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In reply please  
refer to: V2-447-3/DS/VP/1

Your reference: 005-002, PPQC2020-010

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31 May 2024

**WHO Prequalification Team (PQT) – Vector Control Products Assessment (VCP)  
Post-Prequalification Change (PPQC)  
WHO Product ID: 005-002  
Case ID: PPQC2020-010**

Dear Ms Hadi,

Thank you for submitting your company's Post-Prequalification Change (PPQC) application on 7 July 2020 for the following product:

- **PermaNet 3.0 – PQ Ref # 005-002**

Your submission of long-term community studies for the prequalified product PermaNet 3.0 has been reviewed and found acceptable. The complete change assessment is attached to this acceptance letter.

Our files have been updated accordingly.

Yours sincerely,

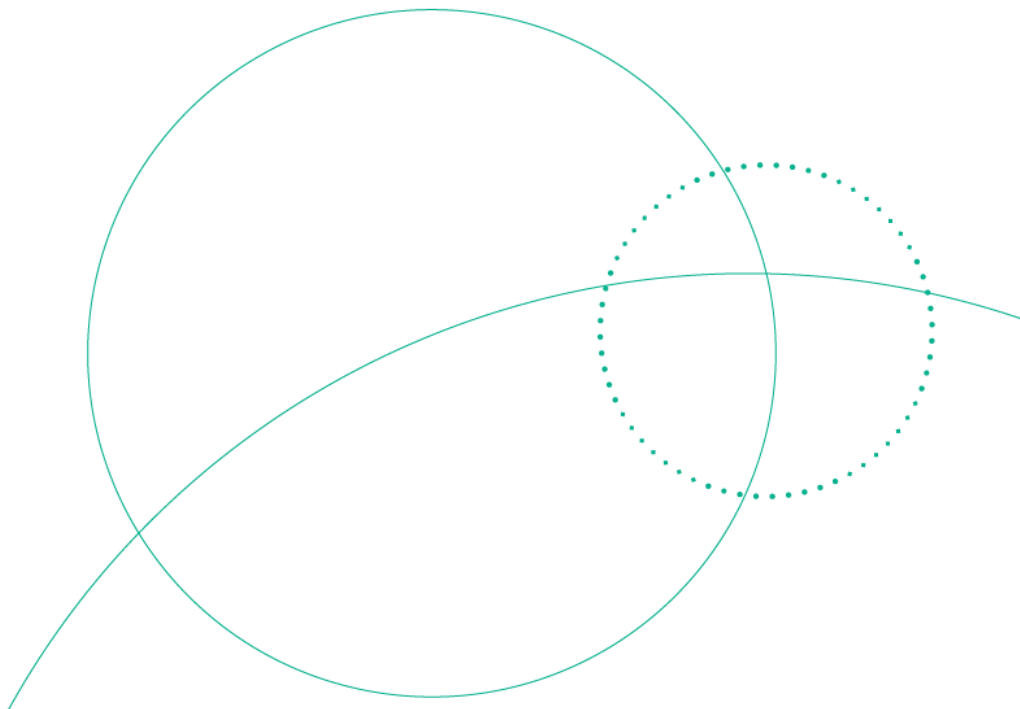
Mr Dominic Schuler  
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WHO Prequalification Programme / Vector Control Product Assessment

# WHO Public Assessment Report: Change assessment

PermaNet 3.0  
(Vestergaard Sarl) 005-002

Long-term community studies assessment



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# 1. Introduction

The primary purpose for the use of a pesticide is the control of a pest, including disease transmitting vectors. Vector control tools, including formulated pesticides, which provide effective management or control of vectors, may be used as part of a resistance management programme. Vector control products for use in public health are a component of Integrated Vector Management (IVM), which is a programme that relies on a suite of diverse interventions and implementations of best practices to manage the vector and chemical/behavioural resistance.

