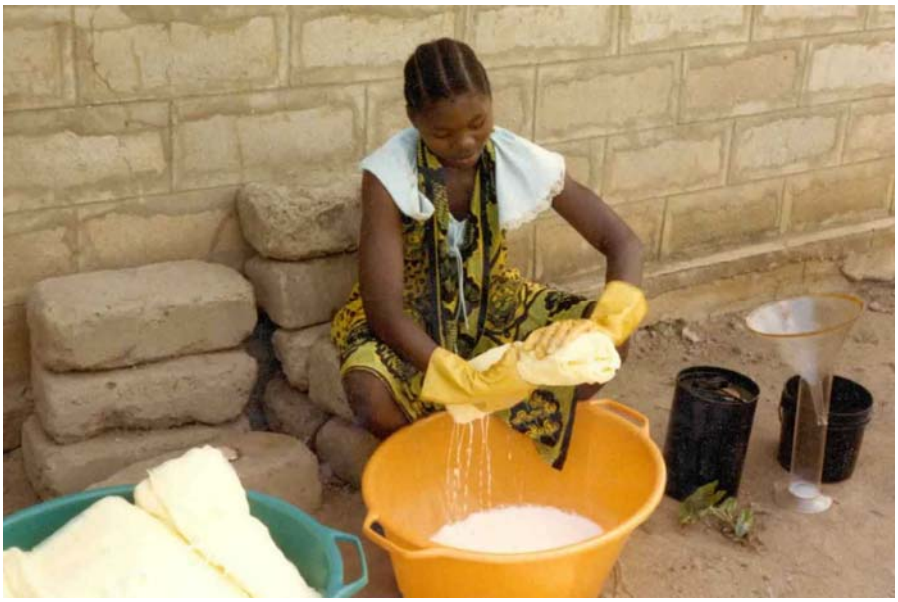
Programmatic Environmental Assessment for Insecticide-Treated Materials in USAID Activities in Sub-Saharan Africa



Prepared by:
Brian Hirsch, USAID/AFR/SD/ANRE
Carl Gallegos, USAID/AFR/SD/ANRE
Walter Knausenberger, USAID/AFR/REDSO-ESA
Andrew Arata, USAID/AFR

In collaboration with:
Michael MacDonald, for the NetMark Program

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Cover photo: Woman treating mosquito net with insecticide. C. Curtis, London School of Hygiene and Tropical Medicine.

Tables

Acronyms

ADI	Acceptable daily intake
BEO	Bureau Environmental Officer
CFR	U.S. Code of Federal Regulations
CS	Capsule suspension
DIY	Do-it-yourself
DNT	Developmental neurotoxicity
EA	Environmental assessment
EC	Emulsifiable concentrate
EW	Emulsion, oil in water
FIFRA	U.S. Federal Insecticide, Fungicide and Rodenticide Act
IEC	Information, education and communication
IEE	Initial Environmental Examination
IPM	Integrated pest management
ITM	Insecticide-treated material
ITMN	Insecticide-treated mosquito net
ITN	Insecticide-treated net
IVC	Integrated vector control
IVM	Integrated vector management
KAPB	Knowledge, attitude, practice and behavior
LD_{50}	Lethal dose, 50% of the test population
LOAEL	Lowest observed adverse effect level
LSHTM	London School of Hygiene and Tropical Medicine
MEO	Mission Environmental Officer
MOE	Margin of exposure
MOS	Margin of safety
NGO	Non-governmental organization
NMCP	National malaria control program
NOAEL	No observed adverse effect level
OTC	Over-the-counter
PEA	Programmatic Environmental AAssessment
PERSUAP	Pesticide Evaluation Report and Safer Use Action Plan
PSI	Population Services International
PVO	Private voluntary organization
RBM	Roll Back Malaria
REO	Regional Environmental Officer
SC	Suspension concentrate
UNICEF	United Nations Children’s Fund
UNFAO	United Nations Food and Agriculture Organization
USAID	U.S. Agency for International Development
USEPA	U.S. Environmental Protection Agency
WHO	World Health Organization
WHOPES	WHO Pesticide Evaluation Scheme
WT	Water-dispersible tablets

1 Summary of findings

The treatment of bednets and curtains with insecticides has been shown to be a cost-effective and efficacious approach to malaria vector control in many situations, and as such provides significant public health benefits. Along with these benefits, however, the use of these treated materials and their re-treatment with insecticides creates tangible risks to human health and the environment throughout the life cycle of the insecticide products. This assessment finds that the public health benefits of these products justify the apparently modest risks. Nonetheless, the risks associated with the use of insecticide-treated materials (ITMs[1]), including bednets and curtains, should be minimized through such steps as proper pesticide product selection, appropriate labeling, and user educational campaigns. Programs should also actively monitor for adverse health and environmental effects, to assure that risks are adequately understood and to allow appropriate and timely interventions to reduce risks.

The use of ITMs can significantly reduce malaria transmission, with estimates of six lives saved per 1,000 children protected by insecticide-treated nets. ITMs are cost-effective and environmentally friendly as compared with alternative vector control measures that use pesticides (with the exception, perhaps, of some low-toxicity biopesticides used in larviciding); a relatively small amount of pesticide is needed to treat nets and other materials, as compared with indoor residual house spraying, space spraying, and larviciding. The products currently used to treat ITMs are also more environmentally sound than other vector control pesticides, such as DDT.

Health and environmental risks from the use of ITMs include potential exposure of humans and the environment during production, distribution, storage, use, and disposal of re-treatment pesticides, and a certain amount of exposure of persons using ITMs to pesticide vapors released from the materials. World Health Organization (WHO)-recommended ITM pesticide products are classified by EPA as only “moderately” toxic to humans, and with adequate safety precautions, the risk of adverse effects from their use is slight, although severe poisonings have been reported with exposure to highly concentrated solutions. However, these products are highly toxic to aquatic organisms, and precautions are necessary to assure that they not contaminate lakes, streams and other bodies of water supporting aquatic life.

Available evidence, including extensive worldwide residential and food-crop use of the pesticides in question, indicates that the associated human health and environmental risks can be acceptably minimized through training, consumer education, and other safety provisions designed into the implementation of USAID ITM programs. A certain amount of risk is tolerable, given the significant public health benefits afforded by these vector control tools. Still, ITMs are a relatively new technology, and some uncertainty remains about the potential for problems as their use expands. One significant question mark is whether users will restrict themselves to using WHO-recommended ITM products, once they have become accustomed to treating their nets, or if they might substitute other,

[1] Note: The most commonly used ITMs are insecticide-treated nets (ITNs), though other ITMs include treated curtains to place over windows, doors, eave gaps and other mosquito entry points.

potentially more hazardous, insecticides out of such motivations as availability and cost savings. USAID programs need to design into their ITM activities a mechanism for monitoring for adverse effects, in order to help identify this and other problems if and when they arise.

The WHO-led global Roll Back Malaria program seeks to dramatically increase the use of insecticide-treated nets. UNICEF and WHO set a goal in 1999 of providing 32 million nets and 320 million net treatments a year for the next 10 years to protect 80% of African households against malaria.[1] If ITM use were to reach these levels, the public health benefits through malaria reduction would likely be tremendous. But the potential also exists that this success could be accompanied by severe pesticide poisonings among the unfortunate few, or by a loss of aquatic life in waterways near poorly run ITM treatment facilities. USAID, and hopefully other donor organizations as well, should implement the risk reduction measures outlined in this assessment in order to minimize human and environmental exposure to ITM pesticides. In addition, monitoring for adverse effects on humans or the environment should be an integral part of USAID programs that use ITMs for vector control, to assure that risks are indeed as low as anticipated, and to be capable of detecting and reducing any problems as early as possible.

Review and revision of this assessment:
Should the conditions and assumptions on which this assessment is based change substantially, the Africa Bureau will need to reevaluate the assessment. For example, if USAID ITM program managers wish to employ different active ingredients in ITMs, because of changes in WHO's recommendations or otherwise, then the risks from the new chemicals in question will need to be reevaluated.

Other references for ITM risk mitigation:
The public health community has taken the issue of risk from ITM pesticides seriously, and effective guidance documents are already available as resources for ITM program managers. WHO's RBM web site hosts a collection of WHO and other documents on all the RBM program issues, including those related to effective and safe use of insecticides in ITM programs. (See http://mosquito.who.int, multiple prevention, insecticide-treated materials). An excellent resource for all aspects of ITM program management, including avoiding environmental or health problems with this technology, is a manual prepared for the Malaria Consortium, titled, "Insecticide Treated Net Projects: A Handbook for Managers."[2]

2 Background

2.1 Use of ITMs for malaria vector control

ITMs are an important tool in vector control, and vector control is one of the key elements of an integrated malaria control program. ("Integrated malaria control" is an approach that combines various methods for preventing and managing the disease burden of malaria.) The key elements of malaria control, as defined by WHO, are:

- Early diagnosis and treatment.
- **Prevention, including vector control**.
- Prevention, early detection, and containment of epidemics.
- Strengthening national capacity for malaria research and monitoring.

The spread of malaria and of drug resistance to the malaria parasite means that it is increasingly important to prevent human contact with the malaria vector through vector control. Vector control strategies include the following (see chapter 5 for more details):

- Personal protection (e.g., insect repellant or mosquito coils);
- Treated bednets, window curtains, eave strips, and other materials;
- Avoidance and diversion of vectors to other animals;
- Insect-proofing houses;
- Insecticide spraying to kill adult mosquitoes;
- Breeding prevention through environmental manipulation;
- Larviciding with chemical or bacterial larvicide and biological control.

Insecticide-treated nets are an improvement over untreated mosquito nets, a technology that has been used for centuries. Untreated nets that are torn or poorly-hung nets still allow access to mosquitoes, and body parts touching an untreated net can still be bitten. Treated nets, on the other hand, kill and repel mosquitoes. Even a torn net can still kill or repel insects before they find access. An entire household's exposure to malaria vectors appears to be reduced by treated materials, even if some individuals do not sleep under a net, potentially because the number of mosquitoes and proportion of them infected with malaria parasites is reduced. By the same token, in some areas an entire community's health can be improved if a sufficient number of members use treated nets.

Treatment of nets with insecticides was first introduced during World War II, using the insecticide DDT. The goal at that time was not malaria reduction but to reduce nuisance biting. Widespread treatment of nets did not begin until the 1980s, after the development of photostable synthetic pyrethroids in the early 1970s. This class of chemicals had the characteristics necessary to be effective as net treatments; they are fast-acting, are effective in small quantities, are relatively stable, adhere to fabric, and are relatively safe for humans.

Large-scale use of insecticide-treated nets started in the 1980s in the Western Pacific Region, and is now one of the major strategies for reducing malaria morbidity and mortality in Africa. At a summit meeting on malaria in Abuja, Nigeria, in April 2000, African heads of state declared their support for the use of ITMs, among other strategies for reducing the toll of malaria. One of the goals of the "Abuja Declaration on Roll Back Malaria in Africa" which came out of the meeting was that, by the year 2005, "…at least 60 percent of children and pregnant women should be sleeping regularly under insecticide-treated mosquito nets (ITNs)."[3]

MALARIA TRANSMISSION

- Malaria is caused by parasites belonging to the genus *Plasmodium,* which are transmitted by the bite of an *Anopheles* mosquito.
- Of the four *Plasmodium* species *falciparum, vivax, malariae* and *ovale)* which affect humans, *P. falciparum* causes most severe malaria illness and death throughout the world.
- *Anopheles* mosquitoes usually bite at night. They become infected with the parasite by feeding on a person with malaria. The parasites develop in the mosquito over a period of days and are transmitted to another person during a future mosquito blood meal.

... AND PATTERNS OF DISEASE

- In high transmission areas—such as in much of sub-Saharan Africa and much of Papua New Guinea—people who have repeated infections develop partial immunity to the disease. Young children and recent arrivals, who have not developed sufficient immunity, and pregnant women, who lose some immunity during pregnancy, are most at risk of malaria. Chronic malaria causes severe anaemia among young children and pregnant women in high transmission areas.
- In low- to moderate-transmission areas—in much of Southern Asia, the Middle East and Latin America—there are seasonal variations in transmission. The whole population is at risk because of low immunity and epidemics can develop rapidly. However, the overall number of new cases in a year is fewer than in high-transmission areas.

From Chavasse et al. 1999

Types of USAID ITM programs

The many USAID programs currently using ITMs vary in scale and methodology. Any examination of potential environmental and health risks from treatment products must take these differences into account. Following are the three general approaches employed in USAID and other public sector ITM programs for net treatment:

1. *Do-It-Yourself (DIY) kits*. Pesticide products are distributed to net owners, generally in very small quantities, so they can treat their own nets at home. WHO recommends that home-use ITM pesticide products be distributed in single-unit dose size only.

2. *Materials treated in a central location by program staff*. Net owners bring their nets and/or other materials to a central location where program staff treat the materials.

3. *Pre-treated, long-lasting nets*. The manufacturer treats the net prior to packaging and sale. Current "long-lasting" nets still need re-treatment within 6 months to 1 ½ years (see chapter 3.4.1 "Insecticide loss over time and by washing") to retain efficacious insecticide concentrations over the life of the net, so this approach does not exist yet as a stand-alone option for net treatment–it must be followed up by some form of re-treatment program.

2.2 USAID environmental review procedures

2.2.1 Overview

USAID regulations[4] require that the Agency assess the environmental effects of its actions before any program it funds is implemented, and that appropriate environmental safeguards be adopted to assure that significant environmental harm is avoided. Typically, the environmental assessment performed for USAID activities is called an Initial Environmental Examination (IEE). An IEE has to provide whatever level of detail is needed to identify potential environmental damage and mitigation measures that will adequately reduce the potential damage. Typically an IEE is a relatively brief document, though some have been quite lengthy and comprehensive. In some cases, USAID and/or its partners must perform a more in-depth analysis of the proposed program because the scope or nature of the proposed activity indicates the potential for significant adverse environmental effects. The analysis performed in such a case is generally termed an Environmental Assessment (EA).

The regulations (22CFR 216.6(d)) also allow a particular type of environmental assessment called a "Program Assessment," also known as a Programmatic Environmental Assessment (PEA), which is used "to assess the environmental effects of a number of individual actions and their cumulative environmental impact in a given country or geographic area, or the environmental impacts that are generic or common to a class of agency actions, or other activities which are not country-specific." One example

of a PEA is the Agency's "Programmatic Environmental Assessment for Locust and Grasshopper Control in Africa/Asia" (1989).

A PEA is not necessarily the last word on the category of action in question, but often must be complemented by a country-specific assessment that addresses implementation details that could not be adequately addressed in the PEA. The Locust PEA, for example, is complemented by Supplemental Environmental Assessments as well as country-level Action Plans for each country in which locust control action is conducted. In the same way, this PEA will not alone suffice to address the full environmental assessment requirements for an ITM activity. A USAID program must also generally prepare a Pesticide Evaluation Report and Safer Use Action Plan (PERSUAP – see chapter 7 for more details) in which the details of risk mitigation measures for that activity are planned.

2.2.2 Pesticide procedures

USAID regulations give specific instructions on what information to consider in performing an environmental assessment of USAID activities involving the procurement or use of pesticides, called "Pesticide Procedures" (22 CFR 216.3(b) – see Annex 1). It is important to note that the term "use" is interpreted broadly by USAID to include *direct or actual use or acquisition*, including handling, transport, storage, mixing, loading, application, cleanup of spraying equipment and disposal of pesticides, as well as the *indirect support to use*, such as provision of fuel for transport of pesticides and providing technical assistance in pesticide management operations. The regulations grant exceptions to the Pesticide Procedures for emergencies and for limited research.

The Pesticide Procedures list 12 factors that must be considered in assessing a pesticide activity. This list is broad, but not exclusive, and assessors can consider additional factors as appropriate. Some key factors include the U.S. registration status of the pesticide, its potential effects on human health and non-target organisms, and the extent to which it is to be used within an integrated pest management program.

The environmental assessment and planning document that the Africa Bureau now requires from most programs in which pesticides will be involved is called a Pesticide Evaluation Report and Safer Use Action Plan (PERSUAP). Previously, essentially the same type of document was referred to as a Pesticide Evaluation Report (PER). A PERSUAP is a document whose scope is designed to meet the information and analysis requirements of the Agency's Pesticide Procedures, and which additionally lays out a plan of action for minimizing the risks involved with the anticipated pesticide use. See chapter 10 for more detailed guidance on preparing a PERSUAP for ITM activities.

2.3 Purpose and approach of the PEA

The purpose of this PEA is to assess environmental impacts that are common to all USAID programs involving insecticide-treated materials, and to provide guidance on how to conduct activity-level assessments and action plans for environmentally sound

implementation of ITM activities. ITMs have undergone considerable evaluation from a variety of scientific and policy bodies, including the WHO. This assessment evaluates the best available information and identifies practical measures that should be taken in USAID programs in order to minimize the risks associated with these products.

This assessment is intended to make it easier to prepare activity-level assessments and action plans (PERSUAPs – see Chapter 10). It will serve as a repository of relevant data, such as risk information about ITM pesticide products, that will be updated as significant new data becomes available. The PEA will also serve as a policy reference, providing guidance on such matters as the type of information that should be included in an activity-level assessment and the type and amount of risk mitigation measures that can be considered adequate in USAID programs.

2.4 Benefits of ITM use in USAID activities

2.4.1 Public Health Benefits

As noted earlier, the spread of malaria and of drug resistance means that prevention, including new approaches to vector control, is becoming increasingly important.[5] The WHO Roll Back Malaria project has made ITMs one of the cornerstones of their effort to reduce malaria, setting the goal in October 1999 of providing 60 million African families with insecticide-treated mosquito nets over the next five years.

Malaria is a major public health problem, so techniques that are effective in preventing this disease have significant public health benefits. WHO gives the following synopsis of the current state of the global malaria crisis:

- Malaria kills at least 1 million people each year, about 3,000 a day.
- Almost 300 million people suffer from acute malaria each year.
- 40 percent of the world's population live in areas with malaria risk, but 9 out of 10 cases occur in Africa south of the Sahara.
- Health systems failure, drug resistance, population movement, deteriorating sanitation, climatic changes and, in some cases, unplanned development activities are all contributing to the spread of malaria. [6]

The efficacy of insecticide-treated bednets or curtains in preventing malaria has been well established. A review of 18 studies of the effectiveness of ITMs (11 of those in Africa) found that, for 1,000 children protected with insecticide-treated nets, about six lives could be saved each year.[7] (This risk difference appears to apply both in a comparison of treated nets versus untreated nets as well as in a comparison of treated nets versus no nets at all.) ITMs also were found to reduce mild episodes of malaria by approximately half, under most transmission conditions.

2.4.2 Environmental benefits

ITMs have environmental advantages over some of the alternative vector control methods. (See chapter 5 for a listing of alternative vector control options.) For example, indoor house spraying requires much more pesticide than with ITMs. A person sleeping under a net effectively acts as "bait' and mosquitoes are killed or repelled after contact with the treated material. Space spraying (e.g., around houses and vegetation with knapsacks or from vehicles) similarly involves a greater volume of pesticide and greater potential for contamination of the environment than the use and re-treatment of ITMs.

