogeneity in entomological risk factors between study arms. Further clarification will be sought, aiming to enable fuller interpretation of the study results.

Although the results did not show a benefit of the Royal Guard net, VCAG awaits the presentation of the 36-month data from the trial in the United Republic of Tanzania to contribute to its understanding of product performance over time.

Recommendations

VCAG requests some additional information intended to ensure that the overall characterization of the trial results is clear and transparent.

- VCAG requests additional information and clarification on the ecological context of the trial and the niche modelling approach used to characterize the variation in entomological characteristics in order to assist interpretation of the epidemiological results. More specifically, the following information would be valuable: EIR over time, including variability of the time-specific and overall estimates; data on the proportion of outdoor biting over time; and resistance phenotypes over the course of the trial.

- VCAG recommends that the applicants conduct additional exploratory analyses to help rule out the possibility that temporary changes in the protocol during COVID-19 restrictions may have affected the outcome measures. For example, participant characteristics evaluated under the baseline and temporary protocols could be compared.
- VCAG also recommends that the SAP be updated to provide more detail on the nature of the statistical models to ensure a clear record of the specific analyses undertaken. For example, it would be useful to summarize exactly how the variables used to constrain the randomization were included as covariates in the analysis (e.g. as mean values or categories and, if the latter, then how these were defined). The subgroup analyses described in section 5.2.1 of the SAP should be explained in more detail and justified.
- Finally, VCAG recommends that the applicants continue to collect information on changes in the impact of pyriproxyfen over time in the Benin trial. VCAG requests that these results be included in the applicant submission next year.

3.3. Intervention class: lethal house lures

The "lethal house lure" intervention class falls under the intervention type of housing modifications. Lethal house lures are a combination of screening mosquito entry points (such as eaves, windows and doors) and treating some or all of these screens with insecticide. The screening helps to channel the warm human-scented air from inside the structure to the upper eaves, attracting host-seeking mosquitoes, which are then exposed to the insecticide. Lethal house lures aim to restrict mosquito entry into houses and kill host-seeking mosquitoes after exposure to an insecticide.

3.3.1. Intervention: EaveTube™ (with and without screening)

Applicant: In2Care®

The In2Care team has interacted with VCAG since 2014 *(5)*. In2Care® EaveTube™ are made of plastic and contain a removable mesh with a static coating that holds powder-formulated insecticides. The tubes are inserted in the eaves of houses during construction. Alternatively, they are placed behind ventilation openings or retrofitted into the wall by drilling, cutting or chiselling. The tubes funnel the indoor human-scented air outwards to attract host-seeking mosquitoes, and the static-coated netting transfers a lethal dose of insecticide particles considered to be effective against highly resistant wild-type mosquito strains. EaveTubes have been developed for malaria vectors.

The results of the first trial conducted with this intervention were from a cluster-randomized controlled trial (cRCT) in Côte d'Ivoire, which commenced in 2017. The efficacy of the lethal house lure intervention was evaluated against clinical episodes of malaria, and the results were presented to VCAG in November 2019 *(6)*. The results demonstrated a substantial impact on malaria incidence, but it was not possible to quantify the relative contribution of the EaveTubes to the overall effect, because they were deployed in combination with house screening. As a result, it is also unclear whether the deployment of the EaveTubes on their own, as envisaged by the manufacturer, has public health value.

At the 12th VCAG meeting (June 2020) *(4)*, the applicants presented plans for a second trial with a factorial cRCT design to be conducted in the United Republic of Tanzania. It was intended that the study would enable the evaluation of EaveTubes as a standalone intervention, as well as in combination with screening. At the 13th VCAG meeting (December 2020) *(7)*, the applicants submitted a proposal to conduct a follow-on study in the same area as their previous trial site in Côte d'Ivoire.

