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Ortho-Isopropoxyphenyl Methylcarbamate (OMS-33) as a Residual Spray for Control of Anopheline Mosquitos

With Special Reference to its Evaluation in the WHO Programme for Evaluating and Testing New Insecticides

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More than 1300 compounds have so far been included in the WHO Programme for Evaluating and Testing New Insecticides, which is designed to disclose compounds that may satisfactorily replace those to which insect vectors of disease have become resistant. The authors describe the successful passage of o-*isopropoxyphenyl methylcarbamate (OMS-33) through the first 6 stages of the 7-stage programme that has been established for compounds intended for use against anopheline mosquitos and conclude that this product is suitable for testing in the final stage—large-scale epidemiological evaluation.*

In operational field trials (at 2 g/m²) OMS-33 has been shown capable of controlling Anopheles stephensi *(in Iran),* An. gambiae *and* An. funestus *(in Nigeria) for 3–4 months,* An. albimanus *(in El Salvador) for 2–4 months and* An. dthali *(in Iran) for 2½ months. It has an airborne effect by which anophelines are killed for a considerable time after OMS-33 has been sprayed, even though they do not make contact with a sprayed surface; this quality would appear advantageous in areas where anophelines enter houses and bite man but do not rest long enough on sprayed surfaces to acquire a lethal dose of insecticide or where significant outdoor biting occurs. The observance of simple safety precautions protects occupants of sprayed houses, spraymen and others from danger. Chemical studies have indicated that commercially produced water-dispersible powders of OMS-33 are stable under field conditions of storage and use.*

Prior to the introduction of residual insecticides, malaria was controlled only in certain areas where the population density and good economic conditions permitted. The discovery of synthetic organic insecticides such as DDT, dieldrin and HCH made it possible for the first time to consider the eradication of malaria on a world-wide basis, since these relatively inexpensive insecticides have a persistent toxicity which lasts for many months after application. However, the emergence of resistance of malaria vectors to DDT, dieldrin and HCH in certain parts of the world has seriously modified progress and in some situations has become one of the major obstacles to achieving the goal of malaria eradication.

Despite intensive research to overcome the problem of resistance, the use of alternative insecticides remains the only solution at present available. Therefore the World Health Organization is making a great effort to develop insecticides other than those to which resistance has occurred.

The WHO collaborative programme for the evaluation and testing of insecticides is based on

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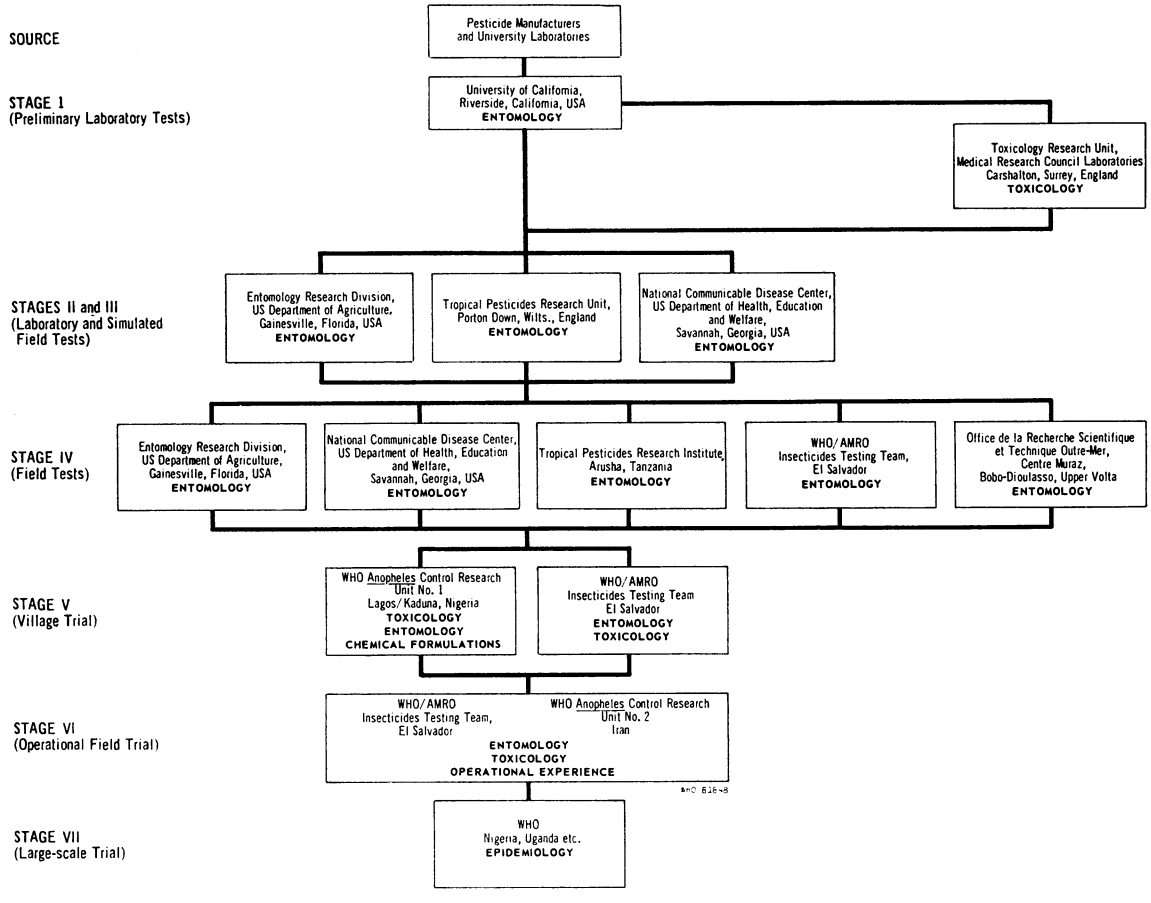
FIG. 1
WHO PROGRAMME FOR EVALUATING AND TESTING NEW INSECTICIDES



newly developed insecticides submitted by the chemical industry to WHO.[1]

These compounds are evaluated by a number of laboratories throughout the world working in collaboration with WHO in a programme of 7 stages, leading from investigation under carefully controlled laboratory conditions to large-scale tests in the field (Fig. 1).

Stage I of the programme involves the laboratory evaluation of the toxicity of new compounds to mosquito larvae and adults and to houseflies. In these screening tests strains of insects both resistant and susceptible to DDT and dieldrin are used. Consideration of the possible human hazard of the new chemical also begins at this stage, with a review of the toxicity data furnished by the manufacturer.

In the next stages, 3 laboratories evaluate the compounds which have shown promise at Stage I on additional species of insects in the laboratory (Stage II) and under simulated field conditions (Stage III). Appropriate tests are carried out against mosquito larvae and adults, houseflies, blackflies, fleas, bed-bugs, lice, *Triatoma* and ticks, with various methods of application. Concurrently, the intrinsic mammalian toxicity of the new compound is established by animal tests.

[1] A comprehensive account of the programme and of the evaluation of a very large number of compounds during the period 1960–67 is contained in unpublished working document WHO/VBC/68.66. A limited number of copies of this document is available to persons officially or professionally interested on request to Distribution and Sales, World Health Organization, 1211 Geneva, Switzerland.

Prior to Stage IV medical toxicologists determine *a priori* safety precautions necessary to protect spraymen and villagers from any hazard due to the insecticide. During the actual spraying of insecticide (Stage IV), studies are made to ascertain that the precautions are sufficient and are being taken as stipulated.

Beginning with Stage IV, investigations of the effectiveness of the new insecticide are carried out differently depending upon the particular species of insect. For the control of adult anopheline mosquitos Stage-IV tests are carried out in experimental huts using naturally entering vector species. An insecticide giving satisfactory results is then tested on a village scale (Stage V). At Stages IV and V, in addition to the entomological evaluation of the insecticide, consideration is given to the stability and suitability of the formulation being supplied. If the compound is satisfactory and effective when used on a village scale it is then tested on a large scale in the field, several thousand houses being sprayed (Stage VI—operational evaluation).

This Stage-VI trial is designed to ascertain whether the active ingredient and the suspensibility of the commercially produced formulation remain stable, whether the formulation can be safely and easily applied to the walls of houses and whether satisfactory control of anophelines is achieved under the conditions of general field operations.

A compound which passes Stage VI is then evaluated epidemiologically (Stage VII): 200 000 or more houses are sprayed, after which entomological and epidemiological data are collected and evaluated. Compounds which pass this final test can be recommended for areas where resistance to other insecticides has interfered with the progress of malaria eradication.

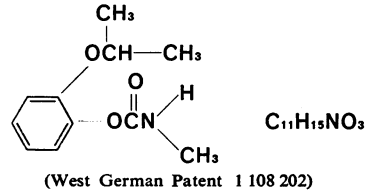
To date more than 1300 compounds have entered the programme of evaluation. Twelve of these successfully met the criteria of the laboratory (Stages I-III) and experimental hut tests (Stage IV) and were recommended for village-scale trials (Stage V). One of them, malathion, successfully passed the village-scale trials, proved to be effective in interrupting transmission of malaria (Stage VII) in Uganda and has been designated by the WHO Expert Committee on Malaria (1968) as an alternative insecticide for malaria eradication in certain circumstances where DDT-resistance has occurred. Another, *o*-isopropoxyphenyl methylcarbamate, as indicated in this paper, was shown to be effective in Stage-VI trials and is now being evaluated epidemiologically in malarious areas. Two others, which did not pass the criteria for residual sprays for control of anophelines have found important uses elsewhere: dichlorvos is effective against many household insects and has permitted a great advance in the disinsection of large aircraft used in international traffic, and fenthion has proved especially effective as a mosquito larvicide in polluted water. Difficulties were encountered with the formulation of fenitrothion during a Stage-VII trial and further evaluation has been suspended temporarily.

One compound, OMS-15 (*m*-isopropylphenyl methylcarbamate) was found to require greater safety precautions for field operations than are applicable in practice; another, carbaryl, was ineffective on mud walls. Further testing of 4 compounds has been deferred for the present for various reasons and 2 are at present being tested in Stage V.

The details that follow in this paper describe the evaluation of the second insecticide to pass successfully from Stage I through Stage VI—the carbamate *o*-isopropoxyphenyl methylcarbamate, designated OMS-33 in the WHO programme for evaluation and testing of new insecticides.[1] For convenience, it will be referred to by the latter designation throughout this paper. (It is or has also been known as Bayer 39007, Baygon, IMPC, UNDEN and propoxur; the name "arprocarb" has also been used but has been applied to another carbamate as well.)

CHEMISTRY [2] AND FORMULATION

The structural formula of OMS-33 is:



$C_{11}H_{15}NO_3$

(West German Patent 1 108 202)

Technical OMS-33 is light yellow with a characteristic phenolic odour. It melts at 87.0°C.

It is comparatively volatile, its half-life at 25°C being 13 days. It is unstable in alkaline conditions, having a half-life of 40 minutes at pH 10.8.

[1] Compounds evaluated in the WHO programme are given serial numbers to which the acronym "OMS" is prefixed.

[2] Interim specifications and methods of analysis for technical OMS-33 and for OMS-33 water-dispersible powders may be obtained on request to Vector Biology and Control, World Health Organization, 1211 Geneva, Switzerland.

Analysis on receipt

The consignment of 2 batches of 50% OMS-33 water-dispersible powder used in the Stage-VI trial at Kaduna, Nigeria, in 1967 (see below) was analysed there by *Anopheles* Control Research Unit No. 1 (ACRU-1) for compliance with the interim specifications for this material. All samples obtained from the 54 drums making up the consignment conformed to those specifications, although a few lumps ranging from 10 g to 20 g were present in 4 drums. There was no evidence of any colour deterioration after accelerated storage and the samples did not show any signs of caking. A few floating particles of OMS-33 which did not suspend in water were observed. After accelerated storage for 1 month an increased amount of these floating particles was found.

The analysis showed the active ingredient in the samples to range from 48.8% to 50.7% w/w and the suspensibility in hard water after accelerated storage to range from 73.0% to 85.2%.

Storage stability

Stability of the material stored in Kaduna was investigated over a period of 6 months; [1] a summary of analytical results over this period is given in Table 1.

