

CTD/WHOPES/97.5
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**REPORT OF THE FIRST WHOPES WORKING GROUP
MEETING**

**WHO/HQ, GENEVA
26-27 June 1997**



**WORLD HEALTH ORGANIZATION
DIVISION OF CONTROL OF TROPICAL DISEASES (CTD)
WHO PESTICIDE EVALUATION SCHEME (WHOPES)**

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Table of contents

	Page
1. Objectives	1
2. Preparatory work	1
3. Conduct of the meeting	1
4. Background/supportive documents	2
5. Insecticides and formulations tested in phases II and III (WHOPES) field trials	5
6. Main results	6
7. Pending questions	12
8. Conclusions	13
Annex I. Bibliography	15
Annex II. List of participants	18

1. Objectives

The purpose of the meeting was to review the reports of field trials of pesticides that have reached the final stages of evaluation by the WHO Pesticide Evaluation Scheme (WHOPES) and to make recommendations to the Division of Control of Tropical Diseases (CTD) for their use in vector control.

The reports submitted to the Working Group related to field trials of indoor residual spraying or bednet impregnation with etofenprox (Mitsui Toatsu Chem., Japan) or deltamethrin (AgrEvo, UK) in one or more of the following formulations: etofenprox (20WP, 20% wettable powder; 20EC, 20% emulsifiable concentrate; 10EW, 10% emulsion oil-in-water) for the purpose of *Anopheles* or *Triatoma* control, and deltamethrin (25SC, 2.5% suspension concentrate) for *Triatoma* control.

2. Preparatory work

All the reports to be reviewed were sent to the participants in April 1997 for advance study to facilitate review at the meeting. In addition, each participant was requested to study specifically one or two related reports and to prepare an abstract of each one, critically analyzing the objectives, methodology and the significant contents and main conclusions of the research, with special reference to the objectives of WHOPES.

The abstracts prepared by participants were also circulated prior to the meeting. The list of the supporting/background documents and participants are presented in Annexes I and II respectively.

3. Conduct of the meeting

The meeting took place at WHO Headquarters in Geneva from 26-27 June 1997. Dr K. Behbehani, Director of CTD, opened the meeting on behalf of the Director-General. Dr Yap Han Heng was appointed as chairman and Dr. J.A. Najera as rapporteur.

In his opening address, Director of CTD highlighted the importance of the WHOPES Programme to support the development of new pesticides for public health use and, in particular, those potentially applicable to the renewed efforts in malaria and dengue control; the coordinated efforts for Chagas disease control in the central and southern America; and the continued development of onchocerciasis control. The need for development and evaluation of new products was emphasized, not only to cope with the problem of multiple resistance, but also to optimize the application of new approaches such as use of impregnated bednets. Director of CTD also referred to the re-orientation of the WHOPES to ensure further strengthening of the programme. The need for capacity building of Collaborating Centres in endemic countries was stressed to improve the quality of work and to speed up evaluation of candidate pesticides and their formulations.

Dr M. Zaim, scientist in charge of WHOPES, reviewed the status of development of the two pesticides and their formulations under consideration, recognizing that the trials under review were planned and executed before the recent redefinition of the WHOPES phases (CTD/WHOPES/IC/96.1). Dr Zaim referred to the large amount of scientific knowledge which exists on etofenprox, and referred to the use of deltamethrin SC, which has become the *de facto* reference for *Triatoma infestans* chemical control. In both cases, a considerable body of information has become available from trials in several countries and, therefore, the WHOPES trials were aimed at confirmation and consolidation of existing knowledge. The meeting proceeded to discussion of the reports, which were presented by the participant who had carried out the preliminary review.

4. Background/supportive documents (Annex I)

Phase II trials of residual spraying of etofenprox WP in Burkina Faso and impregnation of bednets with etofenprox EC in Burkina Faso (Bobo-Dioulasso) and Muheza (Tanzania), demonstrated a high repellent effect of this insecticide in preventing entry into experimental huts and inducing exophily, being one of the most repellent pyrethroids

tested in Bobo-Dioulasso, where the strong excito-repellency was shown also on impregnated bednets at the very low dose (25 mg a.i./m²) tested. Nevertheless, it appears that immediate mortality with etofenprox is lower than with other pyrethroids tested and mosquitos had time to bite once inside the house (gorging rate was 94%); similarly, in the experimental huts in Muheza impregnated bednets at a dose of 200 mg a.i./m² showed one of the lowest ability in preventing feeding (geometric mean of *Anopheles* succeeding in feeding 11.5% vs. 1.4% with permethrin EC at 500 mg a.i./m²), although it produced a relatively high mortality (geometric mean of 64.6% vs 61.2% with permethrin EC); it should be noted that prevention of entry was not reported from Muheza and that results of total mortality in experimental huts did not report separately the mortality inside the hut and after reaching the exit traps.

