WHO Prequalification of Vector Control Products

Annex I. ITN studies

Table 1.1 General		
Report section	**Description**	**Critical parameters to report**
General		
Cover page		
Table of contents		
GLP compliance statement	An official statement of compliance with GLP requirements. The GLP certificate can be provided as part of this section or as an annex to the report	
Results summary	Briefly summarise the results and conclusions of the study. This can be in tabular or narrative text format.	
List of abbreviations	List of abbreviations used in the study report. The use of abbreviations should be kept to a minimum.	
Background	Relevant background information for the study. This can be a brief description of the product and its proposed use.	
Study rationale	A brief description of the rationale for conducting the study and the intent of its use	
Study objectives	List the objectives of the study. Study objectives should be clearly written and described. If the study has been conducted to meet the requirements of multiple bodies, the full list of study objectives can be provided in this section, with those study objectives related to the prequalification product assessment clearly indicated.	
Study endpoints	This section should list and describe all endpoints used in the study, including descriptions of primary and secondary endpoints where relevant. If multiple strains of test systems have been tested in the study, identify the	• Primary endpoints • Secondary endpoints

Table 1.1 General		
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General		
	test system which was used to determine the validity of the study/provide the scientific determination of product performance, and provide a rationale for the selection of said test system as the decision-making strain. Endpoints should be used consistently throughout all data generation for a product, with the exception of early exploratory studies which might be submitted in a dossier as supplementary evidence.	
Criteria for study acceptance	List and describe the criteria for • Acceptance of the study as scientifically valid • Evaluation of the product as having met the requirements for prequalification for that particular study type	• Criteria for controls • Criteria for evaluation of the proposed product as having met the requirements for prequalification for that particular study type, e.g. laboratory assessment
Guidance and protocol deviations	Provide any deviations from either the study protocol (as per GLP requirements) and/or from WHO guidance	• Deviations from the study protocol » As per GLP facility requirements • Deviations from WHO guidance » Evidence-based justifications/rationales » Assessment of the impact on study validity, acceptability, robustness, with additional evidence to support the assessment where necessary » Any adjustments that were made to the study protocol in response to considerations received from WHO as part of a protocol review submission

Table 1.2 Methods		
Report section	**Description**	**Critical parameters to report**
Methods		
1.2.1 Test systems		
Test systems	Description of the test systems used in the study	• Colony maintenance and brief summarised rearing procedures • Light cycle of insectary • Age and physiological status used in bioassays » If multiple bioassays have been used, report the age and physiological status for each method separately • Most recent date of insecticide resistance characterisation (note that the results of the characterisation should be reported in the matrix for mosquito strains https://extranet.who.int/prequal/key-resources/documents/ig-template-msms) • Justification for the selection of test system(s), including reference to the product AI and mode of action, and the characteristics of the test system(s) that make it a suitable choice
1.2.2 Study sites		
Description and selection of study sites (for semi-field studies)	Narrative description of semi-field study site(s), including a justification for the site(s) suitability	• Location • GPS coordinates • Description of seasonal variations and rainfall
1.2.3 Characterisation of vector population(s)		
Characterisation of local vector population (for semi-field studies)	Description and characterisation of the local vector population at semi-field sites, including suitability for use in testing the proposed product	• Vector species and composition, including sibling species, if present • Description of insecticide resistance status and mechanisms (note that the results of the characterisation should be reported in the matrix for mosquito strains)
1.2.4 Test items, product information		
Test and reference items	Description of the batch(es) of test and reference items used in the study.	• The number of batches of test items used in the study • All batch numbers for test and reference items • The number of test and reference items received at the testing facility » The number of test items received per batch of test items

