WHO Prequalification of Vector Control Products

Entomology assessment process

Modules 3 and 5

PURPOSE

This document describes the process of entomology assessment of laboratory, semi-field and community studies submitted as part of the WHO Prequalification of Vector Control Products (PQT/VCP) dossiers. The purpose of this document is to familiarize prospective applicants with the process of the entomological assessment of data submitted in product dossiers, provide details regarding what is considered during the assessment process and specify information that remains internal to WHO and information that is included in the Module 5 WHO public assessment report (WHOPAR).

PROCESS

Application submission and screening

The applicant is responsible for generating the necessary data and compiling the complete product dossier for submission. Once WHO has received the product dossier, it will be screened for completeness, including both an administrative and technical screening, before it is accepted for assessment. WHO will communicate the deficiencies in the documentation and/or the data identified during the screening to the applicant in writing. WHO may request that the applicant provide the necessary information/clarification to complete the product dossier, or if deficiencies are critical in nature, WHO may issue a screening failure letter, effectively cancelling the review of the submission. If a screening failure letter is issued, the applicant may resubmit the application once the identified deficiencies are addressed.

Note: Only complete applications will be accepted for assessment. In situations where additional entomological data are under development at the time of product dossier submission, specific identification of the studies and target dates for submission must be included in the cover letter and product dossier table of contents for consideration in the screening process.

Module 5: Technical screening

During the technical screening, the quality and robustness of submitted entomology studies are assessed, and deficiencies that lead to uncertainty or preclude the full entomology assessment from being conducted are identified.

WHO will communicate identified deficiencies to the applicant in writing. The applicant will be informed that irregularities have been identified in the scientific content of the entomology studies and requested to provide the necessary information and/or explanations to address the questions and thereby enable the advancement of the product dossier to the assessment phase.

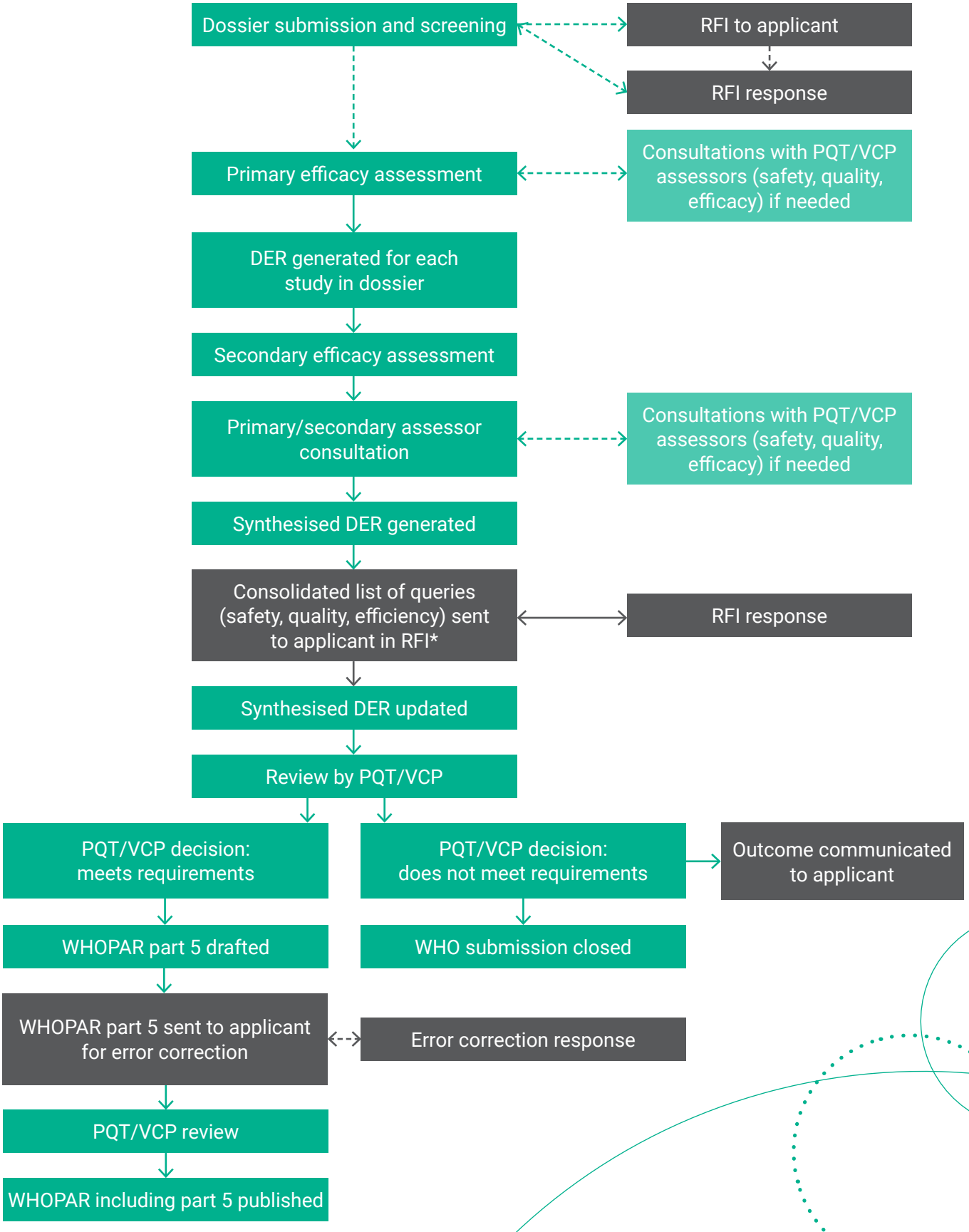
Examples of commonly identified deficiencies include laboratory or supplementary bioassay studies that do not meet the minimum sample size requirements, underpowered semi-field studies and selection/use of controls without scientific justification.