TABLE 1

STORAGE STABILITY OF 50% OMS-33 WATER-DISPERSIBLE POWDER UNDER AMBIENT CONDITIONS AT *ANOPHELES* CONTROL RESEARCH UNIT No. 1, KADUNA, NORTHERN NIGERIA

Number of months of storage	Active ingredient [a] (% w/w)	Suspensibility (%) tested with 2.5% w/v suspension [a]
0 [b]	49.7 (48.8–50.7)	79.1 (73.0–85.2)
1	49.9 (49.1–50.6)	87.8 (79.4–95.1)
2	49.8 (49.0–50.5)	87.1 (78.8–94.5)
3	49.6 (49.0–50.5)	86.7 (77.8–94.6)
4	49.6 (49.0–50.2)	86.7 (77.6–94.9)
6	49.6 (48.5–50.6)	85.7 (79.3–92.1)
8	49.7 (48.5–50.7)	83.2 (77.1–89.3)

[a] Single values given are the averages of 8 analyses. The figures in parentheses show the lowest and highest values found.

[b] Material arrived in Kaduna on 12 June 1967 after surface shipment from the manufacturer in Europe and was analysed on 15–27 June 1967.

The insecticide for the Stage-VI large-scale trial in Iran in 1967 (see below) was stored in four places, Kazerun, Borazjan, Saadabad and Dalaki, in mud-walled rooms with small ventilation openings high on some walls, typical of this area. During the period April to September there was no rain in any of these places and the mean monthly relative humidity did not exceed 35%. The temperature ranged between 34°C and 52°C.

The OMS-33 water-dispersible powder in 150 drums used during the first round of spraying and 120 used during the second round had no visible signs of deterioration and was mixed and applied without difficulty. Some of this material had been stored under the above-described conditions for about 7 months. In the case of 10 drums during the first round and 1 during the second, the insecticide had a lumpy appearance and did not suspend well.

Suitability in use

The sanitarian in charge of the spraying operations at Kaduna found that the formulation was excellent and easy to mix; without having to be stirred, it went rapidly into suspension after a slight rotation of the rinsing tin and went into the pumps without frothing. After about 15 minutes' spraying, there was practically no deposit on the bottom, even when the pumps were not shaken.

In Iran it was generally observed that a good suspension with a layer of foam at the top resulted when the powder was mixed with water. There was no sediment at the bottom of the mixing barrel or in the pumps and no blockage of nozzles occurred except as noted below. However, in the case of the contents of 11 drums (as indicated previously) it was observed that some minute granules floated and did not go into suspension, there was no formation of foam while mixing, sediment was formed in the mixing barrels and pumps, and frequent blockage of nozzles occurred. In spite of these difficulties all but 80 kg of this material, which were retained for analysis, was sprayed in the usual manner.

Samples from these drums were analysed by the Tropical Pesticides Research Unit, Porton Down (see Fig. 1) and compared with a sample received from the manufacturer. All samples were found to disperse satisfactorily in distilled water, to sediment at similar rates and to redisperse readily on mild shaking. In hard water all flocculated; the flock sedimented rapidly but was easily dispersed. The

[1] Ramasamy, M. & Renaud, P. G.; unpublished working document WHO/VBC/68.102. A limited number of copies of this document is available to persons officially or professionally interested on request to Distribution and Sales, World Health Organization, 1211 Geneva, Switzerland.

amount of wetting agent was found to be adequate. One sample from Iran contained a small amount (0.45% by weight) of a white solid which floated on the surface of the suspension. The manufacturer carried out an analysis with similar results. These did not explain a few difficulties reported from the field.

A sample of OMS-33 material collected from strainers of spray cans at Kaduna was also analysed by the Tropical Pesticides Research Unit. It was found to consist of a white powder, lumps which could be readily reduced to white powder, and vegetable material such as grass seeds, stalks and fibres. The amount of material collected on the screens was determined to be less than the amount permitted by specifications to be retained on a BS-200-mesh sieve.

There was evidence of some erosive action of the insecticide on the nozzles in Iran, increasing the discharge rate by about 20% over the normal after 2 weeks of spraying. DDT formulations generally give about 10%–15% increase in discharge rate during a 2-week period. OMS-33 water-dispersible powders, containing 50% diluent, would be expected to be more erosive than those of DDT, which contain only 25% diluent.

It has been concluded after practical field use of over 30 metric tons of the material that the commercially available formulation of OMS-33 water-dispersible powder is satisfactory from the point of view of specifications, tropical storage and suitability for residual spraying.

STAGE I

(Preliminary Screening)

Intrinsic toxicity to anopheline mosquitos

The first stage in the entomological evaluation of candidate insecticides (carried out at the Riverside, Calif., laboratory—see Fig. 1) is a preliminary screening conducted by exposing adult mosquitos to a graduated series of insecticide concentrations in standard acetone solutions applied to filter-paper. The papers are air-dried, rolled and placed in vials.

Twenty mosquitos are placed in each vial, exposed to the residue for 1 hour, and then removed to holding-cages for determination of the 24-hour dosage–mortality curve. This curve is replicated 3 times, each on a different day. From these curves the LD_{50} of OMS-33 for dieldrin-resistant *Anopheles albimanus* was determined to be 0.82 $\mu g/cm^2$ (Georghiou & Metcalf, 1961) compared with 0.23 $\mu g/cm^2$ for DDT.

STAGES II AND III

(Tests of Formulations)

In the laboratory

In the Porton Down laboratory (see Fig. 1) the residual effectiveness of candidate insecticides against a susceptible strain of *An. stephensi* on various substrates is determined. Plywood panels and dried mud bricks were sprayed with aqueous suspensions of water-dispersible powders and stored at 25°C and 50% relative humidity.

Blood-fed *An. stephensi*, 2–3 days old, were exposed in contact with the OMS-33-treated surfaces for varying times and then transferred to cages at 25°C and 70% relative humidity for 24 hours before mortality counts were made.

With deposits of 1 g/m^2 on plywood there was over 70% kill after 1 hour's exposure for the following periods with the following insecticides (Hadaway & Barlow, 1965):

OMS-33	16 weeks
DDT	52 weeks
Dieldrin	42-48 weeks
Lindane	6-8 weeks
Fenthion	26 weeks
Malathion	20 weeks

Similar tests of OMS-33 on plywood panels against *An. quadrimaculatus* by the Gainesville laboratory in 1961 gave mortalities over 70% after 1 hour's exposure for 32 weeks (Gahan et al., 1961).

OMS-33 was thus shown to have reasonable persistence on a semi-porous inert substrate such as plywood. However, its persistence on mud blocks in the laboratory was short, as is the case with most insecticides. Although the laboratory tests on mud blocks made from carefully sieved soil give an indication of the relative persistence of various insecticides on mud surfaces, it has been found that the actual period of persistence observed bears little relation to the period of effectiveness in the field.

In the field

In the field the various surfaces described as " mud " usually contained sand, straw or other non-sorptive materials which were absent from the laboratory test surfaces and the period of persistence of toxicity as measured by bioassays was much longer than found in the laboratory. The results were variable, however, because of differences in test species, dosages, surfaces and other environmental conditions. Reported durations of effective kill on mud and wood surfaces are given in Table 2.

TABLE 2
RESULTS OF FIELD BIOASSAY OF OMS-33 WALL DEPOSITS

Year	Location	Species	Target dosage (g/m²)	Exposure time (min)	Mortality greater than:	Duration (weeks) of effectiveness at mortality level shown in previous column	
						On mud	On wood
1961	Savannah, Ga., USA[a]	*An. quadrimaculatus*	1.0	60	90%	6–10	>20
			2.0	60	90%	6–14	>20
1962	Lagos, Nigeria[b]	*An. gambiae*	1.5	30	70%	10	—
			1.8–2.5	30	70%	—	34
1967	El Salvador[c]	*An. albimanus*	2.0	30	70%	14–27[e]	>27
1967	Iran[d]	*An. stephensi*	2.0	30	80%	10–14	>36

[a] Mathis & Schoof (1963).
[b] World Health Organization, Insecticide Testing unit, unpublished data.
[c] WHO/PAHO, Insecticide Testing Team, unpublished data.
[d] A. G. Carmichael et al., unpublished data.
[e] Less than 1 week on highly sorptive mud.

STAGE IV
(Experimental Hut Trials)

When the results of tests of insecticides at Stages I, II and III were reviewed in March 1961, it was decided that one of the most promising of the new compounds for the control of anopheline mosquitos was OMS-33 and this was accordingly put forward for trial in experimental huts.

At Arusha, Tanzania, in 1961–62, OMS-33 was applied at a nominal dosage of 1.5 g/m² to huts with: (*a*) grass roof and mud walls, or (*b*) grass roof and plywood walls, or (*c*) roof and walls lined entirely with sorptive mud.

The kills of naturally entering *An. gambiae* were calculated from the daily counts of dead mosquitos on the floors plus the numbers, captured in the window traps, that died within 24 hours.

In the huts with grass roofs and plywood walls the over-all mortality remained over 90% for 7 months; in the huts with grass roofs and mud walls the mortalities were 99% the first month, 82% the second and 69% the third; but in the huts lined entirely with sorptive mud the kill was only 52% in the first month (Smith & Hocking, 1963).

The Gainesville laboratory (see Fig. 1) found OMS-33 to be effective in wooden buildings in Arkansas, USA (1962–63); at 2 g/m² the indicated reduction in natural populations of *An. quadrimaculatus* was 96%–100% for 48–62 weeks (Gahan et al., 1965).

At Bobo-Dioulasso, Upper Volta, in 1965, OMS-33 was effective for at least 2 months at 2 g/m² in experimental huts made entirely of mud, but with the surface treated with an oily extract from the fruits of *Butyrospermum* sp. (Coz et al., 1966). The monthly over-all mortalities of naturally entering *An. gambiae* were 98.4% the first month, 90% the second, 44% the third and 16.7% the fourth. During 1965–66, in experimental hut tests in El Salvador, over 80% of naturally entering *An. albimanus* were killed for 8–10 weeks in huts with pole walls and grass roofs, and for 12 weeks in huts with mud walls and grass roofs. When the huts were resprayed after 3 months, at the same dosage (2 g/m²), mortalities remained above 70% for 13 weeks in the mud huts, thereafter fluctuating between 30% and 100% through 32 weeks after spraying.

In 1964 in Arkansas, USA, a new technique—cheesecloth impregnated with OMS-33 at 2 g/m² and hung in wooden buildings for a period of 10 weeks—was used. When all the interior surfaces of the buildings were covered with impregnated cloth, the reduction in the numbers of naturally entering *An. quadrimaculatus* was 96%–100% for 10 weeks. When, in other buildings strips of cloth, 90 cm wide, were hung around the edges of the ceiling and in the

corners, the reduction was 100% for 5 weeks and 82%–99% for the next 5 weeks. When the strips were hung around the ceiling only, or in the corners only, the reduction was 98%–100% for the first 5 weeks and 84%–100% for the next 5 weeks (Gahan et al., 1966).

STAGE V
(Village-Scale Trials)

In 1962 a trial was carried out in the village of Isheri-Olofin, 20 km from Lagos in Nigeria. The village consisted of 32 houses, all of which had mud walls and all but one a tin roof (the exception was thatched). There were about 180 inhabitants in these houses. OMS-33 was sprayed in all but 3 of the houses at a target dosage of 1.5 g/m². Control of *An. gambiae*, as indicated by morning pyrethrum spray catches in the treated houses compared with those in the untreated houses in the village, lasted for 12 weeks or possibly longer, but by that time the mosquito population in the whole area was very low.

In 1963, comparative village-scale trials with fenthion, malathion and OMS-33 were carried out near Borazjan in southern Iran. All insecticides were sprayed at a target dosage of 2 g/m²; fenthion in 2 villages with a total population of 787, malathion in 2 villages with a total population of 490, and OMS-33 in 2 villages with a population of 710. It was estimated that 40% of the surface sprayed was mud and 60% wood and rush mat. The mosquito season finished 12 weeks after the time of application but both fenthion and OMS-33 gave effective control of the population of *An. stephensi* (as shown by morning pyrethrum-spray catches in the houses) for the whole period; malathion gave less effective control for 10–12 weeks.