2.4.3 Resistance and Potential Impact on ITM Benefits

One of the threats to the efficacy of ITMs is the potential for mosquitoes that carry malaria to develop resistance to the pyrethroids that are used to treat nets. Resistance is a problem that threatens the efficacy of public health as well as agricultural pesticides (see box). WHO reports that pyrethroid resistance genes have been identified in malaria vectors in recent years in West Africa, Central America, Turkey, India, Pakistan and parts of the Arabian Peninsula. Resistance management is one of the technical challenges identified in the "Report of the Second International Conference on Insecticide-Treated Nets" held in Dar es Salaam, Tanzania, October 1999.[8] The conference concluded, however, that while "resistance is an important consideration…[it] should not deter wider promotion of ITMs." They further advise that "Management of insecticide resistance will be very difficult to achieve unless some specific compounds are restricted to public health use, since the agricultural sector has a far greater impact on the development of resistance in malaria vectors."

The WHO 20th Report of the Experts Committee on Malaria describes the resistance problem as follows:

> Although considerable hope is now centered on the use of insecticide-treated materials, its success relies almost entirely on pyrethroids, which are the only insecticides currently available for this purpose. Therefore, a high priority must be given to the search for non-pyrethroid insecticides for treating materials. The search for effective and practical strategies for management of insecticide resistance in mosquitoes should be encouraged. Every effort should be made to prolong the useful life of available insecticides and to develop alternative preventive measures.[9]

For the purposes of this environmental assessment, resistance is not yet a significant issue, as it does not yet substantially diminish the efficacy of ITMs as a vector control tool in Africa. *In years to come, however, resistance could have an impact on ITMs that could significantly change this assessment*, in one of two ways:

- resistance could render ITMs an ineffective tool whose benefits might then not outweigh the risks of using pesticides; or
- one resistance management approach that the WHO Pesticide Evaluation Scheme (WHOPES) is pursuing is the approval of other non-pyrethroid pesticides for use

in treating nets.[10] USAID would need to decide whether the use of such proposed new products were sufficiently safe, and whether mitigation actions called for in this assessment were sufficient for the new chemical(s) as well.

> Pesticide use is a powerful selection pressure for changing the genetic makeup of a pest population. Naturally resistant individuals in a pest population are able to survive pesticide treatments. The survivors pass on the resistance trait to their offspring. The result is a much higher percentage of the pest population resistant to a pesticide. In the last decade, the number of weed species known to be resistant to herbicides rose from 48 to 270, and the number of plant pathogens resistant to fungicides grew from 100 to 150. Resistance to insecticides is so common—more than 500 species—that nobody is really keeping score.
>
> Benbrook, Charles M. 1996. Pest Management at the Crossroads. Consumers Union, Yonkers, NY.

3 Alternative pesticide products

3.1 Overview

The distinction must be made between a pesticide active ingredient and a formulated pesticide product. A formulated pesticide product has two main components: the active ingredient(s), which is the chemical that has the desired insecticide action, and the "inert" (other) ingredient(s) (despite the name, all inert ingredients are toxic to some degree). An active ingredient is rarely applied in its pure form, but is usually combined with other ingredients that improve storage, handling, application, effectiveness, or safety. The percent active ingredient(s) and other, or inert ingredient(s), is given on the label.

WHO's "Guidelines on the Use of Insecticide-treated Mosquito Nets for the Prevention and Control of Malaria in Africa" indicate that "the choice of insecticide may depend on the vector susceptibility, established or anticipated efficacy, availability, cost and affordability." The choice will therefore be a program-specific one, made in recognition of factors that must be evaluated on a case-by-case basis. But the choice of pesticide products to use on ITMs is relatively limited.

USAID's "Pest Management Guidelines" (1991) effectively limit the selection of pesticide active ingredients available for use in USAID programs to those that are registered for the same or similar uses by the USEPA. The Guidelines explain that "…[pesticides not registered in the U.S.] would only be considered for use if it can be proven that no USEPA-registered pesticides can work, [and] that sufficient toxicological data exists and is comparable to that required by USEPA for registration…" The Guidelines require further that USAID programs choose the least toxic products that are still effective against the target pest.

In the case of ITN pesticides, all but one of the seven WHO-recommended pesticide products are clearly acceptable for use in USAID programs, as they are registered for similar uses in the U.S. (See table 1 below.) The chemicals currently recommended by WHO for use in ITMs are five synthetic pyrethroids (alpha-cypermethrin, cyfluthrin, deltamethrin, lambda-cyhalothrin, and permethrin) and one "near pyrethroid" (etofenprox). Of these, all have active product registrations in the U.S. except alpha-cypermethrin.

WHO's public health pesticide review program, the WHO Pesticide Evaluation Scheme (WHOPES -- http://www.who.int/ctd/whopes/) provides essential guidance for ITM programs about what products to use. WHO pesticide reviews and recommendations should in general be considered authoritative; they are based upon methodologies developed in open consultation with the international community, including U.S. governmental authorities. WHO recommendations are particularly relevant in the case of ITMs because EPA has few registrations specifically for pesticide treatment of nets.

3.2 WHO recommendations for ITM products

WHOPES recommendations for ITM insecticide products are given by specific formulation. It is important to note that percentage of active ingredient is not the only factor determining efficacy and safety, since both elements are directly affected by formulation. WHOPES' evaluation is based on a consideration of the safety, efficacy, ease of application, and acceptance by residents of proposed pesticide product uses, as well as their cost-effectiveness. See table 1 for a list of the insecticide active ingredients and formulations recommended by WHOPES for ITM use.

3.3 USEPA registration status

USEPA registers pesticides on the basis of scientific information sufficient to demonstrate that their use will not cause unreasonable adverse effects, either to human health or the environment. The Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) requires EPA registration for all pesticides sold in the U.S. It is a violation of FIFRA to use a pesticide in a manner inconsistent with its label.

The USEPA registration status of WHOPES-recommended ITM pesticides is also listed in table 1.

Table 1: WHO recommended insecticides for treatment of mosquito nets for malaria vector control and USEPA registration status of these insecticides

WHO RECOMMENDATIONS				
INSECTICIDE (CAS Reg'n #[a])	**FORMUL-ATION[b]**	**DOSAGE[c]**	**EXAMPLE TRADE NAMES/ MANUFACTURER**	**U.S. PRODUCTS REGISTERED FOR "SIMILAR" USES**
Alpha-cypermethrin 67375-30-8 (not cypermethrin)	SC 10%	20-40	Fendona (BASF) sachets	No alpha-cypermethrin products registered in U.S. Cypermethrin products are registered, but the chemicals have significant differences.
Cyfluthrin 68359-37-5	EW 5%	50	Tempo 20 WP (Bayer Corp. Agric.) Baythroid (Bayer)	3125-380 3125-351
Deltamethrin 52918-63-5	SC 1% and WT 25%	15-25 35-55 for Permanet™	K-Othrine Decis Permanet™ (Vestergaard Frandsen) is pre-impregnated with deltamethrin.	432-763 34147-8
Etofenprox 80844-07-1	EW 10%	200	Vectonet (Mitsui Chemical)	33657-6, first registered in 2001.
Lambda-cyhalothrin 91465-08-6	CS 2.5%[d]	10-15	Icon (Zeneca)	10182-96
Permethrin 52645-53-1	EC 10%	200-500	Ectiban Pramex Pounce 3.2 EC	279-3013 279-3051 279-3014

[a] Chemical Abstract Service Registration Number, a unique chemical identifier.
[b] EC = emulsifiable concentrate; EW = emulsion, oil in water; CS = capsule suspension; SC= suspension concentrate; WT = water-dispersible tablet.
[r] Milligrams of active ingredient per square metre of netting.
[d] WHO specifications under development.
Note: WHO Specifications for public health pesticides, for quality control and international trade, are available on the WHO homepage on the Internet at www.who.int/ctd/whopes.

While alpha-cypermethrin is not registered for use in the U.S., it is important to note that this is not because of risk concerns about products made from this chemical. The lack of registration for an alpha-cypermethrin pesticide product most likely represents the lack of market incentive to register the product in the U.S.[11] Initial registration of a pesticide in the U.S. is an expensive proposition, and registrants must pay periodic registration maintenance fees to keep a U.S. registration active (annual fee of $650 for the first registration held by any registrant and $1,300 for each subsequent registration.)

It is sometimes useful to recognize the chemical classification of these six WHO-recommended ITM chemicals. All are members of the chemical category called "pyrethroids," but the group contains members of three subcategories. Table 2 gives the classifications of these chemicals and some relevant information about the characteristics of their pyrethroid subcategory.

Table 2: Classification of different ITM insecticides

Permethrin	"Third Generation" pyrethroid. Less of an irritant than alpha-cyano pyrethroids.
Deltamethrin Lambda-cyhalothrin Cyfluthrin Alpha-cypermethrin	"Fourth (current) Generation" pyrethroids, also known as "alpha-cyano pyrethroids." Insecticidal activity persists longer than permethrin. Less volume needed to treat nets than permethrin. More reported side effects than permethrin.
Etofenprox	Structurally different from the others (it is termed a "pyrethroid ether" insecticide, and the others are "pyrethroid ester" insecticides[12]), but its activity is similar to permethrin and it is used at a similar dose. The main advantage is that it is hundreds of times less toxic to humans and other mammals than the other ITM pyrethroids.

From The Pesticide Book[13] and ITN Projects: A Handbook for Managers [14]

3.4 Efficacy of alternative pesticide products

As discussed above in the section on the benefits of ITMs, the efficacy of insecticide-treated bednets or curtains in preventing malaria has been well established. But are all ITM treatment products equally efficacious?

WHO considers all of the products listed above to be effective for ITN treatment, when applied at the dosages listed. However, two factors can limit the overall effectiveness of ITN pesticide products: 1) loss of the insecticide by volatilization over time and through washing, and 2) the development of resistance of mosquitoes to the insecticide in question.

3.4.1 Insecticide loss over time and by washing

Of these two factors, ITM efficacy is considered to be more dependent on the amount of washing than on the time after treatment. Generally, a single permethrin treatment will remain effective for six months and the alpha-cyano pyrethroids will last one year or more when the nets are not washed. However, as Table 3 below shows, insecticide concentrations may drop quite drastically as a result of washing. Although some insecticide is lost during each washing, the amount of loss depends on a variety of factors including variations in use of soap, water temperature, and washing action, as well as the wash-resistance of the particular pesticide product and the type of net material. (Some of

the variation seen may also be due to differences in sampling and testing practices used to determine remaining pesticide concentrations.)

Table 3: Loss of insecticide on washing as a percentage reduction in concentration

Prepared by Jane Briggs for the Malaria Consortium[15]

Authors and place	Insecticide	Type of net	No of washes	% reduction in concentration
Miller et al. 1991 The Gambia	Deltamethrin Lambda-cyhalothrin	Nylon	3 3	100% 85%
WHOPES 1999b The Gambia	Deltamethrin (SC &WT)	?	1	50-60%
Kroeger et al. 1997 Nicaragua, Peru, Ecuador & Colombia	Permethrin	Cotton	Several	71%
Lindsay et al. 1991 The Gambia	Deltamethrin Lambdacyhalothrin Permethrin	Polyester	1st wash 2nd wash 1st wash 2nd wash 1st wash 2nd wash	65% 25% (additional) 45% 20% (additional) 53% 10% (additional)
Duffield & Hordle 1997	Deltamethrin	Cotton Synthetic	1st wash Subsequent washes	20-30% 2-3% (additional)
AgrEvo (personal communication)	Deltamethrin	-	1st wash Subsequent washes	50% 10% (additional)

The alpha-cyano pyrethroids are generally considered to be more wash-resistant than permethrin.[16] For standard (not "long-lasting") nets that are washed, it is recommended that permethrin-treated nets be re-treated after the first wash, whereas for nets treated with alpha-cyano pyrethroids, the recommended re-treatment rate is after 2-3 washes.

Wash frequency

The best information on actual wash frequency seems to be that found in the June 2001 document, "NetMark Baseline Survey on Insecticide Treated Materials (ITMs): Cross-National Summary of Findings." Based on interviews of 1,000 persons from each of five African countries – Nigeria, Senegal, Zambia, Uganda and Mozambique – NetMark researchers determined that nets are generally washed quite frequently. "…at least half to three-quarters of nets that were ever washed were washed at least once a month. And in all countries between one-quarter and half of all ever-washed nets were washed at least every two weeks."[17]

So it appears that the majority of users wash their net at least once a month, meaning that the insecticide efficacy period is relatively brief. For most conventionally treated nets, efficacy will be lost after only 2-3 washes, or 2-3 months. It is as yet uncertain how many washes a "long-lasting" net can withstand.

Long-lasting nets
Several companies have begun selling or are currently developing "long-lasting, wash-resistant" nets treated with alpha-cyano pyrethroids. Examples include the BILNET, marketed by Biotech International Ltd. in India, and the Permanet, produced by the Vestergaard-Frandsen Company.

The length of efficacy of long-lasting nets is an open and active research topic. The Vestergaard-Frandsen Company's own studies (reportedly performed according to WHO protocols) indicate that the Permanet remains effective for between 15 and 25 washes[18]. At one wash per month, that would mean a Permanet would remain effective for about 1 ½ years. The net can then be re-treated, as necessary.

WHO is conducting its own studies of the Permanet's efficacy, with completion of laboratory and small-scale field studies expected in spring 2002. Preliminary results from field studies conducted by Kilian et al. in Uganda[19] cast doubt on the manufacturer's efficacy estimates. These results indicate that after six months of field use in villages of western Uganda, the majority of the Permanets no longer showed "optimal bio-activity", though they did perform better than conventionally treated nets. One conclusion of the study was that "the technology of 'long-lasting' insecticide treatment may need further improvement."

An extended efficacy period from pre-treatment is advantageous for malaria prevention and for the environment. Considering the low re-treatment rates that ITN programs are generally experiencing, malaria vector control will clearly be improved by a net that relies less on re-treatment for its efficacy. From the environmental standpoint, the advantage is also clear: the delayed need for re-treatment means less pesticide used and less risk to humans and their environment.

While it appears the efficacy period of current long-lasting nets in the field is not long enough to avoid all need for re-treatment, any technology that delays re-treatment serves the interest of both malaria control and environmental protection. And both of those interests will be best served by a net that needs no re-treatment, a technological target that WHO still hopes the private sector will hit in coming years.

3.4.2 Resistance development

The problem of mosquito resistance development and its potential impact on the efficacy of ITM products is discussed in section 2.4. In their Twentieth Report, the WHO Expert Committee on Malaria explains the severity of the risk to ITM programs that resistance presents, and provides recommendations for addressing the problem:

> Although considerable hope is now centred on the use of insecticide-treated materials, its success relies almost entirely on pyrethroids, which are the only insecticides currently available for this purpose. Therefore, *a high priority must be given to the search for non-pyrethroid insecticides for treating materials.* [Emphasis added.] The search for effective and practical strategies for management of insecticide resistance in mosquitos should be encouraged. Every

effort should be made to prolong the useful life of available insecticides and to develop alternative preventive measures.

3.4.3 Cost concerns

Since public health and household funds are scarce, the cost of an ITM product might affect its attractiveness as a vector control option. However, at first glance, cost differences between products do not appear to be substantial or consistent, so there is no product that stands out as being hands-down more cost-advantageous. NetMark data indicates that net owners in most of the countries surveyed paid around $5 per net, and between $0.74 and $1.73 per net re-treatment. Permanets were not included in NetMark data, as they only entered the market in late 2000. But Population Services International (PSI) in Zambia reported in May 2001 that they were selling Permanets at the cost to the program for somewhat more than a package containing an untreated net plus a deltamethrin treatment dose (a K-O Tab™)—about $6 per Permanet versus a little more than $5 for standard net plus treatment dose.

Nonetheless, a rough comparison of overall costs indicates that Permanets may be a better deal in the long run, though just a bit more costly to start. Assuming a 1 ½-year efficacy period for the Permanet and 3 months between treatment of a standard net, and an average cost of $1.24 for a re-treatment dose, then a standard net's original cost ($5) plus re-treatment products (five additional doses at $1.24 per dose) would bring the cost of a "standard" net treated over that same 1 ½ year period to $11.24, or almost twice the cost PSI Zambia charges for the Permanet. Even if the Permanet's efficacy were to last only 6 months without retreatment, and would need treatment every 3 months thereafter, it would still present a cost advantage of over $1. These are rough figures which will vary by situation, but they serve to show the potential cost advantage of long-lasting nets.

3.5 Conclusion: available products for USAID ITM programs, based on EPA/WHO evaluations

No evidence currently gives sufficient reason to prohibit the use of any of the pesticide products that WHOPES recommends for use with ITMs. However, the goal of reducing risks does favor some products over others (see also chapter 6 on Mitigation Opportunities).

With respect to registration status, five of the six active ingredients have similar registrations in the U.S.. This confirms that the USEPA considers the risk from use of similar products to be acceptable.

For the one chemical without similar U.S. registrations (alpha-cypermethrin), the lack of registration does not appear to be the result of risk concerns, but more likely a lack of a market incentive. Nonetheless, the USAID Pest Management Guidelines (1991) establish a fairly substantial hurdle for using pesticides without U.S. registrations, including demonstration that other pesticides cannot be used instead. The conclusion of this assessment is therefore twofold:

- In light of WHOPES approval for the use of alpha-cypermethrin, and the similarity in characteristics of this chemical to the other synthetic pyrethroids approved for ITM use, together with the lack of evidence of concern by the USEPA about this chemical, there is no apparent reason for concern about the safety of alpha-cypermethrin use in ITM programs.

- In accordance with USAID policy regarding products not registered in the U.S., the use of alpha-cypermethrin can only be authorized if a compelling need can be demonstrated for its use, such as in the case that no other products are available or efficacious. If a program can indeed demonstrate a compelling need for use of alpha-cypermethrin products, then the WHO-recommended formulations of this chemical should be allowed for use in USAID ITM programs.

The choice of pesticide product for use in an ITM program – that is, the formulated product, consisting of the active ingredient and the other "inert" ingredients that make up the product[2] – will be influenced by a variety of factors, including price, availability, and efficacy in that region, as well as environmental concerns. Risks discussed in the following chapter can be addressed in large measure by the choice of pesticide product. In fact, this PEA's primary recommendation toward mitigating environmental risks (see chapter 6 on mitigation measures available) is that programs choose long-lasting nets whenever possible, and a secondary recommendation is to avoid use of permethrin EC formulations. Because of the tremendous impact malaria has on human health and productivity, environmental factors do not seem to outweigh the benefits of treating nets with any of these products, and so all of these options should remain available to USAID programs. Nonetheless, programs are likely to have significant control over which products they use over the long-term, and environmental concerns should weigh heavily in product choice.