PermaNet 3.0 is an ITN incorporated with 4 g/kg deltamethrin and 25 g/kg of the synergist piperonyl butoxide (PBO) in roof fabric and coated with 2.8 g/kg deltamethrin in the side panel fabric. The product is intended to provide personal and community protection from Anopheline mosquitoes as part of malaria control programmes. The premise of the combination of the insecticide and the synergist is that the deltamethrin insecticidal activity provides knockdown and/or kill of mosquitoes and the PBO inhibits mixed function oxidases implicated in resistance in pyrethroid resistant *Anopheles spp.* malaria vectors.

Community studies to characterise the performance of PermaNet 3.0 under operational conditions using bioassays to characterise the availability of active ingredients (AI) and the insecticidal effect of the fabric of the ITN on Anopheline mosquitoes at selected durations of operational use were submitted to WHO as a post-prequalification change application (PPQC2020-010).

## 2. Long-term community studies

Studies conducted in community settings include the investigation of endpoints other than mortality, knockdown and blood-feeding inhibition, for example the community acceptance, fabric integrity and attrition rate of the ITN under investigation. Based on the existing requirements and established decision framework, mosquito knockdown and mortality are considered the primary endpoints for assessment. Therefore, results for these are included within the summaries of these studies. Calculations of blood-feeding inhibition were also included for further entomological characterization of the product.

### 2.1 Operational studies and supplementary bioassays

Data on the operational performance of PermaNet 3.0 in long-term community studies were provided. These data were obtained from studies conducted according to established standards. These summary results are based on ITNs drawn from batches 1 156 14 for Ghana, 1 159 14 for Kenya, and 1 088 14 for India.

Three long-term community studies were presented to evaluate the operational performance of PermaNet 3.0, in Ghana, Kenya and India, conducted 2014-2018. All three studies were conducted as prospective, household-randomised trials. The endpoints used to evaluate bioavailability were 60-minute post-exposure knockdown and 24-hour mortality in cone tests and 24-hour mortality and blood-feeding inhibition in tunnel tests, and in bioassays PermaNet 3.0 was considered met the WHO requirements for community studies if, after three years, at least 80% of sampled ITNs met the criteria of >95% KD or 80% mortality in cone tests and/or >80% mortality or >90% blood-feeding inhibition in tunnel tests.

The negative control for bioassays was untreated net. In the household-randomised trials, the positive control was a prequalified product treated with 1.4 g/kg deltamethrin, hereafter referred to as PC1.

One thousand, seven hundred and fifty-five PermaNet 3.0 ITNs were distributed in the study in Ghana, 1,508 ITNs were distributed in the study in Kenya and 869 ITNs were distributed in the study in India. A randomised sampled of thirty ITNs were sampled per study arm at the baseline of each study, and at pre-determined time points of 6, 12, 18, 24 and 30 months. At the conclusion of the study (36 months), fifty ITNs were sampled from each study arm. Sampled ITNs were subject to destructive sampling and the sampled fabric pieces were used in bioassays to determine the bioavailability of the treatments on the fabric and analysed for chemical content using the high-performance liquid chromatography (HPLC) method referenced in the product specifications. WHO cone tests and tunnel tests were the experimental methods used in bioavailability experiments.

In bioassays, the product was tested against pyrethroid susceptible colonised mosquitoes of: *An. gambiae* s.s. Kisumu strain in Ghana and Kenya, and *An. culicifacies* and *An. stephensi* strains in India. The insecticide resistance status of the *An. gambiae* s.l. vector population in the study site in Ghana was characterised yearly during the study using F1 mosquitoes; this population consistently demonstrated <30% mortality following exposure to the diagnostic doses of permethrin, deltamethrin and cyfluthrin.