Although pyrethroids are generally not recommended for larviciding against mosquitos, the Onchocerciasis Control Programme (OCP) in West Africa has included etofenprox EC at a dose of 0.03 mg a.i./l for 10 minutes, among the seven larvicides currently in use. The effects on non-target organisms were investigated, especially on shrimp, usually very susceptible to pyrethroids. On *Caridina* sp, it had no detectable effect in the field. From bioassays it was shown that six times the operational dose is needed to cause 50% mortality of *Caridina* and 30 times this same dose for 95% mortality. Immediately after application, some increased drift (detachment of total fauna) by use of etofenprox was noted; however no disruption was noted in the relative composition of aquatic invertebrate communities. The observed drift was far below that observed for permethrin. The use of etofenprox by OCP was then approved by the Ecological Group (an independent panel of experts).

Etofenprox is a non-ester pyrethroid insecticide with comparable insect toxicity and a similar mode of action to other pyrethroids. Cross-resistance studies on standard susceptible and resistant laboratory strains of *An. gambiae*, *An. albimanus*, *An. stephensi*, and *Culex quinquefasciatus* showed no effect of carboxylesterase, elevated esterase, altered acetylcholinesterase or glutathione S-transferase-based resistance mechanisms, while cross

resistance to etofenprox occurred in a pyrethroid-resistant strain of *Cx. quinquefasciatus* with both oxidase and *kdr*-like resistance mechanisms.

Trials on the use of impregnated bednets had been conducted in North Viet Nam, with etofenprox EC and EW formulations, and in South Viet Nam and Cambodia with etofenprox EW, all at a dose of 200 mg a.i./m²; all trials indicated a marked effect on resting and biting densities and high residual bioassay mortalities between 4 and 6 months with residual effect on wood one or two months longer than on sorptive materials.

Regarding the efficacy of impregnated bednets on long term use and different storage conditions, as well as their residual effect after laboratory-controlled washing, CDC investigated etofenprox 10 EW (300 & 500 mg a.i./m²) in comparison with permethrin 10% EC (300 & 500 mg a.i./m²) and deltamethrin 2.5% EC (15 & 25 mg a.i./m²), on polyester netting material (100 denier), with the following results:

- (i) Bioassay tests were carried out every three months for one year on impregnated materials kept under three conditions of storage: (a) in the dark (on a drawer); (b) hanging on a laboratory room, exposed to indirect sunlight; and (c) in a greenhouse where the roof was coated with a semi-opaque substance and a heating/air conditioning system which ensured constant temperature. Results with etofenprox were intermediate between the other two insecticides, with deltamethrin clearly showing a stronger residual effect; etofenprox at 500 mg a.i./m², showed a potentially useful residual effect of 6-8 months, although chemical analysis (GLC) showed a faster decay of etofenprox under greenhouse conditions.
- (ii) The effect of washing was investigated, by both bioassay tests and chemical analysis, after one to three washing cycles consisting of: placing the netting sample in a jar containing 100 ml of aqueous 2% SDS; mechanical shaking for 5 minutes; rinsing by shaking for 10 minutes in 300 ml of de-ionized water; and wringing and air drying overnight. Results again showed

etofenprox to be intermediate between the other two insecticides. At the dose of 500 mg a.i./m² it caused about 35% mortality after a second wash, with 3 minutes exposure.

5. Insecticides and formulations tested in phases II & III (WHOPES) field trials

The following insecticides/formulations/doses and target vectors were reviewed:

- For indoor residual spraying

1. Against *Anopheles*

- 1.1 Experimental huts

- Etofenprox 20WP (100, 200 & 400 mg a.i./m²) vs unsprayed hut (Thailand)

- 1.2 Village scale

- Etofenprox 20WP (300 mg a.i./m²) vs DDT 75% WP (2 g a.i./m²) (Thailand)
- Etofenprox 20WP (500 mg a.i./m²) vs unsprayed village (Iran)

- 1.3 Large scale

- Etofenprox 20WP at 300 mg a.i./m² vs malathion (2 g a.i./m²) (Sri Lanka)
- Etofenprox 20WP (100 mg a.i./m²) vs DDT 75% WP (2 g a.i./m²) (Philippines)
- Etofenprox 20WP (200 mg a.i./m²) vs unsprayed village (Indonesia)

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