In El Salvador, 3 villages—El Jocotal, Playa Grande and Cantora—were treated with OMS-33 at 2 g/m² from 29 September to 11 October 1965 and again from 6 to 16 December 1965. These 3 villages had a total of 320 houses, some with walls of poles and some of wattle and daub, but nearly all with thatched roofs. The effectiveness of the treatment was measured by several types of collection, the most effective measurement being the ratio of dead to live mosquitos found in houses in morning collections. During the first weeks after spraying, 100% of the mosquitos found were dead, but this proportion was considerably reduced 7–10 weeks after each application. There were occasional weeks after that, during the 5 months after the second treatment, when more dead than live mosquitos were found. These higher kills were apparently associated with periods of higher humidity. One village, El Jocotal, was given a third treatment in September 1966 and this remained effective for about 3 months.

In 1966, in Northern Nigeria, trials on a village scale were carried out to compare the effectiveness against *An. gambiae* and *An. funestus* of OMS-33 when used as a spray and when applied to houses in the form of impregnated cheesecloth.[1] Two Hausa villages near Kaduna were used for the trials. One, with 81 houses, was sprayed with OMS-33 as a water-dispersible powder at the rate of 2 g/m². The other village, 3 km away, with 111 houses, was treated with a 90-cm-wide strip of cheesecloth, dyed, flameproofed and impregnated with 2 g/m² OMS-33 from an acetone solution, and attached to the upper part of the walls inside the houses. About 35% of the inside surface of the houses was covered with the cloth and the amount of insecticide used averaged about 25 g per house compared with an average of 136 g applied to the sprayed houses. The cheesecloth treatment, as used in this experiment, was more time-consuming and had a shorter period of effectiveness than the spray. There was greater than 85% reduction in the house-resting populations of *An. gambiae* and *An. funestus* as shown by morning pyrethrum-spray catches and door-trap catches (compared with the untreated village) for about 90 days with the cheesecloth treatment and 100 days with the spray treatment, but there was some indication of an earlier increase in the numbers of mosquitos in the village treated with cheesecloth. Chemical analyses showed that the amount of insecticide in the cheesecloth hanging in the houses was reduced to about 1% of the original level after 2–3 months (Pant & Self, 1966).

STAGE VI
(Operational Evaluation)

Large-scale trials of OMS-33 were carried out in 3 areas in 1966–67: southern Iran, El Salvador and Northern Nigeria. In all these areas DDT is ineffective in interrupting malaria transmission for one reason or another.

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[1] Pant, C. P., Ramasamy, M., Renaud, P. G. & Self, L. S.; unpublished working document WHO/VBC/68.101. A limited number of copies of this document is available to persons officially or professionally interested on request to Distribution and Sales, World Health Organization, 1211 Geneva, Switzerland.

Iran

Two large-scale trials were carried out near Borazjan, in the Shabankareh area of the southern coastal plain of Iran in 1966 by the Government of Iran and in 1967 jointly by the Government of Iran and WHO. In this area the main vector of malaria is *An. stephensi*, which is resistant to both DDT and dieldrin. The population of *An. stephensi* is normally low from January to April, increasing in May to a peak in June and July. After a mid-summer low, a secondary peak occurs in September–October, followed by a gradual decline to a minimum population in February. *An. dthali*, a possible vector of malaria, is predominantly exophilic and generally is found in greatest numbers in May and in November. Because of its habits it is not effectively controlled by DDT.

The houses in this area are built of mud with pole and matting ceilings and have very little ventilation. These are generally within compounds formed by high mud walls. The relative humidity during the main transmission season is very low (about 30%), whereas the temperature is high (up to 50°C).

During 1966, the walls of buildings in 26 villages containing a population of 5506 were sprayed at 2 g/m² from 11 to 27 April and again at 1 g/m² from 4 to 24 October of the same year.[1] Entomological observations were made in 4 sprayed and 3 unsprayed villages. The indoor-resting densities of *An. stephensi* in the selected villages were nil for 4 months after the first spraying and those of *An. dthali* nil for 2 months. The catches from exit traps in these villages were also greatly reduced for both species.

During 1967, spraying of OMS-33 was carried out in an enlarged area including 11 000 people. OMS-33 was sprayed at a target dosage of 2 g/m² from 18 May to 30 June and again from 20 September to 8 October 1967.[2] Extensive entomological assessment included indoor pyrethrum-spray, night-biting, outdoor-resting, window-exit-trap and floor-sheet collections; bioassay tests of toxicant on the walls and in the air; serological determination of hosts; and susceptibility tests and dissections to determine the parous/nulliparous ratio.

The numbers of *An. stephensi* and *An. dthali* resting in bedrooms, *kumeha* (shelters) and stables were greatly reduced by the application of OMS-33 (Fig. 2). This insecticide maintained a low density (less than 1 per room) of *An. stephensi* for more than 3 months and of *An. dthali* for more than 2½ months. Outdoor-resting densities in sprayed villages appeared to be similarly affected. Exit-trap and floor-sheet collections indicated that mortality of both species continued to occur for about 4 months.

The residual OMS-33 considerably reduced but did not totally prevent the man-mosquito contact in the villages for at least 3 months.

For 3 months after spraying the numbers of half-gravid and gravid *An. stephensi* were considerably reduced. Similarly the proportion parous of the anopheline population was greatly reduced.

Bioassay of wall surfaces using a 30-minute exposure gave 69% or greater mortality for 126 days after spraying on mud surfaces and 80% or greater mortality for 254 days on non-sorbtive surfaces (wood and palm thatch). Bioassay of air using a 1-hour exposure gave 100% mortality up to 39–70 days in rooms and 60% or greater mortality for 74–88 days (see section on airborne effect and Table 7). At a 1-m distance outside sprayed houses, the airborne lethal effect (1-hour exposure) gave 100% mortality for 39 days.

In this area it is concluded that OMS-33 at 2 g/m² gives excellent control of *An. stephensi* for 3 months or longer and of *An. dthali* for more than 2½ months.

Nigeria

In collaboration with the Government, a large-scale trial was carried out by the *Anopheles* Control Research Unit No. 1 near Kaduna in Northern Nigeria in 1967. An area containing 1800 houses and 4000 people was sprayed at 2 g/m² from 26 June to 26 July 1967 and again between 9 October and 9 November of that year. More than 4300 structures, including animal shelters, granaries and kitchens, were sprayed.

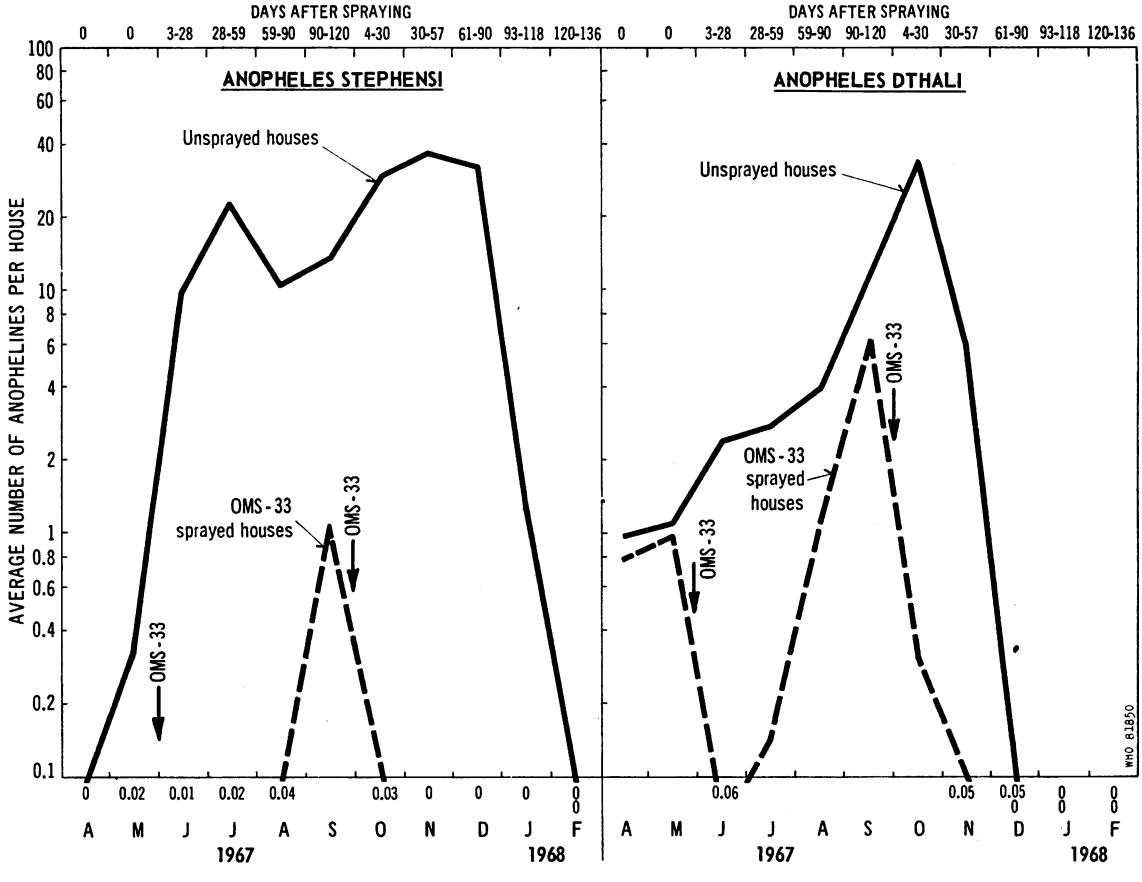
The main malaria vectors are *An. gambiae* and *An. funestus*, both of which are largely endophilic, *An. funestus* more so than *An. gambiae*. Despite the normal house-resting habit of *An. gambiae* females, DDT exerts only limited control because an irritant effect of the insecticide causes them to leave treated surfaces without acquiring a lethal dose.

[1] Samimi, B., Motabar, M. & Rouhani, F.; unpublished working document WHO/VBC/68.64; WHO/Mal/68.646. A limited number of copies of this document is available to persons officially or professionally interested on request to Distribution and Sales, World Health Organization, 1211 Geneva, Switzerland.

[2] Carmichael, A. G., Motabar, M., Sundararaman, S., Rowhani, F. & Golestani, J.; unpublished working document WHO/VBC/68.105. A limited number of copies of this document is available to persons officially or professionally interested on request to Distribution and Sales, World Health Organization, 1211 Geneva, Switzerland.

