World Health Organization

WHO Prequalification Programme / Vector Control Product Assessment

WHO Public Assessment Report: WHOPAR Part 5

Optica ULV

(Clarke International)

P-11637

Efficacy Assessment

Contents

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.

Optica ULV is an ultra-low volume (ULV) liquid containing 1% w/w broflanilide and is intended to be used as a non-thermal aerosol mist for the control of *Aedes* mosquitoes as an outdoor and indoor space spray. The insecticidal mode of action on mosquitoes is through binding to the inter-subunit allosteric site on the insect γ-aminobutyric acid (GABA) receptor, thus inhibiting neurotransmission. The product was tested at 55 - 110 ml/hectare (ha) in outdoor studies and 5.5 – 11.1 ml/1,000 m^2 in indoor studies, as per the manufacturer's recommended application rate range.

Laboratory studies, and small-scale outdoor and indoor studies to characterize the performance of Optica ULV were submitted to WHO as part of the prequalification dossier.

2 Laboratory Studies

Laboratory studies to characterize the effect of the formulated Optica ULV on *Aedes* spp. were submitted to WHO as part of the prequalification dossier.

Supplementary evidence on the characterization of the formulated Optica ULV product under laboratory conditions was submitted. These data were obtained from studies conducted according to established standards and/or Good Laboratory Practices (GLP).

2.1 Intrinsic insecticidal activity of the Optica ULV product

One supplementary study was presented to characterize the intrinsic insecticidal activity of Optica ULV and determine the LD_{50} and LD_{95}. The endpoint used in the characterisation of the product was 48-hour mortality.

Two *Aedes aegypti* test systems were used in the study: *Aedes aegypti* Rockefeller strain, and *Ae. aegypti* Monterrey strain. The colonised Rockefeller test system was used as an insecticide susceptible reference strain; the Monterrey test system was from the local vector population and carries pyrethroid resistance mediated by *kdr* mutations Ile1016 and Cys1534.

The range of concentrations of Optica ULV that were tested in the laboratory study to determine the intrinsic insecticidal activity of the formulated product are presented in Table 1, and the results of the study are presented in Table 2. The LD_{50} and LD_{95} results as determined using one *Ae. aegypti* test

system and topical applications of the formulated Optica ULV product are presented in Table 3. In the intrinsic insecticidal experiments, mortality greater than 90% was observed for all doses greater than 0.19 (µg/mg) by 48 hours post-exposure. The LD_{95} for the resistant test system was 0.416 µg/mg at 48 hours post-exposure.

Table 1. Optica ULV concentrations tested in mortality range finding experiments

Concentration (µg/mg)	Control	Dose A	Dose B	Dose C	Dose D	Dose E
Optica ULV	0	0.19	0.37	1.9	3.8	5.58

Table 2 is presented on page 5.

Table 3. LD_{50}, LD_{95}, and RR50 concentrations of Optica ULV as determined using topical applications against *Ae. aegypti* Rockefeller and Monterrey test systems.

Mosquito Strain	Sample size (n)	Timepoint	LD_{50} µg/mg (95% CI)	LD_{95} µg/mg (95% CI)	RR50 (95% CI)
Ae. aegypti Rockefeller	5,171	24	0.227 (0.223 – 0.231)	0.599 (0.566 – 0.633)	-
		48	0.18 (0.179 – 0.182)	0.417 (0.401 – 0.432)	-
Ae. aegypti Monterrey	5,171	24	0.235 (0.229 – 0.241)	0.655 (0.596 – 0.713)	0.599 (0.566 – 0.633)
		48	0.192 (0.191 – 0.194)	0.416 (0.402 – 0.429)	0.417 (0.401 – 0.432)

Table 2. Intrinsic insecticidal activity of Optica ULV against *Ae. aegypti* Rockefeller and Monterrey strains tested using topical applications of formulated product.