If in the future WHO decides to recommend additional chemicals for use with ITMs, in order to combat resistance development or for other reasons, USAID will likely need to evaluate those chemicals prior to sanctioning their use in USAID ITM programs. While the WHOPES review process is conducted by respected public health experts, USAID's Pest Management Guidelines nonetheless clearly make U.S. registration the standard for evaluating what chemicals can be used in USAID programs.

[2] Active ingredients are the specific chemicals contained in a pesticide product that are designed to kill a particular pest, and "inert" ingredients are any ingredients in the product that are not intended to affect a target pest. Inert ingredients include solvents, emulsifiers, spreaders, and other substances mixed into pesticide products to increase the effectiveness of the active ingredients, make the product easier to apply, or to allow several active ingredients to mix in one solution. Inert ingredients can be as much as 99% of pesticide products. (Pesticide Action Network Pesticide Database, http://www.pesticideinfo.org/documentation3/ref_general1.html)

4 Overall risks from use and treatment of ITMs

All pesticides, by their nature, are toxic to some degree and present the risk of adverse effects under certain conditions. The risk of adverse effects from a pesticide is a factor of the toxicity of the chemical and the degree to which an organism is exposed. An organism can tolerate considerable exposure to a product of very low toxicity, but can tolerate very little exposure to very toxic products without experiencing adverse effects. The risks from the use of ITMs are essentially the following:

- *Risks to humans* from exposure to ITM pesticides during pesticide storage and transport, during net treatment, and during use (exposure to vapors or dermal or oral contact).
- *Risks to the environment*, i.e., non-target organisms other than humans, from accidental exposure to ITM pesticides during storage and transport, from improper disposal, and from the washing of nets in natural bodies of water.

As USAID and other organizations in the Roll Back Malaria partnership scale up their ITM programs with the intent of delivering millions of nets and pesticide treatments, the unit risks from ITM use may not increase, but the overall risk will. It is therefore important to clearly identify the risk factors so that program managers can take early and cost-effective steps to reduce those risks as much as practicable.

It is also important to note that risk assessments – studies to quantify the potential for adverse effects from anticipated exposures – are imperfect. They cannot accurately predict such factors as human behavior. For example, available evidence does not allow us to predict the likelihood that ITM users will follow WHO recommendations in choosing a chemical with which to treat their bed nets. This discussion of risks must therefore be one conducted "on the basis of available evidence," and be subject to revision should additional information point to unexpected adverse effects.

4.1 Risks to humans

A number of assessments have been conducted of the risks of synthetic pyrethroids. From these assessments, the USEPA, WHO and other regulatory bodies have determined that these chemicals are relatively low-toxicity products compared with other insecticides and that the risks of their use with ITMs are acceptably low.

The WHO document "Safety of pyrethroid-treated mosquito nets" is the most authoritative and comprehensive analysis available on the subject of ITM pesticide safety to humans, and except for the addition of particularly noteworthy recent evidence, this PEA will rely for its human risk information largely on WHO's interpretation of the available evidence. The abstract from this document provides the following succinct statement of WHO's position on the human risks of the ITM pesticide products:

> The use of insecticide-treated nets (ITNs) for personal protection against malaria vector *Anopheles* mosquitoes has become popular during the past decade. With the precautions outlined in this paper, field use of pyrethroids—at concentrations recommended for treatment of mosquito nets—poses little or no hazard to people treating the nets or to users of the treated nets. With frequent exposure to low concentrations of pyrethroids, the risk of toxicity of any kind is remote. Pyrethroids entering the systemic circulation are rapidly metabolized to much less toxic metabolites. Toxicologically, pyrethroids have a useful characteristic—the production of skin paraesthesia—which gives an early indication of exposure. This reversible symptom of exposure is due to transient stimulation of peripheral sensory nerves and not a toxic effect. In the retail market, for home use, the provision of proper packaging and labelling, with clear instructions on safe and effective use of the product, are most important. Because many domestic users of pyrethroid "home treatment kits" for ITNs may not be fully literate, it is essential that "instructions for use" should be portrayed via pictograms with supporting text in appropriate local language(s). [20]

A risk assessment by Barlow, Sullivan and Lines (2001)[21] of deltamethrin use on ITNs generally supports the WHO assessment's estimates of low risks presented by this particular product, with the partial exception of a relatively high chronic risk estimate for newborns sleeping under a treated net.

4.1.1 Acute and chronic toxicity of ITM chemicals to humans

[The material in this section is drawn heavily from Zaim et al.[22]]

As mentioned, risk is a factor of both toxicity and exposure. The principle of prevention is best applied to pesticide use by the choice of low-toxicity products.

Since products for treating ITMs will be used by untrained persons in a multitude of relatively uncontrolled settings, and since chronic low-level exposure of adults and children can be expected during use, it is essential that ITN insecticides have low acute and chronic toxicity.

Acute Toxicity

Acute toxicity refers to the adverse effects that may result from single or multiple exposures to a chemical over a relatively short period of time. Table 4 shows the "LD_{50}" values in rats (the most common test animal for mammalian effects) from both oral and dermal administration of pyrethroids commonly used for treating mosquito nets. The LD_{50} is a statistical estimate of the amount of a substance required to kill 50% of a population of test animals. The higher the LD_{50}, the lower the toxicity.

Table 4: Acute oral and dermal toxicity of pyrethroid formulations commonly used for treatment of mosquito nets

(as reported by manufacturers in product Material Safety Data Sheets)

Product	[Acute] Oral toxicity: LD_{50} Value mg/kg bw rats	[Acute] Dermal toxicity: LD_{50} Value mg/kg bw rats
Alpha-cypermethrin 10% SC	4,932	2,000
Cyfluthrin 5% EW	2,100	>5,000
Deltamethrin 1% SC	>10,000	>10,000
Deltamethrin 25% WT	1,965	2,000 rabbit
*Etofenprox 10% EW	>5,000	>5,000
Lambda-cyhalothrin 2.5% CS	>5,000	>4,000
**Permethrin 10% EC	5,000 – 6,000	4,000 – 10,000

*For the acute oral toxicity of etofenprox (a non-ester pyrethroid) 10% EW the exact figure is not available. However, extrapolation from the value for the active ingredient gives a figure of >400,000 mg/kg bw.

*Material Safety Data Sheets of 3 major manufacturers have been consulted for data on permethrin 10% EC.

For the sake of comparison with two common pesticides, DDT and ethyl parathion, the acute oral and dermal toxicity values for the pure active ingredient, or "technical product" are given in table 5. (Note: Technical pesticide products are used to formulate end-use product, and are not typically available to end users. Comparing technical product toxicity is one way of comparing the innate toxicity of a chemical, though the toxicity of the formulated product is what is most relevant to the end user.)

Table 5: Acute oral and dermal toxicity of pyrethroid "technical" products

(primarily as reported in Pesticide Information Profiles of the Extension Toxicology Network, or Extoxnet[23])

Product	Acute Oral toxicity: LD_{50} Value mg/kg bw rats	Acute Dermal toxicity: LD_{50} Value mg/kg bw rats
DDT (technical)	113-800	2,500-3,000
Ethyl parathion (technical)	2-30	6.8-50
Alpha-cypermethrin (technical)	80-500	>2,000
Cyfluthrin (technical)	869-1271	>5,000
Deltamethrin (technical)	128-5,000	>2,940
Etofenprox (technical)	NA	NA
Lambda-cyhalothrin (technical)	56-64	632-696
*Permethrin (technical)	430-4,000	>4,000

To help interpret this comparison, note that ethyl parathion is one of the most acutely toxic pesticides registered in the U.S. Close to the other side of the human acute toxicity spectrum is DDT, which is considered "moderately to slightly toxic" to mammalian species via the oral route, and "slightly to practically non-toxic" (Extoxnet) by the dermal route.

The adverse effects reported by net-dippers include tingling and burning sensations (paraesthesia), eye pain and irritation, swelling of the face, headache and dizziness**.** The paraesthesia can be unpleasant, especially if pyrethroid concentrate comes into contact with the skin of the face. Zaim et al. notes that such paraesthesia has no long-term consequence, further suggesting that paraesthesia can be a useful phenomenon – it is transitory, has no lasting effects, and provides an early warning of exposure.

Transitory side-effects associated with the use of treated nets have also been reported by householders, but most symptoms lasted for less than 24 hours. Effects include skin itching, watery eyes, nasal irritation and sneezing during the first few days after net treatment.

While the transitory nature of acute effects from pyrethroids is undoubtedly typical of the vast majority of poisonings, some reports of poisoning incidents involving pyrethroids point out the potential for serious, irreversible effects, particularly from exposure to highly concentrated products. A 1999 journal article by Müller-Mohnssen[24] reports on 144 adults who fell ill after indoor pyrethroid exposure and experienced lengthy recovery periods, with permanent damage in some cases. In one case study, a woman spilled a concentrated permethrin solution on her leg and hand, and afterward bathed the area with an oil solution. Oil greatly enhances the skin's permeability to lipophilic pesticides like pyrethroids, and this is apparently the primary reason she sustained painful, permanent and debilitating damage to the exposed areas.

Chronic Toxicity

The chronic toxicity of a chemical refers to the potential for adverse effects from long-term exposure. Chronic exposure may be experienced by professional net treatment personnel and by ITM users. Chronic effects from exposures to chemicals can usually be seen at much lower concentrations than needed to elicit effects from acute exposure. Exposure to a certain concentration might have no impact if it is sufficiently brief (acute), but might have an impact if it persists (chronic).

Table 6 below provides figures that allow a comparison of different pyrethroids' chronic toxicity to humans. The "no observed adverse effect level" (NOAEL) and "acceptable daily intake" (ADI) values are determined from standard tests and criteria. NOAEL is the dosage of an insecticide that results in no discernible harm to rats in chronic toxicity studies that include the close examination of all body organs for abnormalities. The ADI is the daily exposure level to the insecticide residue (expressed as mg/kg body-weight) that, over the entire lifetime of a human being, appears to be without appreciable risk, on the basis of all facts known at a given time. This ADI has been calculated from the relevant NOAEL, with a safety factor of 100.

Table 6: The chronic toxicity of insecticides commonly used for treatment of mosquito nets

mg a.i./kg bw/day = milligrams per kilogram of body weight per day (for the rat).
(ADI=acceptable daily intake; NOAEL=no observed adverse effect level. See text.)

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

Formulation Impacts
As mentioned, toxicity is affected by product formulation. Some formulations are more toxic by nature than others. Among available liquid formulations, the water-based products, i.e., CS (capsule suspension or micro-encapsulated), EW (emulsion, oil in water) and SC (suspension concentrate) formulations are less toxic than the EC (emulsifiable concentrate) formulations.

Water-based formulations also have the advantages, over EC formulations, that they are not flammable and they do not have such an unpleasant smell. Permethrin is the only relevant pyrethroid insecticide still generally marketed in EC formulation. For ITNs, only the use of public health grade (as opposed to agricultural) permethrin (EC formulated without harmful solvents) is recommended. "Some agricultural EC formulations are very toxic to humans because of the solvents they contain, so these formulations should never be used for treating nets." [25]

4.1.2 Potential human exposure – oral, dermal and inhalation

People are at risk of exposure to ITM insecticides through the oral, dermal and inhalation routes. Exposures occur for various reasons, some due to typical "occupational" exposure by persons treating ITMs, some due to accidental (or intentional/suicidal) exposure to treatment products, and some due to unavoidable inhalation of vapors while using ITMs.

4.1.3 Occupational exposure

Exposure will occur through the handling of insecticides for treatment of mosquito nets. People directly involved in dipping large numbers of nets are at most risk of such exposures. Such exposures could be expected to result from splashing on the skin, into the eyes, or through ingestion (e.g., workers smoking while treating nets).

4.1.4 Accidental exposure

Any large-scale use of pesticides presents a substantial number of opportunities for accidental exposure. This is a particular concern for pesticide use in developing countries. While the majority of pesticide use occurs in the U.S. and other highly industrialized nations, the vast majority of pesticide poisonings are estimated to occur in developing countries.[26] Commonly-cited reasons for this overabundance of poisonings in developing countries include a lack of sufficient education about pesticide risks and safe handling, poorly or mislabeled containers, and lack of access to personal protective equipment needed for safe pesticide use.

The supply of insecticide "over the counter" (OTC) for treatment of nets by householders has particular safety concerns. As indicated above, ingestion of the contents of even a single application pack of permethrin 10% EC could be lethal to a child. (Note: EC formulations are not recommended by WHOPES for home-use ITM treatments.) The likelihood of accidental exposure in any one household may be relatively slight, but the realization of Roll Back Malaria's goals could see tens of millions of doses of ITM

pesticides entering African households annually. Accidents happen. Children find and eat solid products, users are splashed by concentrated solution while treating nets, pesticide powder finds its way into foodstuffs, etc.

4.1.5 Exposure during use of ITMs

Users can be expected to receive exposure by a variety of routes, including inhalation of insecticide that has volatilized from the net, skin contact with insecticide dislodged from the net through skin contact with the net, and oral exposure from hand-to-mouth transfer and from infants chewing and sucking on the net. Barlow, Sullivan and Lines estimated total exposure from all routes, and the results of these estimates are portrayed in table 8, in the section on "Risks from using ITMs." Those estimates are *based on the following "worst-case" exposure assumptions*:

- *Inhalation exposure*: used the highest estimate from a targeted study of pesticide concentrations in the "breathing zone" of people sleeping under nets; 24-hour exposure; daytime breathing rates, which are typically higher than rates during sleep.
- *Skin contact*: hands, arms, lower legs and feet uncovered, 30% of their total surface area would be in contact with the net. Transfer coefficient of 2.5% (based on study of residue transfer with carpets). 10% of the amount of insecticide dislodged onto the skin could be absorbed.
- *Oral exposure*, from hand-to-mouth and chewing/sucking on the net: 10% of dislodgeable residues present on the hand are transferred to the mouth and swallowed. An area of 50 cm^2 of the net is chewed or sucked overnight and 30% of the insecticide present in that area is sucked out (i.e., the same amount as can be washed out). This oral exposure occurs every night.

One of the study's authors, Dr. Jo Lines of the London School of Hygiene and Tropical Medicine, was asked to review the exposure assumptions used in this risk assessment, for which all of the toxicological input came from Drs. Barlow and Sullivan. See the following section on Risks from Using ITMs for discussion of Dr. Lines' findings.

4.1.6 Risks to humans from ITM use

The bottom line of a pesticide use assessment is a comparison of the anticipated exposure with the toxicity of the product, yielding some measure of the estimated risk presented by the use in question. Since actual exposures in the field will vary, it is important that there be an adequate margin of safety or safety factor in such a theoretical exercise, i.e., the amount of exposure that is capable of causing adverse effects should be much greater than the anticipated exposure (which may end up being greater than anticipated).

4.1.6.1 Occupational exposure risks

Zaim et al. provides the following summary of occupational exposure risks, i.e., the risks of treating ITMs with recommended insecticides:

> *In summary, with [appropriate] precautions…field use of pyrethroids at the concentrations recommended for ITNs poses little or no hazard to those treating the nets...With frequent exposure to low concentrations of pyrethroids, risks of toxicity are remote. Pyrethroids entering the systemic circulation are rapidly metabolized to much less toxic metabolites (WHO, 1991). If symptoms appear after exposure, recovery occurs promptly once the circulating concentration falls. Toxicologically, these compounds have a useful characteristic—the production of skin paraesthesia—which gives an early indication of exposure (WHO, 1991).*

So it would appear that occupational risks from these pesticide products are very low, so long as proper precautions are taken (the use of gloves and face protection, in particular).

The uncertainties inherent in risk assessments should nonetheless be remembered. For example, if concerns about potential endocrine disruption effects of these products turn out to be well founded, then under certain circumstances these products might be much more potent than current evidence indicates. A pregnant woman treating a net might expose her fetus to enough product to affect its development. (On the other hand, ITM use is reported to substantially reduce pre-term delivery.[27]) The principle of prevention must be followed—the lowest-toxicity products should be chosen, and exposures should be avoided as much as possible.

4.1.6.2 Accidental exposure risks

Children are likely to be the most susceptible members of the population, and Zaim et al. provide a rough notion in table 7 below of the risk of acute poisoning presented by home use products through a comparison of the amount of toxic material in such products versus the lethal oral dose for a 10kg child. The "safety factor" in this table is the number of single-net treatment doses that a child would need to consume to reach a lethal oral dose. (Clearly, this comparison is most relevant for single-dose packages.)

Table 7: Estimates of relative safety of pyrethroids for ITNs for supply over the counter

Product	Oral LD_{50} for a 10 kg child (A)[1]	Amount of formulation required for treatment of single net (15 m^2)[2] (B)	Proportion of LD_{50}, for a 10 kg child, contained in a single application pack C: (B/A)	Safety Factor (1/C)
Alpha-cypermethrin 10% SC	50 ml	6 ml	0.12	8
Cyfluthrin 5% EW	42 ml	15 ml	0.36	2.8
Deltamethrin 1% SC	100 ml	40 ml	0.40	2.5
Deltamethrin 25% WT	20 g	1.6 g	0.08	12.5
Etofenprox 10% EW	4,000 ml	20 ml	0.005	200
Lambda-cyhalothrin 2.5% CS	50 ml	12 ml	0.24	4.2
Permethrin 10% EC[3]	50 ml	75 ml	1.5	0.7

[1] Estimated from the oral LD_{50} values for rats, as reported by the manufacturers.
[2] Highest recommended dosage for treatment of the net has been used.
[3] Permethrin EC is marketed as a wide range of concentrations (usually in the range 10 to 55%); this paper considers the case for only the lowest strength formulation (in relation to OTC markets) and even this has by far the lowest safety factor shown above.

The safety factor is highest for etofenprox 10% EW (200) and deltamethrin 25% WT (12.5), but lowest with permethrin 10% EC (0.7). Based on this rough estimate, ingestion of the contents of a single application pack of permethrin 10% EC could be lethal to a child, while a lethal dose would be highly unlikely with any of the other products, particularly the etofenprox product. (Note: WHO does not recommend EC products for home-use ITM treatments.)

The risk comparison made in table 7 is valid for oral exposure. The potential for serious and irreversible poisoning from dermal exposure to pyrethroids, as described in the Müller-Mohnssen report, is apparently presented only by the highly concentrated liquid products. This risk would seem not to exist for solid formulations such as the water-dispersible tablet.

In general, the possibility of accidental exposure is likely to be greater in households where the risks of such pesticide products are not well understood, whether because of illiteracy or simply because pesticides are not commonly used. Ineffective risk communication needlessly raises the potential for accidental exposure.

4.1.6.3 Risks from using ITMs

Zaim et al. determined that "little or no hazard " [or risk] is posed by ITMs to the users of nets treated with recommended pyrethroid products. That assessment is largely confirmed by Barlow, Sullivan and Lines in table 8 below. These researchers used "worst-case"

scenarios (i.e., erring on the side of higher exposure estimates; see discussion above under "Exposure During Use of ITMs") to examine the amount of pesticide that could be absorbed via inhalation, skin contact and oral exposure while sleeping under an ITN, and compared that to the concentrations at which animals experienced effects in chronic toxicity studies. This comparison yields what the researchers term a "margin of safety," which is simply the ratio of the estimated actual exposure to the estimated level at which adverse effects could be expected (the NOEL).

