MALARIA VECTOR CONTROL

INSECTICIDES
FOR
INDOOR RESIDUAL SPRAYING

By:

Dr J.A. Najera & Dr M. Zaim

World Health Organization
Communicable Disease Control, Prevention and Eradication
WHO Pesticide Evaluation Scheme (WHOPES)
## Contents

<table>
<thead>
<tr>
<th>Acknowledgements</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. <strong>Introduction</strong></td>
<td></td>
</tr>
<tr>
<td>1.1 The use of indoor residual spraying in malaria control</td>
<td>4</td>
</tr>
<tr>
<td>1.2 Trends in the use of indoor residual spraying</td>
<td>5</td>
</tr>
<tr>
<td>1.3 Indications for the use of indoor residual spraying</td>
<td>7</td>
</tr>
<tr>
<td>1.4 The WHO Pesticide Evaluation Scheme</td>
<td>10</td>
</tr>
<tr>
<td>1.5 Problems in the choice of insecticides</td>
<td>13</td>
</tr>
<tr>
<td>1.6 Classification of insecticides</td>
<td>15</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>2. <strong>Criteria for the selection of insecticides</strong></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>2.1 Human and environmental safety</td>
<td>16</td>
</tr>
<tr>
<td>2.1.1 Toxicity and hazard</td>
<td>17</td>
</tr>
<tr>
<td>2.1.2 Protective measures</td>
<td>19</td>
</tr>
<tr>
<td>2.1.3 Measurement of exposure</td>
<td>22</td>
</tr>
<tr>
<td>2.1.4 General treatment of insecticide poisoning</td>
<td>24</td>
</tr>
<tr>
<td>2.1.5 Packaging, handling, transport and storage of insecticides</td>
<td>26</td>
</tr>
<tr>
<td>2.1.6 Disposal of insecticides and insecticide containers</td>
<td>29</td>
</tr>
<tr>
<td>2.1.7 Environmental effects</td>
<td>31</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>2.2 Efficacy and residual effect</th>
<th>32</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.2.1 Intrinsic insecticidal effect</td>
<td>32</td>
</tr>
<tr>
<td>2.2.2 Effect of the sprayed surfaces</td>
<td>33</td>
</tr>
<tr>
<td>2.2.3 Spraying cycles</td>
<td>35</td>
</tr>
</tbody>
</table>
2.3 Vector resistance
  2.3.1 Monitoring of resistance
  2.3.2 Mechanisms of resistance and cross-resistance
  2.3.3 Sources of selection pressure and resistance development
  2.3.4 Policies for protection against the development of resistance

2.4 Operational issues
  2.4.1 Organization
  2.4.2 Formulation and dosage
  2.4.3 Erosion of nozzle tips

2.5 Vector ecology and behaviour
  2.5.1 Ecology
  2.5.2 Behaviour

2.6 Social factors
2.7 Cost and cost-effectiveness
2.8 Disposal of obsolete insecticides

3. Purchasing guidelines

4. WHOPES recommended insecticides for indoor residual spraying
  4.1 Organochlorines
    4.1.1 DDT
  4.2 Organophosphates
    4.2.1 Malathion
    4.2.2 Fenitrothion
    4.2.3 Pirimiphos-methyl
4.3 Carbamates
   4.3.1 Bendiocarb  79
   4.3.2 Propoxur  82

4.4 Pyrethroids
   4.4.1 Alpha-cypermethrin  84
   4.4.2 Cyfluthrin  85
   4.4.3 Deltamethrin  87
   4.4.4 Etofenprox  88
   4.4.5 Lambda-cyhalothrin  89

5. References  92
ACKNOWLEDGEMENTS

The Department of Communicable Disease Control, Prevention and Eradication (CPE) wishes to thank the following for their critical review of the document and for their valuable comments and suggestions:

- Dr N Besbelli, Programme on Chemical Safety, World Health Organization, Geneva, Switzerland
- Dr M Coosemans, Institute of Tropical Medicine, Antwerp, Belgium
- Dr L Chadd, Zeneca, Surrey, UK
- Mr K Chanon, Roll Back Malaria, World Health Organization, Geneva, Switzerland
- Dr D Coppen, American Cyanamid, Gembloux, Belgium
- Dr CF Curtis, London School of Hygiene and Tropical Medicine, London, UK
- Dr C Debourg, National Chemicals Inspectorate (Kemi), Solna, Sweden
- Dr P Guillet, Communicable Disease Control, Prevention and Eradication, World Health Organization, Geneva, Switzerland
- Dr P Herath, Candy, Sri Lanka
- Dr J Invest, Aventis, Bucks, UK
- Dr T Itoh, Sumitomo Chemicals, Osaka, Japan
- Dr R Gusmao, World Health Organization, Regional Office for the Americas, Washington D.C., USA
- Dr M Nathan, Communicable Disease Control, Prevention and Eradication, World Health Organization, Geneva, Switzerland
- Dr AM Oliveira-Filho, Lab. de Biologia, Universidade Federal do Rio de Janeiro, Brazil
- Dr J Pronczuk, Programme on Chemical Safety, World Health Organization, Geneva, Switzerland
- Dr VP Sharma, Consultant, WHO Regional Office for South-East Asia, Delhi, India
- Dr T Tanaka, Mitsui Chemicals, Tokyo, Japan
- Dr I Vythillingam, Institute for Medical Research, Kuala Lumpur, Malaysia
- Dr G B White, Douvaine, France

This publication has been funded by the Roll Back Malaria (RBM).
1. INTRODUCTION

The current global malaria strategy includes the selective control of malaria transmission as one of its four main elements (1). Vector control is the most effective way of controlling malaria transmission. Indoor residual spraying remains the most widely used method of vector control and one of the most effective for obtaining a rapid large-scale impact at an affordable cost.

Residual spraying should be used as part of a coherent malaria control programme whenever:
- it responds to epidemiological indications;
- it can be correctly applied;
- its results can be sustained.

The purpose of this document is to help health authorities and other partners to select suitable insecticides for their malaria control programmes. It reviews the main characteristics of the insecticides, the entomological, epidemiological and ecological variables, and the operational requirements which should be taken into consideration when making that choice.

Chief features of spraying

Indoor residual spraying normally refers to the spraying of all the stable surfaces inside human habitations using an insecticide with residual action. The actual surfaces to be sprayed should include all potential resting places for the local Anopheles vectors of malaria and those which may prevent their entry into the house. Ideally these sprayable
surfaces should be determined in accordance with the biting and resting behaviour of local vectors. They normally include the interior surfaces of walls and roofs, the interior and exterior surfaces of doors and windows, and the under surfaces of roof eaves.

**Spraying should be:** a) **total** (meaning that all the dwellings are sprayed); b) **complete**, (covering all sprayable surfaces); c) **sufficient** (ensuring the uniform application of the required insecticide dose to all sprayable surfaces); and d) **regular** (spraying should be repeated at regular intervals so as to ensure that there is an effective residue in place during the transmission season).

It is important to recognize the essential characteristics of spraying when choosing it as a control intervention. **The expected result of indoor residual spraying is mainly to reduce the survival of vector(s) entering houses, whereas antilarval measures are aimed at reducing vector density.** When indoor surfaces have been sprayed with residual contact insecticides, mosquitoes die when they enter and rest in those houses. Most of the main malaria vectors bite in the middle of the night, when people are normally indoors and asleep. Generally, mosquitoes do not rest for any length of time before biting. However, when fully fed, they tend to rest on a nearby wall for at least a few hours. Even semi-sylvatic vectors, which may prefer outdoor daytime resting, rest indoors for some time after feeding there on humans. In addition, particularly in arid areas, a house may be the preferred daytime resting place for the vector, even when people sleep outside and therefore most biting takes place outdoors. In contrast, there are situations where malaria is maintained by people being exposed to transmission outside the village, when occupied in activities requiring that they stay for several nights in the open or in shelters which often have no sprayable surfaces. Where people
work or stay in the open or in limited shelter, spraying of the village may have very little impact on malaria transmission.

It is essential for the success of indoor residual spraying that there is sufficient mosquito-insecticide contact. **Indoor spraying is nearly useless in the control of mosquitoes which bite and rest outdoors.** Domestic animal shelters would normally be considered part of routine indoor spraying programmes.
1.1 The use of indoor residual spraying in malaria control

The discovery of residual insecticides and their rapid effectiveness in controlling malaria transmission led to the intensive use of indoor residual spraying as the main measure of malaria control during the second half of the 20th century in most malaria-endemic countries. Although the expected eradication of the disease was not obtained in most tropical areas, the experience gained led to a solid understanding of the mode of action of residual spraying on vector populations. It showed the problems involved in the operational use of residual insecticides, as well as the influence of ecological and socioeconomic factors on the sustainability of the early success. As a result, the development of malaria control strategies during the last fifty years has moved from an almost exclusive reliance on indoor residual spraying to a main emphasis on disease management and a selective use of transmission control methods adapted to the local epidemiology.

The current global malaria control strategy therefore calls for the selective control of transmission. Indoor residual spraying remains the most generally applicable method of transmission control.

The malaria control strategy has to be flexible and continuously responsive to changes in the effectiveness of the measures adopted. It involves adapting to the epidemiological, operational and social conditions of different areas and accommodating their changes over time. This has implications for the training of human resources. Good training and supervision of the operations are also required to ensure the use of protective measures for spraymen and community inhabitants.
Selective application of insecticides implies a precise definition of the areas to be sprayed and planning of the frequencies and times of application. There must also be clear criteria for when spraying operations are to stop, and for when they are to be continued beyond the initial set time period, or beyond the areas originally defined for spraying. Spraying operations may be limited to certain geographical areas, individual villages or groups of villages, or to specific times of the year, e.g. just before the peak of the transmission season. Selective use of insecticides may reduce costs, decrease the risk of resistance developing, and allow more resources to be allocated to ensuring better coverage in vulnerable areas.

Before spraying it is necessary to make an adequate assessment of the epidemiological situation, and also to assess the epidemiological impact of spraying once it has started. This is achieved by correlating changes in epidemiological indicators with data on quality and coverage of spraying operations, taking proper consideration of any ecological or social change which may have affected those indicators.

1.2 Trends in the use of indoor residual spraying

The tendency since the 1970s has been to decrease the use of indoor residual spraying for malaria control. For example, in the Region of the Americas, the number of houses sprayed each year for malaria control decreased from a high of 15 million houses in 1964 to 1.6 million in 1997. Also, there has been a trend to replace DDT, the most widely used insecticide for malaria control, by other insecticides. DDT use has also declined in the other WHO
regions in favour of other insecticides, particularly pyrethroids, in recent years.

The main reason for the decline in the use of DDT, particularly since the 1980s, has not always been the observed decrease of effectiveness. It has also been the result of adverse publicity on the alleged safety and environmental hazards of DDT and its reduced production and availability, particularly in formulations which meet WHO specifications.

In contrast with this trend, the use of DDT for malaria control in Madagascar has been reinstated on a large scale in the highlands, following a dramatic epidemic in 1986-87. Since then a reported 1.5 million houses have been sprayed. In early 2000, South Africa reverted from using deltamethrin back to DDT. This was because Anopheles funestus had become resistant to pyrethroids but continued to be susceptible to DDT.

In recent years, the use of insecticide (pyrethroid) treated mosquito nets (ITNs) as a potential major prevention measure has been a growing trend. The aim is to replace residual house spraying in national malaria control programmes with ITNs, e.g. in China, Solomon Islands and Viet Nam. Many countries in Africa are trying to adopt this strategy. Nevertheless, although use of ITNs by a high proportion of the population is essential if the community is to be protected (as in indoor residual spraying programmes), coverage in rural areas remains extremely low.

An additional role is now developing for indoor residual spraying as a preventive measure of choice in many cases. This is as a result of the present increased attention to malaria epidemic forecasting and prevention, and to the early detection and control of epidemics. This
requires a good epidemic preparedness plan, including different levels of alert on which to proceed with the refresher training, logistical preparations, delimitation and reconnaissance of the affected area or areas, and eventual launch of the spraying operations.

1.3 Indications for the use of indoor residual spraying

The main indications for the use of indoor residual spraying in malaria control programmes are:

a) the prevention of malaria epidemics, following identifiable alarm signals for a specific epidemic-prone area, e.g. abnormally heavy rain, high humidity or high minimum temperature; migration of large numbers of non-immunes into malaria-endemic areas.

b) the control of epidemics, which have been detected in their early stage of development, and where spraying can be achieved sufficiently early to cut off the peak of transmission.

c) as a complementary measure to chemoprophylaxis, whenever this is used for the protection of labour camps, army or police posts, and other circumstances where groups of non-immune people may be temporarily exposed to high transmission. An important aim of spraying is to reduce the transmission of parasites which may have become resistant, through the use of chemoprophylaxis.
d) the reduction of the peaks of incidence in areas of intense seasonal transmission.

e) long-term use when and where its use accompanies a process of socioeconomic development, which would eventually ensure the sustainability of the results.

Most of the above indications aim to maintain a residual effect for the duration of a transmission season.

Choice of insecticide
After deciding that indoor residual spraying is the right control measure for the circumstances, the next important decision is which insecticide to choose. Each insecticide product has a range of characteristics of its own, directing decisions on suitability for different scenarios. Consideration of these aspects is a central part of making the right decision on which insecticide to use. Chapter 2 reviews all these points in detail.

In outline, the areas to consider are:
- aspects of human and environmental safety;
- the insecticide’s efficacy and residual effect;
- vector resistance;
- operational issues such as formulation and dosage;
- vector ecology and behaviour;
- social factors (such as community mobilization/support for spraying);
- cost and cost-effectiveness.

It is an absolute requirement that any insecticide to be used indoors is safe for humans and domestic animals. This is an essential characteristic, since the insecticide goes on the indoor walls of houses. Even with the most careful precautions, it is impossible to avoid
contact with the insecticide-sprayed surfaces. Sprayed houses should not pose a risk for those who live in them even where there has been an accidental overdose.