The results from bioavailability experiments are presented in Table 1, presented as the proportion of sampled ITNs at each time point that met the current WHO criteria for bioassays. Greater than 80% of PermaNet 3.0 ITNs sampled from the community study sites in Ghana, Kenya and India that had been used for three years under routine household usage conditions met the applicable WHO bioassay criteria for determining the bioavailability of ITN treatments, when tested against pyrethroid susceptible mosquito strains.

**Table 1. Proportion of sampled ITNs in long-term community studies conducted in Ghana, Kenya and India that met the applicable WHO criteria for demonstration of bioavailability in laboratory bioassays (>95% KD or 80% mortality in cone tests and/or >80% mortality or >90% blood-feeding inhibition in tunnel tests).**

Product	Number of sampled ITNs and the proportion passing bioavailability criteria	Study timepoint						
		Baseline	6	12	18	24	30	36
<b>Ghana (<i>An. gambiae</i> s.s. Kisumu strain)</b>								
PermaNet 3.0	Sampled ITNs	30	30	30	30	30	30	50
	Proportion passed (%)	100	100	100	100	96.7	93.3	80
PC1	Sampled ITNs	30	30	30	30	30	30	50
	Proportion passed (%)	100	100	100	96.7	100	90	58
<b>Kenya (<i>An. gambiae</i> s.s. Kisumu strain)</b>								
PermaNet 3.0 roof	Sampled ITNs	30	30	29	29	30	31	50
	Proportion passed (%)	100	100	100	97	93	97	94
PermaNet 3.0 sides	Sampled ITNs	30	30	30	29	30	32	50
	Proportion passed (%)	100	100	100	100	87	100	96
PC1	Sampled ITNs	30	30	30	30	30	29	50
	Proportion passed (%)	100	100	97	97	87	86	90
<b>India (<i>An. culicifacies</i> and <i>An. stephensi</i>)</b>								
PermaNet 3.0 roof	Sampled ITNs	30	30	30	30	30	30	50
	Proportion passed (%)	100	93.3	100	93.3	100	100	98
PermaNet 3.0 side upper panel	Sampled ITNs	30	30	30	30	30	30	50
	Proportion passed (%)	100	100	90	100	100	86.7	92
PermaNet 3.0 side lower panel	Sampled ITNs	30	30	30	30	30	30	50
	Proportion passed (%)	100	100	100	100	100	90	96
PC1	Sampled ITNs	30	30	30	30	30	30	50
	Proportion passed (%)	96.7	93.3	100	93.3	100	100	100

### 2.1.1 Chemical characterization

Data on the deltamethrin and piperonyl butoxide content of sampled ITNs in long-term community studies conducted in Ghana, Kenya and India were provided. The data were collected at the following timepoints: baseline, 12-, 24- and 36- months post-net distribution.

A summary of the chemical characterization data is presented in Table 2. The chemical analysis of deltamethrin content in PC1 (whole net) and PermaNet 3.0 (sides and roof) at the baseline were within the manufacturer's specifications for all study sites. The mean PBO content on the roof of PermaNet 3.0 at the baseline was also within manufacturer's specifications for all study sites.

**Table 2. AI content of sampled ITNs in long-term community studies conducted in Ghana, Kenya and India.**

Net and fabric type	AI content	Study timepoint			
		Baseline	12	24	36
<b>Ghana</b>					
PermaNet 3.0 (sides)	Number of net samples	30	30	30	50
	Mean Deltamethrin content (g/kg)	1.93	1.49	1.20	0.96
	RSD (%)*	7.6			
	Deltamethrin content lost (%)	-	23	38	50
PermaNet 3.0 (roof)	Number of net samples	30	30	30	50
	Mean Deltamethrin content (g/kg)	4.65	3.77	3.60	3.24
	RSD (%)	2.9			
	Deltamethrin content lost (%)	-	19	23	30
	Mean PBO content (g/kg)	25.62	15.64	12.4	9.99
	RSD (%)	2.2			
	PBO content lost (%)	-	39	52	61
PC1	Number of net samples	30	30	30	50
	Mean Deltamethrin content (g/kg)	1.27	0.97	0.88	0.62
	RSD (%)	5.6			
	Deltamethrin content lost (%)	-	24	31	51
<b>Kenya</b>					
PermaNet 3.0 (sides)	Mean Deltamethrin content (g/kg)	1.9	1.3	1.1	0.8
	RSD (%)				
	Deltamethrin content lost (%)	-	32	42	58
PermaNet 3.0 (roof)	Mean Deltamethrin content (g/kg)	4.7	3.1	2.5	2.7
	RSD (%)				