Table 8: "Worst-case" total daily systemic exposures to deltamethrin while sleeping under a net

(From Barlow, Sullivan and Lines, 2001)

		Amounts absorbed systemically (mg/day)		
Route	Assumption	Adult	Child	Newborn
Inhalation	100% absorbed	0.00034	0.00011	0.00003
Skin	10% absorbed	0.016	0.004	0.002
Oral	100% absorbed	0	0.04	0.04
Total in mg/day		0.016	0.044	0.042
Total in mg/kg bw/day		0.0003	0.0044	0.014
Margins of safety		**3300**	**250**	**70**

The Margin of Safety (MOS) for an adult, child and newborn respectively is 3,300, 250 and 70. (Note that there are no units for this number, as it is a ratio.) The difference in these numbers signifies that the estimated risk of an exposed newborn experiencing an adverse effect due to this exposure is 3,300/70=47 times greater than the risk experienced by an exposed adult, a difference related to factors such as more hand-to-mouth and sucking/chewing activity and a lower body weight in children vs. adults. To interpret the acceptability of an MOS, one must compare it with a risk management standard such as that of the USEPA.

Given the data and interpretations thereof that were used to prepare the above table, the USEPA standard states that the "level of concern" for a Margin of Safety (also termed a "Margin of Exposure" or MOE) is 100. In other words, this means that an MOS of 100 or greater is considered by EPA to represent an acceptably low risk.

What does this mean? It means that, according to the Barlow, Sullivan and Lines "worst-case" risk assessment, MOSes for adult and children (estimated to weigh 10kg) are comfortably above the EPA standard of 100. For newborns, however, the MOS is about 100/70, or 1.4 times greater than USEPA's standard for a level of concern. Does this mean that newborns sleeping under ITNs would experience adverse effects? Not necessarily, but without further refinement of the risk assessment, the estimated risk of such effects occurring is slightly greater than the USEPA would generally tolerate.

Reevaluating exposure assumptions

Barlow, Sullivan and Lines suggest in their assessment that a refinement of their exposure estimates in the direction of better describing real-world exposures would lead to lower exposure estimates, and therefore to lower risk estimates. It does seem likely

that, all things being equal, a refinement of the "worst-case" exposure assumptions used in the Barlow, Sullivan and Lines assessment wou ld increase the newborn MOS estimate beyond the EPA standard of 100.

Most of the assessment's estimated exposure (0.04 mg/day, out of an estimated total of 0.042 mg/day) is anticipated to come from chewing and sucking on the net, meaning that a 25% reduction in estimated exposure from that route would improve the estimated MOS to an "acceptable" level. One assumption about the oral route of exposure for newborns that seems unreasonable is that a newborn would receive this exposure every night. In practice, a newborn that did chew on a section of net regularly would have to chew on a different section of net each night in order to continue to ingest insecticide. Furthermore, some products, such as K-O Tabs, contain a bittering agent intended to discourage children from eating the product.

One aspect of the risk assessment that may be open to scientific interpretation, and for which a revised interpretation could be significant, is the choice by Barlow, Sullivan and Lines of the other number used in producing an MOS – the concentration of pyrethroid that seems to produce adverse effects in animal studies. In this case, examining all of the relevant chronic effects studies conducted, the researchers decided that 0.01 mg per kg body weight per day (mg/kg bw/day) is the level most appropriate for use in developing an MOS. That is the highest level that selected animal studies indicate NO adverse effects were seen, otherwise known as the No Observeable Adverse Effect Level (NOAEL). This choice is one dependent on professional judgement. Given the sensitivity of the assessment to changes in interpretation on this issue, it would be prudent to seek review by other researchers of this choice of a NOAEL.

Even if these risk estimates were to hold up under closer examination, or even worsen slightly, this does not mean that the exposures being experienced would necessarily be considered "unacceptable." "Undesirable," yes, but risk management typically considers both risks and benefits, and USAID's environmental statute allows such a balancing of risks versus benefits. In this case, newborns sleeping under an ITN are exposed to some degree of theoretical risk from pesticide exposure, but are at the same time saved to a large extent from well-proven risks from malaria vectors.

One of the study's authors, Dr. Jo Lines of the London School of Hygiene and Tropical Medicine, was asked to review the exposure assumptions used in this risk assessment, for which all of the toxicological input came from Drs. Barlow and Sullivan. Dr. Lines advised the following:[28]

- Barlow and Sullivan's choice of 1 mg/kg bw/day as a NOAEL is appropriate, and this should indeed be considered a NOAEL, rather than a LOAEL. This means that the USEPA standard for an "acceptable" MOS should be 100, not 1000.
- The estimate of oral exposure for newborns used by Barlow and Sullivan was unrealistically high. With more realistic assumptions, "…it quickly becomes clear that a more realistic estimate of the margin of safety [for newborn chronic exposure] would be well over 100-fold."

4.1.7 Uncertainties and their significance

4.1.7.1 Risk assessment assumptions

As described above in the section on chronic risks from using ITMs, the Margin of Safety for newborns sleeping under a treated net was found to be very close to the EPA standard limit of acceptability. Differing assumptions about exposure and differing interpretations of animal toxicity study results could alter the end result of the assessment of chronic risks from the use of ITNs. An altering of exposure assumptions seems likely to reduce the estimated risk to levels that are better than the EPA standard for acceptability. On the other hand, it is difficult to predict whether a reevaluation of animal study results would alter the assessment.

4.1.7.2 Potential for other effects

This class of chemicals, the synthetic pyrethroids, has been studied and used extensively, and they generally appear to be safer alternatives to many older pesticides. Nonetheless, questions remain about whether all of the effects are fully understood.

Endocrine Disruption

Endocrine disruption is interference with normal hormone function "that produces reversible or irreversible biological effects in individuals or populations."[29] Recent studies have begun to indicate the potential for man-made chemicals like PCBs, dioxin and many pesticides to act like hormones and interfere with or disrupt normal body functions. One book that recently brought considerable attention to the potential for endocrine disruption by a variety of chemicals is Our Stolen Future: Are We Threatening Our Fertility, Intelligence and Survival? by Theo Colborn et al. Little evidence is yet available on the subject, and little consensus exists on what chemicals may present the risk of such effects. At present, however, pyrethroids have made some lists as "suspected" endocrine disruptors.[30]

The effects of endocrine disruption may be subtle and difficult to discern, but significant, and infants and fetuses may be most at risk. "In some instances," notes one physician's group, "in utero exposures that would have no effect in adults may permanently alter certain characteristics [of infants and the unborn]—including reproductive, neurological, and immune system parameters." [31]

The Food Quality Protection Act of 1996 mandated that EPA develop an endocrine disruptor screening program. EPA is now implementing such a program, which focuses on providing methods and procedures to detect and characterize endocrine activity of pesticides, commercial chemicals, and environmental contaminants. This program is aimed at gathering the information necessary to identify endocrine disruptors and take appropriate regulatory action. Under a settlement agreement with the Natural Resources Defense Council, EPA should complete this screening program by certain dates, as discussed below.

The first stage of this screening program was to involve "structure activity relationship" analysis to determine which chemicals have the potential to be endocrine-disrupting on

the basis of their chemical structure. The results of this analysis should have been completed by December 31, 2001. Further screening tests will be performed for chemicals whose structure appears to have endocrine-disrupting potential. The initial list of chemicals chosen for further screening studies is to be published by December 31, 2002. “Tier 1” and “Tier 2” screening will be performed by December 31, 2003, and December 31, 2004, respectively. Usable results of this screening program will therefore be available, according to current schedules, no later than early 2005, but potentially earlier.[32]

USAID should monitor the results of the EPA screening program. If solid evidence does link pyrethroids to endocrine disruption, then an assessment of the potential for impacts at the concentrations experienced with ITMs would be appropriate.

Developmental neurotoxicity

Another type of pesticide testing that EPA will require in the near future, and which has the potential to detect subtle effects not yet uncovered, is developmental neurotoxicity (DNT) testing. These studies test the effects of pesticide exposures on the developing brain and nervous system. Concerned environmental groups have called for these studies particularly because of recent research demonstrating that developing organisms are especially vulnerable to chemical agents if the exposure occurs at a critical period during development. In March 1998, the FIFRA (Federal Insecticide, Fungicide and Rodenticide Act) Scientific Advisory Panel reported, “One point of consensus is that the developing human, especially its nervous system, is vulnerable to a variety of toxicants, both pesticides and non-pesticides, and is certainly deserving of our best efforts to afford it protection with the intent of the 1996 Food Quality Protection Act.”[33]

EPA has issued a “Data Call-In” for DNT testing. The first phase will affect pesticides of the organophosphate class. Later phases will include the synthetic pyrethroids. As with endocrine disruption testing, USAID should monitor the results of the DNT testing for potential impact on the conclusions of this PEA.

Special sensitivity of children to pesticides

The National Research Council’s 1993 study, “Pesticides in the Diets of Infants and Children,” had a dramatic impact on the regulation of pesticides in the U.S. because of its findings that both children’s exposure to pesticides and their susceptibility to the toxic effects from that exposure could be significantly greater than that of adults. In pesticide-contaminated environments, children’s hand-to-mouth activities and other exposure-enhancing behaviors tend to increase the amount of pesticide they ingest and get on their skin. And because their internal organs are still developing and maturing, pesticides can have a greater effect on children. For example, these chemicals might not be as rapidly excreted in children as in adults, thereby having a longer period within the body during which to cause damage. Also, there are "critical periods" in human development when exposure to a toxin can permanently alter the way an individual's biological system operates.

The Food Quality Protection Act of 1996 mandated that EPA conduct a review of all new and existing pesticides to assure that they meet a new standard of "reasonable certainty of no harm," considering these exposure and toxicological differences between children and adults. This review is ongoing, and the results from the reevaluation of the ITN pesticide products should be considered as they become available.

4.1.7.3 Human behavior and the potential for use of unapproved pesticides

As discussed previously, the above analysis of toxicity and risks from ITM pesticides presumes that users will follow WHO recommendations and utilize only the recommended pesticides for treating ITMs. The potential exists that users will, in the interest of economy or other reasons, turn to other pesticides for the treatment of their bednets and other materials. "in many developing countries…the selection of pesticides is frequently made after considering price and effectiveness, with less emphasis given to safety."[34] The risks to humans from the use of such "alternative" products could potentially be much higher than with the relatively low-toxicity synthetic pyrethroids, and with no dosage recommendations for guidance, the concentrations applied to nets of these unapproved pesticides could be high. As one example, Chavasse et al. report occasions in which Emusifiable Concentrate formulations of deltamethrin, originally intended for agricultural use, were used for net treatment in an emergency, resulting in vomiting and other side effects among net dippers.

4.1.7.4 Change in WHO-recommended products

With mosquitos that transmit malaria beginning to demonstrate resistance to pyrethroids in West and Southern Africa, WHO is considering pesticides other than pyrethroids for use with ITMs. The human and environmental risks of other chemicals would not necessarily be similar to those of pyrethroids, and must be examined separately.

4.2 Environmental risks

Overview

Aquatic ecosystems can be exposed to ITM pesticides through essentially two routes: washing of nets and improper disposal of remaining net treatment solution. Chavasse et al. (1999) report examples of multiple incidents in which fish were killed by net washing, so at least anecdotal evidence demonstrates that these potent aquatic toxins do have the potential to cause damage by this exposure route.

Two recent studies of the potential aquatic effects of ITM pyrethroid use have been completed, one a literature review and one a computer modeling exercise. While both of these are limited in scope and approach, and their authors recommend further study to remove considerable uncertainties due to data gaps, their preliminary results appear to support three conclusions:

- potential aquatic impacts from ITN washing and improper disposal of treatment solution would be short-lived;

- aquatic effects would be unlikely from just a few nets being washed in a substantial river, stream or pond;
- large numbers of nets washed together might indeed kill aquatic organisms, including fish and other members of the ecosystem.

Summary of findings from literature review -- Briggs
A study conducted by Briggs in February 2000, "A Literature Review of the Environmental Impact on Aquatic Life of Pyrethroids used for Mosquito Net Impregnation in Bolivia," [35] found that current evidence indicates little likelihood of long-term or significant short-term aquatic impacts from bednet washing. Briggs acknowledges the possibility that fish and other aquatic organisms would be killed if large numbers of nets are washed at the same time. But Briggs does not consider such an occurrence to be very likely, and furthermore expects any possible effect to be transient—she believes that aquatic life would recover after cessation of exposure. Nonetheless, the study also indicated that conclusive data on the effect of washing ITNs in small streams, ponds and rivers are unavailable, and further study is needed.

Summary of findings from computer modeling -- Calamari
WHO commissioned another study by Calamari et al., "Preliminary assessment of the potential environmental impact of insecticide-treated nets (ITNs) on aquatic ecosystems."[36] A December 2000 draft of that study was made available for this assessment. Like the Briggs study, this is a preliminary evaluation, and the authors of this study advise that additional confirmatory testing should be conducted. In spite of uncertainties attributed to data gaps, the authors of this study reach conclusions that generally corroborate those of Briggs. In addition, the simulations run by these researchers provide some idea of the relative aquatic risk that the different ITM pyrethroids pose, potentially allowing program managers to reduce aquatic risk through their choice of ITM pesticide.

4.2.1 Toxicity of ITM chemicals to non-target wildlife

Both Briggs and Calamari assert that only short-term (acute) exposures are relevant to the scenario of aquatic exposure to ITM pesticides. This is because:

- these chemicals rapidly adsorb into suspended solids and into sediments;
- in many cases the residues released from nets will be washed downstream; and
- the chemicals break down rapidly to products that are nontoxic to aquatic organisms.

The USEPA acute aquatic toxicity categorizations of the different ITM chemicals are listed in table 9 below.

Table 9: Acute aquatic toxicity of pyrethroid technical formulations of ITM insecticides

Product	Acute Toxicity In Aquatic Organisms*
Alpha-cypermethrin	Very highly toxic
Cyfluthrin	Highly toxic to very highly toxic
Deltamethrin	Highly toxic to very highly toxic
Etofenprox	Slightly toxic to moderately toxic
Lambda-cyhalothrin	Very highly toxic
Permethrin	Slightly toxic to very highly toxic

* USEPA ecotoxicity classes are: Practically non-toxic, Slightly toxic, Moderately toxic, Toxic, Highly toxic, Very highly toxic.

Both Briggs and Calamari report on the toxicity values of these compounds for various aquatic species, so more detail is available from those studies, if needed.

It is important to note that risk is the product of toxicity and exposure. This is an important distinction for ITM pesticides, as the very different amounts of chemical required to treat a net with one chemical versus another has a substantial impact on the relative risk posed by different chemicals. As noted in table 1, WHO recommends treatment of ITNs with 200-500 mg active ingredient (ai) of permethrin per square meter of netting, but only 10-15 mg ai of lambda-cyhalothrin and 15-25 mg of deltamethrin. Naturally, aquatic systems will be exposed to far more active ingredient from washing permethrin-treated nets than from washing nets treated with lambda-cyhalothrin or deltamethrin. An axiom of toxicology is that “the dose makes the poison,” so a large amount of a less toxic product can be as bad as or worse than a small amount of something that is intrinsically more toxic.

4.2.2 Potential environmental exposure

The Briggs study reports evidence from a number of studies showing substantial variability in the amount of insecticide lost in washing. Briggs conjectures that the variations are due to methods of measuring the concentration of insecticide remaining in the net, the type of net material (cotton both absorbs more and loses more than polyester), the washing action and its vigor, whether and which detergent is used, and the temperature of the water. The study adopts a “conservative” estimate of 50% loss on first wash, with 2-20% loss found in the reported studies in subsequent washes.

Briggs reports that pyrethroid availability to aquatic organisms is minimized by the rapid degradation of these products, the fact that they do not bioaccumulate, and by their ready adsorption by soil. Environmental fate studies described in Briggs showed rapid clearance from even standing water – deltamethrin sprayed over trenches of standing water was not detectable after 10 days.

The Calamari study developed a computer model for estimating the concentration of pyrethroids that would likely result from the washing of nets, as well as from the rinsing of buckets used to treat nets. That model can be easily tailored to reflect any given set of conditions, and the authors propose that it be used by researchers in "real case" risk analysis.

For the purposes of this preliminary assessment, the researchers ran several simulations based upon a "typical" village (500 people, 100 households, 3 nets per household), assuming exposure of both a river and a pond, with varying assumptions that ranged from all village nets being washed at once (300 nets) to only 10% being washed at once (30 nets). Calamari used the same estimate as Briggs, of 50% loss on first wash. The Calamari model's exposure estimates are best expressed in comparison with the toxicity of the compounds in question—see also the next section.

4.2.3 Conclusions regarding risks to aquatic organisms from ITMs

Pyrethroids are highly toxic to aquatic organisms, and although only small amounts of these pesticides are likely to be released from a treated net when washed, a sufficient number of nets washed at the same time clearly has the capacity to release enough pesticide product to kill aquatic organisms. Field reports of fish kills coincident with the washing of large numbers of nets is convincing evidence of this capacity. Further evidence of the possibility of adverse effects from washing large numbers of nets and/or improperly disposing of a sufficient quantity of net treatment solution has been documented in the recent studies by Briggs and Calamari.

The authors of the Calamari study combined their estimates of the toxicity of the ITM pyrethroids with their model's estimates of exposure to produce estimates of the amount of aquatic risk presented by ITMs. These risk estimates took the form of a ratio of the estimated concentration over the concentration at which laboratory studies indicate that the representative aquatic species would likely be killed, termed an Exposure Toxicity Ratio (ETR). An ETR of one is the "risk threshold," and represents the exposure level at and above which adverse effects might be expected. Because of considerable uncertainty in this study's results (see below), the authors consider their ETR values to be merely "indicative." The higher the ETR, the more likely that negative effects will be seen.

The authors emphasize that several factors contribute to a high degree of uncertainty in their results. These include a lack of toxicity data describing effects from exposure during the timeframe that they estimate to represent the period of exposure – a matter of minutes or hours. This data gap required the researchers to extrapolate from toxicity studies generated for longer timeframes. Exposure estimates are also uncertain, being subject to variations in factors such as local water conditions and the release rate of chemical from bednets. The authors advise that the degree of uncertainty of the risk assessments based upon their exposure model and toxicity estimates cannot be determined at this point. They recommend resolution of these uncertainties through field validation of the exposure model and generation of toxicity studies that examine the appropriate exposure timeframe.

Keeping in mind the uncertainties in these results, it is instructive to examine the relative risk the Calamari study found for the different ITM chemicals. Deltamethrin and lambda-cyhalothrin appear to present the least risk, permethrin by far the greatest, while cyfluthrin, etofenprox, and alpha-cypermethrin lie close to one another in the middle of this range of risks. ETR values for deltamethrin and lambda-cyhalothrin generally remained below the risk threshold (<1), while ETRs for permethrin always exceeded the risk threshold (>1) and reached as high as 2,500 in one worst-case scenario. It is also worthwhile to note that in almost all of the pond simulations reported by Calamari, including most of the best-case scenarios in which only 10% of the village nets were washed at a time (30 nets), the ETR exceeded the risk threshold.

