Integrated Vector Management Programs for Malaria Vector Control

Programmatic Environmental Assessment

January 2007

Integrated Vector Management Programs for Malaria Control

Programmatic Environmental Assessment

Contract GHS-I-01-03-00028-000-1
Period Ending September 30, 2006

Prepared for
Bureau for Global Health
United States Agency for International Development

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INTEGRATED VECTOR MANAGEMENT PROGRAMS FOR MALARIA VECTOR CONTROL: PROGRAMMATIC ENVIRONMENTAL ASSESSMENT

PROGRAM/ACTIVITY DATA:

Program/Activity Number: GHS-I-01-03-00028-000-1
Country/Region: Global
Program/Activity Title: Integrated Vector Management (IVM) Task Order
Sub-Activity Title: Integrated Vector Management Programs for Malaria Vector Control: Programmatic Environmental Assessment
Prepared By: RTI International
Current Date: January 29, 2007

ENVIRONMENTAL ACTION RECOMMENDED: (Place X where applicable)

Categorical Exclusion: ____ Negative Determination: ____
Positive Determination: _X__ Deferral: ____

ADDITIONAL ELEMENTS: (Place X where applicable)

CONDITIONS: _X__ PVO/NGO: ____

SUMMARY OF FINDINGS

The U.S. Agency for International Development (USAID) Office of Global Health contracted RTI International to conduct a Programmatic Environmental Assessment (PEA) to serve as an umbrella evaluation of environmental and human health issues related to malaria vector control and to assist with the preparation of country- and activity-specific Supplemental Environmental Assessments (SEAs) for malaria vector control programs. This PEA provides USAID project managers with the policy, procedural, and technical guidelines to choose appropriate interventions and insecticides and develop and implement mitigation and monitoring and evaluation activities. This, in turn, will allow Missions to design malaria vector control programs in more efficient and cost-effective ways.

This PEA includes a peer-reviewed human health risk assessment of malaria vector control methods, as well as requirements and recommendations for mitigating potential negative impacts resulting from malaria vector control methods. This PEA describes additional factors to take into consideration when selecting interventions, such as host country laws, international treaties, and multi-sector impacts. It also contains a separate guidance document for preparing SEAs, entitled *Guidance for Developing SEAs for Malaria Vector Control Programs.*

Major findings of this PEA are primarily found in the human health risk assessment, which contributes to the current knowledge about the comparative risk of pesticides used in malaria vector control interventions. Based on the results of the assessment, several conclusions can be drawn with regard to potential risks of practices and pesticides:

- The low predicted risks for ITNs suggest that, from a risk standpoint, this approach may be preferable to IRS

- The relatively high risks predicted for the pesticide container reuse scenario suggest that action should be taken to prevent potentially significant risks from short-term exposures as a result of this activity
- The magnitude of the ingestion and dermal risk estimates for the disposal scenario strongly suggests that burial of pesticides should be prohibited
- Across all IVM practices, DDT is the riskiest pesticide with respect to both noncancer and cancer endpoints and, therefore, should only be used after stringent requirements have been met
- For ITNs, the results for all pesticides except etofenprox and (for children) lambda-cyhalothrin were below levels of concern for preparing and treating nets
- For IRS, the least preferred pesticides with respect to risk are DDT, fenitrothion, and pirimiphos-methyl.

With regards to the environment, this PEA finds that the vast majority of the insecticides used in IRS have harmful effects on fish and other aquatic organisms, as well as bees. As one would expect, larvicides applied directly to water may also be toxic to aquatic life, but the categories of organisms that may be affected vary depending on the larvicial agent. Additionally, while five of the twelve IRS insecticides either persists or bioaccumulates, only DDT both persists and bioaccumulates in the environment.

The environmental action recommended, as a result of the high risk presented by use of some of the chemicals included in the assessment, is a **positive determination**. This determination does not preclude different determinations made in SEAs tiering off from this PEA.

The conditions of this PEA include the key recommendations found within this PEA (described and referenced in the *Executive Summary*). These key recommendations should provide a starting point for country-specific recommendations in SEAs tiering off from this PEA.

APPROVAL OF ENVIRONMENTAL ACTION RECOMMENDED:

CLEARANCE:

Environmental Officer,
Bureau of Global Health: _____ Date: _____
Michael Zeilinger

Environmental Officer,
Africa Bureau: _____ Date: _____
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Environmental Officer,
Asia and Near East Bureau: _____ Date: _____
John O. Wilson

Environmental Officer,
Europe and Eurasia Bureau: _____ Date: _____
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Environmental Officer,
Latin America and
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Victor Bullen

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APPROVAL OF ENVIRONMENTAL ACTION RECOMMENDED:

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Environmental Officer,
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Europe and Eurasia Bureau: __ signed Feb 2, 2007_____
Mohammad Latif

Environmental Officer,
Latin America and
the Caribbean Bureau: ___ signed Feb 26, 2007_____
Victor Bullen

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List of Acronyms

ADD	average daily dose
ATSDR	Agency for Toxic Substances and Disease Registry
BEO	Bureau Environmental Officer
Bti	*Bacillus thuringiensis* israelensis
CAS	Chemical Abstracts Service
CFR	U.S. Code of Federal Regulations
CGIAR	Consultative Group on International Agricultural Research
CSF	cancer slope factor
DAF	dilution and attenuation factor
DDT	dichloro-diphenyl-trichloroethane
EA	environmental assessment
EC	emulsifiable concentrate
EC50	median effective concentration
EIR	entomological inoculation rate
EPA	U.S. Environmental Protection Agency
EXTOXNET	EXtension TOXicology NETwork
GDP	gross domestic product
GEF	Global Environment Fund
GFATM	Global Fund for AIDS, Malaria and Tuberculosis
GIS	geographic information systems
GUP	general use pesticide
HEAST	health effects assessment summary tables
HI	hazard index
HQ	hazard quotient
HSDB	Hazardous Substances Data Bank
IARC	International Agency for Research on Cancer
ICIPE	The International Center for Insect Physiology and Ecology
IEC	Information, Education, and Communication
IEE	Initial Environmental Examination
IPCS	International Program on Chemical Safety
IPM	integrated pest management
IRIS	integrated risk information system
IRS	indoor residual spraying
ITM	insecticide-treated material
ITN	insecticide-treated net
IUCN	The World Conservation Union
IVM	integrated vector management
KAP	knowledge, attitudes, and practices
LADD	lifetime average daily dose
LC50	median lethal concentration
LD50	lethal dose, 50 percent of the test population
LLIN	long-lasting insecticidal net
LOAEL	lowest observed adverse effect level
MEO	Mission Environmental Officer
MHO	Mission Health Officer

MOA	Ministry of Agriculture
MOE	margin of exposure
MOH	Ministry of Health
MOS	Margin of Safety
MPW	Ministry of Public Works
MRL	minimal risk level
MRLs	maximum residue limits
NC	noncancer
NGO	nongovernmental organization
NOAEL	no observed adverse effect level
NOEL	no observed effect level
OFDA	Office of Foreign Disaster Assistance
PAN	Pesticide Action Network
PEA	Programmatic Environmental Assessment
PERSUAP	Pesticide Evaluation Report and Safer Use Action Plan
POPs	persistent organic pollutants
PPE	personal protective equipment
PSCs	pyrethrum spray catches
PVO	private voluntary organization
RAGS	Risk Assessment Guidance for Superfund
RBM	Roll Back Malaria
RED	reregistration eligibility decision
REO	regional environmental officer
RfD	reference dose
RUP	restricted use pesticide
SEA	Supplemental Environmental Assessment
SF	safety factor
SIMA	System Wide Initiative On Malaria And Agriculture
SOP	standard operating procedure
UF	uncertainty factor
ULV	ultra-low volume
UNDP	United Nations Development Program
UNEP	United Nations Environment Program
UNFAO	United Nations Food and Agriculture Organization
UNICEF	United Nations Children’s Fund
USAID	U.S. Agency for International Development
USDA/FAS	U.S. Department of Agriculture/Foreign Agricultural Service
WHO	World Health Organization
WHOPES	WHO Pesticide Evaluation Scheme
WP	wettable powder

Executive Summary

The U.S. Agency for International Development (USAID) Office of Global Health contracted RTI International to conduct a Programmatic Environmental Assessment (PEA) to serve *as an umbrella evaluation of environmental and human health issues* related to malaria vector control and to *assist with the preparation of country- and activity-specific Supplemental Environmental Assessments (SEAs)* for malaria vector control programs. This PEA provides USAID project managers with the policy, procedural, and technical guidelines to *choose appropriate interventions and insecticides* and *develop and implement mitigation and monitoring and evaluation activities*. This, in turn, will allow Missions to design malaria vector control programs in more efficient and cost-effective ways.

The integrated vector management (IVM) PEA is composed of the following sections:

- Section 1—**Introduction**. The introduction provides an overview of the purpose and objectives of the PEA.
- Section 2—**Background on Malaria and Malaria Vector Control**.
- Section 3—**Proposed Actions and Alternatives**. This section discusses proposed actions and alternatives, including indoor residual spraying (IRS), insecticide-treated nets (ITNs) (limited evaluation), environmental management, and larviciding, as well as alternatives that are not recommended (including the "no action" alternative).
- Section 4—**Affected Environment**. This section provides an overview of issues to be considered when discussing the intervention area environment in country specific environmental assessments.
- Section 5—**Human Health and Environmental Consequences.** This section discusses the Phase I screening risk assessment that was conducted for the purpose of informing USAID on the human health risks of IRS, ITNs, and larvicides.
- Section 6—**Mitigation, Monitoring, and Evaluation**.
- Section 7—**Regulatory, Legal, and Institutional Setting**. This section provides an overview of regulatory, policy, and institutional capacity issues to be considered during the preparation of country-specific environmental assessments.
- Section 8—**Training and Institutional Capacity Building**. In this section, the PEA provides suggestions for training and institutional capacity building for program quality and sustainability.
- Section 9—**Cross-Cutting Issues**. Three cross-cutting issues are addressed in this section, including interaction with the agricultural sector, hazardous waste management, and prevention versus treatment of malaria.

- Section 10—**Public Consultation Process**. This section summarizes the public consultation process that was conducted at the scoping stages and for various draft versions of this PEA.
- Section 11—**Bibliography**.

A separate guidance document for preparing SEAs, entitled *Guidance for Developing SEAs for Malaria Vector Control Programs*, can be found in ***Annex C***.

The intended audience and users of this PEA, entitled *Management Programs for Malaria Control: Programmatic Environmental Assessment*, include malaria control program decision makers, designers, and implementers; USAID Washington Program Officers, Mission Health Officers (MHOs), and Mission Environment Officers (MEOs); host country health and environment officials; Office of Foreign Disaster Assistance (OFDA) Officers; individuals preparing Initial Environmental Examinations (IEEs) and SEAs; and the general public.

Key Recommendations

- Prohibit the use of interventions not supported by this PEA (Section 3.5).
- Ensure any intervention chosen complies with international treaties, as well as host country and U.S. government laws, regulations and guidelines (Sections 7.1 and 9.2).
- Use entomological surveillance and disease surveillance to select appropriate locations, interventions, and times for implementation. Location-specific criteria that should be used to select an appropriate intervention include, but are not limited to, climate, vector behavior, vector habitat, cost-effectiveness, pesticide–target environment interactions, political and stakeholder commitment, financial sustainability and human resources, and impacts on agricultural export markets (Sections 6.1 and 9.1).
- Promote host country selection of pesticides based on criteria found in Section 6.1.
- Integrate environmental and human health concerns into the planning stages of the intervention (Section 6.1).
- Determine intervention-specific mitigation, monitoring and evaluation activities to be implemented based on recommendations in this PEA and the insecticide-treated materials (ITM) PEA, as well as consultations with host country stakeholders (Section 6.1).
- Promote host country compliance with requirements and recommendations for dichloro-diphenyl-trichloroethane (DDT) use under the Stockholm Convention (Section 6.1).
- Monitor the implementation and effectiveness of mitigation activities (Section 6.1).

- Monitor the impacts of the intervention on the environment, livestock, workers, and communities. (Environmental monitoring is required for support of DDT use in IRS, and cholinesterase monitoring is required for support of organophosphate use in IRS) (Section 6.1).
- Monitor the effectiveness of the intervention on malaria vector populations (Section 6.1).
- Monitor the effectiveness of the intervention on malaria incidence (Section 6.1).
- Consolidate all monitoring results in a Human Health and Environmental Evaluation report, containing elements listed in the PEA (Section 6.2).
- Adapt management of the malaria vector control program according to results found in the Human Health and Environmental Evaluation Report (Section 6.2).
- Provide training to contractors on factors to consider in intervention and insecticide selection, potential impacts of pesticides, best practices and mitigation measures, adaptive management, and any other identified topics of concern (Section 8.2).
- Provide capacity building activities for senior government officials on factors to consider in intervention and insecticide selection, potential impacts of insecticides, best practices and mitigation measures, appropriate timing and logistics, adaptive management, and any other identified topics of concern (Section 8.3).
- Provide capacity building activities for mid-level management on logistics, data management, best practices and mitigation measures, monitoring and evaluation (of all types mentioned in this PEA), surveillance systems, adaptive management, and any other identified topics of concern (Section 8.4).
- Provide for capacity building of institutions outside the malaria sector to improve intervention mitigation and monitoring capabilities in the host country (Section 8.6).
- Train intervention implementers according to the highest standards available (for instance, WHO guidelines, PEA guidelines, United Nations Food and Agriculture Organization guidelines, equipment manufacturer guidelines, pesticide industry guidelines, ministry guidelines, etc.) (Section 8.5).
- When pesticides are used in an intervention, train pesticide storekeepers, medical practitioners, individuals transporting pesticides, and communities on their roles and responsibilities in preventing unwanted exposure of pesticides (or treating exposure, in the case of medical practitioners) (Section 8.5).
- When hazardous waste or potential obsolete pesticide stocks are identified during planning or implementation of an intervention, follow the protocol described in Section 9.2 of this PEA.

- Assist host countries with activities pertaining to DDT compliance requirements of the Stockholm Convention, if they are using USAID-procured DDT for disease vector control, are Parties to the Convention, and have a DDT use exemption under Stockholm (Section 9.2.3).
- Conduct SEAs to supplement this PEA in accordance with the *Guidance for Developing SEAs for Malaria Vector Control Programs* in ***Annex C***.

1. Introduction

The U.S. Agency for International Development (USAID) estimates 300 to 500 million worldwide cases of malaria occur every year, resulting in up to 2.5 million deaths—mostly among young children. Since the start of USAID's Infectious Disease Initiative in 1998, the Agency has significantly increased its programs and funding to fight malaria, particularly in Africa, where 90 percent of malaria deaths occur. USAID's malaria programs focus on assisting countries to develop the capacity to effectively prevent and treat malaria through an integrated approach—integrated vector management (IVM)—that uses a range of interventions designed to eliminate or greatly reduce malaria transmission. On June 30, 2005, President Bush pledged to increase funding for malaria prevention and treatment by more than $1.2 billion over 5 years, specifically in sub-Saharan Africa. To launch the President's Malaria Initiative, the United States will significantly expand resources for malaria prevention and treatment in Angola, Tanzania, and Uganda starting in 2006; expand to four more highly endemic African countries in 2007; and at least five more in 2008. This effort is expected to cover more than 175 million people in 15 or more of the most affected African countries.

Given this recent expansion of USAID malaria control programs and the Agency's prominent role as a key member of the Roll Back Malaria (RBM) Partnership,[1] it decided to prepare a PEA to evaluate potential generic environmental and human health effects of the various methods composing IVM. As a federal government agency, USAID is subject to U.S. environmental laws and regulations, which are applicable to all its programs, projects, and activities. Implementation of these through environmental impact assessment ensures that USAID development programs are not only economically sustainable but protect the host country's residents, malaria control workers, and environment. Title 22, Code of Federal Regulations, Part 216 (22 CFR 216)—Regulation 216, defines USAID's environmental impact assessment procedures.[2] Regulation 216, Section 216.6 (d) states that "Program Assessments may be appropriate in order 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."

[1] The Roll Back Malaria Partnership, launched in 1998 by the WHO, United Nations Development Program, UNICEF, and the World Bank, aims to provide a coordinated global approach to fighting malaria and halving its burden by 2010.

[2] The complete text of USAID environmental procedures, including pesticides procedures, can be found in **Annex B** of this PEA.

Developing a PEA for IVM is appropriate, as the environmental and human health impacts are, in some respects, generic. The World Health Organization (WHO) only supports the use of twelve pesticides for IRS, and countries generally do not use pesticides that are not supported by WHO for this activity. The potential effects of these IVM chemicals on humans and the environment are similar regardless of location. This PEA addresses the environmental and human health effects of IVM activities that are not country specific. The information contained in this PEA, as indicated by the Code of Federal Regulations, will serve to expedite future USAID environmental documentation processes by providing reference material for Initial Environmental Examinations (IEEs), SEAs, Pesticide Evaluation Reports and Safer Use Action Plans (PERSUAPs), or other individual environmental assessments that address country-specific USAID support for IVM activities.

A preliminary PEA for IVM was prepared in mid-2004. The initial draft was revised in 2005 and 2006, and was vetted with a broad spectrum of stakeholders in Washington, DC, and overseas.

Regulation §216.3(b)—Pesticide Procedures

Factors to be considered when assessing the use of pesticides in project activities:

- EPA registration status of the requested pesticide
- Basis for selection of the requested pesticide
- Extent to which the proposed pesticide use is part of an integrated pest management program
- Proposed method or methods of application, including availability of appropriate application and safety equipment
- Acute and long-term toxicological hazards, either human or environmental, associated with the proposed use and measures available to minimize such hazards
- Effectiveness of the requested pesticide for the proposed use
- Compatibility of the proposed pesticide with target and nontarget ecosystems
- Conditions under which the pesticide is used, including climate, flora, fauna, geography, hydrology, and soils
- Availability and effectiveness of other pesticides or nonchemical control methods
- Requesting country's ability to regulate or control the distribution, storage, use, and disposal of the requested pesticide
- Provisions made for training of users and applicators
- Provisions made for monitoring the use and effectiveness of the pesticide

1.1 Objective of the PEA

The objective of this PEA, as stated in the Scoping Statement (***Annex A***), is to "assist with the preparation of country and activity-specific Supplemental Environmental Assessments (SEAs) and Pesticide Evaluation Reports and Safer Use Action Plans (PERSUAPs) for malaria control projects employing IVM strategies. The intent is that this PEA will serve as an umbrella evaluation of environmental and human health issues related to IVM implementation. The PEA will provide project managers with a technical, policy, and procedural guide for the preparation of environmental assessments of individual projects. Together, the PEA and project assessments are intended to provide a clear basis for deciding, for each project, whether USAID can promote the use of IVM components, and if so, how that should be

done so as to comply with the letter and the spirit of the Agency's environmental regulations."[3]

The intended audience and users of this PEA are USAID Washington Program Officers, Mission Health, and Environment Officers; cooperating country health and environment officials; USAID partners implementing malaria control programs; Office of Foreign Disaster Assistance (OFDA) Officers; consultants preparing Initial Environmental Examinations (IEEs), SEAs, and PERSUAPs; and the general public.

Although this PEA primarily focuses on USAID's malaria control programs, many of the proposed prevention and mitigation measures are relevant to other vector-borne disease control programs, such as dengue fever.

While providing a basis for the development of PEAs, the Code of Federal Regulations also gives specific instructions on what information to consider in developing an environmental assessment (EA) when USAID activities involve the *procurement or use of pesticides*. These Pesticide Procedures are described in the Code of Federal Regulations §216.3(b), which is located in ***Annex B***. It is important to note that the term "use" is interpreted broadly by USAID to include direct or actual acquisition, handling, transport, storage, mixing, loading, application, cleanup, or disposal of pesticides, as well as the indirect support of use, such as provision of fuel for transport of pesticides and providing technical assistance in pesticide management operations. Because countries' IVM strategies typically incorporate methods that use pesticides, the vast majority of EAs conducted for USAID support of IVM must follow these Pesticide Procedures.

Although this PEA fulfills the legal requirement of assessing environmental and health impacts of IVM, a second and perhaps more important aspect of the PEA is its value as a tool for designing and implementing safe, environmentally and socially sound IVM activities. Sound environmental design requires that the human health and environmental impacts associated with various IVM strategies are identified during the design phase and that preventative and mitigation measures are incorporated into the project bidding documents, contracts, and project work plans. Implementation of preventative and mitigation measures should be monitored and evaluated as part of performance progress reports and regular project evaluations.

This PEA provides guidelines and cautions for developing an IVM program. It encourages flexibility within the regulatory bounds of this PEA. Country-specific IVM SEAs and PERSUAPs will provide the level of detail required to define specific IVM options and activities. SEAs and PERSUAPs will more fully compare combinations of IVM tactics to be employed, based on local conditions and risks. This PEA cannot anticipate all combinations of conditions to be encountered in all countries; however, it can identify for closer attention or restrict some of the riskier technology choices, and streamline SEA procedures for lower-risk alternatives.

[3] PEA objective quoted from the PEA Scoping Statement–January 2004.

It should be noted that this PEA does not take the place of technical guidelines for designing and implementing IVM methods.

1.2 PEA Scoping Statement

In January 2004, USAID developed a Scoping Statement, summarized below, for the IVM PEA. The full text of the Scoping Statement and public comment on the statement can be found in ***Annex A***.

In the Scoping Statement, USAID states that this PEA should serve as an umbrella evaluation of environmental and human health issues related to IVM implementation. The PEA is meant to provide project managers with a technical, policy, and procedural guide for the preparation of SEAs that will allow missions to proceed with IVM programs in country. The key issues to be analyzed in detail in the PEA, as defined in the Scoping Statement, are presented in the table below.

Table 1. Key Issues to Be Analyzed in the PEA

Key Issues to Be Addressed	Specific Aspects
Risks to humans from the use of no IVM actions	• Mortality • Morbidity • Social disruption • Impact of economic losses • Shift in focus away from prevention to reaction • Human risks in sum • Uncertainties • Mitigation opportunities
Potential risks to humans from the use of IVM pesticides	• Relatively small quantities of pesticides used with IVM chemical group and formulations available; human risks; uncertainties; mitigation opportunities; toxicity of IVM chemicals to humans, acute and chronic; potential human exposure, oral, dermal, and inhalation; externalities associated with pesticide use and exposure; regulatory and legal issues related to pesticides and health; and enforcement issues related to pesticides and health • Logistics: choice, selection, and availability of least toxic pesticide; labeling toxicity categories by hazard indicator; quality of pesticide and pesticide supplier; proper pesticide labels and training materials in local languages; pesticide distribution from labeled containers to unlabelled containers; pesticide pilferage for unauthorized use or sale; improper pesticide storage; improper pesticide container transport; improper pesticide handling, formulation and use; prohibited empty pesticide container re-use; proper disposal of empty pesticide containers; proper disposal of left-over unusable pesticides; and proper use of safety equipment

Key Issues to Be Addressed	Specific Aspects
	• Training: training on proper use of safety equipment; training on proper calibration of sprayers; presence of pesticide antidotes; proper first aid for pesticide overexposure/poisoning/intoxications; and use of botanical compounds for mosquito treatment • New technologies: use of bacteriological agents for mosquito management; mosquito repellents; mosquito traps containing pesticides; and experimental vaccines • Procedural issue: co-mingling of USAID resources with Ministry of Health (MOH) or other donor pesticides
Potential environmental risks from the use of IVM pesticides, introduction of exotic fish, and water management strategies	• Toxicity of pesticides to nontarget organisms (other than mosquitoes), acute and chronic; invasive species issues with introduction of nonnative fish; environmental consequences; issues of environmental modification of waterways; environmental risks; uncertainties; mitigation opportunities • Toxicity to economically important insects such as crop pollinators; ecosystem disruption through water management strategies; ecosystem disruption through fish introduction; potential soil exposure to pesticides; potential surface and ground water exposure to pesticides; potential protected area and forest resource exposure to pesticides; reduction in biodiversity related to pesticide exposure; potential fishery losses related to pesticide exposure; potential bird losses related to pesticide exposure; pesticide drift from spraying; pesticide bioaccumulation (especially related to dichloro-diphenyl-trichloroethane [DDT]); pesticide wash entering waterways and water resources; disruption of natural predator and pathogen mosquito controls; mosquito resistance to insecticides; resurgence of mosquito populations after predator poisoning; and environmental externalities related to pesticide exposure • New technology: environmental effects of mosquito traps and repellents; and environmental effects of mosquito pheromones
Alternatives to recommended IVM options for malaria control	• Comparison of environmental and health risks and human benefits of different alternatives • Chemical control methods available other than those recommended in this PEA, and risks associated with each • Single tactic approach with and without the use of chemical control methods (e.g., insecticide-treated next [ITN] use alone), efficacy of alternatives in comparison with IVM recommendations, no action, cost comparison of alternative malaria control approaches
Risk mitigation	• What mechanisms are available for reducing adverse effects from IVM pesticide and nonpesticide methods? How effective are they? How reliable?
Decision making	• What criteria should USAID use to decide on whether, when, and how to use various IVM options? • Utilization of WHO guidelines and recommended pesticides • Consideration of the information requirements of the Stockholm Convention before a decision is made to use DDT in an IRS program

Key Issues to Be Addressed	Specific Aspects
	• Comparison of WHO guidelines with EPA regulations • Selection of appropriate pesticides and application methods for use in IVM programs. What criteria to use? • Risks, costs, and efficacy? At discretion of program manager? Availability of effective mitigation? Is this important, or are the benefits overwhelming in all cases? • How adequate are local pesticide regulations, infrastructure, and the institutional settings? • Monitoring: how much is required? For how long? What is a "significant" effect? How to compare risks with benefits? • What would happen in the absence of USAID support for IVM options? • What are the local MOH and larger international (WHO) contexts and frameworks in which programs will operate?
Monitoring mechanisms	• For adverse effects from ITN use and treatment, what mechanisms are available? How effective are they? How reliable?
Components of the Pesticide Evaluation Reports and the Safe Use Action Plans	• The information components to be included in PERSUAPs, which will be part of the SEAs, will be listed in the PEA along with the information, analysis, and mitigation measures that would be needed for any project using IVM options.

1.3 Limitations of the PEA

The Scoping Statement also identified areas that will not be covered by this PEA. These include the following:

- Insecticide-treated nets (ITNs) that require retreatment with insecticides have already been covered in an earlier environmental review, entitled *Programmatic Environmental Assessment for Insecticide-Treated Materials in USAID Activities in Sub-Saharan Africa*. According to the insecticide-treated materials (ITM) PEA, follow-up should be conducted on "continuing research into the potential effects of ITM pesticides" and "better evaluation of the real-life impacts of ITM pesticide use" (p. 52). A risk assessment on malaria control interventions that was conducted for this PEA provides this follow-up with an updated characterization of risks posed to humans through the net-retreatment process. However, this is the only way in which this PEA addresses ITNs, and the reader should refer to the ITM PEA for details on all other aspects of ITN programs, such as environmental consequences, monitoring, and mitigation. Like the interventions addressed in this PEA, USAID is highly supportive of ITN use for malaria vector control.

- Long-lasting insecticidal nets (LLINs),[4] another intervention that USAID supports, will be covered in a revised version of *Programmatic Environmental Assessment for Insecticide-Treated Materials in USAID Activities in Sub-Saharan Africa*.
- Environmental impacts of new technologies under development such as neem, natural pyrethrum, nightshade extracts, copepods, fungi, flatworms, nematodes, diatoms and brown algae, microsporidia and protozoans, predatory bugs and predatory mosquitoes are not covered in this PEA. As these technologies become feasible, economically viable, and commercially available, this PEA should be amended to include them.
- Future scientific findings regarding pesticide safety, for example, pyrethroid insecticides, which comprise the majority of those recommended for mosquito control, may cause human endocrine disruption. This is a poorly understood issue, and in the face of little scientific consensus will not be discussed in depth in this PEA.
- Community small-scale water management (elimination of mosquito breeding sites) enforcement through use of fines, and/or incentives is not addressed in this PEA.

1.4 Assessment Methodology

This PEA was prepared using the numerous secondary sources found in professional journals and in publications by environmental and public health organizations, such as WHO, U.S. Environmental Protection Agency (EPA), the United Nations Food and Agriculture Organization, the United Nations Children's Fund, the World Bank, and others. Public consultation and review was invited at several stages during the PEA process, including review of the scoping statement; review of the initial draft of the PEA; an online discussion of chemicals to be considered by the PEA; a principals meeting held in Washington (March 2006) to comment on the final version of the PEA; and written comments from USAID Mission personnel and interested stakeholders.

[4] LLINs have been developed in response to low retreatment rates of conventional insecticide-treated mosquito nets, especially in Africa. An LLIN is a ready-to-use pretreated mosquito net that requires no further treatment during its expected life span (average 4 to 5 years) (WHO 2002).

2. Background on Malaria and Malaria Vector Control

Malaria acutely infects 300 to 500 million people worldwide, and 1 to 2.5 million people die annually because of the disease. Forty percent of the world's population is at risk of malaria infection. Most of these people live in the world's poorest countries in Africa, Asia, and Latin America. The disease was once present in temperate climates during the mid–twentieth century, but was successfully eliminated. The virulent form of the disease is thought to have been evolving for the past 10,000 years. Malaria is caused by protozoans of the genus *Plasmodium* and is transmitted to humans by mosquitoes of the *Anopheles* genus.

There are four species of human malaria: *Plasmodium vivax*, *P. malariae*, *P. ovale*, and *P. falciparum*. The most common species are *P. vivax* and *P. falciparum*, and the most deadly type of malaria is caused by the latter species. *P. falciparum* is most common in sub-Saharan Africa, which accounts for the exceptionally high malaria mortality rate in this region.

In the late nineteenth century, scientists discovered that the malaria parasite is transmitted from person to person through the bite of female *Anopheles* mosquitoes, which require blood meals to nurture their eggs. *Anopheles* mosquito eggs are deposited individually in slow moving and standing water, where they take several days to mature into adults. One female can produce several hundred eggs over several broods. Adult female mosquitoes bite people from early evening to early morning and, if infected, can transmit the *Plasmodium* parasite to humans. There are between 50 and 60 species of *Anopheles* mosquitoes that transmit malaria worldwide.

When a *Plasmodium*-infected *Anopheles* mosquito takes a blood meal, the parasite enters the human host via the blood system. In the blood stream of the human host, the parasite undergoes a series of changes as part of its complex life cycle. It enters the liver and red blood cells, and finally develops into male and female gametocytes that infect mosquitoes that bite the infected person. Inside the mosquito, the gametocytes mate and form a zygote, which passes from the midgut through various stages until it reaches the salivary glands as sporozoites that are ready to be transmitted to another human when the mosquito takes a blood meal. Parasite development in the mosquito takes 10–14 days or more, depending on species and temperature.

Symptoms of malaria appear about 7–14 days after an infectious mosquito bite, although this varies with different *Plasmodium* species. Typically, malaria produces fever, headache, vomiting, and other flu-like symptoms. It attacks and destroys red blood cells of humans, causing anemia. If drugs are not available for treatment or the parasites are resistant to them, the infection can progress rapidly to become life threatening. Malaria-

infected red blood cells can clog the capillaries that carry blood to the brain (cerebral malaria) or other vital organs, which can cause death.

The clinical features of malaria vary. The classic symptoms include persistent fever, shivering, joint pains, headaches, and repeated vomiting. Severe and complicated malaria causing renal failure, hypoglycemia, anemia, pulmonary edema, shock, and coma can have fatal consequences. Malaria can be cured if promptly diagnosed and adequately treated.

Of the one million people who die annually of malaria, 90 percent of these deaths occur in sub-Saharan Africa, mostly among young children. Many children who survive an episode of severe malaria may suffer from learning impairments or brain damage. Pregnant women and their unborn children are also particularly vulnerable to malaria, which is a major cause of perinatal mortality, low birth weight, and maternal anemia. Outside Africa, approximately two thirds of the remaining cases occur in three countries: Brazil, India, and Sri Lanka. However, malaria is still endemic in more than 100 countries.

Malaria burdens individuals and nations with substantial economic costs. Personal expenditures for malaria prevention include ITNs, ITN retreatment kits, mosquito coils, insecticide sprays, and other protective items. Expenditures on treatment may include doctors' fees, antimalarial drugs, transport to health facilities, and lost wages for caregivers. Public expenditures include government spending to maintain health facilities and health care infrastructures, publicly managed vector control activities, and malaria education and research. In some countries with a heavy malaria burden, the disease may account for as much as 40 percent of public health expenditure, 30–50 percent of inpatient admissions, and up to 50 percent of outpatient visits.

Additional costs of malaria include lower labor productivity (because of sickness and death). This results in lower incomes for individuals and families and lower economic growth in malarious nations. Economists believe that malaria is responsible for a "growth penalty" of up to 1.3 percent per year in some African countries. When compounded over the years, this penalty leads to substantial differences in the gross domestic product (GDP) between countries with and without malaria.

From the late nineteenth century to the early twentieth century, malaria vectors were managed through methods such as wetland drainage (water management) and improvements in housing and screening (physical exclusion). During World War II (1939–1945), the chlorinated hydrocarbon pesticide dichloro-diphenyl-trichloroethane (DDT) was discovered to be extremely effective in controlling mosquitoes, and was used in malaria control as an indoor residual house spray. In the 1950s and early 1960s, WHO conducted mosquito eradication campaigns using DDT. These campaigns were highly effective; however, as mosquito resistance to DDT emerged, costs of the campaigns increased, and efforts to expand campaigns to endemic tropical areas failed, the pursuit of

worldwide malaria eradication was abandoned. Individual countries continued controlling malaria using IRS, with DDT and other chemicals.

World Health Organization Policy on IVM

1. WHO is actively promoting IVM among its Member States to maximize the use of different and most appropriate mosquito control options. In Africa, WHO supports sixteen countries in the development and implementation of national action plans for IVM. These countries developed strategic malaria management plans and have already benefited from staff training on IVM.
2. In January 2003, WHO formalized the Partnership for IVM Program—a framework to coordinate actions for IVM, explore opportunities for mobilizing resources, and identify priority actions at national and international levels.
3. To date, the program has developed a Strategic Framework for IVM for Member States for the Eastern Mediterranean; a training manual on the implementation of IVM published in English and translated into Arabic; and a manual on the use of fish for mosquito control.

In the years following the eradication campaigns, governments relied more heavily on curative services for malaria control. This strategy became problematic with the increasing spread of multi-drug resistant malaria, and consequently highlighted the importance of transmission reduction through vector control. To this end, the distribution of bed nets treated with pyrethroid insecticides, or ITNs, was widely adopted as a malaria control strategy during the 1990s. Use of ITNs and ITMs has increased since 2000, but its success in reducing malaria has varied widely.

IVM emerged as a widely supported malaria control strategy. IVM is a conceptual strategy, rather than a physical strategy. It is a decision-making process for the management of vector populations to reduce or interrupt disease transmission. Contemporary features of IVM include the following:

- Building capacity at the operational level to plan, implement, and monitor and evaluate vector control and its epidemiological and entomological impact
- Emphasizing the management process—that is, the assessment and monitoring used to derive the maximum public health impact from control options
- Using a range of interventions, in combination and synergistically, from environmental management to chemical control
- Collaborating with other public and private sectors that have an impact on vector breeding, such as irrigated agriculture and urban development
- Collaborating with public- and commercial-sector organizations, civil society groups, and the communities themselves to reduce vector breeding, and to adopt more rational and cost-effective control measures.

An IVM-based process should be intrinsically cost effective, have indicators for monitoring efficacy with respect to impact on vector populations and disease transmission, and use acceptable and sustainable approaches compatible with local health systems. It should also ensure compliance with local regulations and customs, and reduce the probability of pesticide resistance in mosquitoes. IVM should recognize that malaria is focal and variable in nature—even within a single district or municipality, there may be

great differences in transmission risk—and, as a result, there is no single answer to vector control that can be applied in all circumstances.

Well-managed vector control programs reduce malaria risk significantly, if they use proven methods for appropriate situations. These methods may include IRS, ITN distribution and retreatment, larviciding of mosquito breeding sites, and environmental management or manipulation.

Even if a country's resources do not allow for full implementation of all chosen vector control interventions, partial implementation may still prove worthwhile. While reducing the rate of malaria transmission through vector control may not have an impact on the parasite prevalence in the community until it is reduced to a very low level, newer analysis shows that an incremental reduction in malaria transmission, or the entomological inoculation rate reduces severe disease (especially severe anemia) and mortality, particularly for children under 1 year of age.

USAID defines IVM as the assessment, choice, implementation, and monitoring of one or more control options for vectors by frontline environmental health workers, communities, and households. USAID states that IVM emphasizes the management process—that is, the assessment and monitoring used to derive the maximum public health impact from control options. Furthermore, USAID considers its own endorsement of IVM an extension of its integrated pest management (IPM) policy developed for the agricultural sector in the 1980s under 22 CFR 216.3(b)(1)(i)(c) (Schroeder, 2003). USAID preferred the IPM concept over one-option pest control systems because it reduced pesticide use and thus pesticide exposure to humans and environment, and it used a multi-pronged approach, which was seen as cheaper and more sustainable in poor countries. However, the primary contrast between IPM and IVM is that IVM uses less insecticide than IPM.

3. Proposed Actions and Alternatives

3.1 IVM Alternatives Evaluated and Not Evaluated in the PEA

The primary impacts of taking no action are disease, human pain and suffering, mortality, a reduction in the quality of life, and economic losses. Malaria affects the health of individuals and national economies alike, and not taking action to control this disease is to not address a major constraint to development. Public and personal expenditures on treatment and prevention, and public-sector expenditures to maintain health care programs and facilities dedicated to malaria create a heavy burden for developing countries. For example, countries with malaria-endemic areas are less able to develop tourism and regional markets or to expand economic activity. A poor quality of life resulting from malaria outbreaks is reflected in suffering and loss of productivity and income on an individual and household level. As the quality of life decreases in general, the natural environment is also affected. For these and many other reasons, the no-action alternative is rejected outright as a nonviable option.

The IVM approach to malaria control emphasizes the development of country- and region-specific programs that integrate the use of chemical and nonchemical vector control methods in a way that reduces or interrupts the transmission of disease.

In organizing this PEA, the malaria control methods assessed have been divided into two categories:

(1) Interventions targeting adult mosquitoes
   - Indoor residual spraying (IRS) using pesticides recommended by the World Health Organization (WHO)
   - Insecticide-treated nets (ITNs) (only human health consequences evaluated)

(2) Interventions targeting mosquito larvae
   - Environmental management methods, including filling breeding sites; lining water sources and canals; physical wetland drainage; biological wetland drainage; impoundment planning; deepening and narrowing of old drains; vegetation manipulation; synchronized cropping and intermittent irrigation; larvivorous fish introduction; and saltwater flooding
   - Larvicidal agents, including bacterial larvicides, methoprene, temephos, and molecular films and oils.

3.2 Methods for Controlling Adults—IRS

IRS is a commonly used malaria vector control method that has been particularly effective in seasonal transmission settings. It is implemented by applying residual insecticides (to which female *Anopheles* mosquitoes have been demonstrated to be

susceptible) to the interior walls of houses and other structures. The insecticide remains on the treated surfaces upon which the mosquitoes will rest before or after taking a blood meal. Several formulations of insecticides are available for this purpose. The residual effect of the insecticide is sufficient to kill resting mosquitoes for a period ranging from 3 to 12 months depending on the insecticide, the surface on which it is applied, and local conditions. The objective of IRS programs is to reduce the mean life span of the female mosquito population below the duration required for development of the parasite life phases that occur in the mosquito, and thereby to substantially reduce the population's ability to sustain malaria transmission. IRS is most effective in areas with seasonal malaria transmission and is typically implemented by teams of spray operators who spray houses in at-risk localities prior to the rainy season, before heavy rains prompt increases in the *Anopheles* vector population. To be effective, IRS must attain coverage rates of at least 85 percent of the houses in a target area.

WHO recommends only twelve chemicals for use in IRS. These twelve and their formulations (Table 2) are evaluated in this PEA.

Table 2. IRS Insecticides Evaluated in this PEA

Commonly Used Pesticide	Formulation
Indoor Residual Spraying	
Bendiocarb	WP
Propoxur	WP
DDT	WP
Fenitrothion	WP
Malathion	WP
Pirimiphos-methyl	WP and EC
Alpha-cypermethrin	WP
Bifenthrin	WP
Cyfluthrin	WP
Deltamethrin	WP
Etofenprox	WP
Lambda-cyhalothrin	WP

EC, emulsifiable concentrate; WP, wettable powder.

3.3 Methods for Controlling Larvae—Larvicidal Agents

Environmental management (either environmental *modification* or *manipulation*) is the method of choice for mosquito control when the mosquito species targeted are concentrated in a small number of discrete habitats (see Section 3.4). In many instances, habitat elimination is not feasible. For these situations, various agents can be applied directly to larval habitats to kill the mosquito larvae. It should be noted that, in most endemic settings, the effectiveness of larval control is extremely limited; thus, it should only be implemented where there is solid entomological monitoring indicating that larval control has an impact. Larvicidal agents include the following:

Bacterial larvicides are bacteria that are registered as pesticides for control of mosquito larvae in outdoor areas such as irrigation ditches, flood water, standing ponds, woodland pools, pastures, tidal water, fresh or saltwater marshes, and storm water retention areas. These products can be applied in the same manner as chemical larvicides. Duration of effectiveness depends primarily on the mosquito species, the environmental conditions, the formulation of the product, and water quality. They are very specific, affecting only mosquitoes, black flies, and midges. Microbial larvicides may be used along with other mosquito control measures in an IVM program. The microbial larvicides used for mosquito control are *Bacillus thuringiensis* israelensis *(Bti)* and *Bacillus sphaericus (B. sphaericus)*:

- *Bti* is a naturally occurring soil bacterium registered for control of mosquito larvae. *Bti* was first registered by U.S. Environmental Protection Agency (EPA) as an insecticide in 1983. Mosquito larvae eat the *Bti* product that is made up of the dormant spore form of the bacterium and an associated pure toxin. The toxin disrupts the gut in the mosquito by binding to receptor cells present in insects, but not in mammals.
- *B. sphaericus* is a naturally occurring bacterium that is found throughout the world. *B. sphaericus* was initially registered by the EPA in 1991 for use against various kinds of mosquito larvae. Mosquito larvae ingest the bacteria, and as with *Bti*, the toxin disrupts the gut in the mosquito by binding to receptor cells present in insects but not in mammals.

Methoprene is a compound first registered by the EPA in 1975 that mimics the action of an insect growth-regulating hormone and prevents the normal maturation of insect larvae. Methoprene is specific to mosquitoes and can be applied in the same way as chemical larvicides.

Temephos is an organophosphate pesticide registered by EPA in 1965 to control mosquito larvae, and is the only organophosphate with larvicidal use. In 2000, EPA identified occupational risks of Temephos and imposed risk mitigation measures to protect workers and applicators. It is an important resistance management tool for mosquito control programs; its use helps prevent mosquitoes from developing resistance to the bacterial larvicides. Temephos is used in areas of standing water, shallow ponds,

swamps, marshes, and intertidal zones. It may be used along with other mosquito control measures in an IVM program. Temephos can be applied by backpack sprayers and right-of-way sprayers in either liquid or granular form.

Monomolecular films are low-toxicity pesticides that spread a thin film on the surface of water, making it difficult for mosquito larvae, pupae, and emerging adults to attach to the water's surface and causing them to drown. Films typically remain active for 10–14 days on standing water.

Monomolecular oils, like films, are pesticides used to form a coating on the surface of water to drown larvae, pupae, and emerging adult mosquitoes. The oils are specially derived from petroleum distillates.

3.4 Methods for Controlling Larvae—Environmental Management

Environmental management for mosquito control aims to induce changes in the environment to disrupt the mosquito life cycle and reduce its propagation by eliminating breeding sites. As the aquatic environment is critical to the mosquito life cycle, environmental management introduces changes to the local hydrology or water-use practices.

Environmental management is a particularly effective approach where mosquito breeding habitats are located in relatively small-scale and readily identifiable areas. It is well-suited to areas that have a high human population density (e.g., urban settings). Environmental management is not intended to replace other control strategies, but rather it aims to help provide a foundation for an integrated approach while reducing human and environmental exposure to insecticides (Lindsay, Summary Report).

Environmental management was used extensively in the early 1900s to control malaria. Beginning in the 1950s, insecticides and antimalarial drugs became the primary tools used to combat this disease. Over the course of time, it has become apparent that what environmental management may lack in short-term effectiveness, compared with insecticides, is compensated for by its ability to control the disease in the long term.

Although little cost-benefit analysis has been done to determine the long- and short-term impacts of environmental management, it would appear that its greatest limitation is the potential *initial* high cost. However, the initial costs associated with environmental management may be negligible if they are conducted as part of a broader development initiative. For example, a city drainage scheme may be designed in a manner that also helps to reduce mosquito breeding sites (Lindsay, Summary Report).

Environmental management can be divided into two compatible approaches:

(1) **Environmental Modification.** Environmental modification implies permanent changes such as landscaping, drainage, land reclamation and filling. It will often entail minor or major infrastructure and may require significant capital investment.

(2) **Environmental Manipulation.** Environmental manipulation is a recurrent activity, requiring proper planning and operation, such as removing aquatic weeds from irrigation and drainage canals, and environmental clean up in urban areas. Environmental manipulation can also include the introduction of larvivorous fish. Environmental manipulation can be incorporated into conventional agricultural practices. Its costs are usually modest, but recurrent.

3.4.1 Environmental Modification

Filling Breeding Sites. Potential mosquito breeding sites can be removed by filling abandoned ditches, borrow pits, ponds, and puddling. Breeding sites are particularly effective in increasing malaria transmission if they are located close to human settlements. Refuse can be used for filling such sites, provided the refuse is compacted and covered in earth to reduce fly problems.

Lining Water Sources and Canals. Hoof- and footprints make ideal breeding habitats for some mosquito species. Lining the edges of community water sources and irrigation canals, or building bridges across common water crossings, can reduce the formation of mosquito breeding habitat. Lining irrigation canals with concrete not only reduces the risk of creating mosquito breeding sites, but also saves water. A concrete lining will increase water flow that, in turn, washes the aquatic stages of mosquitoes out of canal networks. Additionally, if the lining is kept clean of vegetation, it will prevent the establishment of some species of mosquitoes. The reduced water seepage associated with lined canals may also reduce mosquito breeding.

Physical Wetland Drainage

- **Surface Drainage.**[5] A well-constructed drainage system can prevent the formation of small bodies of water suitable for the aquatic stages of mosquitoes. The straightening of streams and the removal of vegetation from stream banks creates conditions for the aquatic stages of mosquitoes to be washed into streams, potentially becoming prey to larvivorous fish.

  Surface drainage requires improving water courses and constructing ditches. These modifications should be constructed following the existing water course in order to prevent water pooling along the drainage channel. Lining drains with concrete, stone, or brick will increase water flow and reduce siltation and weed growth.
- **Subsoil Drainage.** Subsurface drainage is used in wet areas to prevent water logging, improve aeration, and reduce salinization. With this technique, drainage

[5] In many instances, a lack of proper drainage reflects the economic realities of irrigation development, which often is only marginally profitable. Including a drainage component as part of an irrigation activity often pulls the internal rate of return of a project in "the red" and renders the proposed development economically unfeasible.

channels are constructed to provide an outlet for accumulated water. Channels can be filled with rock, rubble, or gravel and covered with vegetation, stones, or pipes.

- **Coastal Swamp Drainage.** Constructing embankments to prevent seawater inundation at high tides can assist drainage of some coastal swamps. Pipes fitted into the embankments with an automatic outflow gate will allow water from the lagoon to be drained at low tide.

Biological Wetland Drainage. Tree planting also has been used to drain boggy ground and has been used as part of an integrated program to reduce malaria transmission and help reforestation for the provision of wood and improvement of water management in Gujarat, India. This approach combines improved drainage and filling with planting of *Eucalyptus* trees. The approach has been used in Zambia to convert a once-prolific area of mosquito breeding in a peri-urban area into a public park.

Impoundments. Impoundment is used to hold water behind an artificial barrier—reservoirs behind dams or small storage ponds. When dams are constructed, mosquito numbers generally fall if many small water bodies are combined into one large area of water. If mosquito larvae occur within dams, the larvae are usually confined to the shoreline as many fish are rapacious predators of mosquito larvae. Mosquito populations will only increase if floating vegetation shields the aquatic stages of mosquitoes from predators. There are several dam design and operation techniques that can be used to reduce the threat of malaria.

3.4.2 Environmental Manipulation

Deepening and Narrowing of Old Drains. The deepening and narrowing of old drains can be used to change the rate of water flow. This technique can be used to create conditions that are not conducive to mosquito breeding.

Vegetation Manipulation. The manipulation of vegetation can be an effective tool to create conditions that are not suitable for mosquito breeding. Tree planting can be used to create shade, and tree removal can be used to expose mosquito breeding sites to direct sun light. Vegetation manipulation can also be used in combination with other environmental modification or manipulation interventions (e.g., swamp draining and ditch filling).

In coastal regions, saltwater lagoons with high algae populations are preferred habitats for some mosquito species. Algae populations can also increase the incidence of mosquito breeding in irrigation canals as the algae may reduce the flow of water. The clearing of algae from these areas has led to high mosquito larvae mortality because it increases fish predation on the mosquito larvae. The algae are most often cleared manually with hoes or rakes.

In some locales, vegetation is actually added to the body of water to reduce the preferred habitat for vectors. Plants in the *Azollaceae* family have substantially reduced malaria vector breeding habitats in various locations in India and Sri Lanka.

Synchronized Cropping and Intermittent Irrigation. Using the synchronized cropping method for rice as an example, rice paddies are left dry for 2 months each year. The periodic wet and dry rice agriculture has led to a significant reduction of adult mosquito populations in Indonesia. Alternatively, fields can be flooded for several days and then left to dry.

Case Study: Larvivorous Fish

In India, *Poecilia reticulata* and *Gambusia affinis* are being mass-produced by fish farmers as part of an environmental management malaria control program. The cost associated with mass fish production and distribution is low because the farmers participate. Under the program, fish are produced in hatcheries and transported to the villages, where they are introduced into village fish ponds.

Improving village income through the sustainable use of natural resources is an important component. Carp fish (a source of farmer food and income) are grown along with *G. affinis* in the farmer's fish ponds.

The tendency of *G. affinis* to remain near the margins of the fish ponds convinced farmers that *G. affinis* does not compete with edible fish for space and food, while it feeds on mosquito larvae at the margins.

Gradually, the practice spread to other farmers in the village. The fish were cultured together for 2 years and there was no adverse impact of *G. affinis* on edible Carp fish. In fact, the mosquito nuisance in the areas culturing *G. affinis* went down to such low levels that it encouraged other farmers to produce *G. affinis* in their ponds. As a result, *G. affinis* fish stocks were available in large numbers.

Larvivorous Fish Introduction. As its name suggests, this approach introduces fish that prey on mosquito larvae into mosquito breeding sites. The use of predatory fish to feed on water-borne mosquito larvae has been one of the most effective biological control interventions for malaria. *Gambusia affinis*, a native of Texas, and *Poecilia reticulate*, a native of South America, have been used in vector control programs around the world for the past 50 years (see text box).

To be successful, certain characteristics are required of the fish species. The fish selected must be a surface feeder, as mosquito larvae are only found on the water surface. In

addition, the fish must be hardy enough to survive transport to the breeding area, variations of water quality and turbidity, and temperature variations.

Several potential negative environmental impacts are associated with introducing larvivorous fish. For example, the introduced fish could potentially have a severe impact on local indigenous fish populations. For this reason, introducing fish into natural environments (e.g., rivers, streams, and ponds) is not recommended. Instead, the introduction of larvivorous fish should be limited to man-made environments—underground and overhead tanks, abandoned septic tanks, open and blocked drains, storm water drains, road culverts, irrigation canals, abandoned wells, and commercial fish ponds.

With the above considerations in mind, the use of local indigenous fish species are preferred over the introduction of exotic fish species. Unfortunately, there remains a need to find species that are adapted to survival under local conditions and in temporary habitats.

Saltwater Flooding. Saltwater flooding can be used to create a habitat that is not conducive to mosquito breeding. For example, flood dikes can be constructed to flood lagoons with salt water. Saltwater flooding can also be used in association with drainage systems (e.g., fish ponds and irrigation systems).

3.5 Alternatives Not Recommended by this Assessment

This PEA strongly recommends against ***spraying open spaces*** around villages or open water sources by aircraft or truck-mounted sprayers or ***spraying room spaces*** (not walls) inside houses as routine control measures. These methods needlessly expose humans and the environment to highly absorbable and potentially dangerous concentrations of insecticide. Furthermore, these two methods waste large quantities of insecticides and require high degrees of coordination and infrastructure, making them very costly options.

This PEA also does not recommend using ***pyrethroid-based larvicides***. Pyrethroids are highly toxic to aquatic life, and water where pyrethroids have been applied should not be used for drinking or bathing water by humans. Additionally, ***motor oil*** should not be used for larviciding.

To prevent epidemics, for instance, during floods and around concentrated populations of refugees, emergency programs, such as those administered by the Office of Foreign Disaster Assistance, may require the use of aerial or truck-mounted sprayers with ultra-low volume (ULV) equipment that produces a fog of droplet-size insecticide. ULV application also requires insecticides to be in technical or very high concentrations of active ingredient. When using ULV methods, precautions need to be taken to make sure that only highly trained insecticide applicators are used and that targeted populations are protected from exposure to the insecticide application. Long-lasting insecticidal nets, tarps, and tents will round out the emergency approach.

3.6 A Note on Developing Technologies

With few exceptions, most of the following controls have not been thoroughly studied, developed, or commercialized. Most work better in laboratory trials than in nature and are not able to recycle themselves in nature; thus, they have little or no commercial value. In various developing country settings, some of these agents may help supplement other control tactics in IVM programs.

Neem Oil. Research in India (Nagpal et al., 1995) has shown that 5 percent neem tree extracts soaked into wood balls controlled *Anopheles stephensi* and *Aedes aegypti* breeding in water storage overhead tanks for 45 days. The International Center for Insect Physiology and Ecology (ICIPE) in Nairobi, Kenya, runs a regional project titled Botanicals for Malaria Control. ICIPE found that neem controlled larvae in the laboratory and in the field. In the field, 1 percent and 3 percent applications halted mosquito pupation during a period of 3 weeks. In addition, mosquito eggs deposited after application either had delayed/abnormal hatching, or failed to hatch. Neem oil holds promise as a locally produced botanical insecticide for local development projects.

Nightshade Extracts. Singh and Bansal (2003) found extracts from the fruit and roots of Indian nightshade to be lethal to *A. culicifacies* and *A. stephensi* larvae. With more study, these may provide an additional larvicidal control agent that villagers could prepare themselves.

Natural Pyrethrum. Extracted from chrysanthemum plants, natural pyrethrum provides a mix of naturally occurring pyrethrins that kill flies, mosquitoes, and related insects. Kenya, the country that pioneered the development of pyrethrum, has three natural pyrethrum emulsifiable concentrate (EC) products under temporary registration for use against mosquitoes: one for larvae, one for adults, and one for mosquito net impregnation (Kenya Pest Control Product Board, 2004).

Copepods. Several species of copepods (small crustaceans) have been found to control mosquito larvae in Australia, Oceana, Brazil, and Vietnam. *Mesocyclops longisetus*, *Metacyclops mendocinus*, *Tropocyclops prasinus*, *Eucyclops serrulatus*, *Eucyclops solitarius*, *Eucyclops ensifer*, and *Macrocyclops albidus* are potential biological control agents for disease-bearing anopheline mosquitoes. In Honduras, another species, *Mesocyclops thermocyclopoides*, provides reasonable control of mosquitoes. Copepods can be easily transported, either actively or passively, often as resistant dry stages, making them a keen biological control agent.

Flatworms. Certain species of *Turbellaria* flatworms attack mosquito larvae in nature; however, there is no commercial potential for their use at the present time.

Nematodes. *Romanomermis iyengari* has been found to be effective parasites of aquatic stages of mosquitoes in rice fields. With more research on production and storage, this genus of nematode may provide a reasonable natural control agent. Salinity, narrow temperature range, and desiccation are limiting factors in establishment and infectivity of *Romanomermis* nematodes. An additional species, *Octomyomermis muspratti*, though

difficult to mass produce and with asynchronous egg hatching, is tolerant of salinity, pollution, and desiccation, and has the potential for dispersal by infected adult mosquitoes.

Fungi. The fungus *Erynia aquatica* is a species known to infect the immature aquatic stages of mosquitoes. The fungus has characteristics that make it an attractive microbial agent: it is capable of causing epizootics; it has been found in both freshwater and brackish water mosquitoes; and it has a resting spore stage that may survive well in storage. The fungus has been found in cooler temperate waters, and thus may not be appropriate for use in the tropics. However, similar species may exist in the tropics, and this topic deserves research focus.

The aquatic fungus *Coelomomyces indicus* has been found to be naturally present in the rice fields infecting anophelines and culicines. Experimental infection of *A. subpictus* larvae by this fungus showed that a crustacean, *Mesocyclops leuckarti*, acts as an intermediate host.

Further, there are species of *Metarhizium*, such as *M. anisopliae*, that may hold promise in the future as mosquito controls, and they have been found to be infectious in a wide range of species.

Diatoms/Brown Algae. Similar to fungi in appearance and life cycle, but more closely related to diatoms and brown algae, *Lagenidium giganteum* is called a "water mold." It parasitizes the larval stage of mosquitoes. The infective stage is a highly mobile spore that searches out and infects mosquito larvae. It will infect and kill most species of mosquito breeding in fresh water and is active at temperatures of 16–32°C.

L. giganteum is both very host specific and has the ability, following a single application, to recycle for months or even years in a given breeding habitat. It has been registered for mosquito control by EPA under the trade name Liginex.

Microsporidia/Protozoans. Two microsporidia (*Nosema algerae* and *Amblyospora indicola*) will infect mosquito larvae. The infection leads to a chronic disease that causes the eventual death of the host. *N. algerae* and *Vavraia culicis* decrease longevity and fecundity in adult mosquitoes; however, they do not show sufficient ability to recycle nor to cause extensive larval mortality. These factors limit their effectiveness as biological control agents. Further, and more important, several species of microsporidia are potential human pathogens, and the taxonomy of the group is not well understood. As a result, research into the use of microsporidia as mosquito control agents has been put on hold.

Mosquito Viruses. Mosquitoes are infected by several viruses. Of these, the baculovirus group, which causes high infectivity and pathogenicity, offers the most promise for biological control potential. However, most virus agents are difficult to mass produce and store for long periods of time. Further study of these, especially in developing countries, is merited.

Predatory Vertebrates. Many species of bats and birds are voracious feeders on mosquito adults, and their protection should be ensured. However, their feeding is not generally sufficient to fully control malarial adult mosquitoes.

Predatory Bugs. Many species of water-going predaceous insects, such as dragonfly larvae and water bugs, eat mosquito larvae and pupae. For instance, adults and nymphs of *Anisops bouveri* will feed on mosquito larvae. Insecticides meant to control mosquito larvae, like temephos and methoprene, will also be toxic to these predators. Oils and monomolecular films may also drown predatory insects that rely on water surface tension for movement or breathing.

Predatory Mosquitoes. Larvae of the mosquito genus *Toxorhynchites*, such as *T. lendens,* will attack and kill mosquito larvae. However, some species are very selective in their oviposition sites, limiting them to tree holes and containers, which greatly restrict their usefulness.

4. Affected Environment

CFR 22 §216 requires that environmental assessments describe the affected environment in detail and identify any potential adverse affects on that environment. Additionally, it requires that environmental assessments of pesticide use describe the "conditions under which the pesticide is used, including climate, flora, fauna, geography, hydrology, and soils." This Programmatic Environmental Assessment (PEA) is broad by nature; and, as such, it cannot provide adequate descriptions of the diverse environments where USAID will support malaria control interventions. Thus, Supplemental Environmental Assessments (SEAs) or Pesticide Evaluation Report and Safer Use Action Plans (PERSUAPs) that fall under the purview of this PEA must address the affected environment on a country-by-country basis.

When SEAs or PERSUAPs address pesticide use for malaria control, most aspects of the affected environment can be detailed in the Pesticide Procedures portion of the document. These aspects include the following:

- Climate of affected/targeted area
- Flora and fauna in affected/targeted area, with specific concern for
  - Endangered species that could be harmed by pesticide exposure
  - Protected areas, forest and water resources where spraying of pesticides should not take place, and where buffer zones may be warranted
- Geography of affected/targeted area
- Hydrology of affected/targeted area
- Soils of affected/targeted area

Other aspects of the affected environment can be addressed in the Affected Environment section, including the following:

- Malaria incidence and prevalence in the country and identification of endemic and epidemic-prone areas (interventions must be conducted where the need is greatest)
- Population in targeted area
- Administrative boundaries
- Socioeconomic data
- Land area targeted
- Ecological zones
- Endangered species that could be harmed by water management techniques (specifically for environmental management)
- Water resources that may be affected by water management strategies (specifically for environmental management)

Further guidance on writing the Affected Environment section of SEAs and PERSUAPs is provided in the SEA Guidance Document in ***Annex C***.

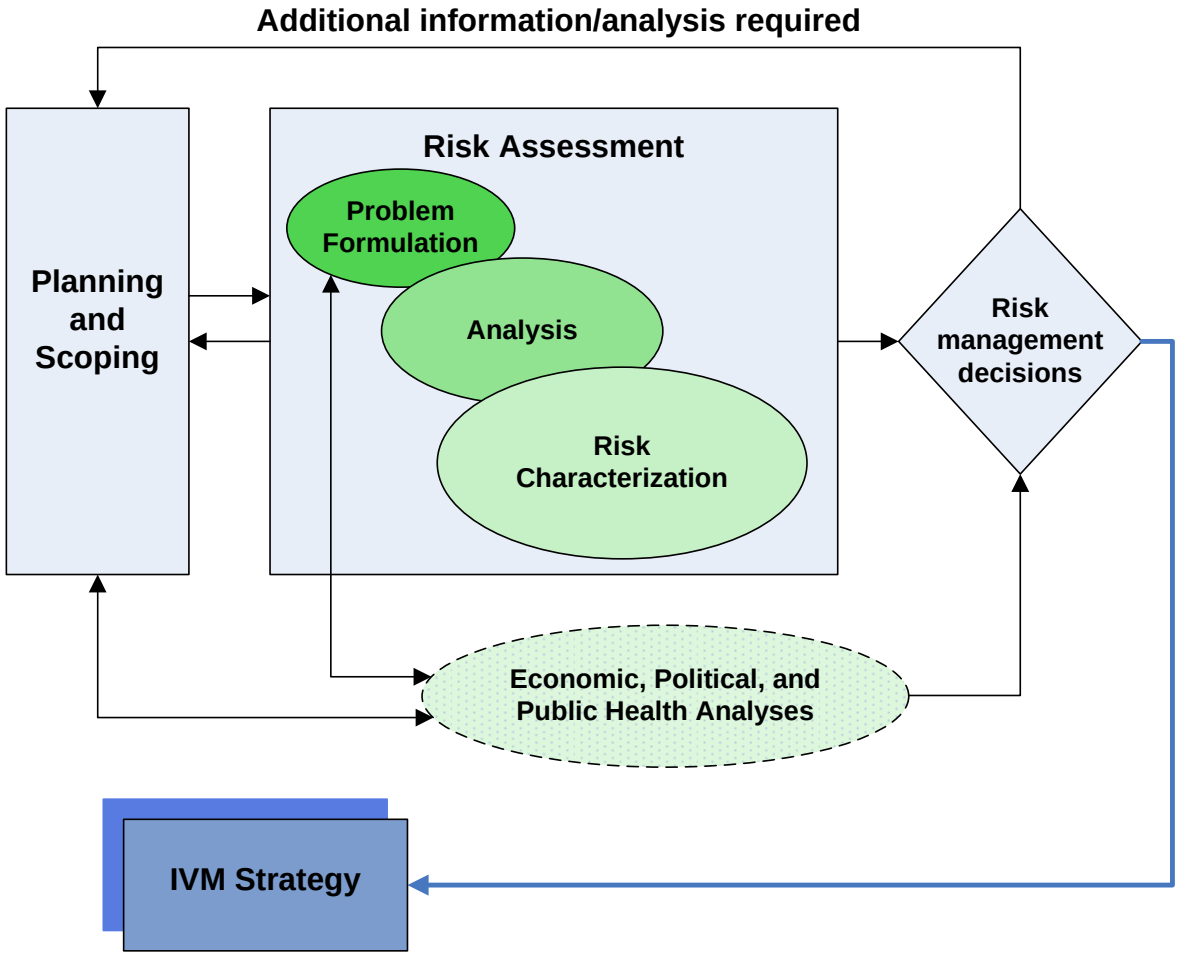
5. Human Health and Environmental Consequences

5.1 Human Health Consequences: Indoor Residual Spraying (IRS), Insecticide-Treated Nets (ITNs), and Larviciding

As part of this PEA, RTI risk assessors developed toxicity profiles and conducted screening assessments for the pesticides used in interventions covered in this PEA. The U.S. Environmental Protection Agency (EPA) provided technical input on the screening tool, which was also peer reviewed by Dr. Douglas Crawford-Brown, Director of the Carolina Environmental Program at the University of North Carolina at Chapel Hill. The risk assessment provides a comprehensive review of the human health effects of malaria vector control interventions. By addressing the exposure pathways specific to IRS, ITN retreatment, and larviciding, the assessment establishes baseline information on the acute, intermediate, and chronic effects of chemicals used in malaria vector control on workers and the general population. No other studies have reviewed the human health impacts of malaria vector control in such an extensive manner. This risk assessment will thus provide USAID with a clearer understanding of the potential effects of its malaria vector control support activities as well as guidance for mitigation actions.

The risk assessment process described is often presented according to three major phases—problem formulation, analysis, and risk characterization—that feed into the decision-making process; this risk assessment adopted a basic framework from recent risk assessment frameworks developed by the EPA (U.S. EPA, 2003, 2004). As Figure 1 suggests, these three phases are not only linked in an iterative framework, but the risk assessment is inextricably linked to the decision-making process. Therefore, the results of the risk assessment may be used to support decisions regarding the appropriateness of the IVM strategy as well as to inform additional data collection and analysis.

Figure 1. Role of the Risk Assessment Framework in Developing IVM Strategy



The remainder of this section describes the risk assessment process, as follows:

- **Section 5.1.1, Problem Formulation,** describes the IVM practices and pesticides covered, presents the conceptual models developed to frame the exposure assessment, and summarizes pesticide characteristics relevant to environmental behavior and health effects. This phase of the risk assessment, which is often referred to as hazard characterization, synthesizes information on the chemical contaminants (in this case, pesticides), application practices and formulations, and potentially exposed receptors. The key activities in the problem formulation are the development of conceptual models and the preparation of an analysis plan.
- **Section 5.1.2, Analysis,** identifies the exposure scenarios assessed in the screening risk assessment and provides a concise description of the methodology developed for the screening risk assessment. The analysis plan describes the selection of algorithms and the key assumptions and data inputs (e.g., exposure duration) required by the screening model. In addition, the selection of health

benchmarks and the calculations for cancer risk and noncancer hazard are presented.

- **Section 5.1.3, Risk Characterization,** presents and discusses the noncancer and cancer risk results of each of the IVM practices and exposure scenarios evaluated in this report. In addition to summarizing the quantitative results, the risk characterization includes a narrative discussion that interprets the results, identifying key uncertainties and limitations in the assessment, providing recommendations for additional data collection and/or analyses, where appropriate.
- **Section 5.1.4, References,** lists the sources referenced in the report.

5.1.1 Problem Formulation

This section describes the problem formulation phase of the risk assessment process, by focusing on defining the "dimensions" for the assessment, which include (1) identifying the practices and stressors (e.g., chemical, physical, or biological) to which humans are exposed, (2) characterizing the properties of the stressors relevant to environmental behavior (e.g., persistence) and toxicity, and (3) describing how stressor releases occur and how humans are likely to be exposed (e.g., acute exposure via dermal contact). The intent of the problem formulation is to characterize the potential hazards associated with the stressors—in this case, pesticides used in IVM for malaria control—and use that information to develop the analysis plan for exposure and risk estimation.

5.1.1.1 IVM Interventions and Pesticides

The following three types of interventions are considered in this risk assessment:

(1) IRS

(2) ITNs

(3) Larviciding

Certain activities are common across all three interventions, such as mixing or preparing the pesticide formulation from a wettable powder (WP) or emulsifiable concentrate (EC) before application. In addition, releases can potentially occur at other points in the lifecycle of the pesticide, including

- **Disposal** of pesticide residuals (e.g., after treating nets) or expired pesticide
- **Reuse of pesticide containers** for drinking water or food
- **Storage** and mishandling of pesticide containers in sheds

The usage of pesticides in the IVM practices, along with the activities required to manage pesticides and pesticide containers throughout the lifecycle of the product, are the primary focus of the conceptual exposure models described in Section 5.1.1.2. Pilferage and subsequent use of stolen pesticides were not included in this screening risk assessment, as data on the parameters for such use cannot be obtained.

Pesticides used for IVM practices vary with respect to physical, chemical, and ecotoxicological properties and cost. In addition, mosquitoes can quickly build up resistance to a particular pesticide. Therefore, effective vector management requires that several alternative pesticides be available for each practice. The pesticides shown in Table 3 are the chemical stressors evaluated for this screening assessment; insecticides that were approved by the World Health Organization (WHO) for IRS and ITNs were addressed, as well as larvicidal agents approved by EPA (see http://www.epa.gov/pesticides/health/mosquitoes/larvicides4mosquitoes.htm). The properties and health effects of these pesticides are described in Section 5.1.1.2.

Table 3. Pesticide Use by Intervention

Pesticide	IRS	ITNs	Larviciding	Pesticide Class	WHO Class[1]	EPA Status[2]	EPA Class[3]	EPA Restrictions[4]
Alpha-cypermethrin	•	•		Synthetic Pyrethroid	II: Moderately Hazardous	Cancelled	No concensus value	n/a
Bendiocarb	•			Carbamate	II: Moderately Hazardous	Cancelled	II: Warning	GUP, RUP
Bifenthrin	•			Synthetic Pyrethroid	II: Moderately Hazardous	Active	II: Warning	RUP
Cyfluthrin	•	•		Synthetic Pyrethroid	II: Moderately Hazardous	Active	I, II: Danger, Warning	GUP, RUP
DDT[5]	•			Organochlorine	II: Moderately Hazardous	Cancelled	II: Warning	n/a
Deltamethrin	•	•		Synthetic Pyrethroid	II: Moderately Hazardous	Active	II, III: Warning, Caution	GUP, RUP
Etofenprox	•	•		Synthetic Pyrethroid	U: Unlikely to present acute hazard in normal use	Active	III: Caution	GUP
Fenitrothion[6]	•			Organo-phosphate	II: Moderately Hazardous	Active,	III: Caution	GUP
Lambda-cyhalothrin	•	•		Synthetic Pyrethroid	II: Moderately Hazardous	Active	II: Warning	RUP
Malathion	•			Organo-phosphate	III: Slightly Hazardous	Active	III: Caution	GUP
Methoprene			•	Insect Growth Regulator	U: Unlikely to present acute hazard in normal use	Active	IV: No Labeling Requirement	GUP
Permethrin		•		Synthetic	II:	Active	II III: Warning,	GUP, RUP

Pesticide	IRS	ITNs	Larviciding	Pesticide Class	WHO Class[1]	EPA Status[2]	EPA Class[3]	EPA Restrictions[4]
				Pyrethroid	Moderately Hazardous		Caution	
Pirimiphos-methyl	•			Organo-phosphate	III: Slightly Hazardous	Active	II III: Warning, Caution	GUP
Propoxur	•			Carbamate	II: Moderately Hazardous	Active	I, II, III: Danger, Warning, Caution	GUP, RUP
Temephos			•	Organo-phosphate	U: Unlikely to present acute hazard in normal use	Active	III: Caution	GUP

GUP, General Use Pesticide; RUP, Restricted Use Pesticide. RUPs can only be used in the United States by trained, certified applicators; usually an indication of risk concerns that must be mitigated in some way.

[1] The classification distinguishes between the more and the less hazardous forms of each pesticide, in that it is based on the toxicity of the technical compound and on its formulations. In particular, allowance is made for the lesser hazards from solids as compared with liquids. The classification is based primarily on the acute oral and dermal toxicity to the rat since these determinations are standard procedures in toxicology. Where the dermal LD_{50} value of a compound is such that it would place it in a more restrictive class than the oral LD_{50} value would indicate, the compound will always be classified in the more restrictive class. Provision is made for the classification of a particular compound to be adjusted if, for any reason, the acute hazard to man differs from that indicated by LD_{50} assessments alone. Table 4 below indicates how WHO determines the toxicity class for pesticides; the terms "solids" and "liquids" refer to the physical state of the active ingredient being classified.

[2] EPA *Registration Status* refers to whether there are any brands or formulations of the pesticide that are registered with EPA as legally available for sale in the United States. If there are, the chemical has an “Active” status; if not it has a “Cancelled” status. It is important to note that the United States, where EPA registration is effective, does not have a malaria problem, does not perform IRS, and has little market for pesticides with important health uses (and where it does use them, generally uses small amounts). Therein lies one of the issues with relying heavily on EPA registration. Many markets are too small for manufacturers to attempt to gain registration status. Therefore, many products that might receive active registration status for the small amounts of insecticide used in health programs, had the United States had a problem with malaria and performed wall spraying, never do. Likewise the EPA will not have specific user risk data for IRS applications nor would it have conducted a risk assessment for that specific use pattern, because IRS applications are not performed in the United States. On the other hand, a product may be registered by EPA, but due to risk concerns, risk mitigation measures could be imposed on its continued use. These risk mitigation measures are often relatively sophisticated and may be difficult to use under developing country conditions.

[3] This table indicates how EPA determines the toxicity class for pesticides.

[4] Some trade names and formulations for the same insecticide active ingredient may be either RUP or GUP, depending on formulation.

[5] DDT is listed in Annex B of the Stockholm Convention on Persistent Organic Pollutants. Parties must register with the Secretariat to use DDT for disease vector control and comply with information collection requirements on production and use of DDT.

[6] Fenitrothion is listed as a GUP. This classification is for the ant bait formulation. Outdoor uses of fenitrothion needed to be RUP for acute and chronic toxicity to nontarget species.

Table 4. U.S. Pesticide Registration Status Determination of Same or Similar Use Patterns

Pesticide	IRS	ITNs	Larviciding	U.S. Registration for Same or Similar Use Pattern	U.S. Registration but No Same or Similar Use Pattern	No U.S. Registration	Notes
Bifenthrin	•			•			Bed nets, indoor carpet, floors, aerosols, and bedding treatments
Cyfluthrin	•	•		•			Multiple residential uses, including foggers and indoor carpets
Deltamethrin	•	•		•			Multiple residential uses, including paint additive, human bedding, and clothing
Etofenprox	•	•		•			Multiple residential uses, including foggers and aerosols
Lambda-cyhalothrin	•	•		•			Multiple residential uses, including bedding
Methoprene			•	•			Larvicide; indoor fog use
Permethrin		•		•			Dust, aerosol, fogger, lice bedding spray, and residential uses
Propoxur	•			•			Multiple residential uses, fogger, and aerosols
Temephos			•	•			Larvicide; multiple public health uses
Fenitrothion	•				•		Many uses broad-spectrum insecticide uses cancelled; only US registered use is in ant/roach baits, child resistant packaging
Malathion	•				•		No residential uses
Pirimiphos-methyl	•				•		No residential uses
Alpha-Cypermethrin	•	•				•	Not Registered—but other forms of cypermethrin registered for residential uses
Bendiocarb	•					•	Cancelled—All uses voluntarily cancelled, 1999; did include residential (carpets, furniture, baseboards, and

Pesticide	IRS	ITNs	Larviciding	U.S. Registration for Same or Similar Use Pattern	U.S. Registration but No Same or Similar Use Pattern	No U.S. Registration	Notes
							floors); risks of concern identified
DDT	•					•	Cancelled

5.1.1.2 Properties and Health Effects of Pesticides

Chemical–Physical Properties

A key component of the problem formulation is the evaluation of data on the environmental behavior of pesticides, such as chemical and physical properties. These properties are assessed to describe a chemical's partitioning between the solid, liquid, and gas phases and are used to model its movement through the environment. This section briefly describes the pesticides used in malaria vector control to identify characteristics that can serve as indicators of environmental behavior.

Table 5 presents key chemical and physical properties for the pesticides. Additional details are provided in ***Annex D***, Input Parameter Tables, Table D-1, Chemical–Physical Properties.

Table 5. Chemical–Physical Properties That Affect Environmental Behavior[1]

Chemical name	Molecular Weight (g/mol)	Solubility (mg/L)	Henry's law constant (atm-m3/mol)	Vapor pressure (atm)	Octanol-water partition coefficient (log)	Reaction half-life in water (days)	Reaction half-life in air (days)	Reaction half-life in soil (days)
Alpha-cypermethrin	4.16E+02	1.00E-02	9.50E-06	1.70E-12	5.16E+00	6.50E+01	7.50E-01	1.40E+01
Bendiocarb	2.23E+02	2.60E+02	3.90E-08	6.60E-09	1.70E+00	2.00E+00	5.00E+00	3.50E+00
Bifenthrin	4.23E+02	1.00E-01	1.00E-06	2.40E-10	6.00E+00	5.55E+02	5.42E-01	1.25E+02
Cyfluthrin	4.34E+02	2.00E+00	5.80E-10	2.67E-12	5.94E+00	NF	NF	5.95E+01
DDT	3.54E+02	2.50E-02	8.30E-06	2.48E-10	6.91E+00	5.60E+01	5.00E+00	5.48E+03
Deltamethrin	5.05E+02	2.00E-03	5.00E-06	2.00E-11	5.43E+00	2.08E+01	NF	4.83E+01
Etofenprox	3.77E+02	1.00E-03	2.26E-08	8.93E-12	7.05E+00	NF	NF	7.90E+01
Fenitrothion	2.77E+02	1.40E+01	9.30E-07	2.80E-07	3.16E+00	6.30E+02	2.67E-01	1.54E+02
Lambda-cyhalothrin	4.50E+02	5.00E-03	9.09E-06	1.97E-12	7.00E+00	7.00E+00	NF	3.00E+01
Malathion	3.30E+02	1.30E+02	4.90E-09	5.25E-08	2.75E+00	2.10E+01	1.50E+00	2.50E+01
Methoprene	3.10E+02	1.40E+00	6.90E-06	3.11E-08	5.50E+00	1.30E+01	6.25E-02	1.00E+01
Permethrin	3.91E+02	6.00E-03	1.90E-06	2.87E-11	6.50E+00	3.30E+01	4.08E-01	3.00E+01
Pirimiphos-methyl	3.05E+02	8.60E+00	7.00E-07	1.97E-08	4.12E+00	NF	1.00E-01	5.90E+00
Propoxur	2.09E+02	1.75E+03	1.43E-09	2.50E-05	1.56E+00	9.32E+01	5.00E-01	2.10E+02
Temephos	4.66E+02	2.70E-01	1.96E-09	1.13E-12	5.96E+00	4.00E+03	1.17E-01	3.00E+01

NF, Not found.

[1]See Annex D for Glossary of Terms.

Values for chemical and physical properties can be found in multiple databases that are maintained and updated by different international, government, and academic groups. These values may differ somewhat from one database to another. When data for a

particular parameter were available from multiple sources, we used the following hierarchy to determine which value to use for the screening assessment:

1. EPA sources such as Reregistration Eligibility Decision (RED) documents
2. Agency for Toxic Substances and Disease Registry (ATSDR)
3. Hazardous Substances Data Bank (HSDB), which is maintained by the U.S. National Library of Medicine
4. Any other reputable database (e.g., the International Program on Chemical Safety's [IPCS's] INCHEM, EXtension TOXicology NETwork [EXTOXNET]).

The environmental behavior of the pesticides used in IVM is described briefly below. Additional details are provided in ***Annex E***, Pesticide Profiles.

- **Alpha-cypermethrin.** Alpha-cypermethrin is a broad-spectrum, nonsystemic, synthetic pyrethroid insecticide used in agricultural—on field crops, fruits, vegetables, and livestock—and residential applications. It is also commonly used as an insecticide to kill mosquitoes to control malaria transmission. Although alpha-cypermethrin is not registered by the EPA, cypermethrin is. USAID does not currently support the use of cypermethrin in IRS because no formulation of cypermethrin has been recommended by WHO for use in IRS at this time.

  In the air, alpha-cypermethrin exists in both vapor and particulate phases. As a vapor, it is broken down by reactions with hydroxyl radicals and ozone. The half-life for these reactions is estimated at 18 hours to 49 days. As a particulate, alpha-cypermethrin is removed from the atmosphere by wet and dry deposition.

  Once in the terrestrial environment, alpha-cypermethrin binds tightly to soil. Volatilization is the major fate process in moist soils; however, the tight bond of alpha-cypermethrin to soil attenuates the volatilization. In nonsterile soil, alpha-cypermethrin is biodegraded by environmental organisms and sunlight. It does not build up in surface soils nor leach to subsurface soils.

  In aquatic environments, alpha-cypermethrin bonds tightly to suspended solids and sediments. Volatilization of alpha-cypermethrin from water is expected; however, this is lessened by its bond with soil. Photodecomposition is also expected. Based on its bioconcentration factor, alpha-cypermethrin has a high potential to bioaccumulate in aquatic organisms. However, the ability of aquatic organisms to rapidly metabolize alpha-cypermethrin suggests that actual bioaccumulation may be lower than the potential.

- **Bendiocarb.** Bendiocarb is a broad-spectrum carbamate insecticide used to control a wide variety of nuisance and disease-vector insects (such as mosquitoes and agricultural insects) and to treat seeds. All registrations for products containing bendiocarb were voluntarily cancelled in 1999. Sales of existing products were allowed until April 2003, and the presence of bendiocarb in or on processed food and animal feed was allowed until April 2005. When applied to

plants, bendiocarb enters the soil both directly and indirectly. In soil, bendiocarb is moderately to very highly mobile. The major fate processes are hydrolysis (in moist soils) and biodegradation. Volatilization is not an important fate process in either moist or dry soils. Biodegradation of bendiocarb is expected to be rapid. Photolysis is important in the photodegradation of bendiocarb in soil. Bendiocarb degrades prior to leaching through soil and its degradation products remain in the upper layers of soil in low concentrations. It is unlikely that bendiocarb will move through soil to groundwater or to surface water through runoff. Bendiocarb is of low persistence in soil.

Water is an important factor in the transport of bendiocarb. However, bendiocarb is of limited hazard in water due to its rapid decomposition under aqueous conditions. In water, bendiocarb is not expected to adsorb to suspended soils and sediments. The major fate processes in water are hydrolysis and biodegradation; volatilization is unimportant. Additionally, direct photolysis is not a major degradative pathway in water and is dependent on the turbidity of the water. In alkaline and neutral environments, hydrolysis is expected to be a major fate process. Bendiocarb does not accumulate in water and, based on soil studies, biodegradation in water is expected to be rapid. Because bendiocarb degrades rapidly in water, bioconcentration in fish is unlikely.

- **Bifenthrin.** Bifenthrin is a pyrethroid insecticide and acaricide used in agricultural and human health applications. Bifenthrin is used to control pests on crops, as well as indoor pests. For mosquito protection, it is used on bed nets and other materials that are treated with bifenthrin to protect the user. Bifenthrin is a restricted use pesticide because of its potential toxicity to aquatic organisms.

  In the terrestrial environment, bifenthrin has a low mobility in soils with large amounts of clay, silt, or organic matter and in sandy soils without much organic matter. In moist soils, volatilization is a major fate process, though this is lessened by absorption in the soil. Depending on the soil type and the amount of air in the soil, the half-life of bifenthrin ranges from 7 days to 8 months. Bifenthrin is expected to biodegrade readily and it is not absorbed by, or translocated, in plants.

  Bifenthrin is fairly insoluble in water, so there is little concern about groundwater contamination through leaching. Volatilization is a major fate process from surface water; however, volatilization is attenuated by bifenthrin's tendency to adsorb to suspended soils and sediments. Based on its bioconcentration factor, bifenthrin has a high potential to accumulate in aquatic organisms. However, the actual bioconcentration may be lower than the potential due to the ability of aquatic organisms to metabolize bifenthrin.

- **Cyfluthrin.** Cyfluthrin is a synthetic pyrethroid insecticide used in agricultural and public health applications. It is commonly used as an insecticide to kill mosquitoes to control malaria transmission. In the air, cyfluthrin exists

predominantly in the particulate phase. As a particulate, cyfluthrin is removed from the atmosphere by wet and dry deposition.

Once in the terrestrial environment, cyfluthrin is highly immobile in soil. Therefore, it does not leach easily into groundwater. Cyfluthrin is one of the more persistent pyrethroids, and its persistence is not significantly affected by soil moisture. The major fate processes in soil are biodegradation and photolysis. Volatilization is not expected to be a major fate process in either moist or dry soils.

In aquatic environments, cyfluthrin binds tightly to soil, is practically insoluble in water, and is less dense than water, which allows it to float on the surface of natural water. Cyfluthrin is stable in water under acidic conditions, but hydrolyzes rapidly under basic conditions. Photolysis is expected to occur in surface waters but volatilization is not. Aqueous hydrolysis is not an important environmental fate process. Cyfluthrin has a high potential to bioaccumulate in aquatic organisms.

- **DDT.** DDT is an insecticide that was once widely used to control insects on agricultural crops and insects that carry diseases such as malaria and typhus. DDT does not occur naturally in the environment and is usually found as a white, crystalline, tasteless, and almost odorless solid. It enters terrestrial and aquatic environments through deposition and accidental spillage.

  Once DDT enters the terrestrial environment, it has a strong affinity for soil and generally remains in the surface layers. As a result of this strong affinity for soil, DDT is quite persistent. The half-life of DDT ranges from 2 to 17 years, depending on soil composition (the warmer and wetter the soil, the shorter the half-life). Therefore, DDT is less persistent in the tropics, where it evaporates and microorganisms degrade it more quickly. The strong affinity for soil also reduces the potential for DDT to leach into groundwater. DDT can be absorbed by some plants and the animals that eat them.

  DDT can enter the aquatic environment in several ways, including direct contact (pouring it into a waterbody), deposition from the atmosphere, and overland transport via erosion and runoff. In surface water, DDT will bind to sediment in the water, settle, and be deposited on the bottom. DDT has some potential to bioaccumulate in marine life because it is absorbed by small organisms, such as plankton and fish. It can accumulate to high levels in fish and marine mammals (such as seals and whales), reaching levels thousands of times higher than in water. In these animals, the highest levels of DDT are found in their adipose tissue (ATSDR, 2002).

  DDT is listed in ***Annex B*** (Restriction) of the Stockholm Convention on Persistent Organic Pollutants. It is allowed to be used for disease vector control in accordance with Part II of the annex. Parties must register with the Secretariat to

use DDT for disease vector control and comply with specific information collection requirements on the production and use of DDT.

- **Deltamethrin.** Deltamethrin is a broad-spectrum synthetic pyrethroid insecticide that was first marketed in 1977 for use in agricultural and public health applications. It is considered the most powerful synthetic pyrethroid. For mosquito control, bed nets and other materials are treated with deltamethrin to protect the user. Deltamethrin is typically formulated as ECs, WPs, ultra-low volume and flowable formulations, and granules (either alone or combined with other pesticides). A dispersible tablet is also used to treat mosquito nets.

  In terrestrial environments, deltamethrin is not expected to be mobile, because it binds tightly to soil particles. It is insoluble in water, and recommended application rates are low. Volatilization from moist soils and biodegradation are major fate processes. However, volatilization is lessened by deltamethrin's tendency to adsorb to soil particles. As with other synthetic pyrethroids, deltamethrin degrades rapidly in soil and plants. It does not bioaccumulate in terrestrial systems.

  Very little leaching to groundwater is expected, because deltamethrin binds tightly to soil and is practically insoluble in water. Volatilization is a major environmental fate process in surface waters, but is lessened by soil adsorption. Deltamethrin breaks down quickly in water, with reported half-lives of 2–4 hours. It has a high potential to bioconcentrate in aquatic organisms.

- **Etofenprox.** Etofenprox is a nonester pyrethroid-like insecticide and acaricide that is used in agricultural, horticultural, and public health applications. For mosquito control, etofenprox is used on bed nets and other materials that are treated with it to protect the user. In soil, studies of adsorption and leaching revealed low translocation. Degradation occurs by oxidation in nonsterile soil. Photodegradation may be an important fate process for degradation of etofenprox from plant surfaces.

  In aquatic environments, the stability of etofenprox is dependent on the conditions. Under laboratory conditions, etofenprox is stable in aqueous solutions. An estimated half-life of more than 1 year is seen at 25°C in neutral and acidic environments in the dark. Under field conditions, etofenprox breaks down more rapidly due to the presence of sunlight.

- **Fenitrothion.** Fenitrothion is a general-use organophosphate insecticide that is mostly used in the control of chewing and sucking insect pests on a wide variety of agricultural crops and in forests, as well as for public health purposes. It is used as a residual contact spray against mosquitoes, flies, and cockroaches. Fenitrothion was introduced in 1959 as a less toxic alternative to parathion, with which it shares similar insecticidal properties. It is used heavily in countries that have banned parathion. In the United States, the use of fenitrothion for mosquito

control was voluntarily cancelled by the manufacturer in 1995, and the only registered use is for containerized ant and roach baits.

In the terrestrial environment, fenitrothion degrades rapidly in most soils with a half-life ranging from 3 to 25 days. Fenitrothion is mostly found in the top 6 inches of soil and is not very mobile and only slightly persistent in soil. Fenitrothion leaches very slowly into groundwater from most soils; however, some runoff can occur.

Fenitrothion can enter the aquatic environment from aerial spraying. It is unstable in water in the presence of sunlight or microbial contamination. Fenitrothion accumulates rapidly in fish, but at low concentrations.

- **Lambda-cyhalothrin.** Lambda-cyhalothrin is a synthetic pyrethroid that is released into the air as a result of its use as an insecticide. Once in the atmosphere, lambda-cyhalothrin, like all pyrethroids, is broken down and degraded rapidly by sunlight and other compounds found in the atmosphere. Often, lambda-cyhalothrin lasts only 1 or 2 days in the atmosphere before being degraded. Any remaining lambda-cyhalothrin will be removed by precipitation and deposited in terrestrial and aquatic environments.

  Lambda-cyhalothrin has a strong affinity for soil and is not easily taken up by the roots of plants and vegetation. It is moderately persistent in the environment, taking a few months to completely degrade (the average half-life ranges from 4 to 12 weeks, depending on soil composition). Also, as a result of its strong affinity for soil, lambda-cyhalothrin is not very mobile in the soil and does not usually leach into groundwater.

  Lambda-cyhalothrin enters the aquatic environment either through direct application or in runoff. Lambda-cyhalothrin is not very soluble in water, so once in a waterbody, it is absorbed strongly by suspended solids and sediments and not expected to be prevalent in the water column. Lambda-cyhalothrin volatilizes slowly from water and soil due to its low vapor pressure and Henry's law constant (ATSDR, 2003a).

- **Malathion**. Malathion is an insecticide that is used for agricultural and nonagricultural purposes. In the United States, it is no longer permitted for any indoor uses. It is released into the environment primarily through spraying on agricultural crops and agricultural sites, spraying for home and garden use, and spraying for public health use in both urban/residential and nonresidential areas. EPA labels for malathion currently recommend that the product be stored at 21°C or less. This is because high temperatures will facilitate the formation of malaoxon, which is substantially more toxic than malathion. Storing malathion at temperatures above 21°C will increase the risks of the use of malathion.

  Once malathion is released in the atmosphere, it can be transported back to surface water and soil by wet and dry deposition. Malathion enters territorial

environments either through direct application or by deposition from the atmosphere. Once in the soil, it degrades rapidly and very little of it appears to volatilize from soil, as indicated by its low Henry's law constant. Although malathion is moderately to highly mobile in soils, it is unlikely to leach through soil and into groundwater due to its low persistence and rapid degradation in the environment.

Once in water, malathion is not expected to absorb to sediment particles, and it usually biodegrades within a few weeks. There is also little potential for malathion to bioaccumulate in marine life. The rate of its breakdown water is dependent on the temperature and pH (ATSDR, 2003b).

- **Methoprene.** Methoprene is a larvicide and growth regulator that is used in agricultural, horticultural, and public health applications. Methoprene was first registered for use in the United States in 1975. In water, methoprene is used to control mosquito larvae, as well as various flies, moths, beetles, and fleas. Methoprene is selective, stable, and potent, though it is not persistent in the environment or toxic to mammals.

  Methoprene binds tightly to soil and is only slightly soluble in water, making it almost immobile in most soil types. It remains only in the top few inches of soil, and studies have indicated that it does not leach from soil. In addition, methoprene is of low persistence in soil and is rapidly and extensively broken down by microbial degradation, which is the major fate process. It also undergoes rapid photodegradation.

  Because methoprene binds tightly to soil and is practically insoluble in water; in fact, very little leaching into groundwater has been reported. Methoprene degrades rapidly in water. Sunlight and temperature play major roles in the breakdown of methoprene in water. Biodegradation and photodegradation are the major fate processes. The potential for bioconcentration of methoprene in aquatic organisms is very high.

- **Permethrin.** Permethrin is a broad-spectrum, nonsystemic, synthetic pyrethroid insecticide registered for use on numerous food/feed crops, livestock and livestock housing, modes of transportation, structures, and buildings (including food handling establishments), and for residential uses. It is also commonly used as an insecticide to kill mosquitoes to control malaria transmission.

  Permethrin enters the atmosphere when it is sprayed in malaria control operations. Like all pyrethroids, permethrin is broken down and degraded rapidly by sunlight and other compounds found in the atmosphere. Often, permethrin lasts only 1 or 2 days in the atmosphere before being degraded. Any remaining permethrin will be removed by precipitation and deposited in terrestrial and aquatic environments.

  Once in the terrestrial environment, permethrin appears to dissipate primarily by binding to the soil and by soil microbial degradation. It is moderately persistent in

soil, but due to its hydrophobicity, permethrin is also extremely immobile in soil and stays in the surface layers. Permethrin is not very soluble in water, resulting in little concern for groundwater contamination.

Permethrin is likely to enter aquatic environments either through direct application or because of runoff. Once in a waterbody, permethrin has a very high affinity for soils and sediment in aqueous systems, and will bind quickly to sediment in the water column (Imgrund, 2003).

- **Pirimiphos-methyl.** Pirimiphos-methyl is a fast-acting, broad-spectrum, noncumulative organophosphate insecticide and acaricide used in agricultural, horticultural, and public health applications. In the United States, no indoor uses are permitted. For public health applications, it is used to control disease-vector insects, including mosquitoes, ants, beetles, bed bugs, cockroaches, fleas, flies, lice, and mites. Pirimiphos-methyl has both contact and fumigant action.

  Pirimiphos-methyl has limited mobility and limited persistence in soil. For a variety of soil types, pirimiphos-methyl has a half-life of less than 1 month. It hydrolyzes rapidly in acidic soils and is stable in neutral and alkaline environments. It also decomposes in sunlight. Because its use is limited outdoors, pirimiphos-methyl is not expected to have a significant impact on aquatic environments. It degrades in water, mainly by hydrolysis, which is attenuated by sunlight. It also volatilizes from still water; however, volatilization is not as significant a fate process as hydrolysis for pirimiphos-methyl.

- **Propoxur.** Propoxur is a broad-spectrum, nonsystemic carbamate insecticide that is used in both agricultural and nonagricultural applications to kill a variety of chewing and sucking pests, as well as mosquitoes, ants, flies, cockroaches, hornets, crickets, and lawn and turf insects.

  In the terrestrial environment, propoxur is expected to be moderately to very highly mobile and moderately persistent in soil. The mobility depends on the soil type and previous exposures to propoxur. In many soil types, propoxur is highly mobile because of its low affinity for soil binding. Hydrolysis and biodegradation in moist soils appear to be the primary modes of degradation. Biodegradation in soil occurs more rapidly in previously exposed soils. Volatilization is not expected to be a major fate process from moist soil surfaces. Propoxur evaporates from soil, with the amount of evaporation increasing with the moisture content of the soil. The half-life ranges from 6 to 8 weeks depending on the soil type. Also, in soil, propoxur shows no or little susceptibility to photolysis. Propoxur moves rapidly through all soil profiles below a 12-inch sampling depth. Its fate and transport characteristics are similar to chemicals that are known to leach into groundwater.

  Propoxur is highly soluble in water and there is a high likelihood of groundwater penetration because it doesn't adsorb strongly to soil. It is relatively stable in

water under neutral or acidic conditions, but hydrolyzes rapidly under alkaline conditions. Reported field half-lives for propoxur range from 14 to 50 days. Volatilization from water is not expected to be a major fate process; however, propoxur is susceptible to photolysis in water. Because propoxur degrades rapidly in water, bioconcentration in fish is unlikely.

- **Temephos.** Temephos is a larvicide that is applied to shallow, stagnant, brackish, and polluted waters; usually, these waters are unsuitable as a source of drinking water. Temephos enters the environment in liquid or granular form. It is unlikely to enter the atmosphere because it is applied directly to waterbodies. Temephos is also unlikely to reach groundwater that would be used for drinking water because of a lack of hydraulic gradient and its relatively short half-life in natural waters. Due to its low vapor pressure and Henry's Law constant, temephos may volatilize slowly from water, but volatilization may be more significant in shallow rivers and waterbodies. Exposure to temephos and its degradation products is primarily associated with treated aquatic environments where mosquito breeding occurs; therefore, terrestrial exposure is expected to be minimal (U.S. EPA, 1999b).

Health Effects

The ability of a pesticide used in IVM to elicit adverse health effects depends on the route of exposure (i.e., ingestion, inhalation, or dermal), the frequency and duration of exposure, the toxicity of the insecticide (by route of exposure), and the sensitivity of the exposed individual. Many of the pesticides considered in this report are cholinesterase inhibitors, so neurological endpoints are frequently attributed to exposure. However, to evaluate the toxicity of each pesticide, we identified pesticide-specific human health benchmarks for each exposure route and duration evaluated in the screening assessment. For noncancer endpoints, the health benchmark represents a point (in milligrams of pesticide per kilogram body weight per day) on the dose–response continuum below which adverse effects would not be anticipated. That is, a dose below the benchmark would not be expected to cause an adverse health effect. For cancer endpoints, the health benchmark represents the potency of the pesticide to cause cancer in humans assuming that *any* exposure is associated with some finite probability of an individual contracting cancer.

This section provides a brief summary of the health endpoints of concern for each of the pesticides evaluated in this screening assessment.

Summary of Health Effects

The health effects of the pesticides considered in this report are described briefly below. Additional details are provided in ***Annex E***, Pesticide Profiles.

- **Alpha-cypermethrin.** Alpha-cypermethrin is a highly active synthetic pyrethroid used to control mosquitoes. It poses a low risk to humans when used at the recommended levels. Alpha-cypermethrin affects the way the nerves and brain normally function by interfering with the sodium channels of nerve cells. Typical

symptoms for acute exposure to high levels of alpha-cypermethrin include irritation of skin and eyes, and neurological effects such as headaches, dizziness, nausea, vomiting, diarrhea, excessive salivation, and fatigue. Inhaled alpha-cypermethrin has been shown to cause paresthesia (a burning, tingling, or stinging of the skin). These effects are generally reversible and disappear within a day of ending the exposure. Alpha-cypermethrin is rapidly metabolized and excreted from the body. Limited data are available for chronic low-level exposures to alpha-cypermethrin; however, it is not expected to be a reproductive or developmental toxicant. Additionally, it is not likely to have mutagenic effects. No data are available on the carcinogenic potential of alpha-cypermethrin.

- **Bendiocarb.** Bendiocarb is a broad-spectrum carbamate insecticide. Bendiocarb exhibits its toxic effects through reversible cholinesterase inhibition and is considered moderately toxic in mammals. In humans, symptoms of bendiocarb toxicity include excessive sweating, salivation, headache, blurred vision, nausea, vomiting, stomach pain, giddiness, slurred speech, tightness in the chest, and muscular twitching. The effects of chronic bendiocarb exposure have not been well documented in humans. In the RED Fact Sheet for bendiocarb, EPA reported that for most of the residential scenarios, including exposure to treated surfaces, there were risks of concern for children and adults.