Even under those conditions of safety, the continuous operational exposure of spraymen means that they are not free of risk. Therefore, it is particularly important to consider effective protective measures to prevent spraymen being contaminated with insecticide. The role of the squad leaders is essential in enforcing safe behaviour and the appropriate use of protective devices (see section 2.1.2).

It is very important to understand the local epidemiology of the disease, not only to decide that spraying is the right measure for the circumstances, but also to make sure that the appropriate insecticide is chosen. The time and place of spraying have to be decided carefully.

After choosing an insecticide it is necessary to assess the impact of spraying, by correlating changes in epidemiological indicators with data on quality and coverage of spraying operations. There must be proper consideration of any ecological or social change which may have affected those indicators.

The nature of the surface on which the insecticide is deposited has a great influence on the duration of the residual effect. This is one of the most important factors in the selection of an insecticide for spraying. It determines the frequency with which spraying has to be repeated. In general, a long residual action is considered desirable.

Many insecticides have other effects on mosquitoes, such as excito-repellency, which may be favourable or detrimental according to circumstances. These
factors should be considered as part of the selection process (see sections 2.3 and 2.5.2 below).

1.4 The WHO Pesticide Evaluation Scheme (WHOPES)

New pesticides or pesticide formulations which appear potentially useful for public health normally undergo a process of independent testing. This is coordinated by the WHO Pesticide Evaluation Scheme (WHOPES). This process ascertains their effectiveness, safety for humans and the environment, and the methods and conditions of their use. The *International Code of Conduct on the Distribution and Use of Pesticides* constitutes the framework of WHOPES in promoting the safe handling and use, efficacy, cost-effective application and quality control of pesticide products/formulations used in public health. **WHOPES develops specifications for pesticides and application equipment (2) for international trade and quality control.**

WHOPES works in close collaboration with: national disease and pest control programmes and national pesticide registration authorities; many international and regional organizations and institutions concerned with pesticide management, legislation and regulation; research institutions; and with industry.

The global objectives of WHOPES are:
- to facilitate the search for alternative pesticides and application methodologies that are safe and cost-effective; and
- to develop and promote policies, strategies and guidelines for the selective and judicious use of pesticides in public health, and to assist and monitor their implementation by the Member States.

In its present form, WHOPES involves a four-phase evaluation and testing programme, the actual activities of which are carried out through a number of collaborating laboratories, research centres and national disease control programmes.

Phase I: Evaluation of technical products or their formulations for their efficacy and persistence is performed on laboratory-bred arthropods. This phase also comprises a study of cross-resistance with the various classes of pesticides currently available and the establishment of tentative diagnostic concentrations to detect vector resistance in the field.

Human and environmental safety evaluation of the compound is also carried out in phase I, in close collaboration with the International Programme on Chemical Safety (IPCS). In addition, minimum laboratory experimentation may also be carried out in this phase, in the WHO collaborating centres. This allows confirmation of the basic toxicological and eco-toxicological information available from the manufacturer or other sources, according to WHO requirements.

Phase II: The evaluation is performed on natural vector populations in the field, on a small scale (e.g. in individual houses or experimental huts), under well-controlled conditions. This is to determine application doses as well as to study the efficacy and persistence of the product. Where appropriate, checks are carried out on how the product affects non-target fauna. Phase II is also the first
opportunity for comments on any harmful effects of the product upon the operators in a field situation.

Phase III: This is a joint undertaking with the participation of WHO, industry and one or more institutions located in malaria-endemic countries. The purpose of this phase is to evaluate the action of a product on a medium or large scale on a specified vector. The evaluation itself comprises entomological, safety and, where appropriate, epidemiological evaluation. The institution supplies qualified staff for implementation, while the manufacturer supplies the insecticide and the funds needed for the trial. WHO takes the technical responsibility for the operation and is involved in the field through independent consultants. All three parties participate in drafting the trial protocol in accordance with a pre-established model that needs to be adapted to each situation. The final report is drafted by the institution, which submits it to WHO for evaluation. The report is then submitted for review to the manufacturer.

A scientific committee (WHOPES Working Group) assists the WHOPES Secretariat in reviewing the reports of the testing/evaluation of pesticides in the Scheme. It also reviews the current information on the products for their intended applications, and makes recommendations to WHOPES on their use in public health. Reports and recommendations of the WHOPES Working Group meetings are published in the form of WHO documents and are widely distributed (3, 4, 5).

Phase IV: This phase is concerned with the establishment of specifications for technical material and the formulations evaluated. Draft specifications proposed by industry are reviewed by members of the WHO Expert Advisory Panel on Vector Biology and Control and WHO collaborating centres. These are then issued as interim specifications.
They are reviewed every five to six years by the WHO Expert Committee on Vector Biology and Control under “Chemistry and specifications of pesticides”. The Committee may recommend publication as full specifications. WHO specifications for pesticides (interim and full) are available on the WHOPES homepage on the Internet www.who.int/ctd/whopes.

1.5 Problems in the choice of insecticides

Insecticides differ considerably in their effects on different species of malaria vectors, depending on many factors. These include the characteristics of the insecticide and its formulation, the ecology and climate of the area and the susceptibility and behaviour of the vector.

Insecticides recommended for indoor residual spraying have been thoroughly tested through the WHOPES programme. Some of the older products have been successfully used in many parts of the world. Nevertheless, when considering any new introduction of an insecticide or formulation, it is essential to undertake small field trials to validate their effectiveness under local conditions (6).

In general WHOPES-approved insecticides should not pose toxicological problems. They may, however, require more or less comprehensive protective clothing for the spraymen and handlers, as well as certain precautions to protect the inhabitants of the sprayed houses. In particular, the need for protective clothing may seriously inhibit the use of some insecticides in hot and humid conditions.
A very important factor for the success of indoor residual spraying is the existence of adequate sprayable surfaces where vectors rest after biting people. In many areas people live or spend long periods of time in houses or shelters which have hardly any walls. The decision to spray the roofs and partial walls of those shelters should be based on epidemiological observations, taking into consideration the behaviour of the vector and the availability of alternative resting places.

Problems of objections by householders may be more important than commonly recognized, e.g. the very noticeable deposit left on the walls by some wettable powder formulations has caused an increasing number of refusals in many programmes, particularly in urban and periurban areas. Similarly, the strong odour of some organophosphate and carbamate insecticides has presented problems. Frequently, household pests, such as bedbugs, develop resistance to the insecticides used for indoor residual spraying, causing the inhabitants to object to spraying even if the Anopheles vectors remain susceptible.

In addition, problems of the cost and availability of insecticides, as well as their storage and distribution, may be important points to consider.

Control programmes, which may contemplate a relatively long-term use of indoor spraying in the control of malaria, must consider the likelihood of development of resistance in vectors. This may depend on the large-scale use of insecticides of the same chemical category in agriculture and for household pest control.
In addition, different groups of insecticides have different spectra of cross-resistance, depending on the resistance mechanism involved. A sequence was therefore proposed for the progressive selection of insecticides as resistance develops to some of them. This sequence is not fixed, since some insecticides lead to the selection of different mechanisms of resistance in different species (see section 2.3.2).

1.6 Classification of insecticides

Insecticides used for malaria control are usually classified on the basis of their chemical categories as follows:

- *Chlorinated hydrocarbons*
  The main representative is DDT. The other members of this family which have been used in malaria control are HCH (lindane) and dieldrin. Both are no longer recommended: HCH because of widespread resistance and dieldrin because of its toxicity to humans.

- *Organophosphates*
  These include malathion, fenitrothion and pirimiphos-methyl.

- *Carbamates*
  These include propoxur and bendiocarb.

- *Pyrethroids*
  These include alpha-cypermethrin, cyfluthrin, deltamethrin, etofenprox and lambda-cyhalothrin.
2. CRITERIA FOR THE SELECTION OF INSECTICIDES

2.1 Human and environmental safety

Safety should be the main consideration in the selection of any preventive intervention; in the case of indoor residual spraying it should be assessed at three different levels:

- **safety for the inhabitants** of sprayed houses, i.e., the insecticide deposit, even in the case of accidental overdose, should not be toxic to any of the inhabitants, including children who may play on contaminated floors;

- **safety for the spraymen** and handlers of the insecticide; although the exposure of these workers would be much higher than that of the inhabitants, adequate protective clothing can prevent it; and

- **safety for the environment**, i.e. safety issues for non-target organisms and the insecticide's biodegradability. When these conditions are not met, it is necessary to consider whether there is a risk of environmental contamination by movement of indoor-sprayed insecticides to the outside, or from inadequate disposal of unused residues.

Safe use of insecticides depends mainly on the choice of an insecticide formulation which is safe both for the inhabitants of sprayed houses, and also for spraymen, packers and mixers of insecticides. Such an insecticide
should involve only relatively simple protective measures, since it is very difficult to ensure the use of complex protective devices by spraymen under tropical conditions. The choice of indoor residual spraying as a measure for malaria control in any particular area should include consideration of whether the necessary safe practices for the protection of the environment could be enforced while the work is carried out and during the handling of the insecticide.

2.1.1 Toxicity and hazard

Toxicity and hazard are not the same. "Toxicity" is the inherent poisonous potency of a compound under experimental conditions. "Hazard" refers to the risk or danger of poisoning when a chemical is used or applied.

Absorption by mammals of most insecticides is by ingestion, inhalation, or through the skin. The relative importance of these three main routes of absorption varies greatly, depending on the insecticide used and its formulation. In the case of skin absorption, different parts of the body vary considerably in their rates of absorption.

A distinction should be made between (a) dermal absorption which produces the same systemic toxicity as other routes of absorption, and (b) the specific dermal or nasal toxicity (paraesthesia and other transient, reversible non-toxic effects) frequently produced by pyrethrins as dermal irritation or sneezing, particularly in sensitive individuals. These latter symptoms generally subside quite rapidly on discontinuing exposure, but they may be very acute and even incapacitating while they last.
For comparative purposes, the toxicity of a product is expressed as acute oral and dermal toxicity to the rat, which is the standard procedure in toxicology, measured as LD$_{50}$.

The LD$_{50}$ value is a statistical estimate of the number of milligrams of toxicant per kilogram of bodyweight required to kill 50% of a large population of test animals.

The common measure of insecticide toxicity, the rat LD$_{50}$, gives an indication of the general risk of acute poisoning by ingestion of the basic compound. In the selection of an insecticide for indoor residual spraying it would be equally, or even more important, to consider the dermal LD$_{50}$, due to the high risk of skin contamination. However, the actual risk presented by spraying depends mainly on the formulation used. This may vary in the concentration of active ingredient and the properties of the formulation. This is the basis for the WHO recommended classification of pesticides by hazard (7), in which they are divided into:

- extremely hazardous (class Ia),
- highly hazardous (class Ib),
- moderately hazardous (class II),
- slightly hazardous (class III),
- unlikely to be hazardous (UH).

The WHO classification (Table 1) is based primarily on the acute and dermal toxicity to the rat, since these determinations are standard procedures in toxicology. Where the dermal LD$_{50}$ value of a compound would place it in a more restrictive class than the oral LD$_{50}$ value would indicate, the compound will always be classified in the more restrictive class. The toxicity of the formulated product will depend on the concentration of active
ingredient, on the physical properties (e.g. solid or liquid), the impurities related to the manufacturing process, and the other components of the formulation which may affect absorption of the compound.

National authorities should request a toxicity profile of the formulated product they intend to use. Table 1 shows the WHO recommended classification of pesticides by hazard. All the WHOPEs recommended insecticide formulations for indoor residual spraying, except for etofenprox (class UH), belong to class III and are based on technical products belonging to class II or class III.

### Table 1. WHO recommended classification of pesticides by hazard

<table>
<thead>
<tr>
<th>Class</th>
<th>LD_{50} for the rat (mg/kg body weight)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Oral</td>
</tr>
<tr>
<td></td>
<td>Solids</td>
</tr>
<tr>
<td>Ia</td>
<td>&lt;5</td>
</tr>
<tr>
<td>Ib</td>
<td>5-50</td>
</tr>
<tr>
<td>II</td>
<td>50-500</td>
</tr>
<tr>
<td>III</td>
<td>&gt;500</td>
</tr>
</tbody>
</table>

2.1.2 Protective measures

All malaria control measures involving the use of insecticides are potentially hazardous. Although the risks presented by properly conducted spraying operations are minimal, communities should be aware that these exist. They should be instructed in the simple precautions needed to reduce exposure. This is especially important with increasing community participation in vector control operations, as many malaria control programmes now rely
on community workers to carry out the spraying with limited supervision.

Community health workers, in areas to be protected by indoor spraying, constitute the most important resource for the protection of the community. The technical information given to them must be simple, practical and well-formulated. It must allow them to grasp the basic concepts of the use of insecticides in malaria control, the potential risks involved and the protective measures to be adopted. Sometimes basic training on pesticide risks is provided in connection with agricultural use, in which case the information for malaria control should be complementary.

The people living in the houses to be sprayed should be told why the insecticide is being applied and when it will happen. They should be given clear instructions about what they have to do before and after their houses have been treated (e.g., they should take all food and cooking equipment out of the house and should stay out of the house themselves during spraying. Children may only go back into the house after the floors have been swept or washed).

Any insecticide which has been spilled onto the ground should be removed. This is particularly to protect children as well as being for the safety of the animals which may enter the house. Concrete surfaces should be washed and earth surfaces should be cleaned by scooping up the damp earth and burying it. Large numbers of insects, such as flies, moths and bed bugs, may be killed and fall on the floor during the indoor spraying operations; this is an insecticide hazard, particularly for chickens. Floors should therefore be carefully swept and the sweepings safely disposed of into pit latrines or by burying in pits dug away from sources of drinking-water.
Spraymen and packers are at a higher risk of contamination with toxic doses, either accidentally or occupationally, while handling the insecticides for packing and mixing. Particular care is needed to protect them.