	<b>Deltamethrin content lost (%)</b>	-	34	47	43
	<b>Mean PBO content (g/kg)</b>	26.1	11	6.6	5.3
	<b>RSD (%)</b>				
	<b>PBO content lost (%)</b>	-	58	75	80
PC1	<b>Mean Deltamethrin content (g/kg)</b>	1.2	0.9	0.7	0.4
	<b>RSD (%)</b>				
	<b>Deltamethrin content lost (%)</b>	-	25	42	67
<b>India</b>					
PermaNet 3.0 side lower panel	<b>Number of net samples</b>	30	30	30	50
	<b>Mean Deltamethrin content (g/kg)</b>	2.86	1.79	1.17	0.88
	<b>RSD (%)</b>	9.2	42.2	69	94
	<b>Deltamethrin content lost (%)</b>	-2.14	36.07	58.21	69
PermaNet 3.0 side upper panel	<b>Mean Deltamethrin content (g/kg)</b>	2.69	1.88	1.09	0.79
	<b>RSD (%)</b>	5.8	36.8	72	98
	<b>Deltamethrin content lost (%)</b>	3.93	32.86	61.07	71
PermaNet 3.0 roof	<b>Mean Deltamethrin content (g/kg)</b>	4.32	3.34	2.8	2.3
	<b>RSD (%)</b>	3.1	16.3	18	25
	<b>Deltamethrin content lost (%)</b>	-8.00	16.50	30.0	47
	<b>Mean PBO content (g/kg)</b>	25.54	11.46	6.8	5.1
	<b>RSD (%)</b>	6.7	52.7	74	95
	<b>PBO content lost (%)</b>	-2.16	54.16	72.8	80.0
PC1	<b>Number of net samples</b>	30	30	30	50
	<b>Mean Deltamethrin content (g/kg)</b>	1.32	0.99	0.6	0.45
	<b>RSD (%)</b>	10.7	42.5	55	88
	<b>Deltamethrin content lost (%)</b>	5.71	29.29	57.14	66.0

\* Between net variation, expressed as the relative standard deviation (RSD)

## 2.2 Operational studies and chemical characterisation conclusions

The submitted long-term community studies demonstrate that the bioavailability of sampled PermaNet 3.0 ITNs after three years of routine household use was sustained against pyrethroid susceptible *Anopheles spp.* using the cone and tunnel tests. The deltamethrin and PBO content of the distributed ITNs were within the manufacturer's specifications at baseline. At 12 months post-distribution, the deltamethrin content of sampled nets was between 16.5% and 36% of the baseline content; at 24 months and 36 months post-distribution the content was between 23% and 61.07% and between 30% and 71% of the baseline content, respectively. The PBO content of sampled ITNs was between 39% and 54.16% of the baseline content at 12 months, between 52% and 72.8% at 24 months and between 61% and 80% at 36 months.

## 3. Long-term community studies conclusions

Based on the studies and information provided, all data requirements for the prequalification assessment of long-term community studies have been satisfied. These data have been relied upon to assess the bioavailability and the impact on pyrethroid susceptible laboratory mosquitoes of the PermaNet 3.0 product for the purpose of characterising the fabric of the product after pre-determined durations of household use under routine conditions. The long-term community studies component of the dossier is considered complete, and the assessment of the submitted information supports the continued prequalification of the product.