Because of the uncertainties in the Calamari study results, it is not possible to make too many decisions about chemical choice based on them. Nonetheless, the results would seem at minimum to argue against the use of permethrin, if that can be avoided. Further, the difference in ETR estimates for deltamethrin and lambda-cyhalothrin are sufficiently below those of the other three – generally an order of magnitude – that it would appear adviseable to choose one of these two chemicals over either cyfluthrin, etofenprox, or alpha-cypermethrin, in the interest of reducing the risk of harm to aquatic ecosystems.

4.2.4 Uncertainties in the aquatic risk assessment, and how to resolve them.

As noted above, the two referenced aquatic risk evaluations for ITMs admit that their findings are preliminary and that, while these evaluations were developed using the best information available, considerable uncertainty remains about a number of factors on which the evaluations were based. Among the data gaps that cause uncertainty in these evaluations, those that seem the most significant are listed below, along with suggestions for how these data gaps might be resolved.

- *How many nets will be washed at once in any one body of water*? This depends on a number of factors, including how successful the Roll Back Malaria (RBM) initiative is at promoting the use of ITMs. Also, to what degree can RBM partners convince net users to wash their nets away from natural bodies of water, in order to reduce aquatic risks? The answers to these questions should become clear as ITM promotional programs progress and begin to report results. ITM programs should be certain to track the net-washing habits of their target population.

- *Just how toxic are the ITM products to aquatic organisms over the relevant timeframe*? Since no short-term aquatic toxicity studies were available to the authors of the Briggs and Calamari studies, they extrapolated from 48-hour and 96-hour toxicity studies to an estimated five-minute exposure period. The extrapolations used by the two different research groups are substantially similar, providing some degree of validation to the methodologies used for those extrapolations. But good toxicity estimates will not be known until toxicity studies are conducted using this 5-minute timeframe.

- *How reliable are the pyrethroid concentration estimates given by Briggs and produced by the Calamari model, and how reliable are the risk estimates*? The reliability of the exposure estimates can be studied with field testing, including sampling to determine actual concentrations of pyrethroids in water bodies where ITMs are washed. If performed together with field tests of the impacts of these concentrations on aquatic organisms, e.g., by studying effects on test fish enclosed in baskets within a stream where ITMs are washed, then the risk estimates could also be validated.

5 Alternatives to ITMs for vector control

As explained in section 2.1, WHO considers vector control to be a key component of malaria control. Choosing the appropriate vector control method requires an understanding of the strengths and weaknesses of the available methods and their likelihood of success in any particular situation.

5.1 Other vector control methods

ITM use is one of many malaria vector control methods available, and while it is generally an effective control method, it is not always the most effective one. A number of vector control approaches are available, and achieving effective control relies in large part upon choosing the appropriate control method for the situation. WHO stresses the importance of "selective vector control," which "involves the targeted use of different vector control methods alone or in combination to prevent or reduce human-vector contact cost-effectively, while addressing sustainability issues." [37] Following is a table listing the different approaches to malaria vector control recognized by WHO. As indicated, a number of these involve pesticides.

Table 10: Malaria Vector Control Methods[38]

- Personal protection:
  - Repellents on skin or clothing; *
  - Protective clothing, untreated;
  - Protective clothing, treated; *
  - Insecticide vaporizers; *
  - Mosquito nets, untreated;
  - Mosquito nets, treated; *
- Treated window curtains, eave strips, and other materials; *
- Avoidance and diversion to other animals;
- Insect-proofing houses;
- Insecticide spraying to kill adult mosquitoes;
  - Indoor house spraying with insecticides (e.g., DDT); *
  - Space-spraying with insecticides (only in "exceptional circumstances"[39]); *
- Breeding prevention:
  - Biological control, e.g., fish that eat mosquito larvae;
  - Environmental management, e.g., to remove standing water;
  - Treating breeding grounds with larvicides. *

Approaches followed by an asterisk (*) involve the use of pesticides.

Treated bednets are not the appropriate choice for some situations, but ITMs are clearly an important vector control tool. For example, WHO advises that indoor house spraying is more suitable for containing epidemics than ITMs. Nonetheless, WHO states that, in

Africa, "where malaria transmission is stable, the use of insecticide-treated materials is the preventive method of choice when used correctly." [40]

As noted in table 10, one of the insecticides used for controlling malaria vectors is DDT, which is employed in indoor house spraying. The WHO "Action Plan for the Reduction of Reliance on DDT in Disease Vector Control[41]" recommends research into "the effectiveness, sustainability, and affordability" of insecticide-treated materials as one of the handful of approaches to replacing DDT use in malaria vector control. (Under the terms of the Stockholm Convention on Persistent Organic Pollutants, signed May 22, 2001, 127 governments agreed to phase out the use of DDT as soon as safe, affordable, and effective alternatives are available.)

5.2 Integrated vector management

5.2.1 Definition of IVM

Integrated vector management (IVM) (also called integrated vector control, or IVC) is a term used to refer to the public health equivalent of integrated pest management (IPM) in agriculture; it is generally the application of IPM principles in the practice of vector control.[42] Without attempting to give a "definitive" definition of either IVM or IPM, following are a few working definitions of each:

IVM

- "a vector or pest control strategy based on a combination of techniques such that it is not possible to increase efficacy or decrease adverse side-effects by using any additional methods."[43]
- "Targeted and site-specific use of available measures, taking into consideration the technical and operational feasibility, resources and infrastructure." [44]
- "A process of evidence-based decision-making procedures aimed to plan, deliver, monitor and evaluate targeted, cost-effective and sustainable combinations of regulatory and operational vector control measures, with a measurable impact on transmission risks, adhering to the principles of subsidiarity, intersectoriality and partnership."[45]

IPM

- "A sustainable approach to managing pests by combining biological, cultural, physical, and chemical tools in a way that minimizes economic, health, and environmental risks."[46]
- "In order to accomplish long-range, intelligent, and environmentally sound pest control, the management and manipulation of pests must be accomplished using not just one but all available pest control methods. This combination of methods into one thoughtful, ecologically valid program is referred to as Integrated Pest Management (IPM)."[47]

5.2.2 Recommended IVM practices

One description of the application of IPM principles to mosquito control is explained in "Florida Mosquito Control" :

> A typical mosquito control program employing IPM principles first determines the species list and abundance of mosquitoes through larval and adult surveys and then uses the most efficient and effective means of control. In some situations, water management programs or sanitation programs can be instituted to reduce breeding areas. When this approach is not practical, then a larviciding program is used so that specific breeding areas can be treated. Where larviciding is not effective adulticides are used. The choice of larvicides and adulticides used is based on the species targeted for control and environmental restrictions.
>
> An important part of an IPM program is public education. Public participation can do much to reduce breeding sites of domestic mosquitoes. Public education can be most effective during disease epidemics to educate the public concerning mosquito habits and ways individuals can protect themselves from mosquito attack."[48]

Described above is a focus on environmental management, which reduces breeding areas and thereby reduces the population of vectors. This places the emphasis on prevention and avoids the use of pesticides to kill adult mosquitoes. The Florida public health authorities consider ecological soundness and effectiveness in devising their vector control program.

As noted in the IVM and IPM definitions, a vector control program should be site-specific and use available measures. WHO's malaria vector control guidance advises that "Non-discriminatory reliance on a single approach or tool should be discouraged."[49]

5.2.3 Integrated vector management and its relationship to ITM use in USAID activities

ITMs are a relatively low-risk approach to vector control, certainly as compared to other pesticide-reliant methods such as house and space spraying, so ITMs meet the important IPM/IVM criteria of minimizing environmental risks. To help assure that ITMs are appropriately matched up with other available vector control approaches, another essential aspect of IPM/IVM, USAID programs should coordinate with the appropriate national, and/or regional, and/or local malarial and vector control strategies and activities.

The USAID Environmental Health Project, or EHP, (www.ehproject.org) is currently working with the WHO Africa Regional Office and others to develop IVM as a fundamental component of malaria control programs in Africa. This IVM initiative includes research into the cost-effectiveness of larval and environmental control, as well as technical and programmatic guidelines for IVM. Connected with this effort, EHP and WHO are building capacity for vector control and safe use of pesticides among municipal and district-level environmental health staff.

IPM and IVM both rely heavily on good information and good planning. There appears to be a widespread need to build capacity within national programs to conduct environmental impact assessments for vector control options so that national programs can be well informed.[50] Without such assessments, it would be difficult to claim that a program is consistent with the principles of IVM.

6 Risk management – mitigation and monitoring

6.1 Risk management decision-making issues

6.1.1 How much risk mitigation is enough?

Pesticides are toxic, and they inherently present health and environmental risks. In developing countries, risk reduction measures employed in the U.S., such as providing use instructions on the label, may be less effective. So what level of mitigation is sufficient? In light of the accidental human poisonings and fish kills that may result from a major scale-up of ITM activities, what level of effort should USAID and partners put forth to help reduce their frequency?

The standard of evaluation for these questions is expressed in the Agency's environmental regulations, in Section 216.6(a): "The purpose of the Environmental Assessment is to provide Agency and host country decision-makers with a full discussion of significant environmental effects of a proposed action. It includes alternatives which would avoid or minimize adverse effects or enhance the quality of the environment *so that the expected benefits of development objectives can be weighed against any adverse impacts upon the human environment* or any irreversible or irretrievable commitment of resources [emphasis added]." That is, an Environmental Assessment is used to develop options, allowing the program managers to choose the most environmentally sound one—as far as practicable. The determination of practicability is where the risks are weighed against the benefits.

USAID, and particularly its host country partners, need to continue to weigh the benefits of ITMs against the risks of their use. This assessment has identified a number of measures whose employment will reduce risks from the use of ITMs, and these are summarized in sections 4.1.5 and 4.2.5. For the most part, these should all be employed, as they are not largely resource-intensive, but the combination of mitigation measures should be decided on a case-by-case basis. For example, in many cases the exclusive use of long-lasting nets may not be appropriate, perhaps because of the somewhat higher initial cost of these nets, or perhaps because of other preexisting untreated nets that the program needs to target with re-treatment products.

On the other hand, it is important to note that the environmental protection goal of avoiding adverse effects from ITMs and the public health goal of widespread ITM use are consistent with one another. Adverse effects, such as reactions to overtreated nets, accidental human poisonings, and fish kills, could detract from the public image of ITMs and reduce the rate of public adoption of this malaria-control tool. Minimizing adverse effects from ITM pesticides is therefore important to the successful promotion of widespread ITM use. It seems that all interests would be served if ITM programs implement mitigation measures, as described herein and elsewhere, sufficient to assure that adverse impacts on human health or the environment from ITM use are rare, not regular occurrences.

6.1.2 The no-action alternative

In an environmental assessment, the "no-action alternative" must be considered. That is, what would be the environmental (including social) impact of simply not taking the action investigated, which in this case is the action of investing in vector control via ITMs? As discussed above, this would decrease the effectiveness of the malaria control programs with which USAID works, since vector control is an essential part of a malaria control program.

As described previously, the impact of malaria on human health and productivity in Africa is enormous. But the environment can be indirectly degraded by malaria, as well. This connection is explained in the following statement of the Institute of Medicine of the National Academy of Sciences (1996):

> When a substantial proportion of a country's population is ill with malaria for five or six months each year, sustained economic development is very difficult to achieve. Countries thus compromised cannot easily become active trading partners...nor are they positioned to decrease their dependence on foreign aid. Similarly, *when child survival is threatened by malaria and other infectious diseases, family planning and environmental quality are simply not priorities*. [Emphasis added.] [51]

The no-action alternative of not implementing measures to control malaria vectors is clearly an undesirable one. Since vector control is considered quite effective at reducing malaria, avoiding vector control in USAID Africa programs would have very negative impacts on human health, productivity, as well as the environment.

6.2 List of key mitigation measures for reducing human and environmental risks from ITM pesticides

Based on the analysis above, below are several important actions that programs should take to minimize the risk of human poisoning and environmental contamination with ITM re-treatment insecticides. Chapter eight of the "ITN Handbook" (Chavasse et al.) does an excellent job of addressing this subject, and many of the following are derived from that document. For safer use guidelines for pesticides in general, also see the section titled, "Design Considerations for Pesticide Management and Safe Use" in the Africa Bureau's "Environmental Guidelines for Small Scale Activities in Africa," Knausenberger et al., 1996.[52]

6.2.1 Choose safer products

- *Long-lasting nets*

True "long-lasting," pre-treated nets that retain their effectiveness over the lifetime of the net would present the ideal solution to ITM pesticide risks to humans and the environment by eliminating the need for re-treatment. Considering that the majority of African users studied were found to wash nets at least once a month[53], the currently-available Permanet, which is supposed to retain efficacy for 20 washes, would remain efficacious for only about 1 ½ years (compared with 2-3 washes, i.e., 2-3 months for most other products). Some evidence suggests that the initial efficacy of Permanets, prior

to the need for re-treatment, might last as little as six months under typical use conditions. Nonetheless, choosing to use such a net is still the best risk reduction measure that an ITM program can take, as it reduces the need for re-treatment and thereby addresses all of the exposure opportunities. As research into long-lasting net technology progresses, and the efficacy period is extended, the environmental advantages of such nets will increase.

- *Safer active ingredients*

Only WHOPES-recommended ITN active ingredients should be used for USAID ITN programs; WHOPES has determined that these chemicals are particularly well suited for use with ITNs because of their efficacy and relatively low toxicity to humans. Among these chemicals, the lower the toxicity of the end use products, the better. Permethrin is probably a choice to be avoided, for example, as it is only available in an EC formulation; this type of formulation contains organic solvents, making the end-use products more toxic than similar products that are water-based. Another reason to avoid permethrin is the high dosage required on the net. By comparison with deltamethrin, for example, the dosage needed on the net and therefore the treatment solution concentration must be about 10 times that of deltamethrin. Since the toxicity of the two products is approximately the same by weight, this means the risk to users from permethrin is much higher than with deltamethrin. Also, as noted in the text, the acute safety factor for the WHO-recommended permethrin formulation is the worst of all the WHO-recommended products.

- *Safer formulations*

Highly concentrated formulations of liquid pyrethroid products are to be avoided as much as possible, and are inappropriate for OTC sale because of the potential for accidental poisoning. Zaim et al. recommends specifically against OTC supply of high concentration permethrin (e.g., 50% EC). Table 5 provides a good comparison of the "safety factor" of the ITM pesticide products. Programs should choose the highest safety factor possible, particularly for OTC products.

Water-based formulations are the only liquid formulations that should be used for OTC distribution, including CS (capsule suspension or micro-encapsulated), EW (emulsion, oil in water) and SC (suspension concentrate) formulations. EC (emulsifiable concentrate) formulations, which are based on toxic organic solvents, should be avoided.

Even better are water-dispersible tablets. Zaim et al. makes a good case for the use of this formulation: "Solid formulations, such as water-dispersible tablets (WT), have many advantages since they are easy to handle, transport and store, and there is less risk of accidental spillage and contamination than with liquids. A bittering agent should be incorporated into the product to prevent deliberate or accidental ingestion, especially by children."

- *Packaging*

Large-volume containers should be avoided whenever possible. Handling ITM pesticides in barrels means measuring out concentrated liquid pesticide product, presenting the opportunity for serious injury through accidental exposure. This also introduces the opportunity for repacking into inappropriate, poorly-labeled containers, increasing the chance of accidental exposure and misuse.

Regarding OTC products, Zaim et al. states, “It is strongly recommended that insecticides for home treatment of ITMs should be presented only in single unit doses. Moreover, if presented as liquid formulation in bottles, use of child-proof caps should be mandatory.”

6.2.2 Assure proper labeling of pesticide products

Particularly for OTC products, but also for products to be used in mass treatment programs, labelling is a crucial risk communication tool. Zaim et al.describes the appropriate labelling as follows:

> *All packs should bear, durably and legibly, in local language, the following information: the formulation (Specification WHO/…) and concentration of the active ingredient; the volume (liquid) or net weight (solid) of the contents; the manufacturer’s identity (name and address) with batch or reference number, date of production and expiry date; together with the minimum cautionary advice necessary to ensure safe and effective use. Pictograms on use of the product and disposal of contaminated materials are essential for users who may have limited literacy. For single-dose packs (i.e., bottles, sachets or tablets), care should be taken to ensure that the above-mentioned information is not easily separated from the insecticide itself.*

To elaborate on Dr. Zaim’s explanation, “minimum cautionary advice necessary to ensure safe and effective use” needs to be defined for the particular situation. What is an appropriate message for one community may be different for another. Research and monitoring on the effectiveness of such label information should be part of a safe use program.

6.2.3 Educate consumers and employees in pesticide safety

For over-the-counter (OTC) products, consumer education materials (including the product label) and other consumer awareness efforts need to address the issue of health and safety in pesticide storage and handling, as well as the environmental risks from disposal of excess treatment solution and from washing nets.

- OTC products should be stored out of reach of children,
- Users should wear appropriate protective equipment when treating nets. For occasional net treatment, impermeable gloves should suffice. Home users cannot be expected to have these available, so gloves should be distributed with each net re-treatment package. For professional net treaters, particularly if they handle

concentrated product prior to dilution for treating nets, face protection is recommended,
- Users should follow practices that reduce exposure as much as possible. For example, gloves used for mixing pesticide solution should be washed on the hands before removal,
- Excess solution should be disposed of in a latrine or garbage pit, out of reach of people and animals and where it cannot be washed into natural bodies of water,
- Nets should be washed in basins of water, not in rivers and streams (see below). The hazard to aquatic organisms should figure prominently on product labels and educational materials.

If the ITN program has its own employees treating nets, then educational materials and training should target these employees as well. The program needs to assure that these employees are themselves adequately trained in safe use of these pesticides and are capable of training others as appropriate.

Field testing of educational programs and materials is important. For example, Chavasse et al.describes the experience of researchers from the London School of Hygiene and Tropical Medicine (LSHTM), who worked with a group of women in Tanzania to develop a home treatment kit for nets. In that process the researchers developed instructions for proper net treatment, which they significantly altered after field testing. One researcher at LSHTM commented on an early draft of this PEA, advising, "It is the responsibility of the insecticide seller to show that the instructions used in DIY kits are safe and effective within the cultural context in which the kits will be sold and used. This means considering what languages are most commonly used in the country concerned. More importantly, it means carrying out local tests to show that the instructions provided are adequate, i.e., can be followed safely and effectively by the great majority of local users." With that in mind, *any USAID program selling a DIY kit needs to demonstrate that the instructions are adequate in the local context.*

Attached as Annex 2 is a sample package insert designed to train DIY kit users in proper use and disposal of the ITN treatment product, providing an example of the type of insert that should accompany such kits. Note that some comments were received in response to the draft version of this PEA regarding ways in which to make that insert more effective for illiterate users, and those comments are included in the annex.