Note: These examples are not an exhaustive list. Any critical deficiency in entomological studies can be flagged and communicated to applicants prior to the product dossier entering the assessment phase.

WHO Prequalification of Vector Control Products
Avenue Appia 20
1211 Geneva 27
Switzerland

For further information, contact:
pqvectorcontrol@who.int
https://extranet.who.int/prequal/vector-control-products

Figure 1. Entomology assessment process



*RFI shown once for visual clarity, can be generated at any stage.

DER data evaluation record
RFI request for information

WHO Prequalification of Vector Control Products
Avenue Appia 20
1211 Geneva 27
Switzerland

For further information, contact:
pqvectorcontrol@who.int
https://extranet.who.int/prequal/vector-control-products

ASSESSMENT BY WHO

Primary entomology assessment

Once an application has been accepted for assessment, the primary reviewer is assigned, and the product dossier is made available to the expert. In some cases, multiple primary reviewers may be assigned to facilitate timely assessments.

Prior to the assessment of the individual entomology study reports, the expert assessor reviews the submitted table of contents to ensure they have received all the necessary documents and the Module 2 summaries for all disciplines to gain an overview of the product, its intent, characteristics, studies and results contained in the product dossier.

During the primary review, the assessor examines the entomological data provided in each scientific study using the relevant WHO guidelines and implementation guidance as a basis for the assessment. If deviations are identified, the assessor notes the deviation, whether a scientific rationale or justification has been provided and whether the justification provided is acceptable. Assessors routinely consult raw scientific data during the primary assessment to verify summarized results and investigate any questions arising from the presentation of results in study reports.

Table 1 includes the minimum list of considerations that expert assessors use during primary entomology assessments.

Document record: The primary assessor generates a data evaluation record (DER) for every assessed study in the product dossier. The DER includes the details of the study purpose and methodology, summarized study results and the assessor's conclusions regarding the completeness of the study and whether the study is adequately conducted for use in decision-making. DERs are internal WHO documents.

Secondary entomology assessment

A senior expert entomology assessor conducts the secondary entomology assessment, which takes place after the primary assessments of the entomology studies submitted in the product dossier are complete. During the secondary assessment, the senior expert assessor reviews the DERs produced during the primary entomology assessment alongside the entomology study reports and the relevant WHO guidelines and implementation guidance. Table 1 includes the minimum list of considerations that the senior expert assessor uses during secondary entomology assessments.

The primary and secondary assessors may consult with one another to identify alignment or disagreement in their identification of questions that must be addressed and interpretations and conclusions made based on the available information in the study report.

If deficiencies in the presented study methodologies and results are identified during the primary and secondary assessments, WHO compiles a consolidated list of queries and communicates to the applicant using a request for information (RFI).* Once responses to the RFI have been received from the applicant, the responsible assessor reviews the responses and determines whether the responses are sufficient to address the identified issues, thereby allowing for the continuation/closing of the assessment phase. Following the review of the additional information in response to an RFI, WHO may request further clarification/information for the same issues and identify additional issues for which further information is required.