  Additionally, bendiocarb is not expected to have reproductive effects in humans at the expected exposure levels. It has not been shown to be mutagenic in animals. EPA has classified bendiocarb as "noncarcinogenic to humans."

- **Bifenthrin.** Bifenthrin is a pyrethroid insecticide used in agricultural and human health applications including mosquito control. As a synthetic pyrethroid, bifenthrin affects the nerves and brain. Symptoms of acute exposure may include skin and eye irritation and neurological effects such as headache, dizziness, nausea, vomiting, diarrhea, excessive salivation, fatigue, irritability, and numbness. Inhalation of pyrethrins may cause a localized reaction of the upper and lower respiratory tracts. In mammals, pyrethroids are generally of low toxicity due to their rapid biotransformation. No toxicity data for chronic bifenthrin exposure are available in humans. EPA has classified bifenthrin as a "possible human carcinogen."

- **Cyfluthrin.** Cyfluthrin is a synthetic pyrethroid. It is not expected to cause long-term problems in humans when used under normal conditions. Cyfluthrin has both contact and stomach poison action and it can affect the nerves and brain. Typical symptoms for acute human exposure are skin and eye irritation. Dermal exposure to cyfluthrin has been shown to cause paresthesia (a burning, tingling, or stinging of the skin) which may lead to a numbness lasting up to 24 hours. Skin irritation may be immediate or delayed for up to 2 hours. In animals, exposure to high levels of cyfluthrin causes nervous system effects such as irritability, excessive salivation, incoordination, tremors, convulsions, and even death. Cyfluthrin is

rapidly metabolized and excreted from the body. Limited data are available for chronic low-level exposures of humans to cyfluthrin. Based on animal studies, it is not expected to be a reproductive or developmental toxicant. Additionally, cyfluthrin does not show any mutagenic potential. No evidence of carcinogenic potential of cyfluthrin has been reported in animals.

- **DDT.** DDT is a broad-range organochlorine insecticide. It was banned in the early 1970s in the United States and in most industrial countries, mainly because of its persistence in the environment and enormous volumes used in agriculture. DDT has been used in large populations for more than 60 years with little evidence of acute toxicity, except from accidental exposures. In these relatively rare instances, DDT acts by impairing the conduction of nerve impulses. Symptoms of acute exposure to high levels of DDT by any route include mild altered sensations, tremors, convulsions, and respiratory depression. Additional effects observed in humans after acute DDT exposure include headaches; nausea and vomiting; diarrhea; numbness; paresthesia (a burning, tingling, or stinging of the skin); increased liver enzyme activity; irritation of the eyes, nose, or throat; altered gait; and malaise or excitability. In humans, oral exposure is thought to be most significant. In addition to potential acute effects, DDT is believed to be an endocrine disruptor. Recent data indicate that exposure to DDT in amounts necessary for malaria control may cause preterm birth decreased birth weight, early weaning, and pregnancy loss. The International Agency for Research on Cancer (IARC) has classified DDT in Group B2, “probable human carcinogen.”
- **Deltamethrin.** Deltamethrin is a powerful broad-spectrum synthetic pyrethroid. It is of moderate toxicity to mammals as it is rapidly metabolized and does not accumulate. It poses low risk to humans when used at levels recommended for its designed purpose. Deltamethrin exhibits its toxic effects by affecting the way the nerves and brain normally function by interfering with the sodium channels of nerve cells. Typical symptoms of acute exposure are irritation of skin and eyes and neurological effects such as severe headaches, dizziness, nausea, anorexia, vomiting, diarrhea, excessive salivation, and fatigue. Tremors and convulsions have been reported in severe poisonings. Inhaled deltamethrin has been shown to cause reversible cutaneous paresthesia (a burning, tingling, or stinging of the skin). Limited data exist for humans following chronic exposures. However, the following effects are suspected to be a result of chronic exposures in humans: choreoathetosis, hypotension, prenatal damage, and shock. Chronic occupational exposure to deltamethrin causes skin and eye irritation. IARC has classified deltamethrin as “not classifiable as to its carcinogenicity in humans.”
- **Etofenprox.** Etofenprox is a nonester pyrethroid-like insecticide. Like other pyrethroids, it acts on the central nervous system. Its toxicity is also similar to that of other pyrethroids. WHO has classified etofenprox as a low risk for acute toxicity in humans under conditions of normal use. Limited chronic human exposure data are available. Based on animal studies, etofenprox is not expected

to have any developmental, reproductive, mutagenic, or genotoxic effects on humans. Etofenprox is not a cholinesterase inhibitor, but rather affects the thyroid and kidneys in animals. With respect to carcinogenicity, EPA has classified it in Group C, as a "possible human carcinogen."

- **Fenitrothion.** Fenitrothion is an organophosphate insecticide that is nonsystemic and not persistent. It can cause overstimulation of the nervous system due to cholinesterase inhibition, which may result in nausea, dizziness, confusion, and at very high exposures, respiratory paralysis and death. Chronic symptoms of toxicity in humans include general malaise, fatigue, headache, loss of memory and ability to concentrate, nausea, thirst, weight loss, cramps, muscular weakness, and tremors. Reproductive and developmental toxicity have been reported in animal studies. EPA has classified fenitrothion as a Group E chemical, with "evidence of noncarcinogenicity for humans." However, the broad-spectrum insecticide uses have been cancelled in the United States, and it is now only registered for use in ant and roach baits with child-resistant packaging.
- **Lambda-cyhalothrin.** Lambda-cyhalothrin is a synthetic pyrethroid that is a more biologically active form than cyhalothrin. It is used to control pests (including mosquitoes) in agricultural, public, and animal health settings. Typical symptoms for acute exposure to high levels of lambda-cyhalothrin include tingling, burning, or numbness (particularly at the point of skin contact); dizziness; headache; nausea; tremors; incoordination of movements; paralysis or other disrupted motor functions; convulsions; and loss of consciousness. These effects are generally reversible because lambda-cyhalothrin breaks down rapidly in the body. Lambda-cyhalothrin is not considered to have any teratogenic, mutagenic, or genotoxic effects on humans. It has been classified by EPA as a Group D chemical, "not classifiable as to human carcinogenicity."
- **Malathion.** Malathion is a nonsystemic, broad-spectrum organophosphate insecticide that is used in a wide variety of applications, including agricultural, veterinary, and public health uses, such as the control of mosquitoes. Malathion causes neurological effects by inhibiting cholinesterase in the blood and brain. In general, malathion is thought to exhibit low toxicity via acute oral, dermal, and inhalation exposure. However, acute exposure to high concentrations of malathion can cause numbness, headaches, sweating, abdominal cramps, blurred vision, difficulty breathing, respiratory distress, and loss of consciousness. Limited data from chronic human exposures indicate that the nervous system is the main target organ of chronic malathion toxicity. EPA has classified malathion as having "suggestive evidence of carcinogenicity."[6] Malathion is no longer permitted in the United States for any indoor uses.

[6] Under EPA's new system, group letters are no longer used to classify chemicals. As this process is being phased in, some chemicals—like malathion—are identified under the new system.

- **Methoprene.** Methoprene is a larvicide and growth regulator that acts by interfering with the life cycle of the insect rather than by direct toxicity. It prevents insects from reaching maturity or reproducing. EPA has classified methoprene as toxicity class IV, slightly to almost nontoxic. It is selective, stable, and potent, though not persistent in the environment or toxic to mammals. It presents no long-term hazard other than to the target species. It has low potential for acute oral or inhalation toxicity. It is not a skin or eye irritant or skin sensitizer and is of low acute dermal toxicity. Limited data are available for humans following chronic exposures to methoprene; however, no chronic, reproductive, developmental, mutagenic, or carcinogenic effects have been seen in humans or animals. Methoprene is rapidly and completely metabolized.
- **Permethrin.** Permethrin is a synthetic pyrethroid used for controlling mosquitoes. Permethrin is of low risk to humans when used at recommended levels. However, like many of the pesticides assessed in this report, permethrin is a cholinesterase inhibitor and can affect the nerves and brain. Typical symptoms for acute exposure to high levels of permethrin include irritation of skin and eyes, and neurological effects such as headaches, dizziness, nausea, vomiting, diarrhea, excessive salivation, and fatigue. Inhaled permethrin has been shown to cause paresthesia (a burning, tingling, or stinging of the skin). These effects are generally reversible and disappear within a day of ending the exposure. Low-level, chronic exposures to permethrin do not generally cause neurological effects in humans, because permethrin is rapidly metabolized and excreted from the body. Permethrin is not likely to have reproductive, teratogenic, or mutagenic effects. EPA has classified pyrethrins as "likely to be carcinogenic to humans by the oral route."
- **Pirimiphos-methyl.** Pirimiphos-methyl is a fast-acting, broad-spectrum, non-cumulative organophosphate insecticide and acaricide. Like other organo-phosphates, pirimiphos-methyl acts by inhibiting cholinesterase activity. It is of low mammalian toxicity. Early symptoms of pirimiphos-methyl exposure include excessive sweating, headache, weakness, giddiness, nausea, vomiting, stomach pains, blurred vision, slurred speech, and muscle twitching. Symptoms of more severe poisoning may include convulsions, coma, loss of reflexes, and loss of sphincter control. EPA has concluded that there are insufficient animal data to assess the chronic, reproductive, developmental, or mutagenic toxicity of pirimiphos-methyl. The carcinogenic potential of pirimiphos-methyl could not be determined.
- **Propoxur.** Propoxur is a broad-spectrum nonsystemic carbamate insecticide. It exhibits its toxic effects through reversible cholinesterase inhibition and has moderate toxicity in mammals. The liver and the nervous system are the main organs affected by propoxur in both humans and animals. Short-term exposures may cause effects on the nervous system, liver, and kidneys, as well as respiratory failure and convulsions. In humans, symptoms of acute oral poisoning include red

blood cell cholinesterase inhibition with mild transient cholinergic symptoms including nausea, vomiting, sweating, blurred vision, and tachycardia. Long-term inhalation exposures in humans results in cholinesterase inhibition, headaches, nausea, and vomiting. EPA has classified propoxur in Group B2 as a "probable human carcinogen."

- **Temephos.** Temephos is a nonsystemic organophosphate larvicide used in the United States since 1965 for public health reasons, including control of mosquito larvae, but not for use in potable water. It is also used occasionally to treat potable water. Temephos causes its effect by inhibiting cholinesterase, which results in eye irritation, blurred vision, dizziness, nausea, abdominal cramps, diarrhea, salivation, headaches, loss of muscle coordination, and difficulty breathing. Compared with other organophosphates, temephos is of low-to-moderate toxicity. Temephos can be absorbed through the oral, dermal, and inhalation pathways, with dermal exposure being the most likely for humans. However, dermal absorption in an animal study was low (38 percent). It is moderately toxic through dermal and oral exposure and has low toxicity through inhalation exposure. Because of its low toxicity in humans, few studies exist on the human health effects of acute exposure to temephos. No data exist on the carcinogenic effect of temephos in humans, and only very limited data exist for animals. EPA has not classified temephos as a carcinogen.

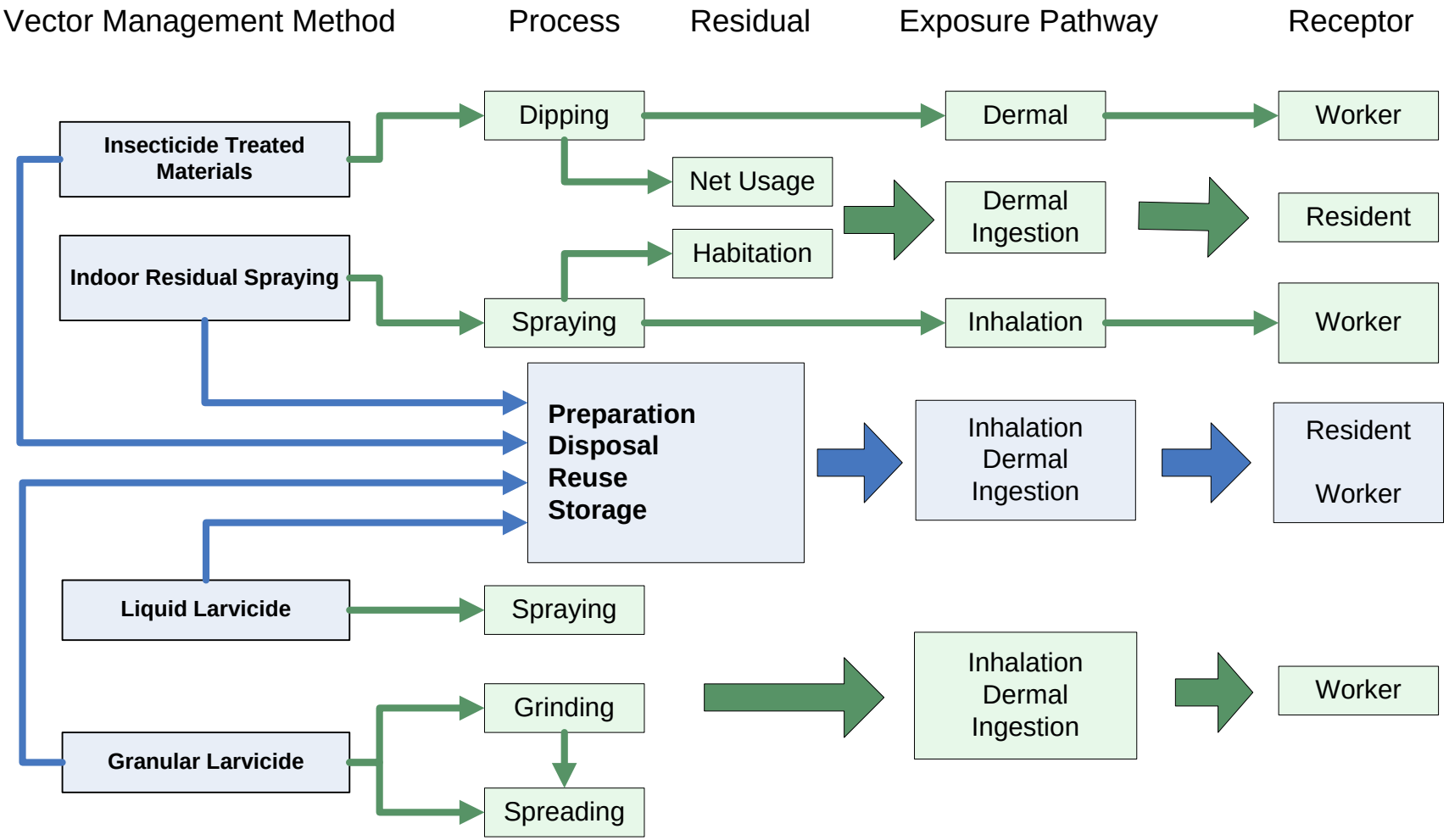
5.1.1.2 Conceptual Models of Exposure

Each IVM intervention involves different processes, from the preparation of the pesticide formulation to the disposal of excess pesticide or contaminated materials. Figure 2 presents an overall conceptual model that shows the main processes involved in the IVM practices and the main resulting pathways that could lead to pesticide exposure for various receptors. The figure also provides a roadmap to the other subsections, which describe the conceptual models for each practice (preparation, IRS, ITNs, larviciding, disposal, reuse, and storage).

Preparation

Most of the pesticides used in IVM do not come in ready-to-use form. Therefore, the worker or resident must first prepare the applied form from the concentrated form. Table 6 lists the concentrated and applied forms of each pesticide.

Figure 2. Overall Conceptual Model for Possible Exposure Pathways from IVM Practices



- Blue boxes and arrows indicate common practices, pathways, and receptors combinations
- Green boxes and arrows indicate IVM-specific practices, pathways, and receptor combinations

Table 6. Formulations of Pesticides Used in IVM

Pesticide	Concentrated Form	Applied Form
Alpha-cypermethrin	Wettable powder, aqueous suspension concentrate	Liquid solution
Bendiocarb	Wettable powder	Liquid solution
Bifenthrin	Wettable powder	Liquid solution
Cyfluthrin	Wettable powder, emulsion	Liquid solution
DDT	Wettable powder	Liquid solution
Deltamethrin	Wettable powder, water dispersible granules, aqueous suspension concentrate, water-dispersible tablet	Liquid solution
Etofenprox	Wettable powder, emulsion	Liquid solution
Fenitrothion	Wettable powder	Liquid solution
Lambda-cyhalothrin	Wettable powder, capsule suspension	Liquid solution
Malathion	Wettable powder	Liquid solution
Methoprene	Emulsifiable concentrate	Liquid solution
Permethrin	Wettable powder, emulsifiable concentrate	Liquid solution
Pirimiphos-methyl	Wettable powder, emulsifiable concentrate	Liquid solution
Propoxur	Wettable powder	Liquid solution

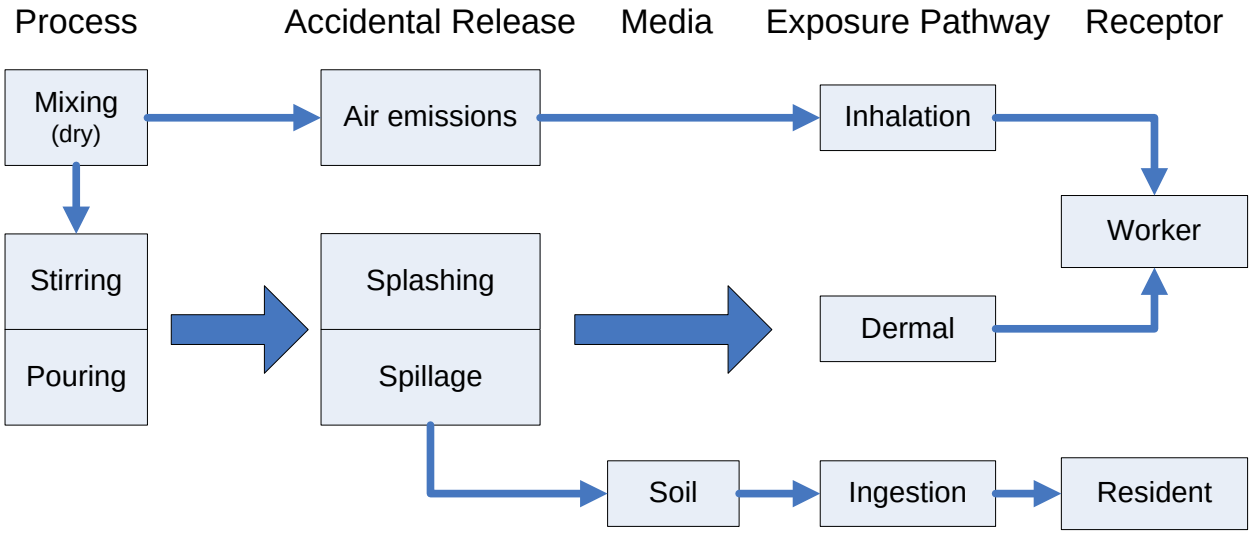
EC, Emulsifiable concentrate; WP, Wettable powder.

To prepare liquid solutions (for IRS, ITNs, and liquid larviciding), the worker or resident mixes the concentrated pesticide (either a powder or concentrated solution) with a solvent (usually water) to the recommended use concentration (which varies by pesticide). For ITNs, the resident leaves the solution in the mixing basin. For IRS and liquid larviciding, the worker pours the solution into an aerosol canister (sprayer). Granular larvicides do not require mixing; instead, the worker pours the granules into a belly grinder or push cart.

Figure 3 presents the conceptual model for exposure from preparation. Preparing pesticide solutions can involve mixing, stirring, and pouring. Spills can also occur. These processes can lead to exposures via inhalation, dermal contact, and incidental ingestion, mostly from releases of pesticide vapors, particulate matter (from powders), and solutions. Vapor releases can occur when liquid concentrated emulsions are diluted. Particulate releases can occur when mixing powdered forms. Workers or residents can

inhale the vapors or the particulates or be exposed through dermal contact. Spills could also pose significant risk, especially for children who ingest the resulting residues that are left on surfaces such as floors.

Figure 3. Conceptual Model for Possible Exposure Pathways from Preparation of Pesticide

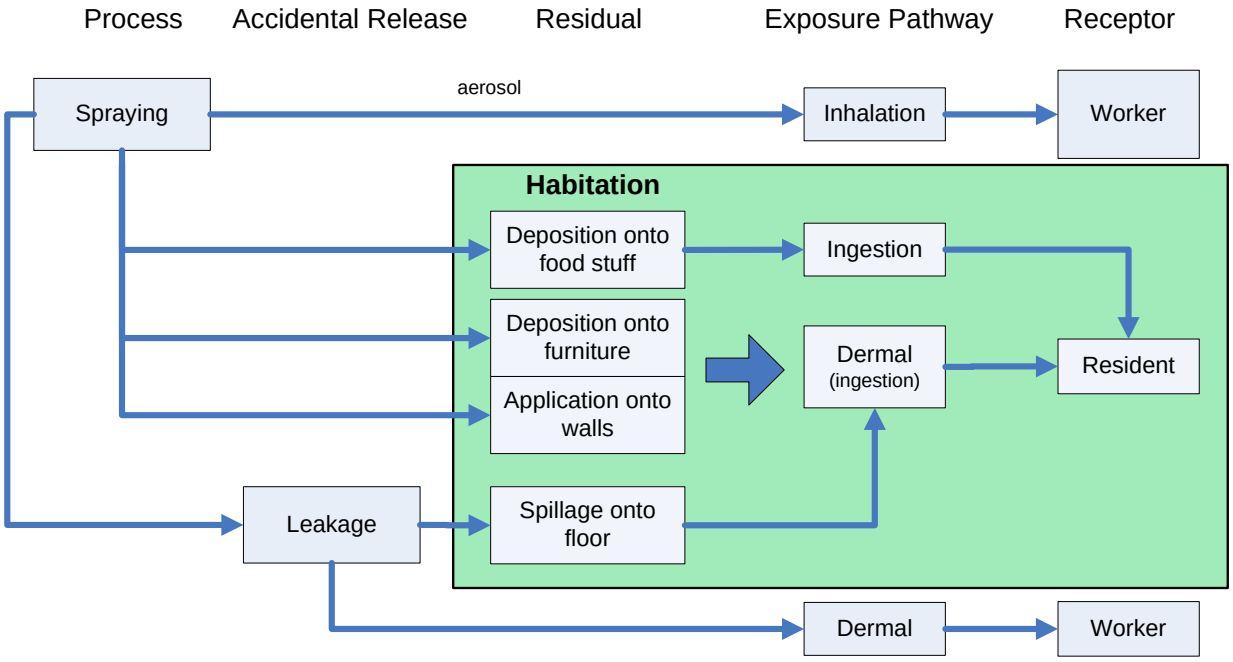


Exposure of the worker or resident to the pesticides during preparation can be greatly reduced if the worker follows best practices.

Indoor Residual Spraying (IRS)

Figure 4 presents the conceptual model for exposure from IRS. Inhalation of aerosol vapors during spraying is the main process for worker exposure during IRS. Residents are mainly exposed through dermal contact with sprayed surfaces and incidental ingestion of insecticide after their houses have been sprayed, especially when food or drink are left in the house during spraying. Leaky equipment can also lead to insecticide exposure through dermal contact with the floors and incidental ingestion by children who may come in contact with the spills before they are cleaned up.

Figure 4. Conceptual Model for Possible Exposure Pathways from IRS

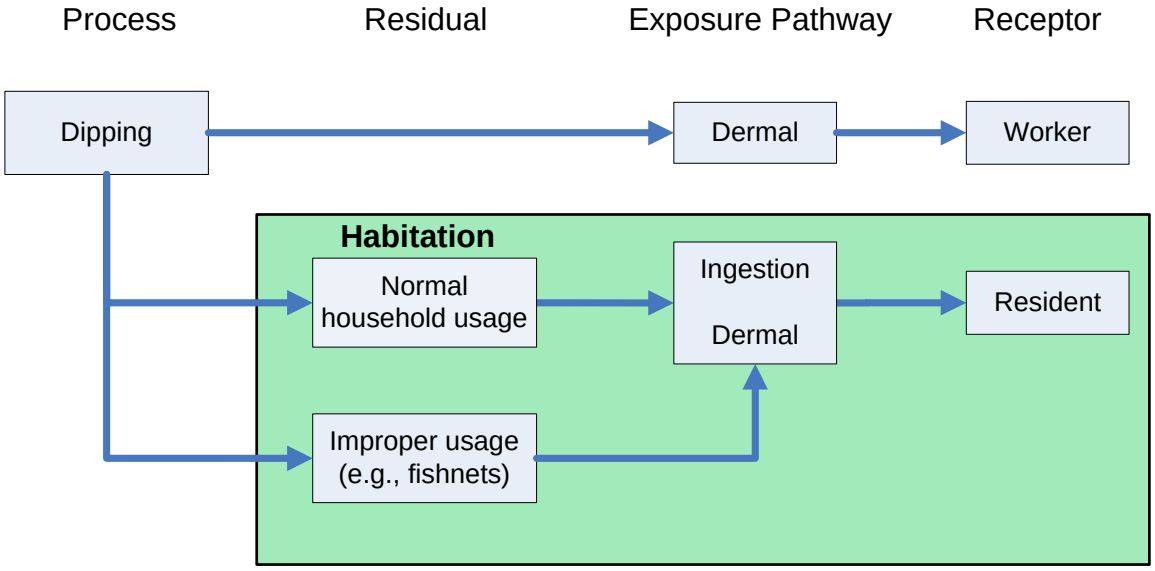


Exposure of the worker and the residents to the insecticide can be greatly reduced if the worker and residents follow best practices. Even if best practices are followed, workers should be closely monitored for acute symptoms, because there will always be some level of exposure. In addition, work-day duration should be monitored to limit exposure as required by safety recommendations (Najera and Zaim, 2002).

Insecticide-Treated Nets (ITNs)

A conceptual model for ITNs is presented in Figure 5. The primary route of exposure is dermal exposure while treating the nets. Dermal exposure to residents can theoretically occur through the use of the bed nets, but the potential exposure is minimal. Ingestion can also occur among children who touch the nets and residents who use the nets for other purposes, such as fishing.

Figure 5. Conceptual Model for Possible Exposure Pathways from ITNs



Exposure of the worker and the residents to the insecticide used in treating bed nets can be greatly reduced if the worker and residents follow best practices.

Larviciding

Conceptual models for liquid and granular larviciding are presented in Figures 6 and 7, respectively. In liquid larviciding, workers are exposed to the larvicide through inhalation of aerosols while spraying. They can also be exposed through dermal contact caused by faulty equipment or improper practices that lead to spills onto soil or directly onto the skin. In granular larviciding, workers are exposed to particulates via inhalation during the grinding process. Grinding is a manual process that could also lead to significant dermal exposure, especially if best practices are not followed. In both forms of larviciding, residents are exposed through dermal contact with surfaces or water sprayed with the larvicides. They can also be exposed through ingestion of water in puddles that have been sprayed or water contaminated with runoff from sprayed areas.

Figure 6. Conceptual Model for Possible Exposure Pathways from Liquid Larviciding

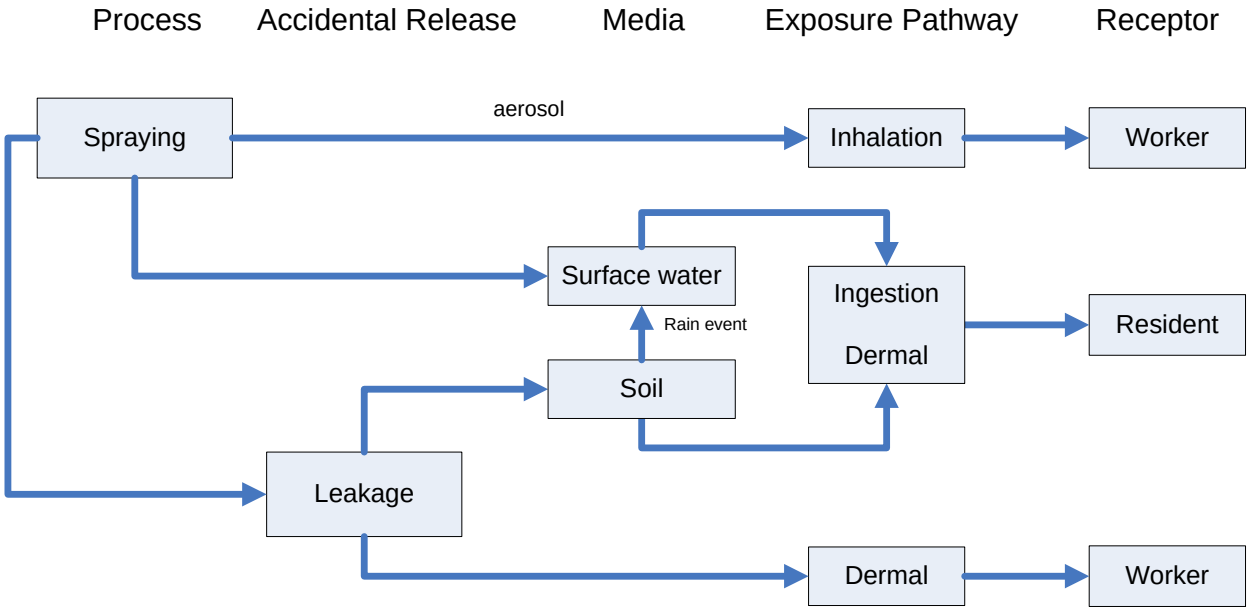
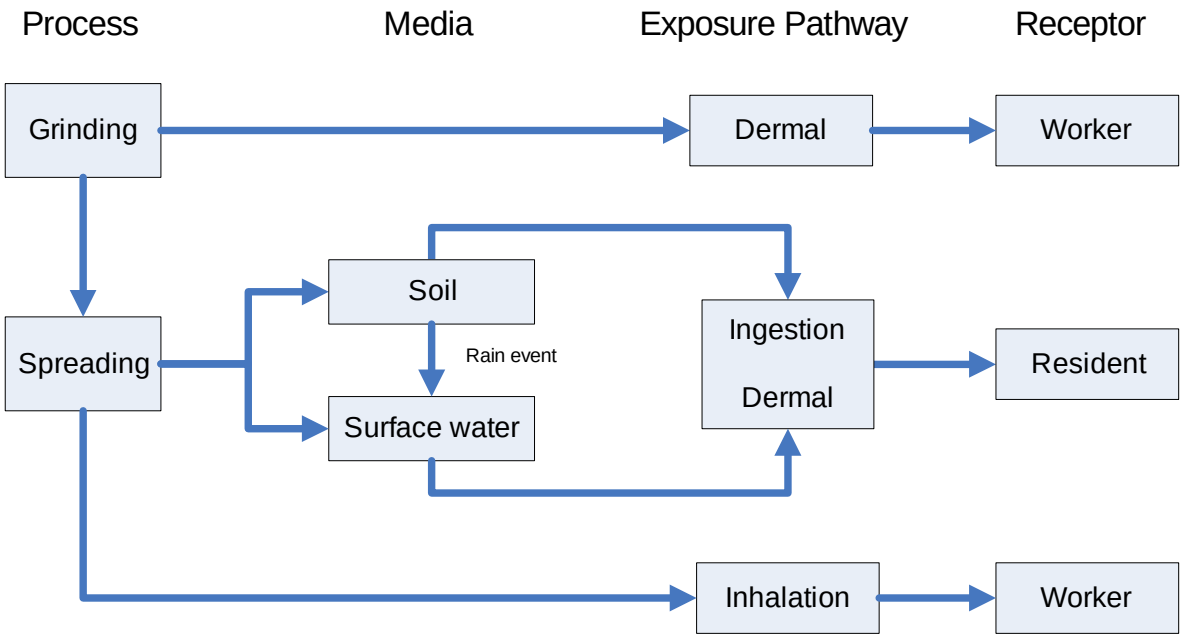


Figure 7. Conceptual Model for Possible Exposure Pathways from Granular Larviciding



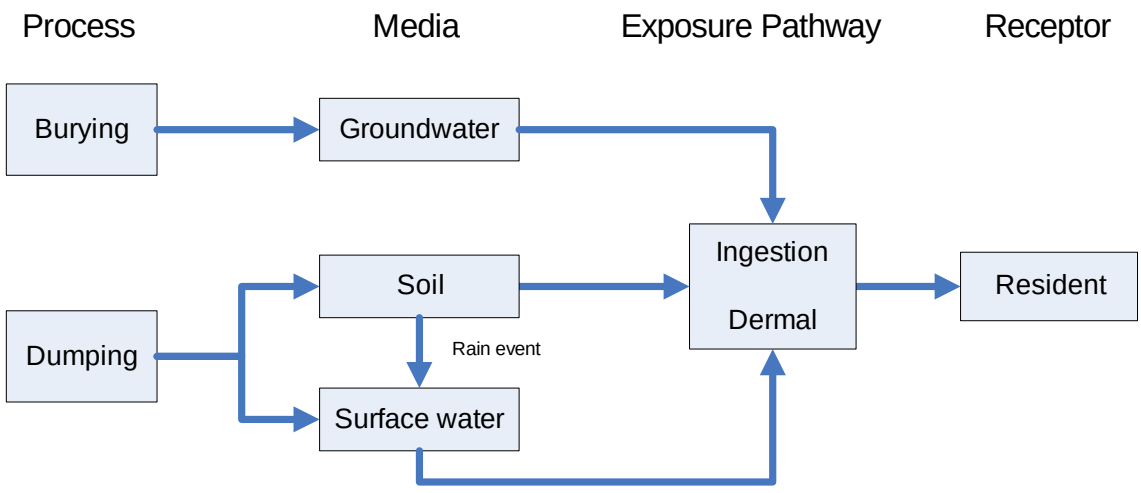
Exposure of the worker and the residents to the larvicides used in larviciding can be greatly reduced if the worker and residents follow best practices. Exposures to untargeted aquatic life and the community at large may occur even if best practices are used, especially if a heavy rain event occurs after spraying and washes recently sprayed puddles into larger bodies of water (e.g., lakes and rivers) that are used for drinking and other household purposes (e.g., washing clothes and dishes).

Disposal

Excess pesticide formulation can be disposed of by burying or dumping onto the soil or surface water. Disposal is a key issue with each IVM intervention that utilizes pesticides.

A conceptual model for disposal of pesticides is presented in Figure 8. Both burying and dumping can lead to dermal exposure to residents who come in contact with the soil or water in which the pesticide was disposed. Ingestion exposure can occur from drinking contaminated surface water. Once the excess formulation gets into the soil, the pesticide can reach the groundwater, which may be used as a water supply via household wells. Residents may then be exposed to this contaminated water by ingestion or by dermal contact when it is used for cleaning purposes.

Figure 8. Conceptual Model for Possible Exposure Pathways from Disposal of Excess Pesticide Formulation



It is not uncommon that excess pesticide formulation, packaging, and even personal protective equipment (PPE) is disposed of by burning. In rare cases, storehouse fires may occur. Although inhaling burned material was not a scenario addressed in this screening assessment, Table 7 highlights the toxic byproducts of the pesticides addressed in this PEA. It should be noted that, often, the burning of plastic packaging and other synthetic waste from malaria control programs may pose a hazard to human health and the environment.

Table 7. Combustion Byproducts of Pesticides

Pesticide	Combustion Byproduct	Extinguishing Instructions
Alpha-cypermethrin	Combustion and/or pyrolysis of alpha-cypermethrin can lead potentially to the production of compounds such as formaldehyde, acrolein, and hydrogen cyanide (UK PID, 2006)	Not available
Bendiocarb	Not available	Not available
Bifenthrin	Not available	Not available
Cyfluthrin	Combustion and/or pyrolysis of cyfluthrin can lead potentially to the production of compounds such as formaldehyde, acrolein, hydrogen cyanide, hydrogen chloride, and hydrogen fluoride (UK PID, 2006)	Not available
DDT	Fires involving DDT may produce irritating or poisonous gases (IPCS PIM, 2006)	Fire fighters should wear self-contained breathing apparatus and chemical protective clothing. For small fires, use dry chemical, CO_2, halon, water spray, or standard foam extinguishment. For larger fires, water spray, fog, or standard foam is recommended. For spills, take up with sand or other noncombustible absorbent material and place into containers for later disposal (IPCS PIM, 2006)
Deltamethrin	Combustion and/or pyrolysis of deltamethrin can lead potentially to the production of compounds such as formaldehyde, acrolein, hydrogen cyanide, and hydrogen bromide (UK PID, 2006)	Not available
Etofenprox	Not available	

Pesticide	Combustion Byproduct	Extinguishing Instructions
Fenitrothion	(For organophosphates generally) Powder, granular, and water-based products will not burn. Most liquid formulations will burn and are miscible with water. The products of combustion may be harmful by inhalation and dermal contamination (IPCS PIM, 2006)	Fire service personnel should extinguish fires with alcohol-resistant foam, water spray, or dry powder. Firefighters should wear full protective clothing including self-contained breathing apparatus (IPCS PIM, 2006)
Lambda-cyhalothrin	Open-burning of lambda-cyhalothrin creates nitrogen oxides, hydrogen chloride, and hydrogen fluoride (WHO, 1997)	Not available
Malathion	(For organophosphates generally) Powder, granular, and water-based products will not burn. Most liquid formulations will burn and are miscible with water. The products of combustion may be harmful by inhalation and dermal contamination (IPCS PIM, 2006)	Fire service personnel should extinguish fires with alcohol-resistant foam, water spray, or dry powder. Firefighters should wear full protective clothing including self-contained breathing apparatus (IPCS PIM, 2006)
Methoprene	Not available	Not available
Permethrin	When heated to decomposition, toxic fumes of hydrogen chloride are emitted (UK PID, 2006)	Not available
Pirimiphos-methyl	(For organophosphates generally) Powder, granular, and water-based products will not burn. Most liquid formulations will burn and are miscible with water. The products of combustion may be harmful by inhalation and dermal contamination (IPCS PIM, 2006)	Fire service personnel should extinguish fires with alcohol-resistant foam, water spray, or dry powder. Firefighters should wear full protective clothing including self-contained breathing apparatus (IPCS PIM, 2006)
Propoxur	Gives off irritating or toxic fumes (or gases) in a fire (IPCS, 1994)	Not available

Pesticide	Combustion Byproduct	Extinguishing Instructions
Temephos	(For organophosphates generally) Powder, granular, and water-based products will not burn. Most liquid formulations will burn and are miscible with water. The products of combustion may be harmful by inhalation and dermal contamination (IPCS PIM, 2006)	Fire service personnel should extinguish fires with alcohol-resistant foam, water spray, or dry powder. Firefighters should wear full protective clothing including self-contained breathing apparatus (IPCS PIM, 2006)

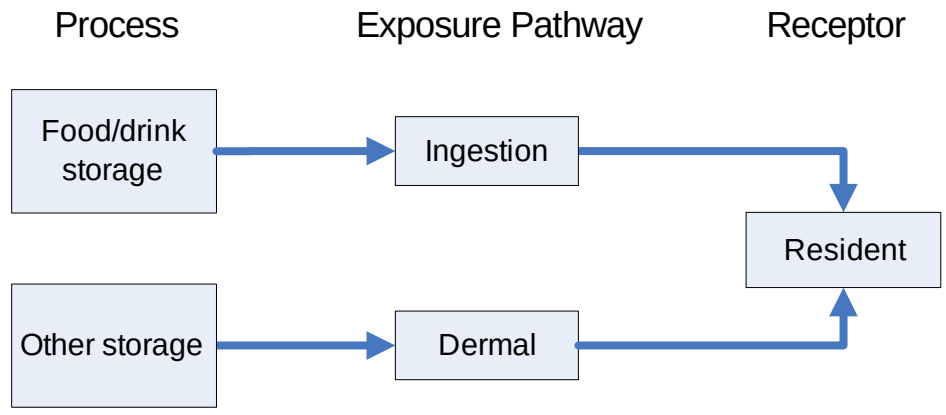
Reuse of Pesticide Containers

Reuse of pesticide containers occurs when best practices for disposal are not followed. Pesticides, especially those bought in bulk amounts, come in large, screw-on top containers that are made of extremely durable materials (i.e., plastics and metals); as a result, the desire to reuse is strong.

A conceptual model for reuse of pesticide containers is presented in Figure 9. Sturdy pesticide containers might be improperly reused to store water or dry food, such as mill or flour, leading to ingestion exposures from drinking water and dermal exposures to the water or food.

Best practices emphasize that no matter how many times a container is cleaned, it should never be used to carry anything other than pesticides. Any container once used to contain potentially harmful chemicals should never be used to hold household items or food stuffs, especially water.

Figure 9. Conceptual Model for Possible Exposure Pathways from Reuse of Pesticide Containers

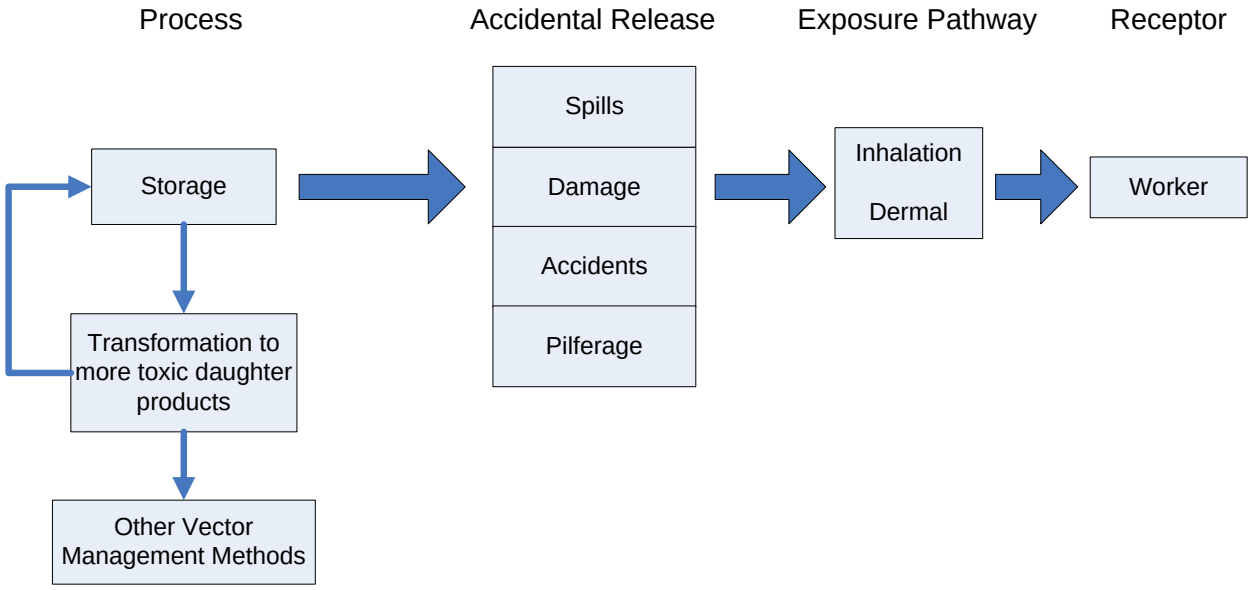


Storage

Proper storage of pesticides is just as important as the recommended use concentrations. Like any potentially harmful chemical, precautions must be taken to minimize any harm or contamination of the environment from the pesticide. United Nations Food and Agriculture Organization's *Pesticide Storage and Stock Control Manual* provides guidelines for the construction and maintenance of large storehouses, and the major principles in these guidelines should guide the location, construction, and management of temporary local storage facilities.

A conceptual model for storage of pesticides is presented in Figure 10. Note that pesticides stored beyond their expiration date may produce daughter products that can be introduced into other vector management methods. Pesticides and daughter products can be released to the environment during storage due to damage to the containers or accidents leading to spills. Workers at the storage facility can be dermally exposed through contact with damaged containers or the contaminated surfaces. In addition, workers may inhale vapors and particulate material released from spills.

Figure 10. Conceptual Model for Possible Exposure Pathways from Storage of Pesticides



5.1.1.3 Analysis Plan

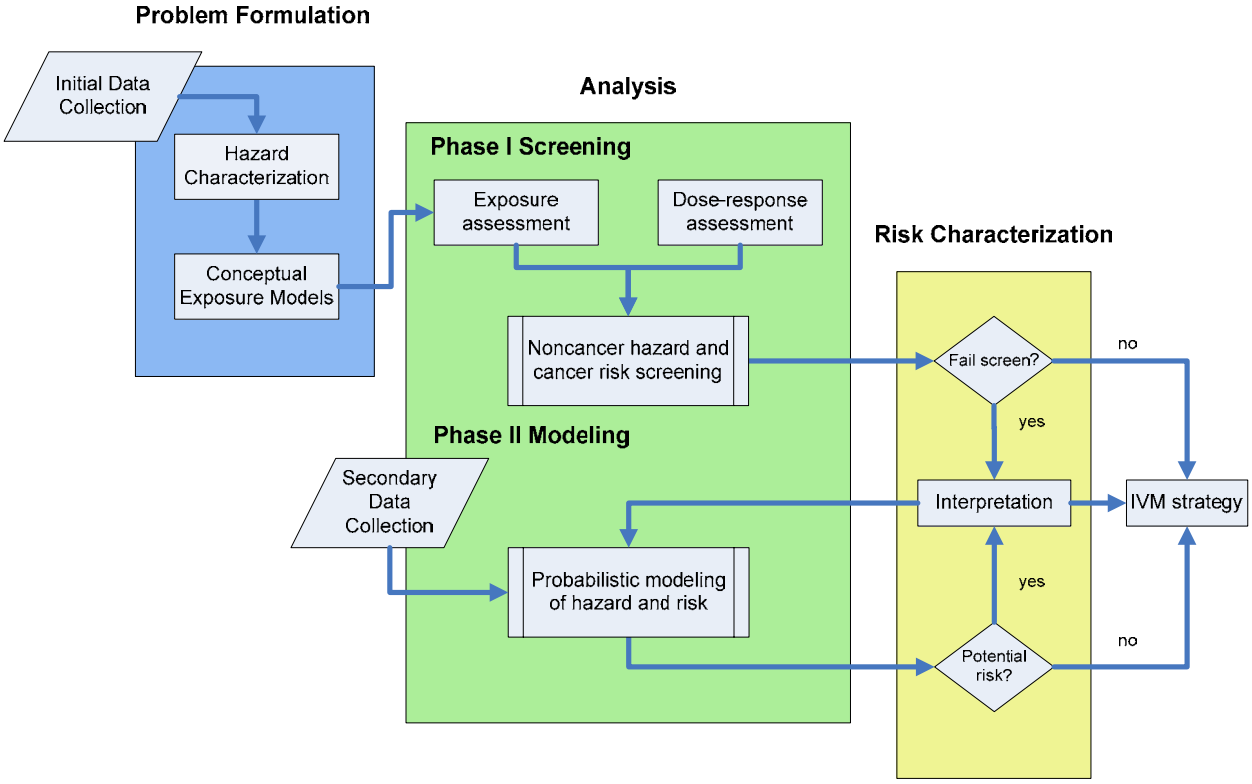
The analysis plan consists of a two-phased approach to characterize the potential health effects associated with pesticides used in implementing various IVM interventions. Figure 11 expands on Figure 1 and provides a more detailed view of the risk assessment process; in particular, it shows that the analysis phase of the risk assessment consists of a Phase I deterministic screening and, pending the results of the risk characterization and

interpretation, a Phase II probabilistic risk simulation. Although both phases are integral to the analysis plan, only a Phase I assessment has been completed for this PEA.

Phase I evaluates exposure scenarios (i.e., combinations of IVM intervention, receptor, exposure pathway, and pesticide) for workers and residents that may be exposed to pesticides through IVM practices. The screening assessment uses a series of simple exposure/risk models to identify scenarios with the potential to result in adverse effects for humans and expresses the results in terms of noncancer HQs (i.e., the ratio of predicted dose to a human health benchmark) and cancer risks (i.e., excess risk of an individual contracting cancer over a lifetime). To facilitate the deterministic screening calculations, we created a spreadsheet that automates the exposure and risk calculations for all of the scenarios and exposure routes considered in this assessment.[7] We made several assumptions in defining the scenarios that tend to increase exposure. For example, to estimate worker exposures, we assumed that workers do not wear PPE. Through literature reviews and consultations with vector control specialists working in the field, we selected reasonably conservative values for the input parameters, such as the exposure duration for workers during the spraying season. The complete set of input data used to populate the screening calculation spreadsheet is presented in ***Annex D***.

[7] The screening algorithms are discussed briefly in this section and in detail in ***Annex G***, Exposure and Risk Calculations.

Figure 11. Detailed View of the Pesticide Risk Assessment Process



Major groups of data inputs for the screening assessment include the following:

- **Concentration parameters** were derived from empirical data and are primarily a function of the physical characteristics associated with handling and application (e.g., formulation type) rather than the chemical properties of individual active ingredients (see U.S. EPA, 1997).
- **Pesticide use parameters** (e.g., application rates) generally describe how pesticides were applied and were largely taken from field investigations that described the use of pesticides for malaria vector management practices.
- **Receptor exposure factors** were derived to represent the characteristics of the African population. For example, the body weight reflects the nutritional status of a person in an African nation that is commonly used in exposure assessment.

In this PEA, only a conservative Phase I screening assessment was completed. This PEA recommends that a Phase II probabilistic risk simulation be used to characterize the uncertainty and variability in the risk estimates by using data on the distribution of values for each of the input parameters and assumptions (e.g., no PPE) of interest.

The risk characterization in Section 5.1.3 describes the Phase I deterministic screening results and makes recommendations as to whether each exposure scenario should be evaluated in the Phase II assessment, based not just on whether the scenario fails the screening, but also on the potential value of a more refined risk assessment for that

particular combination of pesticide, pathway, and receptor. For example, a scenario that fails the screening may fail because we assumed that no PPE was worn (e.g., no rubber gloves worn during treatment), but the use of PPE may eliminate the exposure pathway entirely. In this case, the screening results may be sufficient to support a decision regarding the use (or nonuse) of a particular pesticide or management practice without performing additional modeling, and a more precise estimate of the risk/hazard may be of little value to the decision maker.

5.1.2 Analysis

This section describes the Phase I screening risk assessment methodology developed to evaluate potential risks associated with pesticide use in various IVM interventions. Specifically, we present this analysis in three parts

- **Section 5.1.2.1** provides an overview of the exposure assessment methodology, explains how and why we selected pathways for analysis, summarizes the primary sources that form the basis for the screening methodology, discusses how the exposure durations were matched to endpoints, and covers exposure issues common to various IVM interventions and receptors.
- **Section 5.1.2.2** presents a concise description of the IVM-specific exposure scenarios, assumptions, data, and algorithms used in predicting exposures.
- **Section 5.1.2.3** describes the selection of human health benchmarks as part of the dose–response assessment and the calculation of the risk/hazard metrics for noncancer and cancer endpoints, respectively.

5.1.2.1 Overview of Exposure Assessment

The screening methodology is designed to produce conservative estimates of exposure to pesticides based on experiences in countries where IVM tools have been utilized. Worker exposures during application as well as post-application residential exposures are considered for the dermal, inhalation, and ingestion routes for both adults and children, as appropriate. The exposure assessment focused on specific pathways identified by vector control specialists in the field based on their extensive experience in integrated vector management. The specialists were instrumental in describing and providing parameters for exposure scenarios that would most likely result in the highest doses to workers and residential receptors. In making these selections, the specialists considered factors such as whether workers using a particular method tend to wear protective equipment, whether workers using particular methods exhibit symptoms of acute exposure, the toxicity of the pesticide, and the proximity of application to the home. Table 8 lists the pathways and pesticides evaluated in this screening assessment. ***Annex F***, Pathway List, presents a detailed list of the full universe of exposure pathways and indicates which pathways were considered insignificant (i.e., exposures well below other pathways that were modeled) and which pathways were not included in our current scope (e.g., pilferage and subsequent use of pesticides).

Table 8. Pathways by Pesticide and Intervention

Process	Pathway	Receptor	Alpha-cypermethrin	Bendiocarb	Bifenthrin	Cyfluthrin	DDT	Deltamethrin	Etofenprox	Fenitrothion	Lambda-cyhalothrin	Malathion	Methoprene	Permethrin	Pirimiphos-methyl	Propoxur	Temephos
Preparation																	
Mixing	Inhalation Dermal	Worker Resident	•	•	•	•	•	•	•	•	•	•		•	•	•	
IRS																	
Spraying	Inhalation	Worker	•	•	•	•	•	•	•	•	•	•			•	•	
Spraying, application on walls	Dermal	Resident	•	•	•	•	•	•	•	•	•	•			•	•	
ITNs																	
Treating nets	Dermal	Resident	•			•		•	•		•			•			
Disposal																	
Burying, groundwater	Dermal Ingestion	Resident	•	•	•	•	•	•	•	•		•	•	•	•	•	
Reuse of Pesticide Containers																	
Food/drink storage	Ingestion	Resident	•			•		•	•				•	•	•		•
Storage																	
Spillage	Inhalation	Worker	•	•	•	•	•	•	•	•		•			•	•	

In developing the screening methodology, we reviewed several reports, journal articles, and guidance documents specific to pesticide exposure and risk assessment. Our intent was to ensure that the approach developed for this risk assessment was consistent with common practices in evaluating pesticide risks as well as the current state-of-the-science

in the broader chemical risk assessment community. As appropriate, we discuss when we adopted approaches from existing guidance and explained why we modified our methodology for the IVM risk assessment, particularly in instances where the methods diverge somewhat from typical pesticide risk assessment techniques (i.e., modifications required to address IVM-specific scenarios). In addition to numerous chemical risk assessment projects that we have conducted for EPA, we also undertook a review of materials specific to pesticides, evolving IVM strategies, and international risk assessment guidance; examples of these materials include the following:

- Barlow, S.M., F.M. Sullivan, and J. Lines. 2001. Risk assessment of the use of deltamethrin on bed nets for the prevention of malaria. *Food and Chemical Toxicology 39*: 407–422.
- IPCS (International Program on Chemical Safety). 2005a. INCHEM: Principles for the Assessment of Risks to Human Health from Exposure to Chemicals. Available at www.inchem.org (Accessed July 2005).
- IPCS (International Program on Chemical Safety). 2005b. Dermal Absorption. Available at http://www.who.int/ipcs/methods/dermal_absorption/en/ (February, 2005).
- Najera, J.A., and M. Zaim. 2001. *Malaria Vector Control: Insecticides for Indoor Residual Spraying.* WHO/CDS/WHOPES/2001.3.
- Najera, J.A., and M. Zaim. 2002. *Malaria Vector Control: Decision Making Criteria and Procedures for Judicious Use of Insecticides*. World Health Organization. WHO/CDS/WHOPES/2002.5 Rev 1.
- Rogan, W.J., 2005. Health risks and benefits of bis (4-chlorophenyl)-1,1,1-trichloroethane (DDT). *Lancet* 366: 763–773.
- USAID (United States Agency for International Development). 2002. Programmatic Environmental Assessment for Insecticide-Treated Materials in USAID Activities in Sub-Saharan Africa. Washington, DC: Office of Sustainable Development. January.
- U.S. EPA (Environmental Protection Agency). 1997. *Standard Operating* P*rocedures (SOPs) for Residential Exposure Assessments*. Draft. Office of Pesticide Programs. December 19. Available at http://www.epa.gov/pesticides/trac/science/trac6a05.pdf (accessed September 27, 2005).
- U.S. EPA (Environmental Protection Agency). 1999a. *Guidance for Performing Aggregate Exposure and Risk Assessments*. Office of Pesticides. October 29.
- U.S. EPA (Environmental Protection Agency). 2000a. *A Review of Department of Defense Office of the Special Assistant for Gulf War Illnesses, 3/9/99 DRAFT Environmental Exposure Report: Pesticides in the Gulf*. Washington, DC: Office of Pesticide Programs. February 29.

- WHO (World Health Organization). 2004. A Generic Risk Assessment Model for Insecticide Treatment and Subsequent Use of Mosquito Nets. Communicable Disease Control, Prevention, and Eradication WHO Pesticide Evaluation Scheme.

The methodology described in this report, particularly as it pertains to worker exposures, is largely based on algorithms developed by the EPA Office of Pesticide Programs and referred to as standard operating procedures (SOPs) (U.S. EPA, 1997). The SOPs were very useful in framing the exposure assessment and subsequent risk/hazard calculations. However, because the SOPs were developed to characterize high-end risks associated with residential pesticide use specifically in the United States, some of the algorithms and data are not entirely appropriate for use in estimating risks associated with pesticide use in the developing world as part of an overall IVM strategy (e.g., residual pesticide exposure from contact with carpets is unlikely in most households). In addition, the SOPs were not intended for use in evaluating environmental exposures due to accidental pesticide release following dumping or disposal (for example, the SOPs do not cover ingestion of contaminated groundwater). Therefore, we modified the basic exposure algorithms by incorporating additional variables and modeling constructs used in chemical exposure assessment. Specific examples include the following:

- For most exposure algorithms, averaging time and exposure duration are now explicitly represented (see, for example, U.S. EPA, 1998b). This change enables us to calculate an average daily dose of pesticide over a period of time that can be matched to a health effects benchmark over the length of time that exposure is assumed to occur.
- For dermal exposure, we added algorithms to evaluate direct contact with contaminated groundwater through bathing (U.S. EPA, 2004). In addition, the SOPs for dermal exposure for residents were modified to calculate an absorbed dose per exposure event.
- For acute and intermediate dermal exposures, we adapted the simple screening methodology described in Barlow et al. (2001) and the generic risk assessment model for insecticide treatment (WHO, 2004). This is essentially a mass-based approach that calculates the total amount of pesticide that an individual may contact and estimates the average dose per kilogram of body weight.
- For the groundwater pathways, dilution and attenuation factors (DAFs) were used to represent the natural attenuation of pesticide concentrations that occurs between the release point and the drinking water aquifer. As indicated in Section 2, the scope of this assessment did not include environmental fate and transport modeling and, therefore, the DAF provides a reasonably conservative predictor of pesticide concentration in groundwater.

Most of the algorithms predict an applied dose—the mass of chemical that is inhaled, ingested, or deposited on the skin. Lacking chemical-specific information about the mass of chemical that crosses these barriers (e.g., the gastrointestinal mucosa), we typically

make the conservative assumption that 100 percent of the applied dose is absorbed into the body (i.e., applied dose = absorbed dose). However, the algorithms used to evaluate the dermal exposures through contact with water that is contaminated with pesticides (e.g., dermal contact with treatment solution for bed nets) predict an absorbed dose—the mass of chemical that crosses skin and is absorbed systemically. This is largely a function of the skin permeability to a particular pesticide and is intended to reflect the ability of the skin to prevent chemicals from entering the bloodstream.

For noncancer endpoints, an average daily dose (ADD) is calculated for each route of exposure for the scenario-specific duration (e.g., seasonal exposure for pesticide workers) and averaged over the time period of interest. As described above, the exposure duration represents the actual length of time that a receptor is exposed, and the averaging time represents the period of time over which daily dose should be averaged. For example, a worker that sprays pesticide 6 days a week for 12 weeks is assumed to have an exposure duration of 72 days (6 days/week x 12 weeks) and an averaging time of 84 days (7 days/week x 12 weeks). This averaging time corresponds to an intermediate-term health benchmark (typically 31–90 days).

For cancer endpoints, a lifetime average daily dose (LADD) is calculated that reflects the ADD over a person's entire lifetime. Thus, the LADD is calculated by averaging a dose of any duration over the 50-year lifetime assumed in this assessment. For cancer endpoints, we combined the predicted doses from different routes of exposure to estimate an aggregate exposure per the *Guidance for Performing Aggregate Exposure and Risk Assessments* (U.S. EPA, 1999a).

5.1.2.2 Estimating Exposure to Pesticides

This section provides a concise description of each exposure scenario, the source of the exposure algorithm we selected, and any major modifications that we made to the exposure algorithm. The scenario includes information on the activity (e.g., pesticide preparation), exposure route, receptor, selected assumptions, and data inputs. The exposure algorithms are presented in ***Annex G***, Exposure and Risk Calculations, along with an explanation of each of the input values used in the deterministic screening (e.g., unit exposure factors). Information on the other input parameter values is presented in ***Annex D***, Input Parameters. The complete results from the

IVM Intervention: IRS

Activity: Preparation

Exposure Route: Dermal and Inhalation

Algorithms: *Annex G*, **Tables G-1, G-2, and G-5**

Receptors: Workers (adults)

Assumptions:
- Two 12-week spraying seasons per year
- Spraying occurs 6 days per week
- Fifteen 10-liter tanks used per day

Exposure Duration: 72 days (NC)/144 days (C)

Averaging Time: 84 days (NC)/50 years (C)

Mean Body Weight: 60 kg

exposure assessment are presented in ***Annex H*** in units of applied or absorbed dose, as predicted by the exposure model.

IRS

For IRS, we assessed exposure from preparing (mixing) the insecticide formulation, spraying the insecticide on the interior walls of a residence, and contact with treated walls after spraying. The worker is assumed to be exposed during the mixing and spraying processes, and the resident is assumed to be exposed through dermal contact with treated walls and contaminated surfaces after spraying. Residents could also be exposed through inhalation and dermal contact, or children could even ingest residues.

Preparation—Dermal and Inhalation Exposure

For the preparation of insecticide for IRS, we looked at potential dermal and inhalation exposures for workers mixing the insecticide formulation with water. The algorithms were adapted from the EPA SOP 2.1 (Handler Inhalation and Dermal Potential Doses from Pesticides Applied to Turf) (U.S. EPA, 1997). These algorithms for worker exposures from mixing insecticide formulation were modified to include the amount of formulation used per tank.

For this scenario, we assumed that only adults are involved in mixing IRS insecticides, and we selected the unit exposure for open mixing/loading for WP (DDT, lambda-cyhalothrin, and malathion). For noncancer (NC) endpoints, we evaluated the hazard associated with a single spraying season of 12 weeks, assuming a 6-day work week. For carcinogenic (C) endpoints, we evaluated the risk from two spraying seasons per year averaged over a 50-year lifetime. Because we did not have any information on the tenure of pesticide workers, the cancer risk was calculated for a single year of exposure.

Spraying—Inhalation Exposure

For indoor spraying, we assessed the inhalation exposure of workers during application. The algorithm was adapted from the EPA SOP 6.1.1 (*Inhalation Potential Dose from Painting/Staining in Residential Settings*) (U.S. EPA, 1997). The scenario is based on an application of active ingredient of insecticide per area of the house and takes into account total surface area of the walls of an estimated average size house in Africa and the total number of houses sprayed in 1 day by a worker. Thus, this algorithm for indoor spraying was customized to reflect IRS practices in Africa. We estimated adult exposures as in the preparation scenario described above with respect to exposure

IVM Intervention: IRS

Activity: Spraying

Exposure Route: Inhalation

Algorithms: *Annex G*, **Table G-7**

Receptors: Workers (adults)

Assumptions:

- Two 12-week spraying seasons per year
- Spraying occurs 6 days per week
- 12 houses sprayed per day
- 35.8 m^2 per house

Exposure Duration: 72 days (NC)/144 days (C)

Averaging Time: 84 days (NC)/50 years (C)

Mean Body Weight: 60 kg

duration, averaging time, and body weight (e.g., exposure duration of 72 days for NC endpoints).

Contact with Sprayed Surfaces—Dermal Exposure

IVM Intervention: IRS

Activity: Contact with sprayed surfaces

Exposure Route: Dermal

Algorithms: *Annex G*, **Table G-8**

Receptors: Residents (adults and children)

Assumptions:
- Hands and forearms exposed
- Estimated as a one-time event

Averaging Time: 1 days (NC)/50 years (C)

Mean Body Weight: 60 kg (adult)/40 kg (child)

Residential exposures through dermal contact with indoor surfaces were assumed to occur immediately after spraying; therefore, we considered dermal exposure that occurs in a single day for both adults and children. We did not use the algorithm in EPA SOP 8.2.2 (*Post Application Dermal Dose from Pesticide Residues on Hard Surfaces*) (U.S. EPA, 1997) because it was developed to predict exposures from direct contact with pesticide residuals on carpets, a significantly different exposure scenario than what we would expect in African homes as a result of IRS. We evaluated the approach presented in the *Risk Assessment Guidance for Superfund* (RAGS) (U.S. EPA, 2004) that was designed to calculate the absorbed dose from dermal contact with contaminated water. However, there are significant uncertainties associated with modeling this scenario (e.g., how much contact actually occurs), and the algorithms developed in RAGS were intended for use in estimating chronic exposures to low concentrations of chemical contaminants in environmental media. Therefore, we adapted the approach presented in WHO (2004) to estimate the dose experienced by a person through dermal contact with a pesticide film that adheres to the skin following immersion in a water-based application.

For this scenario, we assumed that residents are exposed through contact with the insecticide residue that adheres to surfaces during spraying. Given the type of pesticide application and the small volume required for the typical home assumed for this analysis, it is reasonable to expect that aerosol particles will settle out of the air, forming a temporary insecticide film on nonwall surfaces. Residents may be exposed to this film through contact with palms and forearms for 1 day; after the first day, the available pesticide residue on contactable surfaces is removed by evaporation of water, friction that occurs during contact, and general cleaning. The total volume of the film that the resident is in contact with is based on studies showing that roughly 8 mL is the maximum amount of a nonviscous liquid likely to be in contact with hands that have been immersed without gloves in a liquid (Barlow et al., 2001). Assuming that only palms and the inside surface of the forearm are in contact, a conservative estimate for the film volume would be about 4 ml. The walls of typical peri-urban African homes are generally constructed of earthen materials (e.g., mud or cement), and because the walls tend to absorb the insecticide, significant long-term dermal exposure through incidental contact with walls is unlikely.

For noncancer endpoints, we assumed that after 1 day, walls and other surfaces are essentially free of any insecticide film; therefore, the averaging time is a single day. For cancer endpoints, we estimated the cancer risk associated with exposure that occurs during a single day and averaged that over a lifetime of 50 years. Thus, this is the incremental cancer risk associated with exposure over a single day; if additional exposures occur, the cancer risk from each event would be added together to estimate a total cancer risk from multiple acute exposures.

IVM Intervention: IRS

Activity: Ingestion of sprayed food

Exposure Route: Ingestion

Algorithms: *Annex G*, **Table G-9**

Receptors: Residents (adults and children)

Assumptions:
- Food is not covered during spraying

Application rate to walls also applied to food

Mass of food based on caloric intake
- Estimated as a one-time event

Exposure Duration: 1 day

Averaging Time: 1 days (NC)/50 years (C)

Mean Body Weight: 60 kg (adult)/40 kg (child)

Sprayed Food—Ingestion Exposure

In addition to dermal exposure from contact with sprayed walls, we evaluated the exposure to food sprayed with pesticide. We assumed that ingestion of contaminated food occurred immediately following spraying for both adults and children. Neither the EPA SOPs nor the WHO Generic Risk Assessment addressed this exposure pathway; the ingestion equations in the EPA SOPs deal with incidental nondietary exposures, and WHO only addressed the ingestion of pesticide pellets. Therefore, this algorithm was developed specifically for this screening assessment.

We assumed that some portion of food items is uncovered during the spraying process. Without information on the type, amount, or common storage practices for food in a residence, we developed a three-part approach to derive a surface area for food assumed to be sprayed with pesticide: (1) estimate the mass of food ingested per day[8] (based on caloric needs and consumption of carbohydrates); (2) convert the mass to a unit volume, using the density of water as a reasonable approximation for the density of food; and (3) use the simple geometry of a cube to estimate the surface area of the food sprayed during IRS (i.e., the top surface of the cube). A flat, rectangular geometry would have produced a more conservative estimate of exposure; however, there are several conservative assumptions built into this scenario and we decided to use the simplest approach possible for the geometry. For instance, we used the pesticide application rate for the wall as the application rate for the food even though we would expect food contamination to occur as the result of aerosol particles settling onto food.

IVM Intervention: ITN

Activity: Preparation

Exposure Route: Dermal and Inhalation

Algorithm: *Annex G*, **Tables G-3, G-4, and G-6**

Receptors: Residents (adults)

Assumptions:

- Nets are treated four times per year
- Resident is involved in mixing for 38 years
- Two nets treated per day

Exposure Duration: 0.007 days (NC)/1.06 days (C)

Averaging Time: 1 day (NC)/50 years (C)

Mean Body Weight: 60 kg (adult)

For noncancer endpoints, we assumed that after 1 day, all contaminated food would be consumed; therefore, the averaging time is 1 day. For cancer endpoints, we estimated the cancer risk associated with exposures occurring in a single day and averaged over a lifetime of 50 years. As with the previous scenario, we are calculating an incremental cancer risk associated with exposure over a single day. Any additional exposures for cancer would need to be added together to estimate a total cancer risk from multiple acute exposures.

[8] The daily food consumption rate reflects the undernourished status of many Africans.

ITNs

For ITNs, we assessed the exposure associated with preparing the insecticide kit to be mixed with water and the direct contact with the insecticide mixture that occurs during treatment of bed nets. Only residents who treat their own bed nets were assessed; community-based operations that treat large numbers of bed nets were assumed to routinely use PPE to eliminate the dermal and inhalation exposure pathways.

Preparation—Dermal and Inhalation Exposure

For the preparation of insecticide for ITNs, we examined both the dermal and inhalation exposure routes. The same algorithm (as modified) used to evaluate the IRS preparation scenario was also used for this scenario.

We assumed that children are not involved in preparing insecticide mixtures, and we selected the unit exposures for open mixing/loading for WP (lambda-cyhalothrin) and EC (permethrin). The insecticide concentration in the mixture was calculated as shown in ***Annex G***, Table G-10 and the amount of formulation used is for one bed net. For noncancer endpoints, we assumed that a resident treats two nets for one household in 1 day. Based on reports from field experts, it takes approximately 6 minutes to prepare the insecticide mixture. For cancer endpoints, we assumed that residents treat the bed nets four times per year to replace the insecticide lost through washing and normal wear, and that the adult (starting at age 13) is involved in mixing until age 50.

IVM Intervention: ITN

Activity: Treating bed nets

Exposure Route: Dermal

Algorithm: *Annex G*, **Table G-10**

Receptors: Residents (adults and children)

Assumptions:
- Hands, forearms, and lower limbs exposed
- Two nets treated per day

Exposure Duration: 1 day

Averaging Time: 1 day (NC)/50 years (C)

Mean Body Weight: 60 kg (adult)/40 kg (child)

Treating ITNs—Dermal Exposure

We evaluated the dermal exposure that occurs during treatment. After reviewing EPA SOP 5.2.2 (*Postapplication Dermally Absorbed Dose from Swimming in Pesticide-Treated Residential Swimming Pools*) (U.S. EPA, 1997), we determined that this algorithm did not explicitly account for the time of travel across the skin, a feature that may be desirable given the very short contact time for treatment (based on reports from field experts, it takes approximately 6 minutes to complete the treatment process). In addition, the SOP was based on a very conservative assumption that 100 percent of the application concentration is available to be absorbed. In addition, we evaluated the appropriateness of algorithms presented in RAGS (U.S. EPA, 2004) to calculate the dermal exposure from treating. These algorithms include a lag time variable that accounts

for the amount of time required for a specific chemical to diffuse through the skin. As with the SOP, the permeability coefficient, exposed skin surface area, and other inputs are needed to estimate the absorbed dose per exposure event. However, the RAGS algorithm is linear with respect to IVM concentration and, for contact with a highly concentrated pesticide solution, this approach will grossly overestimate the absorbed dose. Research has shown that dermal absorption will achieve a maximum rate depending on the availability and properties of the chemical; however, once the maximum rate has been achieved, increasing the concentration to high levels will not increase the absorbed dose, and the exposure-dose profile will reach an asymptote (IPCS, 2005b). Consequently, we used the simple screening approach presented by the WHO (2004) as part of the generic risk assessment model for treating bed nets.

For this scenario, we assumed that both adults and children are involved in treating bed nets (WHO, 2004). The "least safe scenario" was assumed and dermal contact of the hands, forearms, and lower limbs was calculated as described by WHO (2004). The total volume of pesticide solution that the resident is in contact with is based on studies showing that roughly 8 mL is the maximum amount of a nonviscous liquid likely to be in contact with hands that have been immersed ungloved in a liquid (Barlow et al., 2001). Therefore, the total volume to cover the surface area of the hands, forearms, and lower limbs with a film thickness of 0.01 cm is 24 mL of pesticide solution.

For noncancer endpoints, we assumed that a resident treats both nets in the same day; thus, the averaging time is a single day for the acute exposure scenario. For cancer endpoints, we estimated the cancer risk associated with exposure from treating two nets and averaged that over a lifetime of 50 years. Thus, this is the incremental cancer risk associated with exposure over a single day; if additional exposures occur, the cancer risk from each event would be added together to estimate a total cancer risk from multiple acute exposures.

Disposal

Excess or expired pesticide formulation may be disposed of by burying or dumping onto soil or into surface water. Although any of these practices can lead to the contamination of groundwater, the burial of pesticides is of particular concern because of the potentially short distance between the burial and underlying groundwater aquifer.[9] Depending on the quality of the aquifer, groundwater can serve as an important source of drinking and bathing water. For the burial scenario, residents are assumed to be exposed through the ingestion of contaminated groundwater and through dermal contact while bathing.

[9] Pesticides spilled onto soils (rather than buried) are far less likely to contaminate groundwater because of various environmental processes that degrade and/or sorb the pesticide in the unsaturated zone of the soil. Similarly, pesticides dumped into surface waters would also be subject to environmental degradation and sorption to suspended solids and sediment particles. Although dumping could adversely affect humans through direct contact or ingestion, seepage and infiltration into groundwater at levels of concern would be far less likely than in the burial scenario.

For the screening assessment, we did not perform any fate and transport simulations of pesticides released into the subsurface. However, we assumed that the pesticide released from buried containers would be diluted and attenuated by natural environmental processes that would reduce the effective concentration of pesticide at the well. For DDT, we identified a DAF from the *Industrial Waste Management Evaluation Model (IWEM) Technical Background Document* (U.S. EPA, 2002b). Because DAFs were not identified for the other pesticides, we identified a default DAF of 20 suggested by the EPA Superfund program for use in areas where environmental conditions suggest that dilution/attenuation would likely occur (U.S. EPA, 2002a). Given the physical and chemical properties of these chemical compounds, we believe that assuming that no dilution/attenuation occurs would be unrealistically conservative. For these scenarios, we made the simplifying assumption that the well concentration does not change over time. Assuming that the well concentration is at steady-state for the entire period of exposure is based on the premise that there is sufficient pesticide mass in the buried containers to approximate an infinite source.

Disposal

Activity: Drinking of contaminated groundwater

Exposure Route: Ingestion

Algorithm: *Annex G*, **Table G-11**

Receptors: Residents (adults and children)

Assumptions:
- Well concentration remains constant
- Some dilution/attenuation will occur
- All drinking water comes from contaminated well

Exposure Duration: 1 year (NC)/50 years (C)

Averaging Time: 365 days (NC)/50 years (C)

Mean Body Weight: 60 kg (adult)/40 kg (child)

Disposal—Contaminated Groundwater—Ingestion Exposure

For burial of pesticides, we looked at the potential dose from ingestion of contaminated groundwater by adult and child residents. The algorithm presented in ***Annex G*** has been used in numerous EPA groundwater screening assessments (see for example, EPA's *Surface Impoundment Study*, U.S. EPA, 2001); the well concentration is predicted simply by dividing the pesticide concentration by the DAF.

For noncancer endpoints, we assumed that receptors will be exposed daily for a period of 1 year. For cancer endpoints, we assumed that residents are exposed daily and that they remain at the same residence throughout their lifetime. This implies that the person spends their entire life living in the same home and drinking only from the contaminated groundwater well. Following recommendations in RAGS, we adopted a simple screening approach for cancer and used only the adult body weight in the calculations (U.S. EPA, 2004).

Disposal—Bathing with Contaminated Groundwater—Dermal Exposure

Disposal

Activity: Bathing with contaminated groundwater

Exposure Route: Dermal

Algorithm: *Annex G*, **Table G-12**

Receptors: Residents (adults and children)

Assumptions:
- Well concentration remains constant
- Some dilution/attenuation will occur
- Two bathing events per week
- Ten minutes per bathing event

Exposure Duration: 1 year (NC)/50 years (C)

Averaging Time: 365 days (NC)/50 years (C)

Mean Body Weight: 60 kg (adult)/40 kg (child)

In addition to screening ingestion exposure, we also evaluated dermal exposure. The algorithm in ***Annex G*** was adopted from RAGS (U.S. EPA, 2004) for estimating the absorbed dose from dermal contact with contaminated water and is the same algorithm that was used to evaluate dermal exposures during bed net treatment.

The bathing scenario assumes that the resident takes 1 full bath per week and performs daily body washing equivalent to another full bath a week, for a total of 2 bathing events per week. All other assumptions and exposure factors (e.g., body weight) are the same as the ingestion scenario.

Reuse of Pesticide Containers

We evaluated ingestion exposure from the reuse of pesticide containers that contain residual pesticide. The algorithm was adapted from the EPA SOP 5.2.1 (*Postapplication Potential Doses from Incidental Nondietary Ingestion of Pesticide Residues While Swimming*) (U.S. EPA, 1997) for acute ingestion exposures. We modified this algorithm to include a dilution factor that represents the simple volumetric dilution that occurs when the container is filled with water.

Reuse of Pesticide Containers

Activity: Drinking water from pesticide container

Exposure Route: Ingestion

Algorithm: *Annex G*, **Table G-13**

Receptors: Residents (adults and children)

Assumptions:
- Container is used to store drinking water
- Container is not rinsed prior to use
- Five percent of pesticide in container after use
- After first use, remaining pesticide is negligible

Exposure Duration: 1 day (NC)/1 day (C)

Averaging Time: 1 day (NC)/50 years (C)

Mean Body Weight: 60 kg (adult)/40 kg (child)

We assumed that a household uses all of the water in the reused container in a single day as a source of water for drinking, cooking, bathing, cleaning, etc., and that the ingestion of the contaminated water would be the most significant exposure route. For noncancer endpoints, this results in a single exposure that occurs for 1 day. For cancer endpoints, we had no information on how many times a household would acquire a new container and, more importantly, we had no way to determine whether the container would have been used for the same pesticide. The assumption that a household would acquire and reuse an unrinsed container for the same pesticide each year seemed unrealistic and simply too conservative, even for a

deterministic screening analysis. Therefore, we assumed that, for any given pesticide formulation, a household would acquire and reuse an unrinsed container only once during the lifetime.

Storage

During the storage of pesticides, damage to containers may be caused by vermin, defective packaging, or mishandling. We estimated the inhalation exposure that is associated with storing pesticides in a small, poorly ventilated shed. We added a variable to an algorithm adapted from the EPA SOP 2.1 (*Handler Inhalation and Dermal Potential Dose from Pesticides Applied to Turf*) (U.S. EPA, 1997) to represent the number of times a worker enters a storage shed and is potentially exposed to pesticide particles that are re-entrained in the air during loading/unloading activities.

Storage

Activity: Spillage

Exposure Route: Inhalation

Algorithm: *Annex G*, **Table G-14**

Receptors: Workers (adults)

Assumptions:

- Two 12-week spraying seasons per year
- Workers loading/unloading six days per week
- Two trips into storage shed per day
- Shed is approximately 12 m^2

Exposure Duration: 72 days (NC)/144 days (C)

Averaging Time: 84 days (NC)/50 years (C)

Mean Body Weight: 60 kg (adult)

We calculated exposures to adult workers assuming that children would not have access to the pesticide storage sheds. The scenario assumes that there are pesticide bags and containers on either side of the shed, with roughly half the area open. Thus, the effective spill area covers the narrow floor space in the middle of the shed; the residual pesticide powder accumulates on the floor and is emitted into the air each time a worker goes into the shed. For both noncancer and cancer endpoints, the other assumptions correspond to the worker scenarios presented above (e.g., two 12-week spraying seasons each year).

5.1.2.3 Predicting Noncancer Hazard and Cancer Risk

To quantify the potential for adverse health effects due to exposure to each pesticide, we identified human health benchmarks for each exposure route and duration evaluated in the screening assessment. For noncancer endpoints, the health benchmark (expressed in milligrams of pesticide per kilogram body weight per day) represents a point on the dose–response continuum below which adverse effects would not be expected. That is, a dose (the ADD) below the benchmark would not be expected to cause an adverse health effect. The noncancer health benchmark is compared with the predicted dose to calculate the hazard quotient (HQ). An HQ above 1 suggests the potential for adverse effects given the assumptions and data used to define the exposure scenario. Given the conservative design of the screening assessment, an HQ below 1 suggests a very low potential for adverse effects.

For cancer endpoints, the health benchmark represents the potential of the pesticide to cause cancer in humans assuming that *any* exposure is associated with some finite

probability of an individual contracting cancer. The cancer benchmark (expressed in units of [milligrams of pesticide per kilogram body weight per day]$^{-1}$) is multiplied by the LADD (the ADD averaged over the lifetime of 50 years) to calculate the excess risk of cancer for a person due to the exposures received over the course of a lifetime. Although policies vary across environmental programs and countries, an excess cancer risk in the range of 10^{-4} to 10^{-6} is typically regarded as the most relevant to decision makers. A cancer risk below 10^{-6} is generally considered to be below a level of concern for public health.

This section describes the benchmarks used to quantify health effects, and describes how the HQ s and cancer risks were calculated.

Selection of Health Benchmarks

Two types of benchmarks were selected for the screening risk assessment. For noncancer hazard, a reference dose (RfD) specific to the duration of exposure was selected for each pesticide. The RfD is defined by EPA as an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily oral exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. It can be derived from a no observed adverse effect level (NOAEL), lowest observed adverse effect level (LOAEL), or benchmark dose, with uncertainty factors generally applied to reflect limitations of the data used. The degree of uncertainty and confidence levels in RfDs vary and are based on both scientific (i.e., toxicological studies) and policy (i.e., level of conservatism) considerations.

For cancer risk, a cancer slope factor (CSF) was selected for those pesticides for which suitable data were available to support the development of a CSF. The CSF is an upper-bound estimate (approximating a 95 percent confidence limit) of the increased human cancer risk from exposure to an agent over the lifetime of the individual. Unlike RfDs, CSFs do not represent “safe” exposure levels; rather, they relate levels of exposure with a probability of cancer risk.

Health benchmarks were identified from several sources in the following order of preference:

a. EPA’s Reregistration Eligibility Decision (RED) documents
b. EPA’s Integrated Risk Information System (IRIS) (U.S. EPA, 2005)
c. EPA’s Health Effects Assessment Summary Tables (HEAST)
d. ATSDR’s Toxicological Profiles.

For noncancer endpoints, the length of time that workers and residents may be exposed to a pesticide varies by activity (e.g., preparation, spraying, treatment). Therefore, benchmarks were identified for four categories consistent with the definitions presented in the RED documents:

1. Acute ($\leq$1 day)
2. Short-term (>1 day to $\leq$ 30 days)

3. Intermediate-term (>30 days to ≤6 months)
4. Chronic (>6 months).

If benchmarks were not available from a RED document, we obtained chronic and subchronic benchmarks from IRIS or HEAST (i.e., chronic and subchronic RfDs), and used the subchronic benchmarks to evaluate the intermediate-term exposures. In the absence of data from EPA sources, we relied on ATSDR documents to identify acute MRLs (developed for exposures of 1–14 days) to represent acute and short-term exposure durations; intermediate MRLs (developed for exposures of 2 weeks to 1 year) to represent intermediate-term exposures; and chronic MRLs (developed for exposures longer than 1 year) to represent chronic exposures.

The inhalation benchmarks not presented in units of dose were converted to milligrams of pesticide per kilogram body weight per day (mg/kg-day) based on an assumed inhalation rate of 20 m^3/day and an average adult body weight of 70 kg. However, inhalation benchmarks were not available for some of the pesticides that we evaluated in the screening assessment. In those instances, we used a simple route-to-route extrapolation that implicitly assumes that that there are no portal-of-entry effects and the route of administration is irrelevant to the dose delivered to the target organ (U.S. EPA, 2002a). Although EPA has not developed formal guidance for route-to-route extrapolations between oral and inhalation studies, the Superfund program has suggested that oral benchmarks can be used to support inhalation benchmarks.

Similarly, dermal benchmarks were not available for some of the pesticides that were included in the screening. In those instances, we used the methodology recently published by EPA for making route-to-route extrapolations for systemic effects via percutaneous absorption (U.S. EPA, 2004). Oral RfDs are generally expressed as the amount of substance *administered* per unit time and body weight, whereas dermal exposure estimates are expressed as *absorbed* dose. EPA recommends that a default value of complete (i.e., 100 percent) oral absorption be assumed in the absence of data indicating poor gastrointestinal absorption, thereby eliminating the need to adjust the oral toxicity value. However, using the oral absorption default value may result in an underestimate of risk at a level that is inversely proportional to the true oral absorption of the chemical in question (U.S. EPA, 2004). EPA does not recommend adjusting for absorption unless gastrointestinal absorption is less than 50 percent. EPA specifically recommends that DDT not be adjusted as oral absorption ranges from 70 to 90 percent (U.S. EPA, 2004). Additional data indicate that malathion oral absorption is about 89 percent (in 60 minutes) in mice (ATSDR, 2003b); permethrin oral absorption is about 60 percent in rats (ATSDR, 2003a); and cyhalothrin oral absorption ranges from 48 to 80 percent in dogs (WHO, 1990). No quantitative absorption data on temephos were located. Based on this information, no adjustment was made for any of the pesticides of concern and oral toxicity values were used for the dermal assessment.

The human health benchmarks used in this risk assessment are summarized in ***Annex D***, Table D-3, and toxicological profiles are presented in ***Annex E***.

Calculating Noncancer Hazard and Cancer Risk

For noncancer endpoints, there are several methods available for expressing the potential hazard including, for example, the margin of exposure (MOE). For this screening assessment, we chose the hazard quotient (HQ) as the simplest and most transparent metric for noncancer hazard. As discussed previously, the HQ is simply the ratio between the predicted dose and the health benchmark (both are in units of milligrams of pesticide per kilogram body weight per day). There are two features about the HQ that make it particularly useful for screening assessments. First, an HQ greater than 1 is regarded as an indication of potential hazard for any of the four categories of benchmarks identified for comparison with predicted doses for corresponding exposure durations (e.g., acute versus chronic). The benchmarks were derived for the protection of human health and, because appropriate uncertainty factors are already documented for each benchmark, the target HQ of 1 serves as a bright line with which to consider potential hazard. Second, the HQ is scalable in the sense that we can consider the impact on hazard by inspection of some of the parameters. For example, an HQ of 2 in a screening assessment might not require additional modeling if one of the input parameters was shown to be overly conservative by a factor of 5 (for example, suppose that a study showed that only 2 percent of a pesticide is dislodgeable, instead of the assumed 10 percent). As a result, we can state with some confidence that a change in the input parameter would allow a particular exposure scenario to pass the screen.

In addition, we can easily aggregate hazard using a simple summation method that is generally referred to as the hazard index (HI), a method often used in EPA screening assessments. The HI aggregates individual HQs for each route of exposure, as shown in the following equation:

$$HI = HQ_{Oral} + HQ_{Dermal} + HQ_{Inhalation},$$

where the HQ represents the same scenario in all respects except for the route of exposure (e.g., the same receptor and exposure duration). The HI approach is frequently used in screening assessments even in cases where the noncancer endpoints differ depending on the route of exposure. In this assessment, we have made this same conservative simplification and added hazard across exposure route regardless of the endpoint. This aggregation regardless of endpoint is less of a concern when many of the health benchmarks are derived through route-to-route extrapolation.

For cancer endpoints, we use EPA's recommended approach to estimate cancer risk by multiplying the LADD by the cancer potency factor to obtain the incremental excess lifetime cancer risk. The cancer risk estimate represents a person's risk of contracting cancer due to the exposures received over a lifetime. Note that this is a simplification of a very complex process that may depend greatly on the timing of exposure with respect to the life stage of the person (this is discussed further in Section 5.1.3). As with the

noncancer endpoints, the aggregate cancer risk can be calculated using a simple summation, as shown in the following equation:

$$\text{Cancer Risk}_{\text{Total}} = \text{Risk}_{\text{Oral}} + \text{Risk}_{\text{Dermal}} + \text{Risk}_{\text{Inhalation}},$$

where the route-specific cancer risks are calculated for the same receptor assuming all aspects of the scenario are the same. As with noncancer endpoints, this approach does not distinguish between different types of cancers that may be associated with different routes of exposure.

5.1.3 Risk Characterization

This section describes the interpretation and risk characterization of the screening results for noncancer hazard and cancer risk for the IVM practices, pesticides, exposure scenarios, and receptors that are the focus of this report. The risk characterization is presented in three parts:

Section 5.1.3.1 briefly describes the strengths and limitations of the risk assessment, focusing primarily on the screening phase. We discuss key uncertainties and develop the context for how these results should be interpreted and used in decision making.

Section 5.1.3.2 summarizes the noncancer and cancer results. For each IVM practice and pesticide-related activity, we interpret the results with respect to the level of conservatism and the significance of the health endpoints, and provide recommendations for mitigation strategies and/or additional analysis.

Section 5.1.3.3 presents the major conclusions of this screening assessment along with recommendations for Phase II, focusing on the most important sources of uncertainty identified in the assessment and providing specific suggestions for next steps.

5.1.3.1 Strengths and Limitations

As described in Section 5.1.2, the screening methodology is designed to produce conservative estimates of the noncancer hazard and cancer risk from exposure to pesticides used in IVM practices in African countries. We developed this approach with two primary goals in mind: first, to be consistent with current screening methods at EPA and other published methods (e.g., WHO); and second, to support making decisions within a continuum of options. These options include

No further action—The screening results indicate that a particular combination of IVM practice, receptor, exposure pathway, and pesticide does not pose a significant health risk

Conduct further modeling—The screening results suggest that more refined modeling to reduce the conservatism in the risk estimates would be useful before deciding whether further action is warranted

Prohibit a specific use—The screening results justify a recommendation to prohibit the use of a particular combination, and more refined modeling is not needed to justify this prohibition.

The major strengths of the screening approach include the following:

Transparency—The assumptions (implicit and explicit), data, models, and key references are fully explained for each exposure scenario that we evaluated. A clear and complete description of the methodology is essential to the review, further development, and implementation of this risk assessment framework. Thus, the layers of this report is allow the reader to drill down to whatever level of detail is required to support the decision-making process, from uncertainty factors in health benchmarks to justification for exposure averaging times.

Appropriateness—The development of conceptual models that describe the potential exposure pathways of concern was based on a weight-of-evidence approach that considered, in order of importance, (1) descriptions of IVM practices provided by expert workers in the field behavior; (2) published reports and journal articles on occupational and residential pesticide exposures (e.g., exposure routes of concern); (3) toxicological data on absorption potential by route and critical endpoints; and (4) pesticide-specific information on chemical–physical and environmental properties.

Scientific defensibility—The simple screening algorithms used in Phase I of this risk assessment were identified from highly regarded sources that describe the development of risk assessment methods (e.g., EPA reports). For screening purposes, these algorithms provide a sound basis for decisions by considering the nature and timing of exposure and matching those characteristics with the correct endpoint (e.g., acute versus chronic). The methodology has been peer reviewed by an independent risk assessment expert to ensure that this methodology meets high standards for scientific rigor.

Flexibility—To implement the Phase I screening assessment, we created a spreadsheet model that can easily be modified to add and evaluate exposure pathways of interest based on current information from the open literature and field experts. In addition, the phased approach permits significant flexibility in designing technical and management options that satisfy the needs of the decision maker, from requiring further modeling and analysis to eliminating a risky practice.

Despite these strengths, the Phase I screening has some limitations in the following areas:

Dermal exposure assessment—Three types of factors affect the amount of chemical that can be absorbed through the skin: (1) exposure factors (e.g., chemical concentration, area of skin exposed, and behavior with respect to wearing of contaminated clothing); (2) chemical factors (e.g., solubility in different vehicles or irritancy); and (3) skin factors (e.g., metabolism, skin thickness/type, and location of exposure). The available screening models (and most higher-order models) address only a few of these factors that affect dermal exposure and risk, and most screening models are not designed to handle the diversity of exposures considered in this assessment. Thus, there is considerable uncertainty in our risk and hazard results for dermal exposure.

Toxicological data—The available health benchmarks are generally based on oral studies of laboratory animals and extrapolated across multiple exposure durations. The

extrapolation procedures are appropriate for screening level assessments; however, this often results in the use of a single benchmark for acute, subchronic, and chronic exposures. The noncancer benchmarks for chronic exposures are typically recommended for use in addressing acute or intermediate exposures, a practice that is based more in caution rather than on a deep understanding of the toxicology of these compounds. In addition, the data are generally insufficient to support a quantitative assessment of potential effects on sensitive subpopulations in the African population, such as pregnant woman and young children, who may already be under stress because of dietary deficiencies or illness. The overall quality of the toxicological data represents a significant uncertainty in this assessment.

Environmental modeling—This report addresses only public health effects associated with pesticide use in IVM strategies and does not address environmental or ecological effects. However, for compounds such as DDT that bioaccumulate in animal tissues and tend to be highly persistent in the environment, additional screening-level modeling should be performed to characterize the potential for adverse ecological and environmental impacts. Only pesticides that are persistent in the environment warrant further attention in this regard.

Uncertainty and variability—As with all deterministic screening assessments, modeling provides little information from which to characterize the uncertainty in the risk and hazard results. Thus, although we suggest below that an HQ of 200 represents a serious potential for an adverse effect, we are unable to offer a quantitative description of this result with respect to confidence. Although this limitation does not prevent us from developing recommendations using just the screening results, it does prevent us from propagating uncertainty through the modeling to characterize the confidence interval around the risk or hazard result.

5.1.3.2 Noncancer Hazard and Cancer Risk Results

This section summarizes and interprets the results from the screening assessment for each IVM practice and related activity. The noncancer HQs and cancer risk estimates are calculated using the equations in Tables G-15 and G-16, respectively, in ***Annex G***. An HQ greater than 1 is interpreted to indicate the potential for adverse noncancer effects. A cancer risk above 10^{-5} (1E-05) is interpreted to indicate potential cancer risks at a level that is relevant to decision makers.

Tables 9 and 10 summarize the noncancer and cancer results, respectively, for the practices and pesticides considered in this assessment. Table 10 includes only those pesticides for which cancer slope factors were available (DDT, etofenprox, fenitrothion, methoprene, permethrin, and propoxur). Each scenario is identified as "pass" (risk < 10^{-5} or HQ < 1), "fail" (risk > 10^{-5} or HQ > 1), or "NA" (the pesticide is typically not an option for the particular IVM practice or the activity is not relevant to a particular pesticide). Note that the significance of predicted cancer risks is typically determined by risk managers within the context of broader public health issues that acknowledge; for

example, the relevance of other potential threats to human health. These summary tables provide an overview of the scenarios; more detailed discussion is provided in subsequent sections, including discussion of scenarios that warrant further consideration (i.e., those designated as “fail”). The actual risk and HQ values that underlie the pass/fail results in these tables are presented in ***Annex H***.

Table 9. Noncancer Screening Results

Process	Pathway	Receptor	Alpha-cypermethrin	Bendiocarb	Bifenthrin	Cyflutrhin	DDT	Deltamethrin	Etofenprox	Fenitrothion	Lambda-cyhalothrin	Malathion	Methoprene	Permethrin	Pirimiphos-methyl	Propoxur	Temephos
IRS																	
Preparation by mixing	Inhalation	Worker	Pass	Pass	Pass	Pass	Fail	Pass	Pass	Fail	Pass	Pass	NA	NA	Fail	Pass	NA
	Dermal		Pass	Pass	Pass	Pass	Fail	Pass	Pass	Fail	Pass	Pass			Fail	Pass	
Spraying	Inhalation	Worker	Pass	Fail	Pass	Fail	Fail	Pass	Pass	Fail	Fail	Fail	NA	NA	Fail	Fail	NA
Spraying, application on walls	Dermal	Resident-Adult	Pass	Pass	Pass	Pass	Fail	Pass	Pass	Fail	Pass	Fail	NA	NA	Fail	Pass	NA
		Resident-Child	Pass	Pass	Pass	Pass	Fail	Pass	Pass	Fail	Pass	Fail			Fail	Pass	
Spraying, deposition on food	Ingestion	Resident-Adult	Pass	Pass	Pass	Pass	Fail	Pass	Pass	Fail	Pass	Pass	NA	NA	Fail	Pass	NA
		Resident-Child	Pass	Pass	Pass	Pass	Fail	Pass	Pass	Fail	Pass	Fail			Fail	Pass	
ITNs																	
Preparation by mixing	Inhalation	Resident	Pass	NA	NA	Pass	NA	Pass	Pass	NA	Pass	NA	NA	Pass	NA	NA	NA
	Dermal		Pass			Pass		Pass	Pass		Pass			Pass			
Treating nets	Dermal	Resident-Adult	Pass	NA	NA	Pass	NA	Pass	Fail	NA	Pass	NA	NA	Pass	NA	NA	NA
		Resident-Child	Pass			Pass		Pass	Fail		Fail			Pass			

Process	Pathway	Receptor	Alpha-cypermethrin	Bendiocarb	Bifenthrin	Cyflutrhin	DDT	Deltamethrin	Etofenprox	Fenitrothion	Lambda-cyhalothrin	Malathion	Methoprene	Permethrin	Pirimiphos-methyl	Propoxur	Temephos
Disposal																	
Burying, drinking groundwater	Ingestion	Resident-Adult	Fail	Fail	Fail	Fail	Pass	Fail	Fail	Fail	NA	Fail	Fail	Fail	Fail	Fail	NA
		Resident-Child	Fail	Fail	Fail	Fail	Pass	Fail	Fail	Fail		Fail	Fail	Fail	Fail	Fail	
Burying, bathing with groundwater	Dermal	Resident-Adult	Pass	Fail	Pass	Pass	Pass	Pass	Fail	Fail	NA	Pass	Fail	Fail	Fail	Pass	NA
		Resident-Child	Pass	Fail	Pass	Pass	Pass	Pass	Fail	Fail		Fail	Fail	Fail	Fail	Pass	
Reuse of Insecticide Containers																	
Food/drink storage	Ingestion	Resident-Adult	Fail	NA	NA	Fail	NA	Fail	Fail	NA	NA	NA	Fail	Fail	Fail	NA	Fail
		Resident-Child	Fail			Fail		Fail	Fail				Fail	Fail	Fail		Fail
Storage																	
Spillage	Inhalation	Worker	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	NA	Pass	NA	NA	Pass	Pass	NA

Table 10. Cancer Screening Results

Process	Pathway	Receptor	DDT	Etofenprox	Permethrin	Propoxur
IRS						
Preparation by mixing	Inhalation	Worker	Pass	Pass	NA	Pass
	Dermal		Fail	Pass		Pass
Spraying	Inhalation	Worker	Fail	Pass	NA	Pass
Spraying, application on walls	Dermal	Resident-Adult	Fail	Pass	NA	Pass
Spraying, deposition on food	Ingestion	Resident-Adult	Pass	Pass	NA	Pass
ITNs						
Preparation by mixing	Inhalation	Resident	NA	Pass	Pass	NA
	Dermal			Pass	Pass	
Treating nets	Dermal	Resident-Adult	NA	Pass	Pass	NA
Disposal						
Burying, drinking groundwater	Ingestion	Resident-Adult	Pass	Fail	Fail	Fail
Burying, bathing with groundwater	Dermal	Resident-Adult	Pass	Fail	Fail	Fail
Reuse of Insecticide Containers						
Food/drink storage	Ingestion	Resident-Adult	NA	Pass	Pass	NA
Storage						
Spillage	Inhalation	Worker	Pass	Pass	NA	Pass

Indoor Residual Spraying (IRS)

For IRS, noncancer hazard was below levels of concern for all practices and exposures for alpha-cypermethrin, bifenthrin, deltamethrin, and lambda-cyhalothrin, and therefore are good choices for an IRS program when considering human health risks. The

screening results for DDT and fenitrothion suggested a significant potential for adverse health effects via the inhalation and dermal exposure routes; significant cancer risks were predicted only for DDT, a tumor promoter (Dich et al., 1997). Not surprisingly, for the dermal exposure route, child exposures produced higher estimates for noncancer endpoints than adult exposures. Inhalation exposures were typically lower than dermal exposures estimated for most pesticides. Therefore, this section focuses primarily on the potential effects associated with DDT usage

Preparation—Dermal and Inhalation Exposure

IVM Intervention: IRS

Activity: Preparation

Receptors: Workers (adults)

Pesticides, endpoints of concern:

- DDT (HQ = 2, 200)
- DDT (cancer risk = 4E-04)
- Fenitrothion (HQ = 3, 10)
- Pirimiphos-methyl (HQ = 2,200)

For the preparation of insecticide for IRS, potential dermal and inhalation risks were estimated for workers mixing the insecticide formulation with water. Predicted dermal risks were well above predicted inhalation risks.