WHO has prepared draft guidance on how to use to safely use and treat ITNs (currently only in French, titled, "Instructions pour le traitement et utilisation des moustiquaires impregnees d'insecticide")[54] that will be a useful reference to include in USAID ITM programs when it becomes available. It is likely to be too long to use as a package insert, but it will be ideal training material for public health workers and ITM program staff, and might also be useful, in an abridged for, in the preparation of package inserts for net users.

6.2.4 Create a safe and environmentally sound workplace for net treatment facilities

If direct net re-treatment by program staff is anticipated, then the program is responsible for creating a safe and environmentally sound workplace for net re-treatment. Some of the measures that should be taken are the following:

- Train staff in the safe handling of these pesticides, disposal of waste and cleanup of spills. Impermeable gloves and face protection should be worn by anyone handling concentrated solution and by persons treating nets.
- Minimise the effects of inhaling solvent vapors by treating nets in a well-ventilated area and using shallow basins for dipping so that the vapors can escape. The best approach to this problem is to choose water-based formulations.
- Ensure insecticide is safely transported and stored, away from foodstuffs and accidental access by untrained persons and children.
- Provide materials for and operating procedures for cleaning up spills.
- Provide facilities and operating procedures for disposing of excess insecticide solution, as needed. (See below for discussion.)
- Dispose of empty pesticide containers properly. (See below for discussion.)
- Train staff in appropriate emergency response in the case of pesticide poisoning, and make certain treatment facilities have soap and water and medical charcoal available. (Refer to the Annex, “Treatment of Pyrethroid Poisoning,” for details on emergency response procedures.)

Program managers need to also carefully examine the United Nations Food and Agriculture Organization (UNFAO) Pesticide Management Guidelines, particularly the UNFAO “Pesticide Storage and Stock Control Manual” [55].

6.2.5 Dispose of leftover insecticide solution properly

Avoid contaminating water sources with leftover insecticide solution after net dipping or with empty insecticide containers, to avoid killing fish and other organisms in local waters. This is likely to be the greatest problem with mass treatment programs, as the potential for large volumes of remaining solution is greatest. Leftover solution, if all the solution is not absorbed by the net, should be dumped into a latrine or garbage pit. Similarly, empty liquid pesticide containers should be rinsed before disposal (see below), and the rinse water disposed of properly.

6.2.6 Dispose of pesticide containers properly

A common problem with pesticide use in developing countries is the tendency to reuse pesticide containers to carry water and other materials, exposing users to ingestion of these products. The UNFAO "Pesticide Storage and Stock Control Manual" explains, "An empty pesticide container can never be cleaned completely of pesticide and should be disposed of in a way that ensures it cannot be used for other purposes."

UNFAO provides the following recommendations for container disposal:

- Empty containers should always be cleaned out, as far as practicable, before disposal;
- If possible, they should then be disposed of according to UNFAO recommendations.
- As long as they are not heavily contaminated, cardboard and fibreboard containers should be burnt on a fire in the open (except those contaminated with phenoxy acid herbicides). [Note – any burning should be upwind.]
- Heavily contaminated material and all other containers should be rendered unusable and sent to a central location for disposal by the national authority.

The UNFAO manual provides other guidance generally targeted to institutional pesticide facilities, such as how to properly decontaminate large containers, clean up spills, and dispose of unused pesticides. Indeed, the UNFAO manual appears to be addressed primarily to institutional pesticide use, rather than to residential users, and is quite appropriate for commercial-scale ITN treatment operations. For persons using single-dose ITN treatment products in their homes, the suggestion that containers be sent to a central location for disposal may not be practical.

The USAID *Environmental Guidelines for Small-Scale Activities in Africa* has the following to say on the question of disposal: "Containers cleaned [by triple-rinsing] are still not safe to use for any other purpose. Glass containers should be broken and plastic or metal containers punctured or crushed. Containers can then be buried in an isolated area at least 50 cm below ground surface."

Chavasse et al. recommends the following regarding disposal of excess pesticide and packaging for DIY kits: "Leftover insecticide should be poured down a latrine or onto dry ground. Avoid disposing of insecticide in streams or ponds. Bury packaging or throw it in a latrine." This advice seems quite practical and appropriate for the small amounts of pesticides involved with DIY kits, and consistent with the *USAID Environmental Guidelines*.

6.2.7 Increase accidental poisoning response capacity

Accidental poisonings of some degree or another will inevitably result from the widespread distribution of ITM pesticides, and efforts should be made to increase the capacity to respond effectively. For mass net treatment facilities, workers should be

trained in the appropriate response to accidental exposure, and the necessary materials for washing eyes and skin should be available on-site. Refer to the Annex, "Treatment of Pyrethroid Poisoning" for details on proper emergency response, or to the ITN Handbook's (Chavasse) section on "Diagnosing and Treating Pyrethroid Poisoning." Programs focusing on OTC products should also work with local health facilities to increase their awareness of the potential for and proper treatment of pyrethroid poisonings.

6.2.8 Perform quality control of ITM pesticide products

Pesticides of poor quality—containing insufficient active ingredient, too much of it, or impurities—threaten both efficacy as well as safety, as these formulation problems can affect the toxicity profile of the product. A 2001 joint report by WHO and UNFAO estimated that 30 percent of pesticides marketed in developing countries do not meet internationally accepted quality standards.[56] Efforts should be made to assure that pesticide products being purchased or promoted are of good quality and contain what they are supposed to contain. Pesticide stocks should also be managed properly so as to avoid allowing the products to expire. WHO specifications for public health pesticides, for quality control and international trade, are available on the WHO homepage on the Internet at www.who.int/ctd/whopes.

6.2.9 Monitor for adverse health and environmental impacts and unsafe practices

Potential health and environmental impacts of ITM pesticides are not likely to be recognized unless ITM programs actively look for them. Assuming that ITM programs already conduct monitoring and evaluation (M & E) of the efficacy of their public health intervention, the environmental issues should be built into that M & E program. For example, field evaluation teams should ascertain whether nets are being washed, with what products nets are being treated (only WHO-recommended ITM products?), and whether persons have become ill as a result of using these products or if they have seen dead fish.

6.2.10 Manage the storage, transport and disposal of pesticide appropriately

An ITM program's handling of pesticides affords opportunities for spills and for human and environmental exposures during storage, transport and disposal of the product. The UNFAO's "International Code of Conduct on the Distribution and Use of Pesticides" specifies appropriate pesticide management protocols, and references detailed guidelines on best practices with regard to storage, transport and disposal of pesticides. Refer to the Code of Conduct at:
http://www.fao.org/waicent/FaoInfo/Agricult/AGP/AGPP/Pesticid/Code/PM_Code.htm
and the UNFAO Pesticide Management Guidelines at:
http://www.fao.org/waicent/FaoInfo/Agricult/AGP/AGPP/Pesticid/Code/Guide.htm.

6.2.11 Help create local capacity to regulate ITMs

In many African countries, the regulatory program for public health and agricultural pesticides is severely limited by lack of staff, expertise and resources. With USAID and other donors attempting to promote the widespread and longterm use of ITMs, it is important to strengthen the national, regional and local government regulatory structure, which will have the role of assuring the efficacy and safe use of ITM products and other pesticides over the long run. For example, USAID programs may want to provide technical assistance in the registration of ITM products in target countries, as well as training for government staff in the environmental aspects of ITMs.

6.3 Monitoring mechanisms for adverse effects from ITM use and treatment

Monitoring for adverse effects should be a responsibility actively assumed by USAID ITM programs. Human pesticide poisonings and environmental contamination events occur with disturbing regularity in agricultural programs in developing countries, but these tend to come to the attention of authorities and researchers only when attempts are made to look for them. The absence of incident reports from agricultural or public health arising from pesticide use in Africa, without efforts to search them out, will never suffice as evidence that such incidents are not occurring.

One example of this pattern appears in "Challenges for improving surveillance for pesticide poisoning: policy implications for developing countries" (2001), in which London and Bailie[57] reported on pesticide poisoning surveillance activities conducted in the Western Cape province of South Africa. This research shows that only a tenth of the pesticide poisonings occurring in that agricultural region are reported to poison control centers or other health authorities. Similarly, in "Cultivating Crisis: the Human Cost of Pesticides in Central America,"[58] Murray describes a systematic effort conducted in 1985 to document the scope of pesticide poisonings in Leon, Nicaragua. Researchers estimated that only 23% of the pesticide poisonings occurring in the region appeared in official illness reports. The revised estimates of poisoning frequency made pesticide poisoning by far the leading cause of work-related illness and injury. The same principle holds as true in Africa as in Central America—poor health care systems and other factors lead to great underreporting of pesticide poisonings and environmental contamination.

Monitoring is also a responsibility assigned by USAID's environmental regulations: "Monitoring. To the extent feasible and relevant, projects and programs for which Environmental Impact Statements or Environmental Assessments have been prepared should be designed to include measurement of any changes in environmental quality, positive or negative, during their implementation." (22CFR, 216.3(a)(8))

One example of a monitoring tool is a questionnaire, an example of which is attached as Annex 2. This questionnaire has been administered by USAID missions to managers of USAID ITM programs in several African countries. One of the functions such a tool serves is to provide a mechanism for reporting on human and environmental adverse

effects that program staff might detect during their work with the community served by the program's ITM activities.

6.4 Risk management issues for further analysis

As discussed above, issues that merit followup and further analysis include (but are not limited to) the following:

- Continuing research into the potential effects of the ITM pesticides, particularly including endocrine disruption and developmental neurotoxicity. Studies commissioned by the USEPA and other organizations need to be monitored for the possibility that they might change the conclusions of this assessment.
- Resistance and its impact on ITM effectiveness.
- Better evaluation of the real-life impacts of ITM pesticide use, as programs scale up their delivery of ITM pesticides. Are poisoning incidents seen, and why? Are aquatic ecosystems affected by these pesticides?

7 Environmental review and documentation for ITM use in USAID activities

7.1 Overview of review requirements

As described in Chapter 2, all USAID activities are subject to evaluation via, at minimum, an Initial Environmental Examination (IEE). And because of risk concerns presented by pesticides, the USAID environmental regulations require that at least the 12 factors outlined in the Pesticide Procedures (22CFR 216.3(b)(1)(i)(a-l)), including USEPA registration status, anticipated conditions of use, etc., be addressed in the IEE for any program that includes assistance for the procurement or use of pesticides. For an evaluation of ITM programs, the Africa Bureau and the Global Bureau are generally requiring the preparation of what is termed a "Pesticide Evaluation Report and Safer Use Action Plan" (PERSUAP), a document that covers the 12 Pesticide Procedures factors and focuses on the development of local-level risk mitigation actions. Further details about what to include in a PERSUAP are given below.

Why is a local-level assessment such as a PERSUAP needed for USAID pesticide programs? To help in understanding the utility, consider the U.S. system for promoting pesticide safety. When the USEPA registers pesticides for use in the United States, it specifies the manner in which the product can be "safely" used (i.e., with an acceptably small risk), including safety equipment needed when applying the pesticide, how to apply it, the allowed uses, etc. But the context in which EPA makes these registration decisions is important to note. An extensive system of capabilities and resources exist in this country that help give EPA confidence these specifications will be followed and the product will be used appropriately. These include a 97% literacy rate meaning most of the population can read labels; close control by EPA over the content of the label; training requirements and programs for those pesticide products that require applicator certification; worker protection requirements; occupational safety regulations; and relatively effective federal, state and local enforcement mechanisms. In allowing the use of certain pesticides in its African programs, USAID cannot rely on the same societal capabilities and resources that the USEPA does to assure appropriate use of the product. The preparation of a PERSUAP gives a program manager the opportunity to consider practical actions by which to reduce the risks of using pesticide products in a program, taking into consideration the context in which the products will be used, the particular elements of the program, and the different capacities of the partners involved.

7.2 Who prepares a PERSUAP?

The Pesticide Procedures require that the analysis outlined in those Procedures be included in the IEE for any program funding pesticide use or procurement. Therefore, the IEE for any and every USAID program supporting ITM procurement and use must describe the results of an analysis performed in accordance with the Pesticide Procedures.

That said, decisions on the best approach to take in performing such an analysis may be made on a case-by-case basis. The Africa Bureau is preparing guidance on that question. One proposal is that one PERSUAP be prepared for each country, to include all USAID ITM programs in that country under one PERSUAP "umbrella." Each of the IEEs covering an ITM program in that country could then be amended with a brief reference to the PERSUAP of the country in question. For further guidance on this question, refer to the appropriate Mission Environmental Officer (MEO), Regional Environmental Officer (REO), or the Africa Bureau Environmental Officer (BEO).

7.3 Components of an activity-level PERSUAP

A PERSUAP basically consists of two parts, a "PER" and a "SUAP." The Pesticide Evaluation Report (PER) section addresses the 12 informational elements required in the Agency's Pesticide Procedures. The Safer Use Action Plan (SUAP) puts the conclusions reached in the PER into a plan of action, including assignment of responsibility to appropriate parties connected with the ITM program. Much of the information needed in the PER section is covered in this PEA and can be copied from or referenced here.

Table 11 below provides detailed guidance for developing a PERSUAP for ITM programs, following the organizational framework of the 12 Pesticide Procedures elements. In addition to furnishing information on each element in turn, programs should develop an action plan which distills the risk mitigation actions to which the program is committing and outlines steps by which they are to be implemented. This action plan should identify roles and responsibilities of different partners involved.

Program managers preparing a PERSUAP should contact their MEO, REO or the BEO for the Africa Bureau to obtain a copy of a good (and recent) example of a PERSUAP. This is another way to assure that program managers are apprised of any updated information that surfaces after completion of this PEA.

Table 11: Guidance for the development of a PERSUAP for ITM programs

USAID "Pesticide Procedures" Element and Description (from USAID Pest Management Guidelines, 1991)	Specific Guidance for ITM PERSUAP
a. **USEPA registration status of the proposed pesticide**. USAID is effectively limited to using pesticide active ingredients registered in the U.S. by the U.S. Environmental Protection Agency for the same or similar uses.	In the PERSUAP: *Reference the appropriate chapter of the ITM PEA or other USAID guidance as appropriate for the USEPA registration status and WHO recommendation. Also identify the registration status in the host country. Identify the formulated pesticide product to be used*. Only WHO-recommended pesticide active ingredients and formulations should be used in USAID ITM programs. One pesticide active ingredient currently recommended by WHO for ITM use is not registered in the U.S.—alpha-cypermethrin. Nonetheless, if a compelling need to use this chemical can be demonstrated by the program in question, as required under USAID Pest Management Guidelines for the use on non-U.S. registered pesticides, then this use should be authorized. Host country pesticide registration procedures must also be identified and followed. See also PEA chapter 3.
b. **Basis for selection of the pesticide**: This refers to the economic and environmental rationale for choosing a particular pesticide. In general, the least toxic pesticide that is effective is selected.	In the PERSUAP: *Explain the basis for selection of the pesticide product to be used, including active ingredient and formulation.* Pesticide product selection may be driven by a number of factors, including efficacy, price, availability, safety, etc. All things being equal, an ITM program should choose the pesticide active ingredient and formulation that presents the least overall risk. Formulation is a key determinant of toxicity, and should be considered in selecting a particular pesticide product. Formulation also has an impact on exposure; for example, water-dispersible tablets eliminate the the potential for poisoning through accidental exposure to concentrated liquid product. Packaging can have a significant impact on exposure potential. Large containers necessarily introduce hazardous product transfer steps, as well as the possibility that the product will end up in a smaller, poorly labeled container. On the other hand, unit-dose products intended for use in the home carry the risk of accidental exposure to family members such as young children. Information, education, communication materials and training programs need to be designed to address the risk factors presented by the pesticide product of choice. The least amount of risk is undoubtedly presented by so-called "long-lasting nets." Since the biggest risk of exposing humans or the environment to ITM pesticides comes from re-treatment, a net that reduces or eliminates the need for re-treatment has significant environmental advantages.

	See also PEA chapters 3 and 4.
c. **Extent to which the proposed pesticide use is, or could be, part of an IPM [or IVM] program**: USAID policy promotes the development and use of integrated approaches to pest management whenever possible. This section discusses the extent to which the proposed pesticide use is incorporated into an overall IPM strategy.	In the PERSUAP: *Describe the extent to which the proposed ITM product(s) is/are or could be a part of an IVM program. Describe the connection between the USAID activity and regional, national and local malaria control programs (as appropriate).* Integrated pest management, and its public health counterpart, integrated vector management, is USAID policy because it is the most effective, economical, and safest approach to pest and vector control. "Integrated pest management attempts to control pests in an economically and environmentally rational manner; it emphasizes non-chemical tactics which cause minimal disruption to the ecosystem."[59] USAID programs should assure that the choice of ITMs was made after consideration of other vector control options available, and that this is the most effective and environmentally sound option available. As discussed in chapter 5, several other vector control options also involve the use of pesticides – indoor residual house spraying, space spraying, larviciding, etc.—but in larger volumes than ITMs. So ITMs appear to be a natural component of an IVM program, which has reduced pesticide use as one of its goals. The availability and effectiveness of other pesticides and non-ITN technologies should be examined in the PERSUAP. One essential means of promoting an integrated approach to public health vector management is to assure that the ITM activity in question is integrated appropriately with regional, national and local malaria control programs. In the interest of resistance management, among other reasons, it is important also to promote connections between the public health and the agricultural sectors in their control of pests in the area of the activity. See also PEA chapter 5.
d. **Proposed method or methods of application, including the availability of application and safety equipment**: This section examines in detail how the pesticide is to be applied and the measures to be taken to ensure its safe use.	In the PERSUAP: *As stated, describe in detail how the pesticide is to be applied and the measures to be taken to ensure its safe use.* Re-treatment is the event in the life cycle of ITM pesticides likely to offer the greatest opportunity for human exposure. Most re-treatment involves dipping, whether in the home or otherwise. In addition, eye, and preferably face, protection should be worn by applicators who treat bednets regularly. Provision should be made to assure that users have gloves available during re-treatment, and it is essential that both professional applicators as well as home users wear these. If it seems necessary in order to assure that gloves are used during home treatment of nets, then gloves should be distributed with each package of over-the-counter ITM pesticide products; many programs already do this. Container size and design can be a factor in determining the likelihood of accidental exposure. For example, in a mass re-treatment program, small "squeeze and pour" bottles that eliminate the need to measure pesticide in a separate container are much less likely to cause spills and are environmentally advantageous over 20-liter drums that require

	transfers to smaller containers. With home use products, care should be taken to assure that the container does not leak or break with expected handling, transfers its contents easily, and is child resistant. Single-dose tablets appear to meet those criteria better than many other options, but the available products should be evaluated on a case-by-case basis. This subject is also addressed in the following section E, and reference can therefore be made here to section E. See also PEA chapters 4 and 6.
e. **Any acute and long-term toxicological hazards, either human or environmental, associated with the proposed use, and measures available to minimize such hazards**: This section of the IEE examines the acute and chronic toxicological data associated with the proposed pesticide. In addition to hazards, this section of the IEE also discusses measures designed to mitigate any identified toxicological hazards, such as training of applicators, use of protective clothing, and proper storage.	In the PERSUAP: *Reference the appropriate section of the PEA and/or other material on this subject. Describe measures the program will take to reduce the potential for exposing humans or nontarget organisms to ITM pesticides. Also describe monitoring measures that will allow the program to identify problems with users applying other non-WHO approved pesticides to ITMs.* **It is recommended that this be the key section of the PERSUAP, in which the majority, or perhaps all, of the planned mitigation measures are described.** To address this element, the PERSUAP should briefly summarize the toxicity to humans and other non-target organisms of the ITM products chosen for the program in question, the potential exposure opportunities presented by those products, and the risk reduction actions the program will take to minimize such exposure opportunities. Potential toxicological hazards are described in depth in chapter 4 of this Programmatic Environmental Assessment. Thus it should be sufficient in an activity-level PERSUAP to reference PEA, chapter 4, without needing to reiterate those hazards. However, what the PERSUAP should expand upon in this section is how the country-level program will respond to the mitigation measures recommended in PEA chapter 6, "Mitigation measures for human and environmental risk reduction." **The reviewer should address each of the mitigation measures recommended in this section, noting how and to what extent the particular risk reduction measure will be implemented.** See also PEA chapters 4 and 6.

