



Safety of Pyrethroid-treated mosquito nets

Fact sheet

WHO/CDS/CPE/WHOPES/99.5
ENGLISH ONLY
DISTR.: GENERAL

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II INTRODUCTION II

Malaria accounts for a large part of the disease burden of poor countries, causing over a million deaths a year, mainly in African children. There are an estimated 300-500 million episodes of acute illness annually, affecting up to one in ten of the world's population.

Insecticide treated mosquito nets effectively reduce malaria morbidity and mortality in many different epidemiological settings. Their use may not only benefit the people who are actually sleeping under them, but when used by the majority of the community, people who sleep without treated nets may also receive fewer infective bites.

Table 1 lists the insecticide products which have successfully passed the WHO Pesticide Evaluation Scheme (WHOPES), and gives the recommended dosages for treatment of mosquito nets against malaria vectors. All listed products are pyrethroid insecticides which are presently the only group of insecticides recommended for this use. This is due to their safety for humans and repellency, high knock down effect, irritancy and efficacy at low dosages, for mosquitoes. WHO specifications for the listed products, used for quality control, are available on request from WHO Pesticide Evaluation Scheme, Department of Control, Prevention and Eradication, Programme on Communicable Diseases, World Health Organization, 1211 Geneva 27, Switzerland, and are also available on the WHO homepage on the Internet (www.who.ch/ctd).

Table 1. WHO recommended insecticides for treatment of mosquito nets for malaria vector control.

INSECTICIDE	FORMULATION ¹	DOSAGE ²
<i>Alpha-cypermethrin</i>	SC 10%	20-40
<i>Cyfluthrin</i>	EW 5%	50
<i>Deltamethrin</i>	SC 1% and WT 25%	15-25
<i>Etofenprox</i>	EW 10%	200
<i>Permethrin</i>	EC 10%	200-500

¹ SC= suspension concentrate; EW=emulsion, oil in water; WT=water dispersible tablet; EC: emulsifiable concentrate.

² Milligrams of active ingredient per square metre of netting.

³ WHO specifications under development

This document reviews the toxicity and hazards of insecticides and insecticide treated mosquito nets and provides relevant recommendations on their safe use. Special consideration has been given to supply of insecticide products for treatment of mosquito nets "over the counter".

II TOXICITY AND HAZARDS II

Toxicity and hazard are not synonymous terms. Toxicity is the inherent poisonous potency of a compound under experimental conditions, while hazard refers to the risk or danger of poisoning when a chemical is used or applied.

The toxicity of pyrethroids is due to their affinity for and intrinsic effect on receptors or targets within the sodium channels essential for nerve conduction. Being highly lipophilic, pyrethroids pass through cell membranes and are absorbed through the skin, by inhalation and by ingestion. However, their rapid metabolism greatly lowers the magnitude of the resultant toxicity.

People are at risk of exposure to insecticides through accidental swallowing or drinking of the insecticide products, inhaling solvent vapours of EC formulations, splashing the product into the eyes or onto the skin during the net treatment, and insecticide residues during the net use.

CHRONIC TOXICITY

The chronic toxicity of the common insecticide products used for treatment of mosquito nets are presented in *Table 2* as the relevant "no observed adverse effect level" (NOAEL) and acceptable daily intake (ADI). NOAEL is the dosage of an insecticide that results in no discernible harm to experimental animals in chronic toxicity studies that include the close examination of all body organs for abnormalities. The ADI is the daily exposure level of the insecticide residue, expressed as mg/kg body weight, that, over the entire lifetime of a human being, appears to be without appreciable risk, on the basis of all facts known at a given time, and has been calculated from the relevant NOAEL, with a safety factor of 100. Thus, for example, an ADI of 0.01 mg of active ingredient/kg body weight is a safety standard value which corresponds to daily intake (licking) of 0.1 mg active ingredient of the insecticide, by a 10 kg child, from the treated net. At the target dosage of 25 mg/m², such an amount of insecticide is present on an area of 6 x 6 cm. However, pyrethroids bind strongly to the fabric and even in washing with soap and water, only part of the insecticide is removed. Therefore there is no indication to suggest that the accidental licking of the net would pose a health hazard to the child.

Table 2. The chronic toxicity of insecticides commonly used for treatment of mosquito nets.

PRODUCT	RELEVANT NOAEL mg a.i./kg bw/day	ADI mg a.i./kg bw (safety factor of 100)
<i>Alpha-cypermethrin</i>	1.5	0-0.02
<i>Cyfluthrin</i>	2	0-0.02
<i>Deltamethrin</i>	1	0-0.01
<i>Etofenprox</i>	3.1	0-0.03
<i>Permethrin</i>	5	0-0.05

In long-term toxicity studies of pyrethroid insecticides commonly used for treatment of mosquito nets, there have been no teratogenic, carcinogenic or mutagenic effect in experimental animals. The volatility of pyrethroids is also low; given the low dosages of insecticide used for the treatment of nets, the risk of inhalation toxicity by the users of treated nets is remote.

ACUTE TOXICITY

Table 3 shows the LD₅₀ values in rats from both oral and dermal administration of the common insecticides used for treating mosquito nets. The LD₅₀ is a statistical estimate of the amount of a substance required to kill 50% of a population of test animals. These values are relevant for comparing with single or multiple exposures of the insecticide over a relatively short period of time that might be encountered accidentally or by a person handling the product.