Dose (µg/mg)	Product concentration (µg)	Mean mortality (%, 95% CI)								
		15'	30'	45'	60'	75'	90'	12 h	24 h	48 h
Ae. aegypti (Rockefeller)										
0.19	0.54	0.0	0.0	0.0	0.0	1.9 (1.1 - 2.7)	2.4 (1.4 - 3.3)	24.1 (21.5 - 26.7)	35.6 (32.7 - 38.5)	52.8 (49.8 - 55.8)
0.37	1.08	0.0	0.0	0.0	0.0	2.6 (1.6 - 3.6)	3.3 (2.2 - 4.4)	45.0 (41.9 - 48.1)	81.8 (79.5 - 84.2)	92.8 (91.1 - 94.4)
1.9	5.40	76.8 (74.2 - 79.3)	79.3 (76.9 - 81.8)	91.6 (89.9 - 93.3)	100.0	100.0	100.0	100.0	100.0	100.0
3.8	10.80	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
5.58	16.20	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
Ae. aegypti (Monterrey)										
0.19	0.54	0.0	0.0	0.0	0.0	2.4 (1.5 - 3.3)	2.9 (1.9 - 3.9)	22.6 (20.1 - 25.1)	36.2 (33.3 - 39.1)	50.2 (47.2 - 53.3)
0.37	1.08	0.0	0.0	0.0	0.0	2.7 (1.7 - 3.7)	3.4 (2.3 - 4.5)	50.3 (47.2 - 53.4)	80.7 (78.2 - 83.1)	93.5 (91.9 - 95.0)
1.9	5.40	75.5 (72.9 - 78.2)	79.1 (76.6 - 81.6)	92.8 (91.2 - 94.3)	100.0	100.0	100.0	100.0	100.0	100.0
3.8	10.80	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
5.58	16.20	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0

3 Small-scale field studies

Based on the existing requirements and established decision framework, mosquito mortality is considered the primary endpoint for assessment.

Data on the semi-field performance of Optica ULV were provided. These data were obtained from studies conducted according to established standards and/or Good Laboratory Practices (GLP).

3.1 Outdoor applications

Seven small-scale studies (four primary evidence, three supplementary evidence) were presented to characterize the efficacy of the product in outdoor settings. The primary evidence studies were conducted in Tanzania (Study 1), Malaysia (Study 2) and Brazil (Studies 3 and 4). The supplementary evidence studies were conducted in Mexico (Study 5) and the United States of America (Studies 6 and 7).

In all studies, the product was tested in open areas that contained no obstructions to the spray cloud. The application rates of Optica ULV were 54-55 ml/hectare (ha) (Studies 1, 2, 3, 5, 6), 73 ml/ha (Study 5) and 109-110 ml/ha (Studies 1, 2, 4, 5, 7). The endpoint used to assess the entomological efficacy of the product was 48-hour mortality, assessed using cages of mosquitoes placed at 25, 50, 75 and 100 metres downwind from the spray line (30.5, 61 and 91.5 metres in supplementary studies conducted in the United States of America).

The product was predominantly tested using insecticide susceptible strains of *Ae. aegypti* and *Aedes albopictus,* excepting Study 1, in which both insecticide susceptible and insecticide resistant strains of *Ae. aegypti* were used. The results for the insecticide susceptibility testing of the resistant *Ae. aegypti* Kinondoni test system are presented in Table 4.

The results for the small-scale outdoor studies are presented in Table 5 (Studies 1-7). In all studies, mortality greater than 90% was observed by 48 hours post-spray at all tested dosages and distances; at 24 hours post-spray, mortality greater than 80% was observed.

Table 4. Insecticide susceptibility testing of *Ae. aegypti* Kinondoni test system in Tanzania, using WHO cylinder tests.

Test system	Classification	M24 (%, 95% CI)					
		Permethrin (4%)	Deltamethrin (0.03%)	Alpha-cypermethrin (0.05%)	Lambda-cyhalothrin (0.05%)	Bendiocarb (0.1%)	Pirimiphos methyl (60 mg/m^2)
Ae. aegypti (Kinondoni)	Insecticide resistant	3 (0.93-5.07)	28 (21.24-34.75)	16 (7.06-24.94)	34 (18.70-49.30)	97 (94.93 -99.07)	29 (19.82-38.17)

Table 5. Observed knockdown (KD) and mortality in small-scale outdoor studies conducted using Optica ULV against *Ae. aegypti spp.* in Tanzania, Malaysia, Brazil, Mexico, and The United States of America.