The screening results for DDT and pirimiphos-methyl indicate a significant potential for noncancer hazard due to dermal exposure during preparation. However, several aspects of the screening assessment suggest that the relatively high HQ values probably overestimate the potential for neurological effects in workers. For DDT, dermal exposure is not believed to be as likely when DDT is mixed in a WP form (as it usually is for IRS). For both DDT and pirimiphos-methyl, the lag time—the time from initial contact with the skin until the material enters the blood supply—may not be sufficient to allow steady-state diffusion across the stratum corneum to occur (Semple, 2004). Because the screening equation implicitly assumes that steady state *has* been reached, the predicted exposure is likely to be overestimated. Similarly, the predicted dose algorithm assumes that 100 percent of the highly concentrated preparation is absorbed, but the actual amount absorbed may be significantly less. For example, Semple (2004) suggests that when the applied concentration is increased, penetration increases up to a certain point and then reaches a plateau (Rougier et al., 1999; Skog and Wahlberg, 1964, as cited in Semple, 2004). Although a linear relationship between dose applied and percutaneous absorption level may exist for a range of concentrations, the nature of that relationship may change at very high concentrations.

Recommendations

The relatively high risk/hazard estimates for DDT and pirimiphos-methyl suggest the potential for adverse health effects from repeated acute dermal exposure, including reproductive, neurological, and cancer endpoints. The inherent conservatism in the screening approach notwithstanding, we used simple mass calculations to estimate that approximately 0.6 mg of pesticide is in contact with the skin, an amount that corresponds to less than 1 mL. Significant care would be required to ensure that less than 1 mL of these pesticides contacted the skin during preparation.

Given current deficiencies in the available data and modeling approaches for dermal effects from acute exposures to highly concentrated pesticide solutions, it is highly likely that a probabilistic modeling approach would produce similar hazard results, unless we consider the uncertainty inherent in the benchmarks selected for this analysis. Therefore, improving the relevance of the risk assessment results to decision making should involve a more extensive evaluation of the underlying toxicological studies and evaluation of less conservative methods for extrapolating acute benchmarks from chronic or subchronic data. For instance, the studies on which the EPA's noncancer benchmark for DDT were based are very old (around 1950), and the literature on human exposures does not indicate that the threshold is anywhere near 0.0005 mg/kg-day. Indeed, the data cited by EPA and ATSDR suggest that effects in humans are not found until approximately 35 mg/day, which translates into a health benchmark of 0.5 mg/kg-day for noncancer endpoints. In more recent studies, even the animal data seem to suggest a threshold of effect (e.g., a LOAEL) of around 20–50 mg/kg-day.

In addition to recommending improvements in the benchmark development and/or modeling for Phase II, we strongly suggest that workers be adequately trained and provided with PPE to ensure the appropriate handling of pesticides during preparation.

Spraying—Inhalation Exposure

IVM Intervention: IRS

Activity: Spraying

Receptors: Workers (adults)

Pesticides, endpoints of concern:

- Bendiocarb (HQ = 6)
- Cyfluthrin (HQ = 8)
- DDT (HQ = 100)
- DDT (cancer risk = 2E-04)
- Fenitrothion (HQ = 200)
- Malathion (HQ = 2)
- Pirimiphos-methyl (HQ = 90)
- Propoxur (HQ = 20)

Potential risks due to inhalation of aerosolized pesticides were estimated for workers during indoor spraying. The predicted hazards were above levels of concern for 8 of the 12 pesticides evaluated for this usage.

As with the preparation scenario described on page 81, the screening results for DDT indicate the potential for significant noncancer (e.g., developmental, reproductive, neurological, or immunological) and cancer endpoints. DDT is believed to be absorbed via the inhalation route, and best practices may not be sufficient to mitigate moderate to severe health impacts for workers due to frequent exposure during the spraying season. Similarly, potentially significant noncancer hazards were predicted for fenitrothion, pirimiphos-methyl, and propoxur.

Significant sources of uncertainty include (1) the quantification of exposure concentrations to which workers are exposed and (2) the evaluation of health impacts associated with intermittent exposures that occur during spraying. The screening approach does not characterize the air concentrations and particle sizes to which workers are exposed nor does it represent the amount of time spent during spraying under which inhalation exposure can occur. With respect to the health impacts, intermittent exposures to chemicals that accumulate in the body can, over time, create a situation in which even

a marginal exposure can result in moderate to severe noncancer health effects. In this type of exposure scenario, the benchmarks may not represent an adequate level of protection.

Recommendations

Even using PPE, worker exposures during spraying activities are not completely preventable. Given the frequency of exposure, the potential to accumulate DDT in the tissues, and the nature and potential severity of health effects associated with DDT exposure, we recommend refining the modeling approach to more accurately characterize the cumulative dose received over a spraying season. For example, approaches develop for occupational exposure assessments can be adopted for this purpose to further evaluate the risks from intermittent exposures to pesticides during spraying. We currently recommend that DDT be used only after stringent requirements have been met.

Contact with Sprayed Surfaces—Dermal Exposure

IVM Method: IRS

Activity: Contact with Sprayed Surfaces

Receptors: Residents (adults & children)

Pesticides, endpoints of concern (child):

- DDT (HQ = 2,000)
- Fenitrothion (HQ = 100)
- Malathion (HQ = 20)
- Pirimiphos-methyl (HQ = 80)

Potential risks to residents who come in contact with sprayed surfaces were estimated using a set of conservative assumptions based on total potential mass that could come in contact with the skin. Potentially significant risks were predicted for 4 of the 12 pesticides. The level of conservatism is evidenced by the fact that the HQ for dermal exposures to workers is lower than the HQ for residents who come in contact with pesticide residues (note that different algorithms were used in the two scenarios). In particular, our assumption that the resident comes in contact with an 8-mL film of pesticide is probably not realistic (the amount of solution that the worker comes in contact with due to splashing during mixing is less than 1 mL). The simple screening approach adopted for this scenario includes significant uncertainty in the algorithm chosen (e.g., number of exposure events is not represented) and supporting data (e.g., volume deposited on skin is based on studies in which the hands were immersed in solution). This scenario also implicitly includes hand-to-mouth behavior because the entire mass of pesticide that reaches the skin is assumed to be absorbed systemically. Thus, from a mass balance perspective, the dermal dose would have to be reduced if some portion of the pesticide that sorbs to skin were ingested.

Recommendations

The transitory nature of the exposure in this scenario seems unlikely to produce effects at a level of severity that would warrant substantial changes in the IRS practices. However, given the relatively high noncancer hazard estimates, further evaluation of this scenario appears to be warranted. As suggested earlier with respect to preparations, a significant source of uncertainty rests with the development of health benchmarks, particularly for less-than-chronic exposures. Any additional probabilistic efforts should include the benchmarks among the parameters that are varied. In addition, it is strongly recommended that surfaces other than walls be covered during spraying and/or cleaned immediately after spraying activities are completed. These prophylactic measures should drastically reduce risk through dermal contact following IRS and can be accomplished in a simple, cost-effective manner. Cloths and rags used in the protection and cleaning of surfaces should be handled carefully to prevent secondary exposures to pesticide residuals.

IVM Method: IRS

Activity: Eating sprayed food

Receptors: Residents (adults & children)

Pesticides, endpoints of concern (child):

- DDT (HQ = 1,000)
- Fenitrothion (HQ = 40)
- Malathion (HQ = 10)
- Pirimiphos-methyl (HQ = 40)

Sprayed Food—Ingestion Exposure

Potential risks to residents who eat food that has been left uncovered during spraying were evaluated based on the conservative assumptions that food is left uncovered and is sprayed directly. Not surprisingly, potentially significant risks were predicted for the same four pesticides for which risks were predicted for dermal contact. The ingestion of spray-contaminated food could be particularly significant for food items that are not peeled or cooked, because the cooking process tends to volatilize and break down pesticides. For the screening assessment, we assumed that any sprayed food items that were eaten contained all of the pesticide that was initially applied during spraying. As with other residential exposure scenarios, we modeled this scenario on a single-event basis (i.e., risks associated with one occurrence) because we did not have information on the extent to which food was actually sprayed and how long it would take the occupants to eat the contaminated food.

Recommendations

As with the dermal contact scenario, the transitory nature of the exposure in this scenario seems unlikely to produce effects at a level of severity that would warrant substantial changes in the IRS practices. Given that this pathway can be eliminated by simply removing or covering the food prior to spraying, we do not recommend additional modeling of this scenario: the risks for this scenario could be reduced to essentially zero if aerosol contact with food is prevented. Residents should be educated to take appropriate steps to prevent food from being sprayed.

Insecticide-Treated Nets (ITNs)

For practices associated with the treatment of bed nets, we evaluated six pesticides: alpha-cypermethrin, cyfluthrin, deltamethrin, etofenprox, lambda-cyhalothrin, and permethrin. We also reviewed published results on deltamethrin to compare the relative conservatism in our screening methodology with findings by other researchers (Barlow et al., 2001; WHO, 2004). Based on this screening risk assessment and the results presented in studies on deltamethrin, we concluded that only the acute exposure to etofenprox during treatment posed a potential risk via dermal contact. This finding is consistent with other published studies (e.g., Barlow et al., 2001); nevertheless, we recommend that individuals involved in treatment at least wear protective gloves during the process.

IVM Intervention: ITN

Activity: Inhalation and dermal exposure during mixing; dermal exposure during treatment

Receptors: Residents (adults and children)

Pesticide, endpoint of concern (adult):

- Etofenprox (HQ = 5)
- All other results were below levels of concern

Disposal

Activity: Drinking contaminated groundwater; bathing in contaminated groundwater

Receptors: Residents (adults and children)

Pesticide, endpoint of concern:

- All pesticides except for DDT had HQs ranging from 7 to 40,000 and cancer risks ranging from 7E-03 to 1E-01

Disposal

Risk estimates were developed for the ingestion of contaminated groundwater and for dermal contact while bathing after burial of 13 different pesticides. Significant risks were not predicted for DDT, due to the high DAF reported by EPA (U.S. EPA, 2002b). However, noncancer hazard for chronic ingestion and bathing were above levels of concern for virtually every other pesticide considered. The predicted HQs for noncancer hazard ranged from 7 to 40,000, and the predicted cancer risks ranged from 7E-03 to 1E-01. We consider these results (for both noncancer and cancer endpoints) to be unrealistically high for both the drinking water and bathing scenarios.

The exposures and concomitant risk and hazard results predicted for disposal in the screening assessment are driven largely by the assumption that pesticides are buried in an amount and location that strongly favors groundwater contamination. For example, the screening algorithm implicitly assumes that the pesticide is buried in an area with a potable aquifer and that the receptor wells are directly in the path of groundwater flow (i.e., along the centerline of the plume). Similarly, the default DAF of 20 does not reflect the chemical-specific properties for a specific chemical, such as its potential to degrade in the environment and its tendency to sorb to organic matter (both of these properties will significantly increase the DAF, resulting in lower groundwater concentrations and lower risk or hazard). Thus, the disposal scenario presents a highly conservative estimate of the

potential for adverse effects and underscores a basic weakness of screening-level assessments: for chemicals with complex environmental behavior (e.g., substantial potential for biodegradation), the screening assessment may grossly overpredict the potential for adverse effects for scenarios involving a significant environmental fate and transport component. In addition, the screening approach assumes that the pesticide is essentially an infinite source that continues to contaminate the groundwater throughout the residents' lifetimes.

Recommendations

Although the predicted risks are well above levels of concern, we do not recommend further analysis of this pathway. As suggested above, these results reflect an overly conservative screen of a complicated environmental fate and transport pathway that is highly dependent on site-specific conditions. Although many groundwater models are available that, with appropriate development of supporting data (e.g., soil type and infiltration rate), could produce scientifically defensible estimates of groundwater well concentrations and risks, these screening results are sufficient to demonstrate that the practice of burying pesticides in the proximity of drinking water wells (or surface water bodies) has the potential to cause significant risks to public health through *chronic* exposures. For example, the mismanagement of malathion can pose risks to groundwater supplies because of its solubility and breakdown into the highly toxic isomalathion. Therefore, we strongly recommend that pesticide burial (outside of permitted, engineered landfills) be prohibited to prevent contamination of valuable water supplies.

Reuse of Pesticide Containers

Activity: Drinking water from pesticide container

Receptors: Residents (adults and children)

Pesticide, endpoint of concern:

- All pesticides at levels of concern, with HQs ranging from 40 to 4,000

Reuse of Pesticide Containers

Noncancer hazard and cancer risk from the reuse of pesticide containers for drinking water were screened for eight pesticides. The noncancer hazard estimates were above levels of concern for all pesticides, but all the cancer risks were below levels of concern. The significant hazard predicted for temephos was surprising, because this compound is often used as a treatment for drinking water supplies to prevent mosquito larvae from developing. In this instance, the magnitude of the dose (830 mg) from using containers that contain residual pesticide was sufficient to indicate a strong potential for neurological effects (e.g., dizziness, tremors, and difficulty breathing) typical of organophosphates. Adverse effects suggested by the results for several other pesticides such as permethrin were also unexpected; permethrin has been shown to be of low toxicity for the ingestion route of exposure.

Recommendations

Based on the screening results, it is apparent that the reuse of pesticide containers may result in adverse effects in the short term, depending on the type of compound. However, further analysis of this scenario is not necessary. The screening results strongly suggest that acute health effects *may* be significant as a result of container reuse.

Storage

The risks of inhalation of pesticides as the result of inadequate storage controls (spillage) were estimated for all relevant pesticides. Based on the screening results, this scenario does not appear to warrant further consideration.

5.1.3.3 Conclusions and Recommendations

The Phase I screening provides a great deal of information about potential risks associated with pesticide use in IVM and allows for the comparison of different pesticides and management strategies. These comparisons should be integrated into decision making on IVM strategies and selection of pesticides (see Section 6.1.2 for more detail on rational pesticide selection).

In addition, the screening results are useful in identifying the drivers for scenarios with risk levels of concern. For these "risky" scenarios, data development and/or more refined modeling can be used to more accurately characterize the potential health risks. For example, the level of conservatism in the risk estimates can be decreased by replacing default values for key parameters with actual study values or distributions of values and modifying simplifying modeling assumptions that tend to produce conservative estimates of risk (e.g., using activity patterns to model exposure). Additional research may not only enhance our ability to characterize pesticide risks, but also increase the value of information that we provide to the decision maker. Thus, the focus of this section is to

- Summarize the major conclusions from the Phase I screening by comparing the risks across different interventions and insecticides, and
- Identify where additional research could be valuable and provide recommendations for next steps.

Comparing Interventions and Insecticides

The key to interpreting risk screening results is to remember that they provide insight into potential risks and relative risks; they are based on the precautionary principle and, therefore, are intended to avoid underestimating the actual risks. Thus, the screening results are very useful for comparing options based on relative risks and to determine, in a general sense, the potential for adverse health effects for scenarios in which high levels of exposure are likely. The screening results are not intended to represent the actual risks that will occur in the field; however, screening results below levels of concern are strongly suggestive that the combination of exposure scenario, pathway, and pesticide will not pose significant health risks. Moreover, within the broader decision-making

context of the PEA, the screening assessment provides information on risk only, without consideration of the economics of a particular pesticide application or the efficacy of the pesticide in controlling malaria (see Section 6.1.1 on selection of intervention and Section 6.1.2 on rational pesticide selection).

Noncancer Results

Tables 11–13 distill the noncancer risk screening results for easy interpretation and use in the selection of interventions and pesticides. In this assessment, noncancer risk is a comparison of an individual's potential dose from a malaria control activity relative to a protective health benchmark at which the likelihood of an adverse health effect is presumed to be very low. This comparison, called an HQ, is calculated as a ratio of the potential dose to the protective health benchmark. Thus, if an individual's potential exposure to a pesticide during a malaria control activity is calculated as 1E-01 mg/kg-day and the health benchmark is 1E-01 mg/kg-day, the ratio of the two (HQ) would equal 1. If the dose to which an individual is exposed is 1E-02 mg/kg-day, and this value is compared with the same health benchmark, the HQ would be 1E-01, which is below 1, indicating that the dose was not of concern with respect to the health endpoint for which the study was conducted. For screening risk analyses, an HQ value of 1 is typically the threshold above which the EPA and this PEA considers the exposure to be of potential concern. HQs in this assessment ranged from essentially zero to 51,000; thus the screening results ranged from below levels of concern (i.e., HQ less than 1) to above levels of concern (i.e., HQ greater than 1).

To estimate the total noncancer risk for a given scenario, the HQs for each pathway and practice were added together for a particular pesticide. For instance, the total noncancer risk for occupational exposure in IRS (typically referred to as the hazard index [HI]) was obtained by adding HQs derived for inhalation and dermal exposures from preparing the pesticide solution, as well as the HQ for inhalation exposure that occurs during spraying. When the sum of the relevant HQs differed between children and adults, the higher sum was selected. Then, the pesticides for each IVM practice were categorized based on the sum of the relevant HQs. Pesticides in the "Risk Below" category are those where the sum of the relevant HQs were lower than 1. Pesticides in the "Low Risk" category are those where the sum of the relevant HQs ranged from 1 to less than 10. Pesticides in the "Moderate Risk" category are those where the sum of the relevant HQs ranged from 10 to less than 100. Pesticides in the "High Risk" category are those where the sum of the relevant HQs were 100 or higher.

Table 11. Risk Results for IRS[1]

Occupational Exposure				Residential Exposure			
Risk Below Level of Concern	**Low Risk**	**Moderate Risk**	**High Risk**	**Risk Below Level of Concern**	**Low Risk**	**Moderate Risk**	**High Risk**
Alpha-cypermethrin	Bendiocarb	Propoxur	DDT	Alpha-cypermethrin		Malathion	DDT
Bifenthrin	Cyfluthrin		Fenitrothion	Bifenthrin			Fenitrothion
Etofenprox	Lambda-cyhalothrin		Pirimiphos-methyl	Bendiocarb			Pirimiphos-methyl
Deltamethrin	Malathion			Cyfluthrin			
				Deltamethrin			
				Etofenprox			
				Lambda-cyhalothrin			
				Propoxur			

[1] This table reflects categorization based on sum of HQs for exposure due to preparation/inhalation, preparation/dermal and spray/inhalation practices/pathways. There is no difference in categorization when the spillage/inhalation pathway is taken into account.

Table 12. Risk Results for ITN Retreatment[1]

Risk Below Level of Concern	Low Risk	Moderate Risk	High Risk
Alpha-cypermethrin	Etofenprox		
Cyfluthrin	Lambda-cyhalothrin		
Deltamethrin			
Permethrin			

[1] This table reflects categorization based on sum of HQs for exposure due to post-spray/dermal and post-spray/ingestion practices/pathways.

Table 13. Risk Results for Container Reuse

Risk Below Level of Concern	Low Risk	Moderate Risk	High Risk
		Alpha-cypermethrin	Etofenprox
		Cyfluthrin	Methoprene
		Deltamethrin	Pirimiphos-methyl
		Permethrin	Temephos

Cancer Results

Tables 14–18 distill the cancer risk screening results for easy interpretation. In contrast to the HQ, excess cancer risk is a probability of an individual developing cancer during their lifetime due to exposures that are presumed to occur for a given scenario. For example, an excess cancer risk of 1E-06 is interpreted to mean that the probability of an individual developing cancer during their lifetime from the scenario-specific exposure is 1 in 1 million. Equivalently, this is the probability that out of 1 million individuals that receive the same exposure, 1 individual will develop cancer. For screening risk assessments, a cancer risk of 1E-06 is often selected as the target above which EPA and this PEA considers the exposure to be of potential concern. In this assessment, four pesticides had excess cancer risks ranging from 9E-10 (the individual has a 9 in 1 billion chance of

developing cancer during their lifetime from the exposure) and 3E-01 (the individual has a 3 in 10 chance of developing cancer during their lifetime from the exposure).

Table 14. Risk Results for Groundwater Contamination[1]

Risk Below Level of Concern	Low Risk	Moderate Risk	High Risk
DDT		Alpha-cypermethrin	Bendiocarb
		Bifenthrin	Etofenprox
		Cyfluthrin	Fenitrothion
		Deltamethrin	Malathion
		Permethrin	Methoprene
			Pirimiphos-methyl
			Propoxur

[1] This table reflects exposure to pesticides from dermal contact and ingestion of groundwater contaminated with pesticides that have been buried.

Key	
Risk Below Level of Concern	HQ < 1
Low Risk	HQ 1 to <10
Moderate Risk	HQ 10 to < 100
High Risk	HQ ≥ 100

Benchmarks for cancer endpoints were only available for four pesticides: DDT, etofenprox, permethrin, and propoxur. Thus, the cancer results can only be compared for this subset of IVM chemicals.

To create the summary data in Tables 14–18, excess cancer risks for each pathway and practice were added together to represent the total risk for a particular individual from a

particular pesticide. For instance, the total risk for occupational exposure in IRS was obtained by adding excess cancer risks for inhalation and dermal exposure from preparing the pesticide solution, as well as the excess cancer risk for inhalation that occurs during spraying. The pesticides for each IVM practice were categorized based on the sum of the relevant excess cancer risks calculated for adults. As is typical of screening level risk assessments, cancer risks were only estimated for adults as a simplification to avoid calculating cancer risk with changing body weights and intake rates as the individual ages. Pesticides in the "Risk Below" category are those where the sum of the relevant excess cancer risks were lower than 1E-06. Pesticides in the "Low Risk" category are those where the sum of the relevant excess cancer risks ranged from 1E-06 to less than 1E-05. Pesticides in the "Moderate Risk" category are those where the sum of the relevant excess cancer risks ranged from 1E-05 to less than 1E-04. Pesticides in the "High Risk" category are those where the sum of the relevant excess cancer risks were 1E-03 or higher.

Table 15. Risk Results for IRS[1]

Occupational Exposure				Residential Exposure (Adults)			
Risk Below Level of Concern	Low Risk	Moderate Risk	High Risk	Risk Below Level of Concern	Low Risk	Moderate Risk	High Risk
	Etofenprox		DDT		Etofenprox	DDT	
	Propoxur					Propoxur	

[1] This table reflects categorization based on sum of excess cancer risks for exposure due to Preparation/Inhalation, Preparation/Dermal, and Spray/Inhalation practices/pathways. There is no difference in categorization when the Spillage/Inhalation pathway is taken into account.

Table 16. Risk Results for ITN Retreatment[1]

Risk Below Level of Concern	Low Risk	Moderate Risk	High Risk
Etofenprox			
Permethrin			

[1] This table reflects categorization based on sum of excess cancer risks for exposure due to Post-spray/Dermal and Post-spray/Ingestion practices/pathways.

Table 17. Risk Results for Container Reuse

Risk Below Level of Concern	Low Risk	Moderate Risk	High Risk
	Etofenprox		
	Permethrin		

Table 18. Risk Results for Groundwater Contamination[1]

Risk Below Level of Concern	Low Risk	Moderate Risk	High Risk
DDT			Etofenprox
			Permethrin

[1] This table reflects exposure to pesticides from dermal contact and ingestion of groundwater contaminated with pesticides that have been buried.

Key	
Risk Below Level of Concern	Excess cancer risk < 10-6
Low Risk	Excess cancer risk 10-6 to <10-5
Moderate Risk	Excess cancer risk 10-5 to < 10-4
High Risk	Excess cancer risk 10-4 $\geq$ 10-3

Interpretation of Screening Results

Based on the results above, several conclusions can be drawn with regard to potential risks of practices and pesticides:

- The low predicted risks for ITNs suggest that, from a risk standpoint, this approach may be preferable to IRS
- The relatively high risks predicted for the pesticide container reuse scenario suggest that action should be taken to prevent potentially significant risks from short-term exposures as a result of this activity
- The magnitude of the ingestion and dermal risk estimates for the disposal scenario strongly suggests that burial of pesticides should be prohibited

- Across all IVM practices, DDT is the riskiest pesticide with respect to both noncancer and cancer endpoints and, therefore, should only be used after stringent requirements have been met
- For ITNs, the results for all pesticides except etofenprox and (for children) lambda-cyhalothrin were below levels of concern for preparing and treating
- For IRS, the least preferred pesticides with respect to risk are DDT, fenitrothion, and pirimiphos-methyl.

Some additional conclusions of the screening assessment with respect to exposure pathways and receptors include

- Within a given scenario, the dermal exposure pathway appears to pose potentially greater risks than other pathways
- Worker exposures during the application of pesticide appear to be much more significant than exposures that occur during handling and storage
- The potential risks to residents may be significant for acute contact scenarios, as well as through chronic exposure scenarios following the mismanagement of pesticides
- Predicted risks to children and adults are not significantly different, although noncancer risks for residents are typically higher for children than for adults.

The results from screening assessments should be interpreted with caution because they are based on several assumptions and simplifications that are intended to produce conservative estimates of risk. For example, the extrapolation techniques used to derive the health benchmarks are rooted in regulatory risk assessment, a process that typically does not consider the potential adverse health effects that may occur if a particular chemical is *not* used as intended. As a result, these screening results need to be considered within the decision-making process used in developing IVM strategies. Our interpretation of the screening results may be summarized as follows

- The very high predictions of noncancer hazard and cancer risk are not supported in the literature or by the experience in other countries
- The default assumptions for dermal exposure pathways likely overstates the predicted risks by an order of magnitude or more for acute exposure scenarios
- The groundwater pathway results, although representative of an extreme worst case scenario (e.g., no degradation or natural attenuation), are indicative of potential problems likely to occur if burial is allowed
- The noncancer HQ lacks a metric for severity that is needed to distinguish between debilitating effects and transitory effects so that decision makers can better characterize the public health implications of different IVM strategies with respect to efficacy, cost, and pesticide-induced health effects
- The regulatory approach to deriving health benchmarks (e.g., use of a point estimate for each effect) is a significant source of uncertainty in the screening

results in that it fails to capture the variability in sensitivity in the human population

- Some health benchmarks (e.g., for DDT) are based on toxicological data that may not be consistent with more recent studies and the current state of knowledge
- The methodology used in predicting worker risks does not consider the potential for cumulative effects due to intermittent exposures and, therefore, the effective threshold for adverse effects to workers may decrease over time due to repeated exposures
- The state-of-the-science and available data are wholly inadequate to evaluate potential risks to populations already under stress (e.g., immunocompromised individuals)
- The lack of any environmental modeling represents a significant limitation in this screening assessment, particularly for DDT.

Recommendations for Further Research

The interpretation of the screening results, particularly the results for DDT and for dermal exposures, suggests several key steps to consider for future analyses. These recommended steps are intended to focus resources on improving the relevance of the risk results to support decision making in the development of effective IVM strategies to control malaria. In summary, we recommend the following technical options for Phase II:

- Categorize the severity of effect for acute, intermediate, and chronic endpoints for noncancer hazard. Economists and other researchers have developed various scales to consider the severity of effect in valuing the benefits of regulations or remedial strategies that reduce chemical exposures. We believe that a scale can be developed that is meaningful in the IVM context and would provide decision makers with a useful metric in comparing pesticide selection on the basis of risk.
- Conduct follow-on modeling for scenarios in which remedial steps are recommended, to confirm the predicted reductions in risk. The follow-on modeling can be done simply, using a modified version of the screening model and varying only a few input parameters, or it may be performed using a refined exposure and risk model, as described below. In either case, the follow-on modeling would address the very high risk screening results.
- Conduct limited mass balance modeling using a simple fugacity model to predict the mass loadings to various biotic and abiotic compartments and evaluate environmental and ecological effects. The lack of environmental and ecological modeling is a significant limitation of this risk assessment as it pertains to IVM strategies, especially for DDT, which was banned because of adverse environmental impacts. The mass balance approach is cost effective, can be implemented quickly, and will provide useful information on the potential environmental effects associated with DDT usage or the usage of other highly persistent, highly bioaccumulative pesticides.

- Investigate further the toxicological database underlying the benchmarks for DDT and convene an expert panel to determine the dose range for threshold effects for acute, intermediate, and chronic exposures. The screening results strongly suggest that DDT should be the least preferred pesticide on the basis of risk, and the magnitude of the noncancer and cancer risks warrants additional research to establish a scientifically defensible dose range. Given the likely significance of DDT to the residual spraying program, we believe it is crucial to establish a credible dose-response range that is based on current information and science.
- Conduct further modeling for IRS worker exposures and residential scenarios associated with spraying. Further modeling in Phase II for these scenarios is warranted based on the screening results. We recommend adopting a probabilistic modeling framework that includes a dose–response function when possible to develop better estimates of risk for these scenarios and to characterize the uncertainty in the estimates. In addition, because dermal exposures appear to drive the risk estimates, we recommend incorporating current research on occupational exposure methods to provide a more science-based model to evaluate acute exposures to pesticides.

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5.2 Environmental Consequences—IRS

Eliminating unnecessary human exposure to insecticides is the primary concern in IRS operations, as spray operators and residents are most exposed to insecticides during indoor spraying operations; however, domestic livestock (particularly chickens) and organisms in the environment may also be harmed if operations, cleanup, and disposal are not conducted according to best practices. Table 19 indicates the toxicity of IRS insecticides to nontarget, nonhuman organisms, as well as the persistence of the insecticides and their capacity to bioaccumulate in the environment (not in mammalian bodies). The table is followed by verbal descriptions of the potential ecological effects of each IRS chemical (except etofenprox and pirimiphos-methyl), which is excerpted from the EXTOXNET database.

Table 19. Toxicity of IRS Insecticides to Nontarget Organisms

IRS Insecticide	Mammal	Bird	Fish	Other Aquatic	Bee	Persistence	Bioaccumulate[1]
Alpha-cypermethrin							
Bendiocarb							
Bifenthrin							
Cyfluthrin							
DDT		[2]					
Deltamethrin							
Etofenprox							
Fenitrothion							
Lambda-cyhalothrin							
Malathion							
Pirimiphos-methyl							
Propoxur							

[1] Bioaccumulation in the environment, not in mammalian bodies (mammalian detoxification produces different results).
[2] Low toxicity, but high chronic or bioaccumulation affect on raptors, pelicans.

Key
High Toxicity
Medium to High Toxicity
Medium Toxicity
Low to Medium Toxicity
Low Toxicity
Data Not Found

Alpha-cypermethrin (effects of cypermethrin used here)

- **Effects on birds:** Cypermethrin is practically nontoxic to birds. Its acute oral LD_{50} in mallard ducks is more than 4,640 mg/kg. No adverse reproductive effects occurred in mallards or bobwhite quail given 50 ppp, the highest dose tested.
- **Effects on aquatic organisms:** Cypermethrin is very highly toxic to fish and aquatic invertebrates. The LC_{50} (96-hour) for cypermethrin in rainbow trout is 0.0082 mg/L, and in bluegill sunfish is 0.0018 mg/L. Its acute LC_{50} in *Daphnia magna*, a small freshwater crustacean, is 0.0002 mg/L. Cypermethrin is metabolized and eliminated significantly more slowly by fish than by mammals or birds, which may explain this compound's higher toxicity in fish compared with other organisms. The half-lives for elimination of several pyrethroids by trout are all more than 48 hours, while elimination half-lives in birds and mammals range from 6 to 12 hours. The bioconcentration factor for cypermethrin in rainbow trout was 1,200 times the ambient water concentration, indicating that there is a moderate potential to accumulate in aquatic organisms.
- **Effects on other organisms:** Cypermethrin is highly toxic to bees.

Bendiocarb

- **Effects on birds:** Bendiocarb is moderately toxic to birds.
- **Effects on aquatic organisms:** Bendiocarb is moderately to highly toxic to fish.
- **Effects on other organisms:** Earthworm populations under turf are severely affected by bendiocarb. It is toxic to bees; the LD_{50} is 0.0001 mg per bee.

Bifenthrin

- **Effects on Birds:** Bifenthrin is moderately toxic to many species of birds. There is concern about possible bioaccumulation in birds.
- **Effects on Aquatic Organisms:** Bifenthrin is very highly toxic to fish, crustaceans, and aquatic animals. Because of its low water solubility and high affinity for soil, bifenthrin is not likely to be found in aquatic systems.
- **Effects on Other Animals (Nontarget species):** Bifenthrin is toxic to bees.

Cyfluthrin

- **Effects on Birds:** Cyfluthrin is of low toxicity to upland game birds and waterfowl. Little information was found concerning the toxicity of cyfluthrin to songbirds. LD_{50} values for canaries range from 250 to 1,000 mg/kg.
- **Effects on Aquatic Organisms:** Cyfluthrin is highly toxic to marine and freshwater organisms. Cyfluthrin is exceptionally toxic to the freshwater invertebrate *D. magna*. Marine and estuarine invertebrates are also extremely sensitive to cyfluthrin.

- **Effects on Other Animals (Nontarget species):** Cyfluthrin is highly toxic to bees with an LD_{50} of 0.037 mg/bee (70). Pyrethroids are known to be highly toxic to other beneficial insects.

DDT

- **Effects on Birds**: DDT may be slightly toxic to practically nontoxic to birds. In birds, exposure to DDT occurs mainly through the food web through predation on aquatic and/or terrestrial species having body burdens of DDT, such as fish, earthworms, and other birds. There has been much concern over chronic exposure of bird species to DDT and its effects on reproduction, especially eggshell thinning and embryo deaths. The mechanisms of eggshell thinning are not fully understood. It is thought that this may occur from the major metabolite, DDE (1,1-dichloro-2,2-bis[*p*-chlorophenyl]ethylene), and that predator species of birds are the most sensitive to these effects. Laboratory studies on bird reproduction have demonstrated the potential of DDT and DDE to cause subtle effects on courtship behavior, delays in pairing and egg laying, and decreases in egg weight in ring doves and Bengalese finches. The implications of these for long-term survival and reproduction of wild bird species is unclear. There is evidence that synergism may be possible between DDT's metabolites and organophosphate (cholinesterase-inhibiting) pesticides to produce greater toxicity to the nervous system and higher mortality. Aroclor (polychlorinated biphenyls, or PCBs) may result in additive effects on eggshell thinning.
- **Effects on Aquatic Species:** DDT is very highly toxic to many aquatic invertebrate species. Early developmental stages are more susceptible than adults to DDT's effects. The reversibility of some effects, as well as the development of some resistance, may be possible in some aquatic invertebrates. DDT is very highly toxic to fish species as well. DDT may be moderately toxic to some amphibian species and larval stages are probably more susceptible than adults. In addition to acute toxic effects, DDT may bioaccumulate significantly in fish and other aquatic species, leading to long-term exposure. This occurs mainly through uptake from sediment and water into aquatic flora and fauna, and also fish. Fish uptake of DDT from the water will be size dependent, with smaller fish taking up relatively more than larger fish. The reported bioconcentration factor for DDT is 1,000–1,000,000 in various aquatic species, and bioaccumulation may occur in some species at very low environmental concentrations. Bioaccumulation may also result in exposure to species which prey on fish or other aquatic organisms (e.g., birds of prey).
- **Effects on Other Animals (Nontarget species):** Earthworms are not susceptible to the acute effects of DDT and its metabolites at levels higher than those likely to be found in the environment, but they may serve as an exposure source to species that feed on them. DDT is nontoxic to bees; the reported topical LD_{50} for DDT in

honeybees is 27 µg/bee. Laboratory studies indicate that bats may be affected by DDT released from stored body fat during long migratory periods.

Deltamethrin

- **Effects on Birds:** The reported 8-day LC_{50} for ducks was more than 4,640 mg/kg diet; and more than 10,000 mg/kg diet for quail.
- **Effects on Aquatic Organisms**: As is common with many pyrethroids, deltamethrin has a high toxicity to fish under laboratory conditions. However, in field conditions under normal conditions of use, fish are not harmed. Deltamethrin had an impact on aquatic herbivorous insects. This impact led to an increase of algae. Although the fish (fathead minnows) accumulated the deltamethrin, no mortality could be observed. In laboratory trials, the LC_{50} for fish was 1–10 µg/L. Aquatic fauna, particularly crustacea, may be affected, but fish are not harmed under normal conditions of use.
- **Effects on Other Animals (Nontarget species):** Deltamethrin is considered toxic to bees. The 24-hour oral LD_{50} for technical deltamethrin fed to bees was 0.079 micrograms ai/bee; and the 24-hour oral LD_{50} for the EC formulation of deltamethrin was equal to or greater than 0.4 micrograms ai/bee. The reported contact LD_{50} for bees is 0.05 micrograms ai/bee. Deltamethrin is very toxic over long periods to the predatory mite *Typhodromum pyri.* The parasitic wasp *Encarsia formosa,* released in greenhouses to combat whitefly, is too sensitive to allow a treatment with deltamethrin against excessive outbreaks of whiteflies. Deltamethrin had little or no effect on adults or cocoons of *Apanteles plutellae,* a parasite of the diamond back moth in India. Spiders were also indicated to be strongly affected in field investigations.

Etofenprox

- Etofenprox is slightly to moderately acutely toxic to fish, and affects their behavior, biochemistry, mortality, and physiology. Other organisms are relatively unaffected. No chronic environmental toxicological risks are listed.

Fenitrothion

- **Effects on Birds:** Negative results were observed in studies on delayed neurotoxicity in hens. The oral LD_{50} for chickens was reported as 28 mg/kg. Fenitrothion was found to be highly toxic to upland gamebirds and slightly toxic to waterfowl.
- **Effects on Aquatic Organisms:** The time for achieving the highest levels of uptake and the extent of retention of organophosphate residues by fish was directly related to the extent of persistence of a compound in water. Motsugo fish exposed to 0.6-1.2 mg/L of fenitrothion attained the highest body concentrations (162 mg/kg) after 3 days. Fenitrothion (4.9 mg/kg) persisted longer than 4 weeks in fish (153). Fenitrothion is considered somewhat toxic to fish. The chronic

toxicity of fenitrothion to fish is considered low. The sublethal effects of fenitrothion exposure on fish include:

- **Morpho Anatomical Changes:** Swelling of the abdomen of fathead minnows occurred. Young Atlantic salmon exposed to 1 mg/L swam with distended fins.
- **Behavioral Changes:** There was a pronounced decline in various agonistic behaviors (chasing, vacating, nipping, etc.) within 2 hours of exposure to several concentrations of fenitrothion. Comfort behaviors (flicks, thrusts, etc.) increased with increasing concentration of the toxicant, but declined at higher concentrations. Altered station selection occurred. At higher concentrations, some fish were unable to maintain position and were swept downstream. After a 5-hour exposure, fish swam near the surface with bloated stomachs and heads pointing downward. Movement was slowed so much that Atlantic salmon did not attempt to avoid capture with a dipnet. Salmon parr exposed to 1 mg/L fenitrothion were more vulnerable to predation by brook trout.
- **Biochemical Changes:** Acetylcholinesterase activity was inhibited 13 percent to 25 percent after various sublethal concentrations of fenitrothion. Cholinesterase activity in the erythrocytes, gills, heart, and serum of rainbow trout was reduced within 1 hour after exposure to fenitrothion.
- **Respiratory Effects:** Oxygen consumption of *Labeo rohita* exposed to fenitrothion progressively decreased with increasing concentrations of insecticide. Exposure caused increased ventilation rate and buccal amplitude at concentrations slightly higher than the 48-hour LC_{50}.
- **Effect on Growth:** Orally administrated fenitrothion had no effect on the growth of rainbow trout.

The compound is considered very toxic to crustaceans and aquatic insects and has a medium toxicity to aquatic worms. A freshwater invertebrate toxicity study reported fenitrothion to be very highly toxic to aquatic invertebrates.

- **Effects on Other Animals (Nontarget species):** There is sufficient information to characterize fenitrothion as highly toxic to honeybees (acute toxicity value = 0.383 µg/bee) when bees are exposed to direct treatment or to dried residues on foliage. Fenitrothion is considered toxic to spider mites with long residual action. The long-term effects of fenitrothion and phosphamidon were evaluated on predaceous carabid beetles and lycosid spiders 1 year after treatment of Northwestern Ontario forests at 6 oz/A and 4 oz/A, respectively. The populations of these predators were clearly suppressed in the treated area. The results “did not imply a 1 year persistence of the insecticides, but rather a persistent disturbance of the ecosystem.” The acute oral toxicity of fenitrothion to mule deer was reported to be 727 mg/kg.

Lambda-cyhalothrin

- **Effects on Birds:** Lambda-cyhalothrin's toxicity to birds ranges from slightly toxic to practically nontoxic. There is evidence that it does not accumulate in the eggs or tissues of birds.
- **Effects on Aquatic Organisms:** Lambda-cyhalothrin is very highly toxic to many fish and aquatic invertebrate species. Bioconcentration is possible in aquatic species, but bioaccumulation is not likely. Bioconcentration in channel catfish has been reported as minimal, with rapid depuration (elimination). A bioconcentration factor of 858 has been reported in fish, but concentration was confined to nonedible tissues and rapid depuration was observed.
- **Effects on Other Animals (Nontarget species):** Lambda-cyhalothrin is highly toxic to bees, with a reported oral LD_{50} of 38 ng/bee and reported contact LD_{50} of 909 ng/bee (0.9 µg/bee).

Malathion

- **Effects on birds:** Malathion is moderately toxic to birds.
- **Effects on aquatic organisms:** Malathion has a wide range of toxicities in fish, extending from very highly toxic in the walleye (96-hour LC_{50} of 0.06 mg/L) to highly toxic in brown trout (0.1 mg/L) and the cutthroat trout (0.28 mg/L), moderately toxic in fathead minnows (8.6 mg/L) and slightly toxic in goldfish (10.7 mg/L). Various aquatic invertebrates are extremely sensitive. Malathion is highly toxic to aquatic invertebrates and to the aquatic stages of amphibians. Because of its very short half-life, malathion is not expected to bioconcentrate in aquatic organisms. However, brown shrimp showed an average concentration of 869 and 959 times the ambient water concentration in two separate samples, respectively.
- **Effects on other organisms:** The compound is highly toxic to honeybees.

Pirimiphos-Methyl

- Pirimiphos-methyl is very highly acutely toxic to zooplankton and aquatic insects, moderately acutely toxic to nematodes/flatworms, annelids and fish.

Propoxur

- **Effects on birds:** Propoxur is very highly to highly toxic to many bird species, but its toxicity varies by the species. Acute symptoms of propoxur poisoning in birds include eye tearing, salivation, muscle incoordination, diarrhea, and trembling. Depending on the type of bird, poisoning signs can appear within 5 minutes of exposure, with deaths occurring between 5 and 45 minutes, or overnight. Symptoms in survivors disappeared from 90 minutes to several days after treatment.
- **Effects on aquatic organisms:** Propoxur is moderately to slightly toxic to fish and other aquatic species. The reported 96-hour LC_{50} values are 3.7 mg/L in

rainbow trout, and 6.6 mg/L in bluegill sunfish. The oral LD_{50} for propoxur in bullfrogs is 595 mg/kg. The compound is not expected to accumulate significantly in aquatic organisms. The calculated accumulation factor for propoxur is nine times the ambient water concentration.

- **Effects on other organisms:** Propoxur is highly toxic to honeybees. The oral LD_{50} for propoxur in mule deer is 100–350 mg/kg.

5.3 Environmental Consequences—Larvicides

Microbial or Bacterial Larvicides

These naturally occurring bacteria and spores are found in soil in nature, and are thus not a significant concern to soil or the environment. Extensive testing shows that microbial larvicides do not pose risks to wildlife, nontarget species, or the environment when used according to label directions. Bacterial insecticides that are used for larval control in water are nontoxic to all but a few species of insects. In addition, they are essentially nontoxic to humans, so there are no concerns for human health effects with *Bti* or *B. sphaericus* when they are used according to label directions.

Methoprene

Methoprene breaks down so rapidly in the soil and water that it is unlikely to leach into groundwater. It is used as a larval insecticide in water, and is highly toxic to crustaceans and other aquatic invertebrates that rely on molting for growth. It presents minimal acute and chronic risk to freshwater fish and invertebrates, and estuarine species. Methoprene does not pose unreasonable risks to wildlife or the environment.

Temephos

Because temephos is applied directly to water, it is not expected to have a direct impact on terrestrial animals or birds. Current mosquito larviciding techniques pose some risk to nontarget aquatic species and the aquatic ecosystem. Although temephos presents relatively low risk to birds and terrestrial species, available information suggests that it is more toxic to aquatic invertebrates than alternative larvicides. For this reason, the EPA recommends limiting temephos use to areas where less-hazardous alternatives would not be effective, specifying intervals between applications, and limiting the use of high application rates. As part of its responsibility to reassess all older pesticides registered before 1984, EPA completed its revised risk assessments for temephos in July 2001, and has issued risk management decisions in the final re-registration eligibility decision (RED). The RED document is available on the EPA Web site

Temephos, applied according to the label for mosquito control, does not pose unreasonable risks to human health. It is applied to water, and the amount of temephos is very small in relation to the area covered, less than 1 ounce of active ingredient per acre for the liquid and 8 ounces per acre for the granular formulations. Temephos breaks down within a few days in water, and postapplication exposure is minimal. However, at high

dosages, temephos, like other organophosphates, can over stimulate the nervous system causing nausea, dizziness, and confusion.

Monomolecular Films

Monomolecular films, used according to label directions for larva and pupa control, pose minimal risks to the environment. They do not last very long in the environment, and are usually applied only to standing water, such as roadside ditches, woodland pools, or containers that contain few nontarget organisms. However, they can be toxic to fish and crustaceans, and animals that require the use of water surface tension for survival.

Likewise, when used according to label directions, monomolecular films do not pose a risk to human health. In addition to low toxicity, there is little opportunity for human exposure, because the material is applied directly to ditches, ponds, marshes, or flooded areas that are not drinking water sources.

Monomolecular Oils

Oils, if misapplied, may be toxic to fish and other aquatic organisms. For that reason, the EPA has established specific precautions on the label to reduce such risks. When used according to label directions for larva and pupa control, oils do not pose a risk to human health. In addition to low toxicity, there is little opportunity for human exposure, since the material is applied directly to ditches, ponds, marshes, or flooded areas that are not drinking water sources.

5.4 Human Health and Environmental Consequences—Environmental Management

The environmental consequences associated with environmental management are location-specific. As a result, this PEA can only address the potential negative environmental impacts of environmental management interventions in a broad manner.

Because mosquitoes breed in shallow-water habitats, it is not surprising that most environmental management interventions for malaria control are associated with the manipulation of wetland environments. Wetlands can be broadly categorized as freshwater wetlands (which include swamps, flood plains, riverine forest, and swamp forest), mangroves, and coastal wetlands (including lagoons, estuaries, and tidal mudflats) (Shumway, 1999). In some geographical regions, there are also semi-arid grasslands, which maintain areas of temporary flooding. Wetlands provide a wide range of ecological services including soil erosion and flood control, water purification and pollutant and nutrient retention, groundwater discharge and recharge, and provision of habitat and breeding grounds for wildlife. Disturbing wetlands through environmental management may alter the quantity and quality of the services that wetlands provide.

When wetlands are drained, their soils lose infiltration capacity. As a result, there is potential for increased surface water runoff and soil erosion. Clearing of wetland

vegetation can also cause (or exacerbate, if the wetland has been drained) increased surface water runoff and soil erosion.

Increased water runoff decreases the amount of water available to groundwater and surface water systems (groundwater constitutes a portion of stream flow, river flow, and sometimes pond depth). This can affect the *availability* of groundwater and surface water for human use throughout the year. Increased water runoff (or, alternatively, a change in the composition or clearing of wetland vegetation) may also decrease the ability of the wetland to take up pollutants, potentially diminishing the *quality* of water resources. Increased water runoff may also cause higher peak water flows in streams and rivers during rain events. This increase in water flow may either increase or decrease the mosquito breeding habitat and may also cause flood damage.

Soil erosion can cause siltation and sedimentation of water bodies, including dams and retention ponds. Soil erosion can reduce the life of dams, and may change the conditions for transport and hydropower production. Soil erosion can also decrease agricultural productivity. Agricultural productivity may also decrease as a result of increased soil acidity following wetland drainage.

Draining wetlands or clearing vegetation may decrease habitat and forage for animal species, and consequently decrease plant and animal biodiversity in the ecosystem. Of particular concern may be breeding habitat for migratory birds and animals. In wetlands, vegetation clearing may also decrease spawning ground for aquatic species.

Tree planting may decrease habitat and forage for some animal species (e.g., aquatic species), while increasing it for others (e.g., some bird species). Thus, tree planting changes the ecosystem composition, and may increase or decrease plant and animal biodiversity. This change in ecosystem composition may also decrease the ability of the wetland to take up pollutants, potentially diminishing the quality of water resources. Because tree planting is used to drain wetlands through transpiration, groundwater and surface water resources available for human use may decrease.

In a similar manner, the construction of impoundments may decrease habitat and forage for some species (e.g., terrestrial), while increasing it for others (e.g., aquatic). Impoundments may increase the availability of water resources for upstream communities, but may decrease water availability for downstream communities. Depending on their construction and location, they may increase or decrease infiltration into the groundwater system.

Saltwater flooding may decrease habitat and forage for freshwater aquatic and terrestrial species. It may also decrease the availability of freshwater resources in the target community.

Larvivorous fish are often introduced into commercial fish ponds without negative environment impacts. However, the introduction of exotic fish species into the natural environment (e.g., wetlands and marshes) should only be conducted following approval by the USAID Bureau Environmental Officer (BEO). The introduction of exotic (and

potentially invasive) fish into a natural environment could disrupt existing predator–prey relationships and alter ecosystem composition.

Table 20. Ranking of Environmental Management Interventions from Low Impact to High Impact

Impact Rank	Environmental Management Interventions	Potential Negative Impacts
Little or No Impact	Deepening/narrowing of existing drains	No significant impacts
Little or No Impact	Synchronized cropping/intermittent irrigation	No significant impacts
Low Impact	Filling breeding sites	Increased or decreased habitat and forage for animal species
Low Impact	Lining water sources and canals	Increased flooding
Medium Impact	Saltwater flooding	Reduction in water availability Decreased habitat for freshwater aquatic and terrestrial species
Medium Impact	Larvivorous fish introduction	Altered ecosystem composition on a small or large scale (invasive species problems) Increase or decrease in biodiversity
High Impact	Impoundment construction	Altered upstream and downstream water availability Increased or decreased habitat and forage for animal species Increase or decrease in plant and animal biodiversity Altered ecosystem composition
High Impact	Biological drainage	Reduction in water availability Reduction or enhancement of water quality Increased or decreased habitat and forage for animal species Increase or decrease in plant and animal biodiversity Altered ecosystem composition

Impact Rank	Environmental Management Interventions	Potential Negative Impacts
High Impact	Vegetation manipulation	Reduction of water availability
		Reduction in water quality
		Increased flooding
		Siltation and sedimentation of water bodies, including dams and retention ponds
		Change in conditions for transport and hydropower production
		Decreased agricultural productivity of soil
		Increased or decreased habitat and forage for animal species
		Increase or decrease in plant and animal biodiversity
		Alteration of ecosystem composition
High Impact	Physical drainage	Reduction in water availability
		Reduction of water quality
		Increased flooding
		Siltation and sedimentation of water bodies, including dams and retention ponds
		Change in conditions for transport and hydropower production
		Decreased agricultural productivity of soil
		Increased or decreased habitat and forage for animal species
		Increase or decrease in plant and animal biodiversity
		Alteration of ecosystem composition

6. Mitigation, Monitoring, and Evaluation

6.1 Mitigation and Monitoring: Planning and Recommendations

6.1.1 Selecting an Appropriate Location, Intervention, and Time of Implementation

The Importance of Surveillance

Mitigation of human health and environmental harm starts with the choice of location for one or more malaria control interventions. Knowing where the most malaria cases occur and where environmental conditions promote increased vector prevalence provides guidance in choosing locations where the intervention will have the most impact. Targeting areas for intervention, rather than implementing a broad-spectrum approach, will simultaneously protect more people from malaria and promote judicious use of insecticides, larvicides, and nonchemical interventions.

Sustained surveillance requires substantial technical support and capacity building, and involves the following aspects:

- Gathering historical malaria and environmental data
- Developing computerized databases
- Analyzing historical malaria and environmental data
- Developing protocols and providing training for malaria sentinel sites
- Analyzing seasonal patterns of malaria transmission (where applicable)
- Creating tools for forecasting and detecting malaria epidemics (where applicable)

Location-Specific Appropriateness

The different interventions proposed in this Programmatic Environmental Assessment (PEA) [as well as insecticide-treated nets (ITNs)] are more or less appropriate depending on the intervention location chosen. Entomological monitoring should be conducted to determine the geographic and temporal distribution of vector populations (see Section 6.1.3 under Entomological Monitoring). Different interventions may be better suited to the endemic or epidemic nature of the disease in a particular location. Additionally, environmental factors can be a determinant for selecting (or emphasizing) a particular intervention. In a semi-arid or arid environment, breeding sites are typically found in small, well-defined areas. In such conditions, year-round environmental management and larviciding may provide more benefits at a lower cost than in tropical areas. Population density can indicate which intervention is more suitable; environmental management and indoor residual spraying (IRS) generally have greater impact and cost less per person in urban than in rural areas. Finally, the type of housing structure in the location can dictate the appropriateness of an intervention.

Choosing or emphasizing an intervention that is location-appropriate will ensure that pesticides are used judiciously. Yet even after this step, the intervention may have to be implemented at an appropriate time to maximize impact. This is particularly important in IRS, where spraying should be conducted as close as possible to the start of a rainy season. Larviciding may also be timed in a manner that increases its impact on the vector population. Once a location, one or more location-specific interventions, and the timing of these interventions have been determined, further operational planning and implementation can commence. To ensure that decisions about future interventions make the most impact with the least harm to humans and the environment, surveillance and statistical analysis should be conducted to determine the extent to which each intervention contributes to malaria reduction. Conclusions derived can then be used to adjust which interventions are chosen or emphasized in the future.

Considering Sustainability

The U.S. Code of Federal Regulations (CFR) §216.6 says that the U.S. Agency for International Development (USAID) must consider "indirect effects and their significance" on the environment. This is particularly important when considering the use of pesticides. Procurement of pesticides for countries could result in an increase in obsolete stocks or improper use of the pesticide in the future (e.g., agricultural use). Spray equipment provided for IRS could be used to spray chemicals that have not gone through the USAID environmental review process, or chemicals that are not World Health Organization (WHO) recommended for IRS. Additionally, when a project ends, there is no guarantee that best practices will be followed in future interventions.

To ensure that a USAID-supported intervention is less likely to have negative indirect impacts, USAID should support interventions in host countries where the following conditions prevail:

- Political commitment to the intervention at all levels of government
- Stakeholder commitment to the intervention
- Commitment to addressing human health and environmental concerns of the intervention at all levels of government
- Stakeholder commitment to addressing human health and environmental concerns of the intervention
- Financial sustainability of the intervention in-country
- Future availability of human and institutional resources for implementation, monitoring, and evaluation of the intervention

6.1.2 Planning for the Intervention

Pesticide Selection

The chemicals used in IRS, ITNs, and larviciding all have different properties and are more or less appropriate in different circumstances. The following threshold criteria must be met in making decisions on pesticides used in malaria vector control:

a. Pesticide registration in the host country
b. Acceptability of the pesticide to the national malaria control program
c. Risk to human health
    i. Pesticides must be approved by the WHO and should be preferred based on their safety as described in Section 5.1.3.3.
d. Risk to environment, livestock, and/or agricultural trade

With particular regard to dichloro-diphenyl-trichloroethane (DDT), "viable alternatives to DDT should pose less risk to human health and the environment, be suitable for disease control based on [country]-specific conditions, and be supported with monitoring data (UNEP, 2001)."

Beyond these four threshold considerations, technical and logistical factors must be addressed in comparing and selecting pesticides for malaria vector control. The primary factor to be addressed is

- Vector resistance.

Secondary factors include

- Appropriateness of surface for spraying
- Duration of effectiveness (and implications for cost)
- Cost of pesticide.

Tertiary factors include

e. The need for a pesticide of a different class to prevent resistance
f. Major classes of pesticide used in other vector control interventions that could promote resistance
g. Major classes of pesticide used in the agricultural sector that could promote resistance
h. Host-country capacity to prevent pilferage.

Supplemental Environmental Assessments (SEAs) tiering off from this PEA must describe how these factors have been addressed in the pesticide selection process.

Planning for Health and Safety

The planning process for integrated vector management (IVM) interventions should integrate human health and environmental considerations from the start. When intervention needs are initially assessed and budgets developed, mitigation and monitoring components and costs identified in an SEA or Pesticide Evaluation Report

and Safer Use Action Plan (PERSUAP) should be included. The importance of planning for and implementing mitigation and monitoring activities is illustrated in the Case Study on Malathion Poisoning in Pakistan (see text box). This streamlines logistics and procurement processes and provides more accurate budget estimates.

The mitigation component of an IVM intervention needs assessment should include the following:

- **Description of Mitigation and Monitoring Measures**. This can be simply a list of activities to be conducted.
- **Mitigation and Monitoring Implementation Schedule**. The mitigation implementation schedule should be seamlessly integrated into the overall malaria disease control activity implementation plan. For example, the periodic assessment of mitigation measures should be scheduled the same way that activity workshops are scheduled.
- **Institutional Responsibility**. Responsibilities for implementation of mitigation and monitoring measures should be clearly identified, with the agreement of those identified, and updated regularly (at least annually).
- **Mitigation and Monitoring Costs.** The cost and source of funds for mitigation and monitoring should be included in the initial intervention cost estimates.

SEAs and PERSUAPs should also include the above elements in their Recommended Mitigation Measures sections (see SEA Guidance Document in ***Annex C***). The Recommended Mitigation Measures section should provide detailed descriptions of how mitigation measures should be planned for, implemented, monitored, and evaluated, and what action should be taken when mitigation activities are poorly implemented or fail. The section should also make evident the links between identified potential human health and environmental impacts and mitigation activities. It is important to factor in the reporting and monitoring activities and costs required by Parties to the Stockholm Convention if DDT is used in an IRS program.

Case Study: Malathion Poisoning in Pakistan

Whenever pesticides are used in a malaria control program, there is a risk of human exposure to pesticides and consequent harm to human health. Perhaps the most dramatic recorded instance occurred during a U.S. Agency for International Development– and World Health Organization–-sponsored indoor residual spraying campaign in Pakistan in 1976. During that campaign, 2,800 field workers in the Pakistan malaria control program were diagnosed with organophosphate insecticide poisoning due to malathion exposure. Five deaths were attributed to the organophosphate poisoning.

Baker et al. (1978) documented these poisonings, and even described the work practices that contributed to the extent and intensity of the poisonings:

> During this study, we observed improper work practices which increased dermal exposure to malathion. Spraymen's clothes were wet at the end of the working day, smelled strongly of pesticide, and were worn for several days without washing. Both spraymen and mixers had extensive skin contact with the pesticide during filling and pressurizing of the spray tanks. Some mixers mixed the malathion suspension with their hands. Many spray cans leaked pesticide onto the arms, hands, and chests of spraymen. When spray nozzles became clogged, the spraymen sometimes blew through them to unclog them.
>
> One sprayman died shortly after he consumed food which had been sprayed….
>
> Baker et al. (1978), pages 31–32

Had the mitigation practices recommended in this Programmatic Environmental Assessment—particularly certifying quality of the insecticide, proper storage conditions, and proper training and protective wear—been planned for and implemented during the program, the poisoning would have been avoided. Storage conditions would not have led to the degradation of malathion, leaky spray cans would not have been used, training of spray operators and supervisors would have ensured proper pesticide handling, personal protective equipment would have been worn and washed regularly and reduced exposure, spray operators would have known not to spray food or eat contaminated food, spray operators would have cared for

6.1.3 Mitigation and Monitoring Recommendations

Human health and environmental mitigation activities are intended to reduce adverse human health and environmental impacts that result from activity interventions. Mitigation measures can be categorized into the following types of actions: avoid impact, minimize or diminish effects, rectify or repair by rehabilitation, reduce or eliminate over time, or provide compensation (USAID, 2003). Monitoring is conducted to determine when mitigation is necessary and whether or not mitigation is working successfully. During implementation of the intervention, monitoring can identify negative human health or environmental impacts in time for mitigation measures to be adjusted or additional measures put in place. Therefore, monitoring is a necessary complement to the mitigation of negative human health and environmental impacts. Additionally, 22 CFR 216.3(a)(8) says that, "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 the environmental quality, positive or negative, during their implementation."

The following sections contain general recommendations for mitigation and monitoring activities in all operations, in addition to specific recommendations for IRS, environmental management, and larvicidal agent interventions. Although these

recommendations represent best practices, host-country stakeholders should be involved in reviewing proposed mitigation and monitoring activities to ensure they are technologically appropriate, culturally appropriate, and feasible. Mitigation and monitoring activities should then be adapted to the host-country situation without compromising human health and the environment.

Universal Mitigation and Monitoring Recommendations

Mitigation monitoring, environmental impacts monitoring, entomological monitoring, malaria case monitoring, and *adaptive management* of intervention implementation and the overall vector control strategy based on monitoring activities should be a part of every intervention. However, simply monitoring impacts is not sufficient—close *communication* and *coordination* between the monitoring staff, malaria control specialists, and decision makers is crucial to enacting mitigation activities successfully and managing the intervention appropriately. In past activities, monitoring data collected were either unavailable or of no use to activity managers (USAID, 1999). To the extent possible, mitigation plans should show causal linkage between the intervention and the negative consequences that may occur during or after implementation—in many instances, past monitoring plans were not developed with enough rigor to show such causal linkages (Hecht, 1994). Monitoring and mitigation plans for IVM interventions should avoid such pitfalls.

Mitigation Monitoring. Mitigation monitoring is used to determine if mitigation measures are being implemented and if those measures are effective in preventing or mitigating adverse environmental impacts. During the intervention, mitigation monitoring should be used to assess the effectiveness of mitigation efforts at *regular intervals* (e.g., at the beginning of the intervention, at 25 percent completion, at 50 percent completion). Mitigation efforts should be adjusted to address any negative impacts on human health or the environment that are observed.

Environmental, Livestock, and Human Health Impacts Monitoring. Environmental impacts monitoring measures ecological change over time as a result of program interventions. This type of monitoring uses *key environmental indicators* (e.g., vegetation change, water quality, pesticide levels present in the environment, indicator species populations, depending on the intervention or pesticide used) and *baseline surveys* to determine the impacts of the interventions on target and nontarget environmental areas. When pesticides are used, environmental impacts monitoring can also include the monitoring of impacts on domestic livestock. Livestock monitored may include chickens (for which there is anecdotal evidence of mortality from exposure to carbamates after IRS), ducks, geese, bees, fish, goats, cattle, and pigs. Additionally, human health effects from pesticide use can be monitored either indirectly, by using patches on the body to measure exposure, or directly, by sampling urine or blood (depending on the pesticide). This type of monitoring could be implemented for both those who apply pesticide and

community residents. An environmental monitoring plan for the environment, livestock, or human health should be developed using the following steps:

- Determine the reason for monitoring (e.g., assess the impacts of activity interventions, identify environmental impacts, and monitor mitigation measures)
- Formulate specific questions to be answered by monitoring
- Select indicators
- Determine the monitoring tools required to measure indicators
- Gather and integrate existing data (consider methods of data storage and analysis)
- Identify environmental "hot spots" (location of ecosystems and species at high risk)
- Design a sampling scheme
- Establish baseline conditions
- Establish targets for each indicator
- Validate the relationship between indicators and planned results
- Analyze trends and recommend management actions (e.g., environmental mitigation measures) (USAID, 1996)

Entomological Monitoring. The primary function of entomological monitoring associated with vector management is to assure that interventions are effective. Such monitoring is essential for IRS and larval control and, though not as critical, should also be implemented in areas where only ITNs have been deployed. The monitoring program must include at least the first three types of tests described below; the fourth category should also be included when possible.

Determine vector susceptibility to available insecticides. Susceptibility studies detect the presence of individuals in the vector population that are physiologically resistant to the insecticide being tested. For IRS, susceptibility studies can be conducted by using WHO test strips or CDC bottle assays on adults caught in the wild or adults reared from immature larvae. Although the CDC bottle assays have the advantage of testing a sample of the same chemical batch being applied, the WHO test strips enable more comparability across countries and time. Where possible, both should be done. Larvicides are generally tested for efficacy in small-scale field trials. In addition to the above "in vivo" resistance information, it is also possible to collect large numbers of the vector species for analysis by polymerase chain reaction (PCR) to determine the frequency of genetic markers that code for pesticide resistance in the local vector population. Nevertheless, PCR analysis should not be used as a substitute for "in vivo" resistance analysis.

Verify that the insecticide was applied properly and had an immediate effect. This involves routine follow-up observations. For IRS, wall bioassays are used to verify there is sufficient residual pesticide on the walls of sampled structures to kill vector mosquitoes, and to monitor the loss of residual efficacy over time. An analogous assay

may be done for ITNs, either with the same type of cone used on the wall, or by forming a "basket" with the treated netting. For larviciding, routine inspection of treated breeding sites will verify that mosquito larvae are no longer present immediately after larvicide treatment and will detect new larvae when they are present. Note that, in most malaria-endemic settings, the effectiveness of larval control is extremely limited; it should only be implemented where there is solid entomological monitoring indicating its effectiveness.

Determine the geographic and temporal distribution of vector populations. To target areas where vector control for malaria is needed, it is necessary to determine where malaria transmission occurs and the length of the transmission season by establishing when populations of adult vectors are present. This can be done by using a variety of collection techniques, including human landing catches, CDC light traps, cattle-baited hut or net collections, nonbaited hut or net collections, pyrethrum spray catches (PSCs), and window exit traps.

Measure the impact of the intervention on the vector population and/or malaria transmission intensity. Several different techniques are used to monitor the vector population and/or the frequency and infectivity of vector biting. In general, the intention is to determine whether the vector management program has substantially reduced the vector population or survivorship, as indicated either by a reduction in the number of mosquitoes that can be collected, a reduction in mosquito biting, or, as detected through mosquito dissections, the proportion parous (the proportion that have laid at least one batch of eggs). Methods are available for human landing catches, CDC light traps, cattle-baited hut or net collections, nonbaited hut or net collections, PSCs, and window exit traps.

Malaria Case Monitoring. Malaria case monitoring is conducted to assess the impacts of malaria control interventions on target human and mosquito populations. The information obtained from this impact monitoring can be used to determine if the interventions are achieving the desired results and to inform changes in the program.

Indoor Residual Spraying Recommendations

In many respects, IRS is operationally homogeneous. Much of the time, the same types of mitigation actions are recommended for IRS regardless of the insecticide used. These general recommendations are listed in Table 21. Descriptions of some of the general recommendations and additional recommendations specific to certain classes of insecticide follow the table.

Table 21. IRS Recommendations

Potential Negative Activities/Impacts	Recommended Mitigation Actions
Daily Operations	
Occupational exposure to insecticide from daily indoor residual spraying (IRS) operations	Training of spray operators, team leaders, and supervisors according to best practices, including recognition of insecticide-poisoning symptoms.
	Procurement and proper use of personal protective equipment (PPE) by spray operators, team leaders, and supervisors (cotton overalls, face mask, broad-rimmed hat, rubber gloves, gum boots)
	Training of health workers in insecticide-poisoning treatment
	Procurement and distribution of treatment medicines for insecticide exposure
	Daily on-site personal washing (after spraying)
	Reprimand of spray operators who do not follow proper procedure in all aspects of operations (handling, spraying, hygiene, cleanup)
	Hire of commercial laundry or local wash persons (can be spray operators) for proper washing of overalls.
	Frequent washing of overalls (after spraying)
	Procurement and wearing of PPE by wash person (chemical apron, rubber boots, rubber gloves) if a wash person is hired to clean spray operator PPE
	Procurement and distribution of barrels for progressive rinse, and wash-tubs for overall washing and personal hygiene
	Progressive rinse of sprayers and PPE
	Development and implementation of a human health monitoring plan to determine pesticide impacts on spray operators and residents, particularly when using organophosphates.
	Development and implementation of environmental reporting system for Human Health and Environmental Evaluation Report (see Section 6.2)
Fetal exposure to insecticide from daily IRS operations (female spray operators)	When dichloro-diphenyl-trichloroethance (DDT) is used, institute prohibitions of hiring women of child-bearing age as spray operators.
	Ensure that pregnant or breast-feeding women are not hired as spray operators

Potential Negative Activities/Impacts	Recommended Mitigation Actions
	Distribution of condoms to women spray operators
	Pregnancy tests 1 month into spray campaign
Community and environmental exposure to insecticide from daily IRS operations	Prohibition of spraying in homes where sick persons or pregnant women are living and cannot move outside the home *and* stay outside the home during and 1 hour after spraying
	Development and implementation of environmental reporting system for Human Health and Environmental Evaluation Report (see Section 6.2)
	Prohibition of spraying in protected areas/sensitive ecosystems (e.g., uncultivated wetlands), and spraying with care in residential areas where beekeeping occurs
	Prohibition of spraying in homes where food and utensils have not been removed from the house, and where furniture has not been removed from the house *or* moved to the middle of the room and covered with a cloth by the spray operator
	Information, education, and communication (IEC) campaign, citing importance of removing all food and utensils from house prior to spraying, moving furniture to the center of the room or outside, staying out of the house during and 1 hour after spraying, not allowing children or animals in the house until floor residue is swept outside, educating about potential impacts of insecticide on domestic animals (e.g., chickens eating insects killed by carbamates)
	Procurement of seat covers or sheets for covering cloth vehicle seats
	Covering of cloth interior seats of program vehicles with seat cover or cloth to prevent seat contamination
	Use of gloves for washing interior and exterior of program vehicle
	Wiping of contaminated bed of truck with damp cloth prior to exterior washing of program vehicles
	End-of-program cleaning/decontamination of interior and exterior of vehicle, according to the United Nations Food and Agriculture Organization's (UNFAO) *Pesticide Storage and Stock Control Manual*
	End-of-campaign washing of seat covers and wiping of seats/bed of program vehicle with damp cloths
	Prior to spraying, covering furniture that cannot be moved with cloths provided by the Ministry of Health (MOH), District Health Office, or U.S. Agency for International Development (USAID) program.

Potential Negative Activities/Impacts	Recommended Mitigation Actions
	Reprimand of spray operators who do not follow proper procedure in all aspects of operations (handling, spraying, hygiene, cleanup)
	Frequent washing of cloths used to cover furniture
	Training of spray operators, team leaders, and supervisors according to best practices
	Procurement and distribution of barrels for progressive rinse and wash-tubs for overall washing and personal hygiene
	Progressive rinsing of sprayers and PPE
	Procurement and distribution of materials necessary for collection (in the case of using a commercial laundry for washing spray operator overalls) and decontamination of washtub rinse-water
	Daily collection of laundry rinse-water (from commercial laundry), decontamination of laundry rinse-water, and latrine disposal
	Analysis of decontaminated rinse-water to determine levels of active ingredient
	Storage of all insecticides, empty packaging, barrels, and tubs in storage facilities, reducing use of contaminated goods domestically
	Inscription of all program barrels and tubs as District Health Office property, and labeling with host-country-specific poison indicators, to deter sale and domestic use (e.g., storage of food or water for human or animal consumption) in the event of pilferage
	Secure storage of contaminated plastic sachets for recapture by the manufacturer or disposal at an internationally recognized hazardous waste incinerator
	Shredding or puncturing of plastic packaging materials, making them unusable (unless barrels used for progressive rinse)
	Local disposal of noncontaminated cardboard or paper packaging
	Transport of rinsed packaging materials to a landfill for disposal, or a power plant or cement kiln for reuse as fuel (if they are not recovered by the manufacturer and if host country environmental guidelines allow)
	Development and implementation of environmental and/or livestock monitoring plan to the extent “feasible” and “relevant”

Potential Negative Activities/Impacts	Recommended Mitigation Actions
	Development and implementation of a human health monitoring plan to determine pesticide impacts on spray operators and residents, particularly when using organophosphates
	Development of protocol for decision making when environmental monitoring indicates environmental or agricultural contamination as a result of IRS
	Development and implementation of environmental reporting system for Human Health and Environmental Evaluation Report (see Section 6.2)
Special Circumstances	
Pilferage of insecticide, consequential human and environmental exposure	Construction or renovation of central, permanent storage facilities according to UNFAO's *Pesticide Storage and Stock Control Manual*
	Construction or renovation of temporary storage facilities using main principles of UNFAO's *Pesticide Storage and Stock Control Manual* as a general guideline
	Double-padlocking and guarding of all storage facilities
	Supervision of spray operators
	Development and implementation of environmental monitoring plan
	Development and implementation of environmental reporting system for Human Health and Environmental Evaluation Report (see Section 6.2)
Storehouse fire, inhalation of toxic fumes from insecticide fire	Construction or renovation of central, permanent storage facilities according to UNFAO's *Pesticide Storage and Stock Control Manual*
	Construction or renovation of temporary storage facilities using main principles of UNFAO's *Pesticide Storage and Stock Control Manual* as a general guideline
	Procurement and distribution of emergency equipment to insecticide storage facilities
	Training of storekeepers according to FAO guidelines
	Development and implementation of environmental reporting system for Human Health and Environmental Evaluation Report (see Section 6.2)

Potential Negative Activities/Impacts	Recommended Mitigation Actions
Accidents and spillage during transport and storage, leading to human and environmental exposure	Training of drivers for long-distance transport of insecticide and short-distance transport during the campaign period
	Transport of centrally-stored insecticides according to UNFAO's *Pesticide Storage and Stock Control Manual*
	Construction or renovation of central, permanent storage facilities according to UNFAO's *Pesticide Storage and Stock Control Manual*
	Construction or renovation of temporary storage facilities using main principles of UNFAO's *Pesticide Storage and Stock Control Manual* as a general guideline
	Emergency equipment located in storage facilities
	Storekeeper training for all insecticide storage facilities, both temporary and permanent
	Training of health workers in insecticide-poisoning treatment
	Procurement and distribution of treatment medicines for insecticide exposure
	Development and implementation of environmental reporting system for Human Health and Environmental Evaluation Report (see Section 6.2)
Flooding of storehouse, leading to environmental contamination	Storage facility sites located on high ground, outside of floodplain
Insecticide Quality and Resistance	
Decreased effectiveness of insecticide, lessening impact on malaria incidence	Selection of insecticide to minimize resistance and maximize residuality on surfaces sprayed
	Laboratory testing of insecticide to ensure quality control
	Entomological monitoring of resistance
	IEC campaign, citing importance of not plastering or painting walls after the home has been sprayed
	Data recording on agricultural insecticides for the purpose of knowing how they may contribute to resistance
	Proper insecticide storage by renovation of storage facilities
	Training of spray operators in proper application for specific wall types (e.g., uniform spray speed, constant and accurate spray distance)

Potential Negative Activities/Impacts	Recommended Mitigation Actions
	Procurement and use of sprayers manufactured according to WHO specifications
	Daily sprayer maintenance
	Development and implementation of environmental reporting system for Human Health and Environmental Evaluation Report (see Section 6.2)
Future Activities	
Indirect support of malaria vector control operations that have not undergone environmental review through procurement of sprayers and storage facilities	Importance of an environmental assessment for any pesticides used in IRS will be discussed with MOH and Ministry of Environment staff and online resources for conducting assessments will be provided (http://www.encapafrica.org/)
Adaptive Management (potentially reducing pesticide use for malaria vector control)	Development of a strong malaria surveillance system to target IRS interventions, reducing pesticide use
	Study resting behavior of the target species, so "treatment may be confined to the ceiling or the lower or upper half of walls, or to include the undersides of furniture, outside eaves and porches" (WHO, 2006;23)
	Pursuit of an integrated strategy involving environmental management and larviciding
	Development of protocol/implementation of measures to mitigate mosquito resistance to insecticides (pesticide rotation or mosaicing)
	Submission of Human Health and Environmental Evaluation Report to USAID Contractor, USAID Mission Environmental Officer (MEO), USAID Regional Environmental Officer (REO)

IRS: Description of Some of the General Recommendations

Hygiene Regimen. WHO recommendations in *Pesticides and their Application for the Control of Pests of Public Health Importance* should be followed in every malaria control program utilizing pesticides. The box below details these recommendations.

WHO Recommendations: Personal Hygiene

Scrupulous attention to personal hygiene is an essential component of the safe use of pesticides. For professional spraying staff operating in the tropics, the safety precautions might depend largely on personal hygiene, including washing and changing clothes. A drill for carrying out and supervising personal hygiene, regular washing of protective clothes, and cleaning of equipment should be organized along the following lines:

- Spraying staff should be provided with at least two uniforms to allow for frequent changes.
- Washing facilities with sufficient water and soap should be made available in the field at appropriate locations.
- All working clothes must be removed at the end of each day's operations and a shower or bath taken.
- Working clothes must be washed regularly, the frequency depending on the toxicity of the formulation used.
- Particular attention should be given to washing gloves, as wearing contaminated gloves can be more dangerous than not wearing gloves at all.
- Spray operators must wash before eating.
- Eating, drinking, and smoking during work must be strictly forbidden.
- When work involves pesticides of relatively high toxicity, the hours of work must be arranged so that exposure to the material is not excessive; transport should be arranged so that there is not a long delay between the end of the day's operations and return to base for washing.

For some of the older pesticides, washing with soap can increase dermal absorption from contaminated skin. This underlines the importance of avoiding exposure.

Protocol for Pesticide-Poisoning Treatment. The pesticides supported by USAID for IRS have been fully evaluated by the WHO Pesticide Evaluation Scheme (WHOPES) and can safely be used for malaria control in safe and effective quantities by sprayer operators who are adequately protected from the potential toxic effects. To assure minimum risk of pesticide poisoning, any USAID-sponsored IRS program must assure appropriate safety standards for handling, storing, and disposing of pesticides, as described in Table 21. Safety supervisors, entomologists, and medical specialists should be aware of the:

The mode of action of the pesticide
The significance of diagnostic measures
Recognition of the signs and symptoms of toxic effects; and
The facilities required for treatment of cases of poisoning (WHO, 2006)

The program must assure that spray operators are trained to identify the signs and symptoms of poisoning and to use emergency first aid techniques, including resuscitation. "All workers should know the hazard of the work they are required to carry out. They should understand the real risks involved and should not be led astray by erroneous preconceptions" (WHO, 2006; 13). Because the treatment for poisoning is specific to each pesticide, country-specific treatment and referral guidelines must be developed based on the specific insecticides being used and the local capacity for

poisoning treatment. To assure that appropriate treatment is available in the event of poisoning, the program must assure that country-specific exposure treatment guidelines are developed. Country-specific guidelines should include

- General principles in the management of acute pesticide poisoning
- First-aid procedures and training strategy for spray operators
- Identification of appropriate treatment facilities and assurance that treatment drugs are available (where necessary, the program should provide training to local medical staff to assure that the capability to provide appropriate treatment is established, procure appropriate treatment drugs if not available, and prepare treatment guidelines for the specific country setting and pesticides being used)
- Determination of referral process (transportation of exposure victim, communication with facilities)

In addition, the program should assure financial support for any medical costs incurred in managing or treating the toxic effects of exposure to pesticides used in the program.

When organophosphates are used, cholinesterase activity must be tested prior to the start of spraying and once per week during the spray campaign for all personnel exposed to the insecticide. Spray operators should cease their participation in the spray campaign if their cholinesterase activity decreases to 50% or more of their baseline cholinesterase activity (WHO, 2006).

The program country-level technical manager will be responsible for an evaluation of the capacity of local facilities to treat poisoning by the pesticides being used, including identification of a referral hospital if treatment for exposure cannot be adequately provided for by local health clinics. The institution implementing the program should assure that appropriate short-term technical assistance is provided by the program to provide necessary training of local medical staff.

Guidelines for treatment of poisoning from IRS insecticide are located in ***Annex I.*** These guidelines are adapted from the U.S. Environmental Protection Agency‘s (EPA) *Recognition and Management of Pesticide Poisonings* and WHO’s report, *Malaria Vector Control: Insecticides for Indoor Residual Spraying*.

Training of Drivers. Prior to long-distance transport of the pesticide from the customs warehouse/central storage facility to the target area, drivers should be informed about general issues surrounding the pesticide and how to handle emergency situations (e.g., road accidents). Training for long-distance transport will include the following information:

- For what use the pesticide is intended
- Toxicity of the pesticide
- Understanding security issues, implications of the pesticide getting into the public

- Handling an accident or emergency (according to the United Nations Food and Agriculture Organization's (UNFAO) *Pesticide Storage and Stock Control Manual*)
- Combustibility and combustion byproducts of pesticide

Drivers hired specifically for the 2-month spray campaign period will receive

- Training provided to spray operators (with the exception of sprayer operation and spray practice)
- Training on handling an accident or emergency (according to UNFAO's *Pesticide Storage and Stock Control Manual*)
- Training on handling vehicle contamination (see below)

If vehicles are expected to be used for purposes other than malaria vector control after the program, it is important to ensure that pesticide contamination in the vehicle does not have negative impacts when the vehicle is subsequently used for another purpose (e.g., food transport). Drivers should be responsible for taking care that any cloth vehicle seats are covered to prevent contamination from transportation of spray operators. To prevent pesticide runoff from vehicle washing, drivers should also be responsible for wiping the vehicle bed with a damp cloth prior to washing the exterior of the vehicle. Finally, drivers should be responsible for cleaning and decontaminating the interior of the vehicle and exterior bed at the end of the spray campaign. Drivers should be provided with gloves to wear for cleaning the vehicle. All cloths used in wiping down the interior and bed of the vehicle should be washed with spray operator overalls.

Packaging Disposal Protocol. Noncontaminated pesticide packaging (e.g., boxes or paper) can be disposed of locally—WHO recommends that this packaging be returned to a supervisor for "safe" disposal, and UNFAO recommends disposal at a landfill or "recycling" the packaging as fuel for a cement kiln or power plant (WHO, 2002; Thompson, 2004). UNFAO's "Draft Guidance Document on the Selection of Waste Management Options for the Disposal of Obsolete Pesticides and Contaminated Materials" says that, "The material, from which the containers and packaging are constructed, is generally environmentally harmless in itself and is suitable for recycling or disposal within the country. The degree of residual pesticide contamination within the materials is the only issue that may prevent this from occurring" (Thompson, 2004:60). Any packaging or personal protective equipment (PPE) that has been heavily contaminated should be triple-rinsed, shredded or punctured, and taken to a hazardous waste facility.

Progressive Rinse Method. With this method, several barrels are placed in a line. The first barrel is empty, the second full of water, the third empty, and so on. Leftover pesticide from the day's operations is dumped in the first barrel, water from the second barrel is used to rinse the sprayer, and then poured into the empty third barrel. Water from the fourth barrel is used for a second rinsing of the sprayer, and is then poured into the empty fifth barrel. This continues until the last rinse water is poured into the last

barrel. The contaminated rinse water is then used to fill up the sprayers in the next day's spraying. This method virtually eliminates environmental contamination from sprayer rinse-water.

Triple-Rinse Method. Add a measured amount of water or other specified dilutent so that the container is one-fifth to one-fourth full. Rinse container thoroughly, pour into a tank, and allow it to drain for 30 seconds. Repeat three times. The water rinsate can be used to mix with or dilute more of the same pesticides or it can be sprayed on a wall.

Double-Padlocking. Storage facilities should have two separate locks on all exterior doors, with the key to one lock given to one individual and the key to another lock given to another individual.

IRS: Insecticide-Specific Considerations

Pyrethroids. For lambda-cyhalothrin, hydrolysis can be used to decontaminate containers or packaging material by using a 1:1 mixture (by volume) of:

- either 5 percent sodium hydroxide (caustic soda) solution or saturated (7–10 percent) sodium carbonate (washing soda) solution

  and

- a water/oil soluble solvent, such as denatured alcohol, monoethylene glycol, hexylene glycol, or 2-propanol.

Cover the contaminated surface with this hydrolyzing agent and leave it for seven days (in a secure place to avoid pilferage). Before the resulting waste is disposed of, it must be analyzed to ensure that the active ingredient has been degraded to a safe level (IPCS, 1990).

DDT. Environmental monitoring must always be conducted when USAID supports DDT use in IRS operations; this is primarily because it is persistent in the environment, bioaccumulates in animals and humans, can cause harm to wildlife, and has serious implications for agricultural trade (see Section 9.1.2). Fortunately, the characteristics of DDT that make it environmentally damaging also make it easy to monitor. Additionally, because DDT use is widely banned in the agricultural sector, increases in levels of DDT in the environment can more easily be attributed to its use in IRS (or improper use after any pilferage of DDT intended for IRS).

The dose of DDT required for use in IRS is also quite large, making packaging of DDT charges in water-soluble sachets infeasible. As a result, there are several operational implications that should be considered in addition to the mitigation measures listed in Table 21. First, DDT charges need to be emptied into a bucket and stirred to assure that the insecticide dissolves into solution before being poured into the spray tank. These buckets and stirrers must be used exclusively for the IRS program and not for any domestic purposes. Second, funnels may be needed to prevent spillage of the DDT charge when it is being poured into the tank. Third, because DDT sachets are insoluble, they

need to be exported for disposal at an internationally recognized hazardous waste incinerator or returned to the manufacturer.

Carbamates. Empty carbamate containers can be neutralized by adding alkaline substances. The following procedure is recommended for 200-liter barrels; use proportionally less material for smaller containers:

1. Add 20 liters of water, 250 milliliters of detergent, and 1 kilogram of flake lye or sodium hydroxide.
2. Close the barrel and rotate to wet all surfaces.
3. Let stand for 15 minutes.
4. Drain completely and rinse twice with water. The rinsate should be drained into a shallow pit in the ground located far away from wells, surface water, or inhabited areas.

Containers cleaned by any of the above methods 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.

Like the dose of DDT, the dose of propoxur required for use in IRS is 1–2 g/m^2, making packaging of propoxur charges in water-soluble sachets infeasible. As a result, there are several operational implications that should be considered in addition to the mitigation measures listed in Table 21. First, propoxur charges need to be emptied into a bucket and stirred to assure that it dissolves into solution before being poured into the spray tank. These buckets and stirrers must be used exclusively for the IRS program and not for any domestic purposes. Second, funnels may be needed to prevent spillage of the propoxur charge when it is being poured into the tank. Third, because propoxur sachets are insoluble, they need to be exported for disposal at an internationally recognized hazardous waste incinerator or returned to the manufacturer.

Organophosphates. When organophosphates are used, cholinesterase activity must be tested prior to the start of spraying and once per week during the spray campaign for all personnel exposed to the insecticide. Spray operators should cease their participation in the spray campaign if their cholinesterase activity decreases to 50 percent or more of their baseline cholinesterase activity (WHO, 2006).

Empty organophosphate containers should be triple-rinsed with water and scrubbed inside thoroughly with a household detergent. “Drums that contained an organophosphate should be given an additional rinse with washing soda at 50 grams per liter (5%) and the solution should be allowed to remain in the container overnight” (WHO, 2006; 15).

The dose of fenitrothion, malathion, or pirimiphos-methyl required for use in IRS is also quite large, making packaging of organophosphate charges in water-soluble sachets infeasible. As a result, there are several operational implications that should be considered in addition to the mitigation measures listed in Table 21. First, the charges

need to be emptied into a bucket and stirred to assure that the pesticide dissolves into solution before being poured into the spray tank. These buckets and stirrers must be used exclusively for the IRS program and not for any domestic purposes. Second, funnels may be needed to prevent spillage of the charge when it is being poured into the tank. Third, because the sachets are insoluble, they need to be exported for disposal at an internationally recognized hazardous waste incinerator or returned to the manufacturer.

With regard to storage, EPA recommends that malathion be stored at a temperature of 21°C or lower to prevent degradation of the product to its more toxic product, isomalathion. The need for such storage conditions must be considered when planning an IRS campaign using malathion.

IRS: DDT as a Special Case

WHO has approved twelve insecticides for use in IRS for malaria control. DDT is unique among these insecticides, as it is a persistent organic pollutant (POP); as stated by the Stockholm Convention, POPs such as DDT "possess toxic properties, resist degradation, bioaccumulate and are transported, through air, water, and migratory species, across international boundaries and deposited far from their place of release, where they accumulate in terrestrial and aquatic ecosystems."

The Stockholm Convention places the following **requirements** on Parties to the Convention as stated in Annex B Part II:[10]

1. Notify Stockholm Secretariat and WHO of production and/or use of DDT
2. Restrict production and/or use to disease vector control
3. Produce and/or use DDT in accordance with WHO recommendations and guidelines
4. Use DDT only when locally safe, effective, and affordable alternatives are not available—"Factors to be promoted when considering alternatives or combinations of alternatives shall include the human health risks and environmental implications of such alternatives. Viable alternatives to DDT shall pose less risk to human health and the environment, be suitable for disease control based on conditions in the [countries] in question and be supported with monitoring data."
5. Report on production and/or use of DDT every three years (reporting requirements found at www.pops.int every 3 years.

In addition, Article 7 of the Stockholm Convention requires that Parties must "develop and endeavor to implement a plan for the implementation of [their] obligations under this Convention." These plans are called national implementation plans (NIPs).

[10] Requirements and recommendations from the Stockholm Convention have been paraphrased for easy reading. Please see the complete text of the Convention at www.pops.int for the precise wording of the text.

The Stockholm Convention also lays out the following **recommendations**, "with the goal of reducing and ultimately eliminating the use of DDT":

1. Each Party using DDT should develop and implement an action plan as part of its NIP. That action plan should include:
    a. Development of regulatory and other mechanisms to ensure that DDT use is restricted to disease vector control
    b. Implementation of suitable alternative products, methods, and strategies, including resistance management strategies to ensure the continuing effectiveness of these alternatives
    c. Measures to strengthen health care and to reduce the incidence of the disease.
2. All Parties to the Stockholm Convention, within their capabilities, should promote research and development of safe alternative chemical and nonchemical products, methods, and strategies [for vector control].

As a signatory to the Stockholm Convention, the U.S. Government is committed to ensuring that its support of DDT in developing countries is consistent with Stockholm Convention requirements and recommendations, as well as NIPs prepared by the host countries. Thus, USAID will support the following planning, program, and environmental compliance activities where it supports DDT use in disease vector control:

1. *USAID will base its support of insecticides used in disease vector control on a rational selection process* considering the insecticide's effectiveness in reducing or repelling the vector; risk to human health, the environment, and the agricultural and trade sectors; acceptability in the host country; cost; the need for resistance management; and other considerations.
2. *USAID will only provide support of DDT to Parties that have notified the Stockholm Secretariat and the WHO* of their production and/or use of DDT and that restrict DDT use to disease vector control.
3. *All USAID support of DDT use will follow WHO recommendations and guidelines.*
4. *USAID will assist host-country governments in re-examining the need for DDT* based upon the best available information and in identifying the best choice for IRS chemicals, considering safety, effectiveness, and affordability in accordance with Annex B, Part II of the Stockholm Convention. The selection of alternatives or combination of alternatives for malaria control will take into consideration human health risks and environmental implications; viable alternatives to DDT should pose less risk to human health and the environment, be suitable for disease control based on Stockholm Convention Party–specific conditions, and be supported with monitoring data.
5. *USAID will regularly review and revise SEAs pertaining to DDT every 1 to 3 years, as appropriate*, to ensure that USAID support remains consistent with

stipulations in Annex B, Part II of the Stockholm Convention, the host-country NIP, and Stockholm Convention Party reporting requirements for DDT use.

6. *When local capacity is insufficient, USAID will assist host-country governments in conducting activities to fulfill Stockholm Convention reporting requirements.* To receive USAID support for use of DDT in IRS, the host country must demonstrate concerted effort in developing and following a NIP as well as reporting to the Stockholm Secretariat.
7. *USAID will support the monitoring of DDT in the environments where it is sprayed.* According to CFR Title 22 Section 216, "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."
8. *When local capacity is insufficient, USAID will facilitate appropriate disposal of DDT-contaminated waste* resulting from IRS operations in accordance with the Basel Convention and other relevant regional and international treaties.

Larvicidal Agent Recommendations

Table 22 lists recommendations for larviciding. It is important to note that larviciding can decrease the need for other pesticide-based interventions, which decreases the potential for harm to human health and the environment from pesticide use. Additionally, "persons applying larvicides are generally much less exposed than staff engaged in indoor house treatment, and exposure is confined mainly to the hands and arms" (WHO, 2006; 17).

Table 22. Larviciding Recommendations

Potential Negative Activities/Impacts	Recommended Mitigation Actions
Daily Operations	
Occupational exposure to larvicide from daily operations	Training of spray applicators and supervisors according to best practices.
	Procurement and proper use of personal protective equipment (PPE) by applicators (cotton overalls, face mask, rubber gloves)
	Training of health workers in pesticide-poisoning treatment
	Procurement and distribution of treatment medicines for pesticide exposure
	Reprimand of applicators who do not follow proper procedure in all aspects of operations (handling, application, hygiene, cleanup)
	Procurement and distribution of barrels for progressive rinse and wash-tubs for overall washing and personal hygiene
	Progressive rinse of sprayers and PPE
	Development and implementation of a human health monitoring plan (to determine pesticide impacts on applicators and residents)
Fetal exposure to larvicide from daily operations (female applicators)	Development and implementation of environmental reporting system for Human Health and Environmental Evaluation Report (see Section 6.2)
	Women prohibited from conducting organophosphate application while pregnant or breastfeeding
Community and environmental exposure to larvicide from daily operations	Care should be taken in deciding when to spray, avoiding larviciding before major storm events
	Care should be taken in deciding where to spray, avoiding bodies of water used as drinking water sources for humans or livestock
	Development and implementation of environmental reporting system for Human Health and Environmental Evaluation Report (see Section 6.2)

Potential Negative Activities/Impacts	Recommended Mitigation Actions
	Reprimand of applicators who do not follow proper procedure in all aspects of operations (handling, application, hygiene, cleanup)
	Training of applicators and supervisors according to best practices
	Procurement and distribution of barrels for progressive rinse and wash-tubs for overall washing and personal hygiene
	Progressive rinsing of sprayers and PPE
	Storage of all insecticides, empty packaging, barrels, and tubs in storage facilities, reducing use of contaminated goods domestically
	Inscription of ALL program barrels and tubs as District Health Office property, and labeling with poison stickers, to deter sale and domestic use in event of pilferage
	Daily triple-rinsing of contaminated packaging
	Shredding or puncturing of packaging materials, making them unusable (unless barrels used for progressive rinse)
	Transport of rinsed packaging materials to landfill or, if appropriate for incineration, power plant or cement kiln
	Development and implementation of environmental and/or livestock monitoring plan
	Development and implementation of a human health monitoring plan (to determine pesticide impacts on spray operators and residents)
	Development and implementation of environmental reporting system for Human Health and Environmental Evaluation Report (see Section 6.2)
Special Circumstances	
Pilferage of larvicide, consequential human and environmental exposure	Construction or renovation of central, permanent storage facilities according to the United Nations Food and Agriculture Organization's (UNFAO's) *Pesticide Storage and Stock Control Manual*
	Construction or renovation of temporary storage facilities using main principles of UNFAO's *Pesticide Storage and Stock Control Manual* as a general guideline

Potential Negative Activities/Impacts	Recommended Mitigation Actions
	Double-padlocking of all storage facilities
	Supervision of applicators
	Development and implementation of environmental monitoring plan
	Development and implementation of environmental reporting system for Human Health and Environmental Evaluation Report (see Section 6.2)
Storehouse fire, inhalation of toxic fumes from larvicide fire	Construction or renovation of central, permanent storage facilities according to UNFAO's *Pesticide Storage and Stock Control Manual*
	Construction or renovation of temporary storage facilities using main principles of UNFAO's *Pesticide Storage and Stock Control Manual* as a general guideline
	Procurement and distribution of emergency equipment to larvicide storage facilities
	Training of storekeepers
	Development and implementation of environmental reporting system
Accidents and spillage during transport and storage, leading to human and environmental exposure	Training of drivers for long-distance transport of larvicide and short-distance transport during the campaign period
	Transport of larvicides according to UNFAO's *Pesticide Storage and Stock Control Manual*
	Construction or renovation of central, permanent storage facilities according to UNFAO's *Pesticide Storage and Stock Control Manual*
	Construction or renovation of temporary storage facilities using main principles of UNFAO's *Pesticide Storage and Stock Control Manual* as a general guideline
	Procurement and distribution of emergency equipment to larvicide storage facilities
	Storekeeper training
	Training of health workers in pesticide-poisoning treatment
	Procurement and distribution of treatment medicines for pesticide exposure
	Development and implementation of environmental reporting system for Human Health and Environmental Evaluation Report (see Section 6.2)

Potential Negative Activities/Impacts	Recommended Mitigation Actions
Flooding of storehouse, leading to environmental contamination	Storage facility sites located on high ground, outside of floodplain
Insecticide Quality and Resistance	
Decreased effectiveness of larvicide, lessening impact on malaria incidence	Prohibition of applying larvicidal agents where vector larvae are not present
	Whenever possible, use of “source reduction” (emptying, covering, or filling in breeding sites) instead of application of the larvicidal agent
	Selection of larvicidal agent to minimize vector resistance
	Laboratory testing of larvicidal agent to ensure quality control
	Entomological monitoring of resistance
	Data recording on agricultural pesticides for the purpose of knowing how they may contribute to resistance
	Construction or renovation of storage facilities according to UNFAO’s *Pesticide Storage and Stock Control Manual*
	Procurement and use of sprayers manufactured according to World Health Organization (WHO) specifications
	Daily sprayer maintenance
	Development and implementation of environmental reporting system for Human Health and Environmental Evaluation Report (see Section 6.2)
Future Activities	
Indirect support of malaria vector control operations that have not undergone environmental review through procurement of sprayers and storage facilities	Importance of an environmental assessment for any pesticides used in malaria vector control will be discussed with Ministry of Health (MOH) and Ministry of Environment staff and online resources for conducting assessments will be provided (http://www.encapafrica.org/)

Potential Negative Activities/Impacts	Recommended Mitigation Actions
Adaptive management (potentially reducing larvicide use for malaria vector control)	Development of a strong malaria surveillance system to target interventions, reducing pesticide use
	Pursuit of an integrated malaria vector control strategy
	Development of protocol/implementation of measures to mitigate mosquito resistance to larvicidal agents through rotation or mosaicing
	Submission of Human Health and Environmental Evaluation Report to USAID Contractor, USAID Mission Environmental Officer, USAID Regional Environmental Officer

Environmental Management Recommendations

The site location for an environmental management intervention should be chosen based on larval surveillance—if no vector larvae are present, no intervention should be conducted. When vector larvae are present in an area, the intervention chosen should be based on scientific information about the site, such as soil type and density, slope, species composition, endangered species habitat, and water flow and quality. Additionally, stakeholder and environmental water needs should be assessed and factored into decisions on specific interventions and intervention design.

Adverse environmental and human health impacts in environmental management are heterogeneous, varying according to the intervention chosen. Because the negative environmental impacts of environmental management are location specific, only general impacts and mitigation suggestions are described in this PEA. Table 23 breaks down the potential negative impacts by specific environmental management intervention and provides suggestions for mitigation.

It is important to note that the use of environmental management can decrease the need for pesticide-based interventions, which decreases the potential for harm to human health and the environment from pesticide use.