Updates

For this 15th meeting, the applicants provided VCAG with an update on their plans for future trials. Their submission included a draft protocol and SAP for the new trial in Côte d'Ivoire. This proposed trial has a full CRT design, which will enable the EaveTubes to be evaluated as a standalone tool. It is planned that the trial will be conducted in the same area near Bouake, enabling direct comparison of results with those of the previously published trial *(8)* that tested screening and EaveTubes together.

The applicants also confirmed that a three-arm trial (EaveTubes, screening and pyrethroid-PBO nets) planned in Uganda is going ahead. The Uganda trial design was originally submitted by the United States Centers for Disease Control and Prevention (CDC)/the U.S. President's Malaria Initiative (PMI) and reviewed at the 12th VCAG meeting in April 2020 *(4)*. Based on the pilot study results (as described in the initial presentation during the 12th meeting), the full RCT will proceed with EaveTubes and full house screening as the two independent intervention arms.

Together, the trials in Côte d'Ivoire and Uganda are intended to generate evidence for the assessment of the efficacy of EaveTubes, independent of house screening, in two different settings.

In2Care's submission included questions about whether VCAG would endorse moving forward based on only a single year's data on EaveTubes deployed alone (i.e. in the absence of house screening) from the trials in Uganda and Côte d'Ivoire.

Summary of discussions

VCAG offered its congratulations on the publication of the first Côte d'Ivoire trial, the WHO Prequalification Team's validation of product risk assessment, and the registration of the product in Côte d'Ivoire.

In response to specific questions from In2Care, VCAG confirmed the following points:

- The new two-arm trial design in Côte d'Ivoire is likely to be adequate to evaluate the efficacy of EaveTubes as a standalone intervention, in terms of sample size, power calculations and proposed impact monitoring methods.
- VCAG will be willing to review the interim results of the new Côte d'Ivoire trial after one year of follow-up (since the trial has been appropriately powered for this). The outcome of this review will depend on what the trial results demonstrate.
- The new Côte d'Ivoire trial will contribute evidence to the dossier but will need to be complemented by results from the other trials, particularly evidence of effect in Uganda.
- If two trials are conducted that deploy EaveTubes alone and if both demonstrate significant impact on malaria incidence, then VCAG will be in a position to advise WHO on the public health value of the standalone product.

The trial protocol generally appeared to be of high quality, but VCAG raised several issues that should be considered in more detail before the trials commence. There was also discussion of several choices made by the investigators that are implicit in the protocol. In each case, VCAG expressed concern that the investigators' choice in the existing protocol might make it less likely for the trials to succeed in establishing the efficacy of EaveTubes. These concerns were related to:

- the use of pre-existing pyrethroid long-lasting insecticidal nets (LLINs), rather than pyrethroid-PBO ITNs; and
- the use of a pyrethroid on the insert, given the very high levels of pyrethroid resistance.

The applicants explained that pyrethroid LLINs are the standard of care in Côte d'Ivoire and were used in the first RCT. Therefore, the inclusion of these standard bednets as background interventions will enable comparison of the results of both trials in Côte d'Ivoire, the one conducted a few years ago and the one planned. The Uganda RCT will include pyrethroid-PBO ITNs in all three trial arms.

The applicants also highlighted their published results on pyrethroid-treated static-coated EaveTubes netting, which demonstrated that the polarity-driven insecticide transfer technology increases the efficacy of deltamethrin and beta-cyfluthrin against highly resistant wild-type mosquito strains. The second trial in Côte d'Ivoire and the trial in Uganda will include measurements of bio-efficacy and persistence of pyrethroid-treated static-coated EaveTubes netting against resistant wild-type anophelines in order to confirm the product's effectiveness in areas with very high levels of pyrethroid resistance.

A number of additional technical (mainly statistical) questions about the protocol for the second trial in Côte d'Ivoire were raised with the applicants, and a written response to these questions was received during the period of the meeting.

Recommendations

VCAG recommends that the applicants proceed with their trial plans as presented to the committee, with minor amendments to the protocol as indicated in the discussion. In addition:

- A pre-intervention (baseline) characterization assessment of the wild-type vector resistance intensity should be carried out at the new Côte d'Ivoire study site. Since resistance is dynamic, contemporary measurements of resistance intensity are needed to extrapolate the findings to other studies.
- Entomological data should be included in the interim analysis to be submitted after one year of follow-up in the Côte d'Ivoire trial.