FIG. 2

COMPARISON OF NUMBERS OF ANOPHELINES COLLECTED BY PYRETHRUM SPRAYING OF UNTREATED AND OMS-33-TREATED HOUSES, SHABANKAREH, IRAN, 1967–68



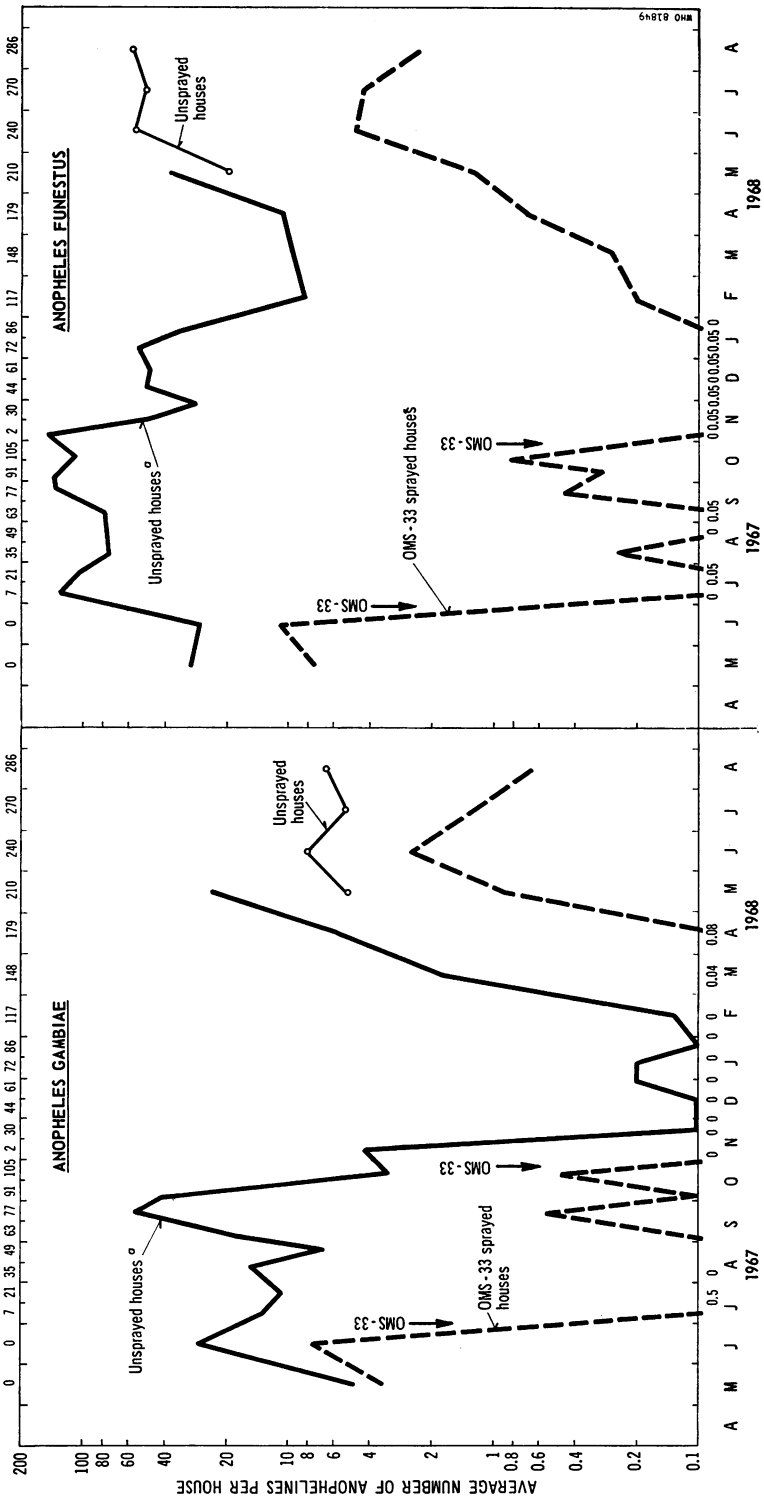
Practically all the houses of the area were of mud walls with grass roofs, some (those of the Hausa) being large and square and some (those of the Gwari) small and round.

Entomological assessment was based on morning pyrethrum-spray catches, door-trap catches and bioassay tests.

A comparison of the average number of *An. gambiae* and *An. funestus* per house collected by pyrethrum spraying in unsprayed and OMS-33-sprayed houses is shown in Fig. 3. It will be noted that the average number per sprayed house rose to about 0.5 at 2½ months after the first spray round for the 2 vector species. Although this figure may be epidemiologically significant, in the comparison area the average number of *An. gambiae* per house was 50 and of *An. funestus* more than 120 at the same time.

Pyrethrum-spray and exit-trap collections following the second OMS-33 spray round (October 1967) indicated that the insecticide also had a pronounced effect in delaying and reducing the population increase during 1968. An *An. gambiae* density of over 1 per house (based on pyrethrum-spray collections) (see Fig. 3) was reached in unsprayed houses in March whereas this density in previously sprayed houses was not approached until May. A peak of 24 *An. gambiae* per house was reached in unsprayed houses (May 1968) but the peak in sprayed houses was only 2.6 (June). It may be noted that the house-resting density of this species in the sprayed area exceeded 1 per house for the month of June only,

FIG. 3
COMPARISON OF NUMBERS OF ANOPHELINES COLLECTED BY PYRETHRUM SPRAYING OF UNTREATED AND OMS-33-TREATED HOUSES, KADUNA, NIGERIA, 1967–68



a During June 1968 the comparison village was sprayed. A near-by comparison village was observed from May onwards.

whereas it exceeded this figure for March through August (end of observations) in the unsprayed area.

A similar phenomenon was observed for *An. funestus*. In unsprayed areas, the density of this species never dropped below 8.5 per house between May 1967 and August 1968. In the sprayed houses the density rose from zero in January 1968, exceeded 1 per house in May and reached a peak of 4.6 per house in June at a time when the density in the unsprayed area was 55 per house. It is considered that such a delay and reduction of house-resting densities in the sprayed villages should have a significant effect on malaria transmission.

The average number of female mosquitos collected per house by pyrethrum spraying and exit traps are given in Table 3. These data indicate excellent control of house-entering *An. gambiae* and *An. funestus* for more than 2 months. During the period between 77 and 119 days after application of OMS-33 females of both species were found resting in houses and surviving 24 hours after being captured in exit traps but the numbers were very low in comparison with the numbers collected from unsprayed houses. No fed or gravid females were among those collected in exit traps up to 63 days after spraying. Between 77 and 119 days after spraying the percentage of fed and gravid females from exit traps surviving 24 hours increased gradually but did not reach the pre-spray value. The indicated reduction in house-frequenting vectors based on pyrethrum-spray and exit-trap collections from sprayed and unsprayed areas was greater than 98% through 119 days (4 months), at which time the area was resprayed.

These data indicate that excellent control of *An. gambiae* and *An. funestus* was maintained for more than 2 months and good control was achieved for 3–4 months.

El Salvador

A large-scale experiment was carried out in the south-eastern part of El Salvador in 1966 and 1967 in collaboration with the Government. Seven rounds of spraying at 2 g/m² were carried out with an interval of 4 months between the first and second rounds and approximately 3-month intervals thereafter (J. R. Austin et al., unpublished data).

The area included about 3000 houses and 13 500 people. The houses were mostly of fairly open construction, with walls of poles or mud and roofs generally of thatch.

The principal vector here is *An. albimanus*, a facultative feeder which can occur in very large and rapidly fluctuating populations. Because of the habits of the vector (irritability to DDT) and of DDT-resistance, that insecticide was only partially effective in this area and became less so as resistance increased after 1960.

Entomological assessment in sprayed villages was made by morning collections of live and dead mosquitos in houses, by collections in wall traps, by night collections on human baits, by bioassays on surfaces and of the airborne effect of the insecticide, and by dissections to determine the longevity of the mosquitos. An unsprayed area was not available for comparison as all surrounding villages had been sprayed with DDT.

Results varied considerably from locality to locality, between well-ventilated and poorly ventilated houses, between villages with houses close together and others with isolated houses, and between dry and rainy seasons. In some compact villages the entire vector population disappeared for up to 14 weeks, while in scattered rural houses, well ventilated and exposed to wind (for example, El Marañón), satisfactory kills lasted sometimes as little as 6 weeks.

The mean night captures from human bait for all 6 villages show a considerable contrast between the period from the first to the second round of spraying and that between the fifth and sixth cycles. The figures (based on over 100 man-hours) for these 2 periods are: June to August 1966, 2.52 *An. albimanus* per man-hour, and June to August 1967, 0.83 *An. albimanus* per man-hour. More than half of this latter number were collected in El Marañón.

Over most of the area, the duration of effective control of *An. albimanus* was generally from 8 to 12 weeks.

To a considerable extent the effectiveness of OMS-33 against more or less exophilic vectors such as *An. albimanus* is due to its ability to kill mosquitos at a distance from a sprayed surface. This airborne effect is discussed below.

AIRBORNE EFFECT OF OMS-33

During experimental hut trials with OMS-33 in El Salvador it was suspected that bioassay and exit-trap results were being affected by contamination with the insecticide that had been sprayed on the interior walls. While investigating this matter, it was discovered that the insecticide actually had an airborne phase which was effective in killing mosquitos

TABLE 3

ANOPHELES GAMBIAE AND *ANOPHELES FUNESTUS* COLLECTED FROM SPRAYED AND UNSPRAYED HOUSES BY PYRETHRUM SPRAYING AND EXIT TRAPS, OMS-33-SPRAYED AREA, KADUNA, NIGERIA, 1967-68

Month	Days after spray	Average number per house [a]										Exit-trap females (sprayed houses)[a]		
		Anopheles gambiae				*Anopheles funestus*				Both vectors				
		Pyrethrum collection		Exit-trap collection (alive)		Pyrethrum collection		Exit-trap collection		Pyrethrum and exit-trap collections		Total no. alive in trap at 24 h	No. fed and gravid alive at 24 h	Fed and gravid alive at 24 h as % of total fed and gravid collected
		Unsprayed	Sprayed	Unsprayed	Sprayed	Unsprayed	Sprayed	Unsprayed	Sprayed	Unsprayed	Sprayed			
1967														
May	0	4.7	3.10	NC	0.70	28.9	7.10	NC	3.10	NC	14.0	645	442	92.8
June	0	26.3	7.50	23.2	6.90	27.5	11.00	18.9	10.80	95.9	36.2	712	640	95.1
July	8	12.4	0.10	14.1	0	123.2	0	65.8	0	215.5	0.1	0	NC	—
	22	10.2	0.05	18.0	0	106.0	0.05	81.9	0	216.1	0.1	0	NC	—
Aug.	35	15.2	0	27.5	0	74.9	0.25	77.9	0.05	195.5	0.3	1	0	—
	49	6.5	0.10	14.1	0.05	77.3	0	74.2	0.05	172.1	0.2	2	0	0
Sept.	63	16.6	0.10	28.6	0.15	79.5	0.05	49.1	0.10	173.8	0.4	3	0	0
	77	52.0	0.55	41.9	1.70	137.3	0.45	71.9	1.05	303.1	3.75	23	10	83.3
Oct.	91	40.1	0.10	58.0	1.20	137.5	0.30	102.5	1.20	338.1	2.80	46	21	100.0
	105	3.2	0.45	NC	1.05	111.0	0.80	79.6	2.15	193.8	4.45	64	35	100.0
	119	NC	0.1	9.2	1.05	NC	0.30	NC	1.45	NC	2.90	50	29	100.0
Nov.	2	4.1	0	5.6	0	149.5	0	79.3	0	238.5	0	0	0	—
	16	0.1	0	0.3	0	48.7	0.05	31.0	0	80.1	0.05	0	0	—
	30	0.1	0	0.1	0	28.2	0.05	13.0	0	NC	0.05	0	0	—
Dec.	44	0.1	0	0.3	0	49.8	0	26.0	0	76.2	0	0	0	—
	61	0.2	0	0.2	0	49.5	0.05	19.3	0.05	69.2	0.1	6	1	—
1968														
Jan.	72	0.2	0	0.5	0	54.8	0.05	18.5	0.10	74.0	0.15	1	1	—
	86	0	0	0.1	0	9.9	0	2.2	0	12.2	0	1	1	—

[a] NC = no collection made; — = percentage not calculated (for collections of less than 20).

TABLE 4

PERCENTAGE MORTALITY OF *AN. ALBIMANUS* IN CAGES AFTER EXPOSURE OF 30–720 MINUTES [a] AT VARIOUS DISTANCES FROM SPRAYED POLE-CONSTRUCTED HOUSES, EL SALVADOR, 1967–68

Date	Days after spraying	Temperature		Relative humidity (%)	Percentage mortality in cages hung at indicated distance [b] and direction from nearest house											
					North			East			South			West		
		°F	°C		60 cm	90 cm	4 m	60 cm	90 cm	4 m	60 cm	90 cm	4 m	60 cm	90 cm	4 m
1967																
29 Nov.	4	77	25.0	60	100	100	—		100	—	100	100	—	100	100	—
6 Dec.	12	72–77	22.2–25.0	62–90	100	100	100	100	100	100	100	100	100	100	100	100
13 Dec.	19	73–80	22.8–26.7	44–55	100	100	100	100	100	100	100	100	100	100	100	100
20 Dec.	26	68–76	20.0–24.4	80	100	100	90	100	100	92	100	100	100	100	94	31
27 Dec.	33	84	28.9	49–60	100	100	100	100	100	100	100	100	100	100	93	93
1968																
4 Jan.	41	80–85	26.7–29.4	46–48	88	86	62	77	67	64	82	87	67	64	77	71
18 Jan.	55	82–87	27.8–30.6	46–48	0	0	20	0	0	0	0	0	0	0	8	0
24 Jan.	61	70–82	21.1–27.8	60–76	38	15	38	54	69	46	69	67	60	38	21	31
3 Feb.	71	77–82	25.0–27.8	48–78	0	0	0	0	42	18	0	20	0	0	0	7
9 Feb.	77	78–79	25.6–26.1	79–81	0	0	0	23	27	36	0	9	0	0	0	0
16 Feb.	84	78–79	25.6–26.1	79–81	0	0	0	0	0	0	18	8	7	0	0	0

[a] Exposure was terminated when 100% were knocked down or after 720 minutes if all were not knocked down by that time. Wind speeds were usually low, being mainly within the range 1 km/h to 15 km/h, with a recorded maximum of 35 km/h.