Protective devices include clothing, hats, gloves and masks or respirators. Clothing and other devices should be as light and comfortable as possible while still protecting against inhalation of insecticide particles and skin contamination. For most spraying programmes which use insecticides of low-acute toxicity (such as DDT and malathion) it has been considered sufficient to wear overalls, broad-brimmed hats to cover the neck of the overalls, gloves, and shoes or boots, the opening of which should be covered by the long trousers of the overalls. The use of fenitrothion, other organophosphates, carbamates and pyrethroids has required the use of light masks to prevent inhalation of insecticide particles. The use of hats, masks and goggles may not be enough to avoid unpleasant facial irritation by some pyrethroids. In this case, visors should be used; these should be of plastic which is resistant against abrasion by the insecticide. The use of respirators is not very practical under tropical climatic conditions. They may, however, be necessary for spraymen working long hours with the more toxic insecticides, such as fenitrothion or bendiocarb.

To prevent unnecessary contamination it is essential to make sure that spraymen are following the right safety precautions. These are: a) hands and face should be washed after filling each pump charge; b) eating, drinking and smoking should be forbidden on the job, except after washing and before starting to spray; c) spraymen’s exposure to insecticide should not be more than six hours each day; d) overalls and hats should be
washed daily, and especially if they have been excessively contaminated; e) spraymen must have a shower at the end of each day's work, particularly when they have been working with organophosphate insecticides; f) if respirators are used, they must fit well around the nose and mouth, they must be washed and dried, and the cartridge must be changed daily or at any time that it becomes obstructed.

Packers and mixers should take extra care. Their work is the most dangerous in terms of the risk of contamination. It is particularly important that they use rubber gloves, masks or respirators, and that they protect their eyes with a visor of clear plastic attached to the hat. Some solid insecticide formulations for indoor residual spraying do not need packers and mixers. They are supplied in water-soluble sachets, containing a single pump charge which minimizes handling.

Squad leaders should enforce safe behaviour and the appropriate use of protective devices. They should understand how to recognize the symptoms of contamination and monitor their group for any signs of poisoning.

It is particularly important to choose the least toxic insecticide for use in very hot and humid climates. This is because, in such conditions, spraymen are more likely to avoid using uncomfortable protective devices when not under direct supervision.

2.1.3 Measurement of exposure

In studies measuring dermal and respiratory exposure (using a standard WHO protocol), in nearly all situations both dermal exposure to insecticide and the resulting
absorption were much greater than respiratory exposure to insecticide and the resulting absorption ($\theta$). Although only traces of insecticide may be taken in while eating or smoking during spraying, the studies showed the importance of maintaining high standards of personal hygiene.

Dermal exposure can be measured directly by using a new disposable overall and gauntlets for a minimum period of one hour during any one day's spraying. Exposure of any particular part of the body may be measured by using standard (10x10 cm) exposure pads, consisting of pieces of $\alpha$-cellulose or white absorbent paper, that are backed with glassine paper, aluminium foil or polyethylene. These can then be sent to a laboratory for analysis.

Another means of monitoring exposure is to take biochemical measurements of the concentration of the insecticide compound or its metabolites in accessible body fluids. The time and frequency of sampling and the volume of the specimen depend on the properties of the compound and the analytical methods available. In most cases it is not possible to perform these analyses in the field so that facilities for preserving and dispatching the samples to a laboratory should be arranged.

Actual monitoring of exposure is not often required in operational programmes with established safety practices. It may be needed when introducing an insecticide in a new area or if there is some suspicion of excessive exposure. In contrast, in the case of organophosphates, it is necessary to monitor the activity of acetyl cholinesterase in spraymen, mixers and any worker who may have been exposed to contamination. This is to prevent exposure reaching a point at which poisoning might occur.
The main methods for determining cholinesterase activity, which may be used under field conditions, are:

- the colorimetric test paper method, which measures activity in the plasma. However, facilities are not always available in the field to separate blood plasma;

- the colorimetric tintometric method, which measures whole-blood cholinesterase activity. This is a more relevant indicator of toxicity than plasma measurements; and

- spectrophotometric methods, which are mainly used in the laboratory, although there are some field spectrophotometers which may be used when more accurate results are required.

Carbamates are also cholinesterase inhibitors. However, the colorimetric methods suitable for identifying contamination with organophosphates cannot be used for carbamate insecticides. This is because reversal of the labile cholinesterase inhibition produced by carbamates takes place faster than the colorimetric reaction measured by the test. Monitoring of carbamate-induced cholinesterase inhibitions would require the use of field spectrophotometers.

2.1.4 General treatment of insecticide poisoning

All countries which spray insecticides, and particularly those which use the more toxic compounds, should develop the capacity to treat potential victims of poisoning. Medical personnel need up-to-date and reliable information and the
required drugs must be easily available in sufficient quantities when needed. The International Programme on Chemical Safety\(^1\) has prepared a poisons information package, INTOX, both on paper and in electronic form, containing information on the physical, chemical and toxicological properties of pesticides, how to analyse them, and how to diagnose, treat and prevent poisoning\(^2\). There is also a handbook on poisoning, for healthcare workers who have no access to hospital facilities, which gives information on how to prevent and manage poisoning cases (9).

Successful treatment of insecticide poisoning depends on the rapid and simultaneous application of measures for: a) alleviation of life-threatening effects; b) removal of non-absorbed material; and c) symptomatic and/or specific treatment.

*The alleviation of life-threatening effects includes* - the removal of secretions and the maintenance of an unobstructed airway. This is achieved by lying the patient in a prone position with head down and to one side; the mouth fully open and the tongue pulled forward. The mouth and pharynx should be cleared with a cloth or by suction. If an obstruction persists it may be necessary to use an oropharyngeal or nasopharyngeal airway or endotracheal intubation.

*The removal of non-absorbed material* - which may be present in the stomach or on the skin. When the insecticide has been swallowed gastric lavage may be required. If the clothing or exposed skin is contaminated, the clothing must be taken off and the skin washed with

---

\(^1\) The International Programme on Chemical Safety is a joint programme of ILO, UNEP and WHO implementing activities related to chemical safety.

\(^2\) See [http://www.intox.org](http://www.intox.org)
soap and clean water for at least 10 minutes. Contamination of the eyes is treated by irrigation of the conjunctiva with clean water for 15 minutes.

Symptomatic and/or specific treatment of insecticide poisoning varies according to the category of insecticide involved. See chapter 4 for details of symptoms of poisoning and treatment of specific recommended insecticides.

2.1.5 Packaging, handling, transport and storage of insecticides

The basic requirements for transportation, storage, handling and disposal are common to all insecticides.

Packaging

Packaging of insecticides must withstand transport, handling and the climatic and storage conditions to which they will be exposed. Insecticide containers should be clearly labelled, rigid and leakproof. The packaging should be strong enough to ensure the integrity of the container for the whole period from packing by the manufacturer to the insecticide's application in the field. The size of the containers should be limited to that which can be easily lifted by one man. Some insecticides, e.g. malathion and deltamethrin, are corrosive to some metals. Water dispersible powders used for indoor spraying must be packaged in moisture-proof plastic bags to maintain their good suspensibility. Many manufacturers offer insecticides in sachets which contain the right amount of insecticide for one pump charge. This avoids the need for re-packaging and considerably reduces the need for handling in the field.
In some countries, formulations are repacked locally into smaller containers for field use. Repacking must be regulated and supervised to avoid poisoning of workers. The quality of the new packaging must be good enough to prevent leakage or alteration of the product. Older products in store should be used before newly purchased products. “Use-by dates” on products should be strictly observed. Insecticides should never be transferred into other storage containers. Keep them in the ones in which they were supplied.

Insecticides to be used for malaria control should comply both with the WHO specifications on formulations and on packing.

Handling
Protective clothing should be used by everyone handling the compound (see section 2.1.2 above). Adequate washing facilities should be available nearby at all times during handling. Eating, drinking and smoking should be prohibited during handling and after handling until the hands and face have been washed. Handling during transport must conform to regulations preventing contamination of workers and food. It must be careful enough to prevent insecticide drums breaking and the contents spilling.

Storage
It is possible for insecticide containers to remain unprotected from the weather for long periods during trans-shipment or storage. This presents risks of deterioration and contamination. Insecticides should be kept away from heat and sources of ignition and stored locked up in a well-ventilated building or warehouse which cannot be accessed by unauthorized persons and children.
As pesticides are valuable but potentially hazardous products, facilities should be available for their safe and secure storage both at central and regional levels. Containers should be stored at a level that is high enough to avoid flooding and should be protected from the sun and rain.

**Storage of insecticides** requires special precautions. To avoid contamination of food and other products, insecticides should be stored in safe separate buildings where they can be protected and properly accounted for. No food or drink should be stored in the same area as the insecticide containers. Insecticides should be kept away from water and from water supplies. In addition, careful precautions should be taken to ensure that insecticides intended for house spraying are not illegally diverted for agriculture use.

**Insecticide products should comply with the tests for stability under extreme conditions of temperature and humidity, so as to ensure their safety under the adverse conditions which may occur during prolonged storage in a tropical climate.**

In particular, it is essential to prevent the degradation of the insecticide under storage conditions. This is to avoid a transformation into more toxic isomers. This occurred in Pakistan in 1978, for example, when a formulation of malathion produced, under tropical storage, the highly toxic iso-malathion, causing several cases of poisoning (10,11).

**Transport**

Transport and handling should also conform to regulations preventing contamination of workers and food. Pesticides must not be transported in vehicles used for the transport of food.
2.1.6 Disposal of insecticides and insecticide containers

The cleaning and disposal, or recycling, of insecticide containers is a serious problem in many developing countries. Many countries have found it difficult to implement existing guidelines. For example, metal containers tend to be reused in a variety of ways without adequate cleaning.

Any insecticide remaining in containers should be emptied into pit latrines, if available, or into pits dug especially for this purpose away from sources of drinking-water. Any insecticide must be diluted with more water before being put into pits.

Paper or plastic containers holding solid insecticide should be shaken to make sure that all the contents are emptied into the spray solution. The empty paper or plastic sacks should be collected by the spray team supervisors and brought to the central storage area for proper disposal by qualified staff, following the UNEP/WHO/FAO guidelines (12).

It is generally recommended that metal insecticide containers are resealed, collected and securely stored. They should be thoroughly rinsed as soon as they are emptied. The rinsate should be used to dilute the next spray solution or safely disposed of into pit latrines, if available, or into pits dug especially for this purpose, away from sources of drinking-water.

Implementation of the guidelines and enforcement of strict disposal rules have been found (by WHO and FAO) to be poor. The WHO Expert Committee on Vector Biology and
Control (13) considered that containers of pesticide formulations which were designated as "slightly hazardous" or "unlikely to present acute hazard in normal use", in the WHO recommended classification of pesticides by hazard (see Table 1, section 2.1.1 above and reference 7), could be reused under the following conditions:

- all pesticide containers should be permanently labelled or embossed, in the relevant languages: “Not for use for food, drink or animal feed”.

- containers that have held only pesticide formulations in Hazard Class III, except for polyethylene containers of formulations of Hazard Class III based on an active ingredient in Hazard Class I or II, should be labelled, in the relevant languages, as follows: “This container may be reused for purposes other than storage of food, drink or animal feed, but only after its contents have been disposed of safely, the container completely refilled with water and allowed to stand for 24 hours, and the whole process repeated twice. After this serial washing, obliterate this label”.

- containers of formulations in Hazard Class Ia, Ib, or II, as well as polyethylene containers of formulations in Hazard Class III based on an active ingredient in Hazard Class I or II, should carry an additional permanent label or embossed warning “When emptied and drained this container must be destroyed”. The method recommended for safe disposal should be described.
The reuse of insecticide containers is always a dangerous practice. Health services should make sure that the containers accepted for reuse have been selected and cleaned by properly trained personnel. Containers that are not washed as described above, should be punctured or otherwise rendered unusable for any other purpose. The containers should not be burned or buried. Such practices are potentially extremely hazardous to human and animal health and the environment. The empty insecticide containers should be returned to the distributor or taken to an approved collection scheme for safe disposal.

The WHO Expert Committee recommended that the product stewardship by industry should be extended to include decontamination of containers of all hazard classes of pesticides (8,13).

2.1.7 Environmental effects

Indoor residual spraying is not considered to be an important source of environmental contamination. Nevertheless, it is essential to make sure that appropriate precautions are taken to prevent undesired effects on non-target organisms. It is particularly important to make sure that unused insecticide suspension is adequately disposed of and that water used for the washing of spray pumps and contaminated materials has been safely disposed of. Particular attention should be given to preventing the washing or rinsing of spray equipment or the disposal of wastage or left-over insecticide in natural water bodies such as lakes or rivers.
2.2 Efficacy and residual effect

2.2.1 Intrinsic insecticidal effect

The effectiveness of an indoor residual spray depends on a complex set of factors. These include: a) the properties of the insecticide (intrinsic toxicity, its mode of action and its stability), and b) its effect on the vector. The effect also depends on the nature of the surfaces on which the insecticide is applied, the type of house construction, the number of domestic animals and the types of their shelters, the ecology of the area, as well as the behaviour of the vectors and the population.

The immediate effect of the insecticides depends mostly on their intrinsic toxicity to the mosquito. Their residual effect depends on their stability, volatility, the formulation used and the nature of the sprayed surfaces.

Knock-down effect - Some insecticides have a very rapid knock-down effect. This is quite distinct from delayed mortality which follows within a period of several hours after exposure. A knock-down effect is particularly noticeable when DDT and pyrethroids are used.

Mosquitoes "knocked down" by pyrethroid insecticides may drop from their resting position on the wall onto the floor. If this happens before they have received a lethal dose they may eventually recover and survive. Nevertheless, in most instances, a knocked down mosquito would be eaten by ants or other scavengers. This is why knockdown is used as an efficacy criterion for pyrethroids.
The ratio of the immediate to the delayed mortality (I/D) is a measure of the capacity of the insecticide to produce rapid vector mortality, sometimes being able to kill the vector before it can feed. That ratio varies considerably even among pyrethroids, from less than 1, for etofenprox, to more than 10 for cyfluthrin.