4. VCAG MEMBERS' DISCUSSION

The Secretariat provided an update on several operational changes intended to improve the communication with and provide updates to wider stakeholders within the vector control community as both the evaluation process and the guidelines process evolve. One change includes the update of the names of intervention types and intervention classes, and the grouping of intervention classes within intervention types (not interfering with the evaluation status of interventions). Further to this point, an interactive platform is being developed, incorporating the recent name changes to the intervention classes. This platform is anticipated to better articulate the linkage between intervention classes, the trials in progress within these intervention classes, and the associated recommendations for established classes. This interactive platform will replace the static PDF version of the "Overview of interventions" table that is currently downloadable from the VCAG website. The new interface for this tool will be more comprehensive, enabling users to search for information by intervention class or meeting participation. This tool is expected to be online and available to the public in early 2022.

Considering the continued COVID-19 pandemic, the Secretariat led a discussion on the future format of VCAG meetings and how to maintain optimal interactions in order to provide quality reviews of applicant submissions. Numerous members noted that they missed the face-to-face meetings, but that virtual meetings did allow for more flexibility. Provisional planning for a face-to-face meeting in the second half of 2022 will proceed, dependent on COVID-19 restrictions. It was also suggested that some members might be able to participate virtually in future in-person meetings, should the technology allow.

5. CONCLUDING REMARKS

The WHO VCAG Secretariat and co-chairs thanked the VCAG members and temporary advisors for their time and effort in reviewing the applicant submissions presented at the meeting and for all of their work preparing the meeting report. The Secretariat acknowledged that the work of WHO is only possible with such contributions from its dedicated members.

Given the continuing COVID-19 pandemic, the 16th VCAG meeting will be held virtually during the week of 28 March 2022.

6. REFERENCES

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ANNEX 1. DECLARATIONS OF INTEREST

The 15th Vector Control Advisory Group (VCAG) meeting was convened to review and evaluate three applicant submissions on novel vector control interventions.

This convening consisted of five categories of invitees, namely:

I. *"members" including the co-chairs, who were each required to complete a Declaration of Interest and Confidentiality Undertaking form;*

II. *temporary advisors, who were each required to complete a Declaration of Interest and Confidentiality Undertaking form;*

III. *participants (applicants), in this case the investigators presenting their research and plans for testing their interventions;*

IV. *observers; and*

V. *WHO staff.*

Respective applicants participated in their own open sessions alongside the members, temporary advisors, WHO staff and observers. Observers participated in the open sessions of two applicant presentations only. Only those individuals who had completed a Declaration of Interest form and WHO staff were allowed to participate in the closed discussion sessions.

Declarations of Interest

Before the meeting, all VCAG members and temporary advisors completed a "Declaration of Interests for WHO experts" form. The VCAG Secretariat assessed the interests declared by the experts and, with the exception of two points described below, determined that the interests were not directly related to the topics under discussion at the meeting.

The following declared interests were assessed as relevant (or potentially relevant) to topics under review at the meeting. The disclosed interests did not warrant full exclusion from the meeting itself, but rather management or partial participation. The mitigating actions taken in relation to the disclosed interests are described.

The reading of these interests at the meeting and their inclusion in this meeting report (and any related documents) constitutes public disclosure.

Dr Hilary Ranson

The research group of Hilary Ranson has received research funding related to the New Nets Project (which involves the Interceptor G2 and Royal Guard nets). Dr Ranson's involvement in the research programme of the New Nets Project was deemed a conflict of interest.

As such, she had no access to any of the submitted documents and was recused from closed discussions leading to the development of VCAG advice to WHO related to the Interceptor G2 and Royal Guard interventions.