[b] Mortality in cages hung 30 cm from the nearest house was similar to that in cages at 60 cm; in the interests of brevity, those results have therefore been omitted from this table.

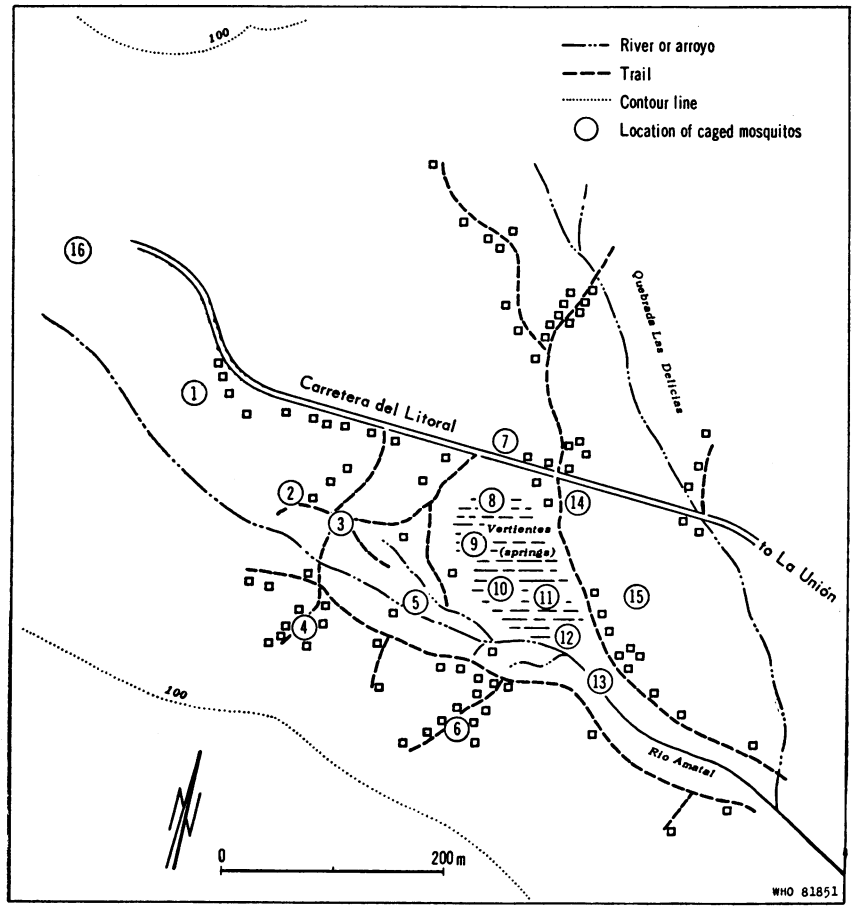
at some distance from the sprayed surface (M. B. O'Bryant & J. R. Austin, unpublished data). Immediately after spraying this effect extended as far as 20 m. In one experimental hut 95% of mosquitos in cages hung at the centre of the hut were killed during an overnight exposure as long as 30 weeks after the walls had been sprayed. In other investigations in El Salvador it was found that during the first week after spraying mosquitos in cages at 30 cm, 60 cm, 90 cm and 4 m from the sprayed surface were all knocked down after an exposure of between 18 and 57 minutes. The time required for knockdown increased with time after spraying, so that at 6 weeks 90%–96% knockdown required an exposure of approximately 12 hours (Table 4).

To define further the airborne effect the village of El Amatal was sprayed with OMS-33 on 16–17 March 1967. On 18 March, 100% mortality was found in all the cages hung within the village. Beginning on 30 March (2 weeks after spraying) caged *An. albimanus* (El Jocotal DDT-resistant colony) were exposed weekly at various localities in the village as indicated in Fig. 4. Exposure was from 18.00 to 06.00 hours. The results are shown in Table 5.

It can be seen from Fig. 4 and Table 5 that there were higher mortalities generally in cages hung within the village for the first 4 weeks, and lower mortalities in cages hung at the village edge or outside the village. The speed and direction of air movement were observed to affect the mortality inside and outside houses. The open style of construction of houses in El Amatal contributed to the effectiveness of the insecticide.

El Amatal is ideally situated to take advantage of an insecticide, such as OMS-33, which has such an effective airborne phase. It is situated in a narrow valley with the stream which produces the mosquitos running directly through it (Fig. 4). This village was sprayed on 30 April 1966, 29 August 1966, 25–28 November 1966, 17 March 1967 and 26 June 1967. During the 16-month period up to 6 September 1967 night-biting collections were made at 2-week

FIG. 4
LOCATION OF MOSQUITO EXPOSURE CAGES IN EL AMATAL VILLAGE, EL SALVADOR, 1967 [a]



[a] See Table 5.

intervals inside and outside sprayed huts with only 12 *An. albimanus* and 14 *An. p. pseudopunctipennis* collected. In fortnightly morning searches for dead or live mosquitos, only 3 live *An. albimanus* and 22 *An. p. pseudopunctipennis* were collected. In the near-by village of Gualoso no live *An. albimanus* and only one *An. p. pseudopunctipennis* were found during these 16 months. It appears from these and other entomological observations that these villages were almost cleared of anophelines by OMS-33. It must be pointed out, however, that in other less favourably situated villages and particularly those with extensive *Anopheles* sources near by, the effect of OMS-33 lasted only 8–9 weeks.

During 1967 bioassays of the airborne effect of OMS-33 were carried out at the *Anopheles* Control Research Unit No. 1 near Kaduna, Nigeria.[1] Ten to 20 laboratory-produced, fed *Aedes aegypti* were placed in mosquito-netting cages and hung in various locations in and around the sprayed village. Exposure extended from sunset (about 18.00 hours) to sunrise the next morning (about 06.00 hours). Results of these tests are shown in Table 6. In this

[1] Pant, C. P. & Joshi, G. P.: unpublished working document WHO/VBC/68.108. A limited number of copies of this document is available to persons officially or professionally interested on request to Distribution and Sales, World Health Organization, 1211 Geneva, Switzerland.

TABLE 5

PERCENTAGE MORTALITY OF DDT-RESISTANT *AN. ALBIMANUS* IN OUTDOOR CAGES 2–6 WEEKS AFTER SPRAYING OF OMS-33

Cage No.[a]	Distance and direction from nearest sprayed house	Percentage mortality at following weeks after spraying[b]				
		2	3	4	5	6
1	10 m W	0	0	5	0	0
2	10 m W	20	46	0	0	0
3	10 m E	88	100	76	0	12
4	10 m E	56	54	22	0	0
5	10 m E	93	100	28	15	NT
6	10 m SE	100	96	100	0	0
7	10 m S	0	NT	31	0	0
8	10 m SW	92	100	82	0	24
9	15 m E	76	100	80	0	32
10	10 m E	96	100	100	20	50
11	25 m W	82	100	NT	9	0
12	30 m NW	92	100	53	0	6
13	15 m W	50	100	90	0	16
14	10 m E	95	100	20	5	6
15	15 m E	70	100	10	0	0
16	Control[c]	1	0	0	0	0

[a] See Fig. 4. [b] NT = not tested. [c] About 100 m W of village.

area, where huts have mud walls, the airborne effect was shown to kill 95% or more of mosquitos at a distance of 27 ft (8.2 m) from sprayed houses for the first 9 days after spraying. At 5 ft–7 ft (1.5 m–2 m) from sprayed houses satisfactory kills (70% or greater) were obtained on the twenty-third day after spraying. In the immediate vicinity of sprayed huts (1 ft–4 ft; 0.3 m–1.2 m) satisfactory kills were attained through day 30. Indoor airborne bioassays at 65 days after spraying showed mortalities between 23% and 100% (average 80.4%). At this time 14 of the 18 cages of mosquitos had a mortality greater than 70%. At 72 and 79 days after spraying the average mortality fell below 70%. However, at these dates 13 out of 18 and 12 out of 17 cages of mosquitos still had mortalities greater than 70%.

The airborne effect of OMS-33 was also observed in the 1967 Stage-VI trial of OMS-33 in south-west Iran. In this area the people live within mud-walled compounds in rooms with mud walls and roofs of palm thatch covered with mud. The airborne phase of OMS-33 brought about satisfactory mortalities after a 1-hour exposure of caged *An. stephensi* for 74–88 days in bedrooms and for 39–46 days in the more open *kumeha* used as shelters in this area (see Table 7). Satisfactory mortalities were attained within 1 m outside the doors of bedrooms and *kumeha* for 28–39 days after spraying.

This airborne phase of OMS-33 gives it a quality that is not found among some of the less volatile

TABLE 6

BIOASSAY OF AIRBORNE EFFECT OF OMS-33 ON CAGED *AEDES AEGYPTI* AT KADUNA, NIGERIA, 1967

Distance from nearest sprayed hut		24-Hour percentage mortality[a] at indicated time after spraying at 2 g/m²											
ft	m	2 days	9 days	16 days	23 days	30 days	37 days	44 days	51 days	59 days	65 days	72 days	79 days
Unexposed controls													
550	168	6 (16)	0 (20)	0 (14)	0 (20)	0 (20)	0 (20)	0 (17)	0 (21)	0 (21)			
320	98	0 (13)	6 (16)	6 (18)	0 (15)	0 (17)	0 (19)	0 (18)	0 (13)	0 (16)			
160	49	—	8 (13)	5 (20)	0 (17)	0 (19)	0 (20)	—	—	—	—	—	—
Exposed mosquitos													
101	31	57 (14)	33 (12)	7 (14)	0 (18)	5 (19)	0 (22)	—	—	—	—	—	—
27	8.2	100 (26)	97 (29)	41 (39)	0 (33)	17 (42)	0 (40)	—	—	—	—	—	—
10–13	3–4	100 (28)	97 (29)	61 (36)	8 (64)	4 (75)	1 (82)	—	—	—	—	—	—
5–7	1.5–2	—	—	—	71 (63)	54 (79)	5 (79)	—	—	—	—	—	—
1–4	03–1.2	100 (180)	100 (145)	99 (168)	84 (183)	70 (237)	43 (246)	33 (258)	4 (358)	2 (42)	—	—	—
Inside huts		100 (64)	100 (35)	100 (29)	99 (75)	100 (78)	100 (76)	100 (61)	96 (198)	62 (277)	80 (343)	66 (367)	56 (394)

[a] Figures in parentheses show number of *Aedes aegypti* exposed in cages from 18 : 00 to 06 : 00 hours.