Application rate (ml/ha)	Distance (m)	Mean mortality (%, 95% CI)				Application rate (ml/ha)	Distance (m)	Mean mortality (%, 95% CI)			
		KD60*	M12	M24	M48			KD60*	M12	M24	M48
Ae. aegypti (Bagamoyo, Tanzania)						*Ae. aegypti* (Kinondoni, Tanzania, insecticide resistant)					
Control				2 (0 – 4)		Control				2 (0 – 5)	
55	25	22 (3 – 37)	100	100	100	55	25	14 (7 – 22)	99 (99 – 100)	100	100
	50	12 (5 – 19)	98 (95-100)	100 (99 -100)	100		50	14 (0 - 28)	96 (88 – 100)	98 (95 – 100)	100 (99 – 100)
	75	5 (1 – 9)	96 (91 – 100)	98 (96-100)	99 (97-100)		75	9 (2 – 16)	92 (78 – 100)	94 (85 – 100)	99 (96 – 100)
	100	3 (1 – 5)	99 (97 – 100)	100	100		100	3 (1 – 5)	100 (99 – 100)	100	100
	Overall	11 (3 - 24)	98 (96 - 101)	100	100		Overall	10 (2 - 18)	97 (91 - 103)	98 (94 - 103)	100
110	25	74 (56 – 93)	97 (91 - 1000	100	100	110	25	62 (46 – 79)	100	100	100
	50	58 (37 – 80)	99 (97 – 100)	100	100		50	35 (17 – 52)	93 (84 – 100)	96 (91 – 100)	100
	75	34 (21 – 46)	99 (97 – 100)	100 (99 – 100)	100		75	13 (3 – 24)	99 (98 – 100)	100	100
	100	31 (13 - 49)	100	100	100		100	9 (3 – 16)	100 (99 – 100)	100	100
	Overall	49 (17 - 82)	99 (97 - 100)	100.0	100.0		Overall	30 (9 - 69)	98 (93 - 100)	99 (96 - 100)	100.0
Ae. aegypti (VCRU, Malaysia)						*Ae. albopictus* (VCRU, Malaysia)					
Control		0		0		Control		0		0	
55	25	7.67 (2.77 - 12.57)	100.0	100.0	100.0	55	25	5.33 (1.09 - 9.57)	98.33 (96.63 - 100)	99.67 (98.94 - 100)	100.0
	50	5.33 (1.52 - 9.14)	100.0	100.0	100.0		50	3.67 (1.14 - 6.2)	95.67 (86.13 - 100)	99.67 (98.94 - 100)	100.0

Table 5. Observed knockdown (KD) and mortality in small-scale outdoor studies conducted using Optica ULV against *Ae. aegypti spp.* in Tanzania, Malaysia, Brazil, Mexico, and The United States of America.