Document record: The secondary assessor produces a synthesized data evaluation record (sDER) that combines the assessments of all the assessed entomology studies in the product dossier. The sDER includes the details of the study purpose and methodology, summarized study results and the assessor's conclusions regarding the completeness of the study and whether the study is robust. If RFIs have been sent to the applicant, the sDER is updated with the responses, along with the assessor's expert opinion regarding whether the responses adequately address the RFI queries. sDERs are internal WHO documents.

The sDER for entomological data is relied upon to inform the prequalification decision-making process by PQT/VCP in addition to the outputs of the safety and quality assessments.

Timing of assessment

Assessment Sessions for Vector Control Products (ASVCP) meetings are planned to be held two times per year.

Although ASVCP meetings are integral to product assessments, neither the initiation nor conclusion of an assessment is tied to the dates of the ASVCP meetings, and applications are accepted throughout the year.

The ASVCP meetings promote the timely completion of assessments and facilitate consultation of assessors from different disciplines, e.g., chemistry and entomology assessors. Assessments for products that cannot be completed during an ASVCP meeting are continued between sessions.

*The RFI step is presented once here to avoid repetition, but an RFI can be generated at any stage.

Table 1. Entomology assessments: considerations for assessments and document records

Assessment considerations	Assessment stage		
	Primary	Secondary	Decision
	Document record		
	DER	sDER	WHOPAR
1. Product information, intended use and mode of action of active ingredients provided.	x	x	x
2. Relevant study identification information provided: • study title • study location • study report code • study report date • study sponsor.	x	x	
3. Statement of GLP compliance/GLP certificate.	x	x	x
4. Study objectives clearly stated and appropriate.	x	x	
5. Criteria for study acceptance described (e.g. for a pyrethroid + PBO insecticide-treated net [ITN], results from metabolically resistant mosquitoes used as the decision-making results). • Criteria for control results acceptance described.	x x	x x	x
6. Relevant specifications for the product and controls described.	x	x	
7. Receipt and storage conditions for the test and control items described.	x	x	
8. Batch numbers for test items and control products listed by study. • For ITNs, the number of nets received per batch and the number of nets used in each study described.	x	x	
9. Product mode of action and intended use described.	x	x	x
10. Has the product been tested using appropriate vector test systems for the mode of action and intended use? • Have the test systems been characterized at appropriate stages within each study?	x x	x x	x x
11. Studies used to characterize the fabric (ITNs) or AI (IRS, larvicides, space sprays, spatial repellents) designed and conducted according to best practice and the available guidance, using appropriate (and validated) methods for the product mode of action and intended use.	x	x	x
12. Mosquito sample sizes used in fabric characterization studies in accordance with available guidance or supported by statistical justification.	x	x	
13. For ITNs, sampling scheme designed according to available guidance and appropriate for the product.	x	x	
14. Semi-field studies conducted in an area where the local vector population is appropriate for assessing the efficacy of the product.	x	x	x

Assessment considerations	Assessment stage		
	Primary	Secondary	Decision
	Document record		
	DER	sDER	WHOPAR
15. Semi-field studies designed and conducted according to best practice and available guidance.	x	x	x
16. Power calculation for semi-field trials and evidence of semi-field study compliance with calculation presented.	x	x	x
17. Supplementary bioassay studies to semi-field studies been designed and conducted according to best practice and available guidance, using appropriate (and validated) methods for the product mode of action and intended use.	x	x	x
18. Mosquito sample sizes used in supplementary bioassays to semi-field studies in accordance with available guidance and implementation guidance or supported by statistical justification.	x	x	
19. Outcome measures appropriately defined for all studies and used consistently.	x	x	
20. Results for all studies presented in tabular format.	x	x	
21. Results presented using appropriate summary statistics as detailed in available guidance and/or best statistical practice.	x	x	
22. Data analyses for all studies conducted according to best statistical practice and relevant available guidance.	x	x	
23. Data analysis methods clearly described.	x	x	
24. Statistical conclusions are robust.	x	x	x
25. All raw data for studies supplied.	x		
26. Raw data supports summarized study reports.	x		
27. Studies categorized into those that can and cannot be used for decision-making.			x

REQUEST FOR PRE-SUBMISSION MEETING AND ADDITIONAL GUIDANCE

Applicant s with questions about data requirements for the entomology components of submissions can contact PQT/VCP via email or request a meeting and/or teleconference by submitting the pre-submission meeting request form.