Table 23. Environmental Management Recommendations

Environmental Management Interventions	Potential Negative Impacts	Mitigation Measures
Environmental Modification		
Filling of breeding sites	Increased or decreased habitat and forage for animal species	Prohibit intervention in sensitive habitats, forest reserves, national parks, wildlife reserves, and endangered species habitats
Lining of water sources and canals	Increased flooding	Assess the impact of increased water flow on other water resources
Impoundment construction	Altered upstream and downstream water availability	Conduct impoundment planning at the water basin level
	Increased or decreased habitat and forage for animal species	Determine water needs (maximum use level) for stakeholders and the environment; assess impacts on water sources prior to intervention, work with stakeholders for appropriate solutions
	Increased or decreased plant and animal biodiversity	Prohibit intervention in sensitive habitats, forest reserves, national parks, wildlife reserves, and endangered species habitats
	Altered ecosystem composition	Design landscape that resembles the natural ecosystem to help conserve water and soil and provide habitat for wildlife
		Integrate buffer strips into intervention design to decrease adverse effects of water runoff and soil erosion
Biological drainage	Reduced water availability	Use environmental information in activity design
	Reduced or enhanced water quality	Determine water needs (maximum use level) for stakeholders and the environment; assess impacts on water sources prior to intervention, work with stakeholders for appropriate solutions
	Increased or decreased habitat and forage for animal species	Prohibit intervention in sensitive habitats, forest reserves, national parks, wildlife reserves, and endangered species habitats
	Increased or decreased plant and animal biodiversity	Design landscape that resembles the natural ecosystem to help conserve water and soil and provide habitat for wildlife
	Altered ecosystem composition	Use native species when introducing vegetation

Environmental Management Interventions	Potential Negative Impacts	Mitigation Measures
Physical drainage	Reduced water availability	Use environmental information in activity design
	Reduced water quality	Determine water needs (maximum use level) for stakeholders and the environment; assess impacts on water sources prior to intervention, work with stakeholders for appropriate solutions
	Increased flooding	Prohibit intervention in sensitive habitats, forest reserves, national parks, wildlife reserves, and endangered species habitats
	Siltation and sedimentation of water bodies, including dams and retention ponds	Design landscape that resembles the natural ecosystem to help conserve water and soil and provide habitat for wildlife
	Change in conditions for transport and hydropower production	Integrate buffer strips into intervention design to decrease adverse effects of water runoff and soil erosion
	Decreased agricultural productivity of soil	Select alternative site
	Increased or decreased habitat and forage for animal species	
	Increased or decreased plant and animal biodiversity	
	Altered ecosystem composition	
Environmental Manipulation		
Deepening/narrowing of existing drains	No significant impacts	Not applicable
Synchronized cropping/intermittent irrigation	No significant impacts	Not applicable
Saltwater flooding	Reduced water availability	Determine water needs (maximum use level) for stakeholders and the environment; assess impacts on water sources prior to intervention, work with stakeholders for appropriate solutions
	Decreased habitat for freshwater aquatic and terrestrial species	Prohibit interventions in sensitive habitats, forest reserves, national parks, wildlife reserves, and endangered species habitats

Environmental Management Interventions	Potential Negative Impacts	Mitigation Measures
		Design landscape that resembles the natural ecosystem to help conserve water and soil and provide habitat for wildlife
Introduction of larvivorous fish	Altered ecosystem composition on a small or large scale (invasive species problems)	Use indigenous larvivorous fish whenever possible
	Increased or decreased biodiversity	Prohibit intervention in sensitive habitats, forest reserves, national parks, wildlife reserves, and endangered species habitats
		Establish a license program for the use of larvivorous fish
Manipulation of vegetation	Reduced water availability	Determine water needs (maximum use level) for stakeholders and the environment; assess impacts on water sources prior to intervention, work with stakeholders for appropriate solutions
	Reduced water quality	Prohibit intervention in sensitive habitats, forest reserves, national parks, wildlife reserves, and endangered species habitats
	Increased flooding	Use native species when introducing vegetation
	Siltation and sedimentation of water bodies, including dams and retention ponds	Design landscape that resembles the natural ecosystem to help conserve water and soil and provide habitat for wildlife
	Change in conditions for transport and hydropower production	Integrate buffer strips into intervention design to decrease adverse effects of water runoff and soil erosion
	Decreased agricultural productivity of soil	Select alternative site
	Increased or decreased habitat and forage for animal species	
	Increased or decreased plant and animal biodiversity	
	Altered ecosystem composition	

6.2 Evaluation and Adaptive Management

Evaluation is a program management tool that links monitoring data to mitigation actions. Evaluation should be used to change or improve mitigation actions taken during

an intervention, identify opportunities for improvement, and inform future decisions on interventions and their management.

A comprehensive Human Health and Environmental Evaluation Report for IRS should include the following:

- Post-spray Campaign Survey, assessing Knowledge, Attitude, and Practices (KAP) of community regarding IRS responsibilities
- Post-training evaluation of spray operators and supervisors, and storekeepers and medical practitioners when applicable
- Post-training evaluation of instructors
- Stock management records (e.g., insecticide sachet accounts)
- Mitigation monitoring reports (monitoring based on mitigation monitoring worksheet)
- Environmental impact monitoring reports
- Entomological monitoring reports
- Malaria case monitoring reports

A comprehensive Human Health and Environmental Evaluation report for larviciding should include the following:

- Post-training evaluation of applicators
- Post-training evaluation of instructors
- Stock management records
- Mitigation monitoring reports
- Environmental impact monitoring reports
- Entomological monitoring reports
- Malaria case monitoring reports

A comprehensive Human Health and Environmental Evaluation report for environmental management should include the following:

- Post-training evaluation of spray operators and supervisors, and storekeepers and medical practitioners when applicable
- Post-training evaluation of instructors
- Mitigation monitoring reports (monitoring based on mitigation monitoring worksheet)
- Environmental impact monitoring reports
- Entomological monitoring reports
- Malaria case monitoring reports

7. Regulatory, Legal, and Institutional Settings

7.1 The National Setting

The overarching regulatory framework for conducting environmental assessments for U.S. Agency for International Development- (USAID) funded projects is U.S. Code of Federal Regulations (CFR) 22 CFR 216 (see ***Annex B***); however, host-country environmental policies, laws, and regulations must also be consulted and considered in preparing Supplemental Environmental Assessments (SEAs) and Pesticide Evaluation Report and Safer Use Action Plans (PERSUAPs). Support for interventions must abide by host-country environmental regulations, as well as USAID regulations.

Long-term sustainability of any economic or social development project requires that the development interventions be well conceived and that a regulatory framework with enforcement capacity exists.

Public participation in the host country is paramount for successful, sustainable, programs. Host-country government ministries involved in malaria control, pesticide use, or other relevant issues, as well as civil society, should participate in the SEA processes from the onset. Not only do these entities possess the information needed to complete the assessment, but involving them also helps guide the selection of alternative approaches and ensures greater local ownership of the program from the start. Table 24 lists key host-country institutions that should be consulted.

Table 24. Host-Country Institutions with Malaria Control Mandates or Related Functions

Institution	Information and Data
Ministry of Health (MOH)	Documents pertaining to malaria control policies, history of control in the country Insecticides registered for use against mosquitoes, pesticide use policies, all donor programs active in the country Maps of vectors and malaria distribution, information about insecticide resistance, pesticide testing procedures, inventories of pesticides and equipment available Organization and malaria control responsibilities in the ministry Measures for treating pesticide poisoning
Ministry of Environment (MOE)	Potential institution for environmental monitoring Documents and maps pertaining to the presence of sensitive habitats, such as world heritage sites, national parks and forests, lists of endangered species and their locations, game parks, bodies of water, and other environmental resources

Institution	Information and Data
Ministry of Agriculture (MOA)	Pesticide registration Listing of agricultural development programs currently using pesticides, and information on classes of pesticides used in various agricultural activities and locations, ways to prevent public health pesticides from being used for agriculture Potential agricultural export impacts isolated to use of various pesticides
Ministry of Public Works (MPW)	May be knowledgeable about sanitation laws, regulations, guidelines, and implementation May also work with the MOH in administering routine campaigns to clean up potential malaria mosquito breeding containers or locations
Regional and local governments	Likely to be responsible for implementing some antimalaria campaign activities; information will need to be collected on how and when this is done Measures of program impact
Universities	Potential institutions for environmental monitoring Research studies and data pertaining to malaria control programs, toxicity assays, experimental approaches
Environmental nongovernmental organizations (NGOs)	Potential institutions for environmental monitoring Information and maps pertaining to the presence of sensitive habitats, such as world heritage sites, national parks and forests, lists of endangered species and their locations, game parks, bodies of water, and other environmental resources
Affected citizens	Recommendations and concerns to be taken into account in deciding upon, planning, and implementing an intervention

7.2 The International Setting

7.2.1 International Treaties

International transport and use of pesticides are governed by three major international treaties:

- The **Basel Convention** on the Control of Transboundary Movements of Hazardous Wastes and their Disposal
- The **Rotterdam Convention** on the Prior Informed Consent Procedure for Certain Hazardous Chemicals and Pesticides in International Trade
- The **Stockholm Convention** on Persistent Organic Pollutants (POPs)

The Basel Convention addresses the transboundary movement, management, and disposal of hazardous wastes, including waste pesticides. Transboundary movements of hazardous waste between Parties can take place only on prior written notification by the exporting state to importing (or transit) states, and the inclusion of movement documents with each shipment. In addition, Parties may not permit hazardous wastes to be exported to or imported from a non-Party except pursuant to an agreement or arrangement that stipulates provisions no less environmentally sound than those provided for by the Basel Convention. Finally, trade in hazardous waste cannot take place under conditions in which such wastes cannot be handled in an environmentally sound manner. Parties are obligated to consider illegal traffic in hazardous wastes as criminal and to notify other Party states upon prohibition of import of hazardous wastes for disposal. Export of waste pesticides may require specific compliance activities by the host-country government.

The Rotterdam Convention addresses the transboundary movement of 22 chemicals, including one chemical used for malaria vector control, dichloro-diphenyl-trichloroethane (DDT). Parties to the Convention must make decisions on each chemical regarding its import, abide by export limitations delineated in the treaty, and notify Parties receiving exported waste according to treaty conditions. Host-country governments are responsible for complying with any import or export treaty conditions applicable to their status as a Party or non-Party. Import or export of the 22 chemicals covered by the Rotterdam Convention, including DDT, may require specific compliance activities by the host-country government.

The Stockholm Convention addresses the production, import, and export of 12 POPs, including DDT. Currently, Parties to the Convention must take measures to eliminate releases of each chemical, with the exception of certain uses listed in the Convention (for example, the exception of DDT use for "disease vector control"). Parties to the Convention must also abide by the Convention's stockpile handling, transport, and disposal requirements intended to eliminate persistent byproducts; thus, management and export of obsolete pesticides may require specific compliance activities by the host-country government.

7.2.2 International Institutions

Several international and regional organizations fund and implement antimalaria initiatives. Coordination and collaboration is essential so as not to duplicate efforts and resources. When writing SEAs, the activities of each of these groups in the country of interest should be researched and catalogued, and recommendations for coordination should be included in the report. Table 25 provides an illustrative list of the organizations and programs that may be funding or implementing malaria control or pesticide management activities in specific countries.

Table 25. Illustrative List of Organizations and Programs

Institution	Program
WHO RBM Program	Roll Back Malaria (RBM) is a global partnership founded in 1998 by the World Health Organization (WHO), the United Nations Development Program (UNDP), the United Nations Children's Fund (UNICEF), and the World Bank with the goal of halving the world's malaria burden by 2010. The RBM program has six strategic elements, which build on the WHO global malaria control strategy: (1) effective management of malaria, including malaria outbreaks; (2) rapid diagnosis and treatment of those who are ill; (3) multiple and cost-effective means of preventing infection; (4) focused research to develop, test, and introduce new products; (5) a well-coordinated movement through stronger capacity in the health-sector and community-level effort; and 6) a dynamic global partnership supported by a coalition of partners working within a common approach.
UNEP GEF projects	The United Nations Environment Program Global Environment Facility (UNEP GEF) helps developing countries fund projects and programs that protect the global environment. The GEF's grants support projects related to biodiversity, climate change, international waters, land degradation, the ozone layer, and persistent organic pollutants (POPs)—a new focal area for GEF, as they are a threat to biodiversity and even have the potential to cause disruption at the ecosystem level.
WHOPES	The WHO Pesticide Evaluation Scheme (WHOPES), set up in 1960, is the only international program that promotes and coordinates the testing and evaluation of new pesticides proposed for public health use. It functions through the participation of representatives of governments, the pesticide industry, WHO Collaborating Centers and university associations, associate laboratories, as well as other WHO Programs, particularly the International Program on Chemical Safety (IPCS). WHOPES facilitates the search for alternative pesticides and application methodologies that are safe and cost-effective and helps develop and promote policies, strategies, and guidelines for the use of pesticides in public health, and ultimately, helps monitor their implementation by the Member States.
Global Fund for AIDS, Malaria, and Tuberculosis	The Global Fund for AIDS, Malaria and Tuberculosis, created in 2001, funds initiatives to fight AIDS, tuberculosis and malaria. Together, these diseases kill more than 6 million people each year, and the numbers are growing. As a partnership between governments, civil society, the private sector, and affected communities, the Global Fund represents an innovative approach to international health financing. The Global Fund attracts resources ($4.7 billion to date) and manages and disburses those resources to fight AIDS, tuberculosis, and malaria, but does not implement programs directly. As a financing mechanism, the Global Fund works closely with other multilateral and bilateral organizations involved in health and development issues to ensure that newly funded programs are coordinated with existing ones. The Global Fund uses its own grants to catalyze additional investments by donors as well as by recipients themselves. In its first two rounds of grant-making, it has committed US $1.5 billion in funding to support 154 programs in 93 countries worldwide.
The Food and Agriculture Organization of the United Nations (UNFAO)	Pesticide Management is an activity carried out within the overall framework of the Plant Protection Service of UNFAO. It is designed to work together with member countries as a partner to introduce sustainable and environmentally sound agricultural practices that reduce health and environmental risks associated with the use of pesticides. The environmental and health impact of pesticides is being reduced through the implementation of several concrete programs on pesticide management, including residue analysis, product standards setting and methods to analyze them, prevention of accumulation of obsolete stocks of pesticides and means to dispose them, and exchange of information on national actions taken to control pesticides.

8. Training and Institutional Capacity Building

8.1 Why Training and Capacity Building?

Training and capacity building are essential components of efforts to assist the host country in developing a sustainable malaria vector control program that ensures the protection of human health and the environment. Different types of training and capacity building are necessary, ranging from in-field training of those who apply pesticides, to local-level management capacity, to ministry decision making.

8.2 Training of Contractors (1 day)

U.S. Agency for International Development (USAID) Mission Environmental Officers (MEOs) and Mission Health Officers (MHOs) should provide short training to contractor program managers and other partners involved in USAID-supported malaria vector control interventions. This training should inform program managers of the importance and methods of integrating human health and environmental concerns into malaria vector control. It should also inform program managers of USAID's expectations for implementation of best practices for human health and the environment as detailed in the Supplemental Environmental Assessment (SEA). Finally, the training should express USAID's expectations that measures to protect human health and the environment be factored into program evaluation. Additional topics for discussion may include

- Factors to consider in intervention selection
- Factors to consider in pesticide selection
- Potential impacts of pesticides
- Best practices and mitigation measures (throughout the life cycle of the intervention or pesticide)
- Adaptive management

8.3 Guidance for Senior Officials (1–2 days)

Ministry of Health (MOH) staff have various specialties within malaria control. It is not always guaranteed that central government staff have knowledge and training on all aspects of malaria vector control, or that decision making for malaria vector control takes into account all appropriate facets.

As a way of supporting sound decision making on malaria vector control across the globe, and as part of country-specific intervention support, USAID should support training for MOH malaria control program managers and other relevant staff to orient them to the elements of well-run integrated vector management (IVM) programs, environmental design, monitoring, and mitigation, including the following:

- Factors to consider in intervention selection
- Factors to consider in pesticide selection
- Potential impacts of pesticides
- Best practices and mitigation measures (throughout the life cycle of the intervention or pesticide)
- Appropriate timing and logistics
- Adaptive management

Additionally, contractor specialists should be paired with counterparts from the MOH malaria control program to provide any on-the-job guidance necessary.

8.4 Mid-Level Management (continuous, time-intensive training as necessary)

Although health systems in the developing world have decentralized and placed responsibility for malaria program implementation on local and regional managers, the management skills necessary for these local and regional managers to perform effectively have not filtered down from central ministry. The result is a lack of capacity to manage malaria vector control programs at the local and regional level.

During the period of USAID support, contractor specialists should be paired with local and/or regional counterparts to provide on-the-job guidance, training, and practice. Contractor specialists, as necessary, should train mid-level management in

- Logistics
- Data management
- Best practices and mitigation measures
- Monitoring and evaluation (of all types mentioned in this Programmatic Environmental Assessment [PEA])
- Surveillance systems
- Adaptive management

Additionally, USAID should facilitate knowledge sharing between ministry staff and local or regional managers. Finally, USAID should promote formal training of mid-level managers as the need for such training arises.

8.5 Training of Implementers (1–3 weeks)

Every malaria vector control intervention requires staff that implement interventions in the field: spray operators, larvicide applicators, insecticide-treated net (ITN) impregnators, environmental management or sanitation workers, and intervention supervisors. Each “agent of implementation” should be trained according to the highest standards available—World Health Organization (WHO) guidelines, PEA guidelines,

United Nations Food and Agriculture Organization (UNFAO) guidelines, equipment manufacturer guidelines, pesticide industry guidelines, ministry guidelines, etc. Because some interventions are seasonal, refresher training prior to each intervention may be necessary.

Others may need training as well. When pesticides are used, storekeepers, medical practitioners, individuals transporting pesticides, and communities need to be educated on their roles and responsibilities in preventing unwanted exposure to pesticides (or treatment of pesticide exposure, in the case of medical practitioners). Essential components of this training are provided in Section 6 of this PEA, Mitigation, Monitoring, and Evaluation.

8.6 Capacity Building outside the Malaria Sector

Malaria vector control activities interact with other sectors, most importantly agriculture and environment. To the extent that a host-country institution wants to become involved in environmental monitoring of malaria vector control interventions, promote responsible pesticide use, prevent pesticide pilferage, etc., USAID-supported interventions should include measures to build the capacity of those institutions and facilitate collaboration between those institutions and the malaria control program.

9. Cross-Cutting Issues

9.1 Malaria Control and the Agricultural Sector

9.1.1 Diversion of Malaria Pesticides for Other Uses

A major problem faced by public health programs around the world is the diversion of public health pesticides to the private sector, primarily the agricultural sector but also private pest control enterprises. For multiple reasons, U.S. Agency for International Development (USAID) support for malaria vector control using pesticides must ensure that public health pesticides are not diverted from their intended use in malaria vector control. First, public health pesticides may not be registered by the host country for alternative uses, or may be explicitly banned for any use beyond disease vector control (as is usually the case with dichloro-diphenyl tricholorethane [DDT]); thus, the use of the pesticide outside the program may be illegal. Second, individuals using diverted pesticides are probably untrained in appropriate application and unaware of mitigation precautions that should be taken to avoid exposure to the individual and the community. Such use may endanger the health of the individual, the health of others in the community, and the environment. Third, such use may affect the agricultural export market for certain goods (see Impacts on Agricultural Export Markets, below). Fourth, the use of diverted pesticides may potentially increase resistance of pests or disease vectors (see Mosquito Resistance, below). Fifth, diversion of pesticides from their intended purpose increases the costs of the malaria vector control program.

9.1.2 Impacts on Agricultural Export Markets

Nations, trading groups of countries, and international institutions often define thresholds for pesticide residues present on agricultural commodities beyond which those commodities cannot be sold on the market. These thresholds are called Maximum Residue Limits (MRLs). Use of public health pesticides in the agricultural sector may increase the risk that agricultural exports exceed importing-country MRLs, reducing economic gains from agricultural exports in the host country. This is of particular concern for DDT, which persists in the environment and accumulates in animal fat. International (CODEX) MRLs are provided in ***Annex J***. European Union MRLs can be found at http://europa.eu.int/comm/food/plant/protection/pesticides. The U.S. Department of Agriculture Foreign Agricultural Service (USDA/FAS) hosts an online database containing MRLs for additional countries at http://www.mrldatabase.com/.[11]

[11] It should be noted that, according to the Health and Consumer Protection Directorate-General of the European Commission's *Guidance Document Key questions related to import requirements and the new rules on food hygiene and official food controls*, the importer is responsible for testing agricultural commodities to assure MRLs are not exceeded (2006).

The impact of public health pesticide use in communities that produce organic agricultural crops is of even greater concern than for those communities producing conventional agricultural crops. In northwestern Tanzania, for example, some farmers produce organic vanilla, which is stored inside the home and would likely be contaminated as a result of IRS operations using any insecticide (not just DDT). This contamination could adversely affect the value of the crop, reducing salability on the market and household income. In these instances, if a locally acceptable solution (e.g., storage at a co-op) cannot be identified, the program should consider supporting the use of ITNs or LLINs instead of IRS to preserve the local economy.

The potential adverse economic impacts of diversion of public health pesticides to the private sector must be addressed through monitoring and mitigation activities in the program. These impacts can also be combated by reducing agricultural demand for public health pesticides. This may be achieved through coordination with the Ministry of Agriculture (MOA), commercial producers, export associations, pesticide manufacturers, and nongovernmental organizations (NGOs) to educate agricultural producers.

9.1.3 Mosquito Resistance

Mosquitoes develop resistance to pesticides by evolving enzyme systems that break down or detoxify pesticides. Currently, three enzyme systems are known to confer resistance. Larvae and adult mosquitoes have developed different systems for resistance, so larval and adult resistance must be analyzed and addressed separately. Furthermore, if different classes of pesticides affect the same enzyme system, as is the case with chlorinated hydrocarbons (such as DDT) and synthetic pyrethroids, there is a high probability that resistance to pyrethroids will develop where there is or was known resistance to DDT. This is called cross-resistance.

Vector resistance is a major threat to effective prevention of malaria. The number of available and effective pesticides for malaria vector control is decreasing. Currently, only the pyrethroid class of insecticides is appropriate for insecticide-treated net (ITN) impregnation and long-lasting insecticidal nets (LLINs). Only four classes of insecticides are recommended by the World Health Organization (WHO) for indoor residual spraying (IRS): organochlorines, pyrethroids, carbamates, and organophosphates. It is vital to manage pesticide programs using methods that reduce the probability of resistance, including temporal rotation of pesticide classes or developing a spatial mosaic to juxtapose use of different pesticide classes for malaria vector control. For larval control, there is only one currently recommended organophosphate, temephos, which could be used in a rotation or spatial mosaic with other larvicidal agents.

In areas where large quantities of pesticides are used for agricultural crops, especially monocultures such as cotton, rice, and soybeans, resistance of mosquitoes may develop much faster than in areas that do not use large quantities of agricultural pesticides. Resistance testing should be conducted in areas targeted for malaria vector control to help develop strategies tailored to the area. USAID support for malaria vector control should

include capacity building for managing resistance and promoting coordination among MOAs and Ministries of Health (MOHs) to reduce vector or pest resistance prompted by agricultural or public health use of pesticides.

9.2 Malaria Control and Hazardous Waste Management

9.2.1 Waste Contaminated with Pesticides

Safe disposal of pesticide-contaminated waste products is a key need for any malaria control program that uses pesticides. When it is not feasible to triple-rinse pesticide-contaminated waste and dispose it within the country, as is the case with plastic insecticide sachets, the program should either arrange for export of the waste to the pesticide manufacturer or to an internationally recognized incineration facility. Both methods of disposal will require bilateral agreements between the waste exporting and importing countries to comply with the Basel Convention and regional conventions (e.g., the Bamako Convention). The Basel Convention in particular sets out a prescribed process for the notification of waste import with import, export, and transit countries being officially informed. In addition, the Stockholm Convention with Basel sets out detailed guidance on the processes through which persistent organic pollutants (POPs) waste must be destroyed. There is currently no facility in Africa that is able to treat or destroy pesticides or pesticide-contaminated material in keeping with accepted international standards and norms (FAO, 2006).

The issue of pesticide-contaminated waste is particularly important in IRS, where some insecticides must be applied in high doses (1–2 g/m^2) to be efficacious. In these instances, the volume of insecticide required is too great to use water-soluble sachet material, so the insecticide is packaged in plastic. Once the insecticide is emptied into the sprayer, these sachets become hazardous waste. In Zambia, only three years of indoor spraying with DDT produced several tons of such waste. During the course of planning and implementation of malaria vector control operations, USAID staff or contractors may observe the presence of this waste. In this case, any USAID staff or contractors conducting supplemental environmental assessments (SEAs), needs assessments, or other planning or implementation operations are obligated to follow the protocol described in Section 9.2.3.

9.2.2 Prevention of Obsolete Pesticide Stocks

In an effort to prevent an increase in obsolete pesticide stocks in the host country, USAID programs for malaria vector control must ensure that

- Pesticide formulation is procured only in quantities that are anticipated to be used within one year *or* within the duration of USAID support for the malaria vector control activity, whichever period is shorter
- Pesticide formulation is procured at such a time that it arrives and can be transported to local storehouses *before* the pesticide application start date

- National malaria program procurement officers are aware of the importance of conducting the above activities to prevent obsolete pesticide stock accumulation
- Public health pesticide storehouse managers at the national, regional, or local level are trained to manage pesticide stocks according to the United Nations Food and Agriculture Organization's (UNFAO) *Pesticide Storage and Stock Control Manual*, unless storehouse managers already manage storage facilities according to these standards.

9.2.3 Obsolete Pesticides—Obligations of USAID and Protocol

Obsolete pesticides are a significant problem in many developing countries. During the course of planning and implementation of malaria vector control operations, USAID staff or contractors may observe the presence of potentially obsolete pesticide stocks. Any USAID staff or contractors conducting SEAs, needs assessments, or other planning or implementation operations are obligated to take the actions detailed below when potentially obsolete stocks are identified during field visits.

First, determine who is responsible for providing the pesticides. If a non–U.S.-government party is responsible for providing the pesticides, the USAID Mission must contact the responsible party and request appropriate action. If the U.S. government is responsible for providing the pesticides, or the responsible party cannot be identified, the pesticides should be analyzed by the manufacturer or an independent laboratory to determine whether the pesticides are still usable. If the pesticides are effective and usable, the pesticide should (if necessary) be repackaged for re-use and applied appropriately (for either public health or agricultural use) under the supervision of the host-country Ministry of Environment (MOE), MOA, MOH, USAID, or an appropriate entity selected through consultation with host-country and USAID stakeholders. Any repackaging and supervision costs must be covered under the budget for the malaria vector control project through which the pesticides were initially identified.

If the pesticides are obsolete and unusable, then cleanup, transport, and disposal of the pesticides should be conducted during the period of USAID support for the malaria vector control project at an appropriate facility (probably outside the host country). Discussions with the MOE, MOA, UNFAO, and pesticide manufacturer should guide the steps taken to dispose of obsolete stocks. The costs of the cleanup, transport, and disposal must be covered under the budget for the malaria vector control project through which the obsolete pesticides were initially identified. Export of obsolete pesticides for disposal may require the host-country government to comply with provisions outlined in the Basel, Rotterdam, and/or Stockholm Conventions. See Section 7.2.1, International Treaties, for general information on these conventions, which govern intercountry transport of hazardous waste, including obsolete pesticides.

10. Public Consultation Process

The public consultation process for this programmatic environmental assessment (PEA) was conducted in several phases:

- On May 4, 2004, a public hearing was held in Washington, DC, on the Scoping Statement
- An electronic comments session on the draft PEA took place from July through September 2005. The e-mail requesting comments was broadcast to U.S. Agency for International Development (USAID) officers, nongovernmental organizations (NGOs), private sector interests, international organizations, and health and agriculture researchers throughout the world
- Public comment on the PEA (and corresponding annexes) took place from March 15 to April 14, 2006; this review included host-country counterparts and stakeholders
- A final public comment meeting was held in Washington, DC, on March 29, 2006
- A comment meeting was held with the U.S. Environmental Protection Agency (EPA) and Department of State Office of Environmental Policy in Washington, DC, on July 6, 2006

The PEA team paid particular attention to ensure views and comments were obtained from a broad representation of counterparts and other key stakeholders. Comments from each session were carefully considered and included in the final PEA.

Table 26 presents key issues raised at each phase of the public consultation process. The full text of the Scoping Statement can be found in Annex A; the public comments received from March 15 to April 14, 2006, are included in Annex L.

Table 26. Summary of Public Consultation Issues

Consultation Event	Key Issues/Comments
Public Meeting on Scoping Statement	The intent is that this programmatic environmental assessment (PEA) will serve as an umbrella evaluation of environmental and human health issues related to integrated vector management (IVM) implementation. The PEA will provide an administrative framework to facilitate and expedite matters. This framework will be capable of being updated and/or modified. The PEA will meet the need for environmental soundness because the Supplemental Environmental Assessments (SEAs) to be carried out under this umbrella will spell out specific in-country training needs, vector control method efficacy to date and any disposal problems, as well as the in-country resources already in use and planned. For pesticide information, USAID will look to EPA for World Health Organization (WHO)–approved chemicals to be listed in the PEA along with information on EPA registration, use, import/transport, precautions, label information, monitoring, and health issues relative to handling and packaging. The PEA will provide USAID with the rationale to be used to demonstrate results, to gain ongoing funding, to do the job right, and to maximize impacts of its IVM programs in order to ensure funding. The PEA will provide information relative to local problems and solutions with respect to packaging, transportation, and unloading techniques; strength of containers; use of proper formulations; and use of products that can actually be applied and purchased. The PEA will encapsulate best practices and will provide examples of new combinations and solutions that can be used in the SEAs. It will also detail how in-country baseline data can be developed, especially the use of key indicators in the use of adaptive management monitoring components. The PEA will encourage an IVM approach that includes quality of life issues and improves the long-term health of people and the environment. The PEA will encourage SEAs to include target areas and priority sites as well as the kind of training needed in-country. The PEA will need to address cost-benefit implications of what Missions can do to operationalize things. Regarding dichloro-diphenyl-trichloroethane (DDT), there will be a statement up front addressing current evidence, effectiveness, and proper use.

Consultation Event	Key Issues/Comments
Electronic Comments Session July-Sept 2005	IVM has now been explained in the new WHO strategy, and the scope of the PEA is not congruent with the IVM definition and the scope set out in the WHO strategy. IVM is an all-inclusive (chemical and nonchemical vector control measures, community programs, and personal protection) approach that gives guidance in terms of management in specific settings. The basis has to be a sound management team backed up by solid evidence that stays in place permanently. A hierarchical sequencing of vector control interventions is not the best approach, as it predetermines consideration. True to the IVM concept, the interventions selected should be determined by the local conditions of transmission as well as feasibility of implementation, in terms of cost-effectiveness and sustainability. With respect to the use of chemicals, the debate mainly seems to revolve around choosing between indoor residual spraying (IRS) and insecticide-treated nets (ITNs), both of which have been shown to be effective. There needs to be a comparison of interventions according to their costs and cost-effectiveness. Among vector control options, there may be a possibility of shipping DDT from countries that still have useable stockpiles and are looking for ways of disposing of them. To actually have the DDT disposed of in a safe way is costly and cumbersome, and as was agreed at the meeting that set up the WHO DDT action plan, the best way is to use the DDT for what it was originally intended for: IRS. It might be worthwhile to check on the availability of DDT stockpiles, which would only incur initial quality control and transport costs. Use of these stockpiles would be seen as a positive contribution to the DDT issue. It is important to know what levels of exposure are associated with various magnitudes and types of risks, the actual levels of exposure associated with various malaria control practices, and how such potential effects compare with the benefits to be derived from malaria control.
Electronic Session to Review Final Draft	The PEA lacks discussion on important strategic issues such as resource allocation between rural versus urban malaria control and treatment services. The PEA needs to discuss the intense support needed for IRS. The PEA needs to describe the relationship between IRS and ITNs (that it is not an “either/or” decision). The PEA should have more specific information on insecticide resistance.
Summary of Final Review Meeting in Washington, DC	No members of the public attended this meeting.

Consultation Event	Key Issues/Comments
Summary of EPA/Department of State Meeting in Washington, DC	EPA and Department of State will update the PEA in track change to make it more current with the DDT obligations in the Stockholm Convention and will include the recommendation that USAID assist Parties with activities pertaining to Stockholm reporting obligations if DDT is used for IRS in the host country. The reporting obligations (Annex III to decision SC-1/25) should be attached as an annex to the PEA. The Department of State will provide updated language on the Basel Convention. Based on suggestions from EPA, USAID will develop decision criteria for pesticide selection in USAID projects for possible inclusion in the PEA. EPA will provide USAID with a final table based on the 12 WHO pesticides and provide information if the pesticides are registered for the same or similar use patterns in the USA. EPA will work with USAID to develop text for the PEA on how the screening tool should be used. EPA will provide support to USAID on country-level SEAs tiering off from the PEA upon request. USAID will look at its timeline for the PEA and give EPA and State a revised deadline for comments on the PEA.

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http://www.chem.unep.ch/pops/pdf/redelipops/redelipops.pdf (reduce and eliminate POPs)

www.pesticideinfo.org

http://www.ehproject.org

www.who.int/pcs/docs/pcs98-21rev1.pdf

www.who.int/pcs

www.epa.gov/pesticides

www.pic.int

Annex A: Scoping Statement

Note

This *Scoping Statement* is a stand-alone document that has also been included as an Annex to *Management Programs for Malaria Vector Control: Programmatic Environmental Assessment* (the PEA). As a result, it refers to the PEA as a separate document, even though it is here an Annex to the PEA.

The following annotated outline constitutes a "scoping statement" describing the anticipated content of a Programmatic Environmental Assessment that USAID, Bureau for Global Health, Division for Infectious Diseases and Nutrition, Environmental Health Project II plans to conduct in order to evaluate the potential environmental and human health effects of using insecticides, insecticide-treated materials, water management strategies, and mosquito larvae-eating fish in USAID projects to control mosquitoes that transmit malaria. The intent of this scoping statement is to afford an early opportunity to analytical partners and other interested parties to provide input regarding the analytical framework, issues included, and information sources that USAID plans to use in performing this environmental assessment.

Introduction

USAID is developing a Programmatic Environmental Assessment (PEA) for Integrated Vector Management (IVM) programs primarily to assist with the preparation of country- and activity-specific Supplemental Environmental Assessments (SEAs) and pesticide evaluation reports and safer use action plans (PERSUAPs) for malaria control projects employing IVM strategies. The use of an IVM approach generally decreases the amount of pesticides required and used, thus protecting environmental resources and human health. The intent is that this PEA will serve as an umbrella evaluation of environmental and human health issues related to IVM implementation. The PEA will provide project managers with a technical, policy, and procedural guide for the preparation of environmental assessments of individual projects. Together, the PEA and project assessments are intended to provide a clear basis for deciding, for each project, whether USAID can promote the use of IVM components, and if so, how that should be done so as to comply with the letter and the spirit of the Agency's environmental regulations.

Scope and significance of key issues

Scope and significance of key issues to be analyzed in detail in this assessment, and additional issues to be analyzed in country-specific assessments, such as SEAs and PERSUAPs, that follow from this PEA are listed below.

Risks to humans from use of no IVM actions

- Mortality
- Morbidity
- Social disruption
- Impact of economic losses
- Shift in focus away from prevention to reaction
- Human risks, in sum
- Uncertainties

- Mitigation opportunities

Potential risks to humans from use of IVM pesticides

- Overall issues
  - Relatively small quantities of pesticides used with IVM
  - Chemical group and formulations available
  - Human risks, in sum
  - Uncertainties
  - Mitigation opportunities
  - Toxicity of IVM chemicals to humans, acute and chronic
  - Potential human exposure (oral, dermal, and inhalation)
  - Externalities associated with pesticide use and exposure
  - Regulatory and legal issues related to pesticides and health
  - Enforcement issues related to pesticides and health
- Logistical issues
  - Choice, selection, and availability of least-toxic pesticide
  - Labeling toxicity categories by hazard indicator
  - Quality of pesticide and pesticide supplier
  - Proper pesticide labels and training materials in local languages
  - Pesticide distribution from labeled containers to unlabelled containers
  - Pesticide pilferage for unauthorized use or sale
  - Improper pesticide storage
  - Improper pesticide container transport
  - Improper pesticide handling, formulation and use
  - Prohibited empty pesticide container re-use
  - Proper disposal of empty pesticide containers
  - Proper disposal of leftover unusable pesticides
  - Proper use of safety equipment
- Training issues
  - Training on proper use of safety equipment
  - Training on proper calibration of sprayers
  - Presence of pesticide antidotes
  - Proper first aid for pesticide overexposure
  - Use of botanical compounds for mosquito treatment
- New technology issues
  - Use of bacteriological agents for mosquito management

  - Use of mosquito repellents
  - Use of mosquito traps containing pesticides
  - Use of experimental vaccines
- Procedural issue
  - Co-mingling of USAID resources with Ministry of Health/other donor pesticides

Potential environmental risks from use of IVM pesticides, introduction of exotic fish, and water management strategies

- Overall issues
  - Toxicity of pesticides to nontarget organisms (other than mosquitoes), acute and chronic
  - Invasive species issues with introduction of non-native fish
  - Environmental consequences issues of environmental modification of waterways
  - Environmental risks, in sum
  - Uncertainties
  - Mitigation opportunities
- Specific issues
  - Toxicity to economically important insects like crop pollinators
  - Ecosystem disruption through water management strategies
  - Ecosystem disruption through fish introduction
  - Potential soil exposure to pesticides
  - Potential surface and ground water exposure to pesticides
  - Potential protected area and forest resource exposure to pesticides
  - Reduction in biodiversity related to pesticide exposure
  - Potential fisheries losses related to pesticide exposure
  - Potential bird losses related to pesticide exposure
  - Pesticide drift from spraying
  - Pesticide bioaccumulation (especially related to DDT)
  - Pesticide wash entering waterways and water resources
  - Disruption of natural predator and pathogen mosquito controls
  - Mosquito resistance to insecticides
  - Resurgence of mosquito populations after predator poisoning
  - Environmental externalities related to pesticide exposure
- New technology issues
  - Environmental effects of mosquito traps and repellents

  - Environmental effects of mosquito pheromones

Alternatives to recommended IVM options for malaria control—a comparison of environmental and health risks and human benefits

- Overall issue
  - Chemical control methods available other than those recommended in this PEA, and risks associated with each
- Specific issues
  - Single tactic approach with use of chemical control methods
  - Single tactic approach without use of chemical control methods (e.g., ITN use alone)
  - Efficacy of alternatives in comparison with IVM recommendations
  - No action
  - Cost comparison of alternative malaria control approaches
- Risk mitigation
  - What mechanisms are available for reducing adverse effects from IVM pesticide and non-pesticide methods?
  - How effective are they?
  - How reliable?

Decision making: What criteria should USAID use to decide on whether, when and how to use various IVM options?

- Utilization of WHO guidelines and recommended pesticides. Comparison of WHO guidelines with USEPA regulations.
- Selection of appropriate pesticides and application methods for use in IVM programs. What criteria to use? Risks, costs, efficacy? At discretion of program manager?
- Availability of effective mitigation? Is this important, or are the benefits overwhelming in all cases?
- How adequate are local pesticide regulations, infrastructure, and the institutional settings?
- Monitoring: how much is required? For how long?
- What is a "significant" effect? How to compare risks with benefits?
- What would happen in the absence of USAID support for IVM options?
- What are the local MOH and larger international (WHO) contexts and frameworks in which programs will operate?

Monitoring mechanisms

- For adverse effects from ITN use and treatment

- What mechanisms are available?
- How effective are they?
- How reliable?

Components of a PERSUAP

- What information, analysis, and mitigation measures are needed for a project using IVM options?

Identification and elimination from <u>detailed</u> study of issues expected NOT to be significant, or outside of the scope of this assessment

- ITNs that require re-treatment with pesticides have already been covered in detail in an earlier environmental review (ITM PEA) and will not be repeated in such detail, except where long-lasting nets are involved
- Mosquito control pesticide options reviewed and approved by WHO, but not covered in this PEA. Why were certain pesticides chosen for recommendation in the PEA, and others not?
- Future scientific findings regarding pesticide safety. For example, pyrethroid insecticides, which comprise the majority of those recommended for mosquito control, may cause human endocrine disruption. This is a poorly understood issue, and in the face of little scientific consensus, how much attention should be given to such open scientific questions? What type of monitoring is required, and can this function be adequately covered by WHOPES and/or EPA?
- Community small-scale water management (elimination of mosquito breeding sites) enforcement through use of fines, and/or incentives

Schedule of the assessment

- **Timing for preparation of the analysis*:*** Global Health is targeting the first half of calendar year 2004 for completion.
- **Technical planning and review**: A technical planning meeting and review for the PEA will be held during the last week of January 2004.
- **Public consultation*:*** Selected U.S. government agencies and United Nations agencies will be asked to review the draft PEA during April or May of 2004.
- **Decision-making schedule*:*** The draft PEA will be distributed for a brief review period, most likely in late May or early April. Global Health expects to be able to finalize the assessment shortly after that review is complete.
- **Mechanism for periodic update of the assessment*:*** A schedule and mechanism for periodic update of the PEA will occur every 2 weeks during the drafting of the PEA.

Methodology of the assessment

How will the analysis be conducted and which disciplines will be involved?

This analysis will rely on an abundance of reliable information already available in journals and in publications by environmental and public health organizations, such as WHO and EPA, about the potential environmental issues raised by water management and fish introduction strategies and IVM pesticide options. Analyses will be conducted by entomologists with environmental assessment and pesticide specialization, public health officers, and general environmental specialists. It is not expected that additional research will need to be conducted.

Information sources

A variety of published reports and analyses will be used, but a few documents listed below will be particularly valuable references. Global Health will strive to avoid reinventing the wheel, and expects to rely heavily on the analyses resident in these documents, some of which have a scope similar to that taken on by this PEA.

Primary references

World Wildlife Fund. 1999. "Hazards and Exposures Associated with DDT and Synthetic Pyrethroids used for Vector Control" January report. (See: http://wwwwwforg/toxics/progareas/pop/ddthtm)

Hirsch, B., C. Gallegos, W. Knausenberger, and A. Arata 2002 "Programmatic Environmental Assessment for Insecticide-treated Materials in USAID Activities in Sub-Saharan Africa" USAID Africa Bureau Document. 76 pages. (See: http://www.netmarkafricaorg/keyissues/environmental/itm-peadoc)

Walker, K. 2000. "Cost-comparison of DDT and alternative insecticides for malaria control." Medical and Veterinary Entomology 14: 345-354

Walker, K.R., M.D. Ricciardone, and .J Jensen. 2003. Developing an international consensus on DDT: a balance of environmental protection and disease control. Int J Hyg Environ Health 206: 1-13

Primary Web sites

http://www.chemfinder.camsoft.com

http://www.pesticideinfo.org (PAN pesticides database)

http://www.who.int/ctd/whopes/specifications.htm (WHOPES evaluated pesticides)

http://www.epa.gov/opppmsd1/RestProd/rupjun02.htm (EPA restricted use pesticides)

http://www.encapafrica.org/sectors/pestmgmt.htm (PERSUAPs guidance)

http://www.epa.gov/pesticides/biopesticides/ai/all_ais.htm (EPA regulated biopesticides)

http://www.who.int/mediacentre/factsheets/en/

http://w3.whosea.org/malaria/hist.htm

http://www.epa.gov/pesticides/health/tox_categories.htm

http://www.who.int/entity/en/ (who site map)

http://www.who.int/ctd/whopes/ (WHOPES home site)

http://www.unep-wcm.org/protected_areas/ (Agroecological zones)

http://www.mara.org.za/ (Mapping malaria risk in Africa)

http://skonops.imbb.forth.gr/AnoBase/ (Anopheles database)

http://www.who.int/tdr/ (Malaria research and training)

http://www.malaria.org.za/ (Malaria in southern Africa)

http://www.rbm.who.int/ (Roll Back Malaria home site)

http://www.iwmi.cgiar.org/textonly/health/malaria/ (water management techniques)

http://www.paho.org/english/hcp/hct/mal/malaria.htm (PAHO malaria site)

http://www.iwmi.cgiar.org/sima/index.asp (CGIAR systemwide initiative on malaria, ag)

http://www.malaria.org/pressreleases.html (malaria foundation international)

http://www.chem.unep.ch/pops/ivm/ (Partnership for IVM in Africa)

http://www.unep.org/gef/content/index.htm (UNEP/GEF page)

http://www.theglobalfund.org/en/ (Global Fund to Fight AIDS, TB and Malaria)

http://www.pops.int/ (POPs Web site)

http://www.pops.int/documents/convtext/convtext_en.pdf (POPs Convention text)

http://www.chem.unep.ch/pops/pdf/redelipops/redelipops.pdf (reduce & eliminate POPs)

http://www.whoint/ctd/whopes/specifications.htm

http://www.usaid.gov/pop_health/

http://www.ehproject.org

http://www.epa.gov/pesticides/biopesticides/ai/all_ais.htm

http://www.who.int/pcs/docs/pcs98-21rev1.pdf

http://www.who.int/pcs

http://www.epa.gov/pesticides

http://www.pic.int

Annex: Required contents of the scoping statement [From CFR 22, §216.3 (a)(4)] Scope of Environmental Assessment or Impact Statement

(i) Procedure and Content After a Positive Threshold Decision has been made, or a determination is made under the pesticide procedures set forth in 216.3(b) that an Environmental Assessment or Environmental Impact Statement is required, the originator of the action shall commence the process of identifying the significant issues relating to the proposed action and of determining the scope of the issues to be addressed in the Environmental Assessment or Environmental Impact Statement The originator of an action within the classes of actions described in 216.2(d) shall commence this scoping process as soon as practicable Persons having expertise relevant to the environmental aspects of the proposed action shall also participate in this scoping process (Participants may include but are not limited to representatives of host governments, public and private institutions, the AID Mission staff and contractors) **This process shall result in a written statement which shall include the following matters**:

(a) A determination of the scope and significance of issues to be analyzed in the Environmental Assessment or Impact Statement, including direct and indirect effects of the project on the environment

(b) Identification and elimination from detailed study of the issues that are not significant or have been covered by earlier environmental review, or approved design considerations, narrowing the discussion of these issues to a brief presentation of why they will not have a significant effect on the environment

(c) A description of

(1) The timing of the preparation of environmental analyses, including phasing if appropriate,

(2) Variations required in the format of the Environmental Assessment, and

(3) The tentative planning and decision-making schedule; and

(d) A description of how the analysis will be conducted and the disciplines that will participate in the analysis

(ii) These written statements shall be reviewed and approved by the Bureau Environmental Officer

(iii) Circulation of Scoping Statement

To assist in the preparation of an Assessment, the Bureau Environmental Officer may circulate copies of the written statement, together with a request for written comments, within thirty days, to selected federal agencies if that Officer believes comments by such federal agencies will be useful in the preparation of an

Environmental Assessment Comments received from reviewing federal agencies will be considered in the of the Environmental Assessment and in the formulation of the design and implementation of the project, and will, together with the scoping statement, be included in the project file.

Annex B: USAID Environmental Procedures[12] (22 CFR 216)

Text of Title 22, Code of Federal Regulations, Part 216

These procedures have been revised based on experience with previous ones agreed to in settlement of a law suit brought against the Agency in 1975. The Procedures are Federal Regulations and therefore, it is imperative that they be followed in the development of Agency programs.

In preparing these Regulations, some interpretations and definitions have been drawn from Executive Order No. 12114 of 4 January 1979, on the application of the National Environmental Policy Act (NEPA) to extraterritorial situations. Some elements of the revised regulations on NEPA issued by the President's Council on Environmental Quality have also been adopted. Examples are: The definition of significant impact, the concept of scoping of issues to be examined in a formal analysis, and the elimination of certain USAID activities from the requirement for environmental review.

In addition, these procedures: 1) provide advance notice that certain types of projects will automatically require detailed environmental analysis thus eliminating one step in the former process and permitting early planning for this activity; 2) permit the use of specially prepared project design considerations or guidance to be substituted for environmental analysis in selected situations; 3) advocate the use of indigenous specialists to examine pre-defined issues during the project design stage; 4) clarify the role of the Bureau's Environmental Officer in the review and approval process, and 5) permit in certain circumstances, projects to go forward prior to completion of environmental analysis. Note that only minimal clarification changes have been made in those sections dealing with the evaluation and selection of pesticides to be supported by USAID in projects or of a non-project assistance activity.

Sec. Topic

[12] Title 22 of the Code of Federal Regulations, Part 216, with preamble, is presented here in its entirety. Spelling errors have been corrected from the original to facilitate word searching. This version represents the most recent revisions, as of October 9, 1980.

Authority: 42 U.S.C. 4332; 22 U.S.C. 2381.

Source: 41 FR 26913, June 30, 1976, unless otherwise noted.

§216.1 INTRODUCTION

(a) Purpose

In accordance with sections 118(b) and 621 of the Foreign Assistance Act of 1961, as amended, (the FAA) the following general procedures shall be used by A.I.D. to ensure that environmental factors and values are integrated into the A.I.D. decision-making process. These procedures also assign responsibility within the Agency for assessing the environmental effects of A.I.D.'s actions. These procedures are consistent with Executive Order 12114, issued January 4, 1979, entitled Environmental Effects Abroad of Major Federal Actions, and the purposes of the National Environmental Policy Act of 1970, as amended (42 U.S.C. 4371 et seq.) (NEPA). They are intended to implement the requirements of NEPA as they affect the A.I.D. program.

(b) Environmental Policy

In the conduct of its mandate to help upgrade the quality of life of the poor in developing countries, A.I.D. conducts a broad range of activities. These activities address such basic problems as hunger, malnutrition, overpopulation, disease, disaster, deterioration of the environment and the natural resource base, illiteracy as well as the lack of adequate housing and transportation. Pursuant to the FAA, A.I.D. provides development assistance in the form of technical advisory services, research, training, construction and commodity support. In addition, A.I.D. conducts programs under the Agricultural Trade Development and Assistance Act of 1954 (Pub. L. 480) that are designed to combat hunger, malnutrition and to facilitate economic development. Assistance programs are carried out under the foreign policy guidance of the Secretary of State and in cooperation with the governments of sovereign states. Within this framework, it is A.I.D. policy to:

(1) Ensure that the environmental consequences of A.I.D.-financed activities are identified and considered by A.I.D. and the host country prior to a final decision to proceed and that appropriate environmental safeguards are adopted;

(2) Assist developing countries to strengthen their capabilities to appreciate and effectively evaluate the potential environmental effects of proposed development strategies and projects, and to select, implement and manage effective environmental programs;

(3) Identify impacts resulting from A.I.D.'s actions upon the environment, including those aspects of the biosphere which are the common and cultural heritage of all mankind; and

(4) Define environmental limiting factors that constrain development and identify and carry out activities that assist in restoring the renewable resource base on which sustained development depends.

(c) Definitions

(1) CEQ Regulations. Regulations promulgated by the President's Council on Environmental Quality (CEQ) (Federal Register, Volume 43, Number 230, November 29, 1978) under the authority of NEPA and Executive Order 11514, entitled Protection and Enhancement of Environmental Quality (March 5, 1970) as amended by Executive Order 11991 (May 24, 1977).

(2) Initial Environmental Examination. An Initial Environmental Examination is the first review of the reasonably foreseeable effects of a proposed action on the environment. Its function is to provide a brief statement of the factual basis for a Threshold Decision as to whether an Environmental Assessment or an Environmental Impact Statement will be required.

(3) Threshold Decision. A formal Agency decision which determines, based on an Initial Environmental Examination, whether a proposed Agency action is a major action significantly affecting the environment.

(4) Environmental Assessment. A detailed study of the reasonably foreseeable significant effects, both beneficial and adverse, of a proposed action on the environment of a foreign country or countries.

(5) Environmental Impact Statement. A detailed study of the reasonably foreseeable environmental impacts, both positive and negative, of a proposed A.I.D. action and its reasonable alternatives on the United States, the global environment or areas outside the jurisdiction of any nation as described in §216.7 of these procedures. It is a specific document having a definite format and content, as provided in NEPA and the CEQ Regulations. The required form and content of an Environmental Impact Statement is further described in §216.7 infra

(6) Project Identification Document (PID). An internal A.I.D. document which initially identifies and describes a proposed project.

(7) Program Assistance Initial Proposal (PAIP). An internal A.I.D. document used to initiate and identify proposed non-project assistance, including commodity import programs. It is analogous to the PID.

(8) Project Paper (PP). An internal A.I.D. document which provides a definitive description and appraisal of the project and particularly the plan or implementation.

(9) Program Assistance Approval Document (PAAD). An internal A.I.D. document approving non-project assistance. It is analogous to the PP.

(10) Environment. The term environment, as used in these procedures with respect to effects occurring outside the United States, means the natural and physical environment. With respect to effects occurring within the United States see §216.7(b).

(11) Significant Effect. With respect to effects on the environment outside the United States, a proposed action has a significant effect on the environment if it does significant harm to the environment.

(12) Minor Donor. For purposes of these procedures, A.I.D. is a minor donor to a multidonor project when A.I.D. does not control the planning or design of the multidonor project and either (i) A.I.D.'s total contribution to the project is both less than $1,000,000 and less than 25 percent of the estimated project cost, or (ii) A.I.D.'s total contribution is more than $1,000,000 but less than 25 percent of the estimated project cost and the environmental procedures of the donor in control of the planning of design of the project are followed, but only if the A.I.D. Environmental Coordinator determines that such procedures are adequate.

[45 FR 70244, Oct. 23, 1980]

§216.2 APPLICABILITY OF PROCEDURES

(a) Scope

Except as provided in §216.2(b), these procedures apply to all new projects, programs or activities authorized or approved by A.I.D. and to substantive amendments or extensions of ongoing projects, programs, or activities.

(b) Exemptions

(1) Projects, programs or activities involving the following are exempt from these procedures:

(i) International disaster assistance;

(ii) Other emergency circumstances; and

(iii) Circumstances involving exceptional foreign policy sensitivities.

(2) A formal written determination, including a statement of the justification therefore, is required for each project, program or activity for which an exemption is made under paragraphs (b)(l) (ii) and (iii) of this section, but is not required for projects, programs or activities under paragraph (b)(l)(i) of this section. The determination shall be made either by the Assistant Administrator having responsibility for the program, project or activity, or by the Administrator, where authority to approve financing has been reserved by the Administrator. The determination shall be made after consultation with CEQ regarding the environmental consequences of the proposed program, project or activity.

(c) Categorical Exclusions

(1) The following criteria have been applied in determining the classes of actions included in §216.2(c)(2) for which and Initial Environmental Examination, Environmental Assessment and Environmental Impact Statement generally are not required:

(i) The action does not have an effect on the natural or physical environment;

(ii) A.I.D. does not have knowledge of or control over, and the objective of A.I.D. in furnishing assistance does not require, either prior to approval of financing or prior to implementation of specific activities, knowledge of or control over, the details of the specific activities that have an effect on the physical and natural environment for which financing is provided by A.I.D.;

(iii) Research activities which may have an affect on the physical and natural environment but will not have a significant effect as a result of limited scope, carefully controlled nature and effective monitoring

(2) The following classes of actions are not subject to the procedures set forth in §216.3, except to the extent provided herein:

(i) Education, technical assistance, or training programs except to the extent such programs include activities directly affecting the environment (such as construction of facilities, etc.);

(ii) Controlled experimentation exclusively for the purpose of research and field evaluation which are confined to small areas and carefully monitored;

(iii) Analyses, studies, academic or research workshops and meetings;

(iv) Projects in which A.I.D. is a minor donor to a multidonor project and there is no potential significant effects upon the environment of the

United States, areas outside any nation's jurisdiction or endangered or threatened species or their critical habitat;

(v) Document and information transfers;

(vi) Contributions to international, regional or national organizations by the United States which are not for the purpose of carrying out a specifically identifiable project or projects;

(vii) Institution building grants to research and educational institutions in the United States such as those provided for under section 122(d) and Title XII of Chapter 2 of Part I of the FAA (22 USCA §§2151 p. (b) 2220a. (1979));

(viii) Programs involving nutrition, health care or population and family planning services except to the extent designed to include activities directly affecting the environment (such as construction of facilities, water supply systems, waste water treatment, etc.)

(ix) Assistance provided under a Commodity Import Program when, prior to approval, A.I.D. does not have knowledge of the specific commodities to be financed and when the objective in furnishing such assistance requires neither knowledge, at the time the assistance is authorized, nor control, during implementation, of the commodities or their use in the host country.

(x) Support for intermediate credit institutions when the objective is to assist in the capitalization of the institution or part thereof and when such support does not involve reservation of the right to review and approve individual loans made by the institution;

(xi) Programs of maternal or child feeding conducted under Title II of Pub. L. 480;

(xii) Food for development programs conducted by food recipient countries under Title III of Pub. L. 480, when achieving A.I.D.'s objectives in such programs does not require knowledge of or control over the details of the specific activities conducted by the foreign country under such program;

(xiii) Matching, general support and institutional support grants provided to private voluntary organizations (PVOs) to assist in financing programs where A.I.D.'s objective in providing such financing does not require knowledge of or control over the details of the specific activities conducted by the PVO;

(xiv) Studies, projects or programs intended to develop the capability of recipient countries to engage in development planning, except to the

extent designed to result in activities directly affecting the environment (such as construction of facilities, etc.); and

(xv) Activities which involve the application of design criteria or standards developed and approved by A.I.D.

(3) The originator of a project. program or activity shall determine the extent to which it is within the classes of actions described in paragraph (c)(2) of this section. This determination shall be made in writing and be submitted with the PID, PAIP or comparable document. This determination, which must include a brief statement supporting application of the exclusion shall be reviewed by the Bureau Environmental Officer in the same manner as a Threshold Decision under §216.3(a)(2) of these procedures.

Notwithstanding paragraph (c)(2) of this section, the procedures set forth in §216.3 shall apply to any project, program or activity included in the classes of actions listed in paragraph (c)(2) of this section, or any aspect or component thereof, if at any time in the design, review or approval of the activity it is determined that the project, program or activity, or aspect or component thereof, is subject to the control of A.I.D. and may have a significant effect on the environment.

(d) Classes of Actions Normally Having a Significant Effect on the Environment

(1) The following classes of actions have been determined generally to have a significant effect on the environment and an Environmental Assessment or Environmental Impact Statement, as appropriate, will be required:

(i) Programs of river basin development;

(ii) Irrigation or water management projects, including dams and impoundments;

(iii) Agricultural land leveling;

(iv) Drainage projects;

(v) Large scale agricultural mechanization;

(vi) New lands development;

(vii) Resettlement projects;

(viii) Penetration road building or road improvement projects;

(ix) Power plants;

(x) Industrial plants;

(xi) Potable water and sewerage projects other than those that are small-scale.

(2) An Initial Environmental Examination normally will not be necessary for activities within the classes described in §216.2(d), except when the originator of the project believes that the project will not have a significant effect on the environment. In such cases, the activity may be subjected to the procedures set forth in §216.3

(e) Pesticides

The exemptions of §216.2(b)(l) and the categorical exclusions of §216.2(c)(2) are not applicable to assistance for the procurement or use of pesticides.

[45 FR 70244, Oct. 23, 1980]

§216.3 PROCEDURES

(a) General Procedures

(1) Preparation of the Initial Environmental Examination.

Except as otherwise provided, an Initial Environmental Examination is not required for activities identified in §216.2(b)(1), (c)(2), and (d). For all other A.I.D. activities described in §216.2(a) an Initial Environmental Examination will be prepared by the originator of an action. Except as indicated in this section, it should be prepared with the PID or PAIP. For projects including the procurement or use of pesticides, the procedures set forth in §216.3(b) will be followed, in addition to the procedures in this paragraph. Activities which cannot be identified in sufficient detail to permit the completion of an Initial Environmental Examination with the PID or PAIP, shall be described by including with the PID or PAIP: (i) An explanation indicating why the Initial Environmental Examination cannot be completed; (ii) an estimate of the amount of time required to complete the Initial Environmental Examination; and (iii) a recommendation that a Threshold Decision be deferred until the Initial Environmental Examination is completed. The responsible Assistant Administrator will act on the request for deferral concurrently with action on the PID or PAIP and will designate a time for completion of the Initial Environmental Examination. In all instances, except as provided in §216.3 (a)(7), this completion date will be in sufficient time to allow for the completion of an Environmental Assessment or Environmental Impact Statement, if required, before a final decision is made to provide A.I.D. funding for the action.

(2) Threshold Decision. (i) The Initial Environmental Examination will include a Threshold Decision made by the officer in the originating office who signs the PID or PAIP. If the Initial Environmental Examination is completed prior to or at the same time as the PID or PAIP, the Threshold Decision will be reviewed by the Bureau Environmental Officer concurrently with approval of

the PID or PAIP. The Bureau Environmental Officer will either concur in the Threshold Decision or request reconsideration by the officer who made the Threshold Decision, stating the reasons for the request. Differences of opinion between these officers shall be submitted for resolution to the Assistant Administrator at the same time that the PID is submitted for approval.

(ii) An Initial Environmental Examination, completed subsequent to approval of the PID or PAIP, will be forwarded immediately together with the Threshold Determination to the Bureau Environmental Officer for action as described in this section.

(iii) A Positive Threshold Decision shall result from a finding that the proposed action will have a significant effect on the environment. An Environmental Impact Statement shall be prepared if required pursuant to §216.7. If an impact statement is not required, an Environmental Assessment will be prepared in accordance with §216.6. The cognizant Bureau or Office will record a Negative Determination if the proposed action will not have a significant effect on the environment.

(3) Negative Declaration. The Assistant Administrator, or the Administrator in actions for which the approval of the Administrator is required for the authorization of financing, may make a Negative Declaration, in writing, that the Agency will not develop an Environmental Assessment or an Environmental Impact Statement regarding an action found to have a significant effect on the environment when

(i) a substantial number of Environmental Assessments or Environmental Impact Statements relating to similar activities have been prepared in the past, if relevant to the proposed action, (ii) the Agency has previously prepared a programmatic Statement or Assessment covering the activity in question which has been considered in the development of such activity, or (iii) the Agency has developed design criteria for such an action which, if applied in the design of the action, will avoid a significant effect on the environment.

(4) Scope of Environmental Assessment or Impact Statement

(i) Procedure and Content. After a Positive Threshold Decision has been made, or a determination is made under the pesticide procedures set forth in §216.3(b) that an Environmental Assessment or Environmental Impact Statement is required, the originator of the action shall commence the process of identifying the significant issues relating to the proposed action and of determining the scope of the issues to be addressed in the Environmental Assessment or Environmental Impact Statement. The originator of an action within the classes of actions described in §216.2(d) shall commence this

scoping process as soon as practicable. Persons having expertise relevant to the environmental aspects of the proposed action shall also participate in this scoping process. (Participants may include but are not limited to representatives of host governments, public and private institutions, the A.I.D. Mission staff and contractors.)

This process shall result in a written statement which shall include the following matters:

(a) A determination of the scope and significance of issues to be analyzed in the Environmental Assessment or Impact Statement, including direct and indirect effects of the project on the environment.

(b) Identification and elimination from detailed study of the issues that are not significant or have been covered by earlier environmental review, or approved design considerations, narrowing the discussion of these issues to a brief presentation of why they will not have a significant effect on the environment.

(c) A description of (1) the timing of the preparation of environmental analyses, including phasing if appropriate, (2) variations required in the format of the Environmental Assessment, and (3) the tentative planning and decision-making schedule; and

(d) A description of how the analysis will be conducted and the disciplines that will participate in the analysis.

(ii) These written statements shall be reviewed and approved by the Bureau Environmental Officer.

(iii) Circulation of Scoping Statement. To assist in the preparation of an Environmental Assessment, the Bureau Environmental Officer may circulate copies of the written statement, together with a request for written comments, within thirty days, to selected federal agencies if that Officer believes comments by such federal agencies will be useful in the preparation of an Environmental Assessment. Comments received from reviewing federal agencies will be considered in the preparation of the Environmental Assessment and in the formulation of the design and implementation of the project, and will, together with the scoping statement, be included in the project file.

(iv) Change in Threshold Decision. If it becomes evident that the action will not have a significant effect on the environment (i.e., will not cause significant harm to the environment), the Positive Threshold

Decision may be withdrawn with the concurrence of the Bureau Environmental Officer. In the case of an action included in §216.2(d)(2), the request for withdrawal shall be made to the Bureau Environmental Officer.

(5) Preparation of Environmental Assessments and Environmental Impact Statement. If the PID or PAIP is approved, and the Threshold Decision is positive, or the action is included in §216.2(d), the originator of the action will be responsible for the preparation of an Environmental Assessment or Environmental Impact Statement as required. Draft Environmental Impact Statements will be circulated for review and comment as part of the review of Project Papers and as outlined further in §216.7 of those procedures. Except as provided in §216.3(a)(7), final approval of the PP or PAAD and the method of implementation will include consideration of the Environmental Assessment or final Environmental Impact Statement.

(6) Processing and Review Within A.I.D.

(i) Initial Environmental Examinations, Environmental Assessments, and final Environmental Impact Statements will be processed pursuant to standard A.I.D. procedures for project approval documents. Except as provided in §216.3(a)(7), Environmental Assessments and final Environmental Impact Statements will be reviewed as an integral part of the Project Paper or equivalent document. In addition to these procedures, Environmental Assessments will be reviewed and cleared by the Bureau Environmental Officer. They may also be reviewed by the Agency's Environmental Coordinator who will monitor the Environmental Assessment process.

(ii) When project approval authority is delegated to field posts, Environmental Assessments shall be reviewed and cleared by the Bureau Environmental Officer prior to the approval of such actions.

(iii) Draft and final Environmental Impact Statements will be reviewed and cleared by the Environmental Coordinator and the Office of the General Counsel.

(7) Environmental Review After Authorization of Financing.

(i) Environmental review may be performed after authorization of a project, program or activity only with respect to subprojects or significant aspects of the project, program or activity that are unidentified at the time of authorization. Environmental review shall be completed prior to authorization for all subprojects and aspects of a project, program or activity that are identified.

(ii) Environmental review should occur at the earliest time in design or implementation at which a meaningful review can be undertaken, but in no event later than when previously unidentified subprojects or aspects of projects, programs or activities are identified and planned. To the extent possible, adequate information to undertake deferred environmental review should be obtained before funds are obligated for unidentified subprojects or aspects of projects, programs or activities. (Funds may be obligated for the other aspects for which environmental review has been completed.) To avoid an irreversible commitment of resources prior to the conclusion of environmental review, the obligation of funds can be made incrementally as subprojects or aspects of projects, programs or activities are identified; or if necessary while planning continues, including environmental review, the agreement or other document obligating funds may contain appropriate covenants or conditions precedent to disbursement for unidentified subprojects or aspects of projects, programs or activities.

(iii) When environmental review must be deferred beyond the time some of the funds are to be disbursed (e.g., long lead times for the delivery of goods or services), the project agreement or other document obligating funds shall contain a covenant or covenants requiring environmental review, including an Environmental Assessment or Environmental Impact Statement, when appropriate, to be completed and taken into account prior to implementation of those subprojects or aspects of the project, program or activity for which environmental review is deferred. Such covenants shall ensure that implementation plans will be modified in accordance with environmental review if the parties decide that modifications are necessary.

(iv) When environmental review will not be completed for an entire project, program or activity prior to authorization, the Initial Environmental Examination and Threshold Decision required under §216.3(a)(l) and (2) shall identify those aspects of the project, program or activity for which environmental review will be completed prior to the time financing is authorized. It shall also include those subprojects or aspects for which environmental review will be deferred, stating the reasons for deferral and the time when environmental review will be completed. Further, it shall state how an irreversible commitment of funds will be avoided until environmental review is completed. The A.I.D. officer responsible for making environmental decisions for such projects, programs or activities shall also be identified (the same officer who has decision-making authority for the other aspects of implementation). This deferral shall be reviewed and approved by the

officer making the Threshold Decision and the officer who authorizes the project, program or activity. Such approval may be made only after consultation with the Office of General Counsel for the purpose of establishing the manner in which conditions precedent to disbursement or covenants in project and other agreements will avoid an irreversible commitment of resources before environmental review is completed.

(8) 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. This will require recording of baseline data at the start. To the extent that available data permit, originating offices of A.I.D. will formulate systems in collaboration with recipient nations, to monitor such impacts during the life of A.I.D.'s involvement. Monitoring implementation of projects, programs and activities shall take into account environmental impacts to the same extent as other aspects of such projects, programs and activities. If during implementation of any project, program or activity, whether or not an Environmental Assessment or Environmental Impact Statement was originally required, it appears to the Mission Director, or officer responsible for the project, program or activity, that it is having or will have a significant effect on the environment that was not previously studied in an Environmental Assessment or Environmental Impact Statement, the procedures contained in this part shall be followed including, as appropriate, a Threshold Decision, Scoping and an Environmental Assessment or Environmental Impact Statement.

(9) Revisions. If, after a Threshold Decision is made resulting in a Negative Determination, a project is revised or new information becomes available which indicates that a proposed action might be "major" and its effects "significant", the Negative Determination will be reviewed and revised by the cognizant Bureau and an Environmental Assessment or Environmental Impact Statement will be prepared, if appropriate. Environmental Assessments and Environmental Impact Statements will be amended and processed appropriately if there are major changes in the project or program, or if significant new information becomes available which relates to the impact of the project, program or activity on the environment that was not considered at the time the Environmental Assessment or Environmental Impact Statement was approved.

When ongoing programs are revised to incorporate a change in scope or nature, a determination will be made as to whether such change may have an environmental impact not previously assessed. If so, the procedures outlined in this part will be followed.

(10) Other Approval Documents. These procedures refer to certain A.I.D. documents such as PIDs, PAIPs, PPs and PAADs as the A.I.D. internal instruments for approval of projects, programs or activities. From time to time, certain special procedures, such as those in §216.4, may not require the use of the aforementioned documents. In these situations, these environmental procedures shall apply to those special approval procedures, unless otherwise exempt, at approval times and levels comparable to projects, programs and activities in which the aforementioned documents are used.

(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 long-term 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 non-target 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 non-chemical 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 re-registration, 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 re-registration, 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 multi-donor 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 USEPA 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 non-project 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.

[43 FR 20491, May 12, 1978, as amended at 45 FR 70245, Oct. 23, 1980]

§216.4 PRIVATE APPLICANTS

Programs, projects or activities for which financing from A.I.D. is sought by private applicants, such as PVOs and educational and research institutions, are subject to these procedures. Except as provided in §216.2(b), (c) or (d), preliminary proposals for financing submitted by private applicants shall be accompanied by an Initial Environmental Examination or adequate information to permit preparation of an Initial Environmental Examination. The Threshold Decision shall be made by the Mission Director for the country to which the proposal relates, if the preliminary proposal is submitted to the A.I.D. Mission, or shall be made by the officer in A.I.D. who approves the preliminary proposal. In either case, the concurrence of the Bureau Environmental Officer is required in the same manner as in §216.3(a)(2), except for PVO projects approved in A.I.D. Missions with total life of project costs less than $500,000. Thereafter, the same procedures set forth in §216.3 including as appropriate scoping and Environmental Assessments or Environmental Impact Statements, shall be applicable to programs, projects or activities submitted by private applicants. The final proposal submitted for financing shall be treated, for purposes of these procedures, as a Project Paper. The Bureau Environmental Officer shall advise private applicants of studies or other information foreseeably required for action by A.I.D.

[45 FR 70247, Oct. 23, 1980]

§216.5 ENDANGERED SPECIES

It is A.I.D. policy to conduct its assistance programs in a manner that is sensitive to the protection of endangered or threatened species and their critical habitats. The Initial Environmental Examination for each project, program or activity having an effect on the environment shall specifically determine whether the project, program or activity will have an effect on an endangered or threatened species, or critical habitat. If the proposed project, program or activity will have the effect of jeopardizing an endangered or threatened species or of adversely modifying its critical habitat, the Threshold Decision shall be a Positive Determination and an Environmental Assessment or Environmental Impact Statement completed as appropriate, which shall discuss alternatives or modifications to avoid or mitigate such impact on the species or its habitat.

[45 FR 70247, Oct. 23, 1980]

§216.6 ENVIRONMENTAL ASSESSMENTS

(a) General Purpose

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.

(b) Collaboration with Affected Nation on Preparation

Collaboration in obtaining data, conducting analyses and considering alternatives will help build an awareness of development associated environmental problems in less developed countries as well as assist in building an indigenous institutional capability to deal nationally with such problems. Missions, Bureaus and Offices will collaborate with affected countries to the maximum extent possible, in the development of any Environmental Assessments and consideration of environmental consequences as set forth therein.

(c) Content and Form

The Environmental Assessment shall be based upon the scoping statement and shall address the following elements, as appropriate:

(1) Summary. The summary shall stress the major conclusions, areas of controversy, if any, and the issues to be resolved.

(2) Purpose. The Environmental Assessment shall briefly specify the underlying purpose and need to which the Agency is responding in proposing the alternatives including the proposed action

(3) Alternatives Including the Proposed Action. This section should present the environmental impacts of the proposal and its alternatives in comparative form, thereby sharpening the issues and providing a clear basis for choice among options by the decision-maker. This section should explore and evaluate reasonable alternatives and briefly discuss the reasons for eliminating those alternatives which were not included in the detailed study; devote substantial treatment to each alternative considered in detail including the proposed action so that reviewers may evaluate their comparative merits; include the alternative of no action; identify the Agency's preferred alternative or alternatives, if one or more exists; include appropriate mitigation measures not already included in the proposed action or alternatives.

(4) Affected Environment. The Environmental Assessment shall succinctly describe the environment of the area(s) to be affected or created by the alternatives under consideration. The descriptions shall be no longer than is necessary to understand the effects of the alternatives. Data and analyses in the Environmental Assessment shall be commensurate with the significance of the impact with less important material summarized, consolidated or simply referenced.

(5) Environmental Consequences. This section forms the analytic basis for the comparisons under paragraph (c)(3) of this section. It will include the

environmental impacts of the alternatives including the proposed action; any adverse effects that cannot be avoided should the proposed action be implemented; the relationship between short-term uses of the environment and the maintenance and enhancement of long-term productivity; and any irreversible or irretrievable commitments of resources which would be involved in the proposal should it be implemented. It should not duplicate discussions in paragraph (c)(3) of this section. This section of the Environmental Assessment should include discussions of direct effects and their significance; indirect effects and their significance; possible conflicts between the proposed action and land use plans, policies and controls for the areas concerned; energy requirements and conservation potential of various alternatives and mitigation measures; natural or depletable resource requirements and conservation potential of various requirements and mitigation measures; urban quality; historic and cultural resources and the design of the built environment, including the reuse and conservation potential of various alternatives and mitigation measures; and means to mitigate adverse environmental impacts.

(6) List of Preparers. The Environmental Assessment shall list the names and qualifications (expertise, experience, professional discipline) of the persons primarily responsible for preparing the Environmental Assessment or significant background papers.

(7) Appendix. An appendix may be prepared.

(d) Program Assessment

Program Assessments may be appropriate in order 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. In these cases, a single, programmatic assessment will be prepared in A.I.D./Washington and circulated to appropriate overseas Missions, host governments, and to interested parties within the United States. To the extent practicable, the form and content of the programmatic Environmental Assessment will be the same as for project Assessments. Subsequent Environmental Assessments on major individual actions will only be necessary where such follow-on or subsequent activities may have significant environmental impacts on specific countries where such impacts have not been adequately evaluated in the programmatic Environmental Assessment. Other programmatic evaluations of class of actions may be conducted in an effort to establish additional categorical exclusions or design standards or criteria for such classes that will eliminate or minimize adverse effects of such actions, enhance the environmental effect of such actions or reduce the amount of paperwork or time involved in these procedures. Programmatic evaluations conducted for the purpose of establishing additional categorical exclusions under

§216.2(c) or design considerations that will eliminate significant effects for classes of actions shall be made available for public comment before the categorical exclusions or design standards or criteria are adopted by A.I.D. Notice of the availability of such documents shall be published in the Federal Register. Additional categorical exclusions shall be adopted by A.I.D. upon the approval of the Administrator, and design consideration in accordance with usual agency procedures.

(e) Consultation and Review

(1) When Environmental Assessments are prepared on activities carried out within or focused on specific developing countries, consultation will be held between A.I.D. staff and the host government both in the early stages of preparation and on the results and significance of the completed Assessment before the project is authorized.

(2) Missions will encourage the host government to make the Environmental Assessment available to the general public of the recipient country. If Environmental Assessments are prepared on activities which are not country specific, the Assessment will be circulated by the Environmental Coordinator to A.I.D.'s Overseas Missions and interested governments for information, guidance and comment and will be made available in the U.S. to interested parties.

(f) Effect in Other Countries

In a situation where an analysis indicates that potential effects may extend beyond the national boundaries of a recipient country and adjacent foreign nations may be affected, A.I.D. will urge the recipient country to consult with such countries in advance of project approval and to negotiate mutually acceptable accommodations.

(g) Classified Material

Environmental Assessments will not normally include classified or administratively controlled material. However, there may be situations where environmental aspects cannot be adequately discussed without the inclusion of such material. The handling and disclosure of classified or administratively controlled material shall be governed by 22 CFR Part 9. Those portions of an Environmental Assessment which are not classified or administratively controlled will be made available to persons outside the Agency as provided for in 22 CFR Part 212.

[45 FR 70247, Oct. 23, 1980]

§216.7 ENVIRONMENTAL IMPACT STATEMENTS

(a) Applicability

An Environmental Impact Statement shall be prepared when agency actions significantly affect:

(1) The global environment or areas outside the jurisdiction of any nation (e.g., the oceans);

(2) The environment of the United States; or

(3) Other aspects of the environment at the discretion of the Administrator.

(b) Effects on the United States: Content and Form

An Environmental Impact Statement relating to paragraph (a)(2) of this section shall comply with the CEQ Regulations. With respect to effects on the United States, the terms environment and significant effect wherever used in these procedures have the same meaning as in the CEQ Regulations rather than as defined in §216.l(c)(12) and (13) of these procedures.

(c) Other Effects: Content and Form

An Environmental Impact Statement relating to paragraphs (a)(l) and (a)(3) of this section will generally follow the CEQ Regulations, but will take into account the special considerations and concerns of A.I.D. Circulation of such Environmental Impact

Statements in draft form will precede approval of a Project Paper or equivalent and comments from such circulation will be considered before final project authorization as outlined in §216.3 of these procedures. The draft Environmental Impact Statement will also be circulated by the Missions to affected foreign governments for information and comment. Draft Environmental Impact Statements generally will be made available for comment to Federal agencies with jurisdiction by law or special expertise with respect to any environmental impact involved, and to public and private organizations and individuals for not less than forty-five (45) days. Notice of availability of the draft Environmental Impact Statements will be published in the FEDERAL REGISTER. Cognizant Bureaus and Offices will submit these drafts for circulation through the Environmental Coordinator who will have the responsibility for coordinating all such communications with persons outside A.I.D. Any comments received by the Environmental Coordinator will be forwarded to the originating Bureau or Office for consideration in final policy decisions and the preparation of a final Environmental Impact Statement. All such comments will be attached to the final Statement, and those relevant comments not adequately discussed in the draft Environmental Impact Statement will be appropriately dealt with in the final Environmental Impact Statement. Copies of the final Environmental Impact Statement, with comments attached, will be sent by the Environmental Coordinator to CEQ and to all other Federal, state, and local agencies and private organizations that made substantive comments on the draft, including affected

foreign governments. Where emergency circumstances or considerations of foreign policy make it necessary to take an action without observing the provisions of

§1506.10 of the CEQ Regulations, or when there are overriding considerations of expense to the United States or foreign governments, the originating Office will advise the Environmental Coordinator who will consult with Department of State and CEQ concerning appropriate modification of review procedures.

[45 FR 70249, Oct. 23, 1980]

§216.8 PUBLIC HEARINGS

(1) In most instances AID will be able to gain the benefit of public participation in the impact statement process through circulation of draft statements and notice of public availability in CEQ publications. However, in some cases the Administrator may wish to hold public hearings on draft Environmental Impact Statements. In deciding whether or not a public hearing is appropriate, Bureaus in conjunction with the Environmental Coordinator should consider:

(i) The magnitude of the proposal in terms of economic costs, the geographic area involved, and the uniqueness or size of commitment of the resources involved;

(ii) The degree of interest in the proposal as evidenced by requests from the public and from Federal, state and local authorities, and private organizations and individuals, that a hearing be held;

(iii) The complexity of the issue and likelihood that information will be presented at the hearing which will be of assistance to the Agency; and

(iv) The extent to which public involvement already has been achieved through other means, such as earlier public hearings, meetings with citizen representatives, and/or written comments on the proposed action.

(2) If public hearings are held, draft Environmental Impact Statements to be discussed should be made available to the public at least fifteen (15) days prior to the time of the public hearings, and a notice will be placed in the FEDERAL REGISTER giving the subject, time and place of the proposed hearings.

[41 FR 26913, June 30, 1976. Redesignated at 45 FR 70249, Oct. 23, 1980]

§216.9 BILATERAL AND MULTILATERAL STUDIES AND CONCISE REVIEWS OF ENVIRONMENTAL ISSUES

Notwithstanding anything to the contrary in these procedures, the Administrator may approve the use of either of the following documents as a substitute for an Environmental

Assessment (but not a substitute for an Environmental Impact Statement) required under these procedures:

(1) Bilateral or multilateral environmental studies, relevant or related to the proposed action, prepared by the United States and one or more foreign countries or by an international body or organization in which the United States is a member or participant; or,

(2) Concise reviews of the environmental issues involved including summary environmental analyses or other appropriate documents.

[45 FR 70249, Oct. 23, 1980]

§216.10 RECORDS AND REPORTS

Each Agency Bureau will maintain a current list of activities for which Environmental Assessments and Environmental Impact Statements are being prepared and for which Negative Determinations and Declarations have been made. Copies of final Initial Environmental Examinations, scoping statements, Assessments and Impact Statements will be available to interested Federal agencies upon request. The cognizant Bureau will maintain a permanent file (which may be part of its normal project files) of Environmental Impact Statements, Environmental Assessments, final Initial Environmental Examinations, scoping statements, Determinations and Declarations which will be available to the public under the Freedom of Information Act. Interested persons can obtain information or status reports regarding Environmental Assessments and Environmental Impact Statements through the A.I.D. Environmental Coordinator.

[45 FR 70249, Oct. 23, 1980]

(22 U.S.C. 2381; 42 U.S.C. 4332)

Dated October 9, 1980

Joseph C. Wheeler

Acting Administrator

Annex C: Guidance for Developing SEAs for Malaria Vector Control Programs

Note

This *Guidance for Developing SEAs for Malaria Vector Control Programs* is a stand-alone document that has also been included as an annex to *Management Programs for Malaria Vector Control: Programmatic Environmental Assessment* (the PEA). As a result, it refers to the PEA as a separate document, even though it is here an annex to the PEA.

Introduction

Before Reading this Document

If you are a prospective preparer of Supplemental Environmental Assessments (SEAs) for malaria vector control programs, it is **essential** that you read the following resources prior to reading this document:

- USAID (Agency for International Development). 2005a. *Environmental Compliance Procedures, Title 22 Code of Federal Regulations (CFR), Part 216.* Available at http://www.usaid.gov/our_work/environment/compliance/reg216.pdf.
- USAID (Agency for International Development). 2005b. *USAID Environmental Procedures Training Manual.* Available at http://www.encapafrica.org/EPTM.htm.
- USAID (Agency for International Development). 2006. *Management Programs for Malaria Vector Control: Programmatic Environmental Assessment.*
- USAID (Agency for International Development). 2002. *Programmatic Environmental Assessment for Insecticide-Treated Materials in USAID Activities in Sub-Saharan Africa.*

These documents provide in-depth information about environmental compliance procedures in the U.S. Agency for International Development (USAID) and context for this guidance document.

The SEA: Part of USAID Environmental Compliance

Under the U.S. Code of Federal Regulations (22 CFR §216), malaria vector control activities supported or planned by USAID must undergo environmental examination. To assist USAID missions in planning malaria vector control interventions, USAID recently drafted a Programmatic Environmental Assessment (PEA), *Management Programs for Malaria Vector Control: Programmatic Environmental Assessment* (USAID, 2006), that provides a broad view of the human health and environmental impacts that could result from implementation of malaria vector control interventions. However, the PEA cannot account for intercountry and interregional variation regarding issues such as the capacity to manage pesticides used for vector control and the environment likely to be impacted. For this reason, SEAs must be developed to describe in-country impacts of interventions and describe country-specific activities to minimize those impacts. This process of using the PEA as the basis on which the country-specific SEA is developed is called “tiering.” Tiering off from the PEA saves substantial time and money by not having to repeat environmental review that applies generically to all activities within a program. Tiering also ensures basic consistency and quality across all of the program’s activities, no matter where they are undertaken.

Whenever an in-country malaria vector control activity involves "assistance for the procurement or use, or both, of pesticides," SEAs supplementing the PEA must address the pesticide procedures found in 22 CFR 216.3(b). The pesticide procedures list 12 factors to address in SEAs and are described in the following chapters.

In sum, the SEA should be looked upon as the overall picture within the country. The SEA should address the human health and environmental impacts that may occur as a result of USAID support of malaria vector control activities.

The purpose of a malaria program is to save lives and reduce illness and suffering. The purpose of the SEA is to optimize these goals by ensuring malaria control programs use only safe and efficacious pesticides and use them in the way that will minimize inadvertent poisonings and intoxications; by ensuring the natural resources on which people depend for their daily food production and nutrition are not damaged; by ensuring that long term development is promoted by avoiding disruption of agricultural exports by avoiding misuse of malaria pesticides on agricultural crops; and, by participating in international environmental agreements such as the Stockholm Convention on Persistent Organic Pollutants, among others.

When to Prepare an SEA

Since there are minor variations in the way USAID bureaus approach 22 CFR 216 in order to address special circumstances in their regions, *it is important to consult with the Bureau Environmental Officer (BEO) about his or her expectations prior to development of the environmental assessment*. Because the majority of USAID-supported malaria interventions occur in Africa, this section will discuss the types of environmental assessments that need to be conducted for various types of malaria vector control interventions.

Within the Africa Bureau, the level of analysis in the SEA for a country-specific malaria project will depend on which pesticides are proposed to be used. In all cases the SEA will include a *Pesticide Evaluation Report and Safer Use Action Plan (PERSUAP).* The PERSUAP is a name given for the part of the SEA that addresses the 12 factors required by the pesticide procedures in 22 CFR 216.3(b). The level of analysis in the PERSUAP can be more streamlined in cases where all pesticides being proposed for a malaria project are registered by the U.S. Environmental Protection Agency (EPA) for same or similar use without restriction. If one or more pesticides are registered for same or similar use but with restrictions (restricted use pesticides), then the level of analysis will be greater. Should one or more pesticides not be registered for same or similar use or be cancelled-use pesticides, then the level of analysis in the PERSUAP portion of the SEA would be greatest in order to justify their selection and use.

In all cases public participation is required since each SEA is an amendment to the PEA. The level of public participation will track the degree of analysis in the PERSUAP that is driven by the type of pesticides proposed. It will also be affected by other aspects of the

SEA. The degree and method of public participation is decided by the USAID Mission undertaking the SEA in consultation with their BEO.

Who Prepares an SEA

SEAs should be prepared during the initial planning stages of one or more interventions in-country before an intervention or pesticide has been chosen and before funding has been committed. The SEA will guide the decision-making process in designing the overall approach to fighting malaria in the country – it is not done after basic decisions are made since it would be ineffective at that point. The SEA is also a living document used for adaptive management of the malaria program throughout the life of the project. It is a day-to-day management tool, and amendments to the SEA are likely as new information or new directions emerge. The individuals preparing the SEA may be employees of the contractor who will implement the intervention or an independent contractor. Quality control is provided by the host mission staff with the final decision for sufficiency being made by the BEO in the approval process.

Individuals preparing an SEA should be well acquainted with the possible human health and environmental impacts of the intervention and best practices to mitigate those impacts. These individuals also need sufficient experience with interpretation and implementation of USAID environmental procedures, parallel procedures of the host country, and the environmental impact assessment and review process. SEA preparers will be aided substantially by guidance provided in the *Management Programs for Malaria Vector Control: Programmatic Environmental Assessment* (USAID, 2006).

The SEA preparers should conduct their work in conjunction with specialists in the various interventions considered, host-country malaria control program staff, any regional or local health program staff, and any other stakeholders affected by the interventions considered including local communities and nongovernmental organizations. Specialists should furnish details about the design and implementation of their respective interventions. It is especially important for SEA preparers to work closely with USAID Mission staff so monitoring, mitigation, and evaluation activities can be incorporated into overall project planning.

The USAID Mission health team and the USAID Mission Environmental Officer (MEO) should be actively involved in the preparation of the SEA. This can be achieved by accompanying the SEA preparers on site visits and participating in discussions, or simply posing questions or making comments or suggestions when the SEA is initially drafted. Once the SEA has been drafted, it must be signed by the preparers, cleared by the activity manager or SO team leader, the MEO, and the Regional Environmental Advisor (REA). It is then signed by the mission director prior to submitting it to the BEO for their bureau, who after consulting with the Global Health Bureau's BEO shall make the decision whether to approve the SEA and sign it if they do. Communication with the BEO throughout the process is useful to avoid having the draft SEA returned for revisions.

Components of an SEA

22 CFR 216.6 (c) describes the content and form that should be used for all USAID environmental assessments, including SEAs. The following sections examine each component of the SEA in detail. The text boxes in each section contain the CFR text. These are followed by discussion of what the section should contain to comply with CFR text and address malaria-specific issues. When relevant, the section will provide additional guidance for on-the-ground research.

Acronyms

Provide a list of all acronyms and abbreviations used in the SEA.

Table of Contents

A table of contents at the beginning of the document will enable readers to find relevant information quickly.

Summary

> The summary shall stress the major conclusions, areas of controversy, if any, and the issues to be resolved.

Along with these aspects, the summary may include discussion of the intervention in the context of the timeframe of USAID support, other USAID actions, Ministry of Health (MOH) initiatives, and the activities of other donors. If pesticides are to be procured or used, the ones for which approval is requested shall be listed in this summary. Mitigative measures required by the SEA will also be listed with page number references to where they are more fully described in the text of the SEA.

Background and Purpose

> The Environmental Assessment shall briefly specify the underlying purpose and need to which the Agency is responding in proposing the alternatives, including the proposed action.

To explain the purpose and need for the proposed action, this section should describe the background of malaria and malaria control in the country and the intervention target area. To the extent possible, this section should include information on the following:

- Malaria in the country and intervention target area
  - Malaria parasite species
  - Malaria endemic and epidemic risk areas
  - Start, end, and duration of highest malaria transmission
  - Malaria incidence
  - Malaria prevalence

  - Malaria vector species
- History of malaria control in the country and intervention target area
  - Historical use of insecticides
  - Previous house spraying campaigns
  - Insecticide-treated net (ITN) distribution targets and mechanisms
  - Previous environmental management campaigns
  - Previous use of larviciding
- Current malaria control policies
  - Interventions supported by the MOH
  - Rationale for interventions selected
  - Status of intervention implementation or success
  - Pesticide use policies
  - Current capacity of clinics and hospitals and their workers to diagnose and treat pesticide intoxications
  - Baseline data for pre-existing presence of the pesticides being proposed to be used by the project, both in the target populations of communities to be treated and in the natural environment and agricultural crops in the area to be able to monitor and measure safe and correct use
- Administration of malaria control activities
  - Role of national malaria control program
  - Existence and role of separate department of vector borne diseases
  - Authority of the MOH versus local or regional malaria control programs
- Other donor activities

Additionally, this section should describe the effectiveness of the malaria interventions already in place and provide some indication of whether they need strengthening through training, better planning, more efficient management, or other processes.

Much of this information can be obtained by talking to national malaria control program staff and reviewing existing relevant documents, such as a national strategic plan for malaria control. Local or regional malaria control program staff may also provide valuable information on the history of malaria and malaria control in the target area and the status of intervention implementation and success. In some instances the SEA team may need to develop this information.

Alternatives Including the Proposed Action

This section should present the environmental impacts of the proposal and its alternatives in comparative form, thereby sharpening the issues and providing a clear basis for choice among options by the decision maker. This section should explore and evaluate reasonable alternatives and briefly discuss the reasons for eliminating those alternatives that were not included in the detailed study; devote substantial treatment to each alternative considered in detail including the proposed action so that reviewers may evaluate their comparative merits and risks; include the alternative of no action; identify the Agency's preferred alternative or alternatives, if one or more exists; and include appropriate mitigation measures not already included in the proposed action or alternatives.

Affected Environment

The Environmental Assessment shall succinctly describe the environment of the area(s) to be affected or created by the alternatives under consideration. The descriptions shall be no longer than is necessary to understand the effects of the alternatives. Data and analyses in the Environmental Assessment shall be commensurate with the significance of the impact with less important material summarized, consolidated or simply referenced.

This section overlaps with section h of the Pesticide Procedures section, which is addressed in Environmental Consequences. When preparing an SEA for an intervention supporting pesticide use, put the information that would be included in this section in the Pesticide Procedures section (see below). When preparing an SEA for environmental management, where pesticides are not used, this section should include the conditions under which the environmental management intervention will take place, including climate, flora, fauna, geography, hydrology, and soils.

The affected environment also includes the human environment. Include information on the administrative divisions in the target area so that when administrative entities are referenced in subsequent sections, they will be familiar to the reader. In addition, include the populations that will be affected by the intervention. The national malaria control program and the local or regional malaria control program can usually provide this information.

Environmental Consequences

This section forms the analytic basis for the comparisons under [Alternatives Including the Proposed Action]. It will include the environmental impacts of the alternatives including the proposed action; any adverse impacts that cannot be avoided should the proposed action be implemented; the relationship between short-term uses of the environment and the maintenance and enhancement of long-term productivity; and any irreversible or irretrievable commitments of resources which would be involved in the proposal should it be implemented. It should not duplicate discussions in [Alternatives Including the Proposed Action]. This section of the Environmental Assessment should include discussions of direct effects and their significance; indirect effects and their significance; possible conflicts between the proposed action and land use plans, policies and controls for the areas concerned; energy requirements and conservation potential of various alternatives and mitigation measures; natural or depletable resource requirements and conservation potential of various requirements and mitigation measures; urban quality; historic and cultural resources and the design of the built environment, including the reuse and conservation potential of various alternatives and mitigation measures; and means to mitigate adverse environmental impacts.

Not every aspect listed here is relevant for malaria vector control interventions. Thus, only the points described below need to be considered.

Any adverse effects than cannot be avoided. For alternatives involving pesticide use, unavoidable adverse effects include human and environmental exposure from emergencies, such as spills or fires, and possible effects from residential or occupational exposure that **cannot** be mitigated. For alternatives involving environmental management, unavoidable impacts on water resources used by humans and other organisms, destruction of flora and fauna, reduction of biodiversity, etc. (see Table 11 in the integrated vector management [IVM] PEA), should be described here.

Any irreversible or irretrievable commitments of resources. For alternatives involving pesticide use, the MOH often acquires new insecticides or larvicides, storage facilities, vehicles, application equipment, and protective wear and accoutrements that could be used in future interventions with chemicals that have not undergone environmental review or pilfered and used for activities not related to malaria control, potentially harming human health and the environment.

Discussion of direct and indirect effects and their significance. Direct effects can be characterized as negative and positive. The negative impacts of the intervention are discussed in depth in other parts of the SEA and need only very brief mention here. The positive effects of the intervention, such as providing protection against malaria to a target area population; reduced incidence of adult morbidity, miscarriages, low birth-weight, and adverse effects on malaria-induced fetal neurodevelopment; and reduced incidence of malaria-related childhood anemia, complications, organ failure, and death can be described briefly here.

Indirect effects can be considered equivalent to “irreversible commitments of resources,” in that support of malaria vector control interventions may result in procurement of

pesticides, equipment, storage facilities, vehicles, or other commodities that can be used for purposes other than those intended or that adhere to best practices.

Conflicts with other policies, plans, or controls for the areas under consideration. It is crucial that malaria vector control interventions supported by USAID do not contradict U.S. or host-country laws, regulations, and policies or international treaties (Stockholm, Basel, Rotterdam) to which the United States or the host country are party. It is also important to identify whether the proposed action contradicts the goals of other host-country or donor activities in the target area.

Provide an overview of the local environmental and public health regulations as they apply to malaria vector control. This would include any information on

- Pertinent national legislation
- International treaties (Stockholm, Basel, Rotterdam, or other applicable treaties)
- National environmental assessment procedures
- Systems for registration of chemicals
- Guidelines for control operations.

Consult with the Ministries of Health, Environment, and Agriculture and donor projects to ensure that all aspects of the intervention are legal or complementary to current activities in the target area.

To the extent a country may need advice or assistance in complying with the requirements of international treaties, especially the Stockholm Convention on Persistent Organic Pollutants, the SEA will need to identify how the USAID malaria activity will provide the needed training and/or support.

Environmental impacts of the alternatives, including the proposed action. The environmental impacts of alternatives involving pesticide use will be addressed in the Pesticide Procedures (see below). Thus, for alternatives involving pesticide use, simply highlight in this section the primary human health and/or environmental risks of the interventions considered. For alternatives involving environmental management, however, the environmental impacts should be described in depth here.

Pesticide procedures. 22 CFR 216.3(b) requires that when "a project includes assistance for procurement or use, or both, of pesticides," that the Initial Environmental Examination or subsequent Environmental Assessment address the following 12 factors:

a. EPA 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 IVM program
d. The proposed method or methods of application, including availability of appropriate application and safety equipment

e. Any acute and long-term 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

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

Guidance on addressing these factors appears in the following chapter of this guidance, Pesticide Procedures.

Required and recommended mitigation measures. This subsection is the most vital part of the SEA. An SEA is meaningless if the actions required and/or recommended are not implemented. This section serves to expedite planning and budgeting for monitoring, mitigation, and evaluation activities. It provides a synopsis of monitoring, mitigation, and evaluation measures that logistical needs assessors, program managers, host-country government staff, and other stakeholders can easily incorporate into project planning. This section should include the type of impact monitored, mitigated, or evaluated and which entity is responsible for the monitoring, mitigating, or evaluating action. Use the recommended mitigation measures in the PEA for IVM (USAID, 2006) and the PEA for insecticide-treated materials (ITMs) (USAID, 2002) as a guide for recommended mitigation measures in the SEA. Additionally, if pesticide stocks are identified that need to be analyzed and either repackaged or disposed, describe the location of the stocks and the procedures that must be taken to handle those stocks during the program (see the PEA for IVM for the protocol for finding potentially obsolete pesticide stocks).

An SEA is a living document and process. The SEA must include a workable plan for ongoing monitoring of environmental soundness to identify any problems that may develop and create a workable mechanism to address them through amendments to the SEA. This may include mechanisms for measuring pesticide levels in people – both sprayers and residents of sprayed houses, as well as in the surrounding environment. This is especially critical for any pesticides that are not registered by EPA for same or similar use without restrictions.

Preparation Methodology

The Environmental Assessment shall list the names and qualifications (expertise, experience, professional discipline) of the persons primarily responsible for preparing the Environmental Assessment or significant background papers.

In this section, provide a brief methodology for the SEA, including the dates of visits to the host country, names and qualifications of the SEA preparers, and credits to individuals in the host country who provided information for the SEA. If the SEA involved public comment (see Public Comment chapter), provide the date of the scoping meeting, scoping meeting participants, and dates of the host-country public comment period.

Bibliography

List the resources used in preparing the SEA, such as host-country documents and governments, journal articles, United Nations or U.S. best-practice guidelines, the IVM or ITM PEA, or other "significant background papers."

Appendices

An appendix may be prepared.

Appendices can be useful in organizing the SEA so that only the most critical information for decision making is in the body of the SEA. If the SEA involved public comment, include the scoping statement and any public comments on the SEA as appendices.

Pesticide Procedures

As previously described, 22 CFR §216.3(b) mandates the consideration of 12 factors when a project includes "assistance for procurement or use, or both, of pesticides." In this chapter, each factor is discussed in sequence. For each factor, a text box highlights the relevant guidance from USAID's *Pest Management Guidelines* (USAID, 1991), and two subsections provide guidance specific to malaria vector control on what to write and how to obtain information required to consider the factor (for some factors, these are presented in a tabular format instead of two subsections, where there is a relationship between what to write and how to obtain information).

(a) EPA Registration Status of the Requested Pesticide

What to Write

This section should include the following essential information:

- Host-country registration status

- EPA registration status as
  - General Use Pesticide (GUP)
  - Restricted Use Pesticide (RUP)
  - Cancelled (state reasons for cancellation—e.g., health concerns, no market incentive)
  - Not Registered
- Pesticide formulation and percent of active ingredient
- Registration of any same or similar uses. (Note: Larvicides should have same or similar uses in the United States; however, the closest "same or similar use" for insecticides is indoor pest control, because insecticides are not used for Indoor Residual Spraying (IRS) or ITN programs in the United States.)

The section may also include the following optional information:

- Chemical Abstracts Service number (CAS number)
- Trade name
- Manufacturer

Sources of Information

For Host-Country Registration

Each country should have a pesticide registration office. This registration office, typically in the Ministry of Agriculture (MOA), may or may not handle the registration of pesticides for *public health* use—sometimes these pesticides are registered by the MOH. The national malaria control program is likely to know which institution registers public health pesticides.