TABLE 7

BIOASSAY OF AIRBORNE EFFECT OF OMS-33, BORAZJAN, IRAN, 1967

Location of bioassay cage	Distance from sprayed roof	24-Hour percentage mortality [a] at indicated time after spraying at 2 g/m²												
		9 days	18 days	28 days	32 days	39 days	46 days	53 days	63 days	70 days	74 days	81 days	88 days	95 days
Control	—	0 (44)	8 (50)	0 (50)	0 (50)	0 (50)	0 (48)	0 (50)	0 (50)	0 (50)	0 (50)	0 (50)	0 (50)	0 (50)
Room A [b]	1 m	100 (50)	100 (50)	100 (50)	100 (50)	100 (50)	100 (50)	100 (50)	93 (48)	84 (50)	71 (48)	73 (49)	50 (50)	29 (48)
	2 m	100 (50)	100 (50)	100 (50)	100 (50)	100 (45)	66 (50)	60 (50)	78 (51)	72 (50)	64 (50)	56 (50)	33 (48)	16 (50)
	1 m outside	—	—	—	—	100 (48)	—	—	0 (50)	0 (50)	0 (50)	0 (50)	0 (45)	0 (50)
Room B [c]	1 m	100 (50)	100 (48)	100 (48)	100 (47)	100 (50)	100 (48)	100 (50)	100 (50)	100 (50)	92 (50)	94 (50)	75 (48)	58 (50)
	2 m	100 (50)	100 (50)	100 (50)	100 (50)	100 (49)	100 (50)	100 (50)	93 (48)	92 (50)	83 (50)	88 (48)	40 (50)	41 (51)
	1 m outside	—	—	78 (50)	71 (48)	100 (50)	40 (50)	0 (47)	0 (50)	0 (50)	0 (50)	0 (50)	0 (45)	0 (50)
Kumeh [d]	1 m	100 (49)	100 (50)	100 (50)	90 (49)	94 (50)	88 (50)	32 (50)	20 (50)	24 (50)	—	—	—	—
	2 m	100 (46)	100 (49)	100 (52)	82 (50)	86 (49)	68 (50)	9 (49)	6 (49)	14 (50)	—	—	—	—
	1 m outside	—	—	70 (50)	68 (50)	54 (48)	0 (43)	0 (50)	0 (50)	0 (50)	—	—	—	—
Temperature °C		30	31	28	29	29	24	23	24	20	21	21	16	15
Rel. humidity %		41	42	52	51	56	75	80	51	73	72	72	71	95

[a] Figures in parentheses show number of *Anopheles stephensi* exposed in cages for 1 hour.
[b] Room A: mud-covered, thatch-roofed room with 2 open doors and 1 open window.
[c] Room B: mud-covered, thatch-roofed room with 1 open door and 1 open window.
[d] *Kumeh*: thatch-roofed shelter of more open construction with 1 open door and 1 open window.

insecticides which are applied as residual sprays for the control of anopheline mosquitos. This is an obvious advantage in those areas where mosquitos may enter houses and bite without resting for a sufficient time on sprayed surfaces to pick up a lethal dose of the insecticide or where significant outdoor biting occurs. It has been suggested that in those areas where a certain amount of peridomiciliary transmission is responsible for the persistence of malaria, this insecticide might exert sufficient airborne toxicity to bring such transmission to an end.

TOXICOLOGICAL STUDIES

OMS-33 is a carbamate insecticide of moderate mammalian toxicity. Its toxic properties have been studied extensively in experimental animals in the laboratories collaborating in the WHO insecticide-evaluating programme and in other institutes. Acute toxicity data for OMS-33 for different animal species as obtained in the Medical Research Council Laboratories, Carshalton, England (see Fig. 1), and from the manufacturer are shown in Table 8.

TABLE 8

TOXICITY DATA OBTAINED ON DIFFERENT LABORATORY ANIMALS AFTER A SINGLE ADMINISTRATION OF OMS-33

Species	Oral LD_{50} (mg/kg body-weight)		Dermal LD_{50} (mg/kg body-weight)	
	Male	Female	Male	Female
Rat	116 [a]		>1 000 [b]	
	95 [b]	104 [b]		
Mouse	109 [a]	82 [a]		
Guinea-pig	100 [a]			
Chicken	40 [b]	150 [a]		
Starling	15–20 [b]			
Redwinged Blackbird	2–6 [b]			

[a] Data from Medical Research Council Laboratories, Carshalton, England.
[b] Manufacturer's data.

The mechanism of intoxication by OMS-33 consists of inhibition of acetylcholinesterase and of a consecutive accumulation of excessive amounts of acetylcholine in effector organs. Anticholinesterase activity of OMS-33 determined on purified bovine erythrocyte cholinesterase titrigraphically, after the enzyme had been incubated with inhibitor for 30 minutes at 25°C and pH 7.4, gave an I_{50} value of 7.0×10^{-7} M (Simeon, 1966).

The observed signs in poisoned animals are mostly, but not exclusively, of a cholinergic nature. Owing to the relatively rapid spontaneous reactivation of inhibited enzyme (Wilson, Hatch & Ginsburg, 1960; Reiner & Simeon-Rudolph, 1966)—carbamoylated cholinesterase reactivates more rapidly than phosphorylated enzyme—animals recover relatively rapidly after a single sublethal dose. Thus, after an intravenous injection of a single dose (10.6 mg/kg) of OMS-33 in rats, symptoms developed immediately and in surviving animals lasted for 45 minutes and included very pronounced tremor and fasciculations and only slight salivation (Wilhelm & Vandekar, 1966). Within 20–60 minutes after a single intramuscular injection of OMS-33 into rats at a dose of 1 mg per kg of body-weight, pronounced reductions in both brain and plasma cholinesterase, down to about 60% activity, were found without any noticeable symptoms of poisoning (Pleština & Vandekar, 1966). No cumulative inhibitory effect could be demonstrated on plasma cholinesterase in rats which were inoculated with OMS-33 intramuscularly 6 days a week for 2 weeks in doses corresponding to about 1/20 of the LD_{50} (Svetličić & Fajdetić, 1965).

As with the other carbamates, OMS-33 gave a large ratio between the LD_{50} dose and the dose causing signs of poisoning of 50% of the animals (ED_{50}), the LD_{50}/ED_{50} ratio being about 32 for both intravenous and intramuscular routes of injection (Vandekar et al., 1965). Studies of the tolerance to OMS-33 at different rates of intravenous infusion into rats (Vandekar & Fajdetić, 1966) showed that, while a decrease in the rate of infusion of insecticide was accompanied by a remarkable increase in tolerance regarding the lethal dose, no increase in dose necessary to produce the first symptoms was observed at the rates of infusion employed. On the grounds of these results it was concluded that occupational overexposure to the OMS-33 will produce symptoms of headache, nausea and/or vomiting at doses well below lethal levels, while at a certain rate of absorption exposure may be continued for long periods without danger of poisoning.

In studies (Pleština, 1968) on volunteers, including one of the authors, who took a total oral dose of OMS-33 of 0.75 mg per kg of body-weight or of 1 mg per kg of body-weight, both divided into 5 portions at half-hour intervals, symptomless depression of erythrocyte cholinesterase—down to about 60% activity—was observed. Assays performed by a spectrophotometric method (Ellman et al., 1961) showed that cholinesterase recovered to 100% activity within 3 hours of cessation of dosing. After a single dose of 0.36 mg per kg a rapid fall in erythrocyte cholinesterase—down to 57% activity within 10 minutes—was observed and was associated with short-lasting (about 5 minutes) stomach discomfort and moderate redness and sweating in the face. The cholinesterase recovered to its normal value within 3 hours. In all instances an increased excretion of phenol derivatives, as determined by the method of Dawson et al. (1964), was observed, which apparently returned to normal 3–5 hours after cessation of exposure. After a single oral dose of 1.5 mg per kg of body-weight, a rapid fall in erythrocyte cholinesterase activity was found by the spectrophotometric method, the lowest value (27% activity) being determined 15 minutes after injection. No symptoms were observed at that time but moderate discomfort described as " pressure in the head " was present. A few minutes later symptoms developed, including blurred vision, profound perspiration and vomiting. These symptoms lasted for less than 1 hour and their disappearance was consistent with rapid recovery of erythrocyte cholinesterase activity. No significant inhibition of plasma cholinesterase could be determined spectrophotometrically throughout the experiment.

On the grounds of the results obtained from the above published and unpublished investigations, some of which included studies on other monomethyl carbamates and, for the sake of comparison, some organophosphorus compounds, it has been concluded that although, according to their biological action, carbamates belong to the group of anticholinesterase insecticides, their properties differ markedly from those of organophosphorus compounds. This is consistent with the differences in the kinetic data on the action of these two classes of cholinesterase. Thus, while inhibition in the early stages is rapid, it is difficult to produce a severe degree of inhibition of the carbamates because the rate of reactivation approaches that of inactivation. These differences in behaviour as enzyme inhibitors are important when the toxic effects of carbamates and organo-

phosphorus compounds are compared (WHO Expert Committee on Insecticides, 1967, pp. 10-11).

SAFETY EVALUATION

Observations on safety were made during all the field testing of OMS-33 from village-scale trials (Stage V) onwards. The observations are summarized below with information on the safety precautions that were taken.

Village-scale trials

Lagos, Nigeria, 1962. OMS-33 was sprayed at a target dose of 1.5 g/m² in a village of 32 houses and at 2 g/m² in 6 houses in another village.

A total of 190 people, including 10 spraymen, were exposed and 10 people reported reactions to the compound in the form of a discrete skin eruption. The eruptions were of the contact dermatitis type and caused fairly severe itching. They disappeared after 5 days with topical application of calamine.[1] One sprayman complained, on one occasion, of chest tightness, dyspnoea, tingling under the skin and a bitter taste in the mouth; he recovered spontaneously.

Iran, 1963. OMS-33 was sprayed in 2 villages in southern Iran in the autumn of 1963. The total population exposed was about 700. Six spraymen were engaged and worked for 3–4 days. No symptoms whatever were reported among either spraymen or villagers. Accidental spillage of the carbamate solution caused a mild burning sensation that disappeared as soon as the material was washed off.

Lagos, Nigeria, 1964. OMS-33 was sprayed again in a village-scale trial by 3 spraymen for 4 days (Vandekar & Svetličić, 1966). No clinical symptoms whatever developed among either the spraymen or the 125 residents.

In the three above-mentioned trials the spraymen were under constant supervision to ensure that safety precautions were carried out. Safety measures included the wearing of protective clothing and of respirators which prevented the inhalation of droplets.

[1] As skin eruptions had never been reported before, the Medical Research Council Laboratories, Carshalton, and the manufacturers retested the same formulation and found no eruptions in men, rats or guinea-pigs. At the Insecticides Testing Unit at Lagos, 11 Africans and 6 Europeans were exposed in early 1963 to pure OMS-33 as 3.75% alcohol solution, exposed and not exposed to light; no effects were noted, except that one African had a slight rash in the light-protected test. In addition, 5 houses were sprayed, 30 people being exposed thereby; no rashes or other symptoms occurred.

El Salvador, 1965. A somewhat larger village-scale trial covering 320 houses in 2 weeks was performed in El Salvador. A working day of 7 hours was adopted initially and a minimum of protective equipment was used (plastic helmet, long-sleeved shirt and trousers). Transitory symptoms occurred occasionally in spraymen during the first week of spraying, but after the men had become accustomed to the hard work and high temperatures and had learned how to avoid the heaviest mist fall-out, there were no more complaints or signs of intoxication.

In the second round of spraying there were transient reactions of nausea, vomiting and dizziness in 4 out of 5 spraymen on one day only, when they worked 8 hours in unusual heat and sprayed 9 houses each. Several sick children were observed, 6 of whom were on the itinerary of one sprayman, who was later found to have leaking equipment which had caused excessive contamination of the floors and furniture. In addition, the houses concerned were distant from a water-point and the inhabitants were most sparing with water for washing.

Large-scale field trials

El Salvador, 1966-67. As mentioned earlier, a large-scale operational field trial with 7 rounds of spraying was carried out during 1966 and 1967 in an area with 13 000 inhabitants in El Salvador. A total of 3020 houses was sprayed in April-May 1966 by 10 men working 5½ weeks and 5 men working 1½ weeks. The spraymen worked 5½ days a week and sprayed 7 hours a day in the first round. The working day was increased in the second round (August-September 1966) when 12 men sprayed for 8 hours a day. Precautions were taken to reduce contamination of the floors inside the houses in both rounds of the large-scale trial. In the second round one squad was given disc flow-regulators and these were observed to reduce considerably the mist fall-out and rebound of the insecticide.

In 350 man-days worked in the first round, symptoms were reported by spraymen on 20 occasions, but not all symptoms were due to OMS-33 intoxication. Nausea (8 times) and headache (6 times) were the most common complaints. Spraymen generally recovered after a brief rest and some recovered even while continuing to work. All worked on the day following the appearance of symptoms without further trouble.

Among residents, children 1–4 years old occasionally manifested evidence of intoxication, but only during the first day after spraying. Such children had

always been playing on contaminated floors or in contact with freshly sprayed surfaces, and had been left unbathed for several hours. Ingestion *via* soiled fingers probably played a role in these cases. Nausea, vomiting, pallor, weakness, excessive sweating and salivation were the usual symptoms and signs. Inability to walk without falling was noted several times. Recovery occurred in a few hours, with or without tincture of belladonna. Many complaints in children were found not to be due to the insecticide.