*Airborne effect* - *Some insecticides exert a lethal effect on mosquitoes at a distance. This may be due to a fumigant effect* which occurs when the vapour pressure of the insecticide is sufficiently high. Perhaps more frequent is the release of particles as dust from sprayed surfaces as mentioned above; this effect depends on the insecticide formulation and the non-sorptive nature of the sprayed surface. Released insecticide particles, carried by convection or other air currents within the sprayed room, may move considerable distances.

Non-contact "airborne" insecticidal effects may be tested by exposing mosquitoes in cages hanging at different distances from the sprayed walls for specified periods of time. It is very important to avoid accidental contamination of the cages with the insecticide during handling.

### 2.2.2 Effect of the sprayed surfaces

*Absorption and adsorption* - The nature of the sprayable surface plays a major role in the duration of the residual effect of the insecticide. The phenomena of sorption (absorption and/or adsorption) of insecticides by sprayed surfaces are important factors. These may considerably limit insecticide availability on the sprayed surface. In general, surfaces of organic origin, such as
wood, bamboo, palm leaves or thatch, and metals are non-sorptive. The persistence of the insecticide on non-sorptive surfaces is related to its volatility. This is dependent on the temperature, and on the physical characteristics of the formulation. The formulation may be responsible for poor adhesiveness of the insecticide crystals. They may fall off or be easily removed. The insecticide can also become covered by soot. In contrast, an insecticide applied on mud surfaces may be absorbed into the body of the mud, reducing its availability at the surface. This absorption occurs gradually at a speed related to the particle size of the insecticide, its rate of diffusion in the mud and to the volatility of the insecticide. In some types of mud the insecticide may be adsorbed. This means that the particles of the insecticide become fixed to the surface of the mud particles and cannot be picked up by mosquitoes resting on the mud surface.

Sorption is partly influenced by temperature, but is mainly dependent on humidity. High humidity favours diffusion. This not only increases absorption in general, but may also bring to the surface absorbed particles (desorption), when the concentration at the surface had diminished by volatility during a previous dry period. Humidity also facilitates the contact of the insecticide with the cuticle of the resting mosquito. It thus favours the effectiveness of the insecticide.

In addition, the heat of the sun on metal roofs may rapidly inactivate the insecticide deposits, as well as increasing the risk of the insecticide particles flaking off. These risks should be taken into consideration in areas where the use of corrugated iron roofs, for example, may be increasing, as is often the case in many rural tropical areas.

*Inactivation* - The insecticide may be inactivated by some types of surfaces. *Alkaline surfaces, such as*
whitewashed walls, affect organophosphate, carbamate and pyrethroid insecticides.

2.2.3 Spraying cycles

To ensure people's protection during the transmission season, the insecticide chosen should ideally have a residual effect as long as the transmission season plus the operational period required to spray the whole area.

Spraying should be repeated at regular intervals in order to achieve effective control over the required period of time. Each spraying of all sprayable houses in an area over a period of time is called a "spray round". The repetition of spraying operations at regular intervals is called the "spraying cycle". It is normally expressed in terms of the interval between repetitions, e.g., in a six-month cycle, spraying is repeated every six months. **The spraying cycle should be determined in accordance with the duration of residual effect and the duration of the transmission season.**

The need to maintain the insecticidal effect during the malaria season may lead to the selection of an insecticide which can cover the whole season with only one round, rather than one which would require two rounds. Where there is continuous transmission the spraying cycle should be determined by the duration of residual effect. Many programmes have made their spraying rounds last as long as the spraying cycle, in order to keep spraymen employed throughout the year.

**The timing of spraying is most critical when it is necessary to protect an area during a transmission season with a single round of spraying. The whole round should be completed before the beginning of**
transmission, but the residual effect on the first houses sprayed should not be lost before the end of the season. This would in general require very short spraying rounds. Even in areas of perennial transmission there are usually seasonal peaks when maximum insecticidal effect should be assured. The timing of spraying should be chosen so that the most malarious areas are sprayed just before the peak of transmission.

If there is a high rate of new construction or renewal of sprayed surfaces (such as re-plastering and re-thatching) there will be a need for mop-up operations. In that case it may be more cost-effective to spray all structures at shorter intervals with an insecticide or dosage which gives shorter residual effect.

2.3 Vector resistance

An essential characteristic in the choice of an insecticide is the susceptibility of the malaria vectors in the area of concern. This may vary with time as resistance can develop as a result of continuous exposure to the insecticide.

True insecticide resistance, or physiological resistance, can be defined as the ability, in a population of insects, to tolerate doses of an insecticide which would prove lethal to the majority of individuals in a normal population of the same species; developed as a result of selection pressure by the insecticide.

Cross-resistance is the resistance to an insecticide developed in a mosquito population by selection pressure from another insecticide sharing the same resistance mechanism, often but not necessarily belonging to the same chemical category.
Multiple resistance is the simultaneous resistance to several insecticides of different categories (organochlorines, organophosphates, carbamates, pyrethroids), normally acquired by separate exposure to the different insecticides.

Insecticide avoidance - Vectors may avoid the effect of an insecticide sprayed indoors. The term “behavioural resistance” has been used to describe the way that vectors survive in a sprayed area by avoiding sufficient contact with the sprayed surfaces. Indoor spraying is ineffective when the vector does not come into the house for biting or resting. This may either be because of the vector’s natural behaviour which prevents them from resting on the sprayed surfaces long enough to absorb a lethal dose, or because of "excito-repellency", which is when the insecticide causes the vector to avoid it. This effect is discussed below (2.5 Vector ecology and behaviour) and should be studied before considering the use of indoor residual spraying.

2.3.1 Monitoring of resistance

WHO has developed a practical test to detect resistance in mosquitoes. The production and distribution of standard kits and impregnated papers for the test are organized by WHO. The susceptibility test kits include detailed instructions on how to do the tests and can be requested from the Department of Communicable Disease Control, Prevention and Eradication, World Health Organization, 1211 Geneva 27, Switzerland.

The assessment of vector susceptibility is a basic step in the planning and the epidemiological
evaluation of any malaria control programme considering the use of insecticides. Testing should be carried out:

- to establish the baseline susceptibility of the different vectors in the area;

- to monitor the possible changes throughout the period of insecticide application;

- to identify the mechanisms (14) of resistance and cross-resistance spectrum; and

- to assess the vector's susceptibility to potential alternative insecticides if there is a need for change.

Baseline information on susceptibility requires the determination of dose-response regression lines from tests with a range of insecticide concentrations. In a normally susceptible population the distribution of the logarithms of the doses required to kill individual insects is normally distributed. Hence the mortalities of samples of insects give a straight line, if plotted on probit mortality – log concentration paper. Such a line gives the concentrations which would produce specified mortalities, e.g. LC₅₀, LC₉₀, LC₉₉. Low mortality in the controls is an indication of the validity of the test. Tests with control mortality exceeding 20% are considered invalid. When the control mortality is between 5% and 20% the test mortalities should be corrected using Abbott's formula (15).

For practical purposes, it has been found useful to establish a "discriminating concentration", that is, a concentration which would kill all susceptible individuals. Survivors at such concentration would
clearly be resistant. This discriminating concentration has been commonly established as double the estimated LC$_{99.9}$ as determined, by the method described above, for a given species in different areas of its distribution. The discriminating concentrations of insecticides have absolutely no relationship to the field application rates. They are only used for monitoring insecticide resistance in the mosquito population.

The tests should be carried out indoors in premises which are free from contamination with insecticides, avoiding low relative humidity and extremes of temperature. Female mosquitoes used for the test should ideally be non-blood fed of known age (24-48 hours post-emergence) issued from larval and/or pupal collections or first generation from wild caught females. When only field-collected females can be used, their physiological status (unfed, blood-fed, semi-gravid, gravid) should be carefully recorded (15,16). Although it is recommended to use female mosquitoes only, it is recognized that there is seldom a large difference in susceptibility between the sexes.

The currently recommended discriminating concentrations for the insecticides used as indoor residual spraying for malaria control are shown in Table 2, adapted from WHO (15).
Table 2. Discriminating concentrations of insecticides for adult malaria vectors

<table>
<thead>
<tr>
<th>Insecticide class</th>
<th>Insecticide</th>
<th>Discriminating concentration (exposure period 60 minutes)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Organochlorines</td>
<td>DDT</td>
<td>4%</td>
</tr>
<tr>
<td>Organophosphates</td>
<td>Malathion</td>
<td>5%</td>
</tr>
<tr>
<td></td>
<td>Fenithrothion</td>
<td>1%</td>
</tr>
<tr>
<td>Carbamates</td>
<td>Propoxur</td>
<td>0.1%</td>
</tr>
<tr>
<td></td>
<td>Bendiocarb</td>
<td>0.1%</td>
</tr>
<tr>
<td>Pyrethroids</td>
<td>Alpha-cypermethrin</td>
<td>0.05(^2)</td>
</tr>
<tr>
<td></td>
<td>Permethrin</td>
<td>0.75%</td>
</tr>
<tr>
<td></td>
<td>Deltamethrin</td>
<td>0.05%</td>
</tr>
<tr>
<td></td>
<td>Lambda-cyhalothrin</td>
<td>0.05%(^3)</td>
</tr>
<tr>
<td></td>
<td>Cyfluthrin</td>
<td>0.15%</td>
</tr>
<tr>
<td></td>
<td>Etofenprox</td>
<td>0.5%</td>
</tr>
</tbody>
</table>

1 2 hours for *Anopheles sacharovi*  
2 Tentative diagnostic concentration  
3 0.1% for *Anopheles sacharovi*

2.3.2 Mechanisms of resistance and cross-resistance

Physiological resistance is due to a variety of mechanisms, which can be classified in two main types:

- *Detoxification/sequestration enzyme-based resistance*  
  This occurs when enhanced levels or modified activities of specific enzymes detoxify or sequester the insecticide before it reaches its target. These may be specific for a particular insecticide with a narrow spectrum of activity. For example, glutathione S-transferase is responsible for most examples of DDT resistance. A specific carboxylesterase detoxifies malathion. Others may have a broad spectrum and confer cross-resistance to a variety of insecticides. For
example, a number of esterases and oxidases confer cross-resistance to organophosphates (including malathion), DDT, some carbamates and pyrethroids.

- Target-site resistance
  This occurs when there is a modification of the target (amino acids in the proteins responsible for insecticide binding at its site of action), preventing such binding. The target sites become insensitive or are reduced in number. This type includes the main mechanism of resistance to carbamates (propoxur and bendiocarb being the most commonly used), which also produces cross-resistance to organophosphate insecticides. This is mainly due to the selection of vectors possessing an altered acetyl cholinesterase (AchE), which is not inhibited by the insecticide. This makes resistant individuals almost totally insensitive to the insecticide. The targets of synthetic pyrethroids and DDT are the sodium channels of the nerve axons. Certain amino acid changes, due to the kdr gene, prevent the coupling of the insecticide to the proteins that constitute the ligand-dependent sodium channels of the nerve cell membrane, which thus become insensitive to the insecticide.

Some resistance mechanisms are shared by different insecticides. This explains the phenomenon of cross-resistance. Table 3 summarizes the insecticide resistance mechanisms most commonly reported in major malaria vectors.

Specific biochemical tests are now available for most detoxification types of resistance mechanisms and the modified AchE. Polymerase chain reaction (PCR) assays are also available for several mechanisms, including kdr mutation. These permit the diagnosis of the mechanism responsible for resistance in the field. This will indicate to
which other insecticides the vector population may be cross-resistant. This information is of great importance in the selection of an insecticide for indoor spraying.

Table 3. Major insecticide resistance mechanisms in malaria vectors.

<table>
<thead>
<tr>
<th>Resistance mechanism</th>
<th>DDT</th>
<th>OP</th>
<th>C</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Esterases</td>
<td>+</td>
<td></td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Oxidases</td>
<td></td>
<td>+</td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Insensitive acetylcholinesterases</td>
<td>+</td>
<td></td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Specific carboxylesterase</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glutathione S-transferase</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insensitive sodium channels</td>
<td>+</td>
<td></td>
<td></td>
<td>+</td>
</tr>
</tbody>
</table>

OP = Organophosphates; C = Carbamates; P = Pyrethroids

**Genetics of resistance - Pre-existing gene frequency** -
Each mechanism of resistance is genetically determined. It can be inherited as a recessive or a more or less dominant character. The dominance of the resistance character is an important determinant of the speed of selection of resistance. If the heterozygotes survive, this allows a rapid build-up of the frequency of the resistance genes from initial rarity.

The most common mechanism for DDT resistance is the glutathion-S-transferase enzyme. Its recessive character is presumably one of the main reasons why the development of resistance to DDT has been slow in most places.

In contrast, the resistance to dieldrin is inherited as a dominant character. This presumably explains the very rapid development of resistance to this insecticide, which was one of the reasons for abandoning its use. Similarly,
resistance to carbamates is inherited as a partially dominant character, with high survival of the heterozygotes.

Protection afforded by the resistance mechanism -
Resistance ratio -

The various resistance mechanisms provide different degrees of protection to the resistant individuals. This may be expressed as the "resistance ratio", i.e. the ratio of the LC$_{50}$ of the resistant population to the susceptible population. In the case of detoxification mechanisms, such as those commonly selected by DDT and organophosphate insecticides, the resistance ratio may be from 2x to 100x. In the case of site target insensitivity, the resistance ratio varies, from 30x to 50x in the case of kdr resistance in Anopheles gambiae, to over 1000x in the case of altered AchE, responsible for resistance to organophosphates and carbamates. The higher the resistance ratio, the better the resistant individuals survive increased doses of the insecticide or increased exposure time to it, and therefore the selection of resistance is more rapid.