For EPA Registration

The PEA for malaria vector control interventions and the PEA for ITMs contain information on EPA registration of World Health Organization (WHO)–recommended pesticides; if there is a question as to the status of a pesticide, search EPA's Web site (www.epa.gov) or contact EPA's Office of Pesticides to confirm the current status since this status can and does change from time to time as new information becomes available to EPA.

(b) The Basis for Selection of the Requested Pesticide

What to Write

Describe how each of the criteria listed in Section 6.1.2 of the PEA for IVM (and listed again in this section) were considered in the host country's decision to use a particular pesticide. Four threshold criteria must be met in making decisions on pesticides used in malaria vector control:

- Pesticide registration in the host country
- Acceptability of the pesticide to the national malaria control program
- Risk to human health—pesticides must be approved by the WHO and should be preferred based on their safety as described in USAID's *Programmatic Environmental Assessment for Integrated Vector Management*
- Risk to environment, livestock, and/or agricultural trade.

Beyond these four threshold considerations, technical and logistical factors must be addressed in comparing and selecting insecticides for malaria vector control. The primary factor to be addressed is

- Vector resistance

Secondary factors include

- Appropriateness of surface for spraying
- Duration of effectiveness (and implications for cost)
- Cost of insecticide

Tertiary factors include

- The need for an insecticide of a different class to prevent resistance
- Major classes of insecticides used in other vector control interventions that could promote resistance
- Major classes of insecticides used in the agricultural sector that could promote resistance
- Host-country capacity to prevent pilferage

Sources of Information

The person or institution deciding which pesticide to use may include

- Minister of health
- National malaria program manager
- National malaria program vector control specialist
- A body of key technical experts and stakeholders, such as the National IRS Technical Team in Zanzibar.

Also consult individuals involved in pesticide selection to complete this section.

(c) The Extent to Which the Proposed Pesticide Use Is Part of an Integrated Pest Management Program

What to Write

Describe the extent to which the national malaria control program supports the following interventions:

- Environmental management
- Larviciding
- IRS
- ITNs

If the national malaria control program does not support a certain intervention, describe where and when that intervention may be appropriate. Discuss possibilities for combining the goals and regulations of other sectors with those of the malaria control program. For example, Uganda national law mandates that each district conduct sanitation work for public health; such activities could be adapted to reduce vector breeding sites.

Sources of Information

Typically, the national malaria control strategy details the extent to which different vector management options are considered, and target populations or geographic areas that correspond to those options (for example, ITN distribution free of cost to pregnant women and children under 5 years old). Discuss with national and regional or local malaria control program staff the extent to which the various vector control options are supported, both ideologically and financially. Additional stakeholders, such as public works officers, may provide additional perspectives.

(d) The Proposed Method or Methods of Application, Including Availability of Appropriate Application and Safety Equipment

Examine in detail how the pesticide is to be applied and the measures that will be taken to ensure its safe use, using the guideline in the table below.

What to Write	Sources of Information
• General introduction to the intervention; include the purpose for which pesticides are used in that intervention	• PEA and other Environmental Assessments
• Describe the specific method of pesticide preparation and application	• In-field specialist, trainer, IRS program manager, needs assessor, and/or national, regional or local malaria vector control specialists
• Describe the method, duration, and general content of training for workers and supervisors	• In-field specialist, trainer, IRS program manager, needs assessor, and/or national, regional or local malaria vector control specialists
• Describe methods for protecting workers and supervisors from exposure	• PEAs for IVM and ITMs, WHO manuals, industry manuals (see *Resources* chapter)
• Describe method of supervision	• In-field specialist, trainer, IRS program manager, needs assessor, and/or national, regional or local malaria vector control specialists
• Describe how intervention workers and supervisors are chosen	• National malaria control program, local or regional malaria control program

(e) Any Acute and Long-Term Toxicological Hazards, Either Human or Environmental, Associated with the Proposed Use, and Measures Available to Minimize Such Hazards

Describe measures the program will take to reduce the potential for exposing humans or nontarget organisms to selected pesticides using the guidelines in the table below. Also describe monitoring measures that will allow the program to identify problems with users applying pesticides and with people who live in intervention areas. The level of monitoring for higher risk pesticides is expected to be proportionally higher than for ones that are registered by EPA for same or similar use without restrictions.

What to Write	Sources of Information
• Acute and long-term toxicological hazards to humans	• Include Pesticide Profile (from Annex E of the PEA for IVM) as an annex to the SEA and reference it
• Steps to prevent occupational exposure	• Reference Pesticide Procedures section (d)
• Steps to prevent residential exposure, typically information, education, and communication (IEC) campaigns through a local subcontractor or local health office	• Methods of communication from local health office or potential subcontractor, critical information content from the PEA for IVM and ITMs
• Steps to mitigate pesticide poisoning, including information provided to target area health practitioners and medicines necessary for treatment	• Target area hospital or health facility manager, Ministry of Health formulary office
• Steps to inform or train drivers transporting pesticide (for long-distance travel and daily operations)	• PEA for IVM
Steps to monitor pesticide levels in a statistically significant sample of workers implementing the intervention and/or potential beneficiaries of the intervention. (A mechanism for making corrections or reconsidering pesticide selection or how it is applied must be created, including how to Amend the SEA). Baseline data on the current situation regarding any pre-existing use of the proposed pesticides and their levels in people and the environment should be summarized in this section.	• EPA, host country health and environment authorities, and private-sector specialists; see also the WHO's *Field surveys of exposure to pesticides—Standard Protocol* published in 1982 for guidance.

(f) The Effectiveness of the Requested Pesticide for the Proposed Use

What to Write

- Describe the vector species and its/their resistance to the chosen insecticide or larvicide in the target location, if that information is available
- Describe the impact (or potential impact) of agricultural pesticide use on vector resistance
- Describe steps to ensure quality of the pesticide imported. Some producers, especially those based in developing countries, may not manufacture pesticides to WHO specifications, which can result in pesticides with harmful contaminants and/or reduced efficacy of the product. A practical system to ensure testing of pesticides for purity and potency is needed.
- Reference Pesticide Procedures section (l) for program monitoring activities that will be conducted to determine pesticide efficacy
- For IRS, describe the insecticide's appropriateness for the wall construction material(s) used in the target location.
- For IRS, describe the extent to which the community will accept the intervention taking into account the education that will be provided to individuals through the IEC campaign. Widespread community acceptance of the activity is necessary for it to be effective.

Sources of Information

The national malaria control program and the local or regional malaria control program will have information on vector resistance. The MOA, a local or district agriculture office, or area nonprofit organizations may have information on the impact (or potential impact) of agricultural pesticide use. The MOH or the MOA should have facilities for reliably testing imported insecticides; if no facilities are available in the host country, ask where pesticides can be independently tested in the region by a laboratory not affiliated with either the producer or the broker. Local, regional, or national NGOs, local administrative officers, as well as Ministries of Agriculture, Trade, Natural Resources, or Environment will be able to provide their perspectives on the intervention's acceptability to the community

(g) Compatibility of the Proposed Pesticide with Target and Nontarget Ecosystems

What to Write

This section examines the potential effect of the pesticide on organisms other than the target pest–both wildlife and domestic (for example, the effect on the bee colonies kept in the area). Nontarget species of concern also include birds, fish, bats, dragonflies and

other predator species that naturally reduce mosquito populations. Discuss the potential for negative impact on nontarget species and identify appropriate steps the program will take to mitigate potential adverse impacts. Describe key concerns based on the pesticide's toxicity to nontarget organisms and opportunities for negative impacts on nontarget organisms typically associated with noncompliance with best practices (for example, pesticide pilferage, locating a storehouse in a flood plain, improper dumping of pesticide in water bodies). Larviciding of open water (if it is part of the proposed program) and the effects of improper use of pesticides after pilferage should receive special attention in this section.

Describe the steps the program will take to *monitor* and *mitigate* these potential impacts, referencing Pesticide Procedures sections (d) and (e) when appropriate. Under 22 CFR §216.3(a), projects and programs for which Environmental Assessments are prepared must include measurement of any changes in environmental quality, positive or negative, during their implementation "to the extent feasible and relevant."

Sources of Information

The PEAs on IVM and ITMs indicate toxicity to nontarget organisms. Major concerns about how environmental contamination will occur can be discussed with in-field specialists, the program manager, the Ministry of Environment, and the national malaria control program. Typical mitigation and monitoring steps are described in the PEAs on IVM and ITMs.

(h) The Conditions under Which the Pesticide Is To Be Used, Including Climate, Flora, Fauna, Geography, Hydrology, and Soils

What to Write

Describe the environmental conditions under which the pesticide is to be used, identifying environmental factors that might accentuate (or diminish) the risk of non-target organisms' exposure to pesticides, discussing the need for any additional mitigative measures to reduce exposure risk (citing Pesticide Procedures (g) as needed). Describe aspects of the environment that may be particularly sensitive or subject to contamination as a result of the intervention, and provide a brief overview of the monitoring and mitigation efforts to prevent negative environmental impacts (citing Pesticide Procedures (g) as needed). Discuss any pertinent information on the target area and corresponding peripheral areas, such as:

- Geographic location of target area
- Land area of target location
- Ecological zone
- Climate
- Range and average temperatures
- Range and average rainfall

- Seasonal weather patterns
- Sensitive ecosystems
- Protected areas
- Forest resources
- Common flora and fauna
- Endangered fauna
- Surface water resources
- Groundwater resources (including water table depth, when available)
- Soil types.

Sources of Information

General land area maps can be found on the United Nations Web site or just by searching on the internet. One might expect the Ministry of Environment or a similar ministry to have the information listed above; however, these ministries usually do not have summary information on specific areas in the country. Sometimes the best places to get this information are local environmental nonprofit organizations, local donor projects dealing with the environment, or a search on the internet. (An institution may even have geographic information system [GIS] maps containing this information.) Surface water resources, groundwater resources, and soil types may be found through the Food and Agriculture Organization (FAO) Web site, although the MOA may also have this information. Lists of endangered species can be acquired through the World Conservation Union (IUCN) Red List of endangered species.

(i) The Availability and Effectiveness of Other Pesticides or Nonchemical Control Methods

What to Write

Identify other WHO-recommended malaria control chemicals that could be used in the intervention, taking into account host-country pesticide laws and regulations. Describe the potential for using environmental management for malaria vector control, taking into consideration host-country sanitation laws and environmental regulations.

Sources of Information

The MOA and the MOH should know which WHO-recommended chemicals are registered in-country and could be used. The MOH should know what the sanitation laws require and how they can be leveraged to attain malaria control program goals. The Ministry of Environment will know the regulatory constraints on nonchemical approaches to malaria vector control, such as drainage projects, wetland destruction, etc.

(j) The Requesting Country's Ability to Regulate or Control the Distribution, Storage, Use, and Disposal of the Requested Pesticide

Examine in detail how the pesticide is to be distributed and stored, and how waste materials will be disposed, using the guideline in the table below.

What to Write	Sources of Information
General	
If there are local, regional, or national laws, regulations, or guidelines on distribution, storage, and disposal of pesticides, describe them, describe how well they are actually implemented, and the measures the program will take to follow those guidelines.	The MOA and the Ministry of Environment can provide information on national government laws, regulations, and guidelines on pesticide distribution, storage, and disposal.
Describe any capacity-building activities the program will undertake to improve the host-country distribution, storage, and disposal capacity for pesticides.	Discussions with the national malaria control program, the needs assessor, and local and regional officials can elicit suggestions for capacity building for managing distribution, storage, and disposal of pesticides.
Distribution	
Describe how the pesticide will be transported to the target area.	In-field specialist, IRS program manager, needs assessor, national regional or local malaria vector control specialists
Storage	
Describe the current pesticide storage infrastructure in the target area, measures to protect and control it, and whether the location is sufficient to avoid flooding.	Site visit with needs assessor, and local malaria vector control specialist
Describe the number of storage facilities that are needed for the operation, and where they will be located.	In-field specialist, IRS program manager, needs assessor, national malaria vector control specialists
Describe any construction or renovations that must be undertaken for storage facilities to comply with standards described in UNFAO's Pesticide Storage and Stock Control Manual, including necessary emergency equipment and any need for storekeeper training.	Site visit and UNFAO's Pesticide Storage and Stock Control Manual
Describe measures taken to keep storage facilities secure, such as locating the site in a secure area, storing pesticides off the ground, on sturdy shelving, in a well organized manner and maintaining inventory controls and records, double-padlocking, and guarding. Security of storage facilities is vital to preventing pilferage. Describe process for safe disposal of pesticides that may become obsolete or unusable.	In-field specialist, IRS program manager, needs assessor, national malaria vector control specialist, and PEA recommendations

What to Write	Sources of Information
Disposal	
Describe anticipated waste materials from operations, including but not limited to • Insecticide containers, wrappers, and/or sachets • Rinse-water from cleaning personal protective equipment (e.g., overalls, gloves, face shield or mask), sprayers, and spray operators themselves (for IRS)	Pesticide manufacturer, PEA recommendations, in-field specialist, IRS program manager, needs assessor, national malaria vector control specialist
Describe whether or not waste materials are expected to be contaminated with insecticide.	Pesticide manufacturer, in-field specialist, IRS program manager, needs assessor, national malaria vector control specialist
Describe procedures to deal with contaminated materials; it is particularly important to ensure that empty pesticide containers are not reused for domestic purposes.	Typically PEA recommendations and UNFAO guidelines; check to make sure any host-country laws and international treaties are followed

(k) The Provisions Made for Training of Users and Applicators

What to Write

Generally describe the training that will be provided to users and applicators. Reference Pesticide Procedures sections (d) and (e).

Sources of Information

Pesticide Procedures sections (d) and (e).

(l) The Provisions Made for Monitoring the Use and Effectiveness of the Pesticide

What to Write

Describe the elements of a Human Health and Environmental Evaluation Report (described in the PEA for IVM), their purpose, the activities that must be conducted to achieve that purpose, and the parties responsible for those activities, using the table below as a guide.

Environmental Reporting Elements	Purpose	Activities and Responsible Parties
Post-training evaluation of applicators and supervisors, storekeepers, and medical practitioners	Preliminary assessment of trainees' understanding of training material	Trainers responsible for developing evaluation forms, conducting evaluation, and providing report to program manager and contractor
Post-training evaluation of instructors	Determine effectiveness of training	Program manager responsible for evaluating instructor quality, reporting to contractor
Pesticide stock management reports	Track insecticide leakage/pilferage	Team leaders and supervisors responsible for recording data and submitting it to logistics coordinator or data manager for data aggregation and reporting to program manager and contractor
Mitigation monitoring reports	Identify gaps in implementation of best practices, need for corrective action	Program manager, logistics manager, and/or select supervisors will be responsible for spot-checks of operations. Data manager responsible for synthesizing data and reporting to program manager and USAID contractor
Human exposure monitoring reports	Ensure the program is improving overall health and livelihoods of people	Contractor or subcontractor responsible for collecting baseline data, intermittent data during and after spray operations, and reporting to the program manager and USAID contractor
Environmental impact monitoring reports	Determine whether IRS is exposing sensitive species and ecosystems to pesticide	Contractor or subcontractor responsible for collecting baseline data, intermittent data during and after spray operations, and reporting to the program manager and USAID contractor
Entomological monitoring reports	Determine effectiveness of IRS on reducing mosquito population	Vector control division and national malaria control program of the MOH
Reports on malaria incidence and morbidity	Determine effectiveness of IRS on reducing malaria incidence and morbidity	Health center heads are responsible for collecting malaria incidence and morbidity data (baseline and subsequent) and sending it to the district vector control officer
		The USAID program data manager and regional or local health office counterpart are responsible for synthesizing data and reporting findings to the program manager and USAID contractor
Post-intervention survey, assessing knowledge, attitudes, and practices (KAP) of community regarding community roles and responsibilities	Identify information that requires more emphasis or different communication strategy before the next phase or intervention	IEC subcontractor responsible for survey design, implementation, data analysis, and reporting

The report may exclude some of these elements, depending on the nature of the intervention, the nature of USAID support, the country situation, and USAID and stakeholder concerns.

Sources of Information

The PEA for IVM should be a general guide for monitoring procedures. Details on entomological monitoring can be acquired from the in-field specialist, needs assessor, program manager, or national malaria control program. Environmental and human health monitoring procedures should be determined by a credible host-country institution or other subcontractor.

Public Comment Process

All SEAs must have some degree of public participation. At a minimum, draft SEAs should be provided to individuals consulted during the SEA development process, and the SEA should then be revised based on their suggestions. This is often an acceptable practice for pesticides registered for general use by EPA. For pesticides that EPA has designated as restricted-use pesticides or for pesticides whose registration has been cancelled by EPA, stricter public comment guidelines may apply. The degree of public participation required should be discussed with the USAID Mission undertaking the SEA and the BEO.

If an MOH is receptive to the idea of public comment, USAID should work with the ministry to organize and implement a public comment process that conforms to host-country regulations. Most host countries will have laws or regulations that deal with environmental assessment and public participation; to the extent that there are such laws and regulations, they can be the basis for conducting public comment in a country. If no laws or regulations exist concerning public participation, the host-country government, USAID Mission, and BEO should discuss.

The only guidance for public comment provided by the CFR is in 22 CFR 216.6(e), which states that “Missions will encourage the host government to make the Environmental Assessment available to the general public of the recipient country.” Thus if a MOH rejects making an SEA available to the public, the Mission should try again by educating the ministry as to why it is important, and work with it to conduct a public comment process either through the government, NGOs, or other nongovernmental channels. There may be rare cases where a mission finds that a host-country government is so averse to civil society that it is not possible to undertake any kind of public participation.

Resources

This chapter provides a comprehensive list of resources that might be necessary in preparing SEAs or providing guidance to host-country governments on a variety of topics related to malaria vector control and pesticide management.

USAID Environmental Compliance

The following documents are essential references for USAID guidance on environmental compliance:

- USAID (Agency for International Development). 2005a. *Environmental Compliance Procedures, Title 22 Code of Federal Regulations, Part 216.* Available at http://www.usaid.gov/our_work/environment/compliance/reg216.pdf.
- USAID (Agency for International Development). 2005b. *USAID Environmental Procedures Training Manual.* Available at http://www.encapafrica.org/EPTM.htm.
- USAID (Agency for International Development). 2002. *USAID/AFR Guidance: Preparing PERSUAPs for Pesticide Programs in Africa*. Available at http://www.encapafrica.org/docs/pest-pesticide%20mgmt/PERSUAP%20Guidance.doc.

Storage

Storage capacity and conditions are essential to minimizing exposure, emergencies, and pilferage. All pesticides used for malaria control activities should be stored according to the guidelines in the following manual:

- FAO (Food and Agriculture Organization). 1996. *Pesticide Storage and Stock Control Manual*. FAO Pesticide Disposal Series. Rome.

Additionally, storehouse managers and storekeepers should be trained to manage pesticide stores according to these best practices.

Transport

Transport of pesticides poses risk of spillage, contamination of the environment, human exposure, and contamination of other transported goods. All pesticides used for malaria control activities should be transported according to the guidelines in the following manual:

- FAO (Food and Agriculture Organization). 1996. *Pesticide Storage and Stock Control Manual*. FAO Pesticide Disposal Series. Rome.

Emergencies and Spills

Mitigation and handling of spill and fire hazards are crucial to preventing human and environmental exposure to pesticides. Of particular concern is inhalation of toxic fumes when pesticides burn in an open flame. Storage facilities should be outfitted for such emergencies, and storehouse managers should be trained in best practices of handling emergency situations according to the guidelines in the following manuals:

- FAO (Food and Agriculture Organization). 1996. *Pesticide Storage and Stock Control Manual*. FAO Pesticide Disposal Series. Rome.
- World Health Organization (WHO). 2006. *Pesticides and their application for the control of vectors and pests of public health importance*. 6th ed. Department of Control of Neglected Tropical Diseases, WHO Pesticide Evaluation Scheme.

Additionally, any fire-fighting or emergency services should be trained on handling pesticide emergencies, and notified immediately when any emergencies occur.

Poison Control

In the event that spray operators or residents experience symptoms of pesticide exposure, treatment should be available and accessible. To that end, physicians in health facilities, health centers, and hospitals should be trained in recognizing and treating poisoning symptoms. Treatment medicines should be available in health facilities, health centers, and hospitals. The following manual should be used to guide training and treatment on pesticide poisoning in malaria vector control programs:

- Reigart JR, Roberts JR. 1999. *Recognition and Management of Pesticide Poisonings. 5th Edition.* U.S. Environmental Protection Agency, Washington, DC.

Decontamination and Disposal

Proper decontamination and disposal of expired insecticides, contaminated rinse and wash water, and contaminated packaging products is necessary to mitigate human and environmental exposure to pesticides. The following guidelines should be used to choose decontamination and disposal options that suit the host-country situation:

- Thompson, R. 2004. *Guidance Document: The Selection of Waste Management Options for the Disposal of Obsolete Pesticides and Contaminated Materials.* Draft. Food and Agriculture Organization (FAO). Rome.
- World Health Organization (WHO). 2006. *Pesticides and their application for the control of vectors and pests of public health importance*. 6th ed. Department of Control of Neglected Tropical Diseases, WHO Pesticide Evaluation Scheme.

Pesticide Application Equipment

Pesticide application equipment (e.g., compression sprayers) should be manufactured according to WHO standards, and safety equipment (e.g., face shield, overalls) should be

procured and worn according to WHO standards. The following documents fully describe specifications for pesticide application equipment:

- WHO (World Health Organization). 2000. *Manual for Indoor Residual Spraying—Application of Residual Sprays for Vector Control*. Geneva.
- Najera, J. and Zaim, M. 2002. *Malaria Vector Control: Decision-Making Criteria and Procedures for Judicious Use of Insecticides.* World Health Organization. Geneva.
- WHO (World Health Organization). 1990. *Equipment for Vector Control. 3rd Edition*. Geneva

Pesticide Quality Control

Pesticide procured for public health use should be tested for quality assurance. Regardless of whether the pesticide is tested in the host country or whether a sample is sent outside the host country, the following specifications should be used to determine the quality of the pesticide:

- WHO (World Health Organization). 2002. *Specifications for Public Health Pesticides*. Geneva.

Pesticide Labels

The durability, design, and information content of pesticide labels are crucial to ensuring safe use of pesticides. Pesticide manufacturers should adhere to the guidelines for pesticide labels contained in the following manual:

- FAO (Food and Agriculture Organization). 1995. *Guidelines on Good Labeling Practice*. Rome.

Resistance Monitoring

Resistance monitoring is crucial to the appropriate selection and targeted use of pesticides for malaria vector control. Resistance monitoring should be conducted according to the following guidelines:

- WHO (World Health Organization). 1998. *Techniques to Detect Insecticide Resistance Mechanisms (Field and Laboratory Manual)*. Geneva.
- WHO (World Health Organization). 1998. *Test Procedures for Insecticide Resistance Monitoring in Malaria Vectors, Bio-efficacy and Persistence of Insecticide-Treated Surfaces*. Report of the WHO Informal Consultation, Geneva, 28039, September 1998. Geneva.

Additionally, resistance management practices should be implemented in malaria vector control programs in accordance with the following guidelines:

- WHO (World Health Organization). 2003. *The Manual for Insecticide Resistance Management in Vectors and Pests of Public Health Importance.* Geneva.

Finally, ministries of health and agriculture should work together to ensure agricultural use of pesticides will not adversely impact vector control efforts, and vice versa.

Additional Resources

In addition to the best practices guidelines referenced in the preceding sections, several manuals have been published that may provide further guidance for malaria vector control strategies involving pesticides:

Chavasse, D. and Yap, H. 1997. *Chemical Methods for the Control of Vectors and Pests of Public Health Importance*. Geneva.

FAO (Food and Agriculture Organization). 1988. *Post-Registration Surveillance and Other Activities in the Field*. Rome.

FAO (Food and Agriculture Organization). 1988. *Guidelines for the Retail Distribution of Pesticides with Particular Reference to Storage and Handling at Point of Supply to Users in Developing Countries*. Rome.

FAO (Food and Agriculture Organization). 1990. *Personal Protection When Working with Pesticides in Tropical Climates*. Rome.

FAO (Food and Agriculture Organization). 1991. *Initial Introduction and Subsequent Development of a Simple National Pesticide Registration and Control Scheme*. Rome.

FAO (Food and Agriculture Organization). 1994. *Provisional Guidelines on Tender Procedures for the Procurement of Pesticides*. Rome.

FAO (Food and Agriculture Organization). 1995. *Disposal of Bulk Quantities of Obsolete Pesticides in Developing Countries*. Rome. (Note: this is guidance for governments.)

FAO (Food and Agriculture Organization). 2002. *International Code of Conduct on the Distribution and Use of Pesticides (Revised Version)*. Rome.

FAO (Food and Agriculture Organization). 2002. *Manual on Development and Use of UNFAO and WHO Specifications for Pesticides*. Plant Production and Protection Paper No. 173. Rome.

FAO (Food and Agriculture Organization), WHO (World Health Organization), and UNEP (United Nations Environment Program). 1999. *Guidelines for the Management of Small Quantities of Unwanted and Obsolete Pesticides*. FAO Pesticide Disposal Series, No. 7. Rome.

Najera, J. and Zaim, M. 2001. *Malaria Vector Control: Insecticides for Indoor Residual Spraying*. Geneva.

United Nations. 2002. *Recommendations on the Transport of Dangerous Goods: Model Regulations*. 10th revised edition. New York.

UNEP (United Nations Environment Program). 2001. *Stockholm Convention on Persistent Organic Pollutants*. Geneva.

WHO (World Health Organization). 1996. *Report of the WHO Informal Consultation on the Evaluation and Testing of Insecticides.* WHO/HQ, Geneva, 7-11 October 1996. Geneva.

WHO (World Health Organization). 1997. *Guidelines for Poison Control*. Geneva.

WHO (World Health Organization). 1997. *Report of the First WHOPES Working Group Meeting.* WHO/HQ, Geneva, 26–27 June 1997.

WHO (World Health Organization). 1998. *Review of Alpha-Cypermethrin 10% SC and 5% WP and Cyfluthrin 5% EW and 10% WP*. Report of the Second WHOPES Working Group Meeting: WHO/HQ, Geneva, 22–23 June 1998.

WHO (World Health Organization). 1999. *Review of Deltamethrin 1% SC and 25% WT and Etofenprox 10% EC and 10% EW*. Report of the Third WHOPES Working Group Meeting: WHO/HQ, Geneva, 23–24 September 1999.

WHO (World Health Organization). 1999. *Safe and Effective Use of Household Insecticide Products: Guide for the Production of Educational and Training Materials*. Geneva.

WHO (World Health Organization). 2000. *Guidelines for the Purchase of Public Health Pesticides*. Geneva.

WHO (World Health Organization). 2001. *Information, Education and Communication: Lessons from the Past, Perspectives for the Future*. Occasional paper. Geneva.

WHO (World Health Organization). 2001. *Chemistry and Specification of Pesticides.* Sixteenth Report of the WHO Expert Committee on Vector Biology and Control. WHO Technical Report Series No. 899. Geneva.

WHO (World Health Organization). 2001. *Review of IR3535, KBR 3023, (RS)-Methoprene 20% EC, Pyriproxyfen 0.5% GR, and Lambda-Cyhalothrin 2.5% CS.* Report of the Fourth WHOPES Working Group Meeting, WHO/HQ, Geneva, 4–5 December 2000.

WHO (World Health Organization). 2001. *Review of Olyset Net and Bifenthrin 10% WP.* Report of the Fifth WHOPES Working Group Meeting: WHO/HQ, Geneva, 30–31 October 2001.

WHO (World Health Organization). 2003. *Spray Space Application of Insecticides for Vector and Public Health Pest Control—A Practitioners Guide*. Geneva.

WHO (World Health Organization). 2003. *Draft Guidelines on the Management of Public Health Pesticides.* Report of the WHO Interregional Consultation, Chiang Mai, Thailand, 25–28 February 2003. Geneva.

WHO (World Health Organization). 2005. Recommended Classifications of Pesticides by Hazard: Guidelines to Classification 2004. Geneva.

Annex D: Input Parameter Tables

Table D-1: Chemical/Physical Properties

Parameter	Minimum Value	Maximum Value	Mean Value	Reference	Comments
Alpha Cypermethrin (67375-30-8)					
Henry's law constant (atm-cu m/mol)			9.50E-06	HSDB, 2005	
Melting Point (K)			3.50E+02	IPCS, 2005	
Molecular Weight (g/mol)			4.16E+02	IPCS, 2005	
Octanol-water partition coefficient (LOG) (unitless)			5.16E+00	IPCS, 2005	
Reaction half-life in air (d)			7.50E-01	HSDB, 2005	hydroxyl radicals
Reaction half-life in air (d)			4.90E+01	HSDB, 2005	ozone
Reaction half-life in soil (d)	7.00E+00	1.40E+01		HSDB, 2005	
Reaction half-life in water (d)			8.00E+00	HSDB, 2005	model river
Reaction half-life in water (d)			6.50E+01	HSDB, 2005	model lake
Solubility (mg/L)	5.00E-03	1.00E-02		IPCS, 2005	
Vapor pressure (atm)			1.70E-12	IPCS, 2005	at 20 oC

Table D-1: Chemical/Physical Properties

Parameter	Minimum Value	Maximum Value	Mean Value	Reference	Comments
Bendiocarb (22781-23-3)					
Henry's law constant (atm-cu m/mol)			3.90E-08	HSDB, 2005	
Melting Point (K)			4.00E+02	HSDB, 2005	
Molecular Weight (g/mol)			2.23E+02	HSDB, 2005	
Octanol-water partition coefficient (LOG) (unitless)			1.70E+00	HSDB, 2005	
Reaction half-life in air (d)			5.00E+00	HSDB, 2005	
Reaction half-life in soil (d)	1.00E+00	3.50E+00		U.S. EPA, 1999b	aerobic
Reaction half-life in water (d)			3.30E-01	U.S. EPA, 1999b	at pH 9
Reaction half-life in water (d)			2.00E+00	U.S. EPA, 1999b	at pH 7
Reaction half-life in water (d)			4.65E+01	U.S. EPA, 1999b	at pH 5
Solubility (mg/L)			2.60E+02	HSDB, 2005	at 25 oC
Vapor pressure (atm)			6.60E-09	U.S. EPA, 1999b	at 25 oC

Table D-1: Chemical/Physical Properties

Parameter	Minimum Value	Maximum Value	Mean Value	Reference	Comments
Bifenthrin (82657-04-3)					
Henry's law constant (atm-cu m/mol)			1.00E-06	HSDB, 2005	
Melting Point (K)			3.40E+02	EXTOXNET, 2005	
Molecular Weight (g/mol)			4.23E+02	EXTOXNET, 2005	
Octanol-water partition coefficient (LOG) (unitless)			6.00E+00	EXTOXNET, 2005	
Reaction half-life in air (d)			5.42E-01	HSDB, 2005	hydroxyl radicals
Reaction half-life in air (d)			7.00E+00	HSDB, 2005	ozone
Reaction half-life in soil (d)	6.50E+01	1.25E+02		HSDB, 2005	
Reaction half-life in water (d)			5.55E+02	HSDB, 2005	model lake
Reaction half-life in water (d)			5.00E+01	HSDB, 2005	model river
Solubility (mg/l)			1.00E-01	HSDB, 2005	temperature not specified
Vapor pressure (atm)			2.40E-10	HSDB, 2005	

Table D-1: Chemical/Physical Properties

Parameter	Minimum Value	Maximum Value	Mean Value	Reference	Comments
Cyfluthrin (baythroid) (68359-37-5)					
Henry's law constant (atm-cu m/mol)			5.80E-10	HSDB, 2005	
Melting Point (K)			3.30E+02	HSDB, 2005	
Molecular Weight (g/mol)			4.34E+02	HSDB, 2005	
Octanol-water partition coefficient (LOG) (unitless)			5.94E+00	HSDB, 2005	
Reaction Half-life in air ()			NF		
Reaction half-life in soil (d)			5.95E+01	PAN, 2005	aerobic
Reaction half-life in soil (d)			3.36E+01	PAN, 2005	anaerobic
Reaction half-life in water ()			NF		
Solubility (mg/L)			2.00E+00	HSDB, 2005	at 20 oC
Vapor Pressure (atm)			2.67E-12	HSDB, 2005	at 25 oC
DDT (50-29-3)					
Henry's law constant (atm-cu m/mol)			8.30E-06	ATSDR, 2003a	temperature not reported
Melting Point (K)			3.82E+02	EXTOXNET, 2005	
Molecular Weight (g/mol)			3.54E+02	EXTOXNET, 2005	
Octanol-water partition coefficient (LOG) (unitless)			6.91E+00	HSDB, 2005	
Reaction half-life in air (d)			5.00E+00	HSDB, 2005	at 25 oC
Reaction half-life in soil (d)	7.30E+02	5.48E+03		EXTOXNET, 2005	
Reaction half-life in water (d)			5.60E+01	EXTOXNET, 2005	lake water
Reaction half-life in water (d)			2.80E+01	EXTOXNET, 2005	river water
Solubility (mg/L)			2.50E-02	ATSDR, 2003a	at 25 oC, pH not reported
Vapor pressure (atm)			2.48E-10	EXTOXNET, 2005	at 25 oC

Table D-1: Chemical/Physical Properties

Parameter	Minimum Value	Maximum Value	Mean Value	Reference	Comments
Deltamethrin (52918-63-5)					
Henry's law constant (atm-cu m/mol)			5.00E-06	HSDB, 2005	
Melting Point (K)			3.70E+02	IPCS, 2005	
Molecular Weight (g/mol)			5.05E+02	IPCS, 2005	
Octanol-water partition coefficient (LOG) (unitless)			5.43E+00	IPCS, 2005	
Reaction half-life in air (d)			NF		
Reaction half-life in soil (d)	3.43E+01	4.83E+01		HSDB, 2005	
Reaction half-life in water (d)			1.25E+00	HSDB, 2005	model river
Reaction half-life in water (d)			2.08E+01	HSDB, 2005	model lake
Solubility (mg/L)		2.00E-03		IPCS, 2005	at 20 oC, Reported as < value
Vapor pressure (atm)			2.00E-11	IPCS, 2005	
Etofenprox (80844-07-1)					
Henry's law constant (atm-cu m/mol)			2.26E-08	Chemfinder (SRC), 2005	
Melting Point (K)			3.10E+02	Chemfinder (SRC), 2005	
Molecular Weight (g/mol)			3.77E+02	Chemfinder (SRC), 2005	
Octanol-water partition coefficient (LOG) (unitless)			7.05E+00	Chemfinder (SRC), 2005	
Reaction Half-life in air ()			NF		
Reaction half-life in soil (d)	6.00E+00	9.00E+00		FAO, 1993	lab
Reaction half-life in soil (d)	9.00E+00	7.90E+01		FAO, 1993	field
Reaction half-life in water ()			NF		
Solubility (mg/L)			1.00E-03	Chemfinder (SRC), 2005	at 25 oC
Vapor Pressure (atm)			8.93E-12	Chemfinder (SRC), 2005	at 25 oC

Table D-1: Chemical/Physical Properties

Parameter	Minimum Value	Maximum Value	Mean Value	Reference	Comments
Fenitrothion (122-14-5)					
Henry's law constant (atm-cu m/mol)			9.30E-07	HSDB, 2005	
Melting Point (K)			2.70E+02	IPCS, 2005	
Molecular Weight (g/mol)			2.77E+02	HSDB, 2005	
Octanol-water partition coefficient (LOG) (unitless)			3.16E+00	IPCS, 2005	
Reaction half-life in air (d)			2.67E-01	HSDB, 2005	hydroxyl radicals
Reaction half-life in soil (d)	4.40E+00	1.54E+02		HSDB, 2005	aerobic
Reaction half-life in soil (d)	3.90E+00	1.09E+01		HSDB, 2005	anaerobic
Reaction half-life in water (d)	4.00E+00	8.00E+00		IPCS, 2005	at pH of 5-9 , at 45 oC
Reaction half-life in water (d)	2.00E+02	6.30E+02		IPCS, 2005	at pH of 5-9 (normally found in natural water), at 15 oC
Reaction half-life in water (d)	1.70E+01	6.10E+01		IPCS, 2005	at pH of 5-9, at 30 ℃
Solubility (mg/L)	5.00E+00	1.40E+01		U.S. EPA, 1995	min at 20 oC; max at 30 oC
Vapor pressure (atm)			2.80E-07	U.S. EPA, 1995	at 25 oC

Table D-1: Chemical/Physical Properties

Parameter	Minimum Value	Maximum Value	Mean Value	Reference	Comments
Lambda-Cyhalothrin (91465-08-6)					
Henry's law constant (atm-cu m/mol)			9.09E-06	HSDB, 2005	at 20 oC
Melting Point (K)			3.22E+02	IPCS, 2005	
Molecular Weight (g/mol)			4.50E+02	IPCS, 2005	
Octanol-water partition coefficient (LOG) (unitless)			7.00E+00	IPCS, 2005	
Reaction half-life in air (d)					
Reaction half-life in soil (d)			3.00E+01	NPIC, 2005	
Reaction half-life in water (d)			7.00E+00	NPIC, 2005	
Solubility (mg/L)			5.00E-03	IPCS, 2005	pH not reported
Vapor pressure (atm)			2.96E-08	IPCS, 2005	at 80 oC
Vapor pressure (atm)			1.97E-12	IPCS, 2005	at 20 oC
Malathion (121-75-5)					
Henry's law constant (atm-cu m/mol)			4.90E-09	ATSDR, 2003a	at 25 oC
Melting Point (K)			2.76E+02	EXTOXNET, 2005	
Molecular Weight (g/mol)			3.30E+02	EXTOXNET, 2005	
Octanol-water partition coefficient (LOG) (unitless)			2.75E+00	EXTOXNET, 2005	
Reaction half-life in air (d)			1.50E+00	EXTOXNET, 2005	
Reaction half-life in soil (d)	1.00E+00	2.50E+01		EXTOXNET, 2005	
Reaction half-life in water (d)		7.00E+00		EXTOXNET, 2005	raw river water, reported as < number
Reaction half-life in water (d)			2.10E+01	EXTOXNET, 2005	distilled water
Solubility (mg/L)			1.30E+02	EXTOXNET, 2005	pH not reported
Vapor pressure (atm)			5.25E-08	EXTOXNET, 2005	at 30 oC

Table D-1: Chemical/Physical Properties

Parameter	Minimum Value	Maximum Value	Mean Value	Reference	Comments
Methoprene (40596-69-8)					
Henry's law constant (atm-cu m/mol)			6.90E-06	HSDB, 2005	
Molecular Weight (g/mol)			3.10E+02	HSDB, 2005	
Octanol-water partition coefficient (LOG) (unitless)			5.50E+00	HSDB, 2005	
Reaction Half-life in air (d)	3.33E-02	6.25E-02		HSDB, 2005	
Reaction half-life in soil (d)			1.00E+01	HSDB, 2005	
Reaction half-life in water (d)			1.30E+01	HSDB, 2005	
Solubility (mg/L)			1.40E+00	HSDB, 2005	room temperature
Vapor Pressure (atm)			3.11E-08	HSDB, 2005	at 25 oC
Permethrin (52645-53-1)					
Henry's law constant (atm-cu m/mol)			1.90E-06	HSDB, 2005	temperature not reported
Melting Point (K)	3.07E+02	3.08E+02		HSDB, 2005	
Molecular Weight (g/mol)			3.91E+02	HSDB, 2005	
Octanol-water partition coefficient (LOG) (unitless)			6.50E+00	HSDB, 2005	
Reaction half-life in air (d)			4.08E-01	HSDB, 2005	hydroxy radical
Reaction half-life in air (d)			4.90E+01	HSDB, 2005	ozone
Reaction half-life in soil (d)			3.00E+01	HSDB, 2005	
Reaction half-life in water (d)			3.30E+01	HSDB, 2005	
Solubility (mg/L)			6.00E-03	HSDB, 2005	at 20 oC, pH not reported
Vapor pressure (atm)			2.87E-11	HSDB, 2005	at 25 oC

Table D-1: Chemical/Physical Properties

Parameter	Minimum Value	Maximum Value	Mean Value	Reference	Comments
Pirimiphos-methyl (29232-93-7)					
Henry's law constant (atm-cu m/mol)			7.00E-07	HSDB, 2005	
Melting Point (K)			2.90E+02	HSDB, 2005	
Molecular Weight (g/mol)			3.05E+02	HSDB, 2005	
Octanol-water partition coefficient (LOG) (unitless)			4.12E+00	HSDB, 2005	
Reaction Half-life in air (d)			1.00E-01	HSDB, 2005	
Reaction half-life in soil (d)	5.20E+00	5.90E+00		HSDB, 2005	
Reaction half-life in water ()			NF		varies too much depending on condition
Solubility (mg/L)			8.60E+00	HSDB, 2005	at 20 oC
Vapor Pressure (atm)			1.97E-08	HSDB, 2005	at 20 oC
Propoxur (114-26-1)					
Henry's law constant (atm-cu m/mol)			1.43E-09	HSDB, 2005	
Melting Point (K)			3.60E+02	WHO, 2005	
Molecular Weight (g/mol)			2.09E+02	HSDB, 2005	
Octanol-water partition coefficient (LOG) (unitless)			1.56E+00	WHO, 2005	at 20 oC
Reaction half-life in air (d)			5.00E-01	HSDB, 2005	hydroxyl radicals
Reaction half-life in soil (d)	8.00E+01	2.10E+02		HSDB, 2005	min is silt loam, max is sandy loam
Reaction half-life in water (d)			>365	WHO, 2005	at pH 4, at 22 oC
Reaction half-life in water (d)			1.25E+00	WHO, 2005	at pH 9, at 22 oC
Reaction half-life in water (d)			9.32E+01	WHO, 2005	at pH 7, at 22 oC
Solubility (mg/L)			1.75E+03	WHO, 2005	at 20 oC
Vapor pressure (atm)			2.50E-05	WHO, 2005	at 20 oC

Table D-1: Chemical/Physical Properties

Parameter	Minimum Value	Maximum Value	Mean Value	Reference	Comments
Temephos (3383-96-8)					
Henry's law constant (atm-cu m/mol)			1.96E-09	HSDB, 2005	at 25 oC
Melting Point (K)			3.04E+02	HSDB, 2005	
Molecular Weight (g/mol)			4.66E+02	HSDB, 2005	
Octanol-water partition coefficient (LOG) (unitless)			5.96E+00	HSDB, 2005	
Reaction half-life in air (d)			1.17E-01	HSDB, 2005	
Reaction half-life in soil (d)			3.00E+01	EXTOXNET, 2005	
Reaction half-life in water (d)	4.00E+03			HSDB, 2005	river water, reported as > number
Solubility (mg/L)			2.70E-01	HSDB, 2005	at 20 oC, pH not reported
Vapor pressure (atm)			1.13E-12	HSDB, 2005	at 25 oC

Table D-2: Pesticide Use Data

Vector Management Practice	Pesticide Formulation	Parameter	Minimum Value	Maximum Value	Mean Value	Comments	Reference
Alpha-cypermethrin (67375-30-8)							
IRS	Wettable powder	Application (kg ai/m2)	2.00E-05	3.00E-05			Najera and Ziam, 2002
ITNs	Suspension concentrate	Application (kg ai/m2)			4.00E-05	SC 10%	WHO, 2002b
IRS	Wettable powder	Application frequency (times/year)	2	3		Duration of effective action 4-6 months	Najera and Ziam, 2002
Bendiocarb (22781-23-3)							
IRS	Wettable powder	Application (kg ai/m2)	1.00E-04	4.00E-04			Najera and Ziam, 2002
IRS	Wettable powder	Application frequency (times/ year)	2	6		Duration of effective action 2-6 months	Najera and Ziam, 2002
Bifenthrin (82657-04-3)							
IRS	Wettable powder	Application (kg ai/m2)	2.50E-05	5.00E-05			Najera and Ziam, 2002
IRS	Wettable powder	Application frequency (times/year)	2	4		Duration of effective action 3-6 months	Najera and Ziam, 2002
Cyfluthrin (baythroid) (68359-37-5)							
IRS	Wettable powder	Application (kg ai/m2)	2.00E-05	5.00E-05			Najera and Ziam, 2002
ITNs	Emulsion	Application (kg ai/m2)			5.00E-05		WHO, 2002b
IRS	Wettable powder	Application frequency (times/year)	2.00E+00	4.00E+00		Duration of effective action 3-6 months	Najera and Ziam, 2002
DDT (50-29-3)							
IRS	Wettable powder	Application (kg ai/m2)	1.00E-03	2.00E-03			Najera and Ziam, 2002
IRS	Wettable powder	Application frequency (times/year)	2.00E+00			Duration of effective action 6 months	Najera and Ziam, 2002
Deltamethrin (52918-63-5)							
IRS	Wettable powder	Application frequency (times/year)	2	4		Duration of effective action 3-6 months	Najera and Ziam, 2002

Table D-2: Pesticide Use Data

Vector Management Practice	Pesticide Formulation	Parameter	Minimum Value	Maximum Value	Mean Value	Comments	Reference
			Deltramethrin (52918-63-5)				
IRS	wettable powder and water dispersible granules	Application (kg ai/m2)	2.00E-05	2.50E-05			Najera and Ziam, 2002
ITNs	Suspension concentrate	Application (kg ai/m2)			2.50E-05	SC 1%	WHO, 2002b
ITNs	Water dispensible tablet	Application (kg ai/m2)			2.50E-05	WT 25%	WHO, 2002b
			Etofenprox (80844-07-1)				
IRS	Wettable powder	Application (kg ai/m2)	1.00E-04	3.00E-04			Najera and Ziam, 2002
ITNs	Emulsion	Application (kg ai/m2)			2.00E-04		WHO, 2002b
IRS	Wettable powder	Application frequency (times/year)	2.00E+00	4.00E+00		Duration of effective action 3-6 months	Najera and Ziam, 2002
			Fenitrothion (122-14-5)				
IRS	Wettable powder	Application (kg ai/m2)			2.00E-03		Najera and Ziam, 2002
IRS	Wettable powder	Application frequency (times/year)	2	4		Duration of effective action 3-6 months	Najera and Ziam, 2002
			Lambda-Cyhalothrin (91465-08-6)				
ITNs	Capsule suspension	Application (kg ai/m2)	1.00E-05	1.50E-05			Najera and Ziam, 2002
IRS	Wettable powder	Application (kg ai/m2)	2.00E-05	3.00E-05			Najera and Ziam, 2002
ITNs	Capsule suspension	Application frequency (times/year)	3.00E+00	4.00E+00		Duration of effective action 3-4 months	Najera and Ziam, 2002
IRS	Wettable powder	Application frequency (times/year)	2.00E+00	4.00E+00		Duration of effective action 3-6 months	Najera and Ziam, 2002
ITNs	Capsule suspension	Percent ai	2.50E+00			Percent active ingredient in the insecticide formulation. For a liter.	WHO, 2004b
			Malathion (121-75-5)				
IRS	Wettable powder	Application (kg ai/m2)			2.00E-03		Najera and Ziam, 2002
IRS	Wettable powder	Application frequency (times/year)	4.00E+00	6.00E+00		Duration of effective action 2-3 months	Najera and Ziam, 2002
IRS	Wettable powder	Percent ai	5.00E+01			Percent active ingredient in the insecticide formulation	WHO, 2004b

Table D-2: Pesticide Use Data

Vector Management Practice	Pesticide Formulation	Parameter	Minimum Value	Maximum Value	Mean Value	Comments	Reference
Methoprene (40596-69-8)							
Growth Regulator	Emulsifiable concentrate	Application (kg ai/m2)	2.00E-06	4.00E-06			Najera and Ziam, 2002
Growth Regulator	Emulsifiable concentrate	Application frequency (times/year)					Najera and Ziam, 2002
Permethrin (52645-53-1)							
ITNs	Emulisfiable	Application (kg ai/m2)	2.00E-04	5.00E-04			Najera and Ziam, 2002
ITNs	Emulisfiable	Application frequency (times/year)	3.00E+00	4.00E+00		Duration of effective action 3-4 months	WHO, 2004a
ITNs	Emulisfiable	Percent ai	1.00E+01			Percent active ingredient in the insecticide formulation	WHO, 2004b
Pirimiphos-methyl (29232-93-7)							
IRS	Wettable powder and Emulsifiable concentrate	Application (kg ai/m2)	1.00E-03	2.00E-03			Najera and Ziam, 2002
IRS		Application frequency (times/year)	4.00E+00	6.00E+00		Duration of effection action 2-3 months	Najera and Ziam, 2002
Propoxur (114-26-1)							
IRS	Wettable powder	Application (kg ai/m2)	1.00E-03	2.00E-03			Najera and Ziam, 2002
IRS	Wettable powder	Application frequency (times/year)	2	4		Duration of effective action 3-6 months	Najera and Ziam, 2002
Temephos (3383-96-8)							
Larviciding	Emulsifiable concentrate, granule	Application (kg ai/m2)	5.60E-06	1.12E-05			Najera and Ziam, 2002

Table D-3. Benchmarks*

Exposure Pathway	Duration	Endpoint	Receptor	Value	Units	Reference	Comments
Alpha-cypermethrin (67375-30-8)							
dermal	acute	noncancer		5.0E+00	mg/kg/d	IPCS, 1992	
dermal	chronic	noncancer		5.0E+00	mg/kg/d	IPCS, 1992	
dermal	intermediate	noncancer		5.0E+00	mg/kg/d	IPCS, 1992	
inhalation	acute	noncancer		4.0E+00	mg/kg/d	IPCS, 1992	
inhalation	chronic	noncancer		4.0E+00	mg/kg/d	IPCS, 1992	
inhalation	intermediate	noncancer		4.0E+00	mg/kg/d	IPCS, 1992	
oral	acute	noncancer		2.0E-02	mg/kg/d	ATSDR, 2003b	
oral	chronic	noncancer		1.0E-02	mg/kg/d	U.S. EPA, 2005d	
oral	intermediate	noncancer		1.0E-02	mg/kg/d		chronic RfD
Bendiocarb (22781-23-3)							
dermal	acute	noncancer		5.0E-01	mg/kg/d	U.S. EPA, 1999b	
dermal	chronic	noncancer		1.3E-03	mg/kg/d	U.S. EPA, 1999b	
dermal	intermediate	noncancer		2.0E-01	mg/kg/d	U.S. EPA, 1999b	
inhalation	acute	noncancer		2.0E-03	mg/kg/d	U.S. EPA, 1999b	
inhalation	chronic	noncancer		2.0E-03	mg/kg/d	U.S. EPA, 1999b	
inhalation	intermediate	noncancer		2.0E-03	mg/kg/d	U.S. EPA, 1999b	
oral	acute	noncancer		1.3E-03	mg/kg/d	U.S. EPA, 1999b	
oral	chronic	noncancer		1.3E-03	mg/kg/d	U.S. EPA, 1999b	
oral	intermediate	noncancer		1.3E-03	mg/kg/d	U.S. EPA, 1999b	

Table D-3. Benchmarks*

Exposure Pathway	Duration	Endpoint	Receptor	Value	Units	Reference	Comments
Bifenthrin (82657-04-3)							
dermal	acute	noncancer		2.0E-01	mg/kg/d	U.S. EPA, 2003	
dermal	chronic	noncancer		2.0E-01	mg/kg/d	U.S. EPA, 2003	
dermal	intermediate	noncancer		2.0E-01	mg/kg/d	U.S. EPA, 2003	
inhalation	acute	noncancer		7.0E-03	mg/kg/d	U.S. EPA, 2003	
inhalation	chronic	noncancer		4.0E-03	mg/kg/d	U.S. EPA, 2003	
inhalation	intermediate	noncancer		7.0E-03	mg/kg/d	U.S. EPA, 2003	
oral	acute	noncancer		3.3E-02	mg/kg/d	U.S. EPA, 2003	
oral	chronic	noncancer		4.0E-03	mg/kg/d	U.S. EPA, 2003	
oral	intermediate	noncancer		7.0E-03	mg/kg/d	U.S. EPA, 2003	
Cyfluthrin (68359-37-5)							
dermal	acute	noncancer		3.0E+00	mg/kg/d	IPCS, 1997	
dermal	chronic	noncancer		3.0E+00	mg/kg/d	IPCS, 1997	
dermal	intermediate	noncancer		3.0E+00	mg/kg/d	IPCS, 1997	
inhalation	acute	noncancer		7.0E-04	mg/kg/d	U.S. EPA, 2005e	
inhalation	chronic	noncancer		2.0E-04	mg/kg/d	U.S. EPA, 2005e	
inhalation	intermediate	noncancer		2.0E-04	mg/kg/d	U.S. EPA, 2005e	
oral	acute	noncancer		2.0E-02	mg/kg/d	U.S. EPA, 2005e	
oral	chronic	noncancer		2.4E-02	mg/kg/d	U.S. EPA, 2005e	
oral	intermediate	noncancer		2.4E-02	mg/kg/d		chronic RfD

Table D-3. Benchmarks*

Exposure Pathway	Duration	Endpoint	Receptor	Value	Units	Reference	Comments
DDT (50-29-3)							
oral	acute	noncancer		5.0E-04	mg/kg/d	ATSDR, 2002	
oral	intermediate	noncancer		5.0E-04	mg/kg/d	ATSDR, 2002	
oral	chronic	noncancer		5.0E-04	mg/kg/d	U.S. EPA, 2005a	
inhalation	acute	noncancer		5.0E-04	mg/kg/d		oral benchmark
inhalation	intermediate	noncancer		5.0E-04	mg/kg/d		oral benchmark
inhalation	chronic	noncancer		5.0E-04	mg/kg/d		oral benchmark
dermal	acute	noncancer		5.0E-04	mg/kg/d		oral benchmark
dermal	intermediate	noncancer		5.0E-04	mg/kg/d		oral benchmark
dermal	chronic	noncancer		5.0E-04	mg/kg/d		oral benchmark
oral	chronic	cancer		3.4E-01	per mg/kg/d	U.S. EPA, 2005a	
inhalation	chronic	cancer		3.4E-01	per mg/kg/d	U.S. EPA, 1997	
dermal	chronic	cancer		3.4E-01	per mg/kg/d		oral benchmark
Deltamethrin (52918-63-5)							
dermal	acute	noncancer		1.0E+01	mg/kg/d	Barlow et al., 2001	
dermal	chronic	noncancer		1.0E+01	mg/kg/d	Barlow et al., 2001	
dermal	intermediate	noncancer		1.0E+01	mg/kg/d	Barlow et al., 2001	
inhalation	acute	noncancer		1.0E-02	mg/kg/d	U.S. EPA, 2004b	
inhalation	chronic	noncancer		1.0E-02	mg/kg/d	U.S. EPA, 2004b	
inhalation	intermediate	noncancer		1.0E-02	mg/kg/d	U.S. EPA, 2004b	
oral	acute	noncancer		1.0E-02	mg/kg/d	U.S. EPA, 2004b	
oral	chronic	noncancer		1.0E-02	mg/kg/d	U.S. EPA, 2004b	
oral	intermediate	noncancer		1.0E-02	mg/kg/d	U.S. EPA, 2004b	

Table D-3. Benchmarks*

Exposure Pathway	Duration	Endpoint	Receptor	Value	Units	Reference	Comments
Etofenprox (80844-07-1)							
dermal	acute	noncancer		4.0E-01	mg/kg/d	NYSDEC, 2005	
dermal	chronic	noncancer		3.7E-02	mg/kg/d	NYSDEC, 2005	
dermal	intermediate	noncancer		4.0E-01	mg/kg/d	NYSDEC, 2005	
inhalation	acute	noncancer		1.0E-01	mg/kg/d	NYSDEC, 2005	
inhalation	chronic	noncancer		1.0E-01	mg/kg/d	NYSDEC, 2005	
inhalation	intermediate	noncancer		1.0E-01	mg/kg/d	NYSDEC, 2005	
oral	acute	noncancer		3.7E-02	mg/kg/d	NYSDEC, 2005	
oral	chronic	noncancer		3.7E-02	mg/kg/d	NYSDEC, 2005	
oral	intermediate	noncancer		3.7E-02	mg/kg/d	NYSDEC, 2005	
oral, inhalation, dermal	chronic	cancer		5.1E-03	per mg/kg/d	NYSDEC, 2005	
Fenitrothion (122-14-5)							
dermal	acute	noncancer		1.0E-02	mg/kg/d	U.S. EPA, 1999c	
dermal	chronic	noncancer		1.0E-02	mg/kg/d	U.S. EPA, 1999c	
dermal	intermediate	noncancer		1.0E-02	mg/kg/d	U.S. EPA, 1999c	
inhalation	acute	noncancer		4.0E-04	mg/kg/d	U.S. EPA, 1999c	
inhalation	chronic	noncancer		4.0E-04	mg/kg/d	U.S. EPA, 1999c	
inhalation	intermediate	noncancer		4.0E-04	mg/kg/d	U.S. EPA, 1999c	
oral	acute	noncancer		1.3E-01	mg/kg/d	U.S. EPA, 1999c	
oral	chronic	noncancer		1.3E-03	mg/kg/d	U.S. EPA, 1999c	
oral	intermediate	noncancer		1.3E-03	mg/kg/d	U.S. EPA, 1999c	

Table D-3. Benchmarks*

Exposure Pathway	Duration	Endpoint	Receptor	Value	Units	Reference	Comments
Lambda-Cyhalothrin (91465-08-6)							
oral	acute	noncancer		5.0E-03	mg/kg/d	U.S. EPA, 2002a	
oral	intermediate	noncancer		1.0E-03	mg/kg/d		chronic RfD
oral	chronic	noncancer		1.0E-03	mg/kg/d	U.S. EPA, 2002a	
inhalation	acute	noncancer		8.0E-04	mg/kg/d	U.S. EPA, 2002a	
inhalation	intermediate	noncancer		8.0E-04	mg/kg/d	U.S. EPA, 2002a	
inhalation	chronic	noncancer		8.0E-04	mg/kg/d	U.S. EPA, 2002a	
dermal	acute	noncancer		1.0E-01	mg/kg/d	U.S. EPA, 2002a	
dermal	intermediate	noncancer		1.0E-01	mg/kg/d	U.S. EPA, 2002a	
dermal	chronic	noncancer		1.0E-01	mg/kg/d	U.S. EPA, 2002a	

Table D-3. Benchmarks*

Exposure Pathway	Duration	Endpoint	Receptor	Value	Units	Reference	Comments
Malathion (121-75-5)							
oral	acute	noncancer		1.4E-01	mg/kg/d	U.S. EPA, 2005b	
oral	intermediate	noncancer		3.0E-02	mg/kg/d		chronic RfD
oral	chronic	noncancer		3.0E-02	mg/kg/d	U.S. EPA, 2005b	
inhalation	acute	noncancer		2.6E-02	mg/kg/d	U.S. EPA, 2005b	
inhalation	intermediate	noncancer		2.6E-02	mg/kg/d	U.S. EPA, 2005b	
inhalation	chronic	noncancer		2.6E-02	mg/kg/d	U.S. EPA, 2005b	
dermal	acute	noncancer	adult	5.0E-01	mg/kg/d	U.S. EPA, 2005b	
dermal	acute	noncancer	child	5.0E-02	mg/kg/d	U.S. EPA, 2005b	
dermal	intermediate	noncancer	adult	5.0E-01	mg/kg/d	U.S. EPA, 2005b	
dermal	intermediate	noncancer	child	5.0E-02	mg/kg/d	U.S. EPA, 2005b	
dermal	chronic	noncancer	child	5.0E-02	mg/kg/d	U.S. EPA, 2005b	
dermal	chronic	noncancer	adult	5.0E-01	mg/kg/d	U.S. EPA, 2005b	
Methoprene (40596-69-8)							
dermal	acute	noncancer		1.0E+00	mg/kg/d	ATSDR, 2005	
dermal	chronic	noncancer		1.0E+00	mg/kg/d	ATSDR, 2005	
dermal	intermediate	noncancer		1.0E+00	mg/kg/d	ATSDR, 2005	
inhalation	acute	noncancer		2.5E+01	mg/kg/d	ATSDR, 2005	
inhalation	chronic	noncancer		2.5E+01	mg/kg/d	ATSDR, 2005	
inhalation	intermediate	noncancer		2.5E+01	mg/kg/d	ATSDR, 2005	
oral	acute	noncancer		4.0E-01	mg/kg/d	U.S. EPA, 1991	
oral	chronic	noncancer		4.0E-01	mg/kg/d	U.S. EPA, 1991	
oral	intermediate	noncancer		4.0E-01	mg/kg/d	U.S. EPA, 1991	

Table D-3. Benchmarks*

Exposure Pathway	Duration	Endpoint	Receptor	Value	Units	Reference	Comments
Permethrin (52645-53-1)							
oral	acute	noncancer		2.5E-01	mg/kg/d	U.S. EPA, 2005c	
oral	intermediate	noncancer		2.5E-01	mg/kg/d	U.S. EPA, 2005c	
oral	chronic	noncancer		2.5E-01	mg/kg/d	U.S. EPA, 2005c	
inhalation	acute	noncancer		1.1E-01	mg/kg/d	U.S. EPA, 2005c	
inhalation	intermediate	noncancer		1.1E-01	mg/kg/d	U.S. EPA, 2005c	
inhalation	chronic	noncancer		1.1E-01	mg/kg/d	U.S. EPA, 2005c	
dermal	acute	noncancer		5.0E+00	mg/kg/d	U.S. EPA, 2005c	
dermal	intermediate	noncancer		5.0E+00	mg/kg/d	U.S. EPA, 2005c	
dermal	chronic	noncancer		5.0E+00	mg/kg/d	U.S. EPA, 2005c	
oral	chronic	cancer		9.6E-03	per mg/kg/d	U.S. EPA, 2005c	
inhalation	chronic	cancer		9.6E-03	per mg/kg/d	U.S. EPA, 2005c	
dermal	chronic	cancer		9.6E-03	per mg/kg/d	U.S. EPA, 2005c	
Pirimiphos-methyl (29232-93-7)							
dermal	acute	noncancer		1.5E-02	mg/kg/d	U.S. EPA, 2001	
dermal	chronic	noncancer		7.0E-04	mg/kg/d	U.S. EPA, 2001	
dermal	intermediate	noncancer		7.0E-04	mg/kg/d	U.S. EPA, 2001	
inhalation	acute	noncancer		1.5E-02	mg/kg/d	U.S. EPA, 2001	
inhalation	chronic	noncancer		7.0E-04	mg/kg/d	U.S. EPA, 2001	
inhalation	intermediate	noncancer		7.0E-04	mg/kg/d	U.S. EPA, 2001	
oral	acute	noncancer		1.5E-02	mg/kg/d	U.S. EPA, 2001	
oral	chronic	noncancer		2.0E-04	mg/kg/d	U.S. EPA, 2001	
oral	intermediate	noncancer		2.0E-04	mg/kg/d	U.S. EPA, 2001	

Table D-3. Benchmarks*

Exposure Pathway	Duration	Endpoint	Receptor	Value	Units	Reference	Comments
Propoxur (114-26-1)							
dermal	acute	noncancer		1.0E+01	mg/kg/d	U.S. EPA, 1997c	
dermal	chronic	noncancer		1.0E+01	mg/kg/d	U.S. EPA, 1997c	
dermal	intermediate	noncancer		1.0E+01	mg/kg/d	U.S. EPA, 1997c	
inhalation	acute	noncancer		4.0E-03	mg/kg/d	U.S. EPA, 1997c	
inhalation	chronic	noncancer		4.0E-03	mg/kg/d	U.S. EPA, 1997c	
inhalation	intermediate	noncancer		4.0E-03	mg/kg/d	U.S. EPA, 1997c	
oral	acute	noncancer		5.0E-03	mg/kg/d	U.S. EPA, 1997c	
oral	chronic	noncancer		5.0E-03	mg/kg/d	U.S. EPA, 1997c	
oral	intermediate	noncancer		5.0E-03	mg/kg/d	U.S. EPA, 1997c	
oral, inhalation, dermal	chronic	cancer		3.7E-03	per mg/kg/d	U.S. EPA, 1997c	
Temephos (3383-96-8)							
oral	acute	noncancer		2.0E-01	mg/kg/d	U.S. EPA, 1997	subchronic HEAST (no adjustment for exposure)
oral	intermediate	noncancer		2.0E-01	mg/kg/d	U.S. EPA, 1997	
oral	chronic	noncancer		2.0E-02	mg/kg/d	U.S. EPA, 1997	
inhalation	acute	noncancer		3.0E-03	mg/kg/d	U.S. EPA, 2000d	based on oral data
inhalation	intermediate	noncancer		3.0E-03	mg/kg/d	U.S. EPA, 2000d	based on oral data
inhalation	chronic	noncancer		3.0E-03	mg/kg/d	U.S. EPA, 2000d	based on oral data
dermal	acute	noncancer		3.0E-03	mg/kg/d	U.S. EPA, 2000d	based on oral data
dermal	intermediate	noncancer		3.0E-03	mg/kg/d	U.S. EPA, 2000d	based on oral data
dermal	chronic	noncancer		3.0E-03	mg/kg/d	U.S. EPA, 2000d	based on oral data

*These values are shown to 2 significant figures

Annex D References

Short Reference	Reference
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Glossary

Molecular Weight: The molecular weight, also called formula weight, is the sum of the atomic weights of all the atoms in a molecule (http://www.answers.com/topic/molecular-mass). The molecular weight is a chemical-specific property and is important for the determination of other properties such as the Henry's Law Constant.

Solubility: Solubility is the amount of mass of a compound that will dissolve in a unit volume of solution (http://iaspub.epa.gov/trs/trs_proc_qry.alphabet?p_term_nm=S&p_reg_auth_id=1&p_data_id=79501&p_version=1). Aqueous solubility is an extremely important chemical property because it plays a major role in assessing the migration and fate of chemicals in the environment. In general, a higher solubility is quickly distributed by the hydrologic cycle through biodegradation, where a chemical rapidly and completely dissolves in water and has a low affinity for adsorption to solids. A highly water soluble chemical tends to leach faster (i.e., be mobile in soil) and is more easily degraded by microorganisms. In contrast, chemicals with low solubility have a strong partitioning to the subsurface solids, soil, or sediment. Therefore, a chemical that is highly soluble will be easily transported along with the general flow of water and will demonstrate limited bioconcentration (http://www.crwr.utexas.edu/gis/gisenv98/class/risk/lecture/Lect4/Fate.html#solubility; http://ca.water.usgs.gov/mtbe/fs20396/; http://www.epa.gov/opptsfrs/publications/OPPTS_Harmonized/830_Product_Properties_Test_Guidelines/Series/830-7560.pdf).

Henry's Law Constant: The Henry's Law Constant characterizes the equilibrium distribution of dilute concentrations of volatile, soluble chemicals between gas and liquid. (http://www.epa.gov/ATHENS/learn2model/part-two/onsite/esthenry.htm). The Henry's Law Constant can also be described as the ratio of concentration of a volatile chemical in air to concentration in an aqueous solution (at equilibrium). Henry's Law Constant is important because it can be used as a general indicator of volatility of a chemical, and to estimate amount of a volatile chemical available for inhalation during activities such as spraying of pesticide inside of a residence (http://mepas.pnl.gov/FRAMESV1/physical.html). In general, a compound with a Henry's Law Constant value of 0.05 or larger would be very volatile from water (http://ca.water.usgs.gov/mtbe/fs20396/) while a low Henry's Law Constant value indicates that volatilization from water is slow.

Vapor Pressure: Vapor pressure is the pressure exerted by a vapor in equilibrium with its solid or liquid phase (i.e., it is the pressure at which a liquid will vaporize at a given temperature) (http://www.answers.com/topic/vapor-pressure and http://www.ce.utexas.edu/prof/kinnas/319LAB/Book/fr_book.html). A chemical's vapor pressure is important with respect to the rate at which it will volatilize or evaporate (i.e.,

the transfer of a chemical from water, soil, or plant surfaces to air). Volatilization occurs when pesticide surface residues change from solid or liquid to a gas and each pesticide has a characteristic tendency to become a gas, which is called its vapor pressure. It is also useful in conjunction with other chemical properties (e.g., solubility in water) for estimating partition coefficients between air and water (http://www.crwr.utexas.edu/gis/gisenv98/class/risk/lecture/Lect4/Fate.html#vapor). Once a pesticide is converted to a vapor, the pesticide vapors diffuse a very short distance and then are moved away with the air current (http://extoxnet.orst.edu/faqs/pesticide/pestfate.htm). Vapor pressure is a significant property because during the spraying of a household, a person would be exposed to the volatilized chemical and therefore be at risk of exposure.

Octanol-Water Partition Coefficient: The octanol-water partition coefficient is the ratio of the concentration of a chemical in octanol and in water at equilibrium and at a specified temperature. The octanol-water partition coefficient provides a thermodynamic measure of the tendency of the substance to prefer a nonaqueous or oily milieu rather than water (i.e., its hydrophilic/lipophilic balance) (http://www.wiley.com/WileyCDA/WileyTitle/productCd-0471973971.html). The octanol-water partition coefficient is a chemical-specific property that characterizes a chemical's affinity for water or lipids. This parameter is used to help determine the fate of chemicals in the environment (http://toxics.usgs.gov/definitions/kow.html) and it has been shown to be correlated to water solubility, soil/sediment sorption coefficient, and bioconcentration (http://www.epa.gov/opptsfrs/publications/OPPTS_Harmonized/830_Product_Properties_Test_Guidelines/Series/830-7560.pdf). Specifically, a chemical with a high octanol-water partition coefficient or a compound that is more soluble in octanol (more hydrophobic and lipophilic) is expected to partition out of the water and to bind to soil, suspended particulate matter, or into lipophilic tissue.

Reaction Half-Life: The half-life of a substance is simply the time required for half of the amount originally present to react or degrade in a specified media. (http://www.psigate.ac.uk/newsite/reference/plambeck/chem2/p02143.htm). The half-life is a measure of persistence, which is the ability of a chemical to resist degradation in various media, such as air, soil, water and sediment.

Reaction Half-Life in Water: This property is significant because chemicals with long half-lives, or persistence times, in water have a high potential for accumulation in this medium and also for uptake by living organisms. This property is important for the discussion of the risk from the disposal of a pesticide because pesticides with greater half-lives in water that are disposed of improperly may end up in the surface or groundwater and may adversely impact the environment and human health.

Reaction Half-Life in Air: The reaction half-life in air is a measure of a chemical's persistence in the atmosphere and is significant because a chemical with a long half-life

in the air has a greater potential to be inhaled. This property is especially important for the risk from spraying the inside of a household with insecticide.

Reaction Half-Life in Soil: The reaction half-life in soil is important because chemicals with long persistence times in soil or sediments have a high potential for accumulation in the medium and also for uptake by living organisms. In general, the longer the half-life in soil, the greater the potential for pesticide movement. A pesticide with a half-life greater than 21 days may persist long enough to leach or move with surface runoff before it degrades (http://www.agf.gov.bc.ca/pesticides/c_2.htm). This property is important when discussing the disposal of pesticides because pesticides with a greater half-life in soil will persist longer and will therefore have the ability to leach and present a highly likelihood of human exposure.

Annex E: Pesticide Profiles

Acronym List for Toxicological Profiles

ATSDR	Agency for Toxic Substances and Disease Registry
CSF	cancer slope factor
EC_{50}	median effective concentration (concentration that is lethal to 50% of organisms)
EPA	U.S. Environmental Protection Agency
EXTOXNET	Extension TOXicology NETwork
HSDB	Hazardous Substances Data Bank
IPCS	International Program on Chemical Safety
IRIS	Integrated Risk Information System
LC_{50}	lethal concentration 50 (concentration that is lethal to 50% of organisms)
LD_{50}	lethal dose 50 (dose that is lethal to 50% of organisms)
MRL	minimal risk level
LOAEL	lowest observed adverse effect level
NOAEL	no observed adverse effects level
NOEL	no observed effect level
PAN	Pesticide Action Network
RfD	Reference Dose

SF	safety factor
UF	uncertainty factor
WHO	World Health Organization

Profile for Alpha-Cypermethrin:

CAS Registry Number 67375-30-8

Summary of Insecticide

Chemical History

Alpha-cypermethrin is a highly active synthetic pyrethroid insecticide used to control a wide variety of pests in agricultural and public health applications. It is similar to the natural insecticide pyrethrum, which comes from chrysanthemums; however, it is more effective and longer lasting (ATSDR, 2003; IPCS, 1992). Alpha-cypermethrin is available in technical grade formulation, emulsifiable concentrate, ultra-low-volume formulation, suspension concentrate, and in mixtures with other insecticides (HSDB, 2005; IPCS, 1992). For mosquito control, it is used in bed nets and other materials that are dipped in alpha-cypermethrin to protect the user (WHO, 1997, 1998). It is considered one of the best insecticides for impregnation of traps and screens (WHO, 1997). Alpha-cypermethrin is not currently registered for use in the United States (HSDB, 2005), but cypermethrin is.

Alpha-cypermethrin is of low risk to humans when used at levels recommended for its designed purpose (ATSDR, 2003; HSDB, 2005). However, as a synthetic pyrethroid, alpha-cypermethrin exhibits its toxic effects by affecting the way the nerves and brain normally function by interfering with the sodium channels of nerve cells (ATSDR, 2003; HSDB, 2005). It has moderate acute toxicity and is a suspected endocrine disruptor but does not inhibit cholinesterase (PAN, 2005). EPA has not classified synthetic pyrethroids, including alpha-cypermethrin, as endocrine disruptors. Typical symptoms of acute exposure are irritation of skin and eyes, headaches, dizziness, nausea, vomiting, diarrhea, and excessive salivation and fatigue. Inhaled alpha-cypermethrin has been shown to cause cutaneous paraesthesia or a burning, tingling, or stinging of the skin. However, these effects are generally reversible and disappear within a day of removal from exposure (ATSDR, 2003; HSDB, 2005; PAN, 2005). Alpha-cypermethrin is harmful if swallowed (MSDS, n.d.). Inhalation and dermal exposure are the most likely human exposure routes (HSDB, 2005). Environmental levels of significance are unlikely if alpha-cypermethrin is applied at recommended rates (IPCS, 1992).

Description of Data Quality and Quantity

Comprehensive reviews on the toxicity of alpha-cypermethrin are not widely available but include the following:

- Toxicological Profile for Pyrethrin and Pyrethroids (ATSDR, 2003)
- Environmental Health Criteria 142: Alpha- Cypermethrin (IPCS, 1992)

EPA and ATSDR have developed quantitative oral human health benchmarks (EPA's chronic RfD and ATSDR's acute oral MRL) for cypermethrin. Alpha-cypermethrin makes up one quarter of the racemic mixture cypermethrin and has a similar mode of action. Alpha-cypermethrin is also similar to cypermethrin with regard to the signs of intoxication, target organs effects, and metabolic pathways (IPCS, 1992).

Summary Table

Duration	Route	Benchmark Value	Units	Endpoint	Reference
Acute, Intermediate, Chronic	Inhalation	4	mg/kg/day	Inhalation NOAEL in rats with UF of 100 applied	
Acute	Oral	0.02	mg/kg/day	Acute oral MRL for cypermethrin based on neurological effects in rats with UF of 1000 applied	ATSDR (2003)
Intermediate	Oral	0.01	mg/kg/day	Adopt chronic RfD as intermediate duration	
Chronic	Oral	0.01	mg/kg/day	Chronic oral RfD for cypermethrin based on neurological effects in dogs with UF of 100 applied	U.S. EPA (2005)
Acute, Intermediate, Chronic	Dermal	5	mg/kg/day	Dermal NOAEL in rats with UF of 100 applied	

For inhalation exposure, a NOAEL of 400 mg/m^3 (447 mg/kg/day)[13] was identified for neurological and respiratory effects in rats exposed to alpha-cypermethrin via inhalation for 4 hours (IPCS, 1992). An uncertainty factor of 100 to account for intra- and interspecies variation was applied, for an inhalation benchmark of 4 mg/kg/day. This value is appropriate for all exposure durations.

Due to limited low-dose oral data for alpha-cypermethrin, health benchmarks for cypermethrin were used and are expected to be protective of human health. The acute oral MRL for cypermethrin of 0.02 mg/kg/day is based on a LOAEL of 20 mg/kg for neurological effects (altered gait and decreased motor activity) in rats with an uncertainty factor of 1,000 applied. Long-Evans rats were given single gavage doses of up to 120 mg/kg cypermethrin. Motor activity and FOB were assessed at 2 and 4 hours post-dosing. A NOAEL was not identified (ATSDR, 2003). The chronic oral RfD for cypermethrin of 0.01 mg/kg/day is based on a NOEL of 1 mg/kg/day for systemic effects with an

[13] *Conversion between mg/m^3 and mg/kg/day assumes, for Fischer-344 rats, an average body weight of 0.152 kg and inhalation rate of 0.17 m^3/day (U.S. EPA, 1988).*

uncertainty factor of 100 applied. Beagle dogs were dosed with up to 15 mg/kg/day cypermethrin in corn oil for 52 weeks. During the first week, increased vomiting was observed in dogs at all dose levels. Additionally, throughout the study all dogs passed liquid feces; however, the incidence was 10- and 30-fold higher in the 5 and 15 mg/kg/day groups, respectively. The NOEL identified for this study was 1 mg/kg/day (U.S. EPA, 2005).

For dermal exposure, a NOAEL of 500 mg/kg/day was identified in rats dermally exposed to alpha-cypermethrin once for 24 hours (IPCS, 1992). An uncertainty factor of 100 to account for intra- and interspecies variation was applied, for a dermal benchmark value of 5 mg/kg/day. This value is appropriate for all exposure durations.

Insecticide Background

CASRN:	67375-30-8
Synonyms:	alfamethrin, alphamethrin, alphacypermethrin, alpha-cypermethrin, alfa-cipermetrina, alfacypermetrin, alfa cipremetrin,[1alpha(S*),3alpha]-(+ -)-Cyano(3-phenoxyphenyl)methyl 3-(2,2-dichloroethenyl)- 2,2-dimethylcyclopropanecarboxylate, (1R cis S) and (1S cis R) Enantiomeric isomer pair of alpha-cyano-3-phenoxybenzyl-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropane carboxylate, Pesticide Code 209600(S)-alpha-cyano-3-phenoxybenzyl-(1R)-cis-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylate and (R)-alpha-cyano-3-phenoxybenzyl-(1S)-cis-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylate, WL 85871, cyano(3-phenoxyphenyl)methyl 3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylate (+)-cis isomer, alphametrin, numerous other systematic and non-systematic names (HSDB, 2005; PAN 2005; ATSDR, 2003; MSDS, n.d.)
Chemical Group:	pyrethroid (PAN, 2005)
Registered Trade Names:	Bestox, Fastac, Concord, Dominex, Fendona, Fendona 1.5 SC, Fendona 10 SC, Fendonal WP, Renegade (HSDB, 2005, IPCS, 1992, WHO, 2002), Tenopa SC (alphacypermethrin + flufenoxuron) (HSDB, 2005; PAN 2005; ATSDR, 2003; MSDS, n.d.)

Usage

Alpha-cypermethrin is a pyrethroid insecticide used to combat a wide variety of chewing and sucking insects on field crops, fruits and vegetables, and in forestry uses. It may be applied to crops as either a curative or preventative treatment. Alpha-cypermethrin is also

used in public health applications to control mosquitoes, flies, and other pests. For animal husbandry it is used as an ectoparaciticide and to control flies (HSDB, 2005; IPCS, 1992). Alpha-cypermethrin belongs to the pyrethroid class of insecticides, which have long been used to control mosquitoes, human lice, beetles, and flies (ATSDR, 2003). For mosquito protection, it is used in bed nets and other materials that are dipped into the alpha-cypermethrin to protect the user. Alpha-cypermethrin has been available since 1983 (IPCS, 1992); however, it not currently registered for use in the United States (HSDB, 2005).

Formulations and Concentrations

Alpha-cypermethrin is available in technical grade, emulsifiable concentrates, wettable powder, suspension concentrates, ultra-low-volume liquids, tablets, and in mixtures with other insecticides (HSDB, 2005; IPCS, 1992). Technical grade alpha-cypermethrin is greater than 90 percent pure (HSDB, 2005). Common formulations of alpha-cypermethrin include Fastac, which is available as an emulsifiable concentrate (20–100 g/L), a wettable powder (50 g/kg), a suspension concentrate (15–250 g/L), and an ultra-low-volume liquid (6–15 g/L); and Fendona and Renegade, which are available as an emulsifiable concentrate (50 or 100 g/L), a suspension concentrate (250 g/L), and a wettable powder (50 g/kg). Alpha-cypermethrin is combined with other active ingredients to form other products (IPCS, 1992). WHO has indicated that the content of alpha-cypermethrin in the formulated products must be declared and shall not exceed the listed standards. Technical grade alpha-cypermethrin must have no less than 910 g/kg alphacypermethrin cis 2 ([IR cis] S and [IS cis] R isomers), and the combined content of the cis and trans isomers of alpha-cyano-3-phenoxybenzyl-2,2-dimethyl-3-(2,2-dichlorovinyl-) cyclopropanecarboxylate must be at least 975 g/kg. No more than 1 g/kg of volatile hydrocarbon solvent and 1 mg/kg of triethylamine is permitted. The aqueous suspension concentrate should contain alphacypermethrin cis 2 ([IR cis] S and [IS cis] R isomers) as follows: up to 25 g/kg, ± 15 percent of the declared content; 25 to 100 g/kg, ± 10 percent of the declared content. The alphacypermethrin cis 1:cis 2 isomer ratio must be lower than 5:95 (WHO, 1999).

Shelf Life

Alpha-cypermethrin is stable in acidic and neutral environments. However, it hydrolyzess at pH 12–13 and decomposes at temperatures greater than 220 °C. For practical purposes, field studies have indicated that it is stable to sunlight (IPCS, 1992). It is not compatible with strong oxidizing agents (MSDS, n.d.).

Degradation Products

Based on its structure, alpha-cypermethrin is expected to readily biodegrade in the environment. However, in two tests it did not degrade and therefore cannot be considered readily biodegradable. One of the major transformation products in the microbial

transformation of technical alpha-cypermethrin is 3-phenoxybenzoic acid, which is then transformed to 4-hydroxy-3-phenoxybenzoic acid (IPCS, 1992).

Environmental Behavior

Fate and Transport in Terrestrial Systems

Based on its Koc value, alpha-cypermethrin binds tightly to soil, making it almost immobile in most soil types. In moist soil, volatilization is expected to be the major fate process; however its bond to soil lessens this effect. Volatilization is not a major fate process for dry soil. Biodegradation by environmental organisms in non-sterile soil and by sunlight is expected (HSDB, 2005; IPCS, 1992). Studies have shown that within 2 weeks of treatment with 0.5 kg ai/ha (active ingredient per hectare) of a diluted alpha-cypermethrin emulsifiable concentrate formulation in sandy-clay soil, residues of alpha-cypermethrin were 50 percent less. After 1 year, they were below detection or < 0.01 mg/kg. Similar results were seen after a second and third application to the site indicating that alpha-cypermethrin did not build up in the surface soil. Additionally, no leaching to subsurface soils was observed. Alpha-cypermethrin also does not build up in peat soils (IPCS, 1992).

Fate and Transport in Aquatic Systems

Alpha-cypermethrin binds tightly to suspended solids and sediments in water. It is expected to volatilize from water; however, volatilization is lessened by alpha-cypermethrin's bond with soil. Reported volatilization half-lives are 8 days for a river models and 65 days for a lake model. If adsorption is taken into consideration, the estimated volatilization half-life in a pond model is 125 years. Estimated hydrolysis half-lives are 36 and 4 years at pH 7 and 8 respectively. Alpha-cypermethrin is also expected to undergo photodecomposition. Based on its bioconcentration factor, alpha-cypermethrin has a high potential to bioconcentrate in aquatic organism; however, its potential may actually be lower than this suggests because of the ability of aquatic organisms to rapidly metabolize alpha-cypermethrin (HSDB, 2005).

Human Health Effects

Acute Exposure

Effects/Symptoms

Limited data exist on the acute toxicity of alpha-cypermethrin in humans (IPCS, 1992; HSDB, 2005). Occupationally exposed workers reported only mild skin irritation (IPCS, 1992). The main effects reported from acute exposure to alpha-cypermethrin in humans include skin rashes, eye irritation, itching and burning sensation on exposed skin, and paraesthesia (a result of the direct action of this type of pyrethroid on sensory nerve endings, causing repeated firings in these fibers). Acute inhalation exposures may cause upper and lower respiratory tract irritation. Ingestion of alpha-cypermethrin is also

harmful (HSDB, 2005; MSDS, n.d.). No acute poisonings have been reported (IPCS, 1992).

In rodents, alpha-cypermethrin has moderate to high oral toxicity (HSDB, 2005; IPCS, 1992). Oral LD_{50} values in rats and mice vary greatly and depend on the formulation, concentration, and the vehicle (IPCS, 1992). Acute oral LD_{50} values for technical alpha-cypermethrin range from 79 to 400 mg/kg (in corn oil) in rats (HSDB, 2005; IPCS, 1992; MSDS, n.d.). Although the LD_{50} of 80 mg/kg is considered representative, higher values have been reported. In mice, the reported acute oral LD_{50} of technical alpha-cypermethrin is 35 mg/kg (in corn oil). Oral LD_{50} values for formulated alpha-cypermethrin in rats range from 101 to 174 mg/kg for an emulsifiable concentrate formulation (100 g/L), while 1,804 mg/kg was reported for a suspension concentrate formulation (100 mg/L) and 5,838 mg/kg for an ultra-low-volume liquid formulation (15 g/L) (IPCS, 1992). Clinical signs reported in orally exposed animals are associated with central nervous system activity and included ataxia; gait abnormalities; choreoathetosis; "tip-toe" walk; and increased salivation, lacrimation, piloerection, tremor, and clonic convulsions. Acute dermal exposures are minimally irritating to the skin and eyes of rabbit skin. However, some formulations can cause severe eye irritation that includes corneal opacity and iris damage. Stimulation of the sensory-nerve endings of the skin has been observed in guinea pigs. Reported dermal LD_{50} values of greater than 2,000 mg tech/kg are reported for rats and rabbits (HSDB, 2005; IPCS, 1992). No mortality or signs of toxicity were observed in rats or mice after single dermal applications of up to 500 mg/kg or 4-hour inhalation exposure of mice to 400 mg/m^3. Alpha-cypermethrin is not a dermal sensitizer in guinea pigs (IPCS, 1992).

Treatment

Pyrethroid insecticides and their metabolites can be detected in blood and urine; however, the methods are not practical to use given how quickly these compounds are broken down in the body (ATSDR, 2003). Alpha-cypermethrin poisoning should be treated the same as a pyrethroid poisoning. There are no antidotes for alpha-cypermethrin exposure. Treatment is supportive and depends on the symptoms of the exposed person. Decontamination is all that is necessary for most exposures. If a person exhibits signs of typical pyrethroid toxicity following alpha-cypermethrin exposure (nausea, vomiting, shortness of breath, tremors, hypersensitivity, weakness, burning, or itching), they should immediately remove any contaminated clothing. Any liquid contaminant on the skin should be soaked up and the affected skin areas cleaned with alkaline soap and warm water. The application of topical vitamin E helps to relieve the symptoms of paraesthesia. Eye exposures should be treated by rinsing with copious amounts of saline or room temperature water for at least 15 minutes. Contact lenses should be removed. Medical attention should be sought if irritation, pain, swelling, lacrimation, or photophobia persists. The treatment of ingestion exposures is mostly symptomatic and supportive. Care should be taken to monitor for the development of hypersensitivity reactions with respiratory distress. Gastric decontamination is recommended if large amounts have been

very recently ingested, and oral administration of activated charcoal and cathartic are recommend for ingestion of small amounts or if treatment has been delayed. Vomiting should not be induced following ingestion exposures, but the mouth should be rinsed. The person should be kept calm and medical attention should be sought as quickly as possible. For inhalation exposures, removal to fresh air and monitoring for breathing difficulties, respiratory tract irritation, bronchitis, and pneumonitis are recommended. Oxygen should be administered as necessary (PAN, 2005; HSDB, 2005).

Chronic Exposure

Noncancer Endpoints

Little data are available for humans following chronic exposures to alpha-cypermethrin. Chronic exposure to pyrethrins may cause hypersensitivity pneumonitis characterized by chest pain, cough, dyspnea, and bronchospasm. Because alpha-cypermethrin belongs to this class of chemicals, similar effects may be expected (HSDB, 2005).

Chronic toxicity data are also lacking in animals. No animal data are available for long-term toxicity, reproductive toxicity, teratogenicity, or immunotoxicity (HSDB, 2005; IPCS, 1992). However, chronic toxicity data are available for cypermethrin, including rodent multigenerational reproduction, embryotoxicity, and teratogenicity studies. At doses that produced systemic toxicity, no effects on reproductive parameters or fetal development were observed. Therefore, it is likely that alpha-cypermethrin would also cause no reproductive or developmental effects in rodents because it is a component of cypermethrin. Available data do not indicate that alpha-cypermethrin is mutagenic (IPCS, 1992).

Cancer Endpoints

No data are available on the carcinogenic potential of alpha-cypermethrin (IPCS, 1992).

Toxicokinetics

Like other pyrethroid insecticides, orally administered alpha-cypermethrin, is absorbed via the intestinal tract of mammals, and dermally applied doses are absorbed through intact skin. Little or none is absorbed by inhalation exposures (HSDB, 2005). Most pyrethroids are rapidly broken down by liver enzymes and their metabolites are quickly excreted (HSDB, 2005). The metabolism of synthetic pyrethroids in mammals is generally through hydrolysis, oxidation, and conjugation. Metabolism of alpha-cypermethrin occurs by the cleavage of the ester bond. Studies in rats show that the phenoxybenzyl alcohol and cyclpropan carboxylic ac parts of the molecule are conjugated with sulfate and glucuronide, respectively, before being excreted in urine. Esteric hydrolysis and oxidative pathways occur in rats, rabbits, and humans with esteric hydrolysis being the predominant pathway in humans and rabbits (IPCS, 1992). Within 24 hours of an oral dose of 0.25–0.75 mg in humans, 43 percent was excreted in the urine as free of conjugated cis-cyclprpane carboxlic acid (HSDB, 2005; IPCS, 1992). Orally administered alpha-cypermethrin is eliminated in the urine of rats as the sulfate conjugate

of 3-(4-hydroxyphenoxy) benzoic acid. In the faces it is eliminated partly as unchanged compound. Alpha-cypermethrin levels in tissues are low except for fatty tissues. The reported half-life for elimination from fat is 2.5 days for the first phase of elimination and 17 to 26 days for the second phase (IPCS, 1992).

Ecological Effects

Acute Exposure

Toxicity in Non-Targeted Terrestrial Organisms

Alpha-cypermethrin, like other pyrethroids, is very unlikely to harm terrestrial organisms other than its targets (e.g., mosquitoes and other pests). No toxicity data are available for alpha-cypermethrin in birds. However, cypermethrin has a very low toxicity in birds with acute oral LD_{50} values of greater than 2,000 mg/kg body weight. In feed, the reported LC_{50} values are greater than 10,000 mg/kg diet (IPCS, 1992). As with other pyrethroid insecticides, alpha-cypermethrin is extremely toxic to honey bees. The reported 24-hour oral LD_{50} for alpha-cypermethrin emulsifiable concentrate is 0.13 µg/bee and the 24-hour oral LD_{50} for alpha-cypermethrin in acetone was 0.06 µg/bee. The reported dermal LD_{50}s are 0.03 µg/bee for technical alpha-cypermethrin and 0.11 µg/bee for emulsifiable concentrate (IPCS, 1992). The very high toxicity in bees was not observed in the field, likely as a result of the repellent effect of alpha-cypermethrin, which would limit exposure (IPCS, 1992; HSDB, 2005). Mortality was seen in only 15 percent of honey bees exposed to flowers treated with an emulsifiable concentrate formulation within 48 hours. Other studies using oil-enhanced suspension concentrate formulations showed similarly low toxicity. Additionally, a similar pattern of toxicity was seen in leaf-cutting bees. The toxicity of alpha-cypermethrin to earthworms, Carabid beetles, Syrphid larvae and neuropteran larvae is low while it is relatively high for Linyphiid spiders and Coccinellids (IPCS, 1992).

Toxicity in Non-Targeted Aquatic Systems

Alpha-cypermethrin is very toxic to fish under laboratory conditions, with emulsifiable concentrate formulations being the most toxic (IPCS, 1992); however, these effects are not seen in field studies. Therefore, the hazard to fish from contamination of waterbodies due to overspraying and drift is negligible (IPCS, 1992). Depending on the formulation, the reported 96-hour LC_{50} values range from 0.7 to 350 µg/L (IPCS, 1992). For rainbow trout, the reported 96-hour LC_{50} values range from 2.8 to 350 µg/L (HSDB, 2005; IPCS, 1992). The emulsifiable concentrate formulation is 10 to 70 times more toxic to rainbow trout than the wettable powder or suspension concentrate formulations. However, in field studies, the 14-day LC_{50} for rainbow trout was just 29 g ai/ha for emulsifiable concentrate formulations and greater than 1,000 g ai/ha for suspension concentrate, wettable powder, and micro-encapsulated formulations. For fathead minnows, the reported 96-hour LC_{50} value for technical alpha-cypermethrin was 0.93 µg/L, while the reported 96-hour LC_{50} values for carp range from 0.8 to 11 µg/L depending on the formulation. For fish in the early stages of life, alpha-cypermethrin and cypermethrin toxicity are similar (IPCS,

1992). Alpha-cypermethrin has the potential to accumulate in fish, with a bioconcentration factor of 990 (HSDB, 2005). It has also been shown to be highly toxic to some aquatic invertebrates and aquatic insects (IPCS, 1992).

Chronic Exposure

Due to low rate of application and low persistence of alpha-cypermethrin in both terrestrial and aquatic environments, serious adverse effects are not anticipated from chronic exposures (HSDB, 2005). The hazard of alpha-cypermethrin to fish and aquatic invertebrates is in its acute toxicity. There is no evidence of chronic exposure causing cumulative effects (IPCS, 1992).

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Profile for Bendiocarb:

CAS Registry Number 22781-23-3

Summary of Insecticide

Chemical History

Bendiocarb is a broad spectrum carbamate insecticide first registered in the United States in 1980 for use to control a wide variety of nuisance and disease vector insects, such as mosquitoes, flies, wasps, ants, fleas, cockroaches, silverfish, and ticks. It is also effective against a variety of agricultural insects and to treat seeds against pests (U.S. EPA, 1999a, 1999b; EXTOXNET, 1996). The registration for bendiocarb was voluntarily canceled in 1999 (U.S. EPA, 1999a).

Bendiocarb exhibits its toxic effects through fast-acting, but reversible, cholinesterase inhibition. It has moderate toxicity in mammals (WHO/FAO, 1982), moderate toxicity in birds, and moderate to high toxicity in fish (EXTOXNET, 1996). In humans, symptoms of poisoning are neurological and include headache, blurred vision, nausea, vomiting, giddiness, slurred speech, excessive sweating and salivation, chest tightness, and twitching muscles (WHO/FAO, 1982). Bendiocarb pesticides were formulated as dusts, granules, wettable powders, pellets, and ultra low volume (ULV) sprays (U.S. EPA, 1999a; EXTOXNET, 1996).

Description of Data Quality and Quantity

Review data for bendiocarb are limited. Relevant resources include

- Bendiocarb: Revised HED Chapter for the Reregistration Eligibility Decision (RED) Document (U.S. EPA, 1999b)
- Data Sheet on Pesticides No. 52: Bendiocarb (WHO/FAO, 1982)
- Pesticide Information Profile for Bendiocarb (EXTOXNET, 1996).

EPA has developed quantitative human health benchmarks (acute and chronic oral RfDs and short-, intermediate-, and long-term dermal and inhalation benchmarks) for bendiocarb.

Summary Table

Duration	Route	Benchmark Value	Units	Endpoint	Reference
Acute, Intermediate, Chronic	Inhalation	0.002	mg/kg/day	Inhalation NOAEL (0.00018 mg/L) for neurological effects with UF of 100 applied	U.S. EPA (1999b)
Acute, Intermediate, Chronic	Oral	0.00125	mg/kg/day	Acute and chronic oral RfDs based on neurological effects; adopt chronic for intermediate duration	U.S. EPA (1999b)
Acute	Dermal	0.5	mg/kg/day	Dermal NOAEL for neurological effects of 50 mg/kg/day with UF of 100 applied	U.S. EPA (1999b)
Intermediate	Dermal	0.2	mg/kg/day	Dermal LOAEL for neurological effects of 50 mg/kg/day with UF of 300 applied	U.S. EPA (1999b)
Chronic	Dermal	0.00125	mg/kg/day	Oral NOAEL for neurological effects of 0.125 mg/kg/day with UF of 100 applied	U.S. EPA (1999b)

For inhalation exposure, a NOAEL of 0.00018 mg/L (0.2 mg/kg/day)[14] was identified for whole blood cholinesterase inhibition in rats exposed to bendiocarb via inhalation for 6 hours per day, 5 days per week, for 90 days (Coombs et al., 1995). An uncertainty factor of 100 to account for interspecies and intrahuman variation was applied, for an inhalation benchmark of 0.002 mg/kg/day. This value is appropriate for all exposure durations (U.S. EPA, 1999b).

The acute and chronic oral RfDs of 0.00125 mg/kg/day were based on a NOAEL of 0.125 mg/kg for whole blood cholinesterase inhibition (about 25 percent) in rats exposed via gavage five days per week for two weeks (EPA MRID No. 00059269, no additional citation provided), with an uncertainty factor of 100 applied (10 each for interspecies and intrahuman variability). This value was also adopted for intermediate exposure (U.S. EPA, 1999b).

For acute dermal exposures, a NOAEL of 50 mg/kg/day in rats for whole blood cholinesterase inhibition from a single exposure was identified (EPA MRID No. 00122308, no additional citation provided) and an uncertainty factor of 100 was applied (10 each for interspecies and intrahuman variability). For intermediate dermal exposures, a LOAEL of 50 mg/kg/day for whole blood cholinesterase inhibition from repeated

[14] Conversion between mg/m^3 and mg/kg/day assumes, for Wistar rats, an average body weight of 0.187 kg and inhalation rate of 0.2 m^3/day (U.S. EPA, 1988).

dermal exposures was identified (EPA MRID No. 00122308, no additional citation provided) and an uncertainty factor of 300 was applied (10 each for interspecies and intrahuman variability and 3 for the use of a LOAEL). For chronic dermal exposures, the NOAEL that was used to develop the oral RfDs was used with an uncertainty factor of 100 applied (10 each for interspecies and intrahuman variability) (U.S. EPA, 1999b).

Insecticide Background

CAS #:	22781-23-3
Synonyms:	2,3-isopropylidenedioxyphenyl methylcarbamate (EXTOXNET, 1996), Ent-27695; OMS 1394; (WHO/FAO, 1982), 1,3-Benzodioxol-4-ol, 2,2-dimethyl-, methylcarbamate , 1,3-Benzodioxole, 2,2-dimethyl-4-(N-methylamino-carboxylato)- , 105201 (U.S. EPA PC Code) , 1924 (CA DPR Chem Code) , 2,2-Dimethyl-1,3-benzodioxol-4-yl methylcarbamate, Carbamic acid, methyl-, 2,3-(dimethylmethylenedioxy)-phenyl ester, Carbamic acid, methyl-, 2,3-(isopropylidenedioxy)phenyl ester (PAN, 2005), bencarbate, 1,3-benzodioxole,2,2,-dimethyl-4(n-methylcarbamato), 2,2-dimethyl-1,3-benzodioxol-4-ol methcarbamate, 2,3-isopropylidenedioxyphenyl methylcarbamate, methylcarbamic acid 2,3,-(isopropylidenedioxy)phenyl ester (HSDB, 2005)
Chemical Group:	n-methyl carbamate (PAN, 2005)
Registered Trade Names:	Compounds containing bendiocarb: Ficam, Dycarb, Garvox, Multamat, Multimet, Niomil, Rotate, Seedox, Tattoo, Turcam (EXTOXNET, 1996), NC-6897, Ficam D, Ficam plus, Ficam W, Ficam ULV (HSDB, 2005).

Usage

Bendiocarb is a residual carbamate insecticide that has a variety of indoor and outdoor uses, including the control of mosquitoes, household and ornamental plant pests, and fire ants. It has no registered uses on either food of feed crops (U.S. EPA, 1999b). Most products containing bendiocarb are General Use Pesticides (EXTOXNET, 1996) and are meant for homeowner/residential use. However, some formulations (e.g., wettable powders) are recommended to be used only by pest control operators. Bendiocarb is not a Restricted Use Pesticide (U.S. EPA, 1999b); however, the formulations Turcam and Turcam 2.5 G are classified as *restricted* and may only be used by certified applicators (EXTOXNET, 1996).