Complaints were also received from adults, but the majority checked were found not to be due to insecticides. In those recognized as due to overexposure to OMS-33, the most common reaction was paraesthesia of the mouth, nose or face and respiratory tightness in persons sweeping the floors with too little water immediately after spraying. No case of symptoms attributable to OMS-33 had its onset more than 1 day after the house had been sprayed. All cases were very transient and the persons had usually recovered by the time they were seen by a medical officer.

Among domestic animals, only poultry were affected, and these only in a few households. Illness was almost always attributed to the chickens having eaten cockroaches killed by OMS-33. The only reported deaths were of a few chicks, ducklings and turkey poults, which occurred within a few hours after spraying, and the householders usually accepted their responsibility for lack of care in keeping the poultry from contact with freshly contaminated soil.

The fumigant effect of OMS-33 was studied and was shown to be sufficient to kill mosquitos for upwards of 5 weeks, but harmless to chicks and, as stated above, rarely, if ever, symptom-producing in man.

A striking reduction in complaints, among both spraymen and inhabitants, was observed in the third round of spraying, which took place in the cool, dry season. Also in the later rounds it was found that the number of complaints varied with the climate at the time of spraying, being highest during hot, wet periods (see Table 9). As in earlier rounds, spraymen wore simple protective clothing and changed their uniforms every other day. They worked 8 hours per day with a 1-hour break at noon, and sprayed 8–11 houses daily. They washed their hands when soiled and usually bathed every evening. During 2 weeks of the seventh round of spraying, 12 complaints were received from the spraymen: 9 of these from 6 newly engaged spraymen and only 3 from 14 experienced spraymen.

TABLE 9

COMPLAINTS RECEIVED DURING OPERATIONAL FIELD TRIAL OF OMS-33 IN EL SALVADOR

Spray round	General climate	Man-days of spraying	Complaints	
			Spraymen (no. of incidents)	Residents (% complaining)
1	Dry, then wet	350	20	1.2
2	Wet (hot)	330	40	1.8
3	Dry (cool)	306	7	0.4
4	Dry (hot)	308	19	0.8
5	Wet	330	33	1.1
6	Wet (hot)	276 [a]	0	1.4
7	Dry (cool)	206 [a]	12	0.2

[a] Some houses omitted from spraying.

Iran, 1966. OMS-33 was sprayed in an area of about 300 km², comprising 26 villages with a population of about 6000. The spraying team consisted of 14 spraymen, 2 mixers, 2 foremen, 2 group leaders and 1 chief of operations. Operations were carried out 7 days per week for an average of 7 hours per day. The protective equipment used comprised overalls, helmets with an extension to protect the neck, goggles, surgical-type masks, rubber gloves and rubber boots. The spraymen washed their faces and hands before eating, washed their face-masks every day and their uniforms whenever water for this purpose was available—this being about once or twice a week.

Two mixers experienced dizziness and vomiting 1 day after commencement of spraying. They recovered with a few hours of rest, receiving metaraminol tablets and tincture of belladonna. One of the mixers and a sprayman experienced dizziness, vomiting and sweating 6 days after commencement of spraying, but recovered after 2 days' rest, except for anorexia which persisted for several days after recovery. Another sprayman complained of diarrhoea with abdominal pains 7 days after commencement of spraying.

Among the 426 villagers under observation, 23 had clinical symptoms. Dizziness, headache, vomiting and anorexia were experienced by 21 persons, of whom 3 suffered also from excessive sweating. Two

boys, 10-12 years of age, complained of skin irritation.

During the first spraying round, 21 chickens died 1 day after spraying.

It was reported that, during the second round of spraying, the same spraymen who had shown symptoms in the first round, as well as 3 newly employed spraymen, experienced vomiting, vertigo and palpitations on the first and second days of spraying. They all recovered after taking 15 drops of belladonna tincture and having a rest for the afternoon. Among villagers only 1 woman and a child complained of vertigo.

Iran, 1967. During a 6-week operational field trial in the same area (Vandekar et al., 1968), consisting of 807 man-days of spraying, 25 complaints attributable to OMS-33 were recorded among operators. They consisted of headache (20) and/or nausea (11); both were short-lasting and mild in intensity.

Among the inhabitants of 2 villages more closely observed, 19 persons out of 1052 inhabitants (1.8%) and 10 persons out of 310 inhabitants (3.2%) had complaints that were recorded as attributable to OMS-33. Of the total, 26 complaints were found among adults (3 men and 23 women) and 3 among children, 11-12 years old.

The complaints consisted of headache (29), nausea (10), increased sweating (6) and vomiting (2). Their incidence could be attributed to one or several entries into the house during spraying (18) or immediately after spraying (4), sweeping the floor with or without water (5), or sleeping on a sprayed mat (1).

Two deaths among chickens were reported.

From inhabitants of other villages, totalling about 9600, nearly 50 complaints (about 0.5%) were reported (5 cases among children 2–3 years old and the others among women). Entry into the room during or immediately after spraying appeared to be the main cause of overabsorption.

Nigeria, 1967. Eight spraymen and 1 mixer were engaged in spraying 3 villages and their environs (total population approximately 3500). A total of 118 man-days of work was completed. Three to 10 pump-charges (in most instances 6 to 8) per sprayman per day were sprayed during approximately 5 hours of actual spraying. Throughout the spraying, frequent washing of the hands and face with soap and water was performed. Three different combinations of protective clothing were worn by the operators: (*a*) clean overall daily, sou'wester, respirator, plastic shoes and, for mixer only, rubber gloves; (*b*) as in (*a*) with the exception of the respirator; (*c*) as in (*b*) with rubber gloves for all in addition. No distinction between these 3 sets of precautions could be made on the grounds of whole-blood cholinesterase analyses. Determination of phenols in urine indicated that the skin protection markedly reduced absorption of the insecticide.

Apart from one case of vomiting and "upset stomach" which persisted for more than 2 days and was attributed to intestinal parasites, no complaints were recorded in operators throughout the trial.

No complaints were recorded among the residents of sprayed villages.

Summary of safety evaluations

In no operation did a serious case of poisoning occur, but some complaints were encountered among both spraymen and residents in each operation except that in Nigeria. The first reaction to an overexposure to OMS-33—nausea, headache, excessive sweating and general weakness—made a sprayman stop work. In every case a short rest away from further exposure led to a rapid improvement so that within half-an-hour to an hour work could be resumed and symptoms did not reappear. In El Salvador it was probable that heat exhaustion when humidity was high, coupled with some dehydration and salt depletion, exaggerated by the excessive sweating, induced by OMS-33, contributed to some of the reactions seen among the spraymen.

Safety measures used were limited to simple protective clothing and a good standard of personal hygiene. When personal hygiene was poor and dirty protective clothing was worn, the frequency of reactions rose.

There were reactions to OMS-33 reported by some residents of the sprayed houses in all trials except that in Nigeria. In Iran the complaints often occurred among those who had infringed the recommended precautions by entering the houses during or immediately after spraying or by sweeping the floors with an insufficient amount of water. In El Salvador, small children crawling on floors which had not been swept after spraying sometimes showed reactions. The ill-effects were short-lived and did not lead the residents to refuse to have their houses resprayed in subsequent operations.

It should be recognized that the most common complaints of spraymen and villagers after exposure to OMS-33 (headache, nausea, vomiting, etc.) are common complaints which may be due to various causes and that a group of spraymen or villagers not

exposed to insecticides would mention a certain number of such complaints when questioned. No attempt was made to ascertain the extent of such a "background" of complaints among persons not exposed to OMS-33.

Significance of methods for determining the degree of exposure to OMS-33

In most of the trials listed above, several different field or laboratory methods were employed with a view to evaluating their usefulness in determining the degree of operators' exposure to OMS-33.

By serial blood cholinesterase determinations on operators carried out by a laboratory method in Iran (Vandekar et al., 1968) and Northern Nigeria a pronounced fall in whole-blood cholinesterase activity during the work and a distinct recovery after cessation of exposure were established as an everyday pattern of the enzyme's activity fluctuation. No correlation between the degree of whole-blood cholinesterase inhibition and complaints could be found, most falls in cholinesterase activity—including the largest ones—being unassociated with complaints. Recent studies (Vandekar & Wilford, 1969) have shown that this can be at least partly attributed to the rapid falls of cholinesterase activity during the storage of undiluted samples collected from the workers exposed to OMS-33. In agreement with unpublished results obtained both *in vitro* and in human volunteers, erythrocyte cholinesterase was found to provide a much more sensitive index of exposure to OMS-33 than plasma cholinesterase. No cumulative inhibitory effect could be demonstrated on blood cholinesterase in operators during the 6-week exposure. Limited observations in the El Salvador trials were consistent with these findings.

Exposure to OMS-33 was also measured by determining the level of phenol metabolites in urine by a laboratory method in some of the trials performed in El Salvador and Northern Nigeria. However, excretion of metabolites was often found to be high in spraymen without symptoms, and sometimes to be low in men with symptoms, much apparently depending on the time of collection of the specimen. Somewhat higher excretion was noted on the second day of wearing the protective uniform. Comparative trials had shown that while the wearing of gloves reduced the absorption of OMS-33 by spraymen who washed their hands frequently, the additional protection afforded was not significant. When the degree of cholinesterase depression and the amount of phenols excreted in urine were compared in operators working with or without respirators, but washing their hands and face after each pump-charge, no significant additional protection could be established as being afforded by the respirators.

On the basis of this information it is concluded that—in contrast to what is the case with organophosphorus compounds—routine cholinesterase determination has no practical value in curtailing further exposure to OMS-33. Determination of metabolites in urine, though of theoretical interest, is also of little value as a warning of overexposure. Minor complaints, from which recovery is rapid, serve as early indications of overexposure.

SUMMARY AND CONCLUSIONS

OMS-33 successfully met all the criteria of the three laboratory screening stages (Stages I through III) in the WHO programme for evaluating a residual insecticide for anopheline mosquito control. These laboratory tests indicated that it was intrinsically more toxic than lindane, fenthion, dichlorvos, dieldrin, malathion and DDT to insects already shown to be either susceptible or resistant to one or another of these compounds. The duration of residual effectiveness, particularly on mud surfaces, was indicated to be less than that of DDT and dieldrin. OMS-33 was recommended for field trials against the anopheline mosquitos (Stage IV, experimental hut trials) in 1961.

In the mud and thatch experimental huts at Arusha, Tanzania, 1.5 g/m^2 was effective for more than 2 months. In huts lined entirely with sorptive mud, this dosage was effective for only a short period. In Bobo Dioulasso, Upper Volta, however, in specially treated all-mud huts 2 g/m^2 of the insecticide was effective for at least 2 months. In experimental huts in El Salvador, 80% of the naturally entering *An. albimanus* were killed for 8–10 weeks in huts with pole walls and grass roofs and for 12 weeks in the more enclosed huts of mud with grass roofs.

Village-scale trials (Stage V) of OMS-33 carried out in villages near Lagos, Nigeria, in 1962 at a target dosage of 1.5 g/m^2 gave satisfactory reduction of *An. gambiae* and *An. funestus* for 12 weeks or more. In a trial near Borazjan, Iran, in 1963, OMS-33 at 2 g/m^2 effectively controlled *An. stephensi* for the entire 12-week mosquito season. This same dosage gave satisfactory reductions of *An. albimanus* for 7–10 weeks in village trials in El Salvador, although there were periods of satisfactory kill after this period which were associated with increased

humidity. In a repeat spraying in one village, the effectiveness continued for 12 weeks.

During early field tests with OMS-33, it was suggested that its effectiveness in mud houses might be enhanced if it was impregnated on cheesecloth which was hung in the houses. Some trials in Arkansas, USA, gave 96%–100% control of *An. quadrimaculatus* for the 10 weeks of the experiment. Partial treatment of buildings, consisting of hanging a 90-cm-wide strip of impregnated cheesecloth around the walls, gave 82% or better control for 10 weeks. A trial near Kaduna, Nigeria, indicated that a strip of cheesecloth impregnated with about 25 g of OMS-33 (at 2 g/m²) effectively controlled *An. gambiae* and *An. funestus* for about 90 days whereas a residual treatment of 136 g per house (at 2 g/m²) by conventional residual spraying gave somewhat better control for about 100 days.