Table 1.2 Methods		
Report section	**Description**	**Critical parameters to report**
Methods		
		• Source of all test and reference items • Date of manufacture • Date of receipt at the testing facility • Storage conditions post-receipt • Justification for the choice of positive control(s)
Test and reference items	Description of the fabric and composition of test and reference items	• Material • AI description » Name » Mode of action » Dosage in g AI/kg » Equivalent dosage in g AI/m^2 • Size • Colour
1.2.5 Sample preparation		
Sample preparation	Description of sample preparation	• Sampling plan, including diagram, for each sub-study, e.g. regeneration, wash resistance, and the location of where samples have been taken • The number of nets used in each study • Net cutting procedure(s) • Total number of samples by net/fabric type, batch and study arm • Sample size(s) • Sample storage conditions • Washing method » Container material » Water volume » Water hardness » Volume of soap » pH » Washing time (inc. agitation time where relevant) » Water temperature » Rotations per minute » Rinsing conditions » Drying conditions » Storage conditions » Resting time between washing completion and use in study(ies)

Table 1.2 Methods		
Report section	**Description**	**Critical parameters to report**
Methods		
		• Sample storage and shipment details for chemical analysis • Damage replication (where relevant)
1.2.6 Insecticide resistance status		
Insecticide resistance status of test systems and local vector populations	If insecticide resistance characterisation of test systems has been conducted as part of the study, describe the method. For semi-field studies (open and closed system), describe the methods used to determine the LC_{50} and LC_{90} to the AI(s) used in the proposed product.	• Insecticides tested • Insecticide dosages • Method used, i.e. WHO tube test or bottle bioassay • Total number of mosquitoes tested • Number of mosquitoes per replicate • Number of mosquitoes per test arm • Exposure duration • Post-exposure holding conditions and monitoring • Method for determining LC_{50} and LC_{90} (for local vector populations used in open-system semi-field studies and colonised strains used in closed-system semi-field studies)
1.2.7 Bioassay methods		
Bioassay methods	Description of bioassay method used: Cone tests (if used)	• Environmental conditions (temperature, relative humidity and light cycle) of testing room • Cone board angle • Starvation protocol (if any) • Transport protocol (if any) • Acclimatisation time and temperature(s) for test systems and materials • Time of day when tests were conducted • Number of mosquitoes per replicate • Total number of replicates and number of replicates per net piece and test arm • Exposure duration • Post-exposure holding duration and environmental conditions in holding room • Endpoint recording • Holding receptacle • Timing and placement of sugar sources

Table 1.2 Methods		
Report section	**Description**	**Critical parameters to report**
Methods		
Bioassay methods	Description of bioassay method used: tunnel tests (if used)	• Environmental conditions (temperature, relative humidity and light cycle) of testing room • Starvation protocol • Transport protocol (if any) • Acclimatisation time and temperature(s) for test systems and materials • Time of day when tests were conducted, including start and end times • Total number of replicates, and number of replicates per test arm and net piece • Number of mosquitoes per replicate • Exposure duration • Post-exposure holding duration and environmental conditions in holding room • Endpoint recording • Holding receptacle • Timing and placement of sugar sources
Bioassay methods	Description of bioassay method used: IACT (if used)	• Environmental conditions (temperature, relative humidity) • Starvation protocol • Transport protocol • Acclimatisation time and temperature(s) for test systems and materials • Time of day when tests were conducted, including start and end times • Number of mosquitoes per replicate • Total number of replicates and number of replicates per net piece and test arm • Exposure duration • Post-exposure holding duration and environmental conditions in holding room • Endpoint recording • Holding receptacle • Timing and placement of sugar sources
Bioassay methods	Description of bioassay method used: Experimental hut	• Hut design and measurements • Study arms • Decontamination and/or refurbishment procedure