2.3.3 Sources of selection pressure and resistance development

Practically all anopheline vectors breed in collections of water outside the house, with the exception of A. stephensi which may breed in domestic containers. Males tend not to enter houses, since they live on plant juices. Therefore the selection pressure exerted by indoor spraying is relatively weak. In contrast, exposure of larvae to insecticides affects both sexes. Such exposures of mosquito larvae arise from the deliberate use of insecticides as larvicides or from side effects of control of agricultural pests, particularly by aerial spraying.
of extensive plantations, as is commonly practised in cotton, rice and some tree plantations. Such applications contaminate most breeding places in the area and represent a most effective selection force for insecticide resistance. The majority of the areas where local vectors have developed the highest levels of multi-resistance to practically all available insecticides are where large plantations of cotton have required very frequent applications of mixtures of a wide variety of insecticides.

It is generally unreliable to predict the likelihood of resistance. Some points can, however, generally indicate major risks:

- If the proposed insecticide is extensively used in outdoor applications, especially in agriculture. The same applies to any insecticide which is known to share some resistance mechanisms with the formulation being applied outdoors.

- If systematic laboratory selection succeeds in developing resistance in samples of local vectors. It should be noted that failure to select resistance in the laboratory does not give any security that resistance will not develop. Moreover, laboratory selection tests should not be carried out in malaria-endemic or receptive areas, due to the danger of escape of resistant mosquitoes from laboratory colonies.

- If the resistance mechanism confers a very high protection to resistant individuals (resistance ratio) selection is likely to be faster. The same applies if the heterozygotes are resistant or partially resistant.

- In contrast, if spraying is limited in area or length of time, e.g. if it is limited to the period of the peak of transmission or to the areas at highest risk, selection
could be slower because of the dilution of resistance genes by the immigration of susceptibles from untreated areas.

The experience of several control programmes indicates that the resistance to DDT evolved rather slowly, even when resistance may have been present due to DDT's previous use in agriculture before the beginning of its use in malaria control. In many such situations, spraying retained a useful effect for a long time, since the proportion of resistant mosquitoes in the population increased slowly. For example, in many areas of Central America, DDT was still effective in the field when susceptibility tests gave survival rates of up to 40%. These levels remained relatively stable for several years, well into the 1970s. This contrasts with the much more rapid evolution of resistance to dieldrin and propoxur, for example, which relatively soon affected almost the whole vector population in the sprayed area.

Vector susceptibility is one of the most important factors to determine the effectiveness of an insecticide for malaria control through indoor spraying. The detection of resistance, and the estimation of the proportion of resistant individuals in a vector population, are very important indicators to detect potential changes in the effectiveness of the spraying operation. However, the ultimate criterion is the assessment of its impact through the epidemiological indicators of malaria transmission.

2.3.4 Policies for protection against the development of resistance

Since residual insecticides began to be used both in agriculture and in public health, entomologists have
searched for means to prevent the development of resistance. For some time it was recommended to use insecticides in the sequence: DDT, malathion, fenitrothion, carbamates (propoxur, bendiocarb), pyrethroids. This was based on the fact that the most common resistance mechanisms of DDT and malathion are different and quite specific. Resistance to other organophosphates and to carbamates normally give cross-resistance to malathion. Nevertheless, the number of exceptions has kept growing, as more insecticides from the different categories are being used for different purposes. This leads to the development of varying mechanisms of resistance among the vector populations. For example, in Sri Lanka, resistance to fenitrothion was reported while susceptibility to malathion was maintained. Recently resistance has been reported in South Africa to a pyrethroid (by enzyme detoxification) with cross-resistance to the carbamate propoxur, while maintaining full susceptibility to DDT and to the carbamate bendiocarb.

There is therefore no sequence of insecticide use which applies to all cases. The way the problem has evolved in other areas of distribution of the same vectors may, however, give some guidance in individual cases.

In consequence, the following policies are being suggested, and implemented in some situations:

- Take into account the current and future plans for use of insecticides in all indoor and outdoor applications, including for nuisance insects and in agricultural use.

- Reserve some insecticides for exclusive use in public health. For example, Sri Lanka forbade the use of malathion in agriculture to conserve it for malaria vector control. In general, this is difficult to achieve, since most insecticides are already in agricultural use.
long before their use in public health can be authorized. If the insecticide is useful for agriculture, it is unlikely that regulations could be enforced to ban such use. It would then be necessary to put the same restrictions on all the insecticides which would select for cross-resistance to the restricted compound.

- Use mixtures of unrelated insecticides. This assumes that there is no resistance present in the area of application of the two products used in the mixture. In principle such mixtures would ensure that the rare individuals resistant to compound A, would be killed by compound B and vice versa, while doubly-resistant individuals would be extremely rare. Such a mixture should be prepared by the manufacturer, to avoid problems of mixing incompatible products in the field. Only insecticides with different resistance mechanisms should be combined in such mixtures.

- Rotate the different insecticides used. Although this presents logistical and acceptance problems, it is a simpler solution than dealing with the problems raised by the simultaneous use of two insecticides. This principle has been successfully used in larviciding for the control of Simulium by the Onchocerciasis Control Programme for more than 15 years. It has never been systematically used in indoor residual spraying, changes having been made only after the development of resistance to the first insecticide. In the long run, the consequences of changing insecticide when resistance is detected are probably not different from the effects of a pre-planned rotation.

- Selectively apply insecticides to restrict selection pressure as far as possible, for example limiting coverage by restricting spraying to areas and periods of recognized high epidemic risk, to the areas at
highest risk, or to the season of peak transmission. In these situations it is expected that the resistant genes will be diluted by reproduction during the inter-spraying periods or by the invasion of the sprayed area by susceptible mosquitoes from neighbouring areas.

2.4 Operational issues

2.4.1 Organization

To be effective, indoor residual spraying must have a high level of coverage. That is, it should include almost all the sprayable surfaces in all the houses in the area to be protected with a sufficient dose of insecticide deposit. It is therefore a collective measure for community protection.

When coverage is irregular and poor, spraying is usually a waste of resources. If only a few individuals spray their houses, they get practically no protection, since mosquitoes infected elsewhere could enter their sprayed rooms, bite (and infect) them, although these mosquitoes will most likely die later when resting on the sprayed walls of their house.

Decentralization
In the past, spraying was carried out by centrally organized teams under strict discipline and supervision. Prior to the start of spraying, a detailed geographical reconnaissance was carried out, mapping the location of every house. Spray teams followed pre-planned itineraries and logistics were ensured by a vertical organization. Such strict discipline has been difficult to maintain in most countries, and as a result there has been a steady deterioration of all aspects of the quality of operations. Geographical reconnaissance has not been kept up to
date, staff shortages have weakened supervision, and resistance of nuisance pests has eroded the confidence of people in spraying. Furthermore, people have got tired of preparing houses, and spraymen have become so complacent that they leave rooms or whole houses unsprayed.

Today many countries are decentralizing their health services and operating cost-recovery or cost-sharing systems for most health interventions. In the case of indoor spraying, these policies are leading to increased demand for community participation. This often includes the local recruitment and training of spraymen, who operate under the supervision of local authorities, under the general guidance of district and/or central supervision teams.

There is not yet enough experience to establish organizational models for these forms of decentralized organization. There is no logical reason to consider that they cannot succeed, while there is good evidence that the old "vertical" system was becoming non-functional.

No matter which organizational model is chosen, it will be necessary to provide adequate training, supervision and technical support to strengthen motivation and to ensure logistical requirements. It is also important to create and maintain adequate structures and ensure funding for such activities.

**Sustainability**

It is often difficult, if not impossible, to predict sustainability. Nevertheless, there are situations when non-sustainability is likely, e.g. when long-term operations depend on external funds, or when local populations do not appreciate the programme's usefulness. The sustainability of malaria control requires continuous
political support and commitment to the programme. It also needs the participation of the community or, at least, an acceptance by the community of the intervention. In order to achieve sustainability there must be adequate financial and human resources, with the capacity to determine when and where operations are needed and how achievements are to be maintained.

Logistical support
To achieve an acceptable quality of spraying requires efficient logistical support, well-trained (18) and well-equipped spraymen, especially where insecticides require the use of protective devices. The need to cover all the houses in the area implies a complete knowledge of the geography of that area and sufficient motivation of the spraymen to cover outlying houses and scattered populations.

2.4.2 Formulation and dosage

Formulation
The choice of formulation depends on the type of surface to be sprayed, operational and logistical considerations, and cost.

The traditional formulation used for indoor residual spraying is wettable powder (WP). When the technical material is solid (e.g. DDT), the WP formulations require inert carriers and wetting, suspending and anti-caking agents. To make a WP formulation from a liquid technical material, like malathion, however, the insecticide has first to be adsorbed to a solid carrier, which in turn requires wetting, suspending and anti-caking agents, limiting the maximum concentration of active ingredient in the formulated product. For example, WP formulations of DDT
may contain 75% of the technical material, while those of malathion usually have concentrations between 25%-50%.

When mixed with water and stirred, wettable powders form a suspension. In this mixture of a liquid and an insoluble solid, the small particles of solid are kept in suspension with the help of the wetting and suspending agent and periodic shaking of the spray pump is required.

Two closely interdependent properties are of fundamental importance for WP formulations: suspensibility and particle size. There are “wettability” and “susceptibility” clauses in the specifications for WP formulations. These are to ensure that the product can be rapidly wetted when mixed with water and that a sufficient amount of active ingredient is homogenously dispersed in suspension in the spray liquid. The “wet sieve test” clause of the specifications for WP formulations aims to restrict the content of insoluble particles of sizes which could cause blockage of sprayer nozzles or filters.

Solutions of technical grade insecticides in organic solvents, or emulsions in water, have been used in the past for indoor residual spraying in areas where people object to the unsightly white deposits of the WP formulations. Solutions pose both logistical problems and hazards in transporting and handling the organic flammable solvents. Emulsions are prepared from emulsifiable concentrates (EC) suspended in water.

EC formulations are generally more expensive and more difficult to handle in the field. They are seldom recommended for indoor residual spraying. The “emulsion stability” clause in the specifications for EC formulations is to make sure that enough active ingredient is homogenously dispersed in emulsion to
give a satisfactory and effective mixture during spraying.

New water-based formulations have been developed and are becoming available or being tested. These offer certain advantages for indoor residual spraying. The formulations include:

- suspension concentrate (SC)
  This is a stable suspension of a solid active ingredient in a fluid. It is intended for dilution with water before use. In this sort of product the active ingredient is in the form of crystalline particles. It may therefore be considered as somewhere between an emulsifiable concentrate (EC) and a wettable powder. Suspension concentrate is not absorbed into porous surfaces or through the skin as readily as emulsifiable concentrates, nor does it leave a visible residue, as do wettable powders, since the particles are smaller.

- capsule suspension (CS)
  Here the active ingredient is contained in very small plastic polymer capsules. These are suspended in water for spraying. The capsules release the insecticide slowly, extending the compound's residual life. This differs from agriculture products where quick release may be desirable. They are not readily absorbed by porous surfaces and adhere easily to insects, increasing insect/insecticide contact. They have few odour problems and a good residual effect, as the active ingredient is protected from light and volatility. However, they tend to be more expensive than other formulations, may leave visible deposits (not as much as WP formulations) and spray pumps need to be frequently shaken during application.
- water dispersible granules (WG)
  These offer several advantages over wettable powder, such as a considerable reduction in the risk of inhalation, being relatively dust-free, and the possibility of being measured by volume and not only by weight (as is the case with WP formulations).

As the dosage required of pyrethroids is so much lower than most other insecticides, even their WP formulations do not leave behind unsightly deposits.

**Dosage**

**Dosage is the amount of insecticide applied per unit area.** It is normally expressed as grams or milligrams of active ingredient per square metre (g/m² or mg/m²) of sprayable surface. Doses vary considerably for the different insecticides: DDT and most organophosphates and carbamates are applied at doses of 1 or 2 g/m², bendiocarb at doses of 0.1-0.4 g/m², and most alpha-cyano pyrethroids would be applied at doses of 10-50 mg/m².

**The optimal dosage is the minimum which produces the desired residual effect on common sprayable surfaces.** There is, in theory, a certain flexibility to adjust the dosage in relation to the required effective duration of the insecticide on the surfaces to be sprayed, for example, for the duration of the transmission season. The range of this flexibility is, nevertheless, very limited for most insecticides. Any increase of the recommended dosage is actively discouraged, since this would imply an increase in toxicity. Therefore, only downward dosage adjustments are normally acceptable, e.g. the use of DDT at 1 g/m² instead of the generally recommended 2 g/m². Only with pyrethroids is there a wider possibility of dosage adjustment, due to their considerably larger safety margin.
2.4.3 Erosion of nozzle tips

Different insecticides, and particularly different formulations, differ considerably in their effect on nozzle tips. The formulation of wettable powders usually requires the addition of inert mineral materials, which may be highly abrasive. Abrasion of nozzle tips introduces an added complication to spraying operations, since it may greatly increase, even double, the output of a pump, as well as producing uneven distribution of the insecticide on the sprayed surfaces. Nozzles should be changed following periodic monitoring of output and spray pattern.

The abrasiveness of the formulation should be taken into consideration when selecting the type of nozzle tip to be used. It will be necessary to assess the rate of erosion in the field, and establish a system for periodically changing used nozzle tips.

2.5 Vector ecology and behaviour

2.5.1 Ecology

Malaria transmission requires repeated human-vector contact. This is a function of the tendency of the vector to bite humans and the density of the vector. Transmission also requires the infected mosquito to survive long enough for the parasite to complete its development up to the invasion of the salivary glands with infective sporozoites. The time required for parasite development depends mainly on temperature. The length of life of the vector depends mainly on relative humidity. Vector breeding depends on the availability of suitable water collections.
Variations in rainfall, temperature and relative humidity often determine malarious areas, transmission seasons and epidemic periods.