Common bendiocarb formulations for both agricultural and public health program uses include wettable powders (800, 500 and 200 g active ingredient/kg [g a.i./kg]), granules for soil and turf treatment (30, 50, and 100 g a.i./kg), dust (10 g a.i./kg), suspension

concentrate (500 g a.i./1) for spray or seed treatments, suspension in oil for ULV application (250 g a.i./1), residual sprays, and paint on and granular preparations with bait. The use patterns for bendiocarb in agricultural, horticultural, or forestry applications are reported as follows: soil treatment (300–2,000 g a.i./ha), seed treatment (1–10 g a.i./kg), residual spray (100–1,000 g a.i./ha), and ULV spray (50–500 g a.i./ha). In public health programs, it is reported that the 80 percent wettable powder should be applied only by a professional applicator (WHO/FAO, 1982).

Formulations and Concentrations

- Common formulations of pesticides containing bendiocarb include technical grade, dusts, granules (for soil and turf treatment: 30, 50, and 100 g a.i./kg), wettable powders (800, 500, and 200 g a.i./kg), dust (10 g a.i./kg), suspension concentrate (for spray or seed treatment: 500 g a.i./L) and ULV sprays (in oil: 250 g, a.i./L) (WHO/FAO, 1982; EXTOXNET, 1996). WHO (1999) indicated that the bendiocarb content in various preparations should be declared and contain the following:
- Technical grade bendiocarb: not less than 940 g/kg
- Wettable Powder: above 250 up to 500 g/kg $\pm$ 5% of the declared content or above 500 g/kg $\pm$ 25 g/kg
- Dustable Powder: shall not differ from the declared content by more than -10% to + 35%.
- ULV Liquid: Above 100 up to 200 g/kg $\pm$ 6% of the declared content (WHO, 1999)

Shelf Life

Bendiocarb is reported to be stable below 40^{o}C. Its half-life in aqueous solutions at 25^{o}C is reported as 48 days at pH 5, 81 hours at pH 7, and 45 minutes at pH 9. Bendiocarb degrades slowly at pH 5. Bendiocarb is resistant to oxidation on nonabsorbant surfaces and at low humidity. In sunlight, bendiocarb photo-oxidizes (WHO/FAO, 1982).

Degradation Products

In moist soils and water, a major fate process for bendiocarb is hydrolysis. This is particularly true in neutral and alkaline environments. In neutral hydrolysis, the products are 2,3-isopropylidenedioxyphenol, methylamine, and carbon dioxide (HSDB, 2005). At pHs less than 5, bendiocarb slowly degrades into pyrogallol and acetone (WHO/FAO, 1982). The major degradation product of terrestrial field dissipation on turf is NC-7312 (U.S. EPA, 1999b).

Environmental Behavior

Fate and Transport in Terrestrial Systems

Insecticidal carbamates that are applied to plants reach the soil both directly and indirectly. Degradation of carbamates in soil depends on volatility, leaching, soil moisture, absorption, pH, temperature, photodecomposition, microbial degradation, and soil type (IPCS, 1986). With a Koc range of 28 to 200, moderately to very high mobility is expected if bendiocarb is released in soil (HSDB, 2005). The major fate processes are hydrolysis in moist soils and biodegradation, with volatilization being an unimportant fate process for both dry and moist soils due to the low vapor pressure of bendiocarb. In moist soils, bendiocarb may undergo hydrolysis, and hydrolytic degradation depends on pH (HSDB, 2005; U.S. EPA, 1999b). Biodegradation of bendiocarb is expected to be rapid (HSDB, 2005). The half-life of bendiocarb in soil varies from less than 1 week up to 4 weeks, depending on the type of soil and the pH (EXTOXNET, 1996). The estimated hydrolysis half-life of bendiocarb is 46.5 days at pH 5, 2 days at pH 7, and 0.33 days at pH 9 (U.S. EPA, 1999b). Soil photolysis is important in the photodegradation of bendiocarb in soil. In field dissipation studies on turf, bendiocarb and its degradate NC-7312 are not highly mobile, with intermediate half-lives of 20 days (bendiocarb) and 21 days (NC-7312) (U.S. EPA, 1999b). Bendiocarb degrades before leaching through soil, and degradates remain in the upper layers of soil in low concentrations (U.S. EPA, 1999a, 1999b). It is unlikely that bendiocarb will move through soil to groundwater or to surface water through runoff (U.S. EPA, 1999a). Bendiocarb is of low persistence in soil (EXTOXNET, 1996).

Fate and Transport in Aquatic Systems

Water is an important factor in the transport of carbamates; however, the hazard posed by carbamates under these conditions is limited due to their rapid decomposition under aqueous conditions (IPCS, 1986). In water, bendiocarb is not expected to adsorb to suspended soils and sediments based on its Koc range (28 to 200). The major fate processes in water are hydrolysis and biodegradation; volatilization is an unimportant fate process due to the low vapor pressure of bendiocarb. Additionally, direct photolysis is not a major degradation pathway in water (U.S. EPA, 1999b) and depends on the turbidity of the water (IPCS, 1986). In alkaline and neutral environments, hydrolysis is expected to be a major fate process. Half-lives have been reported of 48 days at pH 5, 4 days at pH 7, and 45 minutes at pH 9 (HSDB, 2005). Bendiocarb does not accumulate in water (EXTOXNET, 1996), and based on soil studies, biodegradation in water is expected to be rapid (HSDB, 2005). Because bendiocarb degrades rapidly in water, bioconcentration in fish is unlikely (U.S. EPA, 1999a). The estimated bioconcentration factor is 12 (HSDB, 2005).

Human Health Effects

Acute Exposure

Effects/Symptoms

Bendiocarb causes toxic effects by the rapid, but reversible, inhibition of cholinesterase in the blood. It is moderately toxic if absorbed through the skin or ingested (EXTOXNET, 1996). Typical signs of acute poisoning are neurological, and include weakness, excessive sweating and salivation, headache, blurred vision, nausea, vomiting, stomach pain, tightness in the chest, muscular twitching, giddiness, slurred speech, confusion, and muscular incoordination (WHO/FAO, 1982; EXTOXNET, 1996). Death from bendiocarb poisoning can result from paralysis of the respiratory system, severe constriction of the lung openings, or stopped breathing (EXTOXNET, 1996). Little data exist on the human health effects of acute exposure to bendiocarb. In humans, the threshold for mild symptoms and blood cholinesterase inhibition is 0.15–0.20 mg a.i./kg for ingestion. No symptoms were reported following repeated hourly doses of 0.1 mg a.i./kg. Studies in human volunteers have shown that both the onset and recovery from cholinesterase inhibition are very rapid (WHO/FAO, 1982). Case reports of accidental bendiocarb exposures report typical symptoms with reversible cholinesterase inhibition. In one case, cholinesterase was inhibited by 63 percent, and the exposed person recovered in less than 3 hours without any medical treatment. Cholinesterase levels returned to normal within 24 hours. In another case, recovery from symptoms occurred within 2 hours after being decontaminated and treated with atropine, with complete recovery by the next day. Bendiocarb is also a mild irritant to the skin and eyes (EXTOXNET, 1996).

In animals, bendiocarb is acutely toxic via the oral, inhalation, and dermal routes (U.S. EPA, 1999b). The oral LD_{50} values of unformulated bendiocarb in various animal species include 34–156 mg/kg in rats, 35–40 mg/kg in rabbits, and 35 mg/kg in guinea pigs. The reported dermal LD_{50} value in rats is greater than 566 mg/kg (EXTOXNET, 1996; IPCS, 1986; WHO/FAO, 1982) and the reported 4-hour LC_{50} in rats is 0.55 mg/L (EXTOXNET, 1996). For formulated bendiocarb compounds, an LD_{50} of 143–179 mg/kg was reported in rats for an 80 percent a.i. water dispersible powder. A dermal LD_{50} of greater than 1,000 mg/kg was reported for an 80 percent a.i. liquid formulation (WHO/FAO, 1982).

As in humans, acute exposure to bendiocarb in animals causes symptoms typical of cholinesterase inhibition (U.S. EPA, 1999a, 1999b). No acute delayed neurotoxicity was observed in hens. Although bendiocarb causes slight eye irritation in animals, it is not considered a skin or eye irritant or a dermal sensitizer (U.S. EPA, 1999b).

Treatment

Exposure to bendiocarb may be determined through laboratory tests that determine cholinesterase levels in blood; however, the enzyme will only be inhibited for a few hours following exposure. Additionally, bendiocarb metabolites may be identified in

urine (WHO/FAO, 1982). Bendiocarb poisoning should be treated in the same way as high-toxicity carbamate poisoning (PAN, 2005). First removing any contaminated clothing and wash affected areas with soap and water. If bendiocarb gets in the eyes, they should be rinsed immediately with isotonic saline or water. Oral exposure to bendiocarb should be treated by rapid gastric lavage with 5 percent sodium bicarbonate if the patient is not already vomiting. Medical attention should be sought. Adults showing signs of bendiocarb toxicity should be treated with 1–2 mg atropine sulfate given intramuscularly or intravenously as needed. Oxygen may be necessary for unconscious patients or those in respiratory distress. Pralidoxime is not effective in treating bendiocarb poisoning (WHO/FAO, 1982).

Chronic Exposure

Noncancer Endpoints

The effects of chronic exposure to bendiocarb in humans have not been well described in the literature, although it is not expected to be toxic at the levels applied to control mosquitoes. When used as a residual mosquito insecticide, few adverse effects were reported by occupationally exposed workers. Those effects that were reported were transient and mild. Additionally, no effects were reported by residents of villages where it was applied (WHO/FAO, 1982).

Subchronic and chronic exposure studies in rats, mice, and dogs have shown that bendiocarb inhibits cholinesterase activity in whole blood, plasma, red blood cells, and the brain (U.S. EPA, 1999a, 1999b; WHO/FAO, 1982). No macroscopic pathology or histological evidence of dermal irritation or treatment-related mortality was observed in a 21-day dermal study in rats. Rats exposed to bendiocarb for 90 days via inhalation showed whole-blood cholinesterase inhibition (U.S. EPA, 1999b). Additionally, bendiocarb does not accumulate in mammalian tissue. There was no evidence of cumulative toxicity in rats or dogs fed bendiocarb for 90 days (WHO/FAO, 1982).

Bendiocarb is not expected to cause reproductive effects in humans. In rats, no effect on fertility and reproduction was seen in rats fed diets containing bendiocarb for three generations. However, very high doses were toxic to dams and pups, as indicated by decreased survival rate and decreased pup weight (EXTOXNET, 1996). No teratogenicity was seen in rats or rabbit fetuses or offspring following pre- and/or postnatal exposures to bendiocarb (U.S. EPA 1999a, 1999b; WHO/FAO, 1982). No evidence of mutagenicity was observed following *in vivo* or *in vitro* exposures to bendiocarb (U.S. EPA, 1999a, 1999b; EXTOXNET, 1996; WHO/FAO, 1982). No irreversible or delayed neurotoxicity has been reported in animals following long-term bendiocarb exposure (WHO/FAO, 1982).

Cancer Endpoints

EPA has classified bendiocarb as a Group E chemical, noncarcinogenic to humans (U.S. EPA, 1999b). The classification is based on the lack of increase in tumors in rat and

mouse studies and is supported by the lack of mutagenicity in somatic cells (U.S. EPA, 1999b). No human data are available.

Toxicokinetics

Bendiocarb can be absorbed through oral, dermal, and inhalation pathways; dermal absorption is especially rapid and is the main route of absorption. Absorption from inhalation, except inhalation of airborne dusts or fine spray mists, is unlikely due to bendiocarb's low vapor pressure (EXTOXNET, 1996; WHO/FAO, 1982). Animal metabolism studies indicate that bendiocarb is rapidly absorbed following oral exposure (U.S. EPA, 1999b). Liver microsome enzymes readily conjugate and metabolize bendiocarb, and it is rapidly excreted. Because of its rapid metabolism and excretion, bendiocarb does not accumulate in mammalian tissues (WHO/FAO, 1982). The majority of an orally administered dose is eliminated in the urine (U.S. EPA, 1999b). In rats fed diets containing up to 10 mg/kg bendiocarb, 89 to 90 percent of the dose was excreted in the urine, 2 to 6 percent was excreted in the feces, and 2 to 6 percent was exhaled. A human subject orally exposed to bendiocarb exhibited a similar excretion pattern (EXTOXNET, 1996). Bendiocarb is excreted mainly as sulfate and beta-glucuronide conjugates of the phenol derivative (WHO/FAO, 1982).

Ecological Effects

Acute Exposure

When applied at the maximum registered application rate, bendiocarb poses acute risk to nontarget terrestrial organisms, such as mammals and birds (WHO/FAO, 1982; U.S. EPA, 1999a). Single broadcast applications on turf may result in high risk to birds, and multiple applications may result in repeated acute effects (U.S. EPA, 1999a). Oral LD_{50} values range from 3.1 mg a.i./kg body weight in mallard ducks to 137 mg a.i./ kg body weight in domestic hens (WHO/FAO, 1982; U.S. EPA, 1999a). However, bendiocarb does not affect avian reproductive parameters (WHO/FAO, 1982). Additionally, bendiocarb has been found to be highly toxic to bees (WHO/FAO, 1982; EXTOXNET, 1996; U.S. EPA, 1999a), with an oral LD_{50} of 0.0001 mg/bee (EXTOXNET, 1996). Additionally, bendiocarb severely affects earthworms under treated turf (EXTOXNET, 1996).

Bendiocarb poses acute risks to freshwater fish, and estuarine and marine animals (U.S. EPA, 1999a). It is moderately to highly toxic to fish, with LC_{50} values ranging from 0.7 to 1.76 mg a.i./L in various species (U.S. EPA, 1999a; WHO/FAO, 1982). The 96-hour LC_{50} for rainbow trout is 1.55 mg/L (EXTOXNET, 1996). When applied at the maximum registered rate, bendiocarb also poses acute risks to freshwater invertebrates (U.S. EPA, 1999a).

Chronic Exposure

Very little data exist for chronic exposure to bendiocarb in nonterrestrial target organisms. In birds, multiple applications of the maximum registered application rate to

turf are expected to result in repeated acute effects. The reproductive effects of chronic exposures cannot be assessed due to limited data (U.S. EPA, 1999a).

Little data exist for chronic exposure to bendiocarb in marine or estuarine organisms. When applied at the maximum registered rate, bendiocarb poses chronic risks to freshwater invertebrates. However, it poses no chronic risk to freshwater fish (U.S. EPA, 1999a).

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Profile for Bifenthrin:

CAS Registry Number 82657-04-3

Summary of Insecticide

Chemical History

Bifenthrin is a pyrethroid insecticide and acaricide used in agricultural and human health applications (EXTOXNET, 1995; WHO/FAO, 1992). It is primarily available as a wettable powder or an emulsifiable concentrate (EXTOXNET, 1995). Bifenthrin is used to control pests on crops and indoor pests (ATSDR, 2003). For mosquito protection, it is used on bed nets and other materials that are dipped in bifenthrin to protect the user. Bifenthrin is a restricted use pesticide due to its potential toxicity to aquatic organisms, and it may only be purchased and used by certified applicators (ATSDR, 2003; EXTOXNET, 1995).

As a synthetic pyrethroid, bifenthrin exhibits its toxic effects by affecting the way the nerves and brain normally function by interfering with the sodium channels of nerve cells (Choi and Soderlund, 2006; EXTOXNET, 1995). Symptoms of acute exposure may include skin and eye irritation, headache, dizziness, nausea, vomiting, diarrhea, excessive salivation, fatigue, irritability, abnormal sensations of the face and skin, and numbness (PAN, 2005). Inhalation of pyrethrins may cause a localized reaction of the upper and lower respiratory tracts (HSDB, 2005). In mammals, pyrethroids are generally of low toxicity due to their rapid biotransformation (HSDB, 2005). EPA has classified bifenthrin as a Class II chemical or moderately toxic. EPA has not classified synthetic pyrethroids, including bifenthrin, as endocrine disruptors. Bifenthrin is highly toxic to fish and other aquatic organisms (EXTOXNET, 1995).

Description of Data Quality and Quantity

Several comprehensive reviews on the toxicity of bifenthrin have been prepared or updated in recent years:

- Toxicological Profile for Pyrethrin and Pyrethroids (ATSDR, 2003)
- Pesticide Residues in Food—1992 Evaluation, Part II: Toxicology—Bifenthrin (WHO/FAO, 1992)
- IRIS summary review (U.S. EPA, 2006)
- Pesticide Information Profile for Bifenthrin (EXTOXNET, 1995).

EPA has developed quantitative human health benchmarks (acute and chronic oral RfDs, intermediate-term oral, and short-, intermediate-, and long-term dermal and inhalation benchmarks) for bifenthrin.

Summary Table

Duration	Route	Benchmark Value	Units	Endpoint	Reference
Acute, Intermediate	Inhalation	0.007	mg/kg/day	Oral NOAEL for neurological effects in dogs at 2.21 mg/kg/day with UF of 300 applied	U.S. EPA (2003)
Chronic	Inhalation	0.004	mg/kg/day	Oral NOAEL for neurological effects in dogs at 1.3 mg/kg/day with UF of 300 applied	U.S. EPA (2003)
Acute	Oral	0.033	mg/kg/day	Acute RfD based on neurotoxicity in rats	U.S. EPA (2003)
Intermediate	Oral	0.007	mg/kg/day	Oral NOAEL for neurological effects in dogs at 2.21 mg/kg/day with UF of 300 applied	U.S. EPA (2003)
Chronic	Oral	0.004	mg/kg/day	Chronic RfD based on neurological effects in dogs	U.S. EPA (2003)
Acute, Intermediate, Chronic	Dermal	0.2	mg/kg/day	Dermal NOAEL for neurological effects in rats at 47 mg/kg/day with UF of 300 applied	U.S. EPA (2003)

For oral exposure, an acute RfD of 0.033 mg/kg/day was derived based on a NOAEL of 32.8 mg/kg/day for neurological effects observed in rats exposed to bifenthrin (study citations not provided), with an uncertainty factor of 1,000 applied to account for the lack of a developmental neurotoxicity study and for interspecies and intrahuman variability (U.S. EPA, 2003). An intermediate NOAEL of 2.21 mg/kg/day was identified for tremors in dogs exposed for 90 days and an uncertainty factor of 300 was applied, resulting in a benchmark of 0.007 mg/kg/day (U.S. EPA, 2003). A chronic oral RfD of 0.004 mg/kg/day was derived based on a NOAEL of 1.3 mg/kg/day for tremors in dogs exposed for 1 year, with an uncertainty factor of 300 applied (U.S. EPA, 2003).

For inhalation exposure, an oral NOAEL of 2.21 mg/kg/day was identified for tremors in dogs exposed for 90 days and an uncertainty factor of 300 was applied (U.S. EPA, 2003). This value (0.007 mg/kg/day) is appropriate to use for short- and intermediate-term inhalation exposures. An oral NOAEL of 1.3 mg/kg/day was identified for tremors in dogs exposed for 1 year and an uncertainty factor of 300 was applied (U.S. EPA, 2003). This value (0.004 mg/kg/day) is appropriate to use for long-term inhalation exposures.

For dermal exposure, a NOAEL of 47 mg/kg/day for neurological effects (staggered gait and exaggerated hind limb flexion) was identified in rats dermally exposed to bifenthrin for 21 days. An uncertainty factor of 300 was applied, for a dermal benchmark value of 0.2 mg/kg/day. This value is appropriate for all exposure durations (U.S. EPA, 2003).

Insecticide Background

CASRN:	82657-04-3
Synonyms:	(2-methyl[1,1'-biphenyl]-3-yl)methyl 3-(2-chloro-3,3,3-trifluoro-1-propenyl)-2,2-dimethylcyclopropanecarboxylate, [1alpha, 3alpha(z)]-(+ -)-3-(2-Chloro-3,3,3-trifluoro-1-propenyl)-2,2-dimethylcyclopropanecarboxylic acid (2-methyl[1,1'-biphenyl]-3-yl)methyl ester, 2-Methylbiphenyl-3-ylmethyl (z)-(1RS,3RS)-3-(2-chloro-3,3,3-trifluoroprop-1- enyl)-2,2-dimethylcyclopropanecarboxylate, [1 alpha, 3 alpha(z)]-(+ -)-(2-Methyl[1,1'-biphenyl]-3-yl)methyl 3-(2-chloro- 3,3,3-trifluoro-1-propenyl)-2,2-dimethylcyclopropanecarboxylate (ATSDR, 2003; EXTOXNET, 1995; HSDB, 2005)
Chemical Group:	pyrethroid (PAN, 2005; EXTOXNET, 1995)
Registered Trade Names:	Talstar, Bifenthrine, Biphenate, Brigade, Bifentrina, Biflex, Capture, FMC 54800, FMC 54800 Technical, OMS3024, Torant (with Clofentezine), and Zipak (with Amitraz), Tarstar (HSDB, 2005; EXTOXNET, 1995; ATSDR, 2003; PAN, 2005)

Usage

Bifenthrin is used as a broad spectrum insecticide and acaricide to combat indoor pests and those on a variety of crops (EXTOXNET, 1995; ATSDR, 2003). It is used to control mosquitoes, beetles, weevils, houseflies, lice, bedbugs, aphids, moths, cockroaches, and locusts. Crops on which bifenthrin is used include alfalfa hay, beans, cantaloupes, cereals, corn, cotton, field and grass seed, hops, melons, oilseed rape, potatoes, peas, raspberries, watermelons, and squash. Bifenthrin belongs to the pyrethroid class of insecticides, which have long been used to control mosquitoes, human lice, beetles, and flies. For mosquito protection, it is used on bed nets and other materials that are dipped into the bifenthrin to protect the user. Bifenthrin for agricultural use is restricted by EPA due to its potential toxicity to aquatic organisms, and it may only be purchased and used by certified applicators (ATSDR, 2003).

Formulations and Concentrations

Bifenthrin is available in technical grade, emulsifiable concentrate, suspension concentrate, wettable powder, ultra-low volume (ULV) liquid, and granules (HSDB,

2005; EXTOXNET, 1995; WHO, 2001). Technical grade bifenthrin may be mixed with carriers or solvents, resulting in the commercial formulations. The label of products containing bifenthrin must contain the word "warning" (EXTOXNET, 1995). Technical grade bifenthrin must have no less than 920 g/kg bifenthrin. The wettable powder should contain > 25–100 g/kg +/- 10% of the declared content, 100–250 g/kg +/- 6% of the declared content, or > 250–500 g/kg +/- 5% of the declared content (WHO, 2001). Bifenthrin that is used on bed nets for malaria control comes in a suspension concentrate dose of 25 mg a.i./m^2 (WHO, n.d.).

Shelf Life

Bifenthrin is photostable and stable to hydrolysis. It volatilizes minimally and is generally stable when stored (EXTOXNET, 1995). Bifenthrin is stable for 2 years at 25–50^{o}C. It is most stable in acidic environments and at pHs from 5 to 9, it is stable for 21 days. Pyrethrins, in general, are stable for a long time in water-based aerosols (HSDB, 2005).

Degradation Products

Pyrethroid insecticides are often formulated with synergists that prevent the breakdown of enzymes and thus enhance the activity of the pyrethroid (ATSDR, 2003). The primary metabolic pathway for the breakdown of bifenthrin is ester hydrolysis (HSDB, 2005). The major degradate of bifenthrin metabolism in soil, biota, and water is 4'-hydroxy bifenthrin (Fecko, 1999).

Environmental Behavior

Fate and Transport in Terrestrial Systems

With Koc values ranging from 131,000 to 320,000, the mobility of bifenthrin in soil ranges from low to immobile (HSDB, 2005; EXTOXNET, 1995). Bifenthrin has a low mobility in soils with large amounts of clay, silt, organic matter and in sandy soils without much organic matter (EXTOXNET, 1995). In moist soils, volatilization is a major fate process, although this is lessened by absorption in the soil (HSDB, 2005). Depending on soil type and the amount of air in the soil, the half-life of bifenthrin ranges from 7 days to 8 months (EXTOXNET, 1995). Bifenthrin is expected to biodegrade readily based on its structure and the biodegradation rates of pyrethroids in general (HSDB, 2005). It is not absorbed by plants and dose not translocate in plants (EXTOXNET, 1995).

Fate and Transport in Aquatic Systems

Bifenthrin is fairly insoluble in water, so it is unlikely to leach to groundwater and cause significant contamination (EXTOXNET, 1995). Volatilization is a major fate process from surface water; however, because bifenthrin is expected to adsorb to suspended soils and sediments, volatilization is attenuated. Volatilization half-lives of 50 days for a model river and 555 days for a model lake have been reported, but if adsorption is

considered, the volatilization half-life of a model pond is 3,100 years. Bifenthrin has a high potential to accumulate in aquatic organisms, with an estimated bioconcentration factor of 190. However, bioconcentration is likely to be lower due to the ability of aquatic organisms to readily metabolize bifenthrin (HSDB, 2005).

Human Health Effects

Acute Exposure

Effects/Symptoms

There are limited data on the acute toxicity of bifenthrin in humans. Bifenthrin is classified as having moderate acute toxicity in mammals (EXTOXNET, 1995; WHO/FAO, 1992; PAN, 2005). Incoordination, irritability to sound and touch, tremors, salivation, diarrhea, and vomiting have been caused by high doses. In humans, no skin inflammation or irritation has been observed; however, bifenthrin can cause a reversible tingling sensation (EXTOXNET, 1995).

In animals, the main signs of acute toxicity include clonic convulsions, tremors, and oral discharge (WHO/FAO, 1992). Reported LD_{50} values for bifenthrin include 54–56 mg/kg in female rats, 70 mg/kg in male rats (EXTOXNET, 1995; WHO/FAO, 1992; HSDB, 2005) and 43 mg/kg in mice (WHO/FAO, 1992). Bifenthrin is slightly toxic through dermal contact, with dermal LD_{50}s of over 2,000 mg/kg in rabbits (WHO/FAO, 1992; HSDB, 2005). Neurotoxicity is a key effect of pyrethroids and is caused by interfering with the sodium channels of nerve cells (ATSDR, 2003; Choi and Soderlund, 2006). In mammals, acute exposure to pyrethroids causes tremors, hyperexcitability, salivation, paralysis, and choreoathetosis. However, delayed neurotoxicity has not been observed (HSDB, 2005). Bifenthrin is not a dermal sensitizer in guinea pigs (EXTOXNET, 1995; HSDB, 2005; WHO/FAO, 1992) and did not irritate either abraded or non-abraded skin of rabbits (WHO/FAO, 1992). In rabbits, it is only slightly irritating to the eyes (EXTOXNET, 1995; WHO/FAO, 1992; HSDB, 2005). Bifenthrin is also a suspected endocrine disruptor (ATSDR, 2003; PAN, 2005).

Treatment

Bifenthrin and its metabolites can be detected in blood and urine during the first few days following exposure (but not later, because these compounds are rapidly broken down in the body) (ATSDR, 2003). Treatment depends on the symptoms of the exposed person. Most casual exposures require only decontamination and supportive care (HSDB, 2005). If a person exhibits signs of typical pyrethroid toxicity following bifenthrin exposure, affected skin areas should be washed promptly with soap and warm water. Medical attention should be sought if irritation or paresthesia occurs. Paresthesia may be prevented or stopped with Vitamin E oil preparations. Corn oil and Vaseline® are less effective and less suitable, and zinc oxide should be avoided (PAN, 2005; HSDB, 2005).

Eye exposures should be treated by rinsing with copious amounts of water or saline. Contact lenses should be removed. Medical attention should be sought if irritation

persists (PAN, 2005; HSDB, 2005). Following oral exposures, the person should be kept calm and medical attention should be sought as quickly as possible. Medical personnel will treat severe intoxications with a sedative and anticonvulsant. Ingestion of large amounts of bifenthrin should be treated with gastric lavage, and small ingestions should be treated with activated charcoal and cathartic (PAN, 2005). For sublethal exposures, vomiting may be induced by ipecac and followed by saline cathartic and an activated charcoal slurry, as long as the person is alert and has a gag reflex (HSDB, 2005).

Chronic Exposure

Noncancer Endpoints

No data are available for humans following chronic exposures to bifenthrin (EXTOXNET, 1995). Dietary studies in dogs, rats, and mice indicate that oral exposure to bifenthrin causes neurological effects such as tremors (U.S. EPA, 2006; WHO/FAO, 1992) but not cholinesterase inhibition (PAN, 2005). In a 1-year feeding study in dogs and a lifetime feeding study in mice, intermittent tremors were observed (U.S. EPA, 2006; WHO/FAO, 1992). In subchronic duration exposure studies in dogs and rats, tremors were also seen at higher exposure levels (U.S. EPA, 2006; WHO/FAO, 1992).

Bifenthrin has the potential to be reproductive toxin (PAN, 2005). Reproductive toxicity has been observed in rats and rabbits at doses lower than those that cause tremors (EXTOXNET, 1995). Teratogenicity was not observed in a 2-generation rat study (EXTOXNET, 1995) or a rabbit teratogenicity study (WHO/FAO, 1992; HSDB, 2005).

Additional effects observed in chronic exposure animal studies include increased body weight and organ-to-body ratios (U.S. EPA, 2006). The mutagenicity data are inconclusive for bifenthrin (EXTOXNET, 1995), but it is unlikely to pose a genetic hazard (WHO/FAO, 1992).

Cancer Endpoints

EPA has classified bifenthrin as Class C, possible human carcinogen (EXTOXNET, 1995; PAN 2005). A 2-year, high dose dietary exposure study in rats reported no evidence of cancer. In mice, however, a significant dose-related increase in urinary bladder tumors was observed in male mice. An increased incidence of lung tumors was observed in female mice (U.S. EPA, 2003; EXTOXNET, 1995).

Toxicokinetics

Bifenthrin is readily absorbed through intact skin (EXTOXNET, 1995; HSDB, 2005) and the gastrointestinal tract (WHO/FAO, 1992). It breaks down in the same way as other pyrethroids (EXTOXNET, 1995). Hydrolysis and hydroxylation are the primary steps in the transformation of bifenthrin. In poultry, bifenthrin metabolism begins with hydroxylation of the 2-methyl carbon of the cyclopropane ring, followed by fatty acid conjugation (WHO/FAO, 1992). Oral administration of radioactive pyrethroids have been shown to distribute to every tissue examined (HSDB, 2005). Bifenthrin can accumulate in

fatty tissues such as skin and ovaries (EXTOXNET, 1995). Bifenthrin metabolism and excretion are rapid. In rats given 4–5 mg/kg bifenthrin, 70 percent of the dose was excreted in urine within 7 days, and 20 percent was excreted in feces (EXTOXNET, 1995). However, another study in rats showed that following oral administration of bifenthrin, 70 to 80 percent was eliminated in the feces within 48 hours while only 5 to 10 percent was eliminated in the urine. Biliary excretion raged from 20 to 30 percent (WHO/FAO, 1992).

Ecological Effects

Acute Exposure

Toxicity in Non-Targeted Terrestrial Organisms

Bifenthrin, like other pyrethroids, is unlikely to harm terrestrial organisms other than its targets, such as mosquitoes and other pests, due to its low persistence in the environment (HSDB, 2005). Bifenthrin has a moderate toxicity in birds (EXTOXNET, 1995). The 8-day dietary LC_{50} values range from 1,280 ppm in mallard ducks to 4,450 ppm in bobwhite quail. Oral LD_{50} values range from 1,800 mg/kg in bobwhite quail to 2,150 mg/kg in mallard ducks. Additionally, concerns about bioaccumulation in birds have been reported. As with other pyrethroid insecticides, bifenthrin is extremely toxic to honey bees (EXTOXNET, 1995; HSDB, 2005).

Toxicity in Non-Targeted Aquatic Systems

Bifenthrin is also known to be toxic to a wide variety of aquatic organisms, including fish, crustaceans, aquatic insects, mollusks, nematodes, flatworms, phytoplankton, and zooplankton (PAN, 2005). Bifenthrin is very toxic to fish (EXTOXNET, 1995); however, because it is not very water soluble and has a high affinity for soil, the risk to aquatic systems is not expected to be high (EXTOXNET, 1995). The high toxicity in fish is illustrated by the low exposures that cause lethality. The reported 96-hour LC_{50} is 0.00015 mg/L in rainbow trout and 0.00035 mg/L in bluegill sunfish (EXTOXNET, 1995; HSDB, 2005). Average LC_{50} values are 17.5 µg/L in sheepshead minnow and 0.36 µg/L in gizzard shad (PAN, 2005). In Daphnia, the reported 48-hour LC_{50} is 0.0016 mg/L (HSDB, 2005). The risk of bioaccumulation of the bifenthrin formulation Talstar®100EC in aquatic organisms is reported to be very high (ASTRACHEM, n.d.). The whole-body bioconcentration factor values for fathead minnow in water T a concentration of 0.0037 µg/L were 21,000 (over 127 days) and 28,000 (over 254 days) (CalDFG, 2000).

Chronic Exposure

Toxicity in Non-Targeted Terrestrial Organisms

No data were located on the chronic toxicity to nontarget terrestrial organisms.

Toxicity in Non-Targeted Aquatic Systems

Chronic exposure of fathead minnow to a 95.7 percent bifenthrin formulation for 246 days resulted in a reported LOEC of 0.41 µg/L, NOEC of 0.30 µg/L, and MATC of 0.351

µg/L. Chronic exposure of fathead minnow to a 96.2 percent bifenthrin formulation for 346 days resulted in a reported LOEC of 0.090 µg/L, NOEC of 0.050 µg/L, and MATC of 0.067 µg/L (CalDFG, 2000).

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Profile for Cyfluthrin:

CAS Registry Number 68359-37-5

Summary

Chemical History

Cyfluthrin is a synthetic pyrethroid insecticide first registered by EPA in 1987. It is used in agricultural and human health applications against a wide variety of pests. It is similar to the natural insecticide pyrethrum, which comes from chrysanthemums; however, it is more effective and longer lasting (ATSDR, 2003). Cyfluthrin has both contact and stomach poison action (EXTOXNET, 1998) and it interferes with nervous system transmissions through inhibition of the sodium channel system (Choi and Soderlund, 2006; WHO, 2004). It is available as the technical product, emulsifiable concentrate, wettable powder, aerosol, granule, liquid, oil-in-water emulsion, dust, concentrate, and ultra-light-volume oil spray (EXTOXNET, 1998; IPCS, 1997). For mosquito control, it is used in bed nets and other materials that are treated with cyfluthrin to protect the user (WHO, 1998). Cyfluthrin can be found in both restricted use pesticides and general use pesticides (EXTOXNET, 1998). When used, it is applied by spraying, dusting, fogging, or impregnation (WHO, 2004; IPCS, 1997). It is considered moderately toxic to mammals (EXTOXNET, 1998). EPA has not classified synthetic pyrethroids, including cyfluthrin, as endocrine disruptors. Typical symptoms of acute human exposure are skin and eye irritation. Dermal irritation may include itching, burning, or stinging, which may lead to a numbness that lasts up to 24 hours. Skin irritation may occur immediately following exposure or be delayed for 1 to 2 hours (EXTOXNET, 1998). In animals, very high doses have been shown to cause nervous system effects, including irritability, excessive salivation, uncoordinated gait, tremors, convulsions, and death (EXTOXNET, 1998; ATSDR, 2003).

Description of Data Quality and Quantity

EPA has developed a quantitative human health benchmark for cyfluthrin (EPA's chronic oral RfD). Several reviews on the toxicity of cyfluthrin have been prepared or updated in recent years and recommended resources include the following:

- Toxicological Profile for Pyrethrin and Pyrethroids (ATSDR, 2003)
- IRIS summary review (U.S. EPA, 2005b)
- Pesticide Information Profiles: Cyfluthrin (EXTOXNET, 1998)
- Toxicological Evaluation of Certain Veterinary Drug Residues in Food. WHO Food Additives Series 39: Cyfluthrin (IPCS, 1997)
- Specifications and Evaluations for Public Health Pesticides: Cyfluthrin (WHO, 2004).

Summary Table

Duration	Route	Benchmark Value	Units	Endpoint	Reference
Acute	Inhalation	0.0007	mg/kg/day	Inhalation NOAEL in rats with UF of 100 applied	U.S. EPA (2005a)
Intermediate, Chronic	Inhalation	0.0002	mg/kg/day	Inhalation NOAEL in rats with UF of 100 applied	U.S. EPA (2005a)
Acute	Oral	0.02	mg/kg/day	Acute RfD based on mammalian neurotoxicity	U.S. EPA (2005a)
Intermediate	Oral	0.024	mg/kg/day	Adopt chronic RfD for intermediate duration	
Chronic	Oral	0.024	mg/kg/day	Chronic RfD based on neurological effects in dogs	U.S. EPA (2005a)
Acute, Intermediate, Chronic	Dermal	3	mg/kg/day	Dermal NOAEL in rabbits with UF of 100 applied	

For inhalation exposure, a NOAEL of 0.00026 mg/L (0.07 mg/kg/day) was identified for body weight effects in rats exposed to beta-cyfluthrin via inhalation for 28 days. A NOAEL of 0.00009 mg/L (0.02 mg/kg/day) was identified for neurological and body weight effects in rats exposed to cyfluthrin via inhalation for 13 weeks. An uncertainty factor of 100 to account for inter- and intraspecies variation was applied, for a short-term inhalation benchmark of 0.0007 mg/kg/day and an intermediate- and long-term inhalation benchmark of 0.0002 mg/kg/day.

For oral exposure, an acute oral RfD of 0.02 mg/kg/day was derived based on a NOAEL of 2 mg/kg/day for acute mammalian neurotoxicity following exposure to beta-cyfluthrin. An uncertainty factor of 100 was applied for inter- and intraspecies variability (U.S. EPA, 2005a). A chronic oral RfD of 0.024 mg/kg/day was derived based on a NOAEL of 2.4 mg/kg/day for neurological effects in dogs exposed to cyfluthrin for 53 weeks. An uncertainty factor of 100 was applied for inter- and intraspecies variability (U.S. EPA, 2005a). An intermediate oral RfD of 0.024 mg/kg/day was derived based on a NOAEL of 2.4 mg/kg/day for neurological effects in dogs exposed to beta-cyfluthrin for 90 days. An uncertainty factor of 100 was applied for inter- and intraspecies variability (U.S. EPA, 2005a).

For dermal exposure, a NOAEL of 250 mg/kg/day (85 percent purity) was identified in rabbits dermally exposed to cyfluthrin 5 times a week for 6 hr/day for 3 weeks (IPCS, 1997). An uncertainty factor of 100 to account for inter- and intraspecies variation was applied, for a dermal benchmark value of 3 mg/kg/day. This value is appropriate for all exposure durations.

Insecticide Background

CASRN:	68359-37-5
Synonyms:	Cyano(4-fluoro-3-phenoxyphenyl) methyl 3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropanecarboxylate; BAY-FCR 1272; (R,S)-alpha-Cyano-4-fluoro-3-phenoxybenzyl-(1R,S)-cis,trans-3-(2,2- dichlorovinyl)-2,2-dimethylcyclopropanecarboxylate; 3-(2,2-Dichloroethenyl)-2,2-diethylcyclopropanecarboxylic acid cyano(4-fluoro- 3-phenoxyphenyl)methyl ester; Cyfluthrine; FCR 1272; (RS)-alpha-Cyano-4-fluoro-3-phenoxybenzyl (1RS, 3RS: 1RS, 3SR)-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylate (ATSDR, 2003; HSDB 2005)
Chemical Group:	pyrethroid (ATSDR, 2003)
Registered Trade Names:	Attotox, Baythroid, Baygon aerosol, Baythroid H, Cyfoxlate, Contur, Laser, Responsar, Solfac, Tempo, Tempo H (ATSDR, 2003; EXTOXNET, 1998)

Usage

Cyfluthrin is effective in combating a broad spectrum of insect pests in agricultural, public health, and structural applications (WHO, 2004; EXTOXNET, 1998). The main agricultural use of cyfluthrin is against chewing and sucking insects on crops (EXTOXNET, 1998; HSDB, 2005; ATSDR 2003). In public health applications, it is used to control mosquitoes, houseflies, and cockroaches (HSDB, 2005). It is primarily a contact insecticide and is applied by residual spraying, fogging, or impregnation (WHO, 2004).

Formulations and Concentrations

Cyfluthrin is available in technical grade, emulsifiable concentrate, wettable powder, aerosol, granules, liquid, oil-in-water emulsion, and ultra-light-volume oil sprays (EXTOXNET, 1998; HSDB 2005). Technical grade cyfluthrin may be mixed with carriers or solvents resulting in the commercial formulations. These commercial formulations may also include ingredients that may potentiate the toxicity compared to technical grade cyfluthrin (EXTOXNET, 2005). WHO indicates that the content of cypermethrin in the formulated products must be declared and shall not exceed the listed standards. Technical grade cyfluthrin must have no less than 920 g/kg cyfluthrin and should contain the four diastereoisomers as follows:

- Diastereoisomer I, (R)-alpha-cyano-4-fluoro-3-phenoxybenzyl-(1R)-cis -3-(2,2-dichlorovinyl)-2,2- dimethylcyclopropanecarboxylate + (S)-alpha, (1S)-cis: 23–27 percent

- Diastereoisomer II, (S)-alpha-cyano-4-fluoro-3-phenoxybenzyl-(1R)-cis -3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylate + (R)-alpha, (1S)-cis: 17–21 percent
- Diastereoisomer III, (R)-alpha-cyano-4-fluoro-3-phenoxybenzyl-(1R)-trans -3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylate + (S)-alpha, (1S)-trans: 32–36 percent
- Diastereoisomer IV, (S)-alpha-cyano-4-fluoro-3-phenoxybenzyl-(1R)- trans -3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylate + (R)-alpha, (1S)-trans: 21–25 percent.

The wettable powder should contain 100 g/kg cyfluthrin +/- 10 percent of the declared content. The oil-in-water emulsion shall contain 50 g/kg or g/L cyfluthrin +/- 10 percent of the declared content at 20 +/- 2 ^{o}C (WHO, 2004, ATSDR, 2003). For malaria control, a 10 percent wettable powder formulation has been found to be safe and effective for indoor residual spraying against malaria vectors at target doses of 15 to 50 mg/m^2, while a 5 percent oil in water emulsion is effective and safe for use in impregnation of bed nets at a dose of 50 mg/m^2 (WHO, 1998).

Shelf Life

Cyfluthrin in water-based aerosols is stable for a long time. It is thermally stable at room temperature. Topical cyfluthrin preparations made with piperonyl butoxide should be stored at temperatures below 40 ^{o}C (and optimally at 15 to 30 ^{o}C) and in tightly closed containers (HSDB, 2005). Australian researchers reported that cyfluthrin is stable and does not break down for up to 52 weeks when used on stored wheat (EXTOXNET, 1998).

Degradation Products

Pyrethroid insecticides are often formulated with synergists that act to prevent the breakdown of enzymes and thus enhance the activity of the pyrethroid (ATSDR, 2003). Cyfluthrin's breakdown products include 4-fluoro-3-phenoxybenzoic acid (PAN, 2005). In soil, the primary breakdown products include carbon dioxide and 4-fluoro-3-phenyl-benzaldehyde (a compound of considerably lower toxicity than the parent compound) (EXTOXNET, 1998).

Environmental Behavior

Fate and Transport in Terrestrial Systems

The use of cyfluthrin as an insecticide may result in its release into the environment via a variety of waste streams (HSDB, 2005). Once in the environment, cyfluthrin is expected to be highly immobile in the soil based on its Koc value (HSDB, 2005; EXTOXNET, 1998). Because it is immobile in soil, cyfluthrin does not easily leach into groundwater (EXTOXNET, 1998).

Cyfluthrin is one of the more persistent pyrethroids and as a result, it is used more often in agricultural applications (ATSDR, 2003). It can be broken down by sunlight, and in surface soils, the reported half-life ranges from 48 to 72 hours. Reported half-lives in German loam and sandy loam soils are 51 to 63 days. Persistence under anaerobic conditions is similar. The persistence of cyfluthrin in soil is not significantly affected by soil moisture content (EXTOXNET, 1998; ATSDR, 2003).

The major fate processes for cyfluthrin in soil are biodegradation and photolysis. Under anaerobic conditions, more than 90 percent biodegradation was reported during an incubation period of 140 days. Anaerobic biodegradation of cyfluthrin initially produces 3-(2,2-dichlorovinyl)2,2-dimethylcyclopropancarboxcylic acid and 4-fluoro-3-phenoxybenzoic acid. Photodegradation was observed when cotton fabric was irradiated for 96 hours in simulated natural sunlight, resulting in almost 75 percent photo-degradation (HSDB, 2005). Volatilization is not expected to be a major fate process from either moist or dry soils (HSDB, 2005).

Fate and Transport in Aquatic Systems

Cyfluthrin binds tightly to soil, is practically insoluble in water, and is less dense than water, allowing it to float on the surface film of natural water (EXTOXNET, 1998; HSDB, 2005). It is stable in water under acidic conditions but hydrolyzes rapidly under basic conditions (EXTOXNET, 1998). On surface waters, cyfluthrin breaks down by photolysis and is not expected to volatilize (EXTOXNET, 1998; HSDB, 2005). In aqueous solutions, an experimental half-life of 16 hours was identified when irradiated by environmentally significant wavelengths of light (HSDB, 2005). Aqueous hydrolysis does not play an important role in the environmental fate of cyfluthrin. Hydrolysis half-lives of 231 days and 2 days were identified at pH 7 and 8, respectively (ATSDR, 2003). Cyfluthrin has a high potential to bioconcentrate in aquatic organisms (HSDB, 2005).

Human Health Effects

Acute Exposure

Effects/Symptoms

Limited data are available on the acute toxicity of cyfluthrin in humans, because pyrethroid poisonings are uncommon. Cases of acute occupational or accidental exposure to pyrethroids resulted in burning, itching, and tingling of the skin which resolved after several hours. Reported systemic symptoms included dizziness, headache, anorexia, and fatigue. Vomiting occurred most commonly after ingestion of pyrethroids. Less commonly reported symptoms included tightness of the chest, paresthesia, palpitations, blurred vision, and increased sweating. In serious cases, coarse muscular fasciculations (twitching), convulsions, and coma were reported (IPCS, 1997). Cyfluthrin is of low toxicity to humans largely due to its poor absorption from the bloodstream and rapid breakdown and excretion. Acute effects of cyfluthrin exposure in humans consist primarily of immediate or delayed skin irritation and immediate eye irritation. Itching,

burning, and stinging of exposed skin can progress to cutaneous paresthesias, which can last up to 24 hours. Sweating, heat, and water can make dermal symptoms worse (WHO, 2004; EXTOXNET, 1998; HSDB, 2005; IPCS, 1997).

As a pyrethroid, cyfluthrin inhibits cholinesterase (HSDB, 2005), and symptoms of acute toxicity in animals may include irritability, excessive salivation, uncoordinated gait, tremors, convulsions, and death (HSDB, 2005; EXTOXNET, 1998). Cyfluthrin is a type II pyrethroid, a class which is known to produce a complex poisoning syndrome involving a progressive development of symptoms. In rats, this manifests as burrowing behavior, coarse tremors, clonic seizures, sinuous writhing, and profuse salivation without lacrimation (HSDB, 2005). Nervous system effects have been reported in acute high-dose exposures of animals to cyfluthrin by oral routes (EXTOXNET, 1998). Neurological effects (e.g., disturbed posture, abnormal motor activity, restlessness, and agitated gate) have also been seen following acute inhalation exposures (ATSDR, 2003). Neurological symptoms following daily dermal doses of $\geq$ 1,845 mg/kg in rats for up to 7 days included pawing and whole body tremors (ATSDR, 2003).

The vehicle used in formulating cyfluthrin significantly affects its toxicity (WHO, 2004). Reported LD_{50} values range from 16 to 1,189 mg/kg body weight, depending on the vehicle used (WHO, 2004). The reported oral LD_{50}s range from 500 to 1,271 mg/kg in rats, 1,401 to 609 mg/kg in mice, greater than 100 mg/kg in dogs, greater than 1,000 mg/kg in rabbits, and greater than 1,000 mg/kg in sheep (EXTOXNET, 1998; HSDB, 2005).The oral LD_{50}s for cyfluthrin in polyethylene glycol and xylene are 500 and 270 mg/kg, respectively (HSDB, 2005), while the oral LD_{50} for a 5 percent water emulsion preparation is reported as 2,100 mg/kg body weight in rats (WHO, n.d.). Inhalation exposures in rats have resulted in 4-hour LC_{50}s ranging from 469 to 592 µg/L and a reported 1-hour LC_{50} greater than 1,089 µg/L (EXTOXNET 1998). The 4-hour LC_{50}s for aerosol and dust exposures in rats are reported as 0.1 mg/L and 0.53 mg/L, respectively (HSDB, 2005). Cyfluthrin is not considered highly toxic via the dermal route of exposure, with a dermal LD_{50} of greater than 5,000 mg/kg in rats (EXTOXNET, 1998; HSDB, 2005). Additionally, it is not a dermal sensitizer or irritant in guinea pigs and rabbits (WHO, 2004; EXTOXNET, 1998; HSDB, 2005) but did induce eye irritation in rabbits (WHO, 2004; HSDB, 2005).

Treatment

Cyfluthrin and its metabolites can be detected in blood and urine; however, the methods are not practical given how quickly these compounds are broken down in the body (ATSDR, 2003). There are no antidotes for cyfluthrin exposure. Treatment depends on the symptoms of the exposed person. If a person exhibits signs of typical pyrethroid toxicity following cyfluthrin exposure (nausea, vomiting, shortness of breath, tremors, hypersensitivity, weakness, burning, or itching), they should immediately remove any contaminated clothing. Any liquid contaminant on the skin should be soaked up and the affected skin areas cleaned with alkaline soap and warm water. Eye exposures should be treated by rinsing with copious amounts of 4 percent sodium bicarbonate or water.

Contact lenses should be removed. Vomiting should not be induced following ingestion exposures, but the mouth should be rinsed. The person should be kept calm and medical attention should be sought as quickly as possible. Medical personnel will treat severe intoxications with a sedative and anticonvulsant. Ingestion of large amounts of cyfluthrin should be treated with gastric lavage using a 5 percent bicarbonate solution followed by powdered activated charcoal. Skin irritation may be treated with a soothing agent; exposure to light should be avoided (PAN, 2005; HSDB, 2005).

Chronic Exposure

Noncancer Endpoints

Little data are available for humans following chronic exposures to cyfluthrin, although it is not likely to cause long-term problems when used under normal conditions (ATSDR, 2003). Available animal data suggest that chronic toxicity is highest by inhalation exposure, with lower toxicity by oral exposure. Dermal exposure has the lowest chronic toxicity (WHO, 2004). Cyfluthrin does not appear to be a reproductive or developmental toxin in animals (HSDB, 2005; WHO, 2004; ATSDR, 2003; EXTOXNET, 1998; WHO/FAO, 1997). However, treatment-related reductions in viability, decreased lactation, and deceased birth weight or weight gain were observed in one 3-generation rat study (ATSDR, 2003; EXTOXNET, 1998; U.S. EPA, 2005b). No developmental or teratogenic effects were observed in several animal studies (HSDB, 2005; EXTOXNET 1998; U.S. EPA, 2005b). In a 1-year dog feeding study, high doses of cyfluthrin caused slight ataxia, increased vomiting, and increased pasty or liquid feces. Decreased body weights were seen in males (U.S. EPA, 2005b). Cyfluthrin does not show any mutagenic potential (HSDB, 2005; WHO, 2004; EXTOXNET, 1998; WHO/FAO, 1997). Decreased weight gain and organ weight changes secondary to body weight are the only significant effects observed in long-term feeding studies in rats, mice, and dogs (WHO/FAO, 1997; EXTOXNET, 1998; U.S. EPA, 2005b). Additionally, reversible damage to the sciatic nerve was observed (EXTOXNET, 1998).

Cancer Endpoints

No evidence of carcinogenic potential has been reported in rats and mice exposed to cyfluthrin (WHO, 2004; EXTOXNET, 1998; WHO/FAO, 1997).

Toxicokinetics

Pyrethroids are rapidly absorbed via inhalation as is indicated by the excretion of their metabolites within 30 minutes of exposures. In workers, plasma cyfluthrin levels confirmed absorption. Oral exposure to pyrethroids results in absorption from the gastrointestinal tract. Cyfluthrin metabolites were identified in the urine of an orally exposed volunteer. Minimal oral absorption was estimated based on the recovery of urinary cyfluthrin metabolites (ATSDR, 2003).

As with other synthetic pyrethroids, biotransformation in mammals exposed to cyfluthrin occurs through hydrolysis of the central ester bond, oxidative attacks at several sites, and

conjugation reactions that produce water-soluble metabolites that are excreted in urine and feces. For cypermethrin, the rapid hydrolytic cleavage of the ester bond is followed by oxidation, which results in carboxylic acid derivatives and phenoxybenzoic acid derivatives that are then excreted as alcohols; phenols; carboxylic acids; and their glycine, sulfate, glucuronide, or glucoside conjugates (ATSDR, 2003). The metabolism of cyfluthrin is biphasic with a rapid initial phase and a slower second phase. This is demonstrated by the elimination of 60 percent of an intravenous dose within the first 24 hours followed by 6 percent elimination during the second 24 hours. Similarly, in feces 20 percent was eliminated on the first day and 3 to 4 percent was eliminated on the second day. Additionally, a single oral dose of cyfluthrin was shown to be 98 percent eliminated within 48 hours (EXTOXNET, 1998). Inhalation of a single dose of cyfluthrin in humans resulted in urinary metabolites within 30 minutes of exposure (ATSDR, 2003; WHO/FAO, 1997).

Elimination of cyfluthrin following inhalation exposure follows first-order kinetics with 93 percent of the dose being excreted within 24 hours of exposure. The elimination half-times for cis-/trans-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropane carboxylic acid (DCCA) and, 4-fluoro-3-phenoxybenzoic acid (FPBA) metabolites and their isomers range from 5.3 to 6.9 hours and remain constant over a range of exposure levels (ATSDR, 2003). Based on occupational human exposure studies, the elimination half-time for cyfluthrin is estimated at 0.5 to 2 hours for plasma and 5 hours for urine (ATSDR, 2003). Oral exposures to cyfluthrin resulted in approximately 60 to 70 percent of the dose being eliminated in the urine and the rest eliminated in the feces (WHO/FAO, 1997).

Ecological Effects

Acute Exposure

Toxicity in Non-Targeted Terrestrial Organisms

Cyfluthrin has a very low toxicity in birds (EXTOXNET, 1998; HSDB, 2005). Oral LD_{50} values range from greater than 2,000 mg/kg in acute tests in bobwhite quail to greater than 5,000mg/kg in subacute tests in mallards and bobwhite quail (EXTOXNET, 1998). Other reported oral LD_{50}s are 4,500 to greater than 5,000 mg/kg in hens (depending on the vehicle used), greater than 2,000 mg/kg in Japanese quail, and 250 to 1,000 mg/kg in canaries (EXTOXNET, 1998; HSDB, 2005). As with other pyrethroid insecticides, cyfluthrin is extremely toxic to honey bees in laboratory tests. The reported LD_{50} is 0.037 mg/bee (EXTOXNET, 1998). However, in the field, serious adverse effects have not been seen due to low application rates and low environmental persistence (HSDB, 2005). Cyfluthrin is also highly toxic to other beneficial insects (EXTOXNET, 1998) but of low toxicity to earthworms (WHO, 2004).

Toxicity in Non-Targeted Aquatic Systems

As with other pyrethroids, cyfluthrin is very toxic to marine and freshwater fish and invertebrates (EXTOXNET, 1998; WHO, 2004). The high toxicity in fish is illustrated by the low exposures that cause lethality. The reported 48-hour LC_{50} for rainbow trout is 0.00068 mg/L, while in bluegill, carp, and golden orfe, the reported LC_{50}s are 0.0015, 0.022, and 0.0032 mg/L, respectively. In sheepshead minnow, an LC_{50} of 0.004 mg/L is reported (EXTOXNET, 1998). The 96-hour LC_{50} values range from 28 ng/L in bluegill sunfish to 330.9 ng/L in golden orfe (HSDB, 2005). In marine and estuarine invertebrates, extreme sensitivity to cyfluthrin is also seen. Reported LC_{50}s include 2.42 ng/L for mysid shrimp. An EC_{50} of 3.2 ng/L was seen in eastern oysters (EXTOXNET, 1998). Cyfluthrin has a high potential to bioconcentrate in aquatic organisms based on the measured BCF of the structurally similar insecticide cypermethrin (HSDB, 2005).

Chronic Exposure

Due to low rate of application and low persistence of cyfluthrin in both terrestrial and aquatic environments, serious adverse effects are not anticipated from chronic exposures (HSDB, 2005).

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Profile for DDT:

CAS Registry Number 50-29-3

Summary

Chemical History

Dichlorodiphenyltrichloroethane (DDT) is a broad range pesticide used since the late 1930s on agricultural crops and to control disease-carrying insects, such as those that spread malaria and typhus. In 1955, a global campaign to eradicate malaria was adopted based on the use of DDT, and endemic malaria in developed countries, subtropical Asia, and Latin America was eradiated by 1967. However, few African countries participated, and the campaign ended in 1969 due to lack of support and developing mosquito resistance to DDT (Rogan and Chen, 2005). DDT was banned in the United States and other industrialized countries in the early 1970s, largely due to its persistence in the environment. However, DDT is still in use today in sub-Saharan African countries to control malaria (ATSDR, 2002). Some studies indicate that DDT (as well as DDE) is an endocrine disruptor in humans. Recent data have indicated that exposure to DDT in amounts necessary for malaria control may cause preterm birth, decreased birth weight, early weaning, and pregnancy loss (IPCS, 2004; Longnecker, 2005; Rogan and Chen, 2005). Acute exposure to high levels of DDT by any route causes neurological effects, including excitability, headache, nausea, vomiting, and dizziness (ATSDR, 2002).

Data on Mexican workers who use DDT show very high levels of DDT in adipose (fat) tissues and serum (Rogan and Chen, 2005). Children are also at risk for increased exposure to DDT and its metabolites via consumption of breast milk and cow's milk. DDT exhibits its toxic effects in humans on the nervous system and liver (ATSDR, 2002).

Description of Data Quality and Quantity

EPA and ATSDR have developed quantitative human heath benchmarks (EPA's chronic RfD and oral and inhalation CSFs and ATSDR's acute and intermediate oral MRLs). Several comprehensive reviews on the toxicity of DDT are available and recommended:

- Toxicological Profile for DDT, DDE, and DDD (ATSDR, 2002)
- IRIS summary review (U.S. EPA, 2005a)
- A recent review article by Rogan and Chen (2005).

Other relevant resources include

- Specifications for Pesticides Used in Public Health (WHO, 1999)
- Environmental Health Criteria 9: DDT and its Derivatives (IPCS,1979)
- Pesticide Information Profile for DDT (EXTOXNET, 2003)

- The Pesticide Action Network (PAN) Pesticide Database (PAN, 2005).

Summary Table

Duration	Route	Benchmark Value	Units	Endpoint	Reference
Acute	Inhalation	0.0005	mg/kg/day	Adopt acute oral MRL as acute inhalation; assume no portal of entry effects	
Intermediate	Inhalation	0.0005	mg/kg/day	Adopt intermediate oral MRL as intermediate inhalation; assume no portal of entry effects	
Chronic	Inhalation	0.0005	mg/kg/day	Adopt chronic RfD as chronic inhalation; assume no portal of entry effects	
Cancer	Inhalation	0.034	per mg/kg/day	Inhalation CSF (calculated from oral data) for benign and malignant liver tumors in rats and mice	U.S. EPA (1997)
Acute	Oral	0.0005	mg/kg/day	Acute oral MRL based on neurodevelopmental effects in mice	ATSDR (2002)
Intermediate	Oral	0.0005	mg/kg/day	Intermediate oral MRL based on liver effects in rats	ATSDR (2002)
Chronic	Oral	0.0005	mg/kg/day	Chronic oral RfD based on liver effects in rats	U.S. EPA (2005a)
Cancer	Oral	0.034	per mg/kg/day	Oral CSF for benign and malignant liver tumors in rats and mice	U.S. EPA (2005a)
Acute	Dermal	0.0005	mg/kg/day	Adopt acute oral MRL as acute dermal; assume no first pass effects and 100% oral absorption	
Intermediate	Dermal	0.0005	mg/kg/day	Adopt intermediate oral MRL as intermediate dermal; assume no first pass effects and 100% oral absorption	
Chronic	Dermal	0.0005	mg/kg/day	Adopt chronic RfD as chronic dermal; assume no first pass effects and 100% oral absorption	
Cancer	Dermal	0.034	per mg/kg/day	Adopt oral CSF as chronic dermal; assume no first pass effects and 100% oral absorption	

For oral exposure, the acute oral MRL of 0.0005 mg/kg/day was derived for DDT based on the LOAEL for neurodevelopmental effects in mice perinatally exposed to DDT (ATSDR, 2002). The intermediate oral MRL of 0.0005 mg/kg/day was derived for DDT based on the NOAEL for liver effects in rats exposed to DDT in the diet (ATSDR, 2002). A chronic RfD of 0.0005 mg/kg/day was derived for DDT based on liver lesions in male and female rats exposed to DDT in the diet for 27 weeks. An oral CSF of 3.4E-1 per mg/kg/day was also derived based on benign and malignant liver tumors in male and female rats and mice chronically exposed to DDT in the diet (U.S. EPA, 2005a).

For inhalation exposure, no noncancer toxicity factors were derived for DDT because adequate experimental data do not exist for this route (ATSDR, 2002; U.S. EPA, 2005a). An inhalation unit risk of 9.75E-5 per $\mu g/m^3$ and an inhalation cancer slope factor of 3.4E-1 per mg/kg/day were calculated from oral data for benign and malignant liver tumors in male and female rats and mice chronically exposed to DDT in the diet (U.S. EPA, 2005a).

For dermal exposure, no dermal toxicity factors have been derived because EPA and ATSDR have not yet identified a method suitable for this route of exposure. However, EPA has developed a simplified paradigm for making route-to-route extrapolations for systemic effects via percutaneous absorption in which complete oral absorption is assumed, thereby eliminating the need to adjust the oral toxicity value (U.S. EPA, 2004). This approach may result in underestimating risk. No adjustment was made and oral toxicity values were used for the dermal assessment.

Background

CASRN:	50-29-3
Synonyms:	(p-chlorophenyl)ethane; dichlorodiphenyl trichloroethane; DDT; 1,1'-(2,2,2-trichloroethylidene)bis(4-chlorobenzene); α-α-bis(p-chlorophenyl)-β, β, β –trichloroethane (ATSDR, 2002)
Chemical Group:	organochlorine (ATSDR, 2002)
Registered Trade Names:	Genitox, Anofex, Detoxan, Neocid, Gesarol, Pentachlorin, Dicophane, Chlorophenothane (ATSDR, 2002) Cesarex, p,p'-DDT, Dichlorodiphenyltrichloroethane, Dinocide, Didimac, Digmar, ENT 1506, Guesapon, Guesarol, Gexarex, Gyron, Hildit, Ixodex, Kopsol, Neocid, OMS 16, Micro DDT 75, Rukseam, R50 and Zerdane (EXTOXNET, 2003).

Usage

DDT is a broad spectrum insecticide that was once widely used. In World War II, it was used extensively to control insect-borne diseases such as malaria and typhus. In the early

1970s, it was banned in the United States and most industrial countries due to its persistence in the environment. Today it is used only in sub-Saharan Africa and in emergency cases to control malaria (ATSDR, 2002).

Formulations and Concentrations

Technical grade DDT is generally used as an insecticide. It is made up of three isomers of DDT, including p,p'-DDT (up to 85 percent), o,p'-DDT (15 percent), and o,o-DDT (trace amounts) (ATSDR, 2002). DDT is available as an aerosol, a dustable powder, an emulsifiable concentrate, in granules, or as wettable powders (EXTOXNET, 2003). DDT that is used for indoor residual spraying is usually a wettable powder that has 75 percent active ingredient. WHO (1999) indicated that the content of p,p'-DDT in the DDT formulation should be declared and contain the following:

- Technical grade DDT: no less than 700 g/kg p,p'-DDT
- Dustable powder: over 25–100 g/kg p,p'-DDT with a permitted tolerance of +/- 10% of the declared content
- Wettable powder: 100–250 g/kg p,p'-DDT with a permitted tolerance of +/- 6% of the declared content, or 250–500 g/kg p,p'-DDT with a permitted tolerance of +/- 5% of the declared content, or greater than 500 g/kg with a permitted tolerance of +/- 25 g/kg.

Shelf Life

DDT has a long shelf life. It is resistant to destruction by light or oxidation (HSDB, 2005).

Degradation Products

DDT breaks down very slowly by dehydrohalogenation into DDE [1,1-dichloro-2,2-bis(p-dichlorodiphenyl)ethylene] and DDE [1,1-dichloro-2,2-bis(p-chlorophenyl)ethane]. In animal systems, these metabolites are stored in body fat and either leave the body slowly if exposure decreases, remain constant in the tissues, or increase with continued exposures (ATSDR, 2002). Stored DDE and DDD are slowly transformed to DDA [bis(dichlorodiphenyl) acetic acid] by other metabolites. DDA and its metabolites are then excreted in the urine (EXTOXNET, 2003).

Environmental Behavior

Fate and Transport in Terrestrial Systems

DDT and its metabolites are highly persistent and bioaccumulate in the environment (ATSDR, 2002). The persistence of DDT in the environment is mainly due to its being soluble in fat and virtually insoluble in water (IPCS, 1979). DDT is released into the air as a result of spraying operations in countries where it is still being used. DDT and its metabolites may also enter the air when they evaporate from contaminated soil and water. They may then be deposited back onto land and surface waters. This cycle of

volatilization and deposition may be repeated numerous times resulting in the movement of DDT in the atmosphere. As a result, DDT and its metabolites have been found in air, sediment, and snow, and accumulated in biota in the Arctic and Antarctic regions. As a result of this ability to undergo long-range global transport, the actual lifetime of DDT and its metabolites is substantially longer than indicated by their estimated half-lives. In the atmosphere, DDT and its metabolites occur as a vapor or are attached to particulates in the air. As a vapor, DDT and its metabolites are broken down by sunlight. DDT is also broken down slowly by microorganisms (ATSDR, 2002).

In most soils, DDT is practically immobile due to its strong affinity to soil, especially organic soil matter (EXTOXNET, 2003). Because DDT and its metabolites (DDD and DDE) stick strongly to the soil, they remain mostly in the surface layers of soil. Soil with DDT bound to it may enter waterways via runoff (ATSDR, 2002). Other routes of loss and breakdown of DDT in soil include volatilization, photolysis, and aerobic and anaerobic biodegradation. Loss from volatilization depends on how much DDT was applied, the amount of organic material in the soil, proximity to the soil-air interface, and the amount of sunlight (EXTOXNET, 2003). Very little DDT will seep into groundwater. The persistence of DDT is soil varies with the type of soil, temperature, and soil moisture (ATSDR, 2002). The typical half-life of DDT in soil ranges from 2 years to 15 years (EXTOXNET, 2003). DDT and its metabolites last for a shorter time in soils that contain more microorganisms, wet soils, and warmer soils (ATSDR, 2002). Because DDT persists in the soil, bioaccumulation in plants has been observed, especially in the root.

Fate and Transport in Aquatic Systems

The two main ways that DDT may be released into surface waters are by direct application for the control of mosquito-borne malaria and by runoff from sprayed areas. Atmospheric transport and drift represent lesser scenarios (EXTOXNET, 2003). DDT is a highly persistent compound with low volatility and low solubility in water, leading to great potential to bioaccumulate in the environment. DDT binds to particles in surface water, settles, and then deposits in the sediment (ATSDR, 2002). Studies have shown that DDT dose not readily break down in estuary sediments. Additionally, DDT has been widely detected in ambient surface water samples in the United States. The reported half-life of DDT in lake and river water is 56 and 28 days, respectively; the half-life in river water is shorter because river water usually has more organic soil matter (EXTOXNET, 2003). The main fate processes in the aquatic environment are volatilization, photodegradation, absorption to water-borne particles, and sedimentation, with the dominant fate process being volatilization. In surface waters, DDT is transformed via biotransformation and photolysis (ATSDR, 2002). DDT is also readily taken up by and accumulates in aquatic organisms (EXTOXNET, 2003).

Human Health Effects

Acute Exposure

Effects/Symptoms

DDT has been used in large populations for more than 60 years with little acute toxicity except from accidental exposures (Rogan and Chen, 2005). DDT impairs the conduction of nerve impulses. In humans, this can cause effects ranging from mild altered sensations to tremors, convulsions, and respiratory depression (ATSDR, 2002). Additional effects observed in humans following acute DDT exposure include headaches; nausea; vomiting; diarrhea; numbness; paresthesia; increased liver enzyme activity; irritation of the eyes, nose, or throat; altered gait; and malaise or excitability (EXTOXNET, 2003; PAN, 2005).

The toxicity of DDT varies with formulation and the exposure pathway. In humans, the oral route is thought to be the most significant. Fatalities have been documented following ingestion of commercial preparations that also contain substances other than DDT (ATSDR, 2002). Children appear to be more susceptible to the fatal effects of DDT than adults (EXTOXNET, 2003). Dermal and inhalation exposures to DDT are more likely in humans if the compound is in solution form (dermal) or aerosol form (inhalation). Exposure through dermal contact is more likely when DDT is in an oily solution than when it is in a wettable powder form, which is the formulation used most often in indoor residual spraying (ATSDR, 2002).

In animals, the toxicity DDT and its analogues have been studied extensively. Acute exposure to high doses of DDT can cause death, with the toxicity dependent upon the formulation. Acute oral LD_{50} values range from 150 to 200 mg/kg in mice, 113 to 800 mg/kg in rats, and 500 to 750 mg/kg in dogs (EXTOXNET, 2003). Deaths were usually a result of respiratory arrest (ATSDR, 2002). DDT is most known for its neurotoxic effects in animals. Similar to its effects in humans, DDT causes hyperactivity, tremor, and seizures in animals. Acute exposure to low doses of DDT can cause subtle neurodevelopmental effects in neonatal mice (EXTOXNET, 2003). Liver effects such as increased liver weights, induction of liver enzymes, and hepatic-cell hypertrophy and necrosis have also been observed (Rogan and Chen, 2005). Because of the hormone altering action of DDT isomers, reproductive and developmental effects have also been seen in laboratory animals. Acute exposure to DDT and its metabolites in food may have negative effects on reproduction (ATSDR, 2002). DDT is very slightly toxic to laboratory animals via acute dermal exposure. LD_{50} values range from 2,500 to 3,000 mg/kg in rats, 1,000 mg/kg in guinea pigs, and 300 mg/kg in rabbits. Acute inhalation exposure of animals to DDT does not result in significant absorption in the lungs (EXTOXNET, 2003).

Treatment

Exposure to DDT may be measured through laboratory tests. DDT and its metabolites (DDE and DDD) may be detected in the blood/plasma, semen, urine, liver, kidney, fatty tissue, skin lipids, breastmilk, and lymphatic tissues (ATSDR, 2002). DDT exposure

should be treated with anticonvulsants (benzodiazepines), oxygen, and cardiopulmonary monitoring. Epinephrine, other adrenergic amines, atropine, and orally administered fats are all contraindicated (PAN, 2005; Reigart and Roberts, 1999).

Chronic Exposure

Noncancer Endpoints

Most chronic exposure human data come from studies of workers who are exposed to DDT in manufacturing facilities or as spray applicators and from epidemiological studies. These studies indicate that chronic oral exposure to small amounts of DDT does not produce toxic effects in humans. However, DDT and its metabolite DDE may alter hormonally mediated endpoints such as lactation duration, maintenance of pregnancy, and fertility. Recent data have indicated that exposure to DDT in amounts necessary for malaria control may cause preterm birth, decreased birth weight, early weaning, and pregnancy loss (Farhang et al., 2005; IPCS, 2004; Longnecker, 2005; Rogan and Chen, 2005; Venners et al., 2005). Increased chances of premature birth, infants that are small for their gestational age, and height abnormalities in children have also been associated with high DDE levels in the blood (ATSDR, 2002). DDT and its metabolites affect male reproductive parameters such as semen volume, sperm count, testosterone ratios, sperm motility, and sperm morphology and DNA damage; these data indicate the possibility of reduced male fertility as a result of occupational and non-occupational exposure to DDT used in IRS (De Jager et al., 2006; IPCS, 2004; Rogan and Chen, 2005). Residential exposure (*in utero* and from breastfeeding) to DDT may delay neurodevelopment in children during their first two years of life (Eskenazi et al., 2006).

In animals, liver effects have been seen following chronic exposure to moderate levels of DDT (ATSDR, 2002). The main effect was localized liver damage. Additional chronic effects in animals include nervous system (tremors, central nervous system cellular chemistry changes, loss of equilibrium), kidneys (adrenal gland and kidney damage), and immune system (reduced antibody formation, reduced immune cells). Those effects were seen at levels much higher than expected human exposure levels (EXTOXNET, 2003).

Cancer Endpoints

IARC has classified DDT in group 2B; a probable human carcinogen (IARC, 1991). EPA has also determined that DDT is a probable human carcinogen (U.S. EPA, 2005a). The available epidemiological evidence regarding carcinogenicity in humans is inconclusive. A slight increase in risk from lung cancer was observed in workers at two DDT production facilities. No other cancer incidences were found in sufficient numbers for analysis. Inconsistent results have been found when comparing serum DDT/DDE levels in people with and without cancer (IARC, 1991). One study indicated a potential link between chronic, high dose DDT exposure and pancreatic cancer in chemical workers but the reliability of the study is questionable. The association between p,p'-DDE and breast cancer has been studied extensively, but studies have failed to show an association (Rogan and Chen, 2005). Studies have indicated that DDT and its metabolites are not

mutagenic (ATSDR, 2002). In animals, DDT has been shown to cause liver and lung cancers (ATSDR, 2002).

Toxicokinetics

DDT is absorbed via inhalation, the gastrointestinal tract, and dermally. In humans, oral exposure to DDT is considered the most significant. Orally, DDT is absorbed from the gastrointestinal tract into the lymphatic system. There is also some absorption into the portal blood. Distribution of DDT to all body tissues then occurs from the lymphatic system and blood. In the tissues, DDT is stored in proportion to the lipid (fat) content of the tissue (ATSDR, 2002). DDT is initially metabolized into DDE and DDD, however these are ultimately transformed into DDA (EXTOXNET, 2003). DDA and its metabolites are eventually excreted in the urine. DDT may also be excreted via feces, semen, and breastmilk (ATSDR, 2002).

Ecological Effects

Acute Exposure

DDT is only slightly toxic to birds. Acute oral LD_{50} values in various bird species include the following: Japanese quail (841 mg/kg), pheasant (1,334 mg/kg), and mallard (2,240 mg/kg). Most avian exposures are a result of the food chain and consumption of aquatic (e.g., fish) or terrestrial (e.g., earthworms or other birds) species that have an accumulated body burden of DDT. However, earthworms are not susceptible to the acute toxic effects of DDT. Additionally, DDT is not toxic to bees. DDT may, however, be toxic to bats as DDT may be released from fat stores during migration (EXTOXNET, 2003).

DDT is highly toxic to many aquatic species. On average, acute exposure to DDT is only slightly toxic to amphibians and phytoplankton; moderately toxic to annelida, mollusks, and zooplankton; highly to very highly toxic to fish; and very highly toxic to crustaceans (PAN, 2005). In fish, the 96-hour LC_{50} values range from 1.5 µg/L in northern pike to 21.5 µg/L in fathead minnows. DDT is very highly toxic to stoneflies, midges, crayfish, sow bugs, and other aquatic invertebrate with 96-hour LC_{50} values ranging from 0.18 to 7.0 µg/L. In aquatic invertebrates, DDT adult stages are less susceptible than developmental stages (EXTOXNET, 2003).

Chronic Toxicity

Chronic exposure to DDT has been linked to reproductive effects in birds. Eggshell thinning and embryo death are two of the main concerns especially in birds of prey. The mechanism of eggshell thinning is thought to be from the major metabolite DDE. Additionally, the reproductive behavior of birds may also be subtlety altered by DDT and DDE exposure. In laboratory studies, changes in courtship behavior, delays in pairing and egg laying, and decreases in egg weight have been observed in some bird species, though it is not clear what these effects mean for the survival of wild bird species. A synergism

may exist between DDT metabolites and organophosphate pesticides to produce greater neurotoxicity and increased deaths (EXTOXNET, 2003).

Chronic exposure to DDT may occur in fish and aquatic species through bioaccumulation. This occurs from the uptake of DDT in sediments and water, with smaller fish taking up higher amounts of DDT. It has been estimated that the half-time elimination of DDT for rainbow trout is 160 days. Bioaccumulation can occur at very low environmental concentrations and the bioconcentration factor for DDT is 1,000 to 1,000,000, depending on the aquatic species (EXTOXNET, 2003).

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Profile for Deltamethrin:

CAS Registry Number 52918-63-5

Summary of Insecticide

Chemical History

Deltamethrin is a broad spectrum synthetic pyrethroid insecticide used in agricultural and human health applications. It was first marketed in 1977 (IPCS, 1990; EXTOXNET, 1995; WHO/FAO, 2001) and has been in use longer than any alpha-cyano pyrethroid with an excellent safety record (WHO/FAO, 1999). It is similar to the natural insecticide pyrethrum, which comes from chrysanthemums; however, it is more effective and longer lasting (EXTOXNET, 1995; WHO/FAO, n.d.; IPCS, 1990). Deltamethrin is considered the most powerful synthetic pyrethroid (EXTOXNET, 1995). For mosquito control, it is used on bed nets and other materials that are dipped in deltamethrin to protect the user (Barlow et al., 2001; EXTOXNET, 1995; WHO/FAO, 2001). Deltamethrin is typically formulated as emulsifiable concentrates, wettable powders, ultra-light-volume (ULV) and flowable formulations, and granules either alone or combined with other pesticides (EXTOXNET, 1995; IARC, 1991). A dispersible tablet is also used to treat mosquito nets (Barlow et al., 2001). Deltamethrin is of moderate toxicity to mammals because metabolizes rapidly and does not accumulate (WHO/FAO, n.d.; WHO/FAO, 1999). It is of low risk to humans when used at levels recommended for its designed purpose (ATSDR, 2003; WHO, 2004). General population exposures are expected to be very low and to occur mostly through public health uses and dietary residues. As a synthetic pyrethroid, deltamethrin exhibits its toxic effects by affecting the way the nerves and brain normally function by interfering with the sodium channels of nerve cells (Choi and Soderlund, 2006). EPA has not classified synthetic pyrethroids, including deltamethrin, as endocrine disruptors. Typical symptoms of acute exposure are irritation of skin and eyes, severe headaches, dizziness, nausea, anorexia, vomiting, diarrhea, excessive salivation, and fatigue. Tremors and convulsions have been reported in severe poisonings. Inhaled deltamethrin has been shown to cause cutaneous paraesthesia (a burning, tingling, or stinging). However, these effects are generally reversible and disappear within a day of removal of the exposure (Barlow et al., 2001; WHO, 2004; ATSDR, 2003; IPCS, 1989, 1990). In animals, the critical effect is neurotoxicity (WHO, 2004).

Description of Data Quality and Quantity

Adequate dose-response studies on the toxicity of deltamethrin exist for oral, dermal, and inhalation exposures. Most are oral exposure studies (WHO, 2004). Several comprehensive reviews on the toxicity of deltamethrin have been prepared or updated in recent years:

- Environmental Health Criteria 97: Deltamethrin (IPCS, 1990)

- Health and Safety Guide No. 30: Deltamethrin Health and Safety Guide (IPCS, 1989)
- A review article by Barlow et al. (2001)
- Pesticide Information Profiles (PIP) for Deltamethrin (EXTOXNET, 1995)
- Data Sheets on Pesticides No. 50—Deltamethrin (WHO/FAO, n.d.)
- A Generic Risk Assessment Model for Insecticide Treatment and Subsequent Use of Mosquito Nets (WHO, 2004)
- Malaria Vector Control—Insecticides for Indoor Spraying (WHO/FAO, 2001)

EPA has developed quantitative human health benchmarks (acute and chronic oral RfDs, intermediate-term oral, and short-, intermediate-, and long-term dermal and inhalation benchmarks) for deltamethrin.

Summary Table

Duration	Route	Benchmark Value	Units	Endpoint	Reference
Acute, Intermediate, Chronic	Inhalation	0.01	mg/kg/day	Oral NOAEL for clinical signs in dogs at 1 mg/kg/day with UF of 100 applied	U.S. EPA (2004)
Acute	Oral	0.01	mg/kg/day	Acute RfD based on neurological effects in rats	U.S. EPA (2004)
Intermediate	Oral	0.01	mg/kg/day	Oral NOAEL for clinical signs in dogs at 1 mg/kg/day with UF of 100 applied	U.S. EPA (2004)
Chronic	Oral	0.01	mg/kg/day	Chronic RfD based on clinical signs in dogs	U.S. EPA (2004)
Acute, Intermediate, Chronic	Dermal	10	mg/kg/day	Dermal NOAEL of 1000 mg/kg/day in rats with a UF of 100 applied	Barlow et al. (2001)

For oral exposure, an acute RfD of 0.01 mg/kg/day was derived based on a NOAEL of 1 mg/kg/day for neurological effects (reduced motor activity) observed in rats exposed to deltamethrin (Crofton et al., 1995), with an uncertainty factor of 100 applied to account for interspecies and intrahuman variability (U.S. EPA, 2004). A chronic oral RfD of 0.01 mg/kg/day was derived based on a NOAEL of 1 mg/kg/day for clinical signs and reduced weight gain in dogs (study citation not provided), with an uncertainty factor of 100 applied (U.S. EPA, 2004). The chronic RfD is appropriate to use for intermediate-term exposures (U.S. EPA, 2004).

For inhalation exposures, the chronic RfD is also appropriate for short-, intermediate-, and long-term exposures (U.S. EPA, 2004).

For dermal exposure, a NOAEL of 1,000 mg/kg/day was identified in rats dermally exposed to deltamethrin for 21 days (study citation not provided). An uncertainty factor of 100 was applied to account for interspecies and intrahuman variability, for a dermal benchmark value of 10 mg/kg/day. This value is appropriate for all dermal exposure durations (Barlow et al., 2001). The large difference between the oral and dermal NOAELs is due to rapid absorption of deltamethrin from the gastrointestinal tract versus low dermal absorption (WHO, 2004; Barlow et al., 2001).

Insecticide Background

CASRN:	52918-63-5
Synonyms:	cyano(3-phenoxy-phenyl)methyl;2-(2,2dibromoethenyl)-2,2-dimethylcyclopropanecarboxylate (CA); alpha-cyano-m-phenoxybenzyl,(1R,3R)-3-(2,2-dibromovinyl)-2,2-dimethyl-cyclopropanl-carboxylate, (S)-alpha-cyano-3-phenoxybenzyl (1R)-cis-3-(2,2-dibromovinyl)-2,2-dimethylcyclopropane-carboxylate, decamethrine, FMC 45498, NRDC 161, OMS 1998, RU 22974, RUP 987 (EXTOXNET, 1995; IARC, 1991; WHO/FAO, n.d.).
Chemical Group:	pyrethroid (PAN, 2005)
Registered Trade Names:	Products containing deltamethrin (NRDC 161 and RU 22974): Butoflin, Butoss, Butox, Cislin, Cislin 2.5% EC, Cislin 2.5% WP, Cislin RTU, Crackdown, Cresus, Decis, Decis-Prime, K-Othrin, K-Orthine, K-Otek, Kordon, Sadethrin (EXTOXNET, 1995; WHO/FAO, n.d.; ATSDR, 2003; IPCS, 1989; IARC, 1991; FPA, 2002).

Usage

Deltamethrin is used to combat pests on a variety of crops, including cotton, fruit, vegetables, coffee, maize, wheat, rapeseed, hops, and soybeans (ATSDR, 2003; EXTOXNET, 1995; IPCS, 1989, 1990). It is also used to control insects in stored grains, to protect cattle from infestation, and in public health applications. It may be applied to foods, field crops, gardens, orchards, and vineyards (WHO/FAO, n.d.). Public health uses include malaria control in Central America and Africa (IPCS, 1990). Deltamethrin belongs to the pyrethroid class of insecticides, which have long been used to control mosquitoes, human lice, beetles, and flies (ATSDR, 2003). For mosquito protection, it is used on bed nets and other materials that are dipped into the deltamethrin to protect the user. All concentrated formulations of deltamethrin were restricted by EPA due to its potential toxicity to aquatic organisms, and it may only be purchased and used by certified applicators (ATSDR, 2003).

Formulations and Concentrations

Deltamethrin is available in technical grade (> 98 percent pure), suspension concentrate, emulsifiable concentrate (25–100 g/L), ultra-low-volume (ULV) concentrate (1.5–30 g/L), wettable powder (25–50 g/kg), flowable powder (7.5–50 g/L), dust powder (0.525 g/kg), and granules (0.5 and 1.0 g/kg) alone or combined with other pesticides (IPCS, 1989, 1990; WHO/FAO, n.d.). Deltamethrin that is marketed for use as a bed net treatment comes in a single 400 mg tablet form (WHO, 2004).

Shelf Life

In storage conditions at 40^{o}C, deltamethrin is stable to light, heat, and air for 6 months and to light and air for 2 years. It is most stable in acidic media and unstable in alkaline environments (EXTOXNET, 1995; IPCS, 1989, 1990; WHO/FAO, n.d.).

Degradation Products

Deltamethrin's major metabolites are free and conjugated Br_2CA, *trans*-hydroxymethyl-Br_2CA, and 3-(4-hydroxyphenoxy)benzoic acid formed by ester cleavage, oxidation, and conjugation (IPCS, 1990).

Environmental Behavior

Fate and Transport in Terrestrial Systems

Deltamethrin is not expected to be mobile in soil, with a Koc ranging from 46,000 to 1,630,000 (HSDB, 2005). Additionally, it binds tightly to soil particles, is insoluble in water, and has low application rates (IPCS, 1989, 1990). Volatilization is a major environmental fate process from moist soils but this is lessened by its adsorption to soil. Another major fate process is biodegradation, with a half-life of several weeks to greater than 100 days (HSDB, 2005). As with other synthetic pyrethroids, deltamethrin degrades rapidly in soil and plants (IPCS, 1990). Degradation occurs within 1 to 2 weeks for soil, and no residues remain on plants after 10 days (EXTOXNET, 1995). Deltamethrin does not bioaccumulate in terrestrial systems (IPCS, 1990).

Fate and Transport in Aquatic Systems

Because deltamethrin binds tightly to soil and is practically insoluble in water, very little leaching into groundwater is expected. In pond water, deltamethrin was absorbed rapidly by sediment, uptake by plants, and evaporation (EXTOXNET, 1995). Volatilization is a major environmental fate process in surface waters but is lessened by soil adsorption. Deltamethrin breaks down quickly in water with reported half-lives of 2 to 4 hours. The estimated volatilization half-life in a model river is 30 hours, and in a model lake, 500 hours. In a model pond, the estimated volatilization half-life is 7 years if adsorption is considered. Deltamethrin has a high potential to bioconcentrate in aquatic organisms. It has an estimated bioconcentration factor of 270. The reported estimated hydrolysis half-life was 36 years at pH 7 and 3.6 years at pH 8 (HSDB, 2005).

Human Health Effects

Acute Exposure

Effects/Symptoms

There are limited data on the acute toxicity of deltamethrin in humans. Acute effects in humans include irritability, headache, salivation, sweating, fever, anxiety, rapid heart beat, diarrhea, dyspnea, tinnitus, runny nose, vomiting, edema, hepatic microsomal enzyme induction, peripheral vascular collapse, serum alkaline phosphatase elevation, tremors, ataxia, convulsions leading to muscle fibrillation and paralysis, and death due to respiratory failure (EXTOXNET, 1995; WHO/FAO, n.d.; IPCS, 1990). Dermatitis is expected after dermal exposures, which often occur as a result of inadequate handling safety precautions during agricultural use (EXTOXNET, 1995; IPCS, 1990). Coma was caused within 15 to 20 minutes at oral exposure levels of 100 to 250 mg/kg (EXTOXNET, 1995). Facial paraesthesia is a common indicator of exposure of humans to high levels (WHO/FAO, n.d.).

In clinical studies in humans, slight irritation but no skin damage was reported in patch tests of deltamethrin put on faces of volunteers (IPCS, 1990). Acute occupational exposures to deltamethrin have resulted mostly in dermal symptoms including itching, burning, and paraesthesia. These are an early, reversible signs of exposure and are due to local, not systemic, exposures (Barlow et al., 2001; IPCS, 1990; EXTOXNET, 1995). Neurological signs such as headaches, dizziness, fatigue, nausea, anorexia, transient EEG changes, muscular fasciculation, and convulsions have also been reported following acute occupational exposures (Barlow et al., 2001; EXTOXNET, 1995). Loss of consciousness, muscle cramps, myosis, and tachycardia were reported in a 13-year-old girl who attempted suicide by ingesting 5 g of deltamethrin (200 mL of a 2.5% EC formulation). After appropriate medical intervention, she recovered completely within 48 hours. Only digestive and hepatic signs were observed in a 23-year-old man who attempted suicide by ingesting 1.75 g of deltamethrin (70 mL of a 2.5% EC formulation) (IPCS, 1990).

Animal studies have indicated that deltamethrin has low acute toxicity; however, this varies greatly depending on the route of administration and the vehicle used (WHO, 2004; Barlow et al., 2001). In acute exposure studies, the mouse is the species most susceptible to deltamethrin toxicity (WHO/FAO, n.d.). Reported oral LD_{50} values range from 19 to 34 mg/kg in mice, 52 to over 5,000 mg/kg in male rats, 30 to 139 mg/kg in female rats, and over 300 mg/kg in dogs (EXTOXNET, 1995; IPCS, 1990; WHO/FAO, n.d.; WHO/FAO, 2001; Barlow et al., 2001). Following acute dermal exposure, the reported LD_{50} is greater than 2,940 mg/kg in rats and dogs and greater than 2,000 mg/kg in rabbits (EXTOXNET, 1995; IPCS, 1990; WHO/FAO, n.d.; WHO/FAO, 2001). The reported inhalation 6-hour LD_{50} in rats is 600 mg/m^3 (IPCS, 1990).

Hyperactivity and hypersensitivity are general characteristics of pyrethroid poisonings. However, the signs of acute deltamethrin poisoning are different from other pyrethroids in that it produces a unique set of effects that occur in a specific sequence in animals.

They begin with chewing, pawing, and burrowing behavior; excessive salivation; and coarse tremors advancing to choreoathetosis and sometimes terminal clonic seizures. Rolling convulsions are especially characteristic of deltamethrin poisoning (WHO/FAO, n.d.; EXTOXNET, 1995). In rabbits and guinea pigs, no primary skin irritation or sensitization was observed following acute dermal exposure to 0.5 g/animal, although transitory ocular irritation was seen in rabbits without immediate rinsing (EXTOXNET, 1995; WHO/FAO, n.d.). However, another study reported skin irritation in rats and guinea pigs (EXTOXNET, 1995). Cardiovascular effects include a rapid fall in blood pressure, severe bradycardia, and EKG changes in intravenously exposed dogs (WHO/FAO, n.d.)

Treatment

Deltamethrin and its metabolites can be detected in blood and urine; however, the methods are not practical given how quickly these compounds are broken down in the body (ATSDR, 2003; WHO/FAO, n.d.). Levels of the degradation products bromide, cyanide, and 3-phenoxybenzyl in urine may be useful indicators in cases of severe toxicity (WHO/FAO, n.d.).

There are no antidotes for deltamethrin exposure (IPCS, 1989; WHO/FAO, n.d.). Treatment depends on the symptoms of the exposed person. If a person exhibits signs of typical pyrethroid toxicity following deltamethrin exposure (nausea, vomiting, shortness of breath, tremors, hypersensitivity, weakness, burning, or itching), they should immediately remove any contaminated clothing. Any liquid contaminant on the skin should be soaked up and the affected skin areas cleaned with alkaline soap and warm water. Eye exposures should be treated by rinsing with copious amounts of 4 percent sodium bicarbonate or water. Contact lenses should be removed. Vomiting should not be induced following ingestion exposures, but the mouth should be rinsed. The person should be kept calm and medical attention should be sought as quickly as possible (PAN, 2005; WHO/FAO, n.d.). Medical personnel will treat severe intoxications with a sedative and anticonvulsant (IPCS, 1989). Ingestion of large amounts of deltamethrin should be treated with gastric lavage using a 5 percent bicarbonate solution followed by powdered activated charcoal. Skin irritation may be treated with a soothing agent and exposure to light should be avoided (WHO/FAO, n.d.)

Chronic Exposure

Noncancer Endpoints

Little data are available for humans following chronic exposures to deltamethrin; however, it is not likely to cause long-term problems when used under normal conditions. In humans, suspected chronic effects include choreoathetosis, hypotension, prenatal damage, and shock (EXTOXNET, 1995). Chronic occupational exposure to deltamethrin caused skin and eye irritation; however, no long-term effects were seen (Barlow et al., 2001; EXTOXNET, 1995). After 1 year of using bednets treated with a target does of 25 mg/m^2 deltamethrin, skin irritation occurred one week after treatment, and runny nose

and sneezing in the first days of use were reported for target does of 10–30 mg/m^2. No chronic effects were reported (Barlow et al., 2001). Data in animals indicate that oral exposure to deltamethrin is not highly toxic (Barlow et al., 2001; EXTOXNET, 1995; WHO/FAO, n.d.).

In studies of reproductive toxicity in rats, no effects were seen on male or female fertility; number of implantation sites; litter size at birth; or pre- or postnatal survival in rats, mice, and rabbits (Barlow et al., 2001). No effects on reproduction were observed in a 3-generation rat study, but slight embryotoxicity was seen (EXTOXNET, 1995; Barlow et al., 2001). Dose-related decreases in maternal weight gain were seen in pregnant mice dosed with deltamethrin on gestational days 7 to 16. However, no effect on the number of implants, fetal mortality, fetal weight, or malformations was seen (EXTOXNET, 1995). Deltamethrin is not teratogenic in mice, rats, or rabbits at doses that produced clinical signs of toxicity in pregnant dams (Barlow et al., 2001; EXTOXNET, 1995; WHO/FAO, n.d.). Mutagenicity studies in mice, rats, and rabbits indicate that deltamethrin is not mutagenic (Barlow et al., 2001; EXTOXNET, 1995; WHO/FAO, n.d.)

Cancer Endpoints

IARC (1991) has classified deltamethrin as a Group 3 chemical, "not classifiable as to its carcinogenicity in humans." No human carcinogenicity data are available for deltamethrin (IARC, 1991; EXTOXNET, 1995). Long-term dietary studies in rats, mice, and dogs did not find evidence of carcinogenicity (IPCS, 1990). Microbial, mammalian cell, and *in vivo* mammalian mutagenicity studies support the evidence that deltamethrin is not carcinogenic (WHO/FAO, n.d.).

Toxicokinetics

Deltamethrin metabolism has not been well studied in humans. It is expected to be similar to metabolism in rodents (Barlow et al., 2001). Deltamethrin is readily absorbed via the gastrointestinal tract, inhalation, and less so through intact skin. The rate at which it is absorbed depends on the carrier or solvent used. Once absorbed, deltamethrin is readily metabolized and excreted (Barlow et al., 2001; IPCS, 1989, 1990; WHO/FAO, n.d). Similar metabolism and excretion patterns have been observed in extensive studies in rats, mice, and cows. Deltamethrin is metabolized in the liver by microsomal esterases and oxidases. It is distributed to the gut wall and liver. The parent compound is cleaved into cyclopropanecarboxylic acid and 3-phenoxybenxyl alcohol, which is then oxidized to 3-phenolbezoic acid. 3-Phenoxybenxoic acid is the major excretion compound. Hydroxylation of this moiety can occur before or after hydrolysis (Barlow et al., 2001; WHO/FAO, n.d.; EXTOXNET, 1995; IPCS, 1990). In rats, approximately 13 to 21 percent of deltamethrin is eliminated unchanged in the urine and feces within 2 to 4 days; however, the metabolites of the cyano substituent are eliminated more slowly. The half-life of deltamethrin in the brains of rats is 1 to 2 days. Levels of the metabolites remain higher, especially in the skin, stomach, and body fat, with a half-life of 5 days in body fat (Barlow et al., 2001; EXTOXNET, 1995). Following oral exposure, deltamethrin is

completely eliminated within 6 to 8 days (WHO/FAO, n.d.). In feces, 7 to 15 percent of the oral dose is found as the parent compound and its hydroxylates; the hydrolysis products are mainly excreted in the urine. A smaller amount is found in the skin as thiocyanate (WHO/FAO, n.d.)

Ecological Effects

Acute Exposure

Toxicity in Non-Targeted Terrestrial Organisms

Deltamethrin, like other pyrethroids, is very unlikely to harm terrestrial organisms other than its targets, such as mosquitoes and other pests (EXTOXNET, 1996). It has a very low toxicity in birds (IPCS, 1990; IPCS, 1989). Oral LD_{50} values range from greater than 1,800 mg/kg in grey partridge to greater than 4,000 mg/kg in ducks (IPCS, 1989). An 8-hour LD_{50} of more than 4,640 mg/kg diet was reported in ducks, and the 8-hour LD_{50} in quail was greater than 10,000 mg/kg diet (EXTOXNET, 1995). As with other pyrethroid insecticides, deltamethrin is extremely toxic to honey bees, with a 24-hour LD_{50} of 0.079 for technical deltamethrin and 0.4 µg ai/bee for the EC formulation. The contact LD_{50} for bees is reported to be 0.05 µg ai/bee. However, in real-life applications, serious effects have not been noticed due to low application rates and lack of environmental persistence. Deltamethrin is also very toxic to *Typhodromum pyri*, a predatory mite; *Encarsia Formosa*, a parasitic wasp; and spiders (EXTOXNET, 1995; IPCS, 1990).

Toxicity in Non-Targeted Aquatic Systems

In the laboratory, deltamethrin is very toxic to fish and aquatic arthropods. However, under normal use conditions in the environment, no deleterious effects have been observed due to its low application rates and lack of persistence (EXTOXNET, 1995; IPCS, 1990). The reported 96-hour LC_{50} value for technical deltamethrin ranges from 0.39 µg/L in rainbow trout to 3.5 µg/L in *Sarotherodon mossambicus*. For the emulsifiable concentrate, LC_{50} values range from 0.59 µg/L in *Salmo salar* (96-hour) to 4.7 µg/L in brown trout (48-hour). For ultra-light volume concentrate, LC_{50} value ranges from 82 µg/L in bleak to 210 µg/L in common carp. In Daphnia, the reported 48-hour LC_{50} for technical deltamethrin is 5 µg/L (IPCS, 1990). Deltamethrin can accumulate in fish. Fathead minnows accumulated deltamethrin without any effect on mortality (EXTOXNET, 1995). Deltamethrin is also highly toxic to aquatic macroinvertebrates such as lobster (IPCS, 1989).

Chronic Exposure

Due to low application rates and low persistence of deltamethrin in both terrestrial and aquatic environments, serious adverse effects are not anticipated from chronic exposures (HSDB, 2005)

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Profile for Etofenprox:

CAS Registry Number 80844-07-1

Summary of Insecticide

Chemical History

Etofenprox is a non-ester pyrethroid-like insecticide and acaricide used in agricultural, horticultural, and public health applications. Its toxicity and mode of action (acting on the central nervous system) are similar to other pyrethroids (WHO/FAO, 1993; WHO, 1999; NIH, 2005). For mosquito control, etofenprox is used on bed nets and other materials that are dipped in it to protect the user. WHO has classified etofenprox as low risk for acute toxicity in humans under normal use conditions (WHO, 1999). Typical symptoms of acute exposure are likely to be similar to other pyrethroid insecticides. At high doses, hunched posture, lethargy, body tremors, and respiratory distress were reported in laboratory animals. Etoxfenprox does not inhibit cholinesterase activity. At high doses, long-term exposure can affect organs such as the thyroid and kidneys. Reproductive and developmental effects are not expected. Etofenprox is available as the technical product and formulated wettable powders and emulsifiable concentrates. Etofenprox is classified as Group C, possible human carcinogen.