Table 1.2 Methods		
Report section	**Description**	**Critical parameters to report**
Methods		
		• Baseline collections and scavenging rate estimation method • ITN hanging method • Storage conditions between testing nights • Method for recording environmental conditions (temperature, relative humidity) • Acclimatisation time for materials • Time of day when tests were conducted, including start and end times • Exposure duration • Transport protocol for collected mosquitoes • Mosquito identification procedure • Post-exposure holding duration and environmental conditions in holding room • Endpoint recording • Holding receptacle • Density of mosquitoes in holding receptacle • Timing and placement of sugar sources
1.2.8 Study design		
Study design	Baseline quality studies	• Number of samples per net, per batch and total • Selected bioassay method(s) • Selected chemical analysis method(s) • Number of bioassay test days and testing plan for each test day, including sample selection • Total number of replicates and number of replicates per net piece/fabric type and test arm
Study design	Wash regeneration studies	• Number of samples per net, per batch and total • Selected bioassay method(s) • Selected chemical analysis method(s) • Study duration • Total number of test days • Regeneration points tested, i.e. 0,1,3…40 days • Sample selection, i.e. random selection procedure • Sample acclimatisation conditions (duration, temperature, humidity) • Number of bioassay test days and testing plan for each test day, including sample selection

Table 1.2 Methods		
Report section	**Description**	**Critical parameters to report**
Methods		
		• Total number of replicates and number of replicates per net piece/fabric type and test arm
Study design	Wash resistance studies	• Number of samples per net, per batch and total • Selected bioassay method(s) • Selected chemical analysis method(s) • Total number of test days • Wash points tested, i.e. 0, 1, 3…25 washes • Sample selection, i.e. random selection procedure • Sample acclimatisation conditions (duration, temperature, humidity) • Number of bioassay test days and testing plan for each test day, including sample selection • Total number of replicates and number of replicates per net piece/fabric type and test arm
Study design	Semi-field studies	• Ethical review board permission • Environmental conditions (temperature, relative humidity) • Number, gender and age range of volunteers • Latin square design • Treatment allocation • Treatment rotation (ITN studies) • Volunteer allocation • Volunteer rotation • Collection period • Cleaning protocol • Total number of collection nights • Exposure duration • Mosquito collection method • Mosquito scoring method • Endpoint recording • Adverse effects monitoring
Study design	Supplemental bioassays to semi-field studies	• Number of samples per net, per batch and total • Selected bioassay method(s) • Selected chemical analysis method(s) • Total number of test days • Wash points tested, i.e. 0, 20 washes

Table 1.2 Methods		
Report section	**Description**	**Critical parameters to report**
Methods		
		• Sample selection, i.e. random selection procedure • Sample acclimatisation conditions (duration, temperature, humidity) • Number of bioassay test days and testing plan for each test day, including sample selection • Total number of replicates and number of replicates per net piece and test arm
1.2.9 Sample size calculations		
Sample size calculation for selected bioassays	Provide a full description of the calculations employed to arrive at the required sample size(s)	• Data source used to parameterize sample size calculations, e.g. previous studies, simulated data • Endpoint used to power study • Point estimate used • Procedure used to estimate the sample size, e.g. simulations, existing software/packages • Details of the procedure that was followed • Assumptions considered, e.g. effect size, power, variability, significance level, and justification(s) for the values of each assumption
Sample size calculations for semi-field studies	Provide a full description of the calculations employed to arrive at the required sample size(s)	• Data source used to parameterize sample size calculations, e.g. previous studies, simulated data • Endpoint used to power study • Point estimate used • Simulation procedure used to estimate the sample size/number of required nights of collection • Details of the procedure that was followed • Assumptions considered, e.g. effect size, power, variability (e.g. differences between huts/chambers, sleepers, collection nights), significance level, and justification(s) for the values of each assumption
1.2.10 Data analysis		
Data analysis for descriptive statistical analyses	Description of the descriptive statistical methods used to summarise and describe data in the report, including	• Number of samples • Number of mosquitoes per study arm • Mean/Median (as appropriate) • Standard deviation • Range