In the course of these field studies it also became evident that there was a considerable airborne effect of this insecticide which made bioassay wall tests inaccurate as a measure of contact effectiveness (*per se*) of sprayed surfaces. Special studies in El Salvador indicated that this airborne effect extended for some distance from sprayed pole-constructed houses. These investigations showed that this airborne toxic effect of the insecticide extended for 20 m or more from freshly sprayed houses and continued to kill more than 60% of DDT- and dieldrin-resistant *An. albimanus* in cages located within 4 m of the nearest sprayed house for 41 days. Although this effect is more pronounced downwind, it has been found to kill mosquitos in all directions from treated houses immediately after spraying. Where sprayed houses are close together this effect seems to extend from house to house, killing many mosquitos before they enter the houses. This same phenomenon has been noted in Nigeria and Iran.

On the basis of results obtained at Stages IV and V, operational field trials (Stage VI) were undertaken in El Salvador, Northern Nigeria and south-west Iran. In Iran, OMS-33 trials carried out by the Government of Iran in 1966 and jointly by the Government of Iran and WHO during 1967, provided good control of DDT- and dieldrin-resistant *An. stephensi* in mud houses for 3–4 months and of *An. dthali* for more than 2½ months. Under the conditions prevailing in Northern Nigeria, effective control of *An. gambiae* (which cannot be adequately controlled by DDT because of its irritability to that insecticide) and of *An. funestus* was achieved for 3–4 months. The first two rounds of spraying with OMS-33 in El Salvador were carried out at 4-month intervals and subsequent rounds at 3-month intervals. Effectiveness varied considerably against DDT- and dieldrin-resistant *An. albimanus*, lasting only 6 weeks in one instance but as long as 14 weeks in compact villages. In one village which was sprayed 5 times over a period of 16 months only 12 *An. albimanus* and 14 *An. pseudopunctipennis* were captured during repeated fortnightly night-biting collections during that period. In morning searches for mosquitos, also at 2-week intervals, only 3 live *An. albimanus* and 22 *An. pseudopunctipennis* were found. In most villages with large productive *An. albimanus* sources near by, the effective control was 8–10 weeks.

It is concluded from the evidence available that OMS-33 applied as a residual spray to houses is effective in controlling *An. funestus*, DDT-irritable/dieldrin-resistant *An. gambiae* and DDT- and dieldrin-resistant *An. stephensi*, exophilic *An. dthali* and DDT- and dieldrin-resistant *An. albimanus* for 2–4 months depending on local conditions. The effectiveness of this insecticide appears to be enhanced in situations where villages are compact, apparently owing to the airborne phase, which kills the vectors at a distance from the sprayed surfaces. It has been suggested that the pronounced airborne phenomenon observed with this insecticide may be successful in interrupting malaria transmission in some areas where the disease persists largely because of peridomiciliary transmission. Investigations are under way to ascertain whether a selected spraying of houses (such as thatch roofs or eave areas only) may have an effect on the mosquitos nearly equal to that observed when the whole house is sprayed and at a considerable saving of insecticide. Additional trials of OMS-33-impregnated cheesecloth will also be carried out when a suitable uniform formulation can be secured.

Observations on the safety of OMS-33 when used as a residual insecticide have been carried out in several village trials (1962–66) and in operational field trials (1966–67) in 3 different parts of the world with a total of more than 4000 man-days of spraying. All these trials were conducted under medical supervision, and laboratory tests to determine cholinesterase inhibition and metabolites in urine were performed. There were minor symptoms among some spraymen and a few inhabitants in 2 trial areas. All patients recovered within a very short time, usually without treatment. Where treatment was given, a few drops of belladonna tincture proved effective. In the case of operators, complaints were

mainly associated with insufficient care and experience in avoiding the inhalation of spray mist or with heavy skin contamination and insufficient washing during the work; in the case of inhabitants, they were usually associated with direct contact with the spray.

OMS-33 needs to be handled with somewhat stricter precautions than are generally taken for applying DDT. Detailed instruction sheets have been prepared to provide field personnel at all levels with the information necessary to ensure safe spraying of OMS-33 as a residual insecticide in houses.

In view of the very marked symptomless daily fluctuation in cholinesterase activity and the absence of a cumulative inhibitory effect during exposure over several weeks, routine cholinesterase examination is of little, if any, practical value in determining when spraymen should be withdrawn to prevent overexposure. On the other hand, minor complaints, such as headache and nausea, cause the operator to stop work, thereby preventing further exposure. He quickly recovers, particularly if he washes the contaminated skin.

Altogether, over 30 metric tons of OMS-33 water-dispersible powder have been used in large-scale operational trials and the commercially available formulations have proved satisfactory from the standpoints of stability under tropical storage, safety, ease of spray applications and entomological effectiveness.

The WHO Expert Committee on Malaria (1968), which met during September 1967, in considering measures for problem areas, reviewed the data from the various stages of the evaluation of OMS-33 and noted the promising results achieved.

In the light of the evidence available, the authors are of the opinion that OMS-33 is suitable for Stage-VII epidemiological evaluation field trials.

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RÉSUMÉ

L'EMPLOI DU MÉTHYLCARBAMATE D'*O*-ISOPROPOXYPHÉNYLE (OMS-33) EN PULVÉRISATIONS À EFFET RÉMANENT POUR LA LUTTE CONTRE LES ANOPHÉLINÉS: ÉVALUATION DE CE COMPOSÉ DANS LE CADRE DU PROGRAMME OMS D'ESSAI ET D'ÉVALUATION DE NOUVEAUX INSECTICIDES

L'OMS-33 a subi avec succès la série d'essais que comportent les stades I à VI du programme OMS d'essai et d'évaluation de nouveaux insecticides destinés à la lutte contre les anophélinés. Le présent article décrit les diverses épreuves auxquelles sont soumis les nouveaux composés et expose les résultats obtenus en ce qui concerne l'OMS-33.

Au cours d'essais opérationnels de grande envergure effectués en Iran, au Nigéria et en El Salvador, on a constaté que l'OMS-33, appliqué à raison de 2 g/m² assurait une lutte efficace contre *Anopheles stephensi*, *An. gambiae* et *An. funestus* pendant 3 à 4 mois, contre *An. albimanus* pendant 2 à 4 mois et contre *An. dthali* pendant 2 mois et demi.

L'OMS-33 possède une action létale à distance due au transport par voie aérienne de particules d'insecticide de sorte que, longtemps après les pulvérisations, les moustiques sont tués même s'ils n'entrent pas en contact avec les surfaces traitées. Au cours d'essais effectués en Iran, 60% et plus des *An. stephensi* exposés en cage pendant

une heure à 1 ou 2 m de distance d'une surface traitée ont été tués. Cette action à distance a été observée pendant une période s'étendant de 74 à 88 jours après la pulvérisation. Un phénomène similaire a été constaté dans des habitations traitées par pulvérisations en El Salvador et au Nigéria du Nord, et même à l'extérieur de certaines maisons, notamment en El Salvador, construites de telle sorte que l'air circule aisément de l'intérieur vers l'extérieur. Il semble que l'on puisse tirer parti de cette propriété de l'OMS-33 dans les endroits où les moustiques pénètrent à l'intérieur des habitations pour attaquer l'homme, mais ne se reposent pas suffisamment longtemps sur les surfaces traitées pour être exposés à une dose létale d'insecticide. On peut également envisager d'utiliser ce composé lorsque la transmission du paludisme résulte principalement de l'agressivité des moustiques en dehors des habitations.

On a procédé à une étude approfondie de la toxicité de l'OMS-33 pour les mammifères. Des mesures de précaution simples permettent d'assurer la protection des personnes exposées, notamment des habitants des maisons traitées et des opérateurs.

Les études chimiques ont montré que la préparation commerciale présentant l'OMS-33 sous forme de poudre dispersable dans l'eau était stable dans les conditions pratiques de conservation et d'emploi. Plus de 30 tonnes du composé ont été utilisées durant les essais sur le terrain.

On a aussi mis à l'étude de nouvelles formulations de l'OMS-33 sous la forme de bandes de gaze imprégnées de l'insecticide pour le traitement partiel des locaux. Ces procédés se sont révélés actifs contre les anophèles pendant une durée de 10 à 12 semaines, mais leur mise au point exige de nouvelles recherches.

REFERENCES

Coz, J., Venard, P., Attiou, B. & Somda, D. (1966) *Méd. trop.*, **26**, 537-543

Dawson, J. A., Heath, D. F., Rose, J. A., Thain, E. M. & Ward, J. B. (1964) *Bull. Wld Hlth Org.*, **30**, 127-134

Ellman, G. L., Courtney, K. D., Andres, V., Jr & Featherstone, R. M. (1961) *Biochem. Pharmacol.*, **7**, 88-95

Gahan, J. B., LaBrecque, G. C. & Wilson, H. G. (1961) *Mosquito News*, **21**, 289-294

Gahan, J. B., Wilson, H. G. & Smith, C. N. (1965) *Bull. Wld Hlth Org.*, **32**, 169-173

Gahan, J. B., Wilson, H. G. & Smith, C. N. (1966) *Bull. Wld Hlth Org.*, **34**, 792-796

Georghiou, G. P. & Metcalf, R. L. (1961) *Mosquito News*, **21**, 303-306

Hadaway, A. B. & Barlow, F. (1965) *Bull. Wld Hlth Org.*, **33**, 129-140

Mathis, W. & Schoof, H. F. (1963) *Mosquito News*, **23**, 145-149

Pant, C. P. & Self, L. S. (1966) *Bull. Wld Hlth Org.*, **35**, 709-719

Pleština, R. (1968) *Prilog poznavanju toksičnih svojstava o-izopropoksifenilmetilkarbamata*, Zagreb (M.Sc. Thesis)

Pleština, R. & Vandekar, M. (1966) *Studies in the toxicology of* N-*methylcarbamates. IV. Symptoms as related to cholinesterase activity.* In: *XVth International Congress on Occupational Health, Vienna, 19–24 September 1966*, Vienna, vol. 2, pp. 525-528

Reiner, E. & Simeon-Rudolf, V. (1966) *Biochem. J.*, **98**, 501-505

Simeon, V. (1966) *Studies in the toxicology of* N-*methylcarbamates. II. Correlation between anticholinesterase activity and acute toxicity.* In: *XVth International Congress on Occupational Health, Vienna, 19–24 September 1966*, Vienna, vol. 2, pp. 521-524

Smith, A. & Hocking, K. S. (1963) *Bull. Wld Hlth Org.*, **29**, 273-277

Svetličić, B. & Fajdetic, T. (1965) *Iugosl. physiol. pharmacol. Acta*, **1**, 196

Vandekar, M. & Fajdetić, T. (1966) *Studies in the toxicology of* N-*methylcarbamates. III. Tolerance of carbamates at different rates of intravenous infusion.* In: *XVth International Congress on Occupational Health, Vienna, 19–24 September 1966*, Vienna, vol. 2, pp. 529-532

Vandekar, M., Hedayat, S., Pleština, R. & Ahmady, G. (1968) *Bull. Wld Hlth Org.*, **38**, 609-623

Vandekar, M., Reiner, E., Svetličić, B. & Fajdetić, T. (1965) *Brit. J. industr. Med.*, **22**, 317-320

Vandekar, M. & Svetličić, B. (1966) *Arh. Hig. Rada*, **17**, 135

Vandekar, M. & Wilford, K. (1969) *Bull. Wld Hlth Org.*, **40**, 91-96

Wilhelm, K. & Vandekar, M. (1966) *Studies in the toxicology of* N-*methylcarbamates. I. Comparative toxicity tests and estimation of persistence of inhibitor in the body.* In: *XVth International Congress on Occupational Health, Vienna, 19–24 September 1966*, Vienna, vol. 2, pp. 517-520

WHO Expert Committee on Insecticides (1967) *Wld Hlth Org. techn. Rep. Ser.*, **356**

WHO Expert Committee on Malaria (1968) *Wld Hlth Org. techn. Rep. Ser.*, **382**

Wilson, I. B., Hatch, M. A. & Ginsburg, S. (1960) *J. biol. Chem.*, **235**, 2312