Description of Data Quality and Quantity

The available data on etofenprox are limited. Relevant references include the following:

- Pesticide Residues in Food – 1993. Evaluation Part II Toxicology. Etofenprox (WHO/FAO, 1993)
- Etofenprox Evaluation (FAO, 1993)
- Summary of Toxicology Data: Etofenprox (CalEPA, 2003)

Summary Table

Duration	Route	Benchmark Value	Units	Endpoint	Reference
Acute, Intermediate, Chronic	Inhalation	0.1	mg/kg/day	NOAEL for systemic effects in rats with UF of 100 applied	NYSDEC (2005)
Acute, Intermediate, Chronic	Oral	0.037	mg/kg/day	Proposed chronic RfD based NOEL in rats with UF of 100 applied	NYSDEC (2005)
Acute, Intermediate	Dermal	0.4	mg/kg/day	LOAEL (skin lesions) in rats with UF of 1,000 applied	NYSDEC (2005)

Duration	Route	Benchmark Value	Units	Endpoint	Reference
Chronic	Dermal	0.037	mg/kg/day	Adopt chronic oral RfD; assume no first pass effects and 100% absorption	NYSDEC (2005)
Cancer	Inhalation, Oral, Dermal	0.0051	per mg/kg/day	CSF for thyroid adenomas and carcinomas in rats	NYSDEC (2005)

For inhalation exposure, a NOEL of 0.04 mg/L (equivalent to 10.6 mg/kg/day) was identified for hematological and systemic effects in rats (study citation not provided) exposed to etofenprox for 90 days (NYSDEC, 2005). An uncertainty factor of 100 was applied to account for intrahuman and interspecies variation. This value is appropriate for all exposure durations.

For oral exposure, EPA calculated a chronic RfD of 0.037 mg/kg/day based on a NOEL in a chronic rat feeding study (study citation not provided). An uncertainty factor of 100 was applied. EPA's Integrated Risk Information System (IRIS) has not yet adopted this value (NYSDEC, 2005). This value is appropriate for all exposure durations.

For dermal exposure, a LOAEL of 400 mg/kg/day for skin lesions was reported (study citation not provided) in a 28-day dermal study in rats (no systemic effects were observed). An uncertainty factor of 1,000 was applied to account for the use of a LOAEL and intrahuman and interspecies variation (NYSDEC, 2005). This value is appropriate for short- and intermediate-term exposures. For long-term exposures, the chronic oral RfD was adopted for dermal exposures.

EPA has classified etofenprox as Group C, possible human carcinogen. To assess potential carcinogenic risks, EPA derived a cancer slope factor (CSF) of 5.1×10^{-3} per mg/kg/day based on increased thyroid follicular cell adenomas and carcinomas in a two-year rat feeding study (NYSDEC, 2005).

Insecticide Background

CASRN: 80844-07-1

Synonyms: Ethofenprox. Ethophenprox, Ephofenprox, 1-((2-(4-Ethoxyphenyl)-2-methylpropoxy)methyl)-3-phenoxy benzene, 3-Phenoxybenzyl 2-(4-ethoxyphenyl)-2-methylpropyl ether, MTI 500, BRN, 707478121 percentEtofenprox aerosol , 1 percentEtofenprox Fogger, 2-(4-Ethoxyphenyl)-2-methylpropyl 3-phenoxybenzyl ether , Benzene, 1-((2-(4-ethoxyphenyl)-2-methylpropoxy)methyl)-3-phenoxy- , Benzene, 1-((2-(4-

	ethoxyphenyl)-2-methylpropoxy)methyl)-3-phenoxy- (9CI) RF 316 , SAN 811 I (NIH, 2005; FAO, 1993; PAN, 2005)
Chemical Group:	non-ester pyrethroid (Hemingway, 1995)
Registered Trade Names:	Carancho 2.5 EC, Polido 2.5 EC, Trebon 10 EC, Trebon 10 EW, Trefic 20 WP, Vectron 10 EW, Vectron 20 WP, Zoecon RF-316 (WHO, 2002; FAO, 1993; PAN, 2005)

Usage

Etofenprox is used as a broad spectrum insecticide to combat a wide variety of pests on an assortment of crops including rice, fruits, vegetables, corn, soybeans, and tea. Etofenprox is effective against Lepidoptera, Hemiptera, Coleoptera, Diptera, Thysanoptera, and Hymenoptera at low rates. Because of its pyrethroid-like activity, it is active against insects that are resistant to carbamate or organophosphorus insecticides, including strains of rice green leafhopper and planthoppers (WHO/FAO, 1993; FAO, 1993). Etofenprox is also used in public health applications, including mosquito control, and on livestock (WHO/FAO, 1993; Hemingway, 1995). Etofenprox is a WHO Pesticide Evaluation Scheme (WHOPES)-recommended insecticide for the indoor spraying of malaria vectors. Application of 0.1 to 0.3 mg/m^2 is effective for 3 to 6 months (WHO, 2003). Technical grade etofenprox (97 percent etofenprox) is labeled for use in pesticide formulations for use in residential, commercial, and industrial uses. Etofenprox aerosol (1 percent) is labeled to kill cockroaches, ants, fleas, ticks, spiders, and other listed insects in residential, commercial, and industrial applications (NYSDEC, 2005). Etofenprox is not a restricted use chemical (PAN, 2005).

Formulations and Concentrations

Etofenprox is available in technical grade, emulsifiable concentrates, and wettable powder formulations (WHO, 1999; FAO, 1993). Technical grade etofenprox is typically 96.3 percent etofenprox with < 1 percent impurities (FAO, 1993). It may be mixed with carriers or solvents resulting in the commercial formulations. The most common formulations are a 20 percent wettable powder and a 20 percent emulsifiable concentrate. These may be used on all crops; however 10 percent or 30 percent formulations are used in some countries (FAO, 1993). WHO indicated that the content of etofenprox in the formulated products must be declared and shall not exceed the listed standards. Technical grade etofenprox must have no less than 985 g/kg etofenprox. The wettable powder should contain > 25–100 g/kg +/- 10% of the declared content, 100–250 g/kg +/- 6% of the declared content, or > 250–500 g/kg +/- 5% of the declared content (WHO, 1999). For mosquito netting treatment, etofenprox is a WHOPES-recommended insecticide at doses of 200 mg ai/m^2 of netting of a 10 percent EW formulation. The amount of etofenprox that is recommended for treatment of mosquito netting is 30 ml of a 10 percent EW formulation (WHO, 2003).

Shelf Life

Etofenprox is stable to temperatures up to 80°C for up to 3 months. At 100°C, it degrades partially. A half-life of 4 days was calculated for radiolabeled etofenprox exposed to high intensity heat lamps (FAO, 1993).

Degradation Products

In soil, etofenprox is broken down by oxidation. The main degradation products are 2-(4-ethoxyphenyl)-2-methylpropyl 3-phenoxybenzoate and 2-(4-ethoxyphenyl)-2-methylpropyl 3-hydroxybenzyl ether. It is metabolized by desethylation of the ethoxyphenyl group, hydroxylation of the phenoxy ring, and oxidation of the benzyl moiety followed by cleavage of the ether linkage to form polar compounds. In animals, conjugates are formed (FAO, 1993).

Environmental Behavior

Fate and Transport in Terrestrial Systems

Studies of adsorption and leaching of etofenprox in Yamanashi sandy loam (78 percent sand, 11 percent silt, 11 percent clay), Chiba light clay (28 percent sand, 39 percent silt, 32 percent clay), and Shizuoka light clay (43 percent sand, 26 percent silt, 31 percent clay) revealed low translocation. Unchanged etofenprox was not found in deeper layers of the soil when it was applied just before application of glass columns. When radiolabeled soil was preincubated, the majority or the radioactivity remained in the top 5 cm of soil. Unchanged etofenprox was not found in the elutes (FAO, 1993).

Under laboratory conditions the half-life of etofenprox in soil is 6 to 9 days, with only minor differences between Yamanashi sandy soil, Chiba light clay soil, and Shizuoka light clay soil. Etofenprox content decreased 15 percent over 3 weeks. Degradation occurred by oxidation to 2-(4-ethoxyphenyl)-2-methylpropyl 3-phenoxybenzoate and 2-(4-ethoxyphenyl)-2-methylpropyl 3-hydroxybenzyl ether. In nonsterile soil, 80 percent of the applied etofenprox was decomposed within two weeks; no degradation occurred in sterile soil (FAO, 1993).

In field studies, the half-life of etofenprox was approximately 79 days in loam soil (8.2 percent clay, 7.5 percent organic carbon), 62 days in clayish loam soil (21 percent clay, 2.4 percent organic carbon), 39 days in volcanic ash loam (10 percent clay, 6.2 percent organic carbon), and 9 days in alluvial clayish loam (2 percent clay, 2.8 percent organic carbon) (FAO, 1993).

Photodegradation may be an important fate process for etofenprox on plant surfaces. Similar degradation pathways have been shown in laboratory studies of photodegradation from glass disc surfaces and in studies on bean leaves (FAO, 1993).

Fate and Transport in Aquatic Systems

Under laboratory conditions, etofenprox is stable in aqueous solutions of 1N NaOH or 1N HCl for a period equal to or greater than 10 days (FAO, 1993). It is stable in neutral and

acidic environments at 25°C and in darkness, with an estimated half-life of greater than 1 year. However, a more rapid breakdown is seen under real life conditions. In city water treated with 200 g/L etofenprox, 70 percent degradation was observed after 1 week and 93 percent after 3 weeks. The rapid degradation was attributed to the presence of sunlight.

Human Health Effects

Acute Exposure

Effects/Symptoms

There are limited data on the acute toxicity of etofenprox in humans. Because its toxicity and mode of action are similar to other pyrethroids, the general symptoms of pyrethroid exposure are expected to occur following acute etofenprox exposure. Technical grade etofenprox is not expected to present an acute hazard to humans under normal use conditions (WHO, 2005; WHO/FAO, 1993).

In mice, rats, and dogs, etofenprox and 1 percent Etofenprox Aerosol have low acute toxicity by oral, dermal, and inhalation routes of exposure (WHO/FAO, 1993, PAN, 2005, NYSDEC, 2005). Reported LD_{50} values for mice exposed to etofenprox (96 percent) were >107.2 for oral exposures and >2.14 g/kg for dermal (24-hour) exposures. In rats, an oral LD_{50} of >42.88 g/kg, a dermal 24-hour LD_{50} of 2.14 g/kg bw, and an inhalation LC_{50} of > 5.9 g/m^3 were reported. The oral LD_{50} in dogs was reported as >5.0 g/kg. The oral LD_{50} of Trebon 20 EC (20 percent etofenprox emulsifiable concentrate) is reported as >5 g/kg in both mice and rats, and the dermal LD_{50} is reported as > 2 g/kg in rats (WHO/FAO, 1993).

Acute oral studies of high-dose exposure to etofenprox showed central nervous system effects in both mice and rats. Dose-related decreases in spontaneous motor activity were observed in mice at high doses. In rats, a dose-related effect on EEG of the frontal lobe was seen at a similarly high dose. In rabbits, a 1 percent etofenprox formulation did not produce much skin or eye irritation. However, technical etofenprox is moderately irritating to the skin but not the eyes. No dermal sensitization was observed in tests on guinea pigs (NYSDEC, 2005; WHO/FAO, 1993). In subchronic (13-week) dietary studies in mice and rats, growth retardation and increased liver weights were observed at lower doses and hunched posture, lethargy, body tremors, and respiratory distress were reported at the highest dose tested (WHO/FAO, 1993).

Treatment

Etofenprox's toxicity and mode of action are similar to other pyrethroids. No chemical-specific data were located on the treatment of etofenprox exposure; however, generalized treatment for pyrethroids should be appropriate. Treatment of etofenprox exposure depends on the symptoms of the exposed person. If a person exhibits signs of typical pyrethroid toxicity following etofenprox exposure (nausea, vomiting, shortness of breath, tremors, hypersensitivity, weakness, burning, or itching), they should immediately

remove any contaminated clothing. Any liquid contaminant on the skin should be soaked up and the affected skin areas cleaned with alkaline soap and warm water. Eye exposures should be treated by rinsing with copious amounts of 4 percent sodium bicarbonate or water. Contact lenses should be removed. Vomiting should not be induced following ingestion exposures, but the mouth should be rinsed. The person should be kept calm and medical attention should be sought as quickly as possible. Medical personnel will treat severe intoxications with a sedative and anticonvulsant. Ingestion of large amounts of etofenprox should be treated with gastric lavage using a 5 percent bicarbonate solution followed by powdered activated charcoal. Skin irritation may be treated with a soothing agent and exposure to light should be avoided (WHO, 1999)

Chronic Exposure

Noncancer Endpoints

Little data are available for humans following chronic exposures to etofenprox. No compound-related effects were reported in workers occupationally exposure to unspecified concentrations of technical etofenprox for 1.5 to 5.5 years. Blood pressure measurements, X-rays, hematology measurements, blood chemistry analysis, urinalysis, and EKGs were taken and interviews conducted (WHO/FAO, 1993).

In chronic animal studies, rodents appear to be the most sensitive species (WHO/FAO, 1993). Following long-term oral exposure, systemic organ toxicity has been observed, including effects on the thyroid, kidneys, and liver in rats, mice, and dogs (NYSDEC, 2005; CalEPA, 2003; WHO/FAO, 1993). A 90-day inhalation exposure of rats resulted in increased heart, lung, liver, and kidney weights (NYSDEC, 2005). Etofenprox is not a cholinesterase inhibitor (PAN, 2005).

Etofenprox exposure does not produce significant reproductive or developmental toxicity in animals (NYSDEC, 2005; CalEPA, 2003). No adverse effects on reproductive parameters were seen in a two-generation feeding study or in segment I and II gavage study where rats were exposed to high levels in the diet and by gavage, respectively (CalEPA, 2003; WHO/FAO, 1993; NYDEC, 2005). No significant developmental toxicity in the absence of maternal toxicity has been reported following etofenprox exposure in animals (NYSDEC, 2005; CalEPA, 2003). Some developmental effects (increased incidence of malformations and visceral abnormalities) have been reported in rat offspring; however, they only occurred at doses that also caused maternal toxicity (WHO/FAO, 1993). Reduced fetal body weight and increased postimplantation loss were observed in rabbits at maternally toxic levels (NYSDEC, 2005).

Etofenprox is not mutagenic. Results from genotoxicity studies in bacteria, mammalian cells, *in vitro*, and *in vivo* in mice were all negative (WHO/FAO, 1993; CalEPA, 2003).

Cancer Endpoints

EPA has classified etofenprox as Category C, possible human carcinogen, and calculated a cancer potency slope factor of 5.1×10^{-3} per mg/kg/day (NYSDEC, 2005). The

available animal data show evidence of carcinogenicity in the absence of any human data (PAN, 2005). An increased incidence of thyroid follicular cell adenomas was seen in a two-year rat feeding study (WHO/FAO, 1993; CalEPA, 2003; NYSDEC, 2005).

Toxicokinetics

Etofenprox is readily absorbed from the gastrointestinal tract of rats given oral doses. Absorption ranged from 48–93 percent; absorption is dose dependent (WHO/FAO, 1993; FAO, 1993). Dermal absorption studies in male rats revealed that more than 90 percent of the total dose of 5, 59, or 184 g/cm^2 was recovered up to 96-hours after applications of ^{14}C-labeled etofenprox. Most of the radioactivity was recovered in the skin wash prior to sacrifice. The absorbed radioactivity was less than 7 percent after 96 hours (CalEPA, 2003). Etofenprox is distributed to fat as the parent compound, where the highest tissue concentrations are observed. Following oral administration, it is rapidly excreted, mainly in feces. Within 5 days, 85 to 90 percent was excreted in the feces, with lesser amounts (3 to 4 percent) in the urine. Only 3 to 4 percent remained in the body after 5 days. Etofenprox is not excreted in bile. It is excreted unchanged in the milk of dairy cows fed diets containing etofenprox. In rats, biotransformation mainly involves desethylation of the ethoxyphenyl group, hydroxylation of the phenoxy ring and oxidation of the benzyl methylene group. Although gastrointestinal absorption occurred at a slower rate in dogs than rats, the major routes of biotransformation were the same (WHO/FAO, 1993; FAO, 1993; CalEPA, 2003).

Ecological Effects

Acute Exposure

Toxicity in Non-Targeted Terrestrial Organisms

No data are available on the toxicity of etofenprox in birds or other non-target terrestrial organisms.

Toxicity in Non-Targeted Aquatic Systems

Etofenprox is toxic to aquatic organisms (WHO, 1999). In fish, etofenprox is slightly to moderately toxic. Slight toxicity is supported by the reported average LC_{50} of 49,000 µg/L in Japanese eel, while moderate toxicity is supported by the reported average LC_{50} of 1,845 µg/L in Mozambique tilapia. In addition to mortality, behavioral, biochemical, and physiological changes have been reported in fish exposed to etofenprox . Behavioral changes were reported in Mozambique tilapia exposed to 1,305 µg/L of the etofenprox formulation Trebon. Biochemical changes were seen in carp exposed to 600 µg/L of a 30 percent emulsifiable concentrate of Trebon for 24 hours, and effects were seen at a mean exposure of 300 µg/L for 15 days. Hematological effects and oxygen consumption changes were seen in Mozambique tilapia at concentrations of 1,400 µg/L of 96.3 percent etofenprox (PAN, 2005)

Chronic Exposure

Due to low application rates and low persistence of permethrin in both terrestrial and aquatic environments, serious adverse effects are not anticipated from chronic exposures (HSDB, 2005). No specific chronic data are available.

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Profile for Fenitrothion:

CAS Registry Number 122-14-5

Summary

Chemical History

Fenitrothion is a general use organophosphate insecticide that is nonsystemic and nonpersistent. It is mostly used in the control of chewing and sucking insects on a wide variety of agricultural crops and in forests, as well as for public health purposes. It is also used as a residual contact spray against mosquitoes, flies, and cockroaches. Fenitrothion is used residentially to control household and nuisance insects (EXTOXNET, 1995; WHO, 2003). Fenitrothion was introduced in 1959 as a less toxic alternative to parathion, with which it shares similar insecticidal properties. Fenitrothion is used heavily in countries that have banned parathion (EXTOXNET, 1995). In the United States, the use of fenitrothion for mosquito control was voluntarily cancelled by the manufacturer in 1995 (U.S. EPA, 1995) and the only registered use is for containerized ant and roach baits (U.S. EPA, 2000b).

The primary route of occupational exposure to fenitrothion is dermal, although inhalation exposures are also possible (U.S. EPA, 1995). Exposure to fenitrothion can cause overstimulation of the nervous system due to cholinesterase inhibition. This may result in nausea, dizziness, confusion, and respiratory paralysis and death at very high exposures (U.S. EPA, 2000b).

Description of Data Quality and Quantity

EPA has developed quantitative human health benchmarks (acute and chronic oral RfDs and inhalation and dermal benchmarks) for fenitrothion. Relevant review data resources include the following

- Reregistration Eligibility Decision (RED) Fenitrothion (U.S. EPA, 1995)
- Pesticide Information Profiles (PIP) for Fenitrothion (EXTOXNET, 1995)
- Specifications for Pesticides Used in Public Health: Fenitrothion (WHO, 1999)
- Pesticide Residues in Food 2000: Fenitrothion (IPCS, 2000).

Summary Table

Duration	Route	Benchmark Value	Units	Endpoint	Reference
Acute, Intermediate, Chronic	Inhalation	0.0004	mg/kg/day	Inhalation NOAEL of 0.2 µg/L (0.2 mg/kg/day) for neurological effects in rats with UF of 100 applied and adjusted for intermittent exposure	U.S. EPA (1999a)
Acute	Oral	0.13	mg/kg/day	Acute oral RfD based on neurological effects in rats	U.S. EPA (1999a)
Intermediate	Oral	0.0013	mg/kg/day	Adopt chronic RfD for intermediate duration	U.S. EPA (1999a)
Chronic	Oral	0.0013	mg/kg/day	Chronic oral RfD for based on NOEL for systemic and neurological effects in dogs	U.S. EPA (1999a)
Acute, Intermediate, Chronic	Dermal	0.01	mg/kg/day	Dermal LOAEL of 3 mg/kg/day for dermal effects in rabbits	U.S. EPA (1999a)

For inhalation exposure, a NOAEL of 0.2 µg/L (0.2 mg/kg/day)[15] was identified in rats (Coombs et al., 1988) exposed to fenitrothion via inhalation for 6 hours per day, 5 days per week, for 90 days (U.S. EPA, 1999a; IPCS, 2000). The concentration was adjusted for intermittent exposure[16] (0.04 mg/kg/day) and an uncertainty factor of 100 was applied to account for interspecies and intrahuman variation, for an inhalation benchmark of 0.0004 mg/kg/day. This value is appropriate for all exposure durations.

For oral exposure, an acute oral RfD was estimated at 0.13 mg/kg/day based on a NOAEL of 12.5 mg/kg/day for acute neurotoxicity in rats (Beyrouty et al, 1992). An uncertainty factor of 100 was applied to account for interspecies and intrahuman variability (U.S. EPA, 1999a). A chronic oral RfD of 0.0013 mg/kg/day was developed by EPA (1995, 1999a) based on a NOAEL of 0.125 mg/kg/day for systemic effects and plasma acetylcholinesterase inhibition in a long-term feeding study in dogs (Spicer, 1986). An uncertainty factor of 100 was applied to account for interspecies and intrahuman variability (U.S. EPA, 1995, 1999a). The chronic RfD was adopted to represent intermediate-term exposures.

For dermal exposure, a LOAEL of 3 mg/kg/day for dermal irritation and desquamation of the epidermis was identified from 21-day dermal rabbit study (Suetake, 1991); no

[15] Conversion between mg/m^3 and mg/kg/day assumes, for female Wistar rats, an average body weight of 0.156 kg and inhalation rate of 0.17 m^3/day (U.S. EPA, 1988).

[16] Adjustment for intermittent exposure is the product of air concentration and exposure of 6/24 hours/day and 5/7 days/week.

neurological effects were observed at this concentration (U.S. EPA, 1995). An uncertainty factor of 300 was applied to account for interspecies and intrahuman variability and the use of a less serious LOAEL, resulting in a dermal benchmark of 0.01 mg/kg/day. This value is appropriate for all exposure durations.

Insecticide Background

CAS#	122-14-5
Synonyms:	O,O-dimethyl O-(4-nitro-m-tolyl) phosphorothioate (U.S. EPA, 1995) methylnitrophos (Eastern Europe) (EXTOXNET, 1995)
Chemical Group:	Organophosphate (EXTOXNET, 1995; U.S. EPA, 2000a)
Registered Trade Names:	Accothion, Agrothion, Bay 41831, Bayer 41831, Bayer S 5660, Cyfen, Cytel, Dicofen, Dybar, Fenitox, Fenstan, Folithion, Kaleit, Mep, Metathion, Micromite, Novathion, Nuvanol, Pestroy, Sumanone, Sumithion, and Verthion (U.S. EPA, 1995; EXTOXNET, 1995)

Usage

Fenitrothion is a broad spectrum organophosphate insecticide and acaricide (IPCS, 2000) most commonly used in agriculture to control chewing and sucking insects on crops such as rice, cereals, fruits, vegetables, stored grains, and cotton. It is also used in forested areas and to control flies, mosquitoes, and cockroaches, and in public health programs (WHO, 2004). In the United States, fenitrothion is only registered for use as a containerized ant and roach bait. In Australia, it is used on stored wheat (U.S. EPA, 2000b).

Formulations and Concentrations

There are several formulations for fenitrothion, each containing varying amounts of the active ingredient. The typical formulations for fenitrothion are dusts (2 percent , 2.5 percent, 3 percent, or 5 percent), emulsifiable concentrate (50 percent), flowable, fogging concentrate (95 percent), and wettable powder (40 or 50 percent). It is also available in granules and ultra-low-volume, oil-based liquid spray (EXTOXNET, 1995). Registered formulation types include 0.01563 percent and 1 percent pellets and granular baits. Emulsifiable concentrates are not registered in the Unites States (U.S. EPA, 2000b). The fenitrothion content for various formulations should be declared as follows: technical grade fenitrothion (no les than 910 g/kg), fenitrothion emulsifiable concentrate and wettable powder (above 250 up to 500 g/kg + 5% of declared content, above 500 g/kg + 25 g/kg) (WHO, 1999).

Shelf-Life

Like many insecticides, fenitrothion should be stored in a locked, well-ventilated facility, preferably one designated only for insecticide storage. It should not be exposed to sunlight and should be stored away from animal feed and foodstuffs (IPCS, 1991).

Fenitrothion is stable for up to two years if stored between 20 and 25°C; storage temperatures should not exceed 40°C. Fenitrothion is unstable when heated above 100°C and may undergo Pishchemuka isomerization and decompose explosively. Decomposition of fenitrothion is promoted by iron. Therefore, fenitrothion should be stored in enamel, aluminum, or glass containers. Fenitrothion is not stable in alkaline environments (EXTOXNET, 1995). Residues of fenitrothion are stable for up to 147 days in wheat and 174 days in wheat gluten when frozen (-18°C) (U.S. EPA, 1995).

Degradation Products

In water, fenitrothion is degraded through photolysis and hydrolysis, with degradation accelerated in the presence of microflora. In soil, fenitrothion is primarily broken down by biodegradation with photolysis also playing a role (WHO, 2003, 2004). Carbon monoxide is the major degradate for aerobic soil metabolism and photolysis. The major nonvolatile degradates for aerobic soil metabolism, anaerobic aquatic metabolism, and photolysis include 3-methyl-4-nitro-phenol (approximately 1 to 22 percent of applied); aminofenitrothion (approximately 13 percent of applied); acetyl-aminofenitrothion (approximately 13 percent of applied); formylaminofenitrothion (4.9 percent of applied); o,o-dimethyl o-(3-carboxy-4-nitrophenyl)phosphorothionte (12.4 percent of applied); fenitrooxon (≤ 4.3 percent of applied); demethylate fenitrothion (approximately 1 percent of applied); and desmethylfenitrooxon (≤ 4.3 percent of applied). Other degradates are present at concentrations less than or equal to 2 percent and include o,o-dimethyl o-(3-methyl-4-nitrophenyl)phosphorothioate-3-methyl-4-nitrophenol; o-methyl (5-methyl o-(3-methyl-4-nitrophenyl)phen-phorothioate; o-methyl o-hydrogen o-(3-methyl-4-nitro-phenyl)phosphate; o,o-dimethyl o-(3-carboxy-4-nitrophenyl)phosphate; 5-methylfenitrothion; and carboxyfenitrooxon. The major degradates in pH 5 and pH 9 solutions are demethylated fenitrothion (10.3 percent of applied) and 3-methyl-4-nitrophenol (1.7 percent of applied). In pH 9 solution, the major degradate is 3-methyl-4-nitrophenol (15.1 percent of the applied), while demethylated fenitrothion accounts for up to 5.6 percent of applied. The major degradate from hydrolysis in pH 5 and pH 7 buffered solutions is demethylated fenitrothion. The major degradate in pH 9 buffered solution is 3-methyl-4-nitrophenol. Seven degradates were identified from photodegradation in soil. In loam soil, the major nonvolatile degradates from aerobic soil metabolism was 3-methyl-4-nitrophenol. Additional degradates included fenitrooxon, desmethylfenitrooxon, and 3-methyl-4-nitroanisole. The major volatile degradate was carbon monoxide (U.S. EPA, 1995).

Environmental Behavior

Fate and Transport in Terrestrial Systems

In most soil types, fenitrothion degrades rapidly with a half-life ranging from 3 to 25 days (U.S. EPA, 1995). Fenitrothion is mostly found in the top six inches of soil and is not very mobile and only slightly persistent in soil (U.S. EPA, 1995). In nonsterile muck and sandy loam soils, a half-life of less than one week is reported. Fenitrothion is intermediately mobile in soils ranging from sandy loam to clay (EXTOXNET, 1995). However, when applied to silty clay loam, silty clay, and sandy loam under laboratory conditions, fenitrothion appears to be immobile (U.S. EPA, 1995). Fenitrothion leaches very slowly into groundwater from most soils; however, some runoff can occur (WHO, 2004).

Fate and Transport in Aquatic Systems

On lakes, surface foam can trap fenitrothion from aerial spraying (EXTOXNET, 1995). In water, fenitrothion is unstable in the presence of sunlight or microbial contamination (WHO, 2003). Laboratory studies at 23^{o}C and pH 7.5 in the dark resulted in a half-life of 21.6 days for buffered lake water and 49.5 days for natural lake water. However, in field experiments, the half-life was 1.5-2 days at pH 7.0-7.5 and 19-23^{o}C (EXTOXNET, 1995). Phenyl labeled [^{14}C]-fenitrothion had a half-life of 4-7 days, while the anaerobic aquatic half-life is reported at 0.82 days. In fish, fenitrothion accumulates rapidly but at low concentrations (U.S. EPA, 1995).

Human Health Effects

Acute Exposure

Effects / Symptoms

Acute oral and dermal experimental data are available for human exposures to fenitrothion. No effect on acetylcholinesterase activity was observed in volunteers following a single oral dose of up to 0.33 mg/kg body weight or repeated doses of up to 0.36 mg/kg body weight/day for 4 days. Volunteers ingested technical-grade fenitrothion via capsule at doses of 0.18 mg/kg/day followed 2 weeks to 5 months later by 0.36 mg/kg/day, with each daily dose continued for 4 consecutive treatments. No significant effect of treatment was seen on blood pressure or pulse, and observed clinical signs were not considered to be treatment related. Transient decreases in erythrocyte cholinesterase activity were observed in two volunteers, but no treatment-related changes in hematological or clinical chemistry parameters were observed. No dermal irritation and no effects on cholinesterase activity were observed in volunteers exposed to up to 0.5 mg/kg/day fenitrothion orally followed by 0.1 mg/kg/day dermally to the arms and face for 9 days (IPCS, 2000).

Case reports of humans accidentally or intentionally ingesting fenitrothion indicate that fenitrothion is lethal at oral doses of 3 g. Additionally, death from respiratory insufficiency was observed 6 days after a man ingested 60 mL of a 50 percent emulsion

in a suicide attempt. Other acute oral effects included paralysis at 1.5 to 6 g. In patients exhibiting paralysis, plasma cholinesterase was inhibited by 40 percent to more than 80 percent. In patients who consumed 50 to 100 mL of a 50 percent fenitrothion solution either accidentally or in suicide attempts, 6 of 16 died within 5 to 22 days, despite receiving medical attention. Intermediate syndrome, characterized by muscular weakness affecting the neck, proximal limb, and respiratory muscles, was observed in 7 of 10 survivors. Of those with intermediate syndrome, plasma cholinesterase activity was not observed at time of hospitalization. Recovery ranged from 5 weeks to more than10 weeks in patients with intermediate syndrome, versus 2 to 4 weeks in those without (IPCS, 2000).

No clinical signs were observed in spray operators or villagers one week after exposure to a 5 percent fenitrothion spray. However, a 40–60 percent decrease in cholinesterase activity was observed in spray operators using fenitrothion indoors for 4 weeks in the absence of clinical symptoms of organophosphate toxicity. Orchard spray operators who inhaled a mean concentration of 0.011 µg/L fenitrothion for 3 consecutive days also showed no clinical signs but had lower maximum plasma concentration of fenitrothion than unexposed operators, with relatively rapid clearance from plasma (IPCS, 2000).

In animals, the acute toxicity of fenitrothion is low. The oral LD_{50} ranges from 240 to 1,700 mg/kg in rats, 715 to 1,400 mg/kg in mice, and 500 mg/kg in guinea pigs (EXTOXNET, 1995; IPCS, 2000). The acute dermal LD_{50} is reported to be 890–5,000 mg/kg in rats and greater than 3,000 mg/kg in mice (EXTOXNET, 1995; IPCS 2000). The acute inhalation LC_{50} ranges from 2.2 to 5.0 mg/L in rats (EXTOXNET, 1995; IPCS 2000). In cats, acute oral toxicity was 142 mg/kg (IPCS, 2000). Toxicity is dependent on sex and vehicle used; males are sensitive than females (IPCS, 2000). This is illustrated by the reported acute toxicity of the fenitrothion preparation Sumithion Technical (97.2 percent); the oral LD_{50} is 330 mg/kg in males and 800 mg/kg in females, and the dermal LD_{50} is 890 mg/kg in males and 1,200 mg/kg in females (U.S. EPA, 1995).

The signs of acute fenitrothion toxicity in animals are consistent with cholinesterase inhibition (IPCS, 2000). In hens, no evidence of delayed neurotoxicity or increased neurological lesions was seen following a single dose (WHO, 2004) or acute administration of Sumithion Technical (97.2 percent) (U.S. EPA, 1995). However, the fenitrothion product Sumithion 50EC has been shown to cause delayed neurotoxicity in adult rats as well as humans (EXTOXNET, 1995). In rats, cholinergic signs and erythrocyte and brain cholinesterase inhibition were seen at a number of doses, but cholinergic signs were seen only when brain cholinesterase was inhibited by more than 58 percent or erythrocyte acetyl cholinesterase was inhibited by more than 38 percent (WHO, 2004).

Technical grade fenitrothion (95 percent) does not cause dermal or ocular irritation in rabbits or dermal sensitization in guinea pigs (IPCS, 2000; U.S. EPA, 1995). However, mild dermal irritation was seen following exposure to Sumithion 8-E (77 percent ai) (U.S. EPA, 1995). Other acute effects in animals include those caused by O,O,S-

trimethyl phosphorothioate, one of the contaminants of fenitrothion, including cytotoxic effects in rat lungs and modulated immune response in mice (EXTOXNET, 1995).

Treatment

Dermal exposure to fenitrothion should be treated by removing contaminated clothing, rinsing the skin with water, washing the exposed areas with soap and water, then seeking medical attention. If fenitrothion gets into the eyes, they should be rinsed with water for several minutes. Contact lenses should be removed if possible and medical attention should be sought. Ingestion of fenitrothion should be treated by rinsing the mouth and inducing vomiting if the person is conscious. Inhalation exposures require removal to fresh air and rest in a half-upright position. Artificial respiration should be administered if indicated and medical attention should be sought (PAN, 2005).

Chronic Exposure

Noncancer Endpoints

Limited data are available on the chronic toxicity of fenitrothion in humans. Chronic symptoms of toxicity in humans include general malaise, fatigue, headache, loss of memory and ability to concentrate, anorexia, nausea, thirst, loss of weight, cramps, muscular weakness, and tremors. At sufficient exposure levels, typical symptoms of cholinergic poisoning may be seen (EXTOXNET, 1995). Mild clinical signs such as nausea and dizziness and whole-blood cholinesterase inhibition were observed in spray operators following occupational exposure to fenitrothion used during a 30-day malaria control operation. However, no treatment-related effects were seen in operators spraying fenitrothion for 5 hours/day, 5 days a week, intermittently for 2 years (IPCS, 2000).

The main toxicological finding from long-term animal studies was cholinesterase activity inhibition (red blood cell, plasma, and brain) in all species studied (IPCS, 2000; U.S. EPA, 1995; EXTOXNET, 1995). Signs of poisoning and cholinergic stimulation were also reported at higher levels.

In animals, reproductive and developmental toxicity are of concern. Developmental effects were seen at doses that were maternally toxic in rats. Reduced body weight, viability, and lactation indices were seen in offspring. In rats and rabbits, no fetal toxicity or treatment-induced malformations were seen at the highest dose tested in the presence of maternal cholinergic signs and decreased body weight gain (WHO, 2004). Others have reported an increase in fetal and skeletal variations at doses causing maternal toxicity (U.S. EPA, 1998). Behavioral effects were observed in rat pups following maternal exposure to Sumithion 50EC on gestation days 7 to 15 and included differences in simple behavioral measures and complex measures, which persisted up to 104 days after birth. No effects were seen at lower levels (EXTOXNET, 1995).

Fenitrothion is not teratogenic, mutagenic, or genotoxic in chronically exposed animals and is not expected to cause those effects in humans (EXTOXNET, 1995). Additionally, fenitrothion did not induce immunotoxicity (WHO, 2004).

Cancer Endpoints

Data on the carcinogenic potential of fenitrothion indicate that it is unlikely to pose a carcinogenic risk to humans. EPA has classified fenitrothion as a Group E chemical, "evidence of noncarcinogenicity for humans" (U.S. EPA, 1995, 1999a). Evidence from animal studies suggests that fenitrothion is not carcinogenic in animals.

Toxicokinetics

Fenitrothion is readily absorbed from the intestinal tract of most mammalian species, with about 90 to 100 percent of the dose absorbed (IPCS, 2000; EXTOXNET, 1995). In rats, oral absorption is approximately 90 to 100 percent within 72 hours, while in humans, it is about 70 percent in 96 hours (IPCS, 2000). Within 24 hours of dermal application, about 45 percent of the applied dose is absorbed (WHO, 2004; IPCS, 2000). In rats, a dermal absorption rate of slightly over 1 percent is suggested as fenitrothion disappeared rapidly during the first hour (EXTOXNET, 1995). Fenitrothion is widely distributed in the body. In rats, the highest concentrations after 48 hours are found in the liver, kidneys, and fat. It is rapidly activated and deactivated (IPCS, 2000). In the liver, fenitrothion is activated by oxidative desulfuration to the activated metabolite fenitrooxon (WHO, 2004; IPCS, 2000). It is then rapidly degraded by demethylation and hydrolysis into the inactive metabolites 3-methyl-4-nitrophenol and dimethylphosphate. Further oxidation to 3-carboxyl-4-nitrophenol is involved in a minor metabolic pathway. In dermally exposed rats, the area of highest concentration (other than skin) of fenitrothion after 31 hours was the cartilaginous part of the bones (EXTOXNET, 1995). Within 24 hours of oral exposures, up to 93 percent of the dose is excreted via the urine, and 5 to 15 percent is excreted in the feces (WHO, 2004; IPCS, 2000; U.S. EPA, 1995). In rats, rabbits, and dogs, seventeen metabolites have been isolated in the urine, and the parent compound was not detected (U.S. EPA, 1995).

Toxicokinetic studies in humans have shown the time to maximal plasma concentration was 1 hour in volunteers who ingested two capsules 12 hours apart that contained 0.09 or 0.18 mg fenitrothion/kg body weight for 4 days. The elimination half-time ranged from 2 to 3 hours for both doses. The maximal plasma concentration following a single oral dose was 0.09 mg/kg body weight 1 day after exposure and 0.84 ng/mL 4 days after exposure. Higher doses resulted in higher maximal concentrations on days 1 and 4 after exposure (1.8 ng/mL and 7.7 ng/mL, respectively). In addition, the elimination half-time of fenitrothion was 2 to 4.5 hours (WHO, 2004; IPCS, 2000). Human studies also indicate that fenitrothion does not accumulate. In humans, doses of 2.5 and 5 mg/man/day administered for 5 days were all excreted within 12 hours without accumulation. Urinary excretion of the metabolite 3-methyl-4-nitrophenol was almost complete within 24 hours in subjects given single oral doses of approximately 0.042 to 0.33 mg/kg body weight fenitrothion. Peak excretion occurred after 12 hours and plasma cholinesterase inhibition was seen in only one subject at the highest dose (EXTOXNET, 1995).

Ecological Effects

Acute Exposure

Fenitrothion has been shown to be moderately to highly toxic to birds (WHO, 2004; U.S. EPA, 1995) and highly toxic to honeybees (U.S. EPA, 1995). It is also toxic to spider mites and has a long residual action (EXTOXNET, 1995). The toxicity of fenitrothion in birds ranges from highly toxic in game birds to slightly toxic in waterfowl. The oral LC_{50} in pheasants was reported as 450–500 ppm for 2-week-old pheasants fed fenitrothion in the diet for 5 days (EXTOXNET, 1995). In bobwhite quail, an LC_{50} of 157 ppm and an LD_{50} of 23.6 mg/kg have been reported (U.S. EPA, 1995; EXTOXNET, 1995). An LD_{50} of 1,190 mg/kg is reported in mallard ducks (EXTOXNET, 1995). The oral LD_{50} for chickens is reported as 28 mg/kg and fenitrothion was negative for delayed neurotoxicity in hens (EXTOXNET, 1995). In honeybees, the oral LD_{50} is reported between 0.02 and 0.38 µg/bee. In mammals, the acute oral toxicity data indicate that fenitrothion is moderately toxic to small mammals. Fenitrothion was acutely toxic to rats at 330 to 355 mg/kg (U.S. EPA, 1995). Additionally, fenitrothion was acutely toxic to mule deer at 727 mg/kg (EXTOXNET, 1995).

Fenitrothion has been shown to be moderately toxic to both warm and coldwater fish (WHO, 2004; U.S. EPA, 1995). Acute 96-hour LC_{50} values range from 1.7 ppm for brook trout to 3.8 ppm for bluegill sunfish, while the 48-hour LC_{50} ranges from 2.0 to 4.1 mg/L in carp. In various North American freshwater fish, the 96-hour LC_{50} values range from 2 to12 µg/L (EXTOXNET, 1995). Studies have shown that the toxicity of fenitrothion in rainbow trout was dependent on the developmental stage of the fish during exposure and the water temperature. Fingerlings and adult fish were the most sensitive, the sacfry stage was intermediate, and embryos were least sensitive to the toxic effects of fenitrothion. Additionally, the toxicity increased as water temperatures increased. In fish, sublethal effects of fenitrothion exposure include morphological and anatomical changes, behavioral changes, biochemical changes, respiratory effects, and effects on growth (EXTOXNET, 1995). Because fenitrothion breaks down rapidly, it does not accumulate in fish (WHO, 2004).

Fenitrothion is highly toxic in freshwater invertebrates. Acute exposure to 95 percent fenitrothion resulted in EC_{50}/ LC_{50} values ranging from 4.3 ppb in *Gammarus* to 11 ppb in *Daphnia magna* (U.S. EPA, 1995). It is also moderately to very highly toxic to estuarine organisms. Acute exposure to 75 percent fenitrothion resulted in EC_{50}/ LC_{50} values ranging from 1.5 ppb in pink shrimp to > 1,000 ppb in Sheepshead minnow (U.S. EPA, 1995).

Chronic Exposure

Chronic toxicity data for non-target terrestrial organisms are limited. Fenitrothion has been shown to cause reproductive impairment in birds. Chronic exposure to 17 ppm fenitrothion reduced egg production in bobwhite quail, with a NOEL of 13 ppm (U.S. EPA, 1995).

Limited data for chronic duration exposures of aquatic organisms were located. In fish, the chronic toxicity of fenitrothion is generally considered to be low (EXTOXNET, 1995). In freshwater fish, studies have reported effects in rainbow trout chronically exposed to 94.5 percent fenitrothion. A LOEL of 88 ppb was determined for weight and length effects, with a NOEL of 46 ppm. In freshwater aquatic invertebrates, chronic exposure to 94.5 percent fenitrothion resulted in a 21 day LOEL of 0.23 ppb for adult daphnid survival in *Daphnia magna* with a NOEL of 0.087 ppb (U.S. EPA, 1995).

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Profile for Lambda-Cyhalothrin:

CAS Registry Number 91465-08-6

Summary

Chemical History

The synthetic pyrethroid lambda-cyhalothrin is a relatively new addition to this insecticide group. It was developed in 1977 and consists of one enantiomeric (i.e., nonsuperimposable, mirror image) pair of isomers and is a more biologically active form than cyhalothrin (IPCS, 1990a). It is used in the control of pests, including mosquitoes, in agricultural and public and animal health settings (EXTOXNET, 1996). The risks of occupational exposures and exposures to the general public are expected to be very low if proper precautions are followed. At the recommended application rates, lambda-cyhalothrin is not expected to cause adverse environmental effects. As is typical of synthetic pyrethroids, the typical symptoms for acute exposure are neurological and include tingling, burning, or numbness sensations (particularly at the point of skin contact), tremors, incoordination of movements, paralysis or other disrupted motor functions. These effects are generally reversible because lambda-cyhalothrin beaks down rapidly in the body (IPCS, 1990a; EXTOXNET, 1996). EPA has not classified synthetic pyrethroids, including lambda-cyhalothrin, as endocrine disruptors.

Description of Data Quality and Quantity

Lambda-cyhalothrin and cyhalothrin are basically the same chemical and differ only in their stereo chemistry and the number of isomers in each mixture (U.S. EPA, 2002a). Cyhalothrin consists of four stereo isomers while lambda-cyhalothrin is a mixture of only two isomers. The two lambda-cyhalothrin isomers are contained in cyhalothrin and they represent 40 percent of the cyhalothrin mixture. The majority of toxicity studies available were conducted using cyhalothrin as the test chemical. Evidence based on subchronic studies in rats suggests that the two mixtures are not biologically different with respect to their mammalian toxicity (U.S. EPA, 2002a).

EPA and ATSDR have developed quantitative human health benchmarks for cyhalothrin (EPA's acute and chronic oral RfDs and short-, intermediate-, and long-term dermal and inhalation benchmarks, and ATSDR's acute and intermediate oral MRLs).

Recommended resources include:

- Environmental Health Criteria 99: Cyhalothrin (IPCS, 1990a)
- Toxicological Profile for Pyrethrin and Pyrethroids (ATSDR, 2003a)
- Pesticide Information Profiles (PIP) for Lambda-cyhalothrin (EXTOXNET, 1996)
- Specifications and Evaluations for Public Health Pesticides for Lambda-cyhalothrin (WHO, 2003)

- Integrated Risk Information System (IRIS) summary review for cyhalothrin (U.S. EPA, 2005b).

Summary Table

Duration	Route	Benchmark Value	Units	Endpoint	Reference
Acute, Intermediate, Chronic	Inhalation	0.0008	mg/kg/day	Inhalation NOAEL for neurotoxicity in rats at 0.08 mg/kg/day (0.3 µg/L) with uncertainty factor (UF) of 100 applied	U.S. EPA (2002b)
Acute	Oral	0.005	mg/kg/day	Acute RfD based on neurotoxicity in dogs	U.S. EPA (2002b)
Intermediate	Oral	0.001	mg/kg/day	Adopt chronic RfD for intermediate duration	
Chronic	Oral	0.001	mg/kg/day	Chronic RfD based on neurological effects in dogs	U.S. EPA (2002b)
Acute, Intermediate, Chronic	Dermal	0.1	mg/kg/day	Dermal NOAEL in rats with UF of 100 applied	U.S. EPA (2002b)

For inhalation exposure, a NOAEL of 0.3 µg/L (0.08 mg/kg/day) was identified for neurotoxicity, decreased body weight, and slight changes in urinalysis parameters in rats exposed to lambda-cyhalothrin via inhalation for 21 days. An uncertainty factor of 100 was applied, for an inhalation benchmark value of 0.0008 mg/kg/day. This value is appropriate for all exposure durations (U.S. EPA, 2002a).

For oral exposure, an acute RfD of 0.005 mg/kg/day was derived based on a NOAEL of 0.5 mg/kg/day for neurotoxicity (ataxia) observed in dogs exposed to lambda-cyhalothrin, with an uncertainty factor of 100 applied (U.S. EPA, 2002a). A chronic oral RfD of 0.001 mg/kg/day was derived based on a NOAEL of 0.1 mg/kg/day for gait abnormalities in dogs exposed to lambda-cyhalothrin, with an uncertainty factor of 100 applied (U.S. EPA, 2002a). The chronic RfD was adopted to represent intermediate exposures.

For dermal exposure, a NOAEL of 10 mg/kg/day was identified in rats dermally exposed to lambda-cyhalothrin for 21 days. An uncertainty factor of 100 was applied, for a dermal benchmark value of 0.1 mg/kg/day. This value is appropriate for all exposure durations (U.S. EPA, 2002a).

Background

CAS #:	91465-08-6
Synonyms:	none (WHO, 2003)
Chemical Group:	synthetic pyrethroid
Registered Trade Names:	Charge, Excaliber, Grenade, Karate, Hallmark, Icon, OMS 0321, PP321, Saber, Samurai, Sentinel, and Matador (EXTOXNET, 1996)

Usage

Lambda-cyhalothrin is a synthetic pyrethroid (IPCS, 1990a) most commonly used for pest control, especially mosquitoes; the insecticide is usually sprayed on interior walls or used to impregnate bed nets (EXTOXNET, 1996). This insecticide is a restricted use pesticide, so it can be purchased and used only by certified applicators (EXTOXNET, 1996). Lambda-cyhalothrin has adulticidal, ovicidal, and larvicidal activity (IPCS, 1990a). In addition to mosquitoes, it is effectively used to control: cockroaches, ticks, fleas, aphids, Colorado beetles, cutworms and butterfly larvae (EXTOXNET, 1996; IPCS, 1990a).

Formulations and Concentrations

There are several formulations for lambda-cyhalothrin, each containing varying amounts of the active ingredient. The typical formulations for lambda-cyhalothrin are

- Technical grade (not less than 810 g/kg lambda-cyhalothrin)
- Emulsifiable concentrate (at 20 +/- 2^{o}C: up to 25 g/l +/- 15% declared content; > 25 g/l to 100 g/l +/- 10% of declared content)
- Wettable powder (up to 25 +/- 15% of declared content: > 25-100 +/- 10 % of declared content)
- Slow release capsule suspension (at 20 +/- 2^{o}C: up to 25 g/l +/- 15% declared content).

The main formulation used for agricultural purposes is the emulsifiable concentrate. The wettable powder formulation is mainly used for public health reasons (WHO, 2003). Lambda-cyhalothrin is commonly mixed with buprofezin, pirimicarb, dimethoate, or tetramethrin, resulting in the usual product (WHO, 2003; EXTOXNET, 1996).

Shelf-Life

This insecticide, like many others, needs to be stored in a cool, dry, and well-ventilated facility (IPCS, 1990a). Lambda-cyhalothrin should not be stored or transported with foodstuffs and household supplies to the limit the potential for cross contamination and human exposure (IPCS, 1990a).

Degradation Products

In the environment, lambda-cyhalothrin degrades through biological and photochemical reactions (IPCS, 1990a). Biological reactions are thought to be more important. Lambda-cyhalothrin will degrade rapidly in soils, remain relatively stable in water, and is usually not found in air due to its low vapor pressure. The main degradation products are 3-(2-chloro-3,3,3-trifluoroprop-1-enyl)-2, 2-dimenthyl-cyclopropanecorboxylic acid, the amide derivative of cyhalothrin, and 3-phenoxybenzoic acid. The degradation is a result of the cleavage of the ester linkage to give two main degradation products, which are further degraded to carbon dioxide. Lambda-cyhalothrin degrades fairly quickly in alkaline conditions, in comparison to neutral or acidic media. It is strongly absorbed in soils and sediments with little tendency for bioaccumulation (IPCS, 1990a).

In water, lambda-cyhalothrin is stable at pH 5. Racemization at the alpha-cyano carbon occurs at pH 7 to pH 9, creating a one to one mixture of enantiomer pairs A and B. The ester bond is hydrolyzesd at pH 9. Additionally, a moderately high rate of photolysis is seen in dilute aqueous solutions (IPCS, 1990a).

Environmental Behavior

Fate and Transport in Terrestrial Systems

In most soil types, lambda-cyhalothrin is not very mobile. Its high reported organic carbon partitioning coefficient (Koc) value reflects its strong affinity for soil. It is retained more in soil with low sand content or high organic matter content (EXTOXNET, 1996). Studies have shown that lambda-cyhalothrin and its degradation products do not leach through soils into groundwater nor are they transported to other compartments of the environment following agricultural uses (IPCS, 1990a).

Lambda-cyhalothrin is moderately persistent in soil with a soil half-life ranging from 4 to 12 weeks. A longer in-field half-life of approximately 30 days is reported for most soils (EXTOXNET, 1996). The half-life is variable because it is dependent on the availability of sunlight, which speeds degradation (IPCS, 1990a).

Fate and Transport in Aquatic Systems

Lambda-cyhalothrin is not expected to be prevalent in surface or groundwater because it has extremely low water solubility and binds tightly to soil. Lambda-cyhalothrin enters surface water largely through surface runoff. Even so, lambda-cyhalothrin is most likely to stay bound to sediment and settle to the bottom. Studies have shown that hydrolysis of lambda-cyhalothrin occurs rapidly at a pH of 9 but not at a pH of 7, though isomerization was observed at a pH of 7. No hydrolysis or isomerization was seen at a pH of 5.

Human Health Effects

Acute Exposure

Effects/Symptoms

No data on accidental human poisonings have been reported. Additionally, no quantitative epidemiological studies are available (IPCS, 1990a). However, under normal use conditions, acute exposure to lambda-cyhalothrin is not expected to represent a hazard in humans. Transient skin sensations such as periorbital facial tingling and burning have been reported following direct skin exposure in laboratory workers and manufacturing workers handling synthetic pyrethroids. This sensation is possibly due to repetitive firing of sensory nerve terminals and usually lasts for a few hours up to 72 hours post-exposure. No neurological abnormalities have been observed upon medical examination (IPCS, 1990a). Lambda-cyhalothrin can irritate the eyes, skin, and upper respiratory tract. Additionally, oral exposure can cause neurological effects, including tremors and convulsions. Ingestion of liquid formulations may result in aspiration of the solvent into the lungs, resulting in chemical pneumonitis. Based on the acute oral toxicity data, lambda-cyhalothrin has been classified as "Moderately Hazardous" (Class II) (WHO, 2003).

In animals, the technical form of lambda-cyhalothrin is moderately toxic; however, toxicity depends on both the formulation (concentration of active ingredient and solvent vehicle) and the route of exposure (EXTOXNET, 1996). Laboratory data indicate that acute oral exposure to lambda-cyhalothrin is moderately to highly toxic in rats and mice and that mice are more susceptible to the toxic effects than rats (WHO, 2003). The oral LD_{50} for lambda-cyhalothrin in corn oil has been reported to range from 56 mg/kg in female rats up to 79 mg/kg in males. A similar LD_{50} is reported for technical grade lambda-cyhalothrin in rats at 64 mg/kg (EXTOXNET, 1996). The oral LD_{50} in mice is reported as 20 mg/kg (IPCS, 1990a). The effects of acute oral exposure are typical of pyrethroid toxicity, including abnormal motor function (WHO, 2003).

Acute inhalation exposures are also highly toxic to animals (WHO, 2003). In the formulated product Karate, the 4-hour LC_{50} in rats is reported as 0.175 mg/L in females and 0.315 mg/L in males (EXTOXNET, 1996).

Lambda-cyhalothrin is less toxic in animals via acute dermal exposure (WHO, 2003). In rats, dermal LD_{50}s of 632 mg/kg for males and 696 mg/kg for females have been reported for the technical product. Studies have also shown the technical product produced no skin irritation to rabbits and is nonsensitizing in guinea pigs. Mild eye irritation was observed in rabbits. However, dermal exposure to the formulated product Karate causes severe primary skin irritation in rabbits and mild skin sensitization in guinea pigs. Other acute dermal effects are related to the nervous system and include tingling, burning sensations, or numbness (EXTOXNET, 1996).

Treatment

Lambda-cyhalothrin and its breakdown products can be detected in blood and urine, but only within a few days of the last exposure (ATSDR, 2003a). Dermal exposure to lambda-cyhalothrin exposure should be treated by removing contaminated clothing and washing the exposed areas with soap and water. If lambda-cyhalothrin gets into the eyes, they should be rinsed with water for several minutes. Contact lenses should be removed if possible and medical attention should be sought. Vomiting should not be induced following ingestion of lambda-cyhalothrin, and medical attention sought. Inhalation exposures require removal to fresh air and rest (IPCS, 1990b)

Chronic Exposure

Noncancer Endpoints

Based on the available data, it is unlikely that lambda-cyhalothrin would cause chronic effects in humans under normal conditions. No specific target organs have been identified in the available chronic studies (EXTOXNET, 1996). Decreased body weight gain and mild neurological effects have been observed in some animal studies (EXTOXNET, 1996; IPCS, 1990a).

Lambda-cyhalothrin is not expected to be teratogenic, mutagenic, or genotoxic in humans. Studies in animals have found no teratogenic or fetotoxic effects in rats or rabbits. Additionally, it was negative in five test strains in the Ames mutagenicity assay (IPCS, 1990a). No mutagenic or genotoxic effects were seen in other in vitro cytogenic assays or chromosomal aberration tests (EXTOXNET, 1996).

Cancer Endpoints

Data on the carcinogenic potential suggest that lambda-cyhalothrin is not carcinogenic in humans. In rats and mice exposed to cyhalothrin, no carcinogenic effects were observed. EPA has classified lambda-cyhalothrin as a Group D chemical, “not classifiable as to human carcinogenicity” (U.S. EPA, 2002a).

Toxicokinetics

Animal studies have been have been conducted in various species to investigate the toxicokinetics of cyhalothrin and lambda-cyhalothrin. Oral cyhalothrin is readily absorbed, metabolized thoroughly, and eliminated as polar conjugates in the urine (IPCS, 1990a). Studies with lambda-cyhalothrin have shown that it also is rapidly metabolized into less toxic water-soluble compounds and excreted in the urine and feces (EXTOXNET, 1996). In mammals, cyhalothrin is metabolized as a result of ester cleavage to cyclopropanecarboxylic acid and 3-phenoxybenzoic acid, and eliminated as conjugates. Tissue levels decline after exposure stops and residues in the body are low (IPCS, 1990a).

Ecological Effects

Acute Exposure

Toxicity to Non-Target Terrestrial Organisms

Like other synthetic pyrethroids, lambda-cyhalothrin has been shown to be toxic to honey bees but has little effect on birds and domestic animals (EXTOXNET, 1996). In birds, the toxicity of lambda-cyhalothrin ranges from nontoxic to slightly toxic. Oral LD_{50} values in mallard duck are reported as greater than 3,950 mg/kg. Dietary LC_{50} values of 5,300 ppm are reported in bobwhite quail. Additionally, there is no evidence of lambda-cyhalothrin accumulation in bird tissues or in eggs (EXTOXNET, 1996). Lambda-cyhalothrin has shown mixed toxicity to other non-target terrestrial organisms. It is extremely toxic to honey bees, with a contact LD_{50} of 0.9 µg/bee and an oral LD_{50} of 38 ng/bee (EXTOXNET, 1996), but has no adverse effect on earthworms (IPCS, 1990a).

Toxicity to Aquatic Organisms

Like other synthetic pyrethroids, lambda-cyhalothrin has been shown to be quite toxic under laboratory conditions to both cold and warm water fish. Acute 96-hr LC_{50} values range from 0.2 to 1.3 µg/L. It is also highly toxic to aquatic arthropods with 48-hr LC_{50} ranging from 0.008 to 0.4 µg/L (IPCS, 1990a; WHO, 2003). In the field, however, these effects are not likely to occur under the recommended use scenarios (WHO, 2003). No serious adverse effects have been observed due to the low rates of application and the lack of persistence in the environments (IPCS, 1990a). Accumulation studies have shown that although bioaccumulation is possible in fish, it is unlikely due to the rapid metabolism of lambda-cyhalothrin (EXTOXNET, 1996).

Chronic Exposure

Toxicity to Non-Target Terrestrial Organisms

No data were located on the chronic toxicity to non-target terrestrial organisms.

Toxicity to Aquatic Organisms

No data for chronic duration exposures of aquatic organisms were located; however, a subchronic study in Sheepshead minnow embryos and larvae showed no effect on hatchability or larval survival when exposed to up to 0.25 µg/L through 28 days post hatching. A significant effect on larval weight was observed at 0.38 µg/L. In an additional subchronic exposure study, survival, growth, and reproduction of *Daphnia magna* were seen at 40 ng/L but not at 2.5 ng/L (IPCS, 1990a).

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Profile for Malathion:

CAS Registry Number 121-75-5

Summary

Chemical History

Malathion is an organophosphate pesticide used in a wide variety of applications, including agricultural, veterinary, and public health uses. In pest eradication programs, malathion is used to eradicate mosquitoes, Mediterranean fruit flies, and boll weevil (ATSDR, 2003b). The primary target of malathion is the nervous system; it causes neurological effects by inhibiting cholinesterase in the blood and brain. Exposure to high levels can result in difficulty breathing, vomiting, blurred vision, increased salivation and perspiration, headaches, and dizziness (U.S. EPA, 2005c). Loss of consciousness and death may follow very high exposures to malathion (ATSDR, 2003b).

Description of Data Quality and Quantity

Several comprehensive reviews on the toxicity of malathion have been prepared or updated in recent years:

- EPA risk assessment for the Reregistration Eligibility Decision (RED) document (U.S. EPA, 2005c)
- IRIS summary review (U.S. EPA, 2005d)
- *Toxicological Profile for Malathion* (ATSDR, 2003b)
- *Specifications and Evaluations for Public Health Pesticides for Malathion* (WHO, 2003).

EPA and ATSDR have developed quantitative human health benchmarks (EPA's acute and chronic oral RfDs, short-, intermediate-, and long-term dermal and inhalation benchmarks and ATSDR's acute inhalation and intermediate oral and inhalation MRLs).

Summary Table

Duration	Route	Benchmark Value	Units	Endpoint	Reference
Acute, Intermediate, Chronic	Inhalation	0.026	mg/kg/day	Inhalation LOAEL for respiratory effects in rats of 25.8 mg/kg/day (0.1 mg/L) with UF of 100 and SF of 10 applied	U.S. EPA (2005c)
Acute	Oral	0.14	mg/kg/day	Acute RfD based on neurological effects in rats	U.S. EPA (2005c)
Intermediate	Oral	0.03	mg/kg/day	Adopt chronic oral RfD for intermediate duration	

Duration	Route	Benchmark Value	Units	Endpoint	Reference
Chronic	Oral	0.03	mg/kg/day	Oral RfD based on neurological effects in rats	U.S. EPA (2005c)
Acute, Intermediate, Chronic	Dermal	0.05 (child) 0.5 (adult)	mg/kg/day	Dermal NOAEL for neurological effects in rabbits with UF of 100 applied (for children, an additional SF of 10 was also applied)	U.S. EPA, 2005c

For inhalation exposure, a LOAEL of 0.1 mg/L (25.8 mg/kg/day, assuming absorption via inhalation route is equivalent to oral absorption) for histopathological lesions in the nasal cavity and larynx of rats was identified for malathion. Uncertainty factors of 10 each were applied to account for interspecies and intrahuman variability and a safety factor of 10 to account for the extrapolation from LOAEL to NOAEL and the severity of effect (U.S. EPA, 2005c). This value is appropriate for short- (1–30 days) and intermediate-term (1–6 months) inhalation exposures; this value was also adopted for chronic (long-term, >6 months) exposures.

For oral exposure, an acute oral RfD of 0.14 mg/kg/day was derived based on the inhibition of red blood cell (RBC) cholinesterase in rats and uncertainty factors of 10 each to account for interspecies and intrahuman variability (U.S. EPA, 2005d). A chronic oral RfD of 0.03 mg/kg/day was derived based on the RBC cholinesterase inhibition in rats and uncertainty factors of 10 each to account for interspecies and intrahuman variability (U.S. EPA, 2005c).

For dermal exposures, a NOAEL of 50 mg/kg/day for plasma, RBC, and brain cholinesterase inhibition in rabbits exposed dermally was identified for malathion. Uncertainty factors of 10 each to account for interspecies and intrahuman variability were applied; a safety factor of 10 to account for susceptibility of young was applied to be protective of children (U.S. EPA, 2005d). This value is appropriate for short- (1–30 days), intermediate- (1–6 months), and long-term (>6 months) dermal exposures.

Background

CASRN:	121-75-7
Synonyms:	1, 2-Di (ethoxycarbonyl) ethyl, *O*, *O*-dimethyl, phosphorodithioate (ATSDR, 2003b), maldison, malathon, mercaptothion, mercaptotion, carbofos (WHO, 2003)
Chemical Group:	organophosphate
Registered Trade Names:	Cekumal, Fyfanon®, Malixol®, Maltox® (ATSDR, 2003b); Celthion, Cythion, Dielathion, El 4049, Emmaton, Exathios, Fyfanon and Hilthion, and Karbofos (EXTOXNET, 1996)

Usage

Malathion is a nonsystemic, broad-spectrum organophosphate insecticide used to control sucking and chewing pests in agricultural and horticultural applications (WHO, 2003). It is also used to control household insects, fleas, ectoparasites in animals, and head and body lice in humans (EXTOXNET, 1996). A major public health use of malathion is to eradicate mosquitoes and Mediterranean fruit flies, with ground application and aerial spraying being the most common methods of application (ATSDR, 2003b).

Formulations and Concentrations

There are several typical formulations for malathion, each formulation varying in the amount of active ingredient (ai) it contains. The typical formulations for malathion are (U.S. EPA, 2005c; ATSDR, 2003b)

- Technical grade (91–95 percent ai)
- Dust (1–10 percent ai)
- Emulsifiable concentrate (3–82 percent ai)
- Ready-to-use liquid (1.5–95 percent ai)
- Pressurized liquid (0.5–3 percent ai)
- Wettable powder (6–50 percent ai).

Malathion may also be used to formulate other pesticides (ATSDR, 2003b).

Degradation Products

In the United States, technical grade malathion is >90 percent pure and contains less than 5 percent impurities (reaction byproducts and degradation products). As many as 14 different impurities have been identified in technical grade malathion (ATSDR, 2003b), some of which are toxic themselves and potentiate the toxicity of malathion. Because of their toxicological properties, relevant impurities include malaoxon (CASRN 1634-78-2), isomalathion (CASRN 3344-12-5), MeOOSPS-triester (CASRN 2953-29-9), MeOOOPS-triester (CASRN 152-18-1), MeOSSPO-triester (CASRN 22608-53-3), and MeOOSPO-triester (CASRN 152-20-5). Both isomalathion and malaoxon are more toxic than malathion, and isomalathion is a potentiator of malathion (WHO, 2003). Degradation products of malathion include dimethyl phosphate, dimethyldithiophosphate, dimethylthiophosphate, isomalathion (a metabolite of malathion), malaoxon, and malathion dicarboxylic acid and are generally the result of impurities or exposure to extreme storage conditions (PAN, 2005).

In dustable powder form, malathion levels decrease when it is stored and it is converted into the more toxic metabolite isomalathion (WHO/FAO, nd). In the environment, malathion is usually broken down into other chemical compounds within a few weeks by water, sunlight and bacteria found in the soil and water (ATSDR, 2003b). At pH 5.0, malathion is reasonably stable to hydrolysis. It hydrolyzes rapidly at pH 7.0 and above or below pH 5.0 (WHO, 2003; ATSDR, 2003b). It is stable in an aqueous solution that is

buffered at a pH of 5.26 (WHO/FAO, nd). In air, malathion is broken down by reacting with sunlight as well as other chemicals found naturally in the air (ATSDR, 2003b). Malathion is generally stable to photolysis (WHO, 2003).

Shelf Life

Malathion levels decline over time during storage. The extent of the decline depends on the type of formulation, as does the increase in isomalathion levels. Technical grade malathion stored at 20°C for 25–30 months lost 3–8 g/kg, while isomalathion levels increased 2.2-2.4 mg/kg. Levels of other impurities did not increase significantly. Malathion stored for 14 days at 54°C declined 2.6 percent as an emulsifiable concentrate, 2.8 percent as a emulsion (oil in water), and 5 percent as a dustable powder, while isomalathion levels increased 0.11 percent, 0.095 percent, and 1.35 percent, respectively (WHO, 2003).

Environmental Behavior

Fate and Transport in Terrestrial Systems

Malathion is released directly into the air during aerial application to target areas such as crops or residential areas. It may also be released via volatilization from crop and ground surfaces. Aerial applications may also release malathion into the soil by way of spray droplets that reach the surface of the soil. This may include spraying and fogging applications. Malathion may also be released into the soil as a consequence of wet deposition applications or when improperly disposed of (ATSDR, 2003b).

In air, malathion may be transported from the site of application to other areas by wind and precipitation. In soils, malathion is moderately to highly mobile, indicating a potential to readily move from soil into groundwater. However, because malathion degrades rapidly in the environment, movement from soil to groundwater is not a significant concern (ATSDR, 2003b).

Malathion degrades through atmospheric photo-oxidation, hydrolysis, and biodegradation. (ATSDR, 2003b). In the atmosphere, malathion breaks down rapidly in sunlight, with a half-life of 1.5 days. In soil, malathion is of low persistence with an average half-life of 6 days. It degrades rapidly depending on the degree of soil binding, which is generally moderate (EXTOXNET, 1996). Malathion degrades more quickly in moist soil (ATSDR, 2003b). The persistence of malathion in vegetation depends largely on the lipid content of the plant. The degradation process is increased with moisture content (EXTOXNET, 1996).

Fate and Transport in Aquatic Systems

Malathion may be released into surface waters through direct applications, spills, runoff from sprayed areas, wet deposition from rain, manufacturing or processing facilities, and wastewater releases (ATSDR, 2003b). The water solubility of malathion is 148 mg/l at 25°C. At pH 5, it is reasonably stable to hydrolysis; however, as pH increases, malathion

hydrolyzess more readily (WHO, 2003). Because it is highly soluble and binds moderately to soil, malathion may also pose a risk to groundwater or surface waters (EXTOXNET, 1996).

In water, malathion degrades relatively quickly due to the action of the water as well as bacteria in the water (ATSDR, 2003b). In water, malathion breaks down into mono- and dicarboxylic acids. However, degradation also depends on the temperature and pH of the water. In river water, malathion breaks down in 1 week, while it is stable in distilled water for 3 weeks. Degradation increases with water temperature, alkalinity, and salinity of the water. Because of its short half-life in water, malathion is not expected to bioaccumulate in aquatic organisms (EXTOXNET, 1996).

Human Health Effects

Acute Exposure

Effects/Symptoms

Similar to other organophosphates, malathion is a cholinesterase inhibitor and interferes with the normal functioning of the nervous system. Malathion exhibits low acute toxicity via ingestion, dermal, and inhalation exposures (ATSDR, 2003b). Human volunteers fed very low doses of malathion for 6 weeks showed no significant effects on blood cholinesterase activity (ATSDR, 2003b). However, acute exposure to high concentrations can cause numbness, headaches, sweating, abdominal cramps, blurred vision, difficulty breathing, respiratory distress, loss of consciousness, and occasionally death. Acute exposure data for humans are limited and come from case reports of accidental poisonings (ATSDR, 2003b).

Several factors affect the toxicity of malathion, including the product purity, route of exposure, gender, and the amount of protein in the diet. Animal studies have shown that malathion is only slightly toxic following acute oral and dermal exposures, with reported LD_{50} values in rats of 1,000–10,000 mg/kg and 400–4,000 mg/kg, respectively. Additionally, as protein levels in the diet decrease, malathion toxicity increases. Females have been shown to be more susceptible to malathion toxicity than males due to differences in metabolism, storage, and excretion (EXTOXNET, 1996). It is uncertain whether children are more susceptible to the toxic effects of malathion; however, animal studies have shown that very young animals are more susceptible to the effects of malathion than older ones when exposed to high levels (ATSDR, 2003b). Weanling male rats acutely exposed to malathion were twice as susceptible to malathion as adults (EXTOXNET, 1996).

Treatment

Exposure to malathion may be determined through laboratory tests of urine and blood that measure breakdown products of malathion in urine or cholinesterase levels in blood (ATSDR, 2003b).

Long-term deleterious effects may be avoided if people exposed to high amounts of malathion are given the appropriate treatment quickly after exposure (ATSDR, 2003b). Oral exposure to malathion should be treated with rapid gastric lavage unless the patient is vomiting. Dermal exposures should be treated by washing the affected area with soap and water. If the eyes have been exposed to malathion, flush them with saline or water. People exposed to malathion who exhibit respiratory inefficiency with peripheral symptoms should be treated via slow intravenous injection with 2–4 mg atropine sulfate and 1,000–2,000 mg pralidoxime chloride or 250 mg toxogonin (adult dose). Exposure to high levels of malathion that result in respiratory distress, convulsions, and unconsciousness should be treated with atropine and a reactivator. Morphine, barbiturates, phenothiazine, tranquillizers, and central stimulants are all contraindicated (WHO/FAO, nd).

Chronic Exposure

Noncancer Endpoints

Most chronic human data come from studies of workers who are exposed to malathion via inhalation or dermally. Chronic exposure data in both humans and animals indicate that the main target of malathion toxicity is the nervous system (ATSDR, 2003b). A two-year rat study showed no adverse effects other than cholinesterase enzyme depression (EXTOXNET, 1996). Chronic animal studies have shown no reproductive or developmental toxicity at doses of malathion that are not maternally toxic. Malathion has been shown to be a contact sensitizer. Recent animal studies indicate that malathion can affect immunological parameters at doses that are lower than those that cause neurotoxicity (ATSDR, 2003b).

Cancer Endpoints

EPA has classified malathion as “suggestive evidence of carcinogenicity” (U.S. EPA, 2005c). While some studies indicate an increased incidence of some forms of cancer in people who are regularly exposed to malathion, such as those exposed occupationally, there is no conclusive evidence that malathion causes cancer in humans. In one study, rodents fed very high doses of malathion in their diet had increased incidences of liver tumors (ATSDR, 2003b; U.S. EPA, 2005c).

Toxicokinetics

Malathion is absorbed via inhalation, the gastrointestinal tract, and dermally (WHO/FAO, 1997). Dermal absorption is dependent on the site and dose applied (ATSDR, 2003b). Malathion is broken down in the liver into metabolites. One of its metabolites is malaoxon, from which malathion exhibits its toxic effects via cholinesterase inhibition (ATSDR, 2003b; U.S. EPA, 2005c; WHO/FAO, 1997). Neither malathion nor its metabolites tend to accumulate in the body and are mostly excreted within a few days (ATSDR, 2003b). Malathion is excreted mostly in the urine with a small amount being excreted in the feces. A very small amount may also be excreted in breastmilk.

Metabolites excreted include the monoacid and diacid of malathion, demethyl malathion, dimethyl phosphate, and O,O-dimethylphosphorothioate. In feces, the majority of material excreted is malathion with a smaller amount being malaoxon (WHO/FAO, 1997)

Ecological Effects

Acute Exposure

Malathion is not expected to pose a hazard to birds and mammals from acute dietary exposure. Malathion exhibits low to moderate toxicity to birds (U.S. EPA, 2005e). Acute oral LD_{50} values in various bird species include blackbirds and starlings (over 100 mg/kg), pheasants (167 mg/kg), chickens (525 mg/kg), and mallards (1,485 mg/kg). Malathion is rapidly metabolized by birds, with 90 percent being excreted in the urine within 24 hours. The toxicity of malathion to reptiles has not been evaluated, but the avian toxicity thresholds have been used to estimate the hazard. Acute effects were reported in one study of the Carolina anole and another on developing snapping turtle embryos (U.S. EPA, 2005e). Malathion is extremely toxic to beneficial insects, including honeybees (U.S. EPA, 2005e; EXTOXNET, 1996).

Malathion also has a wide range of toxicity to species in the aquatic environment, from being quite toxic to walleye with a 96 hr LC_{50} of 0.06 mg/L to being slightly toxic in goldfish with a 96 hr LC_{50} of 10.7 mg/L (EXTOXNET, 1996). In invertebrates and amphibians in their aquatic stages, malathion is also found to be highly toxic. In aquatic invertebrates, EC_{50} values range from 1 µg/L to 1 mg/L. However, since malathion has a very short half-life, there is little potential for bioconcentration in aquatic organisms (EXTOXNET, 1996). Malathion is also highly toxic to the larvae of terrestrial, non-target insects that have aquatic early life stages (U.S. EPA, 2005e).

Chronic Exposure

Although not persistent in the environment, birds may be chronically exposed because current labels do not restrict consecutive applications, intervals, or avoidance of nesting birds. Sublethal effects to birds may include reduced nesting behavior, disorientation, and loss of motor coordination. Studies have shown that chronic malathion exposure in the diet of terrestrial avian species causes moderate toxicity. Bobwhite quail exposed to 350 ppm for 10 weeks exhibited regressed ovaries, enlarged or flaccid gizzards, and a reduction in number of eggs that hatched. At higher exposures, a reduction in the number of eggs produced, viability of embryo, and an increase in cracked eggs was observed, while studies in waterfowl showed low toxicity (U.S. EPA, 2005e).

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Profile for Methoprene:

CAS Registry Number 40596-69-9

Summary

Chemical History

Methoprene is a larvicide and growth regulator that is used in agricultural, horticultural, and public health applications (HSDB, 2005; EXTOXNET, 1996). It is considered a biochemical pesticide because it acts by interfering with the life cycle of the insect instead through direct toxicity. It regulates growth by preventing insects from reaching maturity or reproducing (U.S. EPA, 2005, 2002, 2001, 1991a, 1991b; ATSDR, 2005; EXTOXNET, 1996; HSDB, 2005). Methoprene was first registered for use in the United States in 1975; there are currently 13 registered products. EPA has classified methoprene as toxicity class IV or slightly to almost nontoxic (EXTOXNET, 1996). In food production, methoprene is used on meat, milk, eggs, mushrooms, peanuts, rice, and cereals. As food additive, it prevents the breeding of hornflies in manure. In water, methoprene is used to control mosquito larvae as well as various flies, moths, beetles, and fleas (ATSDR, 2005; EXTOXNET, 1996; U.S. EPA, 2002, 2001, 1991a, 1991b). Methoprene is also used to on mammalian pets to control ectoparasites (U.S. EPA, 2005). It is available as a suspension, emulsifiable and soluble concentrate formulations, briquettes, pellets, sand granules, liquids aerosols, and bait (U.S. EPA, 2002; EXTOXNET, 1996).

Methoprene is selective, stable, and potent but not persistent in the environment or toxic to mammals. It presents no long-term hazard other than to the target species (U.S. EPA, 1991a, 1991b; WHO/FAO, n.d.). It has low potential for acute oral or inhalation toxicity. It is not a skin or eye irritant or skin sensitizer and is of low acute dermal toxicity. No adverse effects have been seen in humans or other non-target species (U.S. EPA, 2005, 2001, 1991a, 1991b). No chronic, oncogenetic, reproductive, developmental, or mutagenic effects have been seen in animals. In mammals it is rapidly and completely metabolized (U.S. EPA, 1991a). In mosquito control uses, there is little chance for human exposure because methoprene is applied directly to ditches, ponds, marshes, or flood areas that are not used for drinking water (U.S. EPA, 2002). Humans can be exposed to methoprene in small amounts through the food supply; through mixing, loading, or application of the pesticide; or while working with treated crops. Methoprene used in mosquito control does not pose a high risk of toxicity to wildlife or the environment. It is of low toxicity to birds and fish and nontoxic to bees; however, it is highly acutely toxic to aquatic invertebrates under laboratory conditions (U.S. EPA, 2005, 2002, 1991a, 1991b).

Description of Data Quality and Quantity

An extensive toxicity database has been compiled for methoprene, which includes acute toxicity batteries, irritation/sensitization studies, subchronic feeding studies, developmental and reproductive toxicity studies, mutagenicity studies, chronic feeding studies, lifetime carcinogenicity studies, and special studies on metabolism and fate and potential for endocrine disruption (U.S. EPA, 2001). Reviews on the toxicity of methoprene have been prepared:

- Registration Eligibility Document Isopropyl (2E, 4E)-11-methoxy-3,7,11-trimethyl-2,4-dodecadienoate (Referred to as Methoprene) (U.S. EPA, 1991a)
- Toxicologic Information About Insecticides Used for Eradicating Mosquitoes (West Nile Virus Control): Methoprene (ATSDR, 2005)
- Residues in Food – 1984. Toxicological Evaluations – Methoprene (WHO/FAO, 1984)
- Data Sheet on Pesticides No. 47. Methoprene (WHO/FAO, n.d.)
- Pesticide Information Profiles: Methoprene (EXTOXNET, 1996)
- The Pesticide Action Network (PAN) Pesticide Database (PAN, 2005).

Summary Table

Duration	Route	Benchmark Value	Units	Endpoint	Reference
Acute, Intermediate, Chronic	Inhalation	25	mg/kg/day	Inhalation NOAEL in rats with a UF of 100 applied	
Acute, Intermediate, Chronic	Oral	0.4	mg/kg/day	Chronic oral RfD based on liver effects in mice	U.S. EPA (1991a)
Acute, Intermediate, Chronic	Dermal	1	mg/kg/day	Dermal NOAEL of 100 mg/kg in rabbits with a UF of 100 applied	

For inhalation exposure, a NOAEL of 20 mg/L (21,000 mg/kg/day)[17] was identified in rats exposed to methoprene via inhalation for 4 hours per day, 5 days per week for 3 weeks (Olson and Willigan, 1972; ATSDR, 2005). The concentration was adjusted for intermittent exposure[18] (2,500 mg/kg/day) and an uncertainty factor of 100 was applied to account for interspecies and intrahuman variation, for an inhalation benchmark of 25 mg/kg/day. This value is appropriate for all exposure durations.

[17] Conversion between mg/m^3 and mg/kg/day assumes, for Wistar rats (species not specified, but Wistars represent the median body weight for laboratory rats), an average body weight of 0.187 kg and inhalation rate of 0.2 m^3/day (U.S. EPA, 1988).

[18] Adjustment for intermittent exposure is the product of air concentration and exposure of 4/24 hours/day and 5/7 days/week.

For oral exposure, a chronic oral RfD of 0.4 mg/kg/day was derived based on a NOAEL of 37.5 mg/kg/day for liver effects (pigmentation) in mice exposed to methoprene for 18 months (Wazeter and Goldenthal, 1975), with an uncertainty factor of 100 applied to account for interspecies and intrahuman variability (U.S. EPA, 1991a). The RfD was adopted to also represent acute and intermediate exposures.

For dermal exposure, a NOAEL of 100 mg/kg was identified in a 30-day rabbit study (Nakasawa et al., 1975). The LOAEL for the study was 300 mg/kg for erythema at the application site (ATSDR, 2005). An uncertainty factor of 100 was applied to account for interspecies and intrahuman variability. This value is appropriate for acute, intermediate, and chronic dermal exposures.

Insecticide Background

CASRN:	40596-69-9
Synonyms:	isopropyl (E,E)-(RS)-11-methoxy-3,7,11-trimethyldodeca-2,4-dienoate, ZR-515; ENT-70460, 1-Methylethyl (E,E)-11-methoxy-3,7,11-trimethyl-2,4-dodecadienoate, 2,4-Dodecadienoic acid, 11-methoxy-3,7,11-trimethyl-, 1-methylethyl ester, (E,E)- , 2,4-Dodecadienoic acid, 11-methoxy-3,7,11-trimethyl-, ispropyl ester, (E,E)-, Isopropyl (2E,4E)-11-methoxy-3,7,11-trimethyl-2,4-dodecadienoate, Isopropyl (2E,4E)-11methoxy-3,7,11-trimethyl-2-4 dodecadienoate, Isopropyl (2E,4E)-11methoxy-3,7,11-trimethyl-2-4 dodecadienoate (methoprene), Isopropyl (E,E)-11-methoxy-3,7,11-trimethyl-2,4-dodecadienoate, Methopreen, Methopren, Methoprene, Methoprene (ANSI), Methoprene Isopropyl (WHO/FAO, 1984; PAN, 2005)
Chemical Group:	Not available (EXTOXNET, 1996)
Registered Trade Names:	Altosid, Altosid Bruquets, Altosid CP10, Altosid SR 10, Altosid IGR, Altosand, Apex, Diacon, Dianex, Extinguish, Fleatrol, Kabat, Manta, Minex, Ovitrol, Pharoid, Precor (EXTOXNET, 1996; U.S. EPA, 2001; WHO/FAO, 1984, n.d; PAN, 2005; HSDB, 2005)

Usage

Methoprene is an insect growth regulator used indoors and outdoors to control a broad spectrum of insect pests in agricultural, horticultural, public health, and household applications. It is used on both food and nonfood crops, ornamentals, livestock, and mammalian pets (WHO/FAO, 1984; U.S. EPA, 2001, 2005; HSDB, 2005). Pest species it is used to control include mosquitoes, horn flies, beetles, tobacco moths, sciarid flies, fleas (eggs and larvae), fire ants, pharoah ants, midge flies, boll weevils, lice, leaf hoppers, plant hoppers, cucumber beetles, cigarette beetles, mites, Indian meal moths,

and others. In public health applications, the most important uses are against flood water mosquitoes (U.S. EPA, 2001, 2005; WHO/FAO, n.d.). Slow-release formulations are applied to prevent the breeding of mosquitoes in places such as rice cultivations, storm drains, ponds, and water treatment works, among others (WHO/FAO, 1984). Because methoprene acts by disruption of insect development, it is not usually used for a quick kill in preharvest situations (WHO/FAO, 1984). Methoprene is used widely in the mushroom cultures to prevent the emergence of sciarid flies, it is mixed into feed supplements for cattle to control adult hornfly breeding in manure, and it is sprayed at food and tobacco handling and storage facilities (WHO/FAO, 1984; HSDB, 2005).

Formulations and Concentrations

Methoprene is available as technical grade product and in formulations including emulsifiable and soluble concentrates, suspension concentrates, granules, briquettes, aerosols, fogging solutions, baits, flowables, encapsulated and feed supplement formulations up to 10 percent ai (HSDB, 2005; EXTOXNET, 1996; WHO/FAO, 1984, n.d.). WHO indicated that the content of methoprene in the formulated products must be declared and shall not exceed the listed standards. Technical grade (RS)-methoprene must have no less than 920 g/kg (RS)-methoprene. The mean content of the highly active trans (E) isomer must be 900 g/kg while the maximum content of the cis (Z) isomer is 20 g/kg. For the (RS)-methoprene emulsifiable concentrate, the (RS)-methoprene content should be $\leq$ 25 g/kg + 15% of the declared content, > 25–100 g/kg + 10% of the declared content, 100–250 g/kg + 6% of the declared content (WHO, 2001).

Shelf Life

Methoprene is a stable compound (WHO/FAO, n.d.). It is stable in sterile aqueous solutions but biodegrades easily by common bacteria, sunlight, and ultraviolet light (WHO/FAO, 1984).

Degradation Products

Methoprene is rapidly and extensively degraded in the soil. The breakdown products include small amounts of nonpolar metabolites, including hydroxyl ester. However, more than 50 percent of the applied dose was converted to carbon dioxide (WHO/FAO, 1984). In humans, methoprene is degraded and excreted in the urine as hydroxyepter (isopropyl 11-hydroxy-3,7,11-trimethyl - 2,4-dodecadienoate), the hydroxyacid (11-methoxy-3,7,11-trimethyl-2,4-dodecadienoic acid), and several lesser metabolites, including 7-methoxycitronellic acid, 7-hydroxycitronellic acid, and 7-methoxycitronellal which are excreted as free compound or conjugates (WHO/FAO, n.d.). Degradation products in unsterile pond water include ZR-724, ZR-725, ZR-669, and recovered methoprene each of which was a 1:1 mixture of cis-2 and trans-2 isomers, although 94 percent of the applied dose was trans-2 methoprene (WHO/FAO, 1984).

Environmental Behavior

Fate and Transport in Terrestrial Systems

Methoprene binds tightly to soil and it is only slightly soluble in water, making it almost immobile in most soil types (EXTOXNET, 1996; ATSDR, 2005). Field leaching studies in sand, sandy loam, silt loam and clay loam have shown that even after repeated washings with water, methoprene remains only in the top few inches of soil (EXTOXNET, 1996; WHO/FAO, 1984). In studies with radiolabeled methoprene, 87 percent of the applied dose was bound to the soil (WHO/FAO, 1984). These results indicate that methoprene does not leach from soil (U.S. EPA, 2001, 1991a, 1991b).

In soil, methoprene is of low persistence (EXTOXNET, 1996; U.S. EPA, 2001, 1991a, 1991b). It is rapidly and extensively broken down in soil (WHO/FAO, 1984). The reported field half-life is up to 10 days, while the half-life in sandy loam soil is about 10 days. The half-life of high application rates (1 pound/acre) of the formulated Altosid product is less than 10 days (EXTOXNET, 1996; ATSDR, 2005; WHO/FAO, n.d.). Methoprene is rapidly broken down by microbial degradation which is the major fate process to mostly carbon dioxide. It also undergoes rapid photodegradation (EXTOXNET, 1996; U.S. EPA, 2001, 1991a, 1991b; WHO/FAO, n.d.).

Additionally, formulated Altosid does not persist in plants. Half-lives of less than 1 day in rice, 2 days in alfalfa, and 3–7 weeks in wheat were reported. Methoprene residues are not expected in plants that are grown in treated soil (EXTOXNET, 1996; ATSDR, 2005).

Fate and Transport in Aquatic Systems

Because methoprene binds tightly to soil and is practically insoluble in water, very little leaching into groundwater has been reported (EXTOXNET, 1996; ATSDR, 2005). Methoprene rapidly degrades in water. Half-lives in ponds have been reported at approximately 30 hours for application of 0.001 mg/L and 40 hours for application of 0.01 mg/L (EXTOXNET, 1996). Sunlight and temperature play major roles in the breakdown of methoprene in water (EXTOXNET, 1996; U.S. EPA, 2001; WHO/FAO, 1984). Half-lives of <1 day for sunlight conditions and > 4 weeks for darkness were reported (ATSDR, 2005). Biodegradation and photodegradation are the major fate processes (EXTOXNET, 1996). The potential for bioconcentration of methoprene in aquatic organisms is very high, as indicated by its bioconcentration factor of 3,400 (ATSDR, 2005).

Human Health Effects

Acute Exposure

Effects/Symptoms

There are limited data on the acute toxicity of methoprene in humans because no obvious signs of poisoning have been reported in humans from either accidental or occupational exposures (EXTOXNET, 1996; WHO/FAO, n.d.). In human health screening studies, no

significant effects were seen (U.S. EPA, 1991a, 1991b). From those data and animal data it is concluded that methoprene has very low acute oral and inhalation toxic potential in humans. It is also not a skin or eye irritant or a skin sensitizer in humans (U.S. EPA, 2001, 1991a, 1991b; WHO/FAO, n.d.).

In animals, acute oral and inhalation exposures to methoprene are almost nontoxic while dermal exposures are only slightly toxic (EXTOXNET, 1996; ATSDR, 2005). Oral LD_{50} values of 2,323 – >34,600 mg/kg in rats, 2,285 mg/kg in mice, and 5,000–10,000 mg/kg in dogs were reported. In rats, 20 percent mortality was seen within 4 months following oral doses of 232 mg/kg/day, while no deaths were seen at 116 mg/kg/day. In rats, an inhalation LC_{50} value of >210,000 mg/m^3 was reported, which was the highest dose tested. Reported dermal LD_{50} values range from > 2,000–10,000 mg/kg in rabbits and are > 5,000 mg/kg in rats (ATSDR, 2005; HSDB, 2005; EXTOXNET, 1996; WHO/FAO, n.d.; NIHE, 2001).

In short-term studies, no inhalation or dermal effects were reported in rats, rabbits, or dogs (U.S. EPA, 2001; WHO/FAO, n.d.; ATSDR, 2005). In subchronic studies, some systemic effects (e.g., increased liver weights and other liver and kidney effects in rats) have been observed at high concentrations (U.S. EPA, 2001, 1991a, 1991b; WHO/FAO, n.d.).

Methoprene is of low dermal toxicity. It does not cause skin or eye irritation in rabbits and it is not a skin sensitizer in guinea pigs (HSDB, 2005; EXTOXNET, 1996; ATSDR, 2005; U.S. EPA, 1991a, 1991b; WHO/FAO, n.d.; NIHE, 2001). No systemic effects were reported in rabbits dermally exposed in a 30-day study; erythema was reported at the application site (ATSDR, 2005; U.S. EPA, 2001). Additionally, hyperemia and edema of the skin was observed following repeated dermal applications (HSDB, 2005). Available data also suggest that methoprene is not genotoxic (NIHE, 2001).

Treatment

No laboratory tests have been identified as indicators of exposure to methoprene, and blood levels have not been established in humans (WHO, n.d.; HSDB, 2005). Because methoprene is of low acute toxicity, there are no clear signs or clinical symptom of toxicity in humans. If a person has been exposed to methoprene and shows signs of illness, treatment before being seen by a physician is supportive. Because no acute toxicity is expected even with ingestion of large doses, any illness seen following exposure is likely due to the solvent used in formulation (WHO/FAO, n.d.). Only following ingestion of large amounts of methoprene should gastrointestinal decontamination be employed. Recommended doses of activated charcoal include 25–100 g in adults and adolescents, 25–50 g in children, and 1 g/kg in infants less than one year old. Dermal exposure should be treated by decontamination of the skin by washing with soap and water. Treatment of ocular exposure consists of flushing the eyes with large amounts of saline or clean water. Medical attention should be sought if irritation continues (HSDB, 2005).

Chronic Exposure

Noncancer Endpoints

Little data are available for humans following chronic exposures to methoprene, though it is not likely to cause long-term problems when used under normal conditions. No overt signs of toxicity have been reported from long-term occupational exposures (EXTOXNET, 1996). Based on animal studies, methoprene is not likely to cause chronic toxicity in human. Animal data indicate that the organ mainly affected by chronic methoprene exposure is the liver. Increased liver weights were reported in a 90-day feeding study in rats. However, these effects were not replicated in 2-year feeding studies in rats or in mice given methoprene in the diet for 90 days (EXTOXNET, 1996; U.S. EPA, 2001; WHO/FAO, n.d.).

Methoprene does not appear to have reproductive, developmental, or neurotoxic effects in animals. No reproductive effects were observed in a 3-generation reproduction study in rats or a 90-day study in dogs (EXTOXNET, 1996; ATSDR, 2005; U.S. EPA, 2001, 1991a, 1991b; WHO/FAO, n.d.; NIHE, 2001). No teratogenic effects were seen in rats, rabbits, or mice (WHO/FAO, n.d.; EXTOXNET, 1996; ATSDR, 2005; U.S. EPA, 1991a, 1991b). Methoprene does not show potential estrogenic, androgenic anabolic, or glucocorticoid effects (U.S. EPA, 2001; WHO/FAO, n.d.).

Cancer Endpoints

Existing data suggest that methoprene is not carcinogenic. Long-term feeding studies in rats and mice showed no increase in tumors (U.S. EPA, 1991a; EXTOXNET, 1996; NIHE, 2001). Additionally, methoprene does not show any mutagenic potential (EXTOXNET, 1996).

Toxicokinetics

Methoprene is absorbed via the gastrointestinal tract, inhalation of spray mist and through intact skin (WHO/FAO, n.d.). Oral absorption is rapid and extensive. It is distributed mainly to organs related to absorption, biotransformation, and excretion (NIHE, 2001). No evidence of accumulation in body tissues or fluids including fat, muscle, liver, lungs, blood, or bile was seen in a study using ^{14}C-labelled methoprene (WHO/FAO, 1984, n.d.). Methoprene is rapidly and completely metabolized and excreted in the urine, feces, and expired air of mammals (EXTOXNET, 1996; U.S. EPA, 2001; ATSDR, 2005; NIHE, 2001). In cattle, methoprene is excreted unchanged and in sufficient quantities in the feces to have the desired effect of killing larvae that breed in the waste (EXTOXNET, 1996). In mice intubated with radiolabeled methoprene, 63.6 percent and 12.3 percent of the radioactivity was excreted within 24 hours in the urine and feces, respectively (ATSDR, 2005).

The metabolism of methoprene occurs mainly by hepatocyte microsomal esterases to methoprene acid. After alpha oxidation, methoprene acid is susceptible to beta oxidation to acetate. It is then further broken down to carbon dioxide or intermediary metabolites

by the Krebs' cycle. It is excreted from the body as carbon dioxide or in urine and feces. Poor intestinal absorption and rapid metabolism of absorbed methoprene may be indicated by the finding of high amounts of unmetabolized methoprene in the feces but not the urine or blood. Products of urinary excretion include the hydroxyepter (isopropyl 11-hydroxy-3,7,11-trimethyl - 2,4-dodecadienoate), the hydroxyacid (11-methoxy-3,7,11-trimethyl-2,4-dodecadienoic acid), and several lesser metabolites including 7-methoxycitronellic acid, 7-hydroxycitronellic acid, and 7-methoxycitronellal. Excretion of the primary urinary products is as free compounds or as conjugates. Methoprene is found in the eggs of laying hens and the milk of lactating cows (WHO/FAO, n.d.) however, no placental transfer was evident in mice (ATSDR, 2005). Approximately 8 percent of the radiolabel was excreted in the milk of lactating cows within 7 days while 19 percent was found in eggs of chickens after 14 days (NIHE, 2001). Most of the radiolabel in most species is excreted within 5 days (NIHE, 2001).

Ecological Effects

Acute Exposure

Toxicity in Non-Targeted Terrestrial Organisms

Methoprene is very unlikely to harm terrestrial organisms other than its targets. It has a very low toxicity in birds (U.S. EPA, 2001, 1991a, 1991b; EXTOXNET, 1996; WHO/FAO, n.d.). Reported oral LD_{50} values include 4,640 ppm in chickens for the formulation Altosid and 2,000 mg/kg for mallard ducks (EXTOXNET, 1996). Reported acute 5–8 day LC_{50} values for Altosid in Mallard ducks and Bobwhite quail were all >10,000 ppm (EXTOXNET, 1996). Similar effects were reported in feeding studies using the technical material (WHO/FAO, n.d.). No reproductive effects or embryotoxicity were seen in mallard ducks and bobwhite quail fed Altosid (U.S. EPA, 2001, 1991a, 1991b; EXTOXNET, 1996; WHO/FAO, n.d.). However, acute oral exposure in birds to higher levels resulted in slowness, reluctance to move, sitting, withdrawal, and incoordination. These effects appeared quickly and persisted for up to 2 days making the birds potentially more susceptible to predation (EXTOXNET, 1996). No toxicity was seen in honeybees or earthworms (EXTOXNET, 1996). The oral and dermal LD_{50} in bees is >1,000 µg/L/bee (HSDB, 2005). An unintended but beneficial effect has been observed in Japanese silk worms where exposure to methoprene extends the time period in which they make silk (WHO/FAO, n.d.).

Toxicity in Non-Targeted Aquatic Systems

Acute effects of methoprene have been reported in a wide variety of aquatic species. It is very highly toxic in aquatic insects, highly toxic in crustaceans, moderately toxic in zooplankton, and slightly toxic in molluscs and fish (PAN, 2005; EXTOXNET, 1996; U.S. EPA, 2001, 1991a, 1991b). In fish, accumulation, behavioral, biochemistry, growth, mortality, and population effects have been reported (PAN, 2005). In freshwater fish, methoprene is more toxic to warm-water fish and less toxic to cold-water fish (U.S. EPA, 1991a, 1991b). No death or toxicity was observed in mosquito fish treated for 10 weeks

in ponds at 56–560 g/ha (WHO/FAO, n.d.). The reported 96-hour LC_{50}s in fish for the formulation Altosid range from 4.4 mg/L to > 100 mg/L in channel catfish and largemouth bass (EXTOXNET, 1996). For technical methoprene, reported LD_{50}s in fish range from 4,000 µg/L in Australian blue-eye to 124,950 µg/L in Mummichog (PAN, 2005).

Methoprene is highly acutely toxic to freshwater invertebrates such as crayfish and Daphnia manga (EXTOXNET, 1996; U.S. EPA 1991a, 1991b). Additionally, it can have high acute toxicity in estuarine and marine invertebrates such as grass shrimp and mud crabs; however, marine invertebrates are less likely to be exposed than estuarine invertebrates since methoprene is used as a mosquito larvicide. Additionally, the rapid degradation of methoprene in water mitigates the risks to estuarine organisms (U.S. EPA, 1991a, 1991b). In arthropods including crustacean, insecta, molluca, shrimp, damselfly, beetle, and tadpole, 24- and 48-hour LC_{50s} were greater than 900 ppb (U.S. EPA, 2001). The reported LC_{50} for freshwater shrimp is > 100 mg/L while it is > 0.1 mg/L for estuarine mud crab (EXTOXNET, 1996). Similar 5-day LC_{50} values for technical methoprene have been reported for crayfish, freshwater shrimp and white and pink shrimp (100 ppm) (WHO, n.d.). A 48-hour EC_{50} of 360 µg/L was reported for Daphnia (HSDB, 2005).

In amphibians, behavioral, developmental, growth, mortality, and population effects have been reported (PAN, 2005). The reported LC_{50} values for *R. catesbeiana* and *R. pipiens* larvae are greater than 10,000 ppb, and in adult *B. woodhousei*, the reported LC_{50} value is greater than the highest dose tested (>1,000 ppb) (U.S. EPA, 2001).

A slight potential for bioconcentration has been reported in bluegill sunfish and crayfish (EXTOXNET, 1996). Methoprene has an estimated bioconcentration factor of 3,400 which suggests that its potential for bioconcentration is very high (ATSDR, 2005).