Table 1.2 Methods		
Report section	**Description**	**Critical parameters to report**
Methods		
	measurements of dispersion	• Precision measurements, e.g. intra- and inter-net/batch variability (where appropriate)
Data analysis for inferential statistical analyses	Description of the fitted inferential model used for each endpoint (including secondary endpoints)	• For each endpoint: » Type of model » Type of endpoint/data » Distribution » Fixed effects (including the type of variable, e.g. continuous or categorial/factor » Random effects (if any) » Justifications for any deviations from published guidance
1.2.11 Selection of wash interval for artificial ageing		
Selection of wash interval for artificial ageing	Description of the process for using the results of the wash regeneration study for the determination of the wash interval to be used for artificial ageing	

Table 1.3. Results

Report section	Description	Critical parameters to report
Results		
Characterisation of local vector population(s)		• Composition of local vector population, including sibling species and seasonal variation (where appropriate)
Baseline quality check	Narrative, tabular and graphical presentation of results of baseline quality check studies	• Evaluation of the results in terms of compliance with the required sample size • Descriptive statistics with measures of dispersion • Summarised tabular results ensuring that each bioassay method (if appropriate) is presented separately and that results for different fabric types and controls are clearly delineated • Intra- and inter-batch variability for each fabric type • Graphical presentation of results • Narrative description of results
Wash regeneration studies	Narrative, tabular and graphical presentation of results of wash regeneration studies Wash interval selected for artificial ageing	• Evaluation of the results in terms of compliance with the required sample size • Summary results for all primary and secondary endpoints, presented by study arm and batch with appropriate measures of dispersion (tabular) • Inferential statistical results (tabular) • Graphical presentation of results • Narrative description of results • Wash interval selected for artificial ageing • The code used for statistical analyses in the format that it was produced (separate file)
Wash resistance studies	Narrative, tabular and graphical presentation of results of wash resistance studies	• Evaluation of the results in terms of compliance with the required sample size • Summary results for all primary and secondary endpoints, presented by study arm and batch with appropriate measures of dispersion (tabular) • Inferential statistical results (tabular) • Graphical presentation of results • Narrative description of results

Table 1.3. Results		
Report section	**Description**	**Critical parameters to report**
Results		
		• The code used for statistical analyses in the format that it was produced (separate file)
Semi-field studies	Narrative, tabular and graphical presentation of results of semi-field studies	• Evaluation of the results in terms of compliance with the required sample size • Summary results for all primary and secondary endpoints, presented by study arm with appropriate measures of dispersion (tabular) • Inferential statistical results (tabular) • Non-inferiority analysis (where appropriate) (tabular, graphical) • LC_{50} of the local vector population to the AI(s) • LC_{90} of the local vector population to the AI(s) • Graphical presentation of results • Narrative description of results • The code used for statistical analyses in the format that it was produced (separate file)
Supplemental bioassays	Narrative, tabular and graphical presentation of results of supplemental bioassays to semi-field studies	• Evaluation of the results in terms of compliance with the required sample size • Summary results for all primary and secondary endpoints, presented by study arm with appropriate measures of dispersion (tabular) • Inferential statistical results (tabular) • Graphical presentation of results • Narrative description of results • The code used for statistical analyses in the format that it was produced (separate file)

Table 1.4. Discussion

Report section	Description	Critical parameters to report
Discussion and conclusions		
Discussion	For each study or sub-study, e.g. small-scale studies in natural breeding sites, an interpretative discussion of the results must be provided.	• Interpretation of the study/sub-study results with reference to the criteria for study acceptability identified in Criteria for study acceptance, e.g. evaluation of the scientific validity of the study based on the parameters of the study and the results of controls » Specific discussions on any methodological deviations, anomalies in results, or other factors which may have impacted the results should be included. • Interpretation of the study/sub-study results with reference to the criteria for study acceptability identified in the Criteria for study acceptance with regards to the evaluation of the proposed product as having met the requirements for prequalification for that particular study type, e.g. laboratory assessment. » Specific discussions on any methodological deviations, anomalies in results, or other factors which may have impacted the results should be included.