f. **Effectiveness of the requested pesticide for the proposed use**: This section of the PERSUAP requires information similar to that provided in item 2, but more specific to the actual conditions of application. This section also considers the potential for the development of pest resistance to the proposed insecticide.	In the PERSUAP: *Explain what recommendations or evidence suggests that the ITM products proposed are effective in the program area. What efforts are being made to monitor for and, as needed, respond to potential problems of pyrethroid resistance among malaria vectors in the program area?* This is an important question, particularly with respect to the goal of malaria prevention, but not one that requires significant attention in a PERSUAP. The ITM pesticides allowed in USAID programs are those recommended by WHO. One of the most important criteria of a WHOPES evaluation is efficacy. Nonetheless, two significant issues in this regard do require attention—mosquito resistance to the pesticide in question, and pesticide quality. Public health use of pesticides is not generally considered to contribute substantially to the development of resistance – that is primarily the result of the more widespread and larger-volume agricultural use – but resistance could determine the choice of pesticide to be used for net treatment. Quality control is another issue of importance, affecting both efficacy and safety. A 2001 joint report by WHO and UNFAO estimated that 30 percent of pesticides marketed in developing countries do not meet internationally accepted quality standards.[60] In the PERSUAP, describe efforts that will be made to assure that pesticide products being purchased or promoted are of good quality. See also PEA chapters 2, 3 and 5.
g. **Compatibility of the proposed pesticide use with target and non-target ecosystems**: This section examines the potential effect of the pesticide on organisms other than the target pest (for example, the effect on bee colonies kept in the area). Non-target species of concern also include birds and fish. The potential for negative impact on non-target species should be assessed and appropriate steps should be identified to mitigate adverse impacts.	In the PERSUAP: *Describe efforts that are being made to minimize environmental exposure to ITM pesticide products.* The toxicity characteristics need not be described at length in the PERSUAP, as those are described in chapter 4 of this PEA and the PERSUAP can reference that chapter. This section of the PERSUAP should describe the environmental risk mitigation measures that the program will take. The key options for environmental risk mitigation, as described in PEA chapter 6, are product choice and exposure reduction. In this section, therefore, describe the relative environmental risk of the product chosen versus the other options. Also describe efforts the program will make to reduce exposure of the environment, through choice of pesticide product and packaging, preparation of educational materials, training, etc. This question might also be covered in response to question (e), and if so, simply reference that section without repeating it. See also PEA chapter 4 and chapter 6.
h. **Conditions under which the pesticide is to be used, including climate, flora, fauna, geography, hydrology, and soils**: This	In the PERSUAP: *Describe the environmental conditions under which the pesticide is to be used, identifying any environmental factors that might be particularly sensitive or subject to contamination from re-treatment operations.* This item refers to particular environmental factors that might accentuate the effects of exposure to ITM pesticides,

	section examines issues such as the potential for contamination of surface and groundwater sources.	and the potential need for measures to reduce those risks. For example, particularly sensitive or valuable aquatic systems adjacent to re-treatment facilities might lead USAID to recommend against the choice of mass net re-treatment, or require more efforts to promote proper pesticide disposal or reduce net washing in these bodies of water. See also PEA chapter 4.
i.	**Availability of other pesticides or non-chemical control methods**: This section identifies other options for control of pests and their relative advantages and disadvantages.	In the PERSUAP*: Describe other vector control options being pursued in the geographic area of the activity, either as part of the USAID activity or otherwise, and explain why this particular vector control method was chosen over other available options.* This item is closely related to item 3 on Integrated Vector Management, and the answer to this is an important part of the explanation to be given in that section. See also PEA chapter 5.
j.	**Host country's ability to regulate or control the distribution, storage, use, and disposal of the requested pesticide**: This section examines the host country's existing infrastructure and human resources for managing the use of the proposed pesticide. If the host country's ability to regulate pesticides is inadequate, the proposed action could result in greater harm to the environment.	In the PERSUAP: *Summarize the host country's capacity and structure for the regulation of public health and agricultural pesticides. Identify the approval/registration status of the pesticide product in the host country.* The host country's capacity and structure for the regulation of public health and agricultural pesticides should be summarized. A critical issue for a USAID ITM activity, or other pesticide activity supported by the Agency, is the extent to which the host country's regulatory oversight will help to control distribution, storage, use and disposal of the pesticide products in question. USAID activities should always be in compliance with local environmental and public laws and regulations, but that is not necessarily enough. If host country regulatory systems and institutions are not sufficient to give a reasonable expectation that environmentally sound practices will be enforced, USAID still bears responsibility for assuring environmental protection at each of these steps in the pesticide life cycle. Since ITM programs generally aim to promote longterm use of ITMs, beyond the life cycle of the program itself, USAID and other donors should accept responsibility for helping assure that the host country infrastructure has the capacity to properly regulate ITM products. Government oversight over pesticides is important for controlling the quality of products as well as their environmentally-sound use and disposal. USAID ITM programs of substantial size should generally include an element of capacity-building work with host country institutions that govern public health pesticide use. These measures should be identified in this chapter of the PERSUAP. See also PEA chapter 6.
k.	**Provision for training of users and applicators**: USAID recognizes that safety training is an essential component in programs involving the use of pesticides. The need for thorough training is particularly acute in	In the PERSUAP: *Describe the provisions made to train and educate those who will be treating nets, from consumers using do-it-yourself kits to professionals conducting mass net re-treatment.* This will have to be tailored to the specific program. For home-use kits, training materials need to accompany nets and re-treatment pesticides. Environmental and safety issues these need to effectively address include the use of protective gloves, the volume of water to use, advice about safe storage of pesticides, and proper disposal of any left-over pesticide solution and containers. If the program will involve mass treatment in central locations, then it is critical that

developing countries, where the level of education of applicators may typically be lower than in developed countries.	the PERSUAP discuss arrangements being made to train net treatment workers. As discussed in chapter 6, it is essential that communication materials such as ITN package inserts be field-tested to verify that they are effective in communicating proper handling, use and disposal techniques to the target audience. In this section of the PERSUAP, a description should be given of the field testing of such materials that was already conducted or that is planned. See also PEA chapters 4 and 6, as well as Annex 3, "Sample insert from ITN package."
l. **Provision made for monitoring the use and effectiveness of this pesticide**: Evaluating the risks and benefits of pesticide use should be an ongoing, dynamic process.	In the PERSUAP: *Describe monitoring and evaluation programs for ITM activities, and the health and environmental safety-related information that is collected via this M and E capacity.* Monitoring programs should actively investigate, to the extent possible, the following issues: • Effectiveness of Information, Education and Communication materials and activities in promoting safe handling, use and disposal of ITM products. • Adverse health and environmental effects and the frequency and severity with which they occur. • Quality control of ITM pesticide products. • Effectiveness of the chosen products and their alternatives, including whether or not resistance is developing. • Safe and effective pesticide use and handling practices by program staff and end users. Included in this is an investigation into the types of pesticide products being used, watching for possible substitution with products not recommended by WHO for ITMs. Questionnaires can be useful tools in a monitoring program. Attached as an annex is an example of a questionnaire used by a national-level coordinator for identifying the nature of and thereby potential problem areas in ITM programs run by different organizations. Something similar might be employed by a program manager for an ITM program with many geographically separate parts. See also PEA chapters 4 and 6.

Annex 1: USAID pesticide procedures

22CFR, §216.3 (b) Pesticide Procedures

(1) Project Assistance. Except as provided in §216.3 (b)(2), all proposed projects involving assistance for the procurement or use, or both, of pesticides shall be subject to the procedures prescribed in §216.3(b)(l)(i) through (v). These procedures shall also apply, to the extent permitted by agreements entered into by A.I.D. before the effective date of these pesticide procedures, to such projects that have been authorized but for which pesticides have not been procured as of the effective date of these pesticide procedures.

(i) When a project includes assistance for procurement or use, or both, of pesticides registered for the same or similar uses by USEPA without restriction, the Initial Environmental Examination for the project shall include a separate section evaluating the economic, social and environmental risks and benefits of the planned pesticide use to determine whether the use may result in significant environmental impact. Factors to be considered in such an evaluation shall include, but not be limited to the following:

(a) The USEPA registration status of the requested pesticide;

(b) The basis for selection of the requested pesticide;

(c) The extent to which the proposed pesticide use is part of an integrated pest management program;

(d) The proposed method or methods of application, including availability of appropriate application and safety equipment;

(e) Any acute and longterm toxicological hazards, either human or environmental, associated with the proposed use and measures available to minimize such hazards;

(f) The effectiveness of the requested pesticide for the proposed use;

(g) Compatibility of the proposed pesticide with target and nontarget ecosystems;

(h) The conditions under which the pesticide is to be used, including climate, flora, fauna, geography, hydrology, and soils;

(i) The availability and effectiveness of other pesticides or nonchemical control methods;

(j) The requesting country's ability to regulate or control the distribution, storage, use and disposal of the requested pesticide;

(k) The provisions made for training of users and applicators; and

(l) The provisions made for monitoring the use and effectiveness of the pesticide.

In those cases where the evaluation of the proposed pesticide use in the Initial Environmental Examination indicates that the use will significantly effect the human environment, the Threshold Decision will include a recommendation for the preparation of an Environmental Assessment or Environmental Impact Statement, as appropriate. In the event a decision is made to approve the planned pesticide use, the Project Paper shall include to the extent practicable, provisions designed to mitigate potential adverse effects of the pesticide. When the pesticide evaluation section of the Initial Environmental Examination does not indicate a potentially unreasonable risk arising from the pesticide use, an Environmental Assessment or Environmental Impact Statement shall nevertheless be prepared if the environmental effects of the project otherwise require further assessment.

(ii) When a project includes assistance for the procurement or use, or both, of any pesticide registered for the same or similar uses in the United States but the proposed use is restricted by the USEPA on the basis of user hazard, the procedures set forth in §216.3(b)(1)(i) above will be followed. In addition, the Initial Environmental Examination will include an evaluation of the user hazards associated with the proposed USEPA restricted uses to ensure that the implementation plan which is contained in the Project Paper incorporates provisions for making the recipient government aware of these risks and providing, if necessary, such technical assistance as may be required to mitigate these risks. If the proposed pesticide use is also restricted on a basis other than user hazard, the procedures in §216.3(b)(l)(iii) shall be followed in lieu of the procedures in this section.

(iii) If the project includes assistance for the procurement or use, or both of:

(a) Any pesticide other than one registered for the same or similar uses by USEPA without restriction or for restricted use on the basis of user hazard; or

(b) Any pesticide for which a notice of rebuttable presumption against reregistration, notice of intent to cancel, or notice of intent to suspend has been issued by USEPA,

The Threshold Decision will provide for the preparation of an Environmental Assessment or Environmental Impact Statement, as appropriate (§216.6(a)). The EA or EIS shall include, but not be limited to, an analysis of the factors identified in §216.3(b)(l)(i) above.

(iv) Notwithstanding the provisions of §216.3(b)(l)(i) through (iii) above, if the project includes assistance for the procurement or use, or both, of a pesticide against which USEPA has initiated a regulatory action for cause, or for which it has issued a notice of rebuttable presumption against reregistration, the nature of the action or notice, including the relevant technical and scientific factors will be discussed with the requesting government and considered in the IEE and, if prepared, in the EA or EIS. If USEPA initiates any of the regulatory actions above against a pesticide subsequent to its evaluation in an IEE, EA or EIS, the nature of the action will be discussed with the recipient government and considered in an amended IEE or amended EA or EIS, as appropriate.

(v) If the project includes assistance for the procurement or use, or both of pesticides but the specific pesticides to be procured or used cannot be identified at the time the IEE is prepared, the procedures outlined in §216.3(b)(i) through (iv) will be followed when the specific pesticides are identified and before procurement or use is authorized. Where identification of the pesticides to be procured or used does not occur until after Project Paper approval, neither the procurement nor the use of the pesticides shall be undertaken unless approved, in writing, by the Assistant Administrator (or in the case of projects authorized at the Mission level, the Mission Director) who approved the Project Paper.

(2) Exceptions to Pesticide Procedures. The procedures set forth in §216.3 (b)(l) shall not apply to the following projects including assistance for the procurement or use, or both, of pesticides.

(i) Projects under emergency conditions.

Emergency conditions shall be deemed to exist when it is determined by the Administrator, A.I.D.. in writing that:

(a) A pest outbreak has occurred or is imminent; and

(b) Significant health problems (either human or animal) or significant economic problems will occur without the prompt use of the proposed pesticide; and

(c) Insufficient time is available before the pesticide must be used to evaluate the proposed use in accordance with the provisions of this regulation.

(ii) Projects where A.I.D. is a minor donor, as defined in §216.1(c)(12) above, to a multidonor project.

(iii) Projects including assistance for procurement or use, or both, of pesticides for research or limited field evaluation purposes by or under the supervision of project personnel. In such instances, however, A.I.D. will ensure that the manufacturers of the pesticides provide toxicological and environmental data necessary to safeguard the health of research personnel and the quality of the local environment in which the pesticides will be used. Furthermore, treated crops will not be used for human or animal consumption unless appropriate tolerances have been established by EPA or recommended by UNFAO/WHO, and the rates and frequency of application, together with the prescribed preharvest intervals, do not result in residues exceeding such tolerances. This prohibition does not apply to the feeding of such crops to animals for research purposes.

(3) Non-Project Assistance. In a very few limited number of circumstances A.I.D. may provide nonproject assistance for the procurement and use of pesticides. Assistance in such cases shall be provided if the A.I.D. Administrator determines in writing that

(i) emergency conditions, as defined in §216.3(b)(2)(i) above exist; or

(ii) that compelling circumstances exist such that failure to provide the proposed assistance would seriously impede the attainment of U.S. foreign policy objectives or the objectives of the foreign assistance program. In the latter case, a decision to provide the assistance will be based to the maximum extent practicable, upon a consideration of the factors set forth in §216.3(b)(l)(i) and, to the extent available, the history of efficacy and safety covering the past use of the pesticide the in recipient country.

Annex 2: Sample environmental impact questionnaire for ITN program managers

The following sample questionnaire is being used by ITM programs in Central and Eastern Africa, with variations currently in use in Malawi, Zambia, Rwanda and Uganda.

Insecticide-Treated Bednets: Environmental Impact Questionnaire

This questionnaire is being circulated to those running (or considering running) programmes involving distribution of insecticide-treated bednets for malaria prevention. If your organization is interested in doing so within the next year but has not been involved in net distribution, many of these questions may not apply to you, but please complete those that do. The main purpose for conducting this survey is to better characterize the way insecticides are handled in insecticide-treated net (ITN) distribution programmes in …. and determine where there may be scope for improving practices to limit risk of adverse occupational and environmental impact of use of these insecticides. This survey is being conducting by …. Anyone interested in obtaining a summary report on results of this survey should contact ...[ADD DETAIL AS APPROPRIATE]

Background: Although use of bed nets to prevent contact with biting insects is ancient, the use of ITNs is quite recent. And, although the efficacy has been demonstrated in pilot programs, the scaling-up to national programs, the distribution and systematic retreating of the nets with insecticides, and the overall sustainability of these programs is now being examined. As a result, there are numerous approaches to distribution, and many organizations sponsoring ITNs as their principal activity, or as part of more comprehensive maternal and child health or environmental health programs. It is important to keep track of these diverse efforts and, at least for those funded by USAID, there are statutory requirements to track and report on any potential environmental impacts that might result from USAID-funded programmes employing insecticides. Although the quantity of insecticides used in any individual ITN is small, the estimated need to treat over 300 million/year world-wide at full scale (as estimated by WHO's Roll Back Malaria effort) will constitute a significant usage of insecticides. Furthermore, although the toxicity of pyrethroid insecticides, used in ITNs, is very low for mammals and birds, these insecticides are quite toxic to organisms living in water such as fish, frogs, aquatic insects and other arthropods.

The use of ITNs should give protection from malaria-bearing mosquitoes with much smaller and more economical amounts of insecticide than would be needed for large-scale residual house spraying (although such spraying can be valuable for focal epidemic control). Likewise, larvicides are very valuable in areas where vector breeding is easily identified, mapped and treated (generally in arid zones), but is generally not a feasible approach to malaria control in the humid tropics, as in Africa, where the vast majority of the cases world's cases of malaria occur.

PLEASE USE THE REVERSE SIDE FOR FURTHER OBSERVATIONS

Section 1: Information on Project/Activty/Programme

1. Name of project/activity/ programme:

2. Responsible organization (if different from above):

3. Location(s):

4. Size of target population served (or planned):

5. What sub-groups of the population are targeted by your programme (e.g. under 5's, pregnant women, chronically ill, lowest socio-economic status)?

6. Funded by: USAID ❑
other donors, specify: ❑

7. Is this: primarily an ITN project? ❑
ITNs are only a component of a more comprehensive project? ❑

8. Starting date (year/month) for net distribution:

9. Expected completion date (year/month) for net distribution activities:

10. a. What is the staffing of the ITN activity/component (e.g, lead partner has coordinator (full-time, part-time?), nature of cooperation with others, e.g. District Malaria Coordinator, village-level committees, health extension agents, etc.):

10. b. Is it linked to a National Malaria Control Program? Yes ❑ No ❑
In what way?