Application rate (ml/ha)	Distance (m)	Mean mortality (%, 95% CI)				Application rate (ml/ha)	Distance (m)	Mean mortality (%, 95% CI)			
		KD60*	M12	M24	M48			KD60*	M12	M24	M48
	75	4.33 (0.57 - 9.23)	99.67 (98.94 - 100)	100.0	100.0		75	1.0 (0.15 - 2.15)	98.67 (95.74 - 100)	100.0	100.0
	100	4.67 (1.64 - 7.7)	98.33 (96.04 - 100)	100.0	100.0		100	2.33 (0.04 - 4.62)	95.33 (92.71 - 97.95)	99.67 (98.94 - 100)	100.0
	Overall	5.5 (3.59 - 7.41)	99.5 (98.93 - 100)	100.0	100.0		Overall	3.08 (1.76 - 4.4)	97.0 (94.65 - 99.35)	99.75 (99.47 - 100)	100.0
Control		0		0		Control		0		0	
110	25	16.0 (13.58 -18.42)	100.0	100.0	100.0	110	25	14.67 (10.86 -18.48)	100.0	100.0	100.0
	50	14.0 (11.46- 16.54)	100.0	100.0	100.0		50	12.33 (8.66 - 16.0)	100.0	100.0	100.0
	75	10.67 (7.54 - 13.8)	100.0	100.0	100.0		75	9.67 (7.65 - 11.69)	100.0	100.0	100.0
	100	9.33 (7.07 - 11.59)	99.67 (98.94 - 100)	100.0	100.0		100	8.67 (6.85 - 10.49)	98.0 (95.97 - 100)	100.0	100.0
	Overall	12.5 (11.11 -13.89)	99.92 (99.75 - 100)	100.0	100.0		Overall	11.33 (9.85 - 12.81)	99.5 (98.98 - 100)	100.0	100.0
Aedes aegypti (Rockefeller, Brazil)						*Aedes aegypti* (United States of America)					
Control		0.0	0.0	0.0	0.5 (0.0 - 1.5)	Control			0.85 (0.51 - 1.19)	1.78 (1.28 - 2.28)	3.5 (2.68 - 4.32)
54	25	7.5 (4.6 - 10.4)	100.0	100.0	100.0	54.8	30.5		21.8 (19.1 - 24.5)	76.3 (73.6 - 79.1)	97.0 (95.9 - 98.1)
	50	11.0 (4.7 - 17.3)	100.0	100.0	100.0		61		17.5 (15.0 - 20.0)	69.3 (66.2 - 72.4)	94.2 (92.6 - 95.7)
	75	14.2 (7.8 - 20.7)	100.0	100.0	100.0		91.5		10.7 (8.6 - 12.7)	59.5 (56.3 - 62.8)	92.3 (90.5 - 94.0)
	100	12.5 (7.0 - 18.0)	100.0	100.0	100.0						
	Overall	10.1 (7.5 - 12.6)	88.9 (81.6 - 96.2)	88.9 (81.6 - 96.2)	88.9 (81.7 - 96.2)		Overall		16.6 (15.2, - 18.1)	68.4 (66.6 - 70.2)	94.5 (93.6 - 95.4)

Table 5. Observed knockdown (KD) and mortality in small-scale outdoor studies conducted using Optica ULV against *Ae. aegypti spp.* in Tanzania, Malaysia, Brazil, Mexico, and The United States of America.

Application rate (ml/ha)	Distance (m)	Mean mortality (%, 95% CI)				Application rate (ml/ha)	Distance (m)	Mean mortality (%, 95% CI)			
		KD60*	M12	M24	M48			KD60*	M12	M24	M48
Control		0.0	0.0	0.0	0.0				2.73 (1.29 - 4.17)	4.65 (2.71 - 6.59)	5.92 (3.57 - 8.27)
109	25	11.0 (5.6 - 16.4)	100.0	100.0	100.0	109.6	30.5		44.3 (37.9 - 50.7)	78.5 (73.2 - 83.8)	100.0
	50	5.5 (1.5 - 9.5)	100.0	100.0	100.0		61		62.0 (55.7 - 68.3)	79.9 (74.7 - 85.1)	100.0
	75	2.0 (0.4 - 3.6)	100.0	100.0	100.0		91.5		51.1 (44.6 - 57.7)	82.5 (77.5 - 87.5)	99.1 (97.9 - 100)
	100	4.8 (2.6 - 6.9)	100.0	100.0	100.0						
	Overall	5.2 (3.4 - 6.9)	88.9 (81.6 - 96.2)	88.9 (81.6 - 96.2)	88.9 (81.6 - 96.2)		Overall		52.5 (48.7 - 56.3)	80.3 (77.3 - 83.3)	99.7 (99.3 - 100)
Aedes aegypti (San Lorenzo, Mexico)						*Aedes aegypti* (San Lorenzo, Mexico)					
Control		0	0	0	0	Control		0	0	0	0
55	25	25.0 (21.23 -28.77)	75.67 (71.41 - 9.93)	94.0 (89.47 -98.53)	100.0	110	25	64.0 (57.06 -70.94)	98.0 (95.97 - 100)	98.33 (96.31 - 100)	100.0
	50	30.0 (24.32 -35.68)	70.33 (64.65 -76.01)	92.33 (86.86 -97.8)	99.33 (97.86 - 100)		50	55.67 (51.84 - 59.5)	97.33 (95.35 - 99.31)	98.67 (97.01 - 100)	100.0
	75	25.33 (19.07 -31.59)	58.33 (49.77 -66.89)	91.0 (87.23 -94.77)	99.67 (98.94 - 100)		75	50.0 (43.82 -56.18)	94.33 (91.37 - 97.29)	95.33 (92.11 -98.55)	100.0
	100	15.67 (8.95 - 22.39)	49.33 (43.07 -55.59)	90.67 (85.91 -95.43)	99.67 (98.94 - 100)		100	61.33 (54.8 - 67.86)	96.0 (94.12 - 97.88)	97.0 (94.8 - 99.2)	100.0
	Overall	24.0 (21.05 -26.95)	63.42 (59.29 -67.55)	92.0 (89.9 - 94.1)	99.67 (99.27 - 100)		Overall	57.75 (54.66 -60.84)	96.42 (95.34 - 97.5)	97.33 (96.22 -98.44)	100.0
Control		0	0	0	0						
73	25	36.67 (25.26 -48.08)	98.33 (96.63 - 100)	100.0	100.0						
	50	40.0 (28.79 -51.21)	99.33 (97.86 - 100)	100.0	100.0						
	75	46.33	97.33	99.0	100.0						