APPENDIX. ENTOMOLOGY STUDY TYPES AND WEIGHT OF EVIDENCE CONSIDERATIONS

Fabric/AI characterization (laboratory studies)

- Defines consistency of material and bioavailability of chemical treatments/formulation.
- Provides baseline data on the effect of treatments on mosquito strains:
  - Susceptible (baseline data);
  - Resistant (with appropriate mechanisms for product intended use and mode of action);
  - Strain characterization data and justifications for the selection of strains must be provided in the dossier.
- Manufacturers should select an appropriate laboratory bioassay that is suitable for the mode of action.
  - If a novel bioassay is used, method validation data must be submitted as part of the dossier.
- Endpoints and outcome measures that are appropriate for the mode of action must be used. Justifications for the selected endpoints must be provided. The selected endpoint(s) must be used consistently throughout the dossier.

Primary evidence

- Studies and sub-studies listed in WHO guidelines, conducted to GLP.

Supplementary evidence

- Additional studies not described in WHO guidelines that further characterize the consistency of the intended effect of the product.

Weight of evidence approach

- Individual studies (and/or sub-studies) are assessed to determine if the product meets the requirements specified in the relevant WHO guidance (for primary evidence studies) and/or the stated study objectives (for supplemental studies).
- Studies are internally categorised into studies that meet requirements and can be used for decision making or studies that do not meet requirements and cannot be used for decision making.
- To meet the requirements for prequalification listing for the laboratory component, all primary requirements must be satisfied.
- In an event where a study has been assessed as meeting requirements, but the quality of evidence is lower, supplementary evidence may be accepted to strengthen the study, provided that the provided that the supplementary evidence demonstrates the same characteristic of the product that was demonstrated in the primary evidence study and the supplementary study has been assessed to be of high quality.

Efficacy (semi-field studies)

- Defines the entomological efficacy of the product, supported by bioassay data to demonstrate product consistency.
- Must be conducted in locations where the vector population is appropriate to demonstrate the AI(s) mode of action and the product intended use.
- Manufacturers should select an appropriate laboratory bioassay that is suitable for the AI(s) mode of action.
  - If a novel bioassay is used, method validation data must be submitted as part of the dossier.
- Endpoints and outcome measures that are appropriate for the product must be used. Justifications for the selected endpoints must be provided. The selected endpoint (s) must be used consistently throughout the dossier.
- Mosquito strains used in supplementary bioassays must have suitable characteristics to demonstrate the AI(s) mode of action
- Product characterization (bioassays). Supports free flying mosquito results.
- Free-flying mosquitoes:
  - data analysis: 20x washed nets;
  - uses manufacturer-defined endpoint dependent on product mode of action and intended use.

Primary evidence

- Studies and sub-studies listed in WHO guidelines, conducted to GLP.

Supplementary evidence

- Additional studies not described in WHO guidelines that further characterize the consistency of the intended effect of the product.

Weight of evidence approach

- Individual studies (and/or sub-studies) are assessed determine if the product meets the requirements specified in the relevant WHO guidance (for primary evidence studies) and/or the stated study objectives (for supplemental studies).
- Studies are internally categorized into studies that meet requirements and can be used for decision making or studies that do not meet the requirements and cannot be used for decision making.
- To meet the requirements for prequalification listing for the semi-field component, all primary requirements must be satisfied.
- In an event where a study has been assessed as meeting requirements, but the quality of evidence is lower, supplementary evidence may be accepted to strengthen the study provided that the supplementary evidence demonstrates the same characteristic of the product that was demonstrated in the primary evidence study and the supplementary study has been assessed to be of high quality.

Comparative entomological efficacy and entomological modelling

- Demonstrates the efficacy of a product, as compared to the first in class product.
- Must be conducted in locations where the vector population is appropriate to demonstrate the product mode of action and intended use.
- Endpoints are specified in guidance documents.
- Data analysis methods are specified in guidance documents.
  - If a novel bioassay is used, method validation data must be submitted as part of the dossier.
- Entomological modelling situates product performance within all products in the relevant class, i.e., not only first in class.

Primary evidence

- Studies conducted as described in relevant guidance documents.

Supplementary evidence

- Entomological modelling that situates the performance of the product amongst the other products in its class.

Weight of evidence approach

- Individual studies (and/or sub-studies) are assessed to see if the product meets the requirements described in the relevant WHO guidance.
- To meet the requirements for prequalification listing for the comparative efficacy component, all primary requirements must be satisfied.
- In an event where one study does not meet the specified requirements to demonstrate non-inferiority, supplemental evidence is consulted to support indications of product performance and a further semi-field trial is requested if indicated.