Section 2: Information on Insecticide Used for ITN treatment/ retreatment:

(Refer to below table for questions at the end of this section)

11. Trade Name(s):

12. Chemical name of active ingredient (e.g. deltamethrin, cyfluthrin, etc):

13. How/why was this insecticide selected?

14. Where and from whom was the insecticide (or treatment/retreatment kits) obtained?

15. Formulation type (e.g. tablet, powder, emulsion, granular, etc.)

16. How is it packaged?
Pre-treated: "long-lasting" nets ❑ , "standard" nets for retreatment ❑

Individual treatments: tablets ❑, sachets ❑, small plastic bottles ❑,
other ❑, specify:

Larger containers: 1 liter ❑, 5 liter ❑, 10 liters ❑,
other ❑, specify:

17. What is the *dilution* of the insecticide used for retreatment (% or ppm)? (if not known, give the weight or volume of insecticide and the volume of water used for dilution)

18. a.What is the *target concentration* expected on the net after pretreatment/treatment/retreatment (ml/ square meter of netting) (if known)?

18. b. What are the recommended retreatmetn conditions (after __ washes, after ___ months, other:_____).

19. a. Does the information provided with the insecticide (such as a label) list any *environmental or safety precautions* that should be taken?
Yes ❑ No ❑
19. b. Are proper use instructions (e.g., washing temp., no ironing, keep out of sun) offered? Yes ❑ No ❑

20. Does the label indicate date of manufacture and expiration? Yes ❑ No ❑

21. Are you aware of the *registration status* of this insecticide and formulation (e.g. host country, US EPA, EU, WHO)? Describe:

WHO-recommended insecticides for ITN treatment for malaria vector control:

Insecticide	Formulation[1]	Dosage[2]
Alpha-cypermethrin	SC 10%	20-40
Cyfluthrin	EW 5%	50
Deltamethrin	SC 1% and WT 25%	15-25
Etofenprox	EW 10%	200
Lambda-cyhalothrin	CS 2.5%	10-20
Permethrin	EC 10%	200-500

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

[2] Milligrams of active ingredient per square metre of netting.

Section 3: Bednets and Distribution

22. If your programme operates through *outlets* or *service-delivery points* (clinics, schools, community groups, retailers, chain stores, etc.), please explain the distribution, relative importance of the respective outlets, and the quantities of nets so distributed and sold:

23. How many nets have been *distributed* to date?

24. How many are *planned* for the life of the project?

25. How many nets planned for the coming year?

26. Is a revolving fund used to purchase more nets and kits? Yes ❑ No ❑
If yes, how many are added over what period?

27. Type(s) and size(s) of nets used ?

28. Are the nets *branded*? Yes ❑ No ❑
If yes, name:

29. Did your programme receive the nets *prepackaged*?

Yes ❑ No ❑

If 'yes', was a *treatment/retreatment kit included*?

N/A ❑ Yes ❑ No ❑

And, did the *packaging include information* on treatment and appropriate net use and care? Yes ❑ No ❑

31. a. Where are the nets obtained?

b. Where are the treatment/retreatment products obtained?

32. What was the price your organization *paid* for nets (US$ equivalent)?

33. What was the price *paid* for treatment/retreatment kits (USD)?

34. What has been the price at which your programme is *selling* the nets (USD)?

35. What has been the price at which your programme is *selling* the treatment/retreatment kits (USD)?

Section 4: Storage, Transport and Disposal

36. In your programme, how are insecticides *stored* before distribution?

37. For *how long* are insecticides stored (maximum time)?

38. Is insecticide purchased for one season _____ or for how long?

_____

Does the supply meet the demand? Yes ❑ No ❑

Will all of the product be used by program end? Yes ❑ No ❑

Why or why not?

39. If insecticides are purchased in large containers (> 1 liter), are these containers taken to field sites for treatment/retreatment?

Yes ❑ No ❑ not applicable ❑

40. Who delivers insecticide to you, or where do you collect it?

41. How are unused, or excess, insecticides disposed of?

42. How do you dispose of packets, sachets, bottles, boxes, etc. that contained insecticides?

Section 5: Treatment and Retreatment

43. In your programme, after how many months, washings, or other conditions is *retreatment* recommended?

44. Is retreatment done (check more than 1, if necessary)? Not applicable ❑

by individual households? ❑

communally? ❑

at retreatment stations (mobile or fixed locations)? ❑

by volunteers ? ❑

for a price? ❑

for all comers (not just project participants) ❑

45. What is the approximate ratio of *new nets sold* to *nets retreated* (or retreatment kits sold) in your programme (e.g. 1000 new nets and 250 retreatment kits last year, therefore ratio of 4:1)?

Section 6: Information, Education and Communication

46. With individual nets and retreatment kits, does your programme pack *use-and-safety instructions* with illustrations and text in language(s) appropriate to the setting?

Yes ❑ No ❑

47. Does your programme separately disseminate (i.e. not packaged with nets or retreatment kits) such use and safety information to your consumers, participating social groups (women's, religious, etc), schools, etc?

Yes ❑ No ❑

48. In your program, is there anyone who provides *individual or group orientation/ teaching* to consumers on the use of nets and demonstrates proper treatment/ retreatment?

Yes ❑ No ❑

If yes, who?

49. If there are people providing such orientation, how were they trained and by whom?

50. Who prepared the written and verbal instructions and use messages that your project uses (e.g. project staff, manufacturer…)?

51. Do you have training materials available (train-the-trainer, posters, informal adult education, etc.). Yes ❑ No ❑. If yes, describe:

52. As your net distribution has grown, would you say the intensity of your IEC efforts has increased proportionally and retained the same quality?

Yes ❑ No ❑ not applicable ❑

Please comment:

53. Are you satisfied that your IEC messages adequately explain the *role of the mosquito* in transmission of malaria, hence the *importance of the ITNs* as a public health measure?

Yes ❑ No ❑ not applicable ❑

Please comment:

Section 7: Environmental, Biological and Human Health Issues

54.. Have residents in your community (-ies) expressed ITN-related concerns that have the potential to reduce acceptability of and demand for ITNs?

Yes ❑ No ❑ not applicable ❑

Please comment:

55. Has anyone complained about skin reactions (e.g. itching) after or while using ITNs?

Yes ❑ No ❑ not applicable ❑

Please comment:

56. What do you think about the following statement? (check one of each of the 2 groups of responses)

Malaria-carrying mosquitoes can develop resistance to the insecticide used in insecticide-treated nets?

I don't think that's true. ❑
I guess that's possible. ❑
Yes, I believe that's true. ❑

That couldn't affect how well our nets work. ❑
That could be a problem for our nets in the future. ❑

57. In your orientation information to new and existing ITN users what, if any, information do you provide explaining that pyrethroid insecticides are very toxic to fish and other aquatic organisms (e.g., frogs, insects, crayfish, etc)?

we have *not* been providing such information ❑
information *is* provided ❑, as described below:

_____

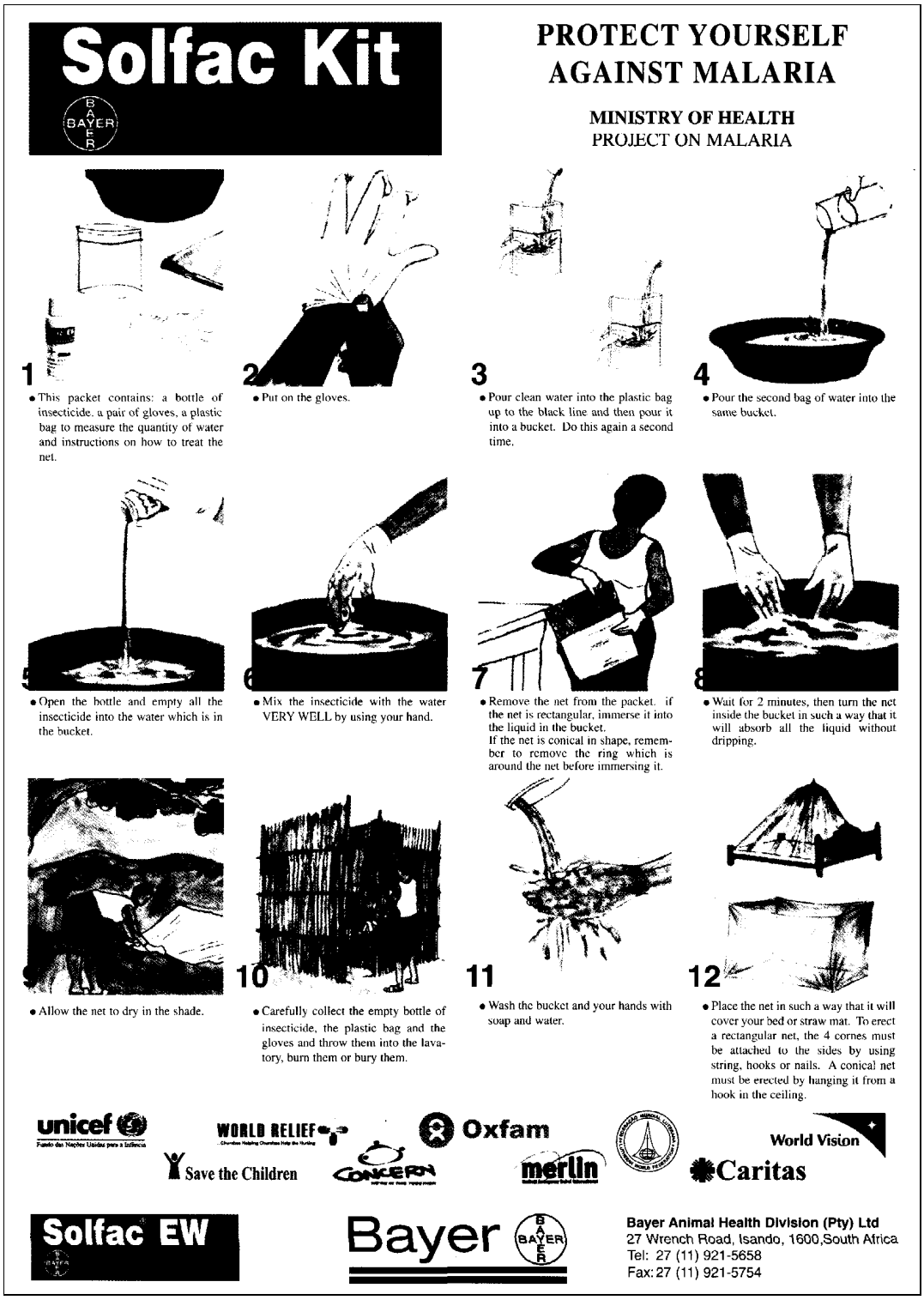
Thank you for taking the time to complete this questionnaire.

Please send it back to:

…
…
National Malaria Control Program

Questionnaire prepared by: Andy A. Arata, Walter I. Knausenberger, and Stephen Hodgins
Last updated: 28 November 2001

Annex 3: Sample insert from ITN package, Population Services International.



Comments regarding this sample insert:

There are many effective elements and proper messages in this package insert designed to accompany do-it-yourself ITN treatment products, but it is difficult to judge the effectiveness of this or any other insert without testing it. As discussed in Chapter 6**, such educational materials should be field-tested to assure that they effectively communicate the necessary information**. Field experience has shown that the developers of such educational materials are frequently surprised by how differently the materials are understood by their users.

Some comments on the above graphic, received from pesticide disposal experts who reviewed a draft version of this PEA, are the following:

- The insert should be designed with the assumption that the user is illiterate, and will only be able to understand the pictures.
- Since the picture shows a person mixing the solution with a gloved hand, in the absence of a glove, the person might be likely to use their bare hand. It might be preferable to depict the person mixing the solution with a stick, which could be easily discarded afterward.
- The user should be advised to leave the pesticide package in the solution into which it is being mixed. This will effectively rinse the package.
- Ideally, a plastic bag should be provided with the product that is large enough to hold all the water needed. If not, then the illustration should show the plastic bag being filled with water twice, as well as being emptied into the bucket twice.
- The insert should include an illustration of washing the bucket. Currently, only words advise users to take this action.
- An illustration should show the user washing the gloves on their hands before removing the gloves, as well as washing their hands after disposal of the gloves and pesticide packaging.
- The “lavatory” should be called a latrine. Also, in some parts of the continent this picture might be thought to depict a house, rather than a latrine, particularly in areas where latrines are not common. Testing should assure that users understand that this is a latrine.
- If there are three disposal options – latrine, burial, burning – then illustrations should depict all three options. Such illustrations should show the items being buried fairly deep. A depiction of burning should show the user wearing a cloth over nose and mouth, burning the items outside the village with smoke moving away from the person and the village.

Annex 4: Treatment of pyrethroid poisoning

(From "Recognition and Management of Pesticide Poisonings, Fifth Edition, 1999." A USEPA-supported publication by Reigart and Roberts. See http://www.epa.gov/pesticides/safety/healthcare)

PYRETHROIDS

These modern synthetic insecticides are similar chemically to natural pyre-thrins, but modified to increase stability in the natural environment. They are now widely used in agriculture, in homes and gardens, and for treatment of ectoparasitic disease. Pyrethroids are formulated as emulsifiable concentrates, wettable powders, granules, and concentrates for ultra low volume application. They may be com-bined with additional pesticides (sometimes highly toxic) in the technical product or tank-mixed with other pesticides at the time of application. AASTAR (discontinued 1992), for instance, was a combination of flucythrinate and phorate. Phorate is a highly toxic organophosphate. Nix and Elimite are permethrin creams applied to control human ectoparasites.

Toxicology

Certain pyrethroids exhibit striking neurotoxicity in laboratory animals when administered by intravenous injection, and some are toxic by the oral route. However, systemic toxicity by inhalation and dermal absorption is low. Although limited absorption may account for the low toxicity of some pyrethroids, rapid biodegradation by mammalian liver enzymes (ester hydrolysis and oxidation) is probably the major factor responsible for this phenomenon. Most pyrethroid metabolites are promptly excreted, at least in part, by the kidney. The most severe, although more uncommon, toxicity is to the central nervous system. Seizures have been reported in severe cases of pyrethroid intoxication. Of 573 cases reviewed in China, there were 51 cases with disturbed consciousness and 34 cases with seizures. Of those, only 5 were from occupational exposure. Seizures are more common with exposure to the more toxic cyano-pyrethroids, which include fenvalerate, flucythrinate, cypermethrin, deltapermethrin, and fluvalinate. There are no reports in the literature of seizures in humans from exposure to permethrin. Apart from central nervous system toxicity, some pyrethroids do cause distressing paresthesias when liquid or volatilized materials contact human skin. Again, these symptoms are more common with exposure to the pyrethroids whose structures include cyano-groups. Sensations are described as stinging, burning, itching, and tingling, progressing to numbness. The skin of the face seems to be most commonly affected, but the face, hands, forearms, and neck are sometimes involved. Sweating, exposure to sun or heat, and application of water enhance the disagreeable sensations. Sometimes the effect is noted within minutes of exposure, but a 1-2 hour delay in appearance of symptoms is more common. Sensations rarely persist more than 24 hours. Little or no inflammatory reaction is apparent where the paresthesia are reported; the effect is presumed to result from pyrethroid contact with sensory nerve endings in the skin. The paresthetic reaction is not allergic in nature, although sensitization and allergic responses have been reported as an independent phenomenon with pyrethroid exposure. Neither race, skin type, nor disposition to allergic disease affects the likelihood or severity of the reaction. Persons treated with permethrin for lice or flea infestations sometimes experience itching and burning at the site of application, but this is chiefly an exacerbation of sensations caused by the parasites themselves, and is not typical of the paresthetic reaction described above. Other signs and symptoms of toxicity include abnormal facial sensation, dizziness, salivation, headache, fatigue, vomiting, diarrhea, and

irritability to sound and touch. In more severe cases, pulmonary edema and muscle fasciculations can develop. Due to the inclusion of unique solvent ingredients, certain formulations of fluvalinate are corrosive to the eyes. Pyrethroids are not cholinesterase inhibitors. However, there have been some cases in which pyrethroid poisoning has been misdiagnosed as organophosphate poisoning, due to some of the similar presenting signs, and some patients have died from atropine toxicity.

Treatment

1. Skin decontamination. Wash skin promptly with soap and water as outlined in Chapter 2 [see excerpt below]. If irritant or paresthetic effects occur, obtain treatment by a physician. Because volatilization of pyrethroids apparently accounts for paresthesia affecting the face, strenuous measures should be taken (ventilation, protective face mask and hood) to avoid vapor contact with the face and eyes.

Vitamin E oil preparations (dL-alpha tocopheryl acetate) are uniquely effective in preventing and stopping the paresthetic reaction. They are safe for application to the skin under field conditions. Corn oil is somewhat effective, but possible side effects with continuing use make it less suitable. Vaseline is less effective than corn oil. Zinc oxide actually worsens the reaction.

2. Eye contamination. Some pyrethroid compounds can be very corrosive to the eyes. Extraordinary measures should be taken to avoid eye contamination. The eye should be treated immediately by prolonged flushing of the eye with copious amounts of clean water or saline. If irritation persists, obtain professional ophthalmologic care.

3. Gastrointestinal decontamination. If large amounts of pyrethroids, especially the cyano-pyrethroids, have been ingested and the patient is seen soon after exposure, consider gastrointestinal decontamination as outlined in Chapter 2. Based on observations in laboratory animals and humans, large ingestions of allethrin, cismethrin, fluvalinate, fenvalerate, or deltamethrin would be the most likely to generate neurotoxic manifestations. If only small amounts of pyrethroid have been ingested, or if treatment has been delayed, oral administration of activated charcoal and cathartic probably represents optimal management. Do not give cathartic if patient has diarrhea or an ileus. [Editor's note: According to the Merck Manual of Diagnosis and Therapy, an "ileus" is a "temporary arrest of intestinal peristalsis."]

4. Other treatments. Several drugs are effective in relieving the pyrethroid neurotoxic manifestations observed in deliberately poisoned laboratory animals, but none has been tested in human poisonings. Therefore, neither efficacy nor safety under these circumstances is known. Furthermore, moderate neurotoxic symptoms and signs are likely to resolve spontaneously if they do occur.

[From Chapter 2: General Principles in the Management of Pesticide Poisonings.]

Skin Decontamination

Decontamination must proceed concurrently with whatever resuscitative and antidotal measures are necessary to preserve life. Shower patient with soap and water, and shampoo hair to remove chemicals from skin and hair. If there are any indications of weakness, ataxia, or other neurologic impairment, clothing should be removed and a complete bath and shampoo given while the victim is recumbent. The possibility of pesticide sequestered under fingernails or in skin folds should not be overlooked. Flush contaminating chemicals from eyes with copious amounts of clean water for 10-15 minutes. If eye irritation is present after decontamination, ophthalmologic consultation is appropriate. Persons attending the victim should avoid direct contact with heavily contaminated clothing and vomitus. Contaminated clothing should be promptly removed, bagged, and laundered before returning. Shoes and other leather items cannot usually be decontaminated and should be discarded. Note that pesticides can contaminate the inside surfaces of gloves, boots, and headgear. Decontamination should especially be considered for emergency personnel

such as ambulance drivers at the site of a spill or contamination. Wear rubber gloves while washing pesticide from skin and hair of patient. Latex and other surgical or precautionary gloves usually will not always adequately protect from pesticide contamination, so only rubber gloves are appropriate for this purpose.

Annex 5: References

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