The ecology of the area can have a strong impact on how well indoor spraying can control malaria. If the vector is able to leave the sprayed room alive, and can easily find a suitable daytime resting place, its survival chances may be the same as in an unsprayed area. In arid areas, however, where the house is often the preferred, or even the only suitable daytime resting place available, a "repelled" vector which leaves the house will be exposed to a considerably higher mortality than in unsprayed areas, even if it avoids being killed by the insecticide. There is no test for this indirect effect, which can only be deduced from the observation of the ecology of the area, the study of vector behaviour and the overall effect on malaria transmission.

2.5.2 Behaviour

The potential effect of indoor residual spraying depends on the tendency of the vector to enter houses and rest on indoor surfaces.

The following terms are used in the discussion of vector behaviour:

- *Exophily* is the tendency of mosquitoes to rest outdoors, during the whole or part of the period of blood digestion and egg development, while *endophily* is the tendency to rest indoors.

- *Exophagy* is the tendency to bite out of doors, while *endophagy* is the tendency to bite indoors.
- *Anthropophily* is the tendency to bite man, while *zoophily* is the tendency to bite animals.

As discussed above, indoor residual spraying has no impact on outdoor resting mosquitoes, i.e., exophilic species. It is noteworthy that exophily and endophily may or may not be associated with exophagy and endophagy. Both resting and biting behaviour are greatly influenced by the availability of suitable daytime resting places and the sleeping behaviour of the human population.

In some cases, a vector population, which was originally endophilic, appears to have changed its behaviour, following indoor residual spraying of the area. This may be a consequence of a genetic selection towards exophily, which has been called behavioural resistance (see section 2.3). It has also been suggested that, in most cases, it may be due to the previous existence of two separate populations, one exophilic and the other endophilic, the latter of which was progressively eliminated by spraying. It is also possible that the vectors were driven out of the houses by the irritant or repellent effect of the insecticide.

The term excito-repellency includes at least three identified effects of insecticides on some vector populations:

a) irritability, which forces resting mosquitoes on a sprayed surface to move away much earlier than on a non-sprayed surface;

b) repellency, which prevents a mosquito from resting on a sprayed surface, after approaching it; and

c) deterrence, which prevents mosquitoes from entering a sprayed room.
There is no fully satisfactory test to monitor these very important effects in the field. A test has been developed for irritability. This is based on the average time a female stays on a treated surface under a bio-assay cone before taking off again. It is a cumbersome and slow test, requiring the observation of individual mosquitoes. The PAHO excito-repellency box was developed in the 1960s; this measures the combination of the three effects. It is also cumbersome and its use has been discontinued even in the Region of the Americas where it originated.

The result of both irritability and repellency may be observed by using exit traps on windows of sprayed and unsprayed rooms. Deterrence may be assessed by using entry traps.

More detailed studies of vector behaviour in relation to spraying may be carried out in experimental huts, by studying the dynamics of entry and exit of unfed, blood-fed, partially gravid and gravid mosquitoes, and estimating the duration of resting in the sprayed rooms, as well as mortality and success in feeding. All mosquitoes collected alive should be kept for recording of mortality within 24 hours. These observations may be carried out by using a combination of entry and exit traps and collecting the dead mosquitoes on sheets covering the floors and horizontal surfaces. A modified experimental hut has also been used, surrounded by a "Colombian curtain". This is a curtain of bednet material which goes around the whole hut and which is lowered at fixed intervals (e.g. every two hours) for a fixed period (e.g. 30 minutes). This interrupts the entry and exit of mosquitoes and allows collection on both sides of the curtain, which thus act as entry and exit traps. After each collection the curtain is raised again to allow the normal entry and exit of mosquitoes (17).
Excito-repellency is important in vector control because its effect is to divert the vector from resting on sprayed surfaces and, therefore, from acquiring a lethal dose of the insecticide. This results in the survival of vectors which have fed in sprayed rooms. This can be estimated by collecting mosquitoes from window traps and observing them for 24 hours (provided the contamination of window traps either by fumigant or particulate effects of the insecticide on trapped mosquitoes can be excluded).

2.6 Social factors

Indoor residual spraying requires collective, coordinated implementation at each of the spray rounds to achieve the required high coverage and adequate dosage. This may need to be regularly repeated for a number of years. Spraying inside houses requires an acceptance of the practice by the population. This is not so essential for most outdoor vector control measures, such as space spraying or anti-larval measures. The operational focus on the house makes indoor spraying particularly suitable for rural areas, where anti-larval measures would be impractical (requiring, for example, the treatment of each rain pool). The requirement to move all furniture away from the walls to expose all the possible mosquito resting places makes spraying a more suitable option for the protection of areas where people have few pieces of furniture.

Today it is unlikely that the types of rigid organization seen previously in vertical antimalarial programmes could be established. Most countries are now decentralizing and promoting community participation in the implementation of health programmes. Both quality of operations and compliance have to be obtained through appropriate
information and education, adequate incentives and the creation of a sense of responsibility and social control.

The prominent role of local authorities in the implementation of vector control requires strong technical support from a core of specialists. These are often located at central or regional level. The sharing of resources through intersectoral collaboration may improve implementation. The active involvement of the communities in the planning and organization of spraying activities may also facilitate operations. For example, communities may provide storage facilities for insecticide, the required water for insecticide suspension, or may help to prepare houses for spraying. Community involvement may also improve coverage by identifying outlying houses. These approaches are still relatively new; it is therefore important that programmes which adopt them should document their experiences and any problems encountered. The main factor influencing community acceptance and participation in vector control has generally been a visible and durable impact on domestic pests.

Planning of spraying requires an understanding of the existing community structures and of the habits of the population with regard to the house, including:

- remaining outdoors in the early hours of the night, which may be important in relation to the biting habits of the vector, but in general means that children are better protected as they often go to bed earlier than adults,

- sleeping habits; vectors biting people sleeping outdoors are not exposed to the insecticide unless the house is the main daytime resting place, as is generally the case in very arid or some urban areas,
- occupations which may take people to outdoor activities where little or no protection is available, such as staying overnight in crop huts, cattle grazing, mining for gold or gems, or tapping of rubber,

- re-plastering or whitewashing of houses or re-thatching of roofs, which may be seasonal or in relation to certain festivities. This requires the adaptation of the spray round or the organization of "mop-up" spraying,

- re-plastering or whitewashing done in order to cover unsightly insecticide deposits. This requires information and education or change of insecticide formulation.

2.7 Cost and cost-effectiveness

The implementation of spraying will usually entail major capital and recurrent costs. These may be borne by the central or local governments, the private sector or the general population.

In most malaria-endemic countries, the purchase of insecticides, which requires "hard" currency, is by far the main component of the total cost of the spraying operation. Many countries obtain insecticides from donors. Because the donations may be time limited, they should be selectively applied. Long-term spraying programmes should not be started until funding has been secured. **Donations may cause a more serious problem when they are of an unsuitable insecticide or formulation, or if they are in excess of requirements. These actions may lead to the eventual accumulation of unsuitable or obsolete insecticides presenting serious problems of disposal.**
The determination of cost should be based on the cost of the product as applied and not strictly on its purchase price. This includes the consideration of the amount of active ingredient in the formulation, cost of shipment and handling (including local transport and storage), as well as dosage, frequency and cost of application.

The value of calculating the cost-effectiveness of interventions is to help policy-makers make decisions about competing uses of resources. The set of available policy options may be clear, but sometimes there is some confusion over what is actually controlled by the decision-maker. Organizational, political and social factors can often impose limits on the appropriate policies; for example, the previous existence of a spraying organization for malaria control. Cost-effectiveness can be improved by sharing resources within the health sector as well as with other sectors. Many malaria services have improved the cost-effectiveness of their interventions by integrating all programmes for the control of vector-borne diseases, or major endemic diseases within a single management structure.

It is generally considered that the estimation of cost-effectiveness is more appropriate to health care interventions than cost-benefit or cost-utility analyses, since the translation of health benefits into monetary terms is not feasible.

The estimation of effectiveness and the possibility of comparing effectiveness of different alternatives requires appropriate indicators. These are often based on the expected impact on entomological and/or epidemiological parameters.
In many countries it is difficult to get reliable data on which to base a cost-effectiveness analysis. Decisions are made on the basis of direct costs, affordability and operational feasibility. It is essential that programmes ensure careful and systematic documentation of resources used, as well as epidemiological and, when possible, entomological data, indicating the impact of the interventions.

2.8 Disposal of obsolete insecticides

The problem of obsolete insecticides is widespread and common. They may be a source of environmental pollution and a threat to human health. The situation is most serious in developing countries where there may be little awareness of the dangers of pesticides and the resources for handling such problems are very limited.

Given the hazards associated with obsolete insecticide stocks and the high cost of safe and environmentally sound disposal, the long-term solution lies in preventive measures. Important preventive measures are: investment in building proper and sufficient capacity for insecticide storage; training of staff in stock management; good storage practices and proper handling of insecticides during transport; refusal of donations in excess of requirements; and clear descriptions of product specifications, including required packaging and labelling (long-life labels), in the tender documents or direct procurement orders. These measures are important to avoid accumulation of obsolete insecticides.

There are no easy disposal methods which are safe, cheap and generally applicable. There are several
methods which definitely should not be used (open burning or burying of bulk quantities of insecticides). These methods are likely to cause severe damage to public health and to the environment.

Different disposal options are available for small or large quantities of product. Those which are acceptable for small quantities may not be suitable for large ones. The definition of a "small" or "large" quantity depends on the health and environmental hazards connected to the product.

The disposal methods that may be considered acceptable vary according to the specific type of products, and require certain conditions. These methods include high temperature incineration, chemical treatment and specially engineered landfill. There are several promising new developments in the field of disposal technology. It is essential to consider the combination of technology and the product on a case-by-case basis. FAO, UNEP and WHO have produced provisional technical guidelines on the disposal of bulk quantities of obsolete pesticides in developing countries (19).
- the name of the insecticide, type of formulation and the intended use,
- the WHO specification number,
- the concentration of active ingredient required,
- the type of packaging (quality and size) required, in conformity with UN packaging specifications, and the kind of labelling, including language,
- the inspection and sampling to be made after completion of the order but before its acceptance,
- the name of the inspection agent and/or laboratory responsible for determining whether the insecticide meets all the requirements of the specification and the purchase order,
- any special requirements that the purchaser may have (e.g. long-term storage). This will guide the manufacturer in the preparation of a satisfactory product.

**An important aspect to be taken into consideration when selecting suppliers is their after-sales service.** This could include technical advice or training. It is also important to check the terms of their return policy in case of failed performance.

**It can be made a pre-condition of the tender that candidate companies supply in advance a sample of the product, accompanied with an official certificate of analysis.** This can be independently checked to see if the product conforms to specifications.

**When the product is delivered, or preferably before shipment, it is wise to take random samples from the consignment for quality control.** These samples should be sent to independent analytical laboratories to ensure that the product conforms to the specifications. This should not be limited to the amount of active ingredient,
3. PURCHASING GUIDELINES

Once an insecticide and its appropriate formulation have been selected on epidemiological and operational grounds, it is essential to choose a good quality product. There may be a variety of suppliers apparently offering the same insecticide in the market. However, products that appear to be similar in fact may not have the claimed level of active ingredient, due to poor manufacturing processes. Even if the product has the correct level of active ingredient, it may suspend badly, block sprayers or give erratic biological performance. A poorly formulated product may deteriorate rapidly under storage and produce toxic derivatives.

It can be a serious mistake to select only the cheapest product offered. In this way purchasing departments can waste money, and serious safety hazards and/or ecological consequences can result.

The WHO specifications for public health pesticides provide exact description of the characteristics of pesticides, and their formulations, approved for use in public health. The specifications are available on the WHOPES homepage on the Internet at <www.who.int/ctd/whopes>.

One of the conditions to be included in any tender for the purchase of insecticides should be: “all products offered must conform to WHO specifications reference “WHO/SIF/.....”. This should exclude suppliers who cannot guarantee quality.

A tender, as well as the subsequent order, for the purchase of an insecticide should state:
but to all physical and chemical properties of the product. Procedures for sampling are available on the WHOPES homepage as given above. **WHOPES offers assistance to national vector and pest control programmes on quality control of pesticides.** The procedures can be carried out on the programmes' behalf at WHO-designated collaborating centres.

**WHO's supply services are available to the national programmes and projects, to agencies under the jurisdiction of the health administration or comparable authority of the Member State and to nongovernmental organizations in official relations with WHO.** This service is also available to other organizations within the United Nations.

The WHO representative offices throughout the world and the various WHO regional offices for Africa, the Americas, South-East Asia, Europe, the Eastern Mediterranean and the Western Pacific can provide further details on how to order using the WHO supply service.
<table>
<thead>
<tr>
<th>Product</th>
<th>Class group</th>
<th>Dosage (g/m²)</th>
<th>Mode of action</th>
<th>Duration of effective action (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DDT WP</td>
<td>OC</td>
<td>1-2</td>
<td>Contact</td>
<td>&gt;6</td>
</tr>
<tr>
<td>Malathion WP</td>
<td>OP</td>
<td>2</td>
<td>Contact</td>
<td>2-3</td>
</tr>
<tr>
<td>Fenitrothion WP</td>
<td>OP</td>
<td>2</td>
<td>Contact &amp; airborne</td>
<td>3-6</td>
</tr>
<tr>
<td>Pirimiphos-methyl WP &amp; EC</td>
<td>OP</td>
<td>1-2</td>
<td>Contact &amp; airborne</td>
<td>2-3</td>
</tr>
<tr>
<td>Bendiocarb WP</td>
<td>C</td>
<td>0.1-0.4</td>
<td>Contact &amp; airborne</td>
<td>2-6</td>
</tr>
<tr>
<td>Propoxur WP</td>
<td>C</td>
<td>1-2</td>
<td>Contact &amp; airborne</td>
<td>3-6</td>
</tr>
<tr>
<td>Alpha-cypermethrin WP &amp; SC</td>
<td>P</td>
<td>0.02-0.03</td>
<td>Contact</td>
<td>4-6</td>
</tr>
<tr>
<td>Cyfluthrin WP</td>
<td>P</td>
<td>0.02-0.05</td>
<td>Contact</td>
<td>3-6</td>
</tr>
<tr>
<td>Deltamethrin WP</td>
<td>P</td>
<td>0.01-0.025</td>
<td>Contact</td>
<td>2-3</td>
</tr>
<tr>
<td>Etofenprox WP</td>
<td>P</td>
<td>0.1-0.3</td>
<td>Contact</td>
<td>3-6</td>
</tr>
<tr>
<td>Lambda-cyhalothrin WP</td>
<td>P</td>
<td>0.02-0.03</td>
<td>Contact</td>
<td>3-6</td>
</tr>
</tbody>
</table>

(1) OC = Organochlorines; OP = Organophosphates; C = Carbamates; P = Pyrethroids.
4. WHOPES RECOMMENDED INSECTICIDES FOR INDOOR RESIDUAL SPRAYING FOR MALARIA VECTOR CONTROL

Safety and effectiveness are essential requirements for an insecticide formulation to be used as an indoor residual spray. The products listed in Table 4 and discussed below have been fully evaluated by the WHO Pesticide Evaluation Scheme (WHOPES). They can therefore be used for malaria vector control in safe and effective quantities by spraymen who are adequately protected from their potential toxic effects (see sections 2.1.1 and 2.1.2).