Table 5. Observed knockdown (KD) and mortality in small-scale outdoor studies conducted using Optica ULV against *Ae. aegypti spp.* in Tanzania, Malaysia, Brazil, Mexico, and The United States of America.

Application rate (ml/ha)	Distance (m)	Mean mortality (%, 95% CI)				Application rate (ml/ha)	Distance (m)	Mean mortality (%, 95% CI)			
		KD60*	M12	M24	M48			KD60*	M12	M24	M48
		(34.0 - 58.66)	(95.35 -99.31)	(97.42 - 100)							
	100	32.0 (20.23 -43.77)	96.33 (92.66 - 100)	98.67 (97.01 - 100)	100.0						
	Overall	38.75 (33.36 -44.14)	97.83 (96.73 -98.93)	99.42 (98.88 -99.96)	100.0						

*M1 for studies conducted in Tanzania and Mexico

3.2 Indoor applications

Four small-scale studies (three primary evidence, one supplementary evidence) were presented to characterize the efficacy of the product in indoor settings. The primary evidence studies were conducted in Malaysia (Study 2) and Brazil (Studies 9 and 10) and the supplementary evidence study was conducted in Mexico (Study 5). In all studies, five-room houses were used as testing sites; the negative control in each study was an untreated house. The application rates of Optica ULV were 5.5 ml/1,000 m^2 (Studies 2, 9 and 5), 7.3 ml/1,000m^2 (Study 5) and 11 ml/1,000m^2 (Studies 2, 10 and 5). The endpoint used to assess the entomological efficacy of the product was 48-hour mortality, assessed using cages of mosquitoes placed in test and control houses.

In Study 2, two insecticide susceptible mosquito test systems were used: *Ae. aegypti* and *Ae. albopictus*. In Studies 9 and 10, the mosquito test system used was insecticide susceptible *Aedes aegypti* Rockefeller strain, and in Study 5 the test system was insecticide susceptible *Aedes aegypti* San Lorenzo strain.

The results for the small-scale indoor studies are presented in Table 6 (Studies 2, 5, 9 - 10). In Study 2, <15% knockdown was observed 60 minutes post-exposure and >90% mortality was observed at 12 hours post-exposure for both application dosages and test systems. In Studies 9 and 10, mortality greater than 90% was observed four hours post-spray and 100% mortality was observed by six hours post-spray at all application rates. In Study 5, 100% knockdown was observed one-hour post-spray and 100% mortality was observed at twelve hours post-spray for all application rates.

Table 6. Observed knockdown (KD) and mortality in indoor small-scale studies conducted using Optica ULV against *Ae. aegypti* VCRU, Rockefeller and San Lorenzo strains in Malaysia, Brazil and Mexico and *Ae. albopictus* in Malaysia.