Dr Tom Smith

Tom Smith currently sits on the Data and Safety Monitoring Board (DSMB) of the New Nets Project (which involves the Interceptor G2 and Royal Guard nets) and was previously involved in modelling the efficacy of Royal Guard in a trial other than the one being reviewed at this meeting. Given that the DSMB of the New Nets Project provides independent oversight of the trial, Dr Smith's participation on the board was not deemed to be a conflict of interest. Similarly, as he is no longer involved in modelling the efficacy of the Royal Guard net in Burkina Faso, it was not deemed to be a conflict of interest for the purpose of reviewing the results of the trial in the United Republic of Tanzania.

These activities have been openly acknowledged and Dr Smith's participation was not restricted in the development of VCAG's advice to WHO related to the Interceptor G2 and Royal Guard interventions.

ANNEX 2. AGENDA

MONDAY, 4 OCTOBER 2021			
Session 1: Welcome and updates		**Presenters/speakers**	**Closed session**
12:45 – 13:00	**Preliminary welcome** Overview of running of meeting Reading of advisors' declarations of interest	WHO VCAG Secretariat	For information
13:00 - 13:20	**Official opening of VCAG meeting** Chair of session: VCAG Co-chairs • Welcome from Acting Director of the Department of Control of Neglected Tropical Diseases • Any other business	Daniel Dagne	For information
Session 2: Presentations from applicants		**Applicant**	**Closed session**
13:30 – 14:45	**Presentation – Interceptor G2® (Tanzanian trial results)** Chair of session: Salim ABDULLA • Applicant presentation • Q&A *Applicants leave the call* • Closed discussion	*ITNs designed to kill host-seeking insecticide-resistant mosquitoes:* Interceptor G2® (BASF)	For guidance
15:15 – 16:30	**Presentation – Royal Guard® (Tanzanian trial results)** Chair of session: Neal ALEXANDER • Applicant presentation • Q&A *Applicants leave the call* • Closed discussion	*ITNs designed to sterilize and/or reduce the fecundity of host-seeking insecticide-resistant mosquitoes:* Royal Guard® (DCT)	For guidance
TUESDAY, 5 OCTOBER 2021			
Session 3: Presentations from applicants		**Applicant**	**Closed session**
12:00 – 13:00	**Presentation – EaveTubes™** Chair of session: Tom SMITH • Applicant presentation • Q&A *Applicants leave the call* • Closed discussion	*Lethal house lures:* EaveTubes (In2Care®)	For guidance
Session 4: Feedback to applicants		**Applicant**	**Closed session**
13:15 – 14:15	**Feedback – Royal Guard® (Tanzanian trial results)** Chair of session: Neal ALEXANDER • Closed discussion *Applicants join the call* • Feedback to applicants	*ITNs designed to sterilize and/or reduce the fecundity of host-seeking insecticide-resistant mosquitoes:* Royal Guard® (DCT)	For guidance
14:45 – 15:45	**Feedback – Interceptor G2® (Tanzanian trial results)** Chair of session: Salim ABDULLA • Closed discussion *Applicants join the call* • Feedback to applicants	*ITNs designed to kill host-seeking insecticide-resistant mosquitoes:* Interceptor G2® (BASF)	For guidance

WEDNESDAY, 6 OCTOBER 2021			
Session 5: Feedback to applicants		**Applicant**	**Closed session**
12:00 – 12:45	**Feedback – Eave Tubes** Chair of session: Tom SMITH • Closed discussion *Applicants join the call* • Feedback to applicants	*Lethal house lures:* Eave Tubes (In2Care)	For guidance
Session 6: VCAG discussion			**Closed session**
12:50 – 13:30	**Discussion among VCAG** Chair of session: VCAG Co-chairs • Update on intervention classes • Discussion session		For discussion
Session 7: VCAG wrap-up			**Closed session**
13:30 – 13:45	**Wrap-up** Chair of session: VCAG Co-chairs		For information

ANNEX 3. LIST OF PARTICIPANTS

VCAG MEMBERS

Co-Chairs

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