4.1 Organochlorines

DDT is the only insecticide of this chemical group which is still recommended for indoor residual spraying. Previously used organochlorines belonged to the cycloidiene subclass, which included dieldrin and HCH. Dieldrin had to be abandoned because of its high acute toxicity to humans. Eventually the whole subgroup became unusable because of the rapid development of resistance by a mechanism common to all cycloidiens.

4.1.1 DDT

DDT is an organochlorine insecticide. It has low volatility and very low solubility in water, but is soluble in fats and organic solvents. It is highly persistent and has a rather long residual effect on most sprayed surfaces. The long persistence in the environment and its high bio-
accumulation in fatty tissues have contributed to the dispersal of residues everywhere, including arctic ice, from agricultural use of DDT in the 1950s and 1960s. This bio-accumulation has resulted in highly toxic effects at the top of food chains, particularly in sharks, eagles and falcons.

It is used at a dosage of 1-2 g/m², giving a residual effect of six months or more. Depending on the surfaces on which it is sprayed and climatic conditions, its effectiveness may last considerably more than one year on wood and thatch, or only 3-4 months on certain mud surfaces.

The development of resistance to DDT has been slow. It is generally associated with its extensive use in agriculture, particularly when mixtures containing DDT and a wide variety of insecticides are used in aerial sprays, exercising pressure on the selection of various mechanisms of resistance. DDT may show cross-resistance to pyrethroids when the kdr gene is involved.

DDT use has considerably declined in recent decades, mainly due to its environmental impact. However, DDT is still one of the most commonly used insecticides for indoor residual spraying. The environmental effects from past agricultural use have resulted in the prohibition of its use outdoors in almost all countries and of all its uses in countries which do not require it for disease control.

DDT is included in the list of Persistent Organic Pollutants (POPs) and negotiations of the global treaty to eliminate certain POPs. Exemption has however been given for the essential uses of DDT in public health till affordable alternatives become available.

The potential environmental contamination from a sprayed house is probably minimal. Even if a sprayed house is
destroyed, its site will normally be used to build a new house and the compacted terrain very seldom would revert to agriculture. Due to the insolubility of DDT in water, its residues will mainly remain in the same place. The main danger of environmental contamination from the use of DDT as an indoor residual spray, would come from the diversion of the insecticide intended for malaria control into agricultural use. A similar danger would occur if containers were inadequately disposed of, or pumps indiscriminately washed in surface waters; all these risks should be prevented by proper education and strict supervision.

a. Toxicology
Absorption route: Absorbed from the gastrointestinal tract and by inhalation. It may also be absorbed through intact skin when in oily solution. This is not applicable to the WP formulations used for malaria control.

Mode of action: DDT is a central nervous system stimulant producing hyperactivity and tremor; convulsions may occur but are less common than with other organochlorine insecticides.

Mammalian toxicity:

- Oral, rat, 113 mg active ingredient/kg body weight
- Dermal, rat, 250-500 mg active ingredient/kg body weight

Note: The WHO recommended classification of the active ingredient is in class II (moderately hazardous), however, the final classification depends on the formulation.

Toxicity to non-mammalian species: Fish: harmful; birds: moderately toxic; other species: harmful to bees.
b. Transportation, storage and handling
All the precautions listed in section 2.1.5 above should be followed.

c. Disposal
Containers with residues must be crushed and returned for proper disposal (see section 2.1.6 above). Care must be taken to avoid subsequent contamination of water sources. Attempts to wash containers in order to use them for other purposes should not be permitted.

d. Symptoms of poisoning
Acute poisoning by DDT is very rare, particularly when used for indoor residual spraying. Nevertheless, it could potentially occur if there is gross mishandling. Early symptoms may include paraesthesia (tingling) of the tongue, lips and parts of the face, in severe cases extending to the extremities. The patient may have a sense of apprehension and disturbance of equilibrium, dizziness, confusion and a characteristic tremor.

e. Treatment before reaching physician
Remove contaminated clothing and wash the affected skin with clean water and soap and flush the area with large quantities of clean water. The patient should be calmed and kept in quiet, shaded conditions and medical assistance should be sought. Oils and fats should not be given. There is no specific antidote. Symptomatic treatment should aim at controlling hyperactivity and in some instances convulsions. Artificial ventilation may be required. Anticonvulsant treatment with soluble barbiturates, diazepam, or paraldehyde should be given in sufficient doses to calm the patient and prevent convulsions.
4.2 Organophosphates

Organophosphates, although rapidly metabolized and eliminated, produce prolonged inhibition of acetylcholinesterase, therefore disturbing the transmission of nerve impulses at the synapses. They may thus produce a cumulative effect after repeated exposure, with recovery requiring the production of fresh acetylcholinesterase. Four considerations apply to the three recommended organophosphates:

a. Toxicology
   This family includes some extremely toxic insecticides, such as parathion. The insecticides recommended for indoor residual spraying have very low (malathion and pirimiphos-methyl) or moderate toxicity (fenitrothion). Specific data on LD$_{50}$ is presented below for each insecticide. Periodical or daily determination of cholinesterase activity, in spraymen and other insecticide handlers, is recommended when spraying organophosphates.

b. Symptoms of poisoning
   Early symptoms of poisoning may include excessive sweating, headache, weakness, giddiness, nausea, vomiting, stomach pains, blurred vision, constricted pupils slurred speech and muscle twitching. Later there may be convulsions, coma, loss of reflexes and loss of sphincter control.

c. Treatment before reaching physician
   Organophosphate poisoning should be considered as a medical emergency, requiring immediate treatment. The affected person should stop work immediately, remove any contaminated clothing, wash the affected skin with soap and clean water and flush the area with large
quantities of clean water. Care must be taken not to contaminate others, including medical or paramedical workers. All squad leaders, and individual spraymen, in the case of dispersed operations, should be trained in first-aid and emergency treatment of intoxication.

Atropine and oximes are the specific antidotes, but their use should be indicated by a physician. There are automatic injectors loaded with atropine sulfate and obidoxime chloride, which could be made available in the field whenever relatively toxic organophosphate insecticides are used in areas without easy access to medical care. Once given the emergency treatment, the patient should be rapidly referred to a hospital for full treatment.

d. Transportation, storage, handling and disposal
The precautions listed in sections 2.1.5 and 2.1.6 above should be followed.

4.2.1 Malathion

Malathion is an organophosphate insecticide. The pure insecticidal compound (technical grade) of malathion is a liquid with relatively low vapour pressure, moderate water solubility and relatively low toxicity. It has been widely used in malaria control since the 1960s, as a 50% WP formulation for indoor residual spraying, and as 95% ULV formulation for space spraying. It was considered, for a long time, as the first potential replacement for DDT in cases of resistance. In Sri Lanka, for example, its use was reserved for public health. As an indoor residual spray it is used at a dosage of 2 g/m² giving a residual effect of 2-3 months. It is rapidly inactivated on alkaline surfaces, such as whitewashed walls, where its effect may last only a few weeks.
Most of its formulations have a strong unpleasant odour, which has been responsible for people's objections to its indoor spraying.

a. Toxicology
Absorption route: Malathion may be absorbed by inhalation, from the gastrointestinal tract or through the intact skin. Malathion has low mammal toxicity and a very good safety record, having been safely used with light protective clothing, overalls and hats. Nevertheless, under storage at high temperature, an inadequately formulated product once produced a very toxic isomer iso-malathion, which caused a number of cases of poisoning in spraymen (10,11). Testing for iso-malathion and for its possible production under storage conditions is now part of the WHO specifications.

Mode of action: Malathion is an indirect cholinesterase inhibitor, after metabolism to malaoxon, its oxygen analogue.

Mammalian toxicity:

- Oral, rat, 1375-2100 mg active ingredient/kg
- Dermal, rat, 4444 mg active ingredient/kg

Note: The WHO recommended classification of the active ingredient is in class III (slightly hazardous), however, the final classification depends on the formulation.

Toxicity to non-mammalian species: it is very toxic to bees and other beneficial insects, moderately toxic to birds and very toxic to fish and crustaceans.
b. Transportation and storage, handling and disposal
The same precautions should be taken as for other organophosphates. When selecting containers it should be remembered that malathion is corrosive to some metals.

c. Symptoms and treatment of poisoning
The same as for organophosphate insecticides, (see above), taking into account the very low toxicity of malathion.

4.2.2 Fenitrothion

Fenitrothion is an organophosphate insecticide. It has been used extensively as an indoor residual spray for malaria control since the 1970s. It is the most toxic for man of the insecticides approved for residual house spraying, with a relatively low margin of safety. Its use therefore requires protective clothing and the monitoring of cholinesterase activity (see sections 2.1.2 & 2.1.3 above). It is used at a dosage of 2 g/m² giving a residual effect of 3-6 months.

a. Toxicology
Absorption route: Absorbed from the gastrointestinal tract as well as from intact skin and by inhalation.

Mode of action: A cholinesterase inhibitor.

Mammalian toxicity:
- Oral, rat, 503 mg active ingredient/kg
- Dermal, rat, 3500 mg active ingredient/kg

Note: The WHO recommended classification of the active ingredient is in class II (moderately hazardous), however, the final classification depends on the formulation.
Toxicity to non-mammalian species. Fish: toxic; birds: moderately toxic; other species: highly toxic to bees and other arthropods.

b. Transportation, storage and handling
Fenitrothion has a higher toxicity than other organophosphates used for indoor residual spraying. Strict discipline is needed in the use of full protective clothing, the use of showers and washing facilities, and the changing and washing of contaminated clothes.

c. Disposal
Containers must be drained and rinsed three times and destroyed with pick axe or hammer, flattened and returned for proper disposal (see section 2.1.6 above). Impermeable gloves and dust masks should be worn during this work.

d. Symptoms and treatment of poisoning
All the comments made above apply to fenitrothion, which is one of the most toxic insecticides approved for indoor residual spraying.

4.2.3 Pirimiphos-methyl

Pirimiphos-methyl is an organophosphate insecticide. It has been tested for malaria control in various parts of the world as a 25% WP and as 25% and 50% EC formulations at doses of 1 to 2 g/m², giving a residual effect of 2-3 months. The EC formulations have virtually no erosion of nozzle-tips and made no unsightly marks on the walls of the sprayed homes.

a. Toxicology
Absorption route: Pirimiphos-methyl may be absorbed from the gastrointestinal tract, through the intact skin and, less commonly, by inhalation of fog, smoke or spray mist.
Mode of action: A cholinesterase inhibitor. The degradation products desethyl pirimiphos-methyl and pirimiphos-methylloxon are also active but of transient stability, and have not figured significantly in mammalian studies.

Mammalian toxicity:

- Oral, rat, 2018 mg active ingredient/kg
- Dermal, rat, >4500 mg active ingredient/kg

Note: The WHO recommended classification of the active ingredient is in class III (slightly hazardous), however, the final classification depends on the formulation.

Toxicity to non-mammalian species: Toxic to fish and birds.

b. Transportation and storage, handling and disposal
See sections 2.1.5 and 2.1.6 above.

c. Symptoms and treatment of poisoning
See sections 4.2 b and c above, taking into consideration the very low toxicity of pirimiphos-methyl.

4.3 Carbamates

Carbamates are fast-acting anticholinesterase (AchE) compounds, with relatively high acute oral toxicity.

a. Toxicology
The inhibition of AchE induced by carbamates is relatively labile. As a result, although symptoms may occur during operational exposure, recovery normally follows once exposure stops.
b. Transportation and storage, handling and disposal
The same precautions should be taken as for the other insecticides, see sections 2.1.5 and 2.1.6 above.

c. Symptoms of poisoning
Symptoms of mild carbamate poisoning are similar to those of organophosphate poisoning. They include excessive sweating, headache, nausea, blurred vision, chest pain, vomiting, excessive salivation and slurred speech. Severe intoxication causes narrowed pupils, muscle twitching, spasms, intestinal convulsions, diarrhoea and laboured respiration. These rapidly subside when spraying is stopped and heavily contaminated clothes removed, particularly if some atropine is given.

d. Treatment before reaching physician
The affected person should stop work immediately, remove any contaminated clothing and wash the affected skin with soap and clean water. The whole contaminated area (including the eyes, if necessary) should be flushed with large quantities of clean water. The patient should be kept at rest and immediate medical aid obtained (showing the product label).

The patient can be treated by atropine but it is often no longer necessary by the time the patient reaches the place where it is available. Oximes are contraindicated for the treatment of carbamate poisoning. Morphine should not be used, but diazepam may be useful for convulsions.

4.3.1 Bendiocarb
Bendiocarb is a carbamate insecticide. It has low vapour pressure, low odour and does not have corrosive and staining properties. This makes it acceptable to most
householders. It is rapidly hydrolysed in alkaline media (such as whitewash) and rapidly degraded in soil.