Application rate (ml/1,000m²)	Mean mortality (%, 95% CI)								
	KD60	M2	M3	M4	M5	M6	M12	M24	M48
Ae. aegypti (VCRU, Malaysia)									
Control	0.0	-	-	-	-	-	-	-	-
5.5	2.73 (1.61 - 3.85)	-	-	-	-	-	95.93 (94.83 - 97.03)	100	100
11	13.53 (7.6, -19.46)	-	-	-	-	-	99.47 (99.12 - 99.82)	100	100
Ae. albopictus (VCRU, Malaysia)									
Control	0.0	-	-	-	-	-	-	-	-
5.5	3.13 (1.97 - 4.29)	-	-	-	-	-	96.0 (95.07 - 96.93)	100	100
11	7.53 (3.98 - 11.08)	-	-	-	-	-	99.27 (98.82 -99.72)	100	100
Ae. aegypti (Rockefeller, Brazil)									
Control	0.0	0.33 (0 -1.76)	0.33 (0 - 1.76)	0.33 (0 - 1.76)	0.33 (0 - 1.76)	0.33 (0 - 1.76)	0.33 (0 - 1.76)	0.33 (0 - 1.76)	0.33 (0 - 1.76)
5.5	40.0 (28.6 - 51.4)	69.0 (45.04 - 92.96)	88.33 (72.36 - 104.3)	97.33 (91.08 - 103.58)	99.33 (96.46 - 102.2)	100.0	100.0	100.0	100.0
11	34.49 (24.07 - 44.91)	70.33 (26.57 - 100)	89.67 (72.76 - 100)	97.67 (96.24 - 99.1)	99.33 (96.46 - 100)	100.0	100.0	100.0	100.0
Ae. aegypti (San Lorenzo, Mexico)									
Control	0	-	-	-	-	-	0	0	0
5.5	100	-	-	-	-	-	100	100	100
7.3	100	-	-	-	-	-	100	100	100
11	100	-	-	-	-	-	100	100	100

4 Efficacy conclusions

Based on the studies and information provided, all data requirements for the prequalification assessment of product efficacy have been satisfied. These data have been relied upon to assess the intrinsic insecticidal activity in laboratory studies and the impact on caged mosquitoes in small-scale field studies of the proposed product for the purpose of characterising the entomological efficacy of the product.

The efficacy component of the dossier is considered complete, and the assessment of the submitted information on efficacy supports prequalification of the product.

Table 7. List of studies related to efficacy submitted to WHO as part of the prequalification dossier

Studies that were relied upon for decision making	
Study number	**Study title**
BIT106 Report 1	The small-scale outdoor study of CMP132-022 adulticide against susceptible and resistant mosquitoes in Tanzania
NAC/023/2023	Ground Ultra-Low Volume Application Field Trials using CMP132-022 as a mosquito adulticide for the control of *Aedes aegypti* and *Aedes albopictus* in Penang, Malaysia
ASR0083.0016.23	Efficacy test of CMP 132-022, with space spray application (Outdoor Low Dose), against mosquitoes of the species *Aedes aegypti*.
ASR0083.0017.23	Efficacy Test of CMP 132-022, with Space Application (Outdoor High Dose), Against Mosquitoes of the Species *Aedes aegypti*.
UCBE-UADY-CL-002	Ground Ultra-Low Volume application to indoor and outdoor field trials using CMP-132-022 as a mosquito adulticide for the control of Aedes aegypti in Merida, Mexico
GBA-1111	Ground ULV Bioassay against Caged Adult Female *Aedes aegypti* and/or *albopictus* Mosquitoes Using CMP132-022
GBA-1114	Ground ULV Bioassay against Caged Adult Female *Aedes aegypti* Mosquitoes Using CMP132-022
ASR0083.0014.23	Efficacy Test of Test Item CMP 132-022, with space spray application (indoor) - ULV, against mosquitoes of the species *Aedes aegypti*
ASR0083.0015.23	Efficacy Test of Test Item CMP 132-022, with space spray application (indoor) - ULV, against mosquitoes of the species *Aedes aegypti*
-	Assessment of intrinsic toxicity in Aedes aegypti through topical bioassay for CMP 132-022
Studies that were not used to inform decision making	
Study number	**Study title**
NAC/021/2023i	Investigation of Blood Feeding Behaviour in *Aedes aegypti* and *Aedes albopictus* following Application by Backpack Sprayer.