Table 3. Acute oral and dermal toxicity of insecticide formulations commonly used for treatment of mosquito nets, as reported by manufacturers in the Material Safety Data Sheets of the products¹.

PRODUCT	ORAL TOXICITY:	DERMAL TOXICITY:
	LD ₅₀ Value mg/kg bw rats	LD ₅₀ Value mg/kg bw rats
Alpha-cypermethrin SC 10%	4,952	2,000
Cyfluthrin EW 5%	2,100	>5,000
Deltamethrin SC 1%	>10,000	>10,000
Deltamethrin WT 25%	1,965	2,000 rabbit
Etofenprox EW 10%	>5,000 ²	>5,000
Permethrin EC 10%	5,000 - 6,000	4,000 - 10,000

¹ The material safety data sheets of 3 major manufacturers have been consulted for provision of data relating to permethrin EC 10%.

² The exact figure for the acute oral toxicity of etofenprox EW 10%, a non-ester pyrethroid, is not available. However, by extrapolation from the figures for active ingredient, it would give a figure of >400,000 mg/kg bw.

As previously mentioned, acute toxicity may occur through treatment and handling of insecticides for treatment of mosquito nets. People directly involved in dipping large numbers of nets are at most risk. However, those who occasionally treat their own net are less exposed to insecticide hazard.

Among available liquid formulations, the water based products, i.e., EW (emulsion, oil in water) and SC (suspension concentrate) formulations, are preferred. They are less smelly and are less flammable, with lower risk of toxicity if they are accidentally swallowed or splashed onto the skin or into the eyes. Permethrin is the only pyrethroid insecticide which is still used as emulsifiable concentrate (EC). However, only the use of public health grade permethrin is recommended.

Solid formulations, such as water dispersible tablets (WT), have many advantages since they are easy to handle, transport and store, and there is less risk of accidental spillage and contamination than with liquids. A bittering agent should be incorporated into the product to prevent deliberate or accidental ingestion, especially by children. The adverse effects reported by net dippers include, tingling and burning sensations (paraesthesia), eye pain and irritation, swelling of the face, headache and dizziness. The paraesthesia can be unpleasant, especially if pyrethroid concentrate comes into contact with the skin of the face. Such paraesthesia has no long term consequence, but users may need to be reassured of this. Noting the marked potential for exposure to the insecticides in the process of treating mosquito nets, use of rubber gloves is essential. Use of mouth and nose mask for dipping large number of nets, especially with EC formulations is recommended.

Transitory side effects associated with the use of treated nets have also been reported by householders. This includes skin itching, eye burning, nasal irritation and sneezing, mainly during the first few days after net treatment, but most lasted for less than 24 hours.

While field use of pyrethroids for treatment of mosquito nets at the recommended use poses little or no hazard to those treating the nets, the supply of insecticide over the counter for treatment of nets by householders has particular safety concerns. Table 4 provides estimates of the relative safety of insecticide products for treatment of mosquito nets if they are to be supplied in do-it-yourself-kits. The safety factor, defined as the reciprocal of the number of single application packs in an oral LD₅₀ for a 10 kg child, is highest for etofenprox 10% EW (200) and deltamethrin 25% WT (12.5), but lowest with permethrin 10% EC (0.7). It is thus apparent that based on this very rough estimation, ingestion of the contents of even a single application pack of permethrin 10% EC could be lethal to a child. Therefore, it is strongly recommended that insecticides for home treatment of mosquito nets should be presented only in single unit doses. Moreover, if presented in liquid formulation in bottles, use of child-proof caps should be mandatory. Over the counter supply of more concentrated formulations of permethrin EC (e.g. 50% EC) should be avoided.

In the retail market, for home use, the importance of proper labelling of insecticide packages and containers and provision of instructions on the safe and proper use of the product is greater than might otherwise be the case. All packages should bear, durably and legibly, in local language, the following information: - the manufacturer's name; the formulation to specification WHO/...; the concentration of the active ingredient; the volume (liquid) or net weight (solid) of the contents; the batch or reference number; the date of manufacture, the expiry date, and the minimum cautionary advice necessary to ensure safe and effective use. In case of single dose packaging, care should be taken to ensure that the above-mentioned information is not easily separated from the insecticide itself.

Table 4. Estimates of the relative safety of insecticide products for supply over the counter.

PRODUCT	ORAL LD ₅₀ for a 10 kg child (A) ¹	AMOUNT OF FORMULATION REQUIRED FOR TREATMENT OF SINGLE NET (15 m ²) (B)	PROPORTION OF LD ₅₀ for a 10 kg child, contained in a single application pack C: (B/A)	SAFETY FACTOR (1/C)
Alpha-cypermethrin 10% SC	50 ml	6 ml	0.12	8
Cyfluthrin 5% EW	42 ml	15 ml	0.36	2.8
Deltamethrin 1% SC	100 ml	40 ml	0.40	2.5
Deltamethrin 25% WT	20 g	1.6 g	0.08	12.5
Etofenprox 10% EW	4,000 ml	20 ml	0.005	200
Permethrin 10% EC	50 ml	75 ml	1.5	0.7

¹ Estimated from the oral LD₅₀ values for rats, as reported by the manufacturers.

² Highest recommended dosage for treatment of the net has been used.