Like other N-methylcarbamates, bendiocarb is a fast-acting anticholinesterase compound, with high acute oral toxicity. It can however be used at low dosages (0.1-0.4 g/m²). The lower dose may be used on non-absorbent surfaces, while the higher dose is required on porous surfaces such as mud walls. The WP formulation should be supplied in water-soluble sachets, each one sufficient for a single pump charge. This avoids handling during weighing of the formulation and the associated exposure of the operators.

The residual effect lasts 2-6 months. This period is longer on surfaces of organic origin (wood, thatch) and shorter on alkaline surfaces. It has been used for malaria control in Turkey and some countries of south-east Asia and Latin America.

a. Toxicology
Bendiocarb may be absorbed from the gastrointestinal tract or, to a limited extent, through intact skin. It is mainly metabolized through hydrolysis and excreted rapidly; there is no accumulation in organs and tissues. Its low vapour pressure makes inhalation unlikely except from airborne spray mist.

Mode of action: Bendiocarb acts through inhibition of cholinesterase activity which is rapidly reversible. The half-life of the inhibited enzyme is approximately 30 minutes.

Mammalian toxicity:
- Oral, male rat, 40-156 mg active ingredient/kg
- Dermal, male rat, > 566 mg active ingredient/kg
Note: The WHO recommended classification of the active ingredient is in class II (moderately hazardous), however, the final classification depends on the formulation.

Toxicity to non-mammalian species. Bendiocarb is toxic to fish and birds, very toxic to domestic hens; and very toxic to bees.

b. Transportation and storage, and disposal
See recommendations for other insecticides (listed in sections 2.1.5 and 2.1.6 above), taking into consideration that Bendiocarb containers should always be made unusable before returning them for proper disposal.

c. Handling
Because of the high toxicity of Bendiocarb, handling of the product should be avoided. Pre-packaged pump charges should be used. These are mixed with water in the pump itself. Because of the low dose used for spraying, the spray itself is not highly toxic.

Bendiocarb has been used in spraying operations by spraymen wearing overalls (washed every day), a broad-brimmed hat, ankle-length canvas shoes and gauze face-masks.

As with other carbamates, monitoring of exposure by simple colorimetric methods for measuring cholinesterase activity is impracticable.

d. Symptoms of poisoning and treatment before reaching physician
The same as for other carbamates, see sections 4.3c and 4.3d above.
4.3.2 Propoxur

Propoxur is a carbamate insecticide. It has been used for indoor residual spraying since the early 1970s as a 50% WP formulation at a dose of 1-2 g/m² giving a residual effect of 3-6 months. Spraying gives a distinct airborne effect on controlling vector activity.

a. Toxicology
Absorption route: Propoxur can be absorbed by inhalation, from the gastrointestinal tract and, to a lesser extent, through intact skin. The compound is rapidly metabolized and does not accumulate in tissues.

Mode of action: Inhibition of cholinesterase, which is relatively rapidly reversible.

Mammalian toxicity:
- Oral, rat, 95 mg active ingredient/kg
- Dermal, rat, >2400 mg active ingredient/kg

*Note:* The WHO recommended classification of the active ingredient is in class II (moderately hazardous), however, the final classification depends on the formulation.

Toxicity to non-mammalian species: Toxic to fish, birds and bees.

b. Transportation and storage, handling and disposal
The same as for other insecticides, listed in sections 2.1.5 and 2.1.6 above.

c. Symptoms and treatment of poisoning
The same as for other carbamates, see 4.3c and d above.
4.4 Pyrethroids

a. Handling
Pyrethroids are skin irritants. Therefore, as well as taking general precautions on handling insecticides, particular care should be taken to avoid contact with skin, eyes, nose and mouth. When handling open containers indoors, use local exhaust ventilation to prevent dust from spreading. Take precautions to prevent formation of explosive mixtures. Keep the formulations away from sources of ignition. In particular, no smoking should be allowed. Make water and fire-fighting products accessible.

b. Disposal
Procedures are the same as for other insecticides, see section 2.1.6 above.

c. Symptoms of poisoning
In normal use only local skin reactions have been reported. Any pyrethroid reaching the systemic circulation will be metabolized rapidly to much less toxic metabolites. The risk of toxicity of any kind, to humans exposed by the usual routes, is extremely remote, even with frequent exposure to the low concentrations used for malaria control. Systemic toxicity has not been seen in users except on very rare occasions when few precautions were taken during packaging of pyrethroids and the whole body was subjected to repeated and often prolonged exposure through soaked clothing (10).

If ingested, nevertheless, these products may produce nausea, vomiting, cough, respiratory distress and convulsions.

The field use of pyrethroids in the recommended concentrations, with the normal precautions for insecticide use, poses little or no hazard to applicators. Skin reactions
such as pruritus, tautness and reddening of the facial skin, partial facial paraesthesia and signs of irritation in the oropharyngeal cavity or coughing, especially when combined with an increase of sensitivity, particularly to touch stimuli, may be signs of dermal contact with or inhalative exposure. These dermal sensations are direct and transitory effects on sensory nerve endings and are not the result of a primary skin irritation. Toxicologically these are useful characteristics, as they provide an early indication of exposure (13).

After breathing in the insecticide spray mist there may be some irritation of respiratory mucous membranes with coughing and sneezing.

d. Treatment before reaching physician
The affected person should stop work, remove any contaminated clothing, wash the affected skin with soap and clean water and flush the area with large quantities of clean water. There is no specific antidote for pyrethroid toxicity. Treatment is symptomatic.

4.4.1 Alpha-cypermethrin

Alpha-cypermethrin is a synthetic pyrethroid. It has a high knock-down effect and a strong excito-repellent effect on anophelines. Alpha-cypermethrin 5% WP and 10% SC have been evaluated at doses of 25-30 mg/m² and found to give a residual effect of 4-6 months.

a. Toxicology
Absorption may occur to some extent after inhalation or dermal exposure but, as with other pyrethroids, alpha-cypermethrin is rapidly metabolized and excreted from the body.
Mode of action: Neurotoxicity through disruption of nerve fibre impulse transmission.

Mammalian toxicity:
- Oral, rat 79 mg active ingredient/kg
- Dermal, rat >2000 mg active ingredient/kg
  **Note:** The WHO recommended classification of the active ingredient is in class II (moderately hazardous), however, the final classification depends on the formulation.

Toxicity to non-mammalian species. Fish: very toxic; birds: low acute oral and dietary toxicity; other species: under normal use conditions it does not pose a significant hazard to non-target organisms, including bees. Under laboratory conditions, it has been observed to be very toxic to bees and aquatic invertebrates.

b. **Transportation and storage, handling and disposal, symptoms of poisoning and treatment before reaching physician**
Action is the same as for other pyrethroids, above, and as listed in sections 2.1.5 and 2.1.6.

**4.4.2 Cyfluthrin**

Cyfluthrin is a synthetic pyrethroid with very low vapour pressure. It is readily hydrolysed under alkaline conditions, but quite stable at pH 7 or below. Cyfluthrin is very strongly adsorbed to organic matter and can be classified as immobile in soil. It can be considered to be moderately bio-accumulating.

As an indoor residual spray for malaria control, at a dosage of 25-50 mg/m², it has a very high knock-down effect and general mortality. It has a relatively low excito-repellent effect, and a residual effect of 3-6 months. It is
available as a 10% WP formulation for indoor residual spraying.

a. Toxicology
The acute toxicity of cyfluthrin varies depending on the vehicle. Toxicity is high by ingestion but cyfluthrin has poor skin penetration. Although as other α-cyano-pyrethroids, it may irritate the eye and skin, 10% WP cyfluthrin is not irritating to the skin and only slightly irritating to mucous membranes.

Absorption route: After oral administration, about 90% was absorbed in the intestine. Absorption after inhalation is also possible. Dermal absorption is very low.

Mode of action: Cyfluthrin acts upon the peripheral nervous system as well as on regions of the central nervous system, e.g. certain binding sites (GABA-receptors) in the brain.

Mammalian toxicity:
- Oral, rat 250 mg active ingredient/kg
- Dermal, rat > 5000 mg active ingredient/kg
  Note: The WHO recommended classification of the active ingredient is in class II (moderately hazardous), however, the final classification depends on the formulation.

Toxicity to non-mammalian species: Cyfluthrin is highly toxic to bees and other arthropods. It shows low toxicity to birds and it is very toxic to fish and aquatic invertebrates.

b. Transportation and storage, handling and disposal, symptoms of poisoning and treatment before reaching physician
Action is the same as for other pyrethroids, as in 4.4a, b, c, d above and as listed in sections 2.1.5 and 2.1.6.
4.4.3 Deltamethrin

Deltamethrin is a synthetic pyrethroid of the alpha-cyano group. It is related to cypermethrin and lambda-cyhalothrin, and is a single isomer pyrethroid. It has been used in malaria control since the late 1970s. It has been widely used for the impregnation of bednets or curtains, but also for indoor residual spraying, in spite of its marked excitoto-repellency, which in some situations may be an advantage as it reduces human-vector contact.

It is used at dosages of 10-25 mg/m² giving a residual effect of 3-6 months. Protective clothing for spraymen should consist of overalls (washed daily), canvas or rubber boots, and hats.

a. Toxicology
Deltamethrin is primarily absorbed from the gastrointestinal tract, but also by inhalation of spray mist.

Mode of action: A neurotoxin, acting primarily on the basal ganglia of the central nervous system, causing repetitive nerve action.

Mammalian toxicity:
- Oral, male rat, 128 mg active ingredient/kg
- Dermal, male rat, 2940 mg active ingredient/kg

Note: The WHO recommended classification of the active ingredient is in class II (moderately hazardous), however, the final classification depends on the formulation.

Toxicity to non-mammalian species: Highly toxic to fish and bees; very low toxicity to birds.
b. Transportation and storage
In addition to the general precautions for the storage of insecticides, care should be taken to prevent deltamethrin's contact with metals, other than aluminium and tin.

c. Handling and disposal
Action should be the same as for other pyrethroids, listed in sections 2.1.5 and 2.1.6 and in section 4.4a above.

d. Symptoms of poisoning and treatment before reaching a physician
Same as other common pyrethroids (see 4.4d above).

4.4.4 Etofenprox

Etofenprox is a synthetic non-ester pyrethroid. It has high vapour pressure and low water solubility. It is the insecticide with lowest acute toxicity to mammals of those recommended for indoor residual spraying. It is used as a WP 20% formulation, at a dosage of 100-300 mg/m² giving a residual effect of 3-6 months.

a. Toxicology
Absorption route: Etofenprox may be absorbed from the gastrointestinal tract or through the intact skin.

Mode of action: Etofenprox disturbs nerve impulses in insect nerve axons.

Mammalian toxicity:
- Oral, rats >10 000 mg active ingredient/kg
- Dermal, rats > 2140 mg active ingredient/kg.

Note: The WHO recommended classification of the active ingredient is in class UH (*unlikely to present
acute hazard in normal use"), however, the final classification depends on the formulation.

Toxicity to non-mammalian species: high to low toxicity to fish; toxic to bees, and low toxicity to birds.

b. Transportation and storage, handling and disposal
Action is the same as for other pyrethroids, listed in sections 2.1.5, 2.1.6 and 4.4a above.

c. Symptoms of poisoning
Etofenprox has extremely low toxicity.

d. Treatment before reaching a physician
Treatment is the same as other pyrethroids, see 4.4e above.

4.4.5 Lambda-cyhalothrin

Lambda-cyhalothrin is a synthetic pyrethroid, of the alpha cyano group, with a core (−CCOCHCN−), as in alpha-cypermethrin and deltamethrin. Lambda-cyhalothrin has low vapour pressure, is essentially insoluble in water and has low volatility. It is available in WP formulation and is used at a dosage of 20-30 mg/m² giving a residual effect of 3-6 months.

a. Toxicology
Absorption route: Lambda-cyhalothrin may be absorbed through the gastrointestinal tract, by inhalation or through the skin. Skin absorption of lambda-cyhalothrin is very low and no systemic effects from skin absorption have been described.

Mode of action: Lambda-cyhalothrin's mode of action is the same as that of other alpha-cyano pyrethroids, primarily affecting the sodium channels in the nerve
membrane and causing a long-lasting prolongation of the transient increase in sodium permeability of the membrane during excitation.

Mammalian toxicity:
- Oral, rat, 79 mg active ingredient/kg (male) and 56 mg/kg (female)
- Dermal, rat, 632 mg active ingredient/kg (male) and 696 mg/kg (female)

Note: The WHO recommended classification of the active ingredient is in class II (moderately hazardous), however, the final classification depends on the formulation.

Toxicity to non-mammalian species: very toxic to fish, toxic to bees, low toxicity to birds.

b. Transportation and storage
The same as for other pyrethroids, listed in section 2.1.5 above.

c. Handling
Suitable protective clothing and gloves should be worn when handling the compound. Contact with skin and eyes should be avoided. Do not breathe spray mist. Spraymen should use visors to avoid intolerable paraesthesia in facial skin (goggles and a mask are not enough). Spraymen should not eat, drink or smoke when using this pyrethroid. They should wash the face and hands before eating, drinking or smoking. Read the label before use.

d. Disposal
Action is the same as for other pyrethroids, see section 2.1.6 above.
e. Symptoms of poisoning
Subjective facial sensation following the handling of product can occur, producing a tingling (paraesthesia), burning, or numb sensation. These symptoms are fully reversible within a few hours and are not signs of systematic toxicity. Nose and throat irritation, sometimes associated with coughing and sneezing, has been described by spray operators.

f. Treatment before reaching physician
Treatment is the same as for other pyrethroids, see 4.4d above.
5. REFERENCES\(^1\)


\(^1\) Listed unpublished documents are available on request from the Department of Communicable Disease Control, Prevention and Eradication, World Health Organization, 1211 Geneva 27, Switzerland.

92


14. Techniques to detect insecticide resistance mechanisms (field and laboratory manual). Geneva,