Chronic Exposure

Methoprene is of minimal chronic risk to freshwater fish, invertebrates, and other estuarine species from use in mosquito products (U.S. EPA, 2001). The use of briquettes poses a potential risk for chronic exposures in estuarine organism since methoprene is released slowly over an extended period of time (U.S. EPA, 1991a, 1991b). However, laboratory and field studies using mosquito product formulations have shown that methoprene dose not reach levels that are toxic to nontarget aquatic species during chronic exposures (U.S. EPA, 2001)

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Profile for Permethrin:

CAS Registry Number 52645-53-1

Summary

Chemical History

Permethrin is a synthetic pyrethroid insecticide used in agricultural and human health applications. It is similar to the natural insecticide pyrethrum, which comes from chrysanthemums; however, it is more effective and longer lasting (WHO/FAO, 1984; IPCS, 1990). For mosquito control, it is used in bed nets and other materials that are dipped in permethrin to protect the user (EXTOXNET, 1996; WHO/FAO, 1984). Permethrin is of low risk to humans when used at levels recommended for its designed purpose (ATSDR, 2003a). However, as a synthetic pyrethroid, permethrin exhibits its toxic effects by affecting the way the nerves and brain normally function by interfering with the sodium channels in nerve cells (Choi and Soderlund, 2006). Typical symptoms of acute exposure are irritation of skin and eyes, headaches, dizziness, nausea, vomiting, diarrhea, and excessive salivation and fatigue. Inhaled permethrin has been shown to cause cutaneous paresthesias or a burning, tingling, or stinging. However, these effects are generally reversible and disappear within a day of removal from exposure (ATSDR, 2003a). EPA has not classified synthetic pyrethroids, including permethrin, as endocrine disruptors.

Description of Data Quality and Quantity

Several comprehensive reviews on the toxicity of permethrin have been prepared or updated in recent years:

- Toxicological Profile for Pyrethrin and Pyrethroids (ATSDR, 2003a)
- An EPA risk assessment for the Reregistration Eligibility Decision (RED) document (U.S. EPA, 2005f)
- IRIS summary review (U.S. EPA, 2005g).

EPA and ATSDR have developed quantitative oral human health benchmarks (EPA's acute and chronic RfDs, short-, intermediate-, and long-term inhalation and dermal benchmarks and ATSDR's acute and intermediate oral MRLs). Other relevant references include

- Environmental Health Criteria 94: Permethrin (IPCS, 1990)
- Specifications for Permethrin (WHO, 1999a).

Summary Table

Duration	Route	Benchmark Value	Units	Endpoint	Reference
Acute, Intermediate, Chronic	Inhalation	0.11	mg/kg/day	Inhalation NOAEL of 0.042 mg/L (11 mg/kg/day) for neurological effects in rats with UF of 100 applied	U.S. EPA (2005f)
Acute, Intermediate, Chronic	Oral	0.25	mg/kg/day	Acute and chronic RfD based on clinical effects in rats	U.S. EPA (2005f)
Acute, Intermediate, Chronic	Dermal	5	mg/kg/day	Dermal NOAEL of 500 mg/kg/day in rats with a UF of 100 applied	U.S. EPA (2005f)
Cancer	Inhalation, Oral, Dermal	0.009567	per mg/kg/day	CSF for lung tumors in female mice	U.S. EPA (2005f)

For inhalation exposure, a NOAEL of 0.042 mg/L (11 mg/kg/day) was identified for neurological effects in rats exposed via inhalation and an uncertainty factor of 100 was applied. This value is appropriate for short- (1–30 days), intermediate- (1–6 months), and long-term (>6 months) inhalation exposures (U.S. EPA, 2005f).

For oral exposure, an acute and chronic oral RfD of 0.25 mg/kg/day was derived based on a NOAEL of 25 mg/kg/day for clinical signs (i.e., aggression, abnormal and/or decreased movement) and increased body temperature observed in rats, with an uncertainty factor of 100 applied (U.S. EPA, 2005f). The acute and chronic RfD was adopted to also represent intermediate exposures.

For dermal exposure, a NOAEL of 500 mg/kg/day was identified in rats dermally exposed for 21 days and an uncertainty factor of 100 was applied. This value is appropriate for all exposure durations (U.S. EPA, 2005f).

To assess potential carcinogenic risks, a cancer slope factor (CSF) of 9.567×10^{-3} per mg/kg/day was derived based on lung tumors in female mice chronically exposed to permethrin in the diet (U.S. EPA, 2005f).

Insecticide Background

CASRN: 52645-53-1

Synonyms: 3-Phenoxyphenyl)methyl3-(2,2-dichloroehenyl)-2,2-dimethylcyclopropanecarboxylate (ATSDR, 2003a)

Chemical Group: pyrethroid

Registered Trade Names: Ambush, BW-21-Z, Cellutec, Dragnet, Ectiban, Eksmin, Exmin, FMC 33297, Indothrin, Kafil, Kestrel, NRDC 143, Pounce, PP 557, Pramex, Qamlin, and Torpedo (EXTOXNET, 1996), Acion, AI3, AMbushfog, BW-21-7, CO-Opex, Matadon, NIA 33297, Outflank, OMS-1821, Perthrine, Picket G, Perigen, PP557, R86557, Stockade, Stomoxin, S-3151, SBP-1513, Talcord, WL43479 (WHO/FAO, 1984)

Usage

Permethrin is used as a broad spectrum insecticide to combat pests on a variety of crops. It is also used to control ectoparasites in animals, biting flies, and cockroaches and is used in greenhouses, gardens, and for termite control (EXTOXNET, 1996). It belongs to the pyrethroid class of insecticides, which have long been used to control mosquitoes, human lice, beetles, and flies (ATSDR, 2003a). For mosquito protection, it is used in bed nets and other materials that are dipped into the permethrin to protect the user. Permethrin for agricultural use is restricted by EPA due to its potential toxicity to aquatic organisms, and it may only be purchased and used by certified applicators (ATSDR, 2003a).

Formulations and Concentrations

Permethrin is available in technical grade, emulsifiable concentrates, dusts, smokes, ultra-low volume (UVL), and wettable powder formulations (EXTOXNET, 1996). Technical grade permethrin may be mixed with carriers or solvents resulting in the commercial formulations. These commercial formulations may also include ingredients that may potentiate the toxicity compared to technical grade permethrin. These ingredients must be identified on the label. WHO indicated that the content of permethrin in the formulated products must be declared and shall not exceed the listed standards. For impregnated mosquito netting, the permissible permethrin content is 20 +/- 3 mg/kg (WHO, 2002). Technical grade permethrin must have no less than 900 g/kg permethrin. The emulsifiable concentrate should contain > 25–100 g/kg +/- 10% of the declared content, 100–250 g/kg +/- 6% of the declared content, or > 250–500 g/kg +/- 5% of the declared content (WHO, 1999a). Permethrin that is used for bed nets comes in the emulsifiable concentrations ranging from 10 to 55 percent active ingredient. The 55 percent emulsifiable concentration is only for professional use (WHO, 1999a).

Shelf Life

Permethrin is stable for 2 years or longer at 50^{o}C. It is most stable in acidic environments and optimal stability is at pH 4. Photochemical degradation occurs in laboratory studies but not in field data. Pyrethrins, in general, are stable for a long time in water-based aerosols (HSDB, 2005).

Degradation Products

Pyrethroid insecticides are often formulated with synergists that act to prevent the breakdown of enzymes and thus enhance the activity of the pyrethroid (ATSDR, 2003a). Permethrin needs to be stored in a dry, cool, well-ventilated location to prevent the risk of it breaking down prior to use. Permethrin's breakdown products include 3-phenoxybenzyl(1RS)-cis, trans-3-(2,2-dichloroviny)-2-2dimethylcyclopropanecarboxylate (PAN, 2005).

Environmental Behavior

Fate and Transport in Terrestrial Systems

Permethrin is moderately stable in the environment (WHO/FAO, 1984). It binds tightly to soil making it almost immobile in most soil types. Studies have shown that permethrin is immobile in clay and loamy sands, while its degradation products have some mobility. As a result, it is not easily taken up by plants or leached into groundwater (ATSDR, 2003a).

In soil, permethrin is of low to moderate persistence (EXTOXNET, 1996). The reported half-life ranges from 30 to 38 days in soil (EXTOXNET, 1996) and < 2.5 days in a sediment and seawater solution. The U.S. Department of Agriculture (USDA) Pesticide Database lists the half-life of permethrin as 4–40 days in aerobic soils. It is broken down largely by microorganisms in nonsterile soil and may also be broken down by sunlight at the surface of soil (ATSDR, 2003a).

Fate and Transport in Aquatic Systems

Permethrin is not expected to be released in large quantities into water because it is generally applied to crops and vegetation aerially or on the ground from sprayers. Nearby waters, however, might be affected by spray drift. Permethrin is prohibited from being applied for mosquito control within 100 feet of lakes, rivers, or streams due to its aquatic toxicity (ATSDR, 2003a). Because permethrin binds tightly to soil and is practically insoluble in water, very little leaching into groundwater has been reported (EXTOXNET, 1996). Due to its low vapor pressure and Henry's law constant, permethrin volatilizes slowly from water. When permethrin is released into water, it rapidly partitions to suspended solids and sediments, which further mitigates volatilization. Studies have shown that greater than 95 percent of permethrin applied directly onto lake sediment was absorbed.

Permethrin breaks down quickly in water. Studies have reported a half-life of < 2.5 days near estuarine areas (EXTOXNET, 1996). Additionally, permethrin undergoes photolysis in sunlit surface waters, with a reported half-life of 14 days in seawater exposed to light (ATSDR, 2003a). In water, a loss of toxicity was observed for permethrin that had aged for 48 hours in sunlight (EXTOXNET, 1996).

Human Health Effects

Acute Exposure

Effects/Symptoms

There are limited data on the acute toxicity of permethrin in humans. Acute effects observed from occupational exposure include burning and itching of the skin of the periorbital area within a few hours of inhalation exposure to permethrin. Ingestion of permethrin causes nausea and vomiting. As a Type I pyrethroid, its primary target is the nervous system (U.S. EPA, 2005f). Typical effects seen following acute exposure to higher levels of permethrin are almost all related to the action of it on the nervous system, as pyrethroids prolong the open phase of the sodium channel during nerve cell excitation. Animal studies have indicated that effects may be caused by repetitive activity in sensory motor nerves (IPCS, 1990; WHO/FAO, 1984). These symptoms of permethrin exposure are transitory and disappear anywhere within a few hours to a few of days once the exposure is discontinued (EXTOXNET, 1996).

In animals, oral and inhalation exposures to permethrin are almost nontoxic. Reported LD_{50} values for technical permethrin range from 430 to 4,000 mg/kg in rats, while a 4-hour LC_{50} of 23.5 mg/L is reported in rats. Permethrin is slightly toxic through dermal contact, with dermal LD_{50}s of over 4,000 mg/kg in rats and over 2,000 mg/kg in rabbits. The toxicity depends on the ratio of cis and trans isomers, with cis being more toxic, and the solvent used (EXTOXNET, 1996; WHO/FAO, 1984). Reported dermal LD_{50} values include > 4,000 mg/kg (no solvent) in rabbits, > 2,500 mg/kg (no solvent) in rats and mice, and 750 mg/kg (in xylene) in rats (WHO/FAO, 1984). Dermal exposure to permethrin has caused mild irritation to both intact and abraded skin of rabbits (EXTOXNET, 1996).

Treatment

Permethrin and its metabolites can be detected in blood and urine; however the methods are not practical given how quickly these compounds are broken down in the body (ATSDR, 2003a; WHO/FAO, 1984). Levels of the degradation product 3-phenoxybenzyl in urine may be useful indicators of exposure (WHO/FAO, 1984).

There are no antidotes for permethrin exposure. Treatment depends on the symptoms of the exposed person. If a person exhibits signs of typical pyrethroid toxicity following permethrin exposure (nausea, vomiting, shortness of breath, tremors, hypersensitivity, weakness, burning, or itching), they should immediately remove any contaminated clothing. Any liquid contaminant on the skin should be soaked up and the affected skin areas cleaned with alkaline soap and warm water. Eye exposures should be treated by rinsing with copious amounts of 4 percent sodium bicarbonate or water. Contact lenses should be removed. Vomiting should not be induced following ingestion exposures, but the mouth should be rinsed. The person should be kept calm and medical attention should be sought as quickly as possible (PAN, 2005; WHO/FAO, 1984). Medical personnel will treat severe intoxications with a sedative and anticonvulsant. Ingestion of large amounts

of permethrin should be treated with gastric lavage using a 5 percent bicarbonate solution followed by powdered activated charcoal. Skin irritation may be treated with a soothing agent and exposure to light should be avoided.

Chronic Exposure

Noncancer Endpoints

Little data are available for humans following chronic exposures to permethrin, though it is not likely to cause long-term problems when used under normal conditions (EXTOXNET, 1996). Chronic occupational exposure to permethrin caused skin and eye irritation in 33 percent of exposed Swedish workers. However, no complaints were reported in volunteers exposed to 0.5 mg/m^3 from an indoor application (WHO/FAO, 1984).

Data in animals indicate that oral exposure to permethrin is not highly toxic, but effects reported are largely neurological. Doses of 5 mg/kg/day for 90 days did not produce effects in dogs (EXTOXNET, 1996) while higher oral doses of 500 mg/kg and greater for 3 months caused transient clinical signs. Mice and rats chronically exposed to dietary levels up to 5,000 mg/kg (mice) and 2,500 mg/kg (rats) exhibited no consistent effects on growth or food consumption (WHO/FAO, 1984). Inhalation and dermal studies in animals indicate that permethrin is nontoxic or minimally toxic. No effects were observed in rats exposed to up to 500 mg/m^3, 6 hours per day, for 13 weeks. Additionally, rabbits dermally exposed to 1.0 g/kg/day on abraded skin for 21 days showed no effects other than moderate skin irritation (WHO/FAO, 1984). Based on the lack of reproductive effects in animals exposed to high oral does of permethrin, human reproductive toxicity is not expected. Additionally, permethrin shows no teratogenic or mutagenic activity (EXTOXNET, 1996; WHO/FAO, 1984).

Cancer Endpoints

EPA has classified permethrin as “likely to be carcinogenic to humans” by the oral route. A long-term, high dose dietary exposure study reported an increased incidence of benign lung and liver tumors in mice. This is supported by equivocal evidence in one strain of rats and structure-activity relationship information (U.S. EPA, 2005f).

Toxicokinetics

Permethrin is readily absorbed via the gastrointestinal tract, inhalation, and less so through intact skin (WHO/FAO, 1984). In mammals, permethrin is rapidly metabolized in the liver (EXTOXNET, 1996). The trans isomer is metabolized by hydrolysis and the cis isomer is not as easily hydrolyzed and is thus more toxic (WHO/FAO, 1984). The hydroysis and oxidation products of permethrin metabolism are quickly excreted in urine and feces with the trans isomers more rapidly excreted than the cis isomers. The primary excretion products of both isomers in most species studied include 4'-HO-3-PBA sulfate (in rats), 4'-HO-3-PBA (trans) and 6-HO-3-PBA (cis) sulfates (in mice), N-(3-phenoxybenzoyl) glutamate (in cows), and cyclopropane-carboxylic acid glucuronides

and 3-PBA glucuronides products in most of the species studied (WHO/FAO, 1984). Permethrin may persist in fatty tissues. The reported half-life in the brain and body fat is 4–5 days (EXTOXNET, 1996).

Ecological Effects

Acute Exposure

Toxicity in Non-Targeted Terrestrial Organisms

Permethrin, like other pyrethroids, is very unlikely to harm terrestrial organisms other than its targets, such as mosquitoes and other pests (EXTOXNET, 1996). Permethrin has a very low toxicity in birds (WHO/FAO, 1984; EXTOXNET, 1996). Oral LD_{50} values range from 9,900 mg/kg for the formulation Pramex in mallard ducks to over 15,500 mg/kg in Japanese quail (EXTOXNET, 1996), while the acute oral LD_{50} for the technical material was >11,275 mg/kg in mallard ducks and >32,000 mg/kg in starlings. Subacute LD_{50}s were >23,000 mg/kg for all bird species tested. No adverse effects or significant accumulation in tissues or eggs were seen in hens exposed to a spray mist of 3.77–11.94 mg/bird (WHO/FAO, 1984). As with other pyrethroid insecticides, permethrin is extremely toxic to honey bees (EXTOXNET, 1996).

Toxicity in Non-Targeted Aquatic Systems

Permethrin is very toxic to fish (EXTOXNET, 1996); however, because it is rapidly absorbed and degraded in the aquatic environment, the risk is of short duration (WHO/FAO, 1984). The high toxicity in fish is illustrated by the low exposures that cause lethality. The reported 48-hour LC_{50} for rainbow trout is 0.0054 mg/L, while in bluegill sunfish and salmon it is 0.0018 mg/L (EXTOXNET, 1996). The 96-hour LC_{50}s range from 0.1–0.5 µg/L in rainbow trout to 15 µg/L in mosquito fish (WHO/FAO, 1984). Permethrin has a low to moderate potential to accumulate in fish, with reported bioconcentration factors of over 700 times the concentrations in water for bluefish and catfish (EXTOXNET, 1996). A bioconcentration factor of 1,900 was reported in eastern oysters following a 28-day incubation (ATSDR, 2003a). Permethrin is also known to be toxic to some aquatic invertebrates, amphibians in larval form, aquatic insects, and crustaceans (WHO/FAO, 1984). A disruption in growth and development of tadpoles has been reported (EXTOXNET, 1996).

Chronic Exposure

Due to low rate of application and low persistence of permethrin in both terrestrial and aquatic environments, serious adverse effects are not anticipated from chronic exposures (HSDB, 2005)

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Profile for Pirimiphos-Methyl:

CAS Registry Number 29232-93-7

Summary of Insecticide

Chemical History

Pirimiphos-methyl is a fast-acting, broad spectrum, noncumulating organophosphate insecticide and acaricide used in agricultural, horticultural, and public health applications (WHO/FAO, 1983, 1974). In public health applications, it is used to control disease vector insects, including mosquitoes, ants, beetles, bed-bugs, cockroaches, fleas, flies, lice, and mites (WHO/FAO, 1983, 1974). Pirimiphos-methyl has both contact and fumigant action (WHO/FAO, 1974). It is applied as a liquid concentrate, ready to use formula, and as treated articles (ear tags) (U.S. EPA, 1999b). It can be applied by closed system containers, low- and high-pressure hand wands, backpack sprayers, tagging equipment, and foggers (U.S. EPA, 2001). Pirimiphos-methyl acts like other organophosphates by inhibiting cholinesterase activity (U.S. EPA, 1999d). It is of low mammalian toxicity (WHO/FAO, 1983). WHO/FAO (1992) has classified it as slightly hazardous. Early symptoms of pirimiphos-methyl exposure include excessive sweating, headache, weakness, giddiness, nausea, vomiting, stomach pains, blurred vision, slurred speech, and muscle twitching. Symptoms of more severe poisoning may advance to convulsions, coma, loss of reflexes, and loss of sphincter control (WHO/FAO, 1983).

Description of Data Quality and Quantity

Comprehensive reviews on the toxicity of pirimiphos-methyl have been prepared:

- Interim Reregistration Eligibility Decision for Pirimiphos-methyl Case No. (2535) (U.S. EPA, 2001)
- IRIS summary review (U.S. EPA, 2006)
- Data Sheet on Pesticide No. 49 – Pirimiphos-methyl (WHO/FAO, 1983).

EPA has developed quantitative human health benchmarks that include an oral acute and chronic RfD and short- and intermediate-term inhalation and dermal benchmarks.

Summary Table

Duration	Route	Benchmark Value	Units	Endpoint	Reference
Acute	Inhalation	0.015	mg/kg/day	Oral LOAEL for neurological effects in rats with UF of 1000 applied; assume no portal of entry effects	U.S. EPA (2001)
Intermediate	Inhalation	0.0007	mg/kg/day	Oral LOAEL for neurological effects in rats with UF of 300 applied; assume no portal of entry effects	U.S. EPA (2001)
Chronic	Inhalation	0.0007	mg/kg/day	Adopt intermediate for chronic duration	U.S. EPA (2001)
Acute	Oral	0.015	mg/kg/day	Acute oral RfD based on a LOAEL of 15 mg/kg/day for neurological effects in rats and UF of 1,000 applied	U.S. EPA (2001)
Intermediate	Oral	0.0002	mg/kg/day	Adopt chronic RfD for intermediate duration	U.S. EPA (2001)
Chronic	Oral	0.0002	mg/kg/day	Chronic oral RfD based on a LOAEL of 0.2 mg/kg/day for neurological effects in rats and UF of 1,000 applied	U.S. EPA (2001)
Acute	Dermal	0.015	mg/kg/day	Oral LOAEL for neurological effects in rats with UF of 1,000 applied; assume no first pass effects and 100% oral absorption	U.S. EPA (2001)
Intermediate	Dermal	0.0007	mg/kg/day	Oral LOAEL for neurological effects in rats with UF of 300 applied; assume no first pass effects and 100% oral absorption	U.S. EPA (2001)
Chronic	Dermal	0.0007	mg/kg/day	Adopt intermediate for chronic duration	

For oral exposure, an acute RfD of 0.015 mg/kg/day was derived based on a LOAEL of 15 mg/kg/day for brain, red blood cell, and plasma cholinesterase inhibition in rats (EPA MRID# 43594101, citation not provided). An uncertainty factor of 1,000 was applied for the use of a LOAEL and the degree of cholinesterase inhibition (10), and intra- and inter-species variability (100) (U.S. EPA, 2001).

A chronic oral RfD of 0.0002 mg/kg/day was derived based on an LOAEL of 0.2 mg/kg/day for plasma cholinesterase inhibition in a subchronic rat study (EPA MRID# 43608201, citation not provided). An uncertainty factor of 1,000 was applied for the use of a LOAEL and data gaps for long-term studies (10), and intra- and inter-species variability (100) (U.S. EPA, 2001). The chronic RfD was used to represent intermediate exposures.

For inhalation and dermal exposure, the oral toxicity endpoints (i.e., LOAELs) were selected for use, and both assume 100 percent absorption and no first pass or portal-of-entry effects (U.S. EPA, 2001). For acute inhalation and dermal benchmarks, an uncertainty factor of 1,000 was applied for the use of a LOAEL and the degree of cholinesterase inhibition (10), and intra- and inter-species variability (100). For intermediate inhalation and dermal benchmarks, an uncertainty factor of 300 was applied for the use of a LOAEL (3) and intra- and inter-species variability (100). The intermediate benchmark was used to represent chronic exposures.

Insecticide Background

CASRN:	29232-93-7
Synonyms:	O-(2-Diethylamino)-6-methyl-4-pyrimidinyl) O,O-dimethyl phosphorothioate, 2-diethylamino-6-methylpyrimidin-4-yl dimethyl phosphorothionate, pirimifosmethyl, methylpirimiphos, pyridimine phosphate, ENT 27699GC, PP511, CMS 1424 (U.S. EPA, 2001, 2006; WHO/FAO, 1983
Chemical Group:	organophosphate (U.S. EPA, 2001; WHO/FAO, 1983)
Registered Trade Names:	Actellic 5E, Atelic, Atellic, Atellifog, Blex, Nu-Gro Insecticide, Nu-Gro 5E, Tomahawk Insecticide Ear Tags, LPM Insecticide Ear Tags, Silosan, Sybol (U.S. EPA, 2001, 2006; WHO/FAO, 1983)

Usage

Pirimiphos-methyl is a fast-acting, broad spectrum organophosphate insecticide and acaricide used to control a wide variety of sucking and chewing pests in agricultural and horticultural applications. It is used in horticultural applications; to clean fruits and vegetables before harvest; to control pests on stored products; and to eradicate nuisance and disease vector insects, including mosquitoes, ants, beetles, bed-bugs, cockroaches, fleas, flies, lice, and mites (WHO/FAO, 1983, 1974). The intended uses of existing products include greenhouse applications, treatment of stored grain and seeds (corn and sorghum) intended for both human and animal consumption, and direct animal applications including incorporation into cattle eartags and sprays (U.S. EPA, 1999c, n.d.). Pirimiphos-methyl is used to control a large number of different insects including, but not limited to, cigarette beetles; confused flour beetles; corn sap beetles; flat grain

beetles; hairy fungus beetles; red flour beetles; sawtoothed beetles; granary weevils; maize weevils; merchant grain beetles; rice weevils; lesser grain borers; and angoumois grain moths, Indian meal moths, and almond moths on corn (seed and whole-grain), rice (whole-grain), wheat (whole-grain), and grain sorghum (seed and whole-grain); mealy bugs; mites (iris bulbs) horn flies and face flies (U.S. EPA, 2001). For malaria control, typical use includes the application of 1 or 2 g pirimiphos-methyl/m^3 of a 2–5 percent suspension to indoor walls and ceilings every 3 months. Ultra-low-volume (ULV) sprays and thermal fogs are additional application methods. To control DDT resistant fleas, a 2 percent dust is applied in rodent burrows. Pirimiphos-methyl is not recommended for use directly on humans or on processed foods (WHO/FAO, 1983; U.S. EPA, 1999c). Current registered uses in the United States include food and non-food uses. Food uses include use on sorghum, corn (gain and seed), nonlactating dairy cattle, beef/range/feeder cattle, and calves. Non-food uses include use on iris bulbs. No residential or public health uses are currently registered in the United States (U.S. EPA, 2001)

Formulations and Concentrations

There are several typical formulations for pirimiphos-methyl, each formulation varying in the amount of active ingredient (ai) it contains. The typical formulations for pirimiphos-methyl include (U.S. EPA, 1999c, 2001; WHO/FAO, 1983) the following:

- U.S. registered formulations: emulsifiable liquid concentrate (57 percent ai), treated ear tags (14 percent and 20 percent ai)
- For agricultural and horticultural uses: emulsifiable concentrate (250–500 g ai/L), ULV concentrate (500 g ai/L), encapsulated formulas (250–400 g ai/kg), dusts (10 and 20 g ai/kg), wettable powders (250 and 400 g ai/kg), fog (100 g ai/L), aerosol (20 g ai/L with pyrethroids), solvent free formulation (900 g ai/kg), smoke generator formulation
- For public health uses: emulsifiable concentrate (250 and 500 g ai/L), ULV concentrate (500 g ai/L), encapsulated formulation (200 g ai/L), dusts (10 and 20 g ai/kg), wettable powder (250 and 400 g ai/kg), fog (100 g ai/L), aerosol (20 g ai/L with pyrethroids), solvent-free formulation (900 g ai/kg), smoke generator formulation
- For household uses: emulsifiable concentrate (80 g ai/L), dusts and aerosols (with pyrethroids) for use in the home and garden.

Degradation Products

Stored pirimiphos-methyl products are broken down by hydrolysis of the phosphorus-ester side chain, which results primarily in the parent hydroxyl-pyrimidine (WHO/FAO, 1974). The main hydrolysis degradates at pH 5, 7, and 9 were 2 (diethylamino)-4-hydroxy-6-methyl pyrimidine and O-2-diethylamino-6-methylpyrimidin-4-yl o-methyl-phosphorothioate (U.S. EPA, 2001). In soil, the major metabolite is the parent hydroxypyrimidine (IV) together with smaller amounts of the related compounds (V) and

(VI). Compound (IV) is the major degradation product in water with only trace quantities of the P=0 analogue (III) detected (WHO/FAO, 1974).

In humans, pirimiphos-methyl is broken down into the degradation products desethyl pirimiphos-methyl and pirimiphos-methyloxon, which are also active and have transient stability (WHO/FAO, 1983). When pirimiphos-methyl is broken down in rats and dogs, the major urinary metabolite (30 percent of administered dose) was 2-ethylamino-4-hydroxy-6-methylpyrimidine. Other metabolites included 4-0(2-diethylamino-6-methylpyrimidinyl-ß-D-glucosiduronic acid (11 percent of dose in dogs), an unidentified phosphorus-containing product likely to be a dealkylated derivative of either pirimiphos-methyl or its oxygen analogue (12 percent of dose in rats), and 2-amino-4-hydroxy-6-methyl pyrimidine (8 percent of dose in rats and 5 percent of dose in dogs) (WHO/FAO, 1992).

Shelf Life

Under normal storage conditions at room temperature, pirimiphos-methyl is stable for up to 6 months. However, it decomposes in sunlight (WHO/FAO, 1983).

Environmental Behavior

Fate and Transport in Terrestrial Systems

Pirimiphos-methyl has limited mobility and persistence in soil (WHO/FAO, 1974). For a variety of soil types, pirimiphos-methyl has a half-life of less than one month (WHO/FAO, 1974). It hydrolyzes rapidly in acidic soils and is stable in neutral and alkaline environments with a half-life of 7.3 days at pH 5, 79 days at pH 7, and 54–62 days at pH 9 (U.S. EPA, 2001). Pirimiphos-methyl decomposes in sunlight (WHO/FAO, 1983).

Fate and Transport in Aquatic Systems

Pirimiphos-methyl is not expected to have a significant impact on water resources due to the lack of significant outdoor uses (U.S. EPA, 2001). It degrades in water mainly by hydrolysis, which is attenuated by sunlight. In sunlight, 50 percent degradation occurs within one day. Volatilization also occurs from still water; however, it is not as significant as hydrolysis (WHO/FAO, 1974).

Human Health Effects

Acute Exposure

Effects/Symptoms

Similar to other organophosphates, pirimiphos-methyl is a cholinesterase inhibitor and interferes with the normal functioning of the nervous system. It causes dose-related reversible decreases in plasma, red blood cell, and brain cholinesterase at very low doses by ingestion, dermal, and inhalation exposures. It is of relatively low acute oral, dermal, and inhalation toxicity (U.S. EPA, 1999b). In two human studies, volunteers were fed a

dose of 0.25 mg/kg/day for up to 56 days. Marginal plasma cholinesterase depression was observed after both dosing periods (U.S. EPA, 1998b, 2006). However, these studies have many deficiencies and should be used as supplemental data. When compared to animal data, they provide some evidence that humans may be more sensitive than animals as is indicated by the lower effect level for cholinesterase inhibition in humans (U.S. EPA, 1999b). No human poisonings from mishaps with pirimiphos-methyl have been reported (WHO/FAO, 1983).

Animal studies have shown that pirimiphos-methyl is only slightly toxic following acute oral and dermal exposures, with reported LD_{50} values in rats of >2,400 mg/kg (U.S. EPA, 1999a). Other reported oral LD_{50}s are as follows: rabbit (male) 1,154–2,300 mg/kg, mouse (male) 1,020–1,360 mg/kg, guinea pig (female) 1,000–2,000 mg/kg, dog (male) > 1,500 mg/kg, and cat (female) 575–1,150 mg/kg. The reported dermal LD_{50} is > 4,500 mg/kg in female rats (WHO/FAO, 1983), >4,050 mg/kg in female rabbits, and 2,200–4,050 mg/kg in male rabbits (U.S. EPA, 2001, 1999a, 1998a). The reported acute inhalation LC_{50} is > 4.7 mg/L for rats (U.S. EPA, 2001, 1999a, 1998a). Among mammals, no one species appears to be more susceptible. However, the hen is appears to be highly susceptible with a reported LD_{50} of 79–80 mg/kg (WHO/FAO, 1983). Clinical signs of exposure include neurotoxicity, excessive salivation, abnormal gait, ataxia, and leg paralysis. Dermal exposure also decreased plasma cholinesterase levels (WHO/FAO, 1983). Eye and skin irritation have been observed in rabbits (U.S. EPA 1999d, 1998b); however, pirimiphos-methyl has not been shown to be a dermal sensitizer in guinea pigs or rats (U.S. EPA, 1998b; WHO/FAO, 1983).

Treatment

Exposure to pirimiphos-methyl may be determined through laboratory tests of urine and blood that measure breakdown products of pirimiphos-methyl in urine or cholinesterase levels in blood. Blood levels of cholinesterase, especially in plasma, are the most useful in diagnosis of poisoning. However, neither urinary or blood tests are specific for pirimiphos-methyl exposure. Early symptoms of pirimiphos-methyl exposure include excessive sweating, headache, weakness, giddiness, nausea, vomiting, stomach pains, blurred vision, slurred speech, and muscle twitching. Symptoms of more severe poisoning may advance to convulsions, coma, loss of reflexes, and loss of sphincter control. Following dermal exposures, the person should stop working and any contaminated clothing should be removed. Exposed areas of skin should be washed with soap and water and flushed with large quantities of water. For oral exposures, vomiting should not be induced unless a potential lethal dose has been ingested and the person is conscious. Care should be taken as the vomitus may contain toxic amounts of the chemical. Once under medical care, potential lethal doses should be treated by rapid gastric lavage unless the patient is already vomiting. Any ocular exposure should be treated by washing with isotonic saline. If no respiratory insufficiency is noted, peripheral symptoms should be treated with 2–4 mg of atropine sulfate and 1,000–2,000 mg pralidoxime chloride or 250 mg toxogonin (adult dose) by slow intravenous injection. If

severe respiratory difficulties, convulsions, and unconsciousness are present, atropine and a reactivator should be given immediately. The airway should be maintained. Morphine, barbiturates, phenothiazine, tranquillizers, and central nervous system stimulants are all contraindicated (WHO/FAO, 1983).

Chronic Exposure

Noncancer Endpoints

Workers in two WHO-supervised health spray program did not show any signs of pesticide poisoning; however, at the end of one of the programs, plasma cholinesterase activity was 70–75 percent of the mean of pre-exposure values. The people living in the spray areas exhibited no signs of poisoning and no effect on cholinesterase activity. Volunteers exposed to 0.25 mg/kg/day for up to 56 days exhibited no toxic effects on liver function or blood tests and an acceptable daily intake (ADI) of 0.01 mg/kg was established (WHO/FAO, 1983).

Chronic exposure data in animals indicates that a main target of pirimiphos-methyl toxicity is the nervous system. Rats repeatedly exposed to high doses of pirimiphos-methyl showed a cumulative inhibitory effect on cholinesterase (WHO/FAO, 1983). In 90-day and 2-year dietary studies in rats, plasma cholinesterase and some erythrocyte and brain cholinesterase inhibition was reported. In a 2-year dog study and an 80-week mouse study, similar effects were observed (WHO/FAO, 1983).

In developmental and reproductive toxicity studies in rats and rabbits, maternal/parental NOELs were less than or the same as offspring NOELs. No increased sensitivity was noted in fetuses or pups. There is no evidence that pirimiphos-methyl is teratogenic in rat or rabbit feeding studies (U.S. EPA, 1998b, 2006; WHO/FAO, 1983). In several mammalian studies, no mutagenic potential was observed (U.S. EPA, 1998b; WHO/FAO, 1983).

Cancer Endpoints

EPA determined that the carcinogenic potential of pirimiphos-methyl could not be determined because a reliable rat carcinogenicity study is lacking (U.S. EPA, 1998b). In an 80-week mouse feeding study, a 78-week mouse feeding study, a 80-week mouse oral study, a 2-year rat feeding study, a 78-week rat feeding study, and a 2-year oral dog study, no evidence of carcinogenic potential was identified (WHO/FAO, 1983; U.S. EPA, 1998b, 2006). Additionally, mammalian mutagenicity studies do not provide any evidence that supports a carcinogenic potential for pirimiphos-methyl (WHO/FAO, 1983).

Toxicokinetics

Pirimiphos-methyl can be absorbed via the gastrointestinal tract, the skin, or, less commonly, by inhalation of fogs, smokes, or spray mists. It is rapidly metabolized and excreted. Pirimiphos-methyl is broken down into desethyl pirimiphos-methyl and

pirimiphos-methyloxon, which are also active and have transient stability. In rats dosed with radiolabeled pirimiphos-methyl, 70 percent was excreted within 24 hours and 100 percent was excreted within 5–6 days. Excretion was mainly in the urine (85 percent) and to a lesser extent, feces (15 percent). Pirimiphos methyl and its metabolites do not accumulate in the liver, kidneys, or fatty tissues of rats and domestic animals following oral exposure (WHO/FAO, 1983).

Ecological Effects

Acute Exposure

Pirimiphos-methyl is not expected to pose a hazard to birds and mammals from acute exposure, because of lack of exposure. In the laboratory, pirimiphos-methyl exhibits relatively high toxicity to birds (WHO/FAO, 1983). Acute oral LD_{50} values in various bird species include chickens (79–80 mg/kg), Japanese quail (140 mg/kg), and green finches (200–400 mg/kg). Dietary LD_{50}s of 630 mg/kg for mallard ducks and 206 mg/kg for bobwhite quail chicks were identified. No lasting adverse effect on hens; chicks; or egg production, quality, or hatchability was seen in studies of chickens fed 4–40 ppm in their diet (WHO/FAO, 1983).

When used for its registered purposes, pirimiphos-methyl is not expected to result in significant exposures of aquatic organisms (U.S. EPA, 2001). Additionally, any risk would be mitigated by its strong tendency to decompose in water and to undergo photo-oxidation (WHO/FAO, 1983). In static tests, the reported 48-hour LC_{50} was 1.4 mg/L in carp and 0.25 mg/L in rainbow trout. The 24-hour LC_{50} for carp was 1.6 mg/L. In flow-through tests, the reported 48-hour LC_{50} was 4.1 mg/L in fathead minnow and 0.53 mg/L in rainbow trout, while the 24-hour LC_{50} was 5.6 mg/L in fathead minnow and 0.78 mg/L in rainbow trout (WHO/FAO, 1983).

Chronic Exposure

Due to low risk of both terrestrial and aquatic acute ecological effects of pirimiphos-methyl, serious adverse effects are not anticipated from chronic exposures. Subchronic 90-day exposure of birds to oral doses of up to 10 mg/kg did not result in clinical or histopathological findings (WHO/FAO, 1983).

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Profile for Propoxur:

CAS Registry Number 114-26-1

Summary of Insecticide

Chemical History

Propoxur is a broad spectrum, nonsystemic carbamate insecticide that was first introduced in 1959. It is used by homeowners and pest control operators in both agricultural and nonagricultural applications to kill a variety of chewing and sucking pests, mosquitoes, ants, flies, cockroaches, hornets, crickets, and lawn and turf insects (U.S. EPA, 1997a, 2000; EXTOXNET, 1996). Propoxur (Baygon) was first registered in the United States for pesticide use in 1963 and currently there are two registered technical products, several manufacturing use only products, and 173 registered products containing propoxur (U.S. EPA, 1997b).

Propoxur exhibits its toxic effects through reversible cholinesterase inhibition (U.S. EPA, 2000). It has moderate toxicity in mammals (WHO/FAO, 1976), high toxicity in birds, and moderate toxicity in fish (EXTOXNET, 1996; U.S. EPA, 1997b). Short-term exposures may cause effects on the nervous system, liver, and kidneys (IPCS, 1994). In humans, symptoms of acute oral poisoning include red blood cell cholinesterase inhibition with mild transient cholinergic symptoms including nausea, vomiting, sweating, blurred vision, and tachycardia. Long-term inhalation exposures in humans results in cholinesterase inhibition, headaches, nausea, and vomiting (U.S. EPA, 2000). Propoxur pesticides are available as emulsifiable concentrates, wettable powders, dusts and powders, baits, aerosols, fumigants, granular baits, containerized baits, pest strips, shelf paper, pet flea collars, and oil sprays (EXTOXNET, 1996; U.S. EPA, 1997a). Applications methods include aerosol can and injection tube; concentrated liquid using a compressed air sprayer or hand or power sprayer; wettable powder using a ready-to-use sprayer liquid, a power or had pressurized sprayer, or a low pressure sprayer for oil soluble liquid (U.S. EPA, 1997b).

Description of Data Quality and Quantity

Extensive review data for propoxur are limited. Relevant resources include

- Propoxur: Registration Eligibility Decision (RED) Document (U.S. EPA, 1997b)
- IRIS summary review (U.S. EPA, 2006)
- Pesticide Information Profile for Propoxur (EXTOXNET, 1996)
- Data Sheet on Pesticides. No. 25: Propoxur (WHO/FAO, 1976)
- International Safety Cards: Propoxur (IPCS, 1994).

EPA has developed quantitative human health benchmarks (acute and chronic oral RfDs and short-, intermediate-, and long-term dermal and inhalation benchmarks) for propoxur.

Summary Table

Duration	Route	Benchmark Value	Units	Endpoint	Reference
Acute, Intermediate, Chronic	Inhalation	0.004	mg/kg/day	Inhalation NOEL (2.2 mg/m3) for neurological effects in rats, adjusted for intermittent exposure and UF of 100 applied	U.S. EPA (1997b)
Acute, Intermediate, Chronic	Oral	0.005	mg/kg/day	Chronic RfD based on LOEL in humans with UF of 30 applied	U.S. EPA (1997b)
Acute, Intermediate, Chronic	Dermal	10	mg/kg/day	Dermal NOAEL for toxicity in rabbits with UF of 100 applied	U.S. EPA (1997b)
Cancer	Inhalation, Oral, Dermal	0.0037	per mg/kg/day	Cancer slope factor based on male rat bladder tumors	U.S. EPA (1997b)

For inhalation exposure, a NOEL of 2.2 mg/m^3 (2.4 mg/kg/day)[19] was identified in rats exposed to propoxur (Pauluhn, 1992, 1994) via inhalation for 6.3 hours per day, 5 days per week for 2 years. Significant plasma, red blood cell, and brain cholinesterase inhibition were observed at higher concentrations (U.S. EPA, 1997b). The concentration was adjusted for intermittent exposure[20] (0.4 mg/kg/day) and an uncertainty factor of 100 was applied to account for interspecies and intrahuman variation, for an inhalation benchmark of 0.004 mg/kg/day. This value is appropriate for all exposure durations. However, the vapor pressure of propoxur is extremely low and significant human exposure via inhalation is not expected (U.S. EPA, 1997b).

For oral exposure, the chronic oral RfD of 0.005 mg/kg/day was calculated based on a LOEL of 0.15 mg/kg for a 40 percent red blood cell cholinesterase inhibition reported in a human exposure study (Vandekar et al., 1971) with an uncertainty factor of 30 applied to account for intrahuman variability (10) and the use of a LOEL (3) (U.S. EPA, 1997b). This value is appropriate for all exposure durations.

For dermal exposure, a NOEL of 1,000 mg/kg/day for lack of toxic effects in a subchronic rabbit study (Diesing and Flucke, 1989) is appropriate for all exposure

[19] Conversion between mg/m^3 and mg/kg/day assumes, for Wistar rats, an average body weight of 0.187 kg and inhalation rate of 0.2 m^3/day (U.S. EPA, 1988).

[20] Adjustment for intermittent exposure is the product of air concentration and exposure of 6.3/24 hours/day and 5/7 days/week.

durations (U.S. EPA, 1997b); an uncertainty factor of 100 was applied to account for interspecies and intrahuman variability. This value is appropriate for all exposure durations. However, studies indicate a very low absorption potential (<20 percent in humans) and/or hazard by the dermal exposure route (U.S. EPA, 1997b).

EPA classified propoxur as a Group B2 chemical, probable human carcinogen. EPA calculated a unit risk of 3.7×10^{-3} per mg/kg/day based on bladder tumors in male rats (U.S. EPA, 1997b).

Insecticide Background

CAS #:	114-26-1
Synonyms:	o-isopropoxyphenyl methylcarbamate (IUPAC); 2-(1-methylethoxy) phenyl methylcarbamate (CA) (WHO, 2005; U.S. EPA 1997b) 2-Isopropoxyphenyl methylcarbamate Phenol, 2-(1-methylethoxy)-,methylcarbamate, Phenol, o-isopropoxy-, methylcarbamate, Propoxur [Phenol, 2-(1-methylethoxy) -, methylcarbamate 2-(1-Methylethoxy)phenyl methylcarbamate PHC (PAN, 2005; IPCS, 1994)
Chemical Group:	carbamate (EXTOXNET, 1996; U.S. EPA 1997b)
Registered Trade Names:	Trade and other names for propoxur include: Arprocarb, Bay, Bay 9010, Bay 5122, Bay 9010, Baygon, Bayer 39007, Bifex, Blattanex, Blattosep, Brifur, Bolfo, BO Q 5812315, Chemagro 9010, Compound 39007 , Dalf dust , DMS 33, ENT 25671, Invisi-Gard, OMS 33, PHC (JMAF), Pillargon, Prentox Carbamate, Propogon, Proprotox, Propyon, Rhoden, Sendra, Sendran, Suncide, Tendex, Tugon, Fliegenkugel, UN Carbamate, Unden, and Undene (WHO, 2005; PAN, 2005; EXTOXNET, 1996; IPCS, 1994; WHO/FAO, 1976; IPCS, 1973)

Usage

Propoxur is a residual carbamate insecticide that has a variety of indoor uses, including the control of mosquitoes, ants, cockroaches, crickets, flies, bees, hornets, wasps, ticks, yellow jackets, bedbugs, fleas, woodlice, and spiders (U.S. EPA, 1997b; WHO, 2005; WHO/FAO, 1976). Indoor food applications include only crack and crevice treatment in food areas (U.S. EPA, 1997b). There are limited outdoor applications consisting mostly of perimeter and spot treatments of nests and lawn and turf insects (U.S. EPA, 1997b, 2000). Crop applications include sugar cane, cocoa, grapes, other fruit, maize, rice vegetables, cotton, lucerne, forestry, and ornamentals (WHO, 2005). Propoxur is used in the control of malaria and in pet flea collars (U.S. EPA, 2000). In public health and agricultural applications, propoxur is applied as a dust or by spraying (WHO, 2005). It is

available in commercial products as a single active ingredient or combined with other pesticides (U.S. EPA, 1997b).

Formulations and Concentrations

Common formulations of pesticides containing propoxur include technical grade propoxur, emulisfiable concentrates, wettable powders, baits, aerosols, fumigants, granules, and oil sprays (EXTOXNET, 1996). Typical formulations and percent propoxur content include ready-to-use liquid (0.5–1 percent), pressurized aerosol liquid (0.25–2 percent), oil-soluble liquid/liquid concentrate (8–19.6 percent propoxur), pastes (2 percent), wettable powders (70 percent), solid baits (0.25–2 percent), pet flea collars (impregnated plastic) (0.4–10 percent), impregnated shelf papers (1 percent), and insecticidal tapes (10 percent) (U.S. EPA, 1997b). Common formulations used for agricultural, horticultural, and forestry applications include wettable powders (50 percent), dusts (1–2 percent), granules, oils, emulsifiable concentrates (200 g/L; 20 percent w/w), pressurized sprays, smokes, baits (various concentrations) (WHO/FAO, 1976; IPCS, 1973).

WHO (2005) indicated that the propoxur content in various preparations should be declared and contain the following:

- Technical grade propoxur: not less than 980 g/kg
- Wettable Powder: 500 g/kg $\pm$ 5% of the declared content.

Shelf Life

Propoxur is reported to be stable under normal storage and use conditions (IPCS, 1973) but unstable in highly alkaline media. The half-life propoxur is reported as 40 minutes at pH 10 at 20^{o}C (WHO/FAO, 1976). WHO (2005) reported that following storage at 54 $\pm$ 2^{o}C for 14 days, 97 percent or greater of the active ingredient must be present in wettable powder formulations.

Degradation Products

In vivo, propoxur is biotransformed by depropylation to 2-hydroxyphenol-N-methylcarbamate and by hydrolysis to the phenol. The glucuronides detected in urine are accounted for by ring hydroxylation and isopropoxy hydroxylation followed by conjugation. Major metabolites in rats include 5-hydroxy-2-isopropoxyphenyl n-methylcarbamate, 2-hydroxyphenyl n-methylcarbamate, o-isopropoxyphenol, o-isopropoxyphenyl, and n-hydroxymethylcarbamate. In mice, the major metabolies include o-isopropoxyphenyl n-hydroxymethylcarbamate. In bean plants, the major metabolites include 4-hydroxy-2-isopropoxyphenyl n-methylcarbamate, 2-hydroxytphenyl n-methylcarbamate, and o-isopropoxyphenyl n-hydroxymethlycarbamate (HSDB, 2005). Limited human data are available. Many propoxur metabolites were found in the urine of a person attempting suicide by ingestion of a large quantity of the emulsifiable concentrate formulation. These were present both as free compound or

conjugated with glucuronide or sulfate. As in other species, biotransformation was from depropoxylation, hydrolysis of the ester bond and ring hydroxylation (IPCS, 1989).

Environmental Behavior

Fate and Transport in Terrestrial Systems

Propoxur is expected to be moderately to very highly mobile and moderately persistent in soil (HSDB, 2005; U.S. EPA, 1997a, 1997b; EXTOXNET, 1996). With a K_{oc} ranging from <1 to 103, high to very high mobility is expected if propoxur is released in soil (HSDB, 2005); however, the mobility depends on the soil type and previous exposures to propoxur. Biodegradation in soil is more rapid in previously exposed soils. In many soil types, propoxur is highly mobile due to its low affinity for soil binding (EXTOXNET, 1996; U.S. EPA, 1997a, 1997b). It evaporates from soil, with the amount increasing with the moisture content of the soil, and the half-life is 6–8 weeks, depending on the soil type (IPCS, 1973). Data from studies of the persistence of propoxur in several soil types suggest that it moves rapidly through all soil profiles below the 12 inch sampling depth. Its fate and transport characteristics are similar to those chemicals that are known to leach into groundwater (U.S. EPA, 1997b).

Hydrolysis appears to be the primary mode of degradation (U.S. EPA, 1997b). At neutral pH, propoxur is hydrolically stable but degrades rapidly at alkaline pH values (U.S. EPA, 1997b). Half-life values of a propoxur in aqueous solutions at 20^{o}C are reported to range from 1 minute at pH 12.8 to 40 minutes at pH 10.8 (IPCS, 1973). Half-life values of 16 days at pH 8, 1.6 days at pH 9, and 0.17 days at pH 10 are reported (U.S. EPA, 1997b). Volatilization is not expected to be a major fate process from moist soil surfaces (HSDB, 2005). The major fate process in moist soils is biodegradation. Under aerobic conditions, biodegradation half-lives of 80 days in silt loam soil and 120 days in sandy loam soil are reported (HSDB, 2005). On inert surfaces, however, volatilization is the main fate process. On a glass surface, 50 percent of a propoxur residue was still present 1.8 hours after application (IPCS, 1973). Propoxur in soil shows no or little susceptibility to photolysis (U.S. EPA, 1997b; IPCS, 1973). Half-lives of several months were reported for the degradation of propoxur under aerobic and anaerobic conditions (U.S. EPA, 1997b).

Fate and Transport in Aquatic Systems

Propoxur is highly soluble in water and there is a high likelihood of groundwater penetration because it does not adsorb strongly to soil particles (HSDB, 2005; EXTOXNET, 1996; U.S. EPA, 1997a). It is relatively stable in water at pH 7 or less but hydrolyzes rapidly at pHs greater than 7 (IPCS, 1973). In a 1 percent aqueous solution at pH 7, propoxur hydrolyzes at a rate of 1.5 percent per day (EXTOXNET, 1996). Reported field half-lives for propoxur are 14–50 days (EXTOXNET, 1996). The hydrolysis half-life of propoxur is reported to be 1 year at pH 4, 93 days at pH 7, and 30 hours at pH 9 (HSDB, 2005). Volatilization from water is not expected to be a major fate process. However, propoxur is susceptible to photolysis in water (U.S. EPA, 1997b). The

half-life of propoxur irradiated with light more than 290 nm is reported as 88 hours (HSDB, 2005). Because propoxur degrades rapidly in water, bioconcentration in fish is unlikely (HSDB, 2005).

Human Health Effects

Acute Exposure

Effects/Symptoms

Propoxur causes its toxic effects by reversible inhibition of cholinesterase. Short-term exposures may cause effects on the nervous system, liver, and kidneys (IPCS, 1994). In humans, symptoms of acute oral poisoning include red blood cell cholinesterase inhibition with mild transient cholinergic symptoms including nausea, vomiting, sweating, blurred vision, and tachycardia (U.S. EPA, 2000). Limited data exist on the human health effects of acute exposure to propoxur. In volunteers, a single oral dose was reported to cause stomach discomfort, sweating, and redness of the face. However transient erythrocyte cholinesterase activity inhibition (up to 27 percent) was observed at a higher level and was associated with vomiting, sweating, and blurred vision (WHO/FAO, 1976). When used to control for malaria, spray operators experienced occasional short-lasting symptoms including nausea, headache, sweating, and weakness from which they quickly recovered (WHO/FAO, 1976; EXTOXNET, 1996). Additionally, some mild reactions were reported by residents where it was applied (WHO/FAO, 1976).

In animals, propoxur is acutely toxic via the oral, inhalation, and dermal routes (U.S. EPA 1997b, 2000; EXTOXNET 1996). Acute inhalation and dermal exposures are moderate to highly toxic while oral exposures are highly to be extremely toxic (U.S. EPA, 1997a, 2000). Propoxur is highly toxic to animals via ingestion. In rats, the oral LD_{50} for propoxur ranges from 68 mg/kg in females to 116 mg/kg in males (EXTOXNET, 1996; WHO/FAO, 1976; U.S. EPA, 1997b). In other species, reported oral LD_{50} values include approximately 100 mg/kg in mice and 40 mg/kg in guinea pigs (EXTOXNET, 1996). Reported dietary levels causing no toxic effects in animals include 300mg/kg/day for mice, 10 mg/kg/day for rats, and 5 mg/kg/day for dogs (IPCS, 1989). Via the dermal route, the reported LD_{50} values in various species include greater than 2,400 mg/kg in rats (EXTOXNET, 1996; WHO/FAO, 1976) and 500 mg/kg to > 2000 mg/kg in rabbits (EXTOXNET, 1996; U.S. EPA, 1997b). Via inhalation, the reported LC_{50} values include a 4-hour LC_{50} of >0.5 mg/L in rats (U.S. EPA, 1997b) and a 1-hour LC_{50} of > 1.44 mg/L (EXTOXNET, 1996).

Similar to its effects in humans, acute exposure to propoxur in animals causes symptoms typical of cholinesterase inhibition (EXTOXNET, 1996; U.S. EPA, 1997b). Cholinesterase depression, muscle spasms, and salivation have been reported within 10 minutes of oral administration in rats (U.S. EPA, 1997b). In rats fed propoxur in their diet for 16 weeks, whole blood cholinesterase was inhibited at dietary levels over 500 ppm while plasma, whole blood, and brain cholinesterase were inhibited at dietary levels

greater than 1,000 ppm at study termination. Signs of cholinesterase inhibition were also observed in both rats and mice within 15 minutes of exposure to different concentrations of propoxur aerosol (WHO/FAO, 1976). Brain pattern and learning ability changes can occur at lower concentrations than those that cause cholinesterase inhibition and/or organ weight changes (EXTOXNET, 1996).

Although propoxur is a mild eye irritant in rabbits, it is not a skin irritant in rabbits or a dermal sensitizer in guinea pigs (U.S. EPA, 1997b). Acute exposure to propoxur is not considered to be teratogenic in rats (WHO/FAO, 1976).

Treatment

Exposure to propoxur may be determined through laboratory tests that determine cholinesterase levels in blood with erythrocyte cholinesterase being a more informative indicator than either plasma or whole blood. However, the enzyme will only be inhibited for a few hours following exposure. Additionally, phenol metabolites may be determined in urine (WHO/FAO, 1976; U.S. EPA, 2000). However, neither of these tests are reliable indicators of total exposure because they are not specific for propoxur (U.S. EPA, 2000).

Propoxur poisoning should be treated by first removing any contaminated clothing, and washing affected skin with soap and water and flushing the area with large amounts of water (WHO/FAO, 1976; IPCS, 1994). If propoxur gets in the eyes, they should be rinsed immediately with isotonic saline or water. Contact lenses should be removed, if possible. Oral exposure to propoxur should be treated by administration of activated charcoal (HSDB, 2005; IPCS, 1994). Rapid gastric lavage with 5 percent sodium bicarbonate is indicated if the patient is not already vomiting. Medical attention should be sought (WHO/FAO, 1976; HSDB, 2005). Inhalation exposures should be treated by removal to fresh air, placing in a half-upright position, monitoring for respiratory distress, and seeking medical attention (HSDB, 2005; IPCS, 1994). Because propoxur is quickly metabolized and symptoms are of a short duration, atropine treatment is not usually necessary by the time the patient reaches medical help (WHO/FAO, 1976). However, adults showing signs of propoxur toxicity should be treated with 1–2 mg atropine sulfate given intramuscularly or intravenously as needed. Oxygen may be necessary for unconscious patients or those in respiratory distress. Pralidoxime is usually not necessary unless the poisoning is severe. Barbiturate and central stimulants are contraindicated (HSDB, 2005; WHO/FAO, 1976).

Chronic Exposure

Noncancer Endpoints

Limited data are available on the effects of chronic exposure to propoxur in humans. Chronic effects are expected to be similar to acute effects (EXTOXNET, 1996). Cholinesterase inhibition, headaches, vomiting, and nausea were reported in humans following chronic inhalation exposure (U.S. EPA, 2000). When used to control for malaria, spray operators experienced occasional short lasting symptoms including nausea,

headache, seating, and weakness from which they quickly recovered (WHO/FAO, 1976). No data are available on human reproductive or developmental effects (U.S. EPA, 2000).

In animals, propoxur is quickly detoxified and does not accumulate in body tissues over time. Daily doses approximating the LD_{50} have been tolerated by rats for long periods of time when the dose was given over the course of the day (EXTOXNET, 1996; WHO/FAO, 1976). Chronic oral exposure to propoxur in animals has been reported to cause cholinesterase inhibition, decreased body weight, liver and bladder effects, and a small increase in neuropathy (U.S. EPA, 1997b, 2000; WHO/FAO, 1976). Significant plasma, red blood cell, and brain cholinesterase inhibition was observed in male and female rats exposed to propoxur in air over a 2-year period (U.S. EPA, 1997b).

The nervous system and liver are the main organs affected by propoxur in both humans and animals (EXTOXNET, 1996). Increased liver weights were observed in rats fed propoxur in feed for 2 years (WHO/FAO, 1976). Reproductive and developmental effects have not been reported in rabbits orally exposed to propoxur. However, some fetotoxicity, decreased litter size, central nervous system impairment in offspring, and decreased fetal weights have been reported in rats orally exposed to propoxur (U.S. EPA, 1997b, 2000; WHO/FAO 1976). The data indicate that reproductive effects in humans are not expected at typical exposure levels and teratogenic effects will occur only at high levels (EXTOXNET, 1996). The available data indicate that propoxur is not mutagenic (EXTOXNET, 1996; U.S. EPA, 1997a).

Cancer Endpoints

EPA's OPP has classified propoxur as Group B2, probable human carcinogen, with a unit risk of 3.7×10^{-3} per mg/kg/day (U.S. EPA, 1997a, 1997b). No information is available on the carcinogenicity of propoxur in humans (U.S. EPA, 2000). A significant increase in bladder papillomas and/or carcinomas was reported in male rats while a significant increase in hepatocellular adenomas and combined adenoma/carcinoma was reported in male mice (U.S. EPA, 1997b, 2000). High dose exposure to propoxur is also associated with an increase in tumors of the uterus (U.S. EPA, 2000).

Toxicokinetics

Like most carbamates, propoxur can be absorbed through the oral, inhalation, and dermal pathways (HSDB, 2005; IPCS, 1994; WHO/FAO, 1976). It is readily absorbed by the lungs (HSDB, 2005) and gastrointestinal tract (IPCS, 1994) but to a lesser extent through the skin (WHO/FAO, 1976). Dermal rat studies indicate that absorption decreases with dose in a nonlinear way. Absorption of a dermal dose of 6.91 $\mu g/cm^2$ was 7.88, 10.2, 17.9, 23.2 and 32.5 percent for durations of 0.5, 1, 2, 4, 8, and 32 hours, respectively, which was a higher rate of absorption than in human studies of 8 and 24 hour exposures. Human studies indicate that the rate of 19.6 percent absorption most closely approximates the rate expected in the field (U.S. EPA, 1997b). Approximately 16 percent of the dose of radiolabeled propoxur applied to the forearms of volunteers was available

for percutaneous absorption (HSDB, 2005). Additionally, the rate of dermal absorption is affected by the solvent used (U.S. EPA, 1997b).

Propoxur and its metabolites are distributed by the lymph system. Metabolism studies in rats exposed to radiolabeled propoxur have shown radioactivity in all organs (especially the intestines) except bones at 1 hour. High concentrations of radioactivity were still present in the gastrointestinal tract, bladder, and mucous membranes of the pharyngeal system after 24 hours. Some radioactivity was still present in the liver, kidneys, and mucous membranes of the pharyngeal region at 48 and 72 hours (U.S. EPA, 1997b). Peak concentrations were seen in the blood (at 15 minutes), brain (1 hour), liver (4 hours), and kidneys (6 hours) after oral exposure to 50 mg/kg propoxur, with the highest concentrations seen in the kidneys and the lowest concentration in the brain (HSDB, 2005). Ingested propoxur is rapidly absorbed, broken down, and excreted in the urine (EXTOXNET, 1996; U.S. EPA 1997b). The major routes of metabolism in rats are depropylation to 2-hydroxyphenyl-N-Methylcarbamate and hydrolysis to isopropoxyl phenyl. Peak circulating and tissue concentrations of isopropxyl phenol were achieved 30–60 minutes after a single oral dose in rats (HSDB, 2005). Because of its rapid metabolism and excretion, propoxur does not accumulate in mammalian tissues (EXTOXNET, 1996). The main route of excretion for propoxur is probably the urine (WHO/FAO, 1976) accounting for 60–95 percent of the dose (HSDB, 2005). In humans, 38 percent of a single oral dose of Baygon was excreted in the urine within the first 24 hours. Of that, most was excreted by the first 8–10 hours (EXTOXNET, 1996). In dermal studies in humans, total excretion was 19.6 percent of the total dermal dose (U.S. EPA, 1997b). Lesser amounts of propoxur are excreted as carbon dioxide (20–26 percent) and in feces (4 percent) (HSDB, 2005).

Ecological Effects

Acute Exposure

Acute exposure to technical grade propoxur is very highly toxic to many bird species (EXTOXNET, 1996; U.S. EPA, 1997b). Remarkable variation in the results of dietary studies of the toxicity of propoxur has been reported. Oral LD_{50} values for 97 percent ai in a 2 percent bait product range from 4.2 mg ai/kg body weight in mourning doves to 120 mg ai/kg body weight in sharp-tailed grouse (U.S. EPA, 1997b; EXTOXNET, 1996). An unexplained phenomenon where, in some instances, birds of a given species are able to metabolize propoxur has been reported. U.S. EPA (1997b) indicated more confidences in the LD_{50} values for Mallard ducks (9.44 mg ai/kg) and Bobwhite quail (1,005 mg ai/kg formulated product). In the diet, subacute 5-day LC_{50} values range from 206 ppm in Northern bobwhite quail exposed to an unknown concentration to greater than 5,000 ppm in Mallard ducks exposed to 98.8 percent ai and Japanese quail exposed to an unknown concentration (U.S. EPA, 1997b). The reported oral LD_{50} in mule deer is 100–350 mg/kg (EXTOXNET, 1996). Additionally, propoxur has been found to be highly toxic to honeybees (EXTOXNET, 1996).

Propoxur is expected to pose a minimal risk to aquatic organisms because of its limited outdoor bait use (U.S. EPA, 1997b). However, when exposures occur, they pose a slight to moderate acute risks to fish and other aquatic species (EXTOXNET, 1996). In freshwater fish, propoxur is moderately toxic with LC_{50} values ranging from >1–10 ppm (U.S. EPA, 1997b). The reported 96-hour LC_{50} values range from 3.7 ppm in rainbow trout exposed to 98.8 percent ai to 25 ppm in fathead minnow exposed to 88 percent ai (U.S. EPA, 1997b; EXTOXNET, 1996). The 96-hour LC_{50} for bluegill sunfish was reported as of 6.6 mg/L (EXTOXNET, 1996).

Propoxur is more toxic in freshwater and estuarine invertebrates. Acute exposure to technical grade propoxur is very highly toxic to freshwater and estuarine invertebrates with EC/LC_{50} values of 0.011 ppm in daphnids, 0.034 ppm in amphipods, 0.18 ppm in stonefly, and 0.041 ppm in pink shrimp (U.S. EPA, 1997b). An oral LD_{50} of 595 mg/kg was reported for propoxur in bullfrogs (EXTOXNET, 1996).

Chronic Exposure

Very little data exist for chronic exposure to propoxur in non-target terrestrial organisms. In birds, no reproductive effects were seen in Northern bobwhite quail fed diets containing greater than 320 ppm (98 percent ai) of propoxur for a number of weeks. No effects on brain cholinesterase were seen at concentrations up to 80 ppm. In Mallard ducks, no reproductive or brain cholinesterase effects were seen in birds fed diets containing 80 ppm (98 percent ai) for 23 weeks. However, reduced egg production and embryo survival were noted at 320 ppm (U.S. EPA, 1997b). Little or no data exist for chronic exposure to propoxur in marine/estuarine organisms. However, no significant accumulation of propoxur is expected in aquatic organisms (EXTOXNET, 1996).

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Profile for Temephos:

CAS Registry Number 3383-96-8

Summary

Chemical History

Temephos is a nonsystemic organophosphate insecticide used in the United States since 1965 for public health reasons (U.S. EPA, 1999b, 2000) to control mosquito, midge, and black fly larvae (EXTOXNET, 1996). It is also used occasionally to treat potable water. Temephos has a low toxicity in mammals, moderate toxicity in birds, and high toxicity in some aquatic organism (HSDB, 2005). All food tolerances for temephos have been revoked (U.S. EPA, 2000). Temephos is available in emulsifiable concentrates (up to 50 percent), wettable powder (50 percent), and granular forms (up to 5 percent) (EXTOXNET, 1996). Because temephos is used primarily as a larvicide to treat bodies of water, the potential for incidental dermal or soil/dust exposure during this usage is minimal (HSDB, 2005). Occupationally exposed workers are the only population with potential elevated risk for temephos exposure due to its limited use pattern and lack of residential, dietary, and drinking water exposures (U.S. EPA, 1999b, 2000; ATSDR, 2005). Although human populations could potentially be exposed to very low levels from potable water that has been treated continually with temephos, little concern exits due to its low toxicity and solubility (ATSDR, 2005).

Description of Data Quality and Quantity

Because temephos is a new larvicide and has a limited use pattern, extensive review data do not exist. Relevant resources include

- Toxicologic Information About Insecticides Used For Eradicating Mosquitoes (West Nile Virus Control): Temephos (ATSDR, 2005)
- Reregistration Eligibility Decision (RED) Document (U.S. EPA, 2000)
- Pesticide Information Profile for Temephos (EXTOXNET, 1996)
- Specifications and Evaluations for Public Health Pesticides for Temephos (WHO, 1999).

EPA has developed quantitative human health benchmarks (intermediate and chronic oral RfDs and short-, intermediate-, and long-term dermal and inhalation benchmarks) for temephos.

Summary Table

Duration	Route	Benchmark Value	Units	Endpoint	Reference
Acute, Intermediate, Chronic	Inhalation	0.003	mg/kg/day	Oral NOEL for neurological effects in rats with UF of 100 applied; assume 100% absorption	U.S. EPA (2000)
Acute	Oral	0.2	mg/kg/day	Adopt intermediate RfD for acute duration	
Intermediate	Oral	0.2	mg/kg/day	Intermediate RfD based on NOAEL in rats with UF of 100 applied	U.S. EPA (1997)
Chronic	Oral	0.02	mg/kg/day	Chronic RfD based on NOAEL in rats with UF of 1000 applied	U.S. EPA (1997)
Acute, Intermediate, Chronic	Dermal	0.003	mg/kg/day	Oral NOEL for neurological effects in rats with UF of 100 applied; assume 38% absorption	U.S. EPA (2000)

For inhalation and dermal exposure, a NOEL of 0.3 mg/kg/day was identified for neurological effects (inhibition of red blood cell [RBC] cholinesterase) in rats fed temephos for 90 days and an uncertainty factor of 100 was applied. This value is appropriate for inhalation and dermal exposures and all exposure durations (U.S. EPA, 2000).

For oral exposure, intermediate and chronic oral RfDs of 0.02 and 0.2 mg/kg/day, respectively, were based on a NOAEL of 200 ppm in rats exposed to 200 ppm in the diet, with uncertainty factors of 100 and 1,000, respectively, applied (U.S. EPA, 1997). The intermediate-duration RfD was adopted to represent acute exposures.

Insecticide Background

CAS #:	3383-96-8
Synonyms:	Phosphorothioic acid, O,O'-(thiodi-4,1-phenylene) bis (O,O'-dimethyl) phosphorothioate; Phosphoric acid, O,O'-(thiodi,1,4-phenylene) O,O,O',O'-tetramethyl ester (U.S. EPA, 2000)
Chemical Group:	organophosphate (EXTOXNET, 1996)
Registered Trade Names:	Compounds containing temephos: Abat, Abate, Abathion, Acibate, Biothion, Bithion, Difennthos, Ecopro, Nimitox, and Swebate (EXTOXNET, 1996)

Usage

Temephos is an organophosphate insecticide that is used to control mosquito larvae. It is used in standing water, shallow ponds, swamps, marshes, intertidal zones, tire piles, and highly polluted waters. There are no registered residential uses for temephos (U.S. EPA, 1999b, 2000). Temephos may also be found in mixed insecticidal formulations such as trichlorfon (EXTOXNET, 1996). U.S. EPA (2000) has reported the use rates for temephos. Granular temephos may be applied at a maximum of 0.5 lbs/ai (active ingredient) per acre. The typical application of temephos in granular form ranges from 0.1–3 lbs/ai/acre. To treat tire piles, the granular application rate is 0.05 lbs/ai/100 ft^2. As an emulsifiable concentrate, temephos may be applied at a maximum of 1.5 fl. oz/acre (0.0469 lbs/ai/acre). The typical application of temephos in the emulsifiable form is 0.5–1.0 fl. oz/acre (0.0156–0.0313 lbs/ai/acre) (U.S. EPA, 1999b, 2000).

Formulations and Concentrations

Temephos is available in emulsifiable concentrates (up to 50 percent), wettable powder (50 percent), and granular forms (up to 5 percent) (EXTOXNET, 1996; U.S. EPA, 1999b, 2000). It is most commonly applied from airplanes and helicopters. Other application methods include backpack power blowers and right-of-way sprayers, horn blowers, belly grinders, and spoons (U.S. EPA, 1999b, 2000). WHO (1999) indicated that the temephos content in the various preparations should be declared and contain the following:

- Technical grade temephos: no less than 800 g/kg
- Emulsifiable concentrate: 250–500 g/kg +/- 10% of the declared content or above 500 g/kg +/- 25 g/kg
- Emulsifiable concentrate for simulium control: 200 g/kg +/- 10 g/kg
- Sand granules:10 g/kg +/- 25% of the declared content.

Shelf Life

Temephos is reported to be stable indefinitely at room temperature (HSDB, 2005); however, no supporting data on its shelf-life could be located.

Degradation Products

In water, temephos degrades slowly, forming degradation products from the sulfide group and the phosphate group through oxidation and hydrolysis, respectively. Hydrolysis occurs in basic or highly acidic water, and temephos is stable in water at pH 5-7. Hydrolysis degradation products include 4,4-thiodiphenol. Photolysis of temephos in methanol through sunlight exposures produces sulfone. A similar reaction may also occur in waters exposed to sunlight. Biodegradation does not occur (HSDB, 2005). Temephos breaks down when heated or burned. Toxic fumes such as phosphorous oxides and sulfur oxides are produced during this process. Temephos reacts strongly with acids and bases (IPCS, 2005).

Environmental Behavior

Fate and Transport in Terrestrial Systems

Based on temephos' very low water solubility and its high affinity for soil, the estimated half-life in soil is around 30 days (EXTOXNET, 1996). The affinity of temephos to soil also suggests that temephos is not extremely mobile in the soil (U.S. EPA, 1999b, 2000). Its very low vapor pressure suggests that it will not significantly volatilize from soil or sediments under most conditions. However, the breakdown products of temephos (temephos sulfoxide, temephos sulfone, temephos sulfide, and sulfone phenols) are more likely to migrate to and remain in water since they do not bind as strongly to soil. In field studies of sediments, temephos was shown to absorb rapidly to organic media and degrade rapidly to low or undetectable concentrations (U.S. EPA, 1999b, 2000). The breakdown of temephos in plants is very slow (EXTOXNET, 1996).

Fate and Transport in Aquatic Systems

Temephos is applied to aquatic environments where mosquitoes breed. It has a low water solubility and a low persistence in water. Several studies found that temephos rapidly degrades in natural waters (ATSDR, 2005; U.S. EPA, 1999b, 2000; EXTOXNET, 1996). Microorganisms and exposure to sunlight are the main ways that temephos degrades and dissipates in water, however, in their absence, temephos does not dissipate significantly (U.S. EPA, 1999b, 2000; EXTOXNET, 1996). In water, temephos would take a very long time to volatilize, as indicated by its very low Henry's law constant, suggesting that it would instead partition to sediment or soil. Hydrolysis is expected within a few days in highly basic or acidic conditions, but temephos is expected to persist longer at pH 5–7 (ATSDR, 2005). Temephos is not likely to reach ground water that would be used for drinking water due to its relatively short half-life in natural waters and the lack of mobility in soil. Because temephos binds to fatty substances, it can bioconcentrate in fish (U.S. EPA, 2000).

Human Health Effects

Acute Exposure

Effects/Symptoms

Temephos causes its toxic effects by the inhibition of cholinesterase. Typical acute toxicity signs are eye irritation, blurred vision, dizziness, nausea, diarrhea, salivation, headaches, loss of muscle coordination, tremors, and difficulty breathing (EXTOXNET, 1996; U.S. EPA, 1999a, 2000; NIOSH, 2004). Compared to other organophosphates, temephos is of low to moderate toxicity (U.S. EPA, 2000). It is moderately toxic through acute dermal and oral exposures and has low toxicity through inhalation exposure (U.S. EPA, 2000). Few studies exist on the human health effects of acute exposure to temephos, presumably due to its low toxicity in humans (ATSDR, 2005). Human volunteers who ingested 256 mg/day for 5 days or 64 mg/day for 4 weeks exhibited no plasma or erythrocyte cholinesterase inhibition (ATSDR, 2005).

In animals, the target organs of acute temephos exposure are the nervous system and liver (EXTOXNET, 1996). Oral LD_{50} values in various animal species include 400–1,300 mg/kg in rats, 400-4,700 mg/kg in mice (EXTOXNET, 1996), and 5,000 mg/kg in cats and dogs (2 percent powder formulation) (EXTOXNET, 1996). In rabbits, a dermal LD_{50} of 1,850 mg/kg in males or 970 mg/kg in females is reported. Similar to its effects in humans, acute high dose exposure to temephos causes neurological effects in animals due to cholinesterase inhibition (U.S. EPA, 1999a, 2000). Effects of cholinesterase inhibition are generally at exposures of 10 mg/kg/day, with liver and other effects seen at higher exposures. However, a few studies have seen cholinesterase effects as low as 1 mg/kg/day (ATSDR, 2005). Although temephos causes slight eye irritation in animals, no skin irritation or dermal sensitization were observed (U.S. EPA, 1999a, 2000). Acute exposures to temephos are not considered to be reproductive or developmentally toxic (U.S. EPA, 1999a, 2000).

Treatment

Exposure to temephos may be determined through laboratory tests to determine cholinesterase levels in blood (WHO/FAO, 1978). Oral exposure to temephos should be treated by rinsing out the mouth and seeking immediate medical attention. For dermal exposures, any contaminated clothing should be removed and the exposed area should be rinsed and then washed with soap and water. Medical attention should be sought. If temephos gets in the eyes, they should be rinsed immediately with copious amounts of water for several minutes. Contact lenses should be removed if possible and medical attention should be sought. Inhalation exposures require removal to fresh air and rest. Artificial respiration should be performed if the person stops breathing, and medical attention should then be sought immediately (IPCS, 2005; NIOSH, 2004).

Chronic Exposure

Noncancer Endpoints

The effects of chronic exposure to temephos in humans have not been well described in the literature, although it is not expected to be toxic at the levels applied to control for mosquitoes. No effects on cholinesterase (plasma or erythrocyte) levels were also seen in residents of a community exposed to < 1 ppm temephos in their water supply for 19 months. Application of 2 percent temephos powder to human subjects and their bedding was deemed safe and effective (ATSDR, 2005).

Chronic-duration exposure studies in animals have shown that temephos can inhibit cholinesterase levels, with symptoms of poisoning occurring at higher levels. A slight decrease in blood and brain cholinesterase activity was seen in dogs chronically exposed to 3–4 mg/kg/day, while severe effects were seen at 14 mg/kg/day. Decreased liver weights were seen in rats fed small doses of temephos for more than 2 years, and rabbits had minor pathological liver changes at 10 mg/kg/day. Temephos is not expected to cause reproductive, teratogenic or mutagenic effects (EXTOXNET, 1996).

Cancer Endpoints

EPA has not classified temephos as a carcinogen (U.S. EPA, 2000). No data exist on the carcinogenic effect of temephos in humans. The existing data suggest that temephos is not carcinogenic. No tumors were reported in rats fed diets containing up to 15 mg/kg/day for 2 years (U.S. EPA, 1999a, 2000).

Toxicokinetics

Temephos can be absorbed through the oral, dermal, and inhalation pathways, with dermal exposure being the most likely and typical (EXTOXNET, 1996). However, in rats, only 38 percent of dermally applied temephos was absorbed (U.S. EPA, 2000). Oral studies in rats have shown that peak bloodstream concentration after a single oral dose of temephos was reached between 5 and 8 hours post-administration, with a half-life of 10 hours. In mammals, most temephos leaves the body unchanged in urine and feces, with only some breakdown products detected (sulfate ester and glucoside conjugates of phenolic hydrolysis) (ATSDR, 2005; EXTOXNET, 1996; WHO/FAO, 1978).

Ecological Effects

Acute Exposure

Temephos is not expected to have a direct effect on terrestrial animals, because it is applied to water so exposures are expected to be low (U.S. EPA, 1999b, 2000). However, it is toxic to nontarget terrestrial organisms such as birds. In birds, temephos may be highly toxic to some species while only moderately toxic to others. The LD_{50}s temephos ranges from 18.9 to 240 mg/kg in California quail and chucker partridge, respectively. However, no significant changes in reproduction were observed in mallard ducks fed diets that contained moderate amounts of temephos (EXTOXNET, 1996). Temephos has been found to be extremely toxic to bees. The direct contact LC_{50} is 1.55 µg/bee (EXTOXNET, 1996).

Temephos is used in shallow water as a larvicide. It has shown a range of toxicity in the aquatic environment depending on its formulation with the emulsifiable concentrate and wettable powders being the most toxic (EXTOXNET, 1996). In fish, temephos has been shown to be slightly to moderately toxic to a variety of species. The most sensitive were the rainbow trout, with an LD_{50} range of 0.16 to 3.49 mg/L. The 96-hour LD_{50} values for the emulsifiable concentrate in various other fish species range from 0.35 mg/L in coho salmon to 6.7 mg/L in Atlantic salmon. The 96-hour LD_{50} values for technical grade temephos in various fish species range from > 10 mg/L in channel catfish to 21.8 mg/L in bluegill sunfish (U.S. EPA, 1999b, 2000).

Temephos is a hydrophobic chemical, so it is more likely to bind to fatty substances; as a result, temephos has the potential to bioconcentrate (U.S. EPA, 1999b, 2000). Some data indicate that there was some bioaccumulation in fish after 20 days of exposure, but temephos was no longer detected 14 days after exposure ended (U.S. EPA, 1999b, 2000).

In aquatic invertebrates, temephos is highly to very highly toxic. This is not surprising because it is an insecticide used to control aquatic larval stages of mosquitoes and other pests. One laboratory study using a 5 percent granular temephos formulation indicated that the emulsifiable concentrate is much more toxic to marine/estuarine aquatic invertebrates than granular formulations (U.S. EPA, 1999b, 2000). The 96-hour LC_{50} values for some freshwater invertebrates include 0.08 mg/kg for Gamma lacustris and 0.01–0.03 mg/kg for stoneflies. One commercial temephos formulation (Abate4E; 46 percent emulsifiable concentrate) is very toxic to saltwater invertebrates, including pink shrimp and oysters. The LC_{50} values for those species are 0.0005 and 0.019 mg/L, respectively. This formulation is not toxic to bull frogs (EXTOXNET, 1996).

Chronic Exposure

Very little data exist for chronic exposure to temephos in nonterrestrial target organisms. Currently, no data exist for potential chronic effects in waterfowl or birds exposed via food. The data that do exist indicate there is little impact (U.S. EPA, 1999b, 2000).

Little data exist for chronic exposure to temephos in marine/estuarine organisms. However, because temephos may be replied repeatedly to water, the chronic exposure of fish is of potential concern. Studies have shown that no chronic effects were seen in fish following 10 applications of a commercial temephos formulation (granular Abate® 2G). Another study showed growth retardation in fish following the application of the liquid Abate® 4E formulation (U.S. EPA, 1999b).

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Annex F: Pathways by Chemical and Intervention

Table F-1. Pathways by Chemical and Practice

Process	Pathway	Receptor	Alpha-cypermethrin	Bendiocarb	Bifenthrin	Cyfluthrin	DDT	Deltamethrin	Etofenprox	Fenitrothion	Lambda-cyhalothrin	Malathion	Methoprene	Permethrin	Pirimiphos-methyl	Propoxur	Temephos
Preparing																	
Mixing	Inhalation Dermal	Worker/ Resident	●	●	●	●	●	●	●	●	●	●	○	●	●	●	○
Mixing, splashing/ spillage, soil	Ingestion	Resident	○	○	○	○	○	○	○	○	○	○	○	○	○	○	○
Indoor Residual Spraying																	
Spraying	Inhalation	Worker	●	●	●	●	●	●	●	●	●	●	NA	NA	●	●	NA
Spraying, deposition to food	Ingestion	Resident	●	●	●	●	●	●	●	●	●	●	NA	NA	●	●	NA
Spraying, deposition to furniture	Dermal	Resident	○	○	○	○	○	○	○	○	○	○	NA	NA	○	○	NA
Spraying, application to walls	Dermal	Resident	●	●	●	●	●	●	●	●	●	●	NA	NA	●	●	NA
Leakage, spillage onto floor	Dermal	Worker	○	○	○	○	○	○	○	○	○	○	NA	NA	○	○	NA

Process	Pathway	Receptor	Alpha-cypermethrin	Bendiocarb	Bifenthrin	Cyfluthrin	DDT	Deltamethrin	Etofenprox	Fenitrothion	Lambda-cyhalothrin	Malathion	Methoprene	Permethrin	Pirimiphos-methyl	Propoxur	Temephos
Insecticide-Treated Nets																	
Treating nets	Dermal	Resident	●	NA	NA	●	NA	●	●	NA	●	NA	NA	●	NA	NA	NA
Normal use of nets	Dermal Ingestion	Resident	○	NA	NA	○	NA	○	○	NA	○	NA	NA	○	NA	NA	NA
Improper use of nets	Dermal Ingestion	Resident	○	NA	NA	○	NA	○	○	NA	○	NA	NA	○	NA	NA	NA
Larviciding (Liquid)																	
Spraying	Inhalation	Worker	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	○
Spraying, surface water	Dermal Ingestion	Resident	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	○
Spraying, leakage, soil	Dermal Ingestion	Resident	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	○
Spraying, leakage, soil, surface water	Dermal Ingestion	Resident	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	○
Spraying, leakage	Dermal	Worker	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	○
Larviciding (Granular)																	
Grinding e	Dermal	Worker	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	○
Spreading, soil	Dermal Ingestion	Resident	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	
Spreading, surface water	Dermal Ingestion	Resident	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	

Process	Pathway	Receptor	Alpha-cypermethrin	Bendiocarb	Bifenthrin	Cyfluthrin	DDT	Deltamethrin	Etofenprox	Fenitrothion	Lambda-cyhalothrin	Malathion	Methoprene	Permethrin	Pirimiphos-methyl	Propoxur	Temephos
Spreading, soil, surface water	Dermal Ingestion	Resident	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	
Spreading	Inhalation	Worker	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	
Disposal																	
Burying, groundwater	Dermal Ingestion	Resident	●	●	●	●	●	●	●	●	NA	●	●	●	●	●	NA
Dumping, soil	Dermal Ingestion	Resident	○	○	○	○	○	○	○	○	NA	○	○	○	○	○	NA
Dumping, soil, surface water	Dermal Ingestion	Resident	○	○	○	○	○	○	○	○	NA	○	○	○	○	○	NA
Dumping, surface water	Dermal Ingestion	Resident	x	x	x	x	x	x	x	x	NA	x	x	x	x	x	NA
Reuse of pesticide-Containers																	
Food/drink storage	Ingestion	Resident	●	NA	NA	●	NA	●	●	NA	NA	NA	●	●	●	NA	●
Other storage	Dermal	Resident	○	NA	NA	○	NA	○	○	NA	NA	NA	○	○	○	NA	○
Storage																	
Spillage	Inhalation	Worker	●	●	●	●	●	●	●	●	NA	●	NA	NA	●	●	NA
Spillage	Dermal	Worker	○	○	○	○	○	○	○	○	NA	○	NA	NA	○	○	NA
Damage	Inhalation Dermal	Worker	x	x	x	x	x	x	x	x	NA	○	NA	NA	x	x	NA

Process	Pathway	Receptor	Alpha-cypermethrin	Bendiocarb	Bifenthrin	Cyfluthrin	DDT	Deltamethrin	Etofenprox	Fenitrothion	Lambda-cyhalothrin	Malathion	Methoprene	Permethrin	Pirimiphos-methyl	Propoxur	Temephos
Accidents	Inhalation Dermal	Worker	x	x	x	x	x	x	x	x	NA	x	NA	NA	x	x	NA
Pilferage	Inhalation Dermal	Worker	x	x	x	x	x	x	x	x	NA	x	NA	NA	x	x	NA

Annex G: Exposure and Risk Calculations

Preparing-Mixing for Indoor Residual Spraying (IRS)

Table G-1. Worker's Intermediate Inhalation Exposure

Parameter	Explanation	Value	Units	Source
Unit exposure	Assumes no PPE worn and open mixing/loading	0.0957 (WP)	mg ai/kg ai	SOPs (U.S. EPA, 1997a)
		0.0026 (EC)		
IVM concentration	See Calculation D-5	Chemical specific data see Table D-17	kg ai/L	Assumption based on collected mass and volume data
Amount of formulation used	Volume of sprayer tank (assumes one sprayer tank used)	10	L/tank	*Manual for IRS* (WHO, 2002a)
Exposure frequency	Number of tanks prepared per day	15	tanks/day	Provided by field worker (2005)
Exposure duration	For noncancer endpoint, based on 12 week spraying season, working 6 days per week	72	Day	Provided by field worker (2005)
	For cancer endpoint, based on 2 spraying seasons per year, 72 days each	144		
Body weight	Adult female mean	60	Kg	WHO (2004a) Generic Risk Assessment
Averaging time	For noncancer endpoints, 12 week spraying season, 7 days per week	84	Day	Provided by field worker (2005)
	For cancer endpoints, assumes a 50 year lifetime	18,250		Assumption

Preparing-Mixing for Indoor Residual Spraying

Table G-2. Worker's Intermediate Dermal Exposure

$$Predicted\ dose = \frac{Unit\ exposure * IVM\ \ concentration * Amount\ of\ \ formulation\ \ used * Exposure\ \ frequency * Exposure\ duration}{Body\ Weight * Averaging\ \ time}$$

Parameter	Explanation	Values	Units	Source
Unit exposure	Assumes no PPE worn and open mixing/loading	9.7002 (WP)	mg ai/kg ai	SOPs (U.S. EPA, 1997a)
		6.3933 (EC)		
IVM concentration	See Calculation D-5	Chemical specific data see Table D-17	kg ai/L	Assumption based on collected mass and volume data
Amount of formulation used	Volume of sprayer tank (assumes one sprayer tank used)	10	L/tank	*Manual for IRS* (WHO, 2002a)
Exposure frequency	Number of tanks prepared per day	15	tanks/day	Provided by field worker (2005)
Exposure Duration	For noncancer endpoint, based on 12 week spraying season working 6 days per week	72	day	Provided by field worker (2005)
	For cancer endpoint, based on 2 spraying seasons per year, 72 days each	144		
Body weight	Adult female mean	60	kg	WHO (2004a) Generic Risk Assessment
Averaging time	For noncancer endpoints, 12 week spraying season, 7 days per week	84	day	Provided by field worker (2005)
	For cancer endpoints, assumes a 50 year lifetime	18,250		Assumption

Preparing-Mixing for Insecticide-Treated Nets (ITN)

Table G-3. Resident's Acute Inhalation Exposure

$$Predicted\ dose = \frac{Unit\ exposure * IVM\ \ concentration * Amount\ of\ \ formulation\ \ used * Exposure\ \ frequency * Exposure\ duration}{Body\ Weight * Averaging\ time}$$

Parameter	Explanation	Value	Units	Source
Unit exposure	Assumes no PPE worn and open mixing/loading	0.0957 (WP) 0.0026 (EC)	mg ai/kg ai	SOPs (U.S. EPA, 1997a)
IVM concentration	See Calculation D-6	Chemical specific data see Table D-17	kg ai/L	Assumption based on collected mass and volume data
Amount of formulation used	Volume of water required to treat one synthetic bed net	1	L/net	Assumption based on *Roll Back Malaria* ITN intervention (WHO, 2002b)
Exposure frequency	Number of nets prepared per day for 1 household	2	nets/day	Provided by field worker (2005)
Exposure duration	For noncancer endpoints, the amount of time spent mixing ITN formulation per event; assumes 5 minutes per net, 2 nets per event	0.007	day	Provided by field worker (2005)
	For cancer endpoints, amount of time spent mixing ITN formulation over a lifetime; assumes a household treats nets 4 times a year for 38 years	1.06		
Body weight	Adult female mean	60	kg	WHO (2004a) Generic Risk Assessment

Parameter	Explanation	Value	Units	Source
Averaging time	For noncancer endpoints, assumes acute exposure	1	day	Provided by field worker (2005)
	For cancer endpoints, assumes a 50 year lifetime	18,250		Assumption

Preparing-Mixing for Insecticide-Treated Nets (ITN)

Table G-4. Resident's Acute Dermal Exposure

$$Predicted\ dose = \frac{Unit\ exposure * IVM\ concentration * Amount\ of\ formulation\ used * Exposure\ frequency * Exposure\ duration}{Body\ Weight * Averaging\ time}$$

Parameter	Explanation	Values	Units	Source
Unit exposure	Assumes no PPE worn and open mixing/loading	9.7002 (WP)	mg ai/kg ai	SOPs (U.S. EPA, 1997a)
		6.3933 (EC)		
IVM concentration	See Calculation D-6	Chemical specific data see Table D-17	kg ai/L	Assumption based on collected mass and volume data
Amount of formulation used	Volume of insecticide formulation required to treat one synthetic bednet	1	L/net	Assumption based on *Roll Back Malaria* ITN intervention (WHO, 2002b)
Exposure frequency	Number of nets prepared per day for 1 household	2	nets/day	Provided by field worker (2005)
Exposure duration	For noncancer endpoints, the amount of time spent mixing ITN formulation per event; assumes 5 minutes per net, 2 nets per event	0.007	day	Provided by field worker (2005)
	For cancer endpoints, amount of time spent mixing ITN formulation over a lifetime; assumes a household treats nets 4 times a year for 38 years	1.06		
Body weight	Adult female mean	60	kg	WHO (2004a) Generic Risk Assessment

Parameter	Explanation	Values	Units	Source
Averaging time	For noncancer endpoints, assumes an acute exposure	1	day	Provided by field worker (2005)
	For cancer endpoints, assumes a 50 year lifetime	18,250		Assumption

Concentration Calculation for Indoor Residual Spraying (IRS)

Table G-5. Insecticide IVM Concentration

$$Insecticide\ \ IVM\ concentration\,(IRS) = \frac{Application * Surface\ area\ house * Houses\ per\ day\,(*1E+06)}{Tank\ volume * Tanks\ per\ day}$$

Parameter	Explanation	Value	Units	Source
Insecticide IVM concentration (IRS)	Mass of ai (kg) per unit volume; calculated based on collected data	Calculated	kg ai/L	Calculated above for use in D-1, D-2, D-8, D-11, D-12
1E+06[21]	Conversion factor for kg to mg	----	mg/kg	NA
Application	Amount of insecticide to be sprayed onto walls	Chemical specific data see Table D-17	kg ai/m^2	Najera and Zaim (2002) Criteria for use of insecticides
Surface area house	Total area of the walls of a house on which the insecticide is sprayed	3.58E+01	m^2/house	World Bank (1996)
Houses per day	Number of houses sprayed per day; assumes 3 houses per hour and working 4 hours per day	12	houses/day	Provided by field worker (2005)
Tank volume	The total volume of one tank of insecticide	10	L/tank	*Manual for IRS* (WHO, 2002a)
Tanks per day	Number of tanks prepared per day	15	tanks/day	Provided by field worker (2005)

[21] For use when concentration should be units of mg ai/m^3 instead of kg ai/m^3.

Concentration Calculation for Insecticide-Treated Nets (ITN)

Table G-6. Insecticide IVM Concentration

$$Insecticide\ IVM\ Concentration = \frac{Application * Area\ of\ bednet(*1E+06)}{Volume}$$

Parameter	Explanation	Value	Units	Source
Insecticide IVM Concentration	Amount of insecticide in kg a receptor will be exposed to during the treatment of one bed net; calculated based on collected data	Calculated	kg ai/L	Calculated above for use in D-2, D-4, D-10, D-11, D-12
1E+06	Conversion factor for kg to mg	----	mg/kg	NA
Application	Amount of insecticide on bed net	Chemical specific data see Table D-17	kg ai/m^2	Najera and Zaim (2002) Criteria for use of insecticides
Area of bednet	Total area of a bed net	15	m^2	Najera and Zaim (2002) Criteria for use of insecticides
Volume	The volume of water for home treatment of bednets; set to the amount of liquid a synthetic bed net absorbs	1	L	WHO (2002b) *Roll Back Malaria* ITN intervention

Indoor Residual Spraying (IRS) Process—During

Table G-7. Worker's Intermediate Inhalation Exposure

$$Predicted\ dose = \frac{Unit\ exposure * Application * Area\ treated * Exposure\ \ frequency * Exposure\ duration}{Body\ Weight * Averaging\ time}$$

Parameter	Explanation	Values	Units	Source
Unit exposure	Assumes a backpack sprayer and no PPE	5.29	mg ai/kg ai	SOPs (U.S. EPA, 1997a)
Application	Amount of insecticide to be sprayed onto walls	Chemical specific data see Table D-17	kg ai/m^2	Najera and Zaim (2002) Criteria for use of insecticides
Area treated	Total area of the walls of a house on which the insecticide is sprayed	3.58E+01	m^2/house	World Bank (1996)
Exposure frequency	Number of houses sprayed per day; assumes 3 houses per hour and working 4 hours per day	12	houses/day	Provided by field worker (2005)
Exposure duration	For noncancer endpoints, assumes 12 week spraying season working 6 days per week	72	day	Provided by field worker (2005)
	For cancer endpoints, assumes 2 spraying seasons per year, 72 days each	144		
Body weight	Adult female mean	60	kg	WHO (2004a) Generic Risk Assessment
Averaging time	For noncancer endpoints, 12 week spraying season, 7 days per week	84	day	Provided by field worker (2005)
	For cancer endpoints, assumes a 50 year lifetime	18,250		Assumption

Indoor Residual Spraying (IRS) Process—Post Application

Table G-8. Resident's Acute Dermal Exposure

$$Absorbed\ dose = \frac{IVM\ Concentration * Volume\ deposited\ onto\ skin\ (IRS)}{Body\ Weight * Averaging\ time}$$

Parameter	Explanation	Values	Units	Source
IVM Concentration	See Calculation D-5	Chemical specific data see Table D-17	mg ai/L	Assumption based on collected mass and volume data
Volume deposited onto skin	The total volume deposited onto the skin from contact with insecticide film on surfaces; assumes contact is with hands and forearms, 4 milliliters on each	8E-03	L	WHO (2004a) Generic Risk Assessment
Body weight	Adult female mean	60	kg	WHO (2004a) Generic Risk Assessment
	10- 12 year old child	40		
Averaging time	For noncancer endpoints, assumes an acute exposure	1	day	Provided by field worker (2005)
	For cancer endpoints, assumes a 50 year lifetime	18,250		Assumption

Indoor Residual Spraying (IRS) Process—Post Application

Table G-9. Resident's Acute Ingestion Exposure

$$Predicted\ dose = \frac{Application * Surface\ area\ of\ food * Exposure\ duration * 1E+06}{Body\ Weight * Averaging\ time}$$

Parameter	Explanation	Value	Units	Source
Application	Mass per unit area of insecticide sprayed onto foodstuff, assume same amount as applied to walls	Chemical-specific see Table D-17	kg ai/m^2	Najera and Zaim (2002) Criteria for use of insecticides
1E+06	Conversion factor for kg to mg	----	mg/kg	NA
Surface area of food	The total surface area of food sprayed and eaten in a single day	0.011	m^2/day	Calculated below
Exposure duration	A person consumes contaminated food for 1 day	1	day	Conservative screening assumption
Body weight	Adult female mean	60	kg	WHO (2004a) Generic Risk Assessment
	10–12 year old child	40		
Averaging time	For noncancer endpoints, assumes an acute exposure	1	day	Provided by field worker (2005)
	For cancer endpoints, assumes a 50 year lifetime	18,250		Assumption

(continued)

Table G-9. (continued)

$$Surface\ Area\ of\ \ food\ (sprayed\ and\ eaten\ per\ day) = \frac{\left(\sqrt[3]{Daily\ volume\ of\ \ food\ eaten}\right)^2}{day}$$

$$Daily\ volume\ \ of\ \ food\ eaten = \frac{Daily\ \ food\ consumption\ rate}{Energy\ value * Density}$$

Parameter	Explanation	Value	Units	Source
Daily food consumption rate	Amount of food an average person consumes in one day	2,200	kcal/day	FAO (2002) World agriculture
Energy value	The value of energy per unit mass for carbohydrates in the diet which reach the colon	2,000	kcal/kg	FAO (1999) Carbohydrates in human nutrition
$Density_{water}$	Assume the major portion of food is made up of water, the mass per unit volume of water	1,000	kg/m^3	NA
Daily volume of food eaten	The total volume of food consumed in a day, assume the shape of the food is a cube		m^3	Calculated above

Treating Insecticide-Treated Nets (ITNs)

Table G-10. Resident's Acute Dermal Exposure

$$Absorbed\ dose = \frac{IVM\ Concentration * Volume\ deposited\ onto\ skin(ITN)}{Body\ Weight * Averaging\ \ time}$$

Parameter	Explanation	Values	Units	Source
IVM Concentration	See Calculation D-6	Chemical specific data see Table D-17	mg ai/L	Assumption based on collected mass and volume data
Volume deposited onto skin	The total volume deposited onto the skin during the treatment of a bed net; assumes the least safe scenario where no gloves are worn	2.4E-02	L	WHO (2004a) Generic Risk Assessment
Body weight	Adult female mean	60	kg	WHO (2004a) Generic Risk Assessment
	10-12 year old child	40		
Averaging time	For noncancer endpoints, assumes an acute exposure	1	day	Provided by field worker (2005)
	For cancer endpoints, assumes a 50 year lifetime	18,250		Assumption

Disposal—Contaminated Groundwater

Table G-11. Resident's Chronic Ingestion Exposure

$$Predicted\ \ dose = \frac{Groundwate\ r\ concentrat\ ion * Water\ \ ingestion\ \ rate * Exposure\ \ Frequency\ \ * Exposure\ \ duration}{Body\ \ weight * Averaging\ \ time}$$

$$Groundwate\ r\ concentrat\ ion = \frac{IVM\ \ concentra\ tion}{DAF}$$

Parameter	Explanation	Values	Units	Source
Groundwater concentration	IVM concentration in GW used as drinking water		mg ai/L	Calculated above
Water ingestion rate	Adult	2	L/day	Exposure Factors Handbook (U.S. EPA, 1997b)
	Child	1		
Exposure frequency	Assumes daily exposure	365	days/years	Assumption
Exposure duration	For noncancer endpoints, assumes one year	1	year	Typical assumption for chronic exposure – noncancer
	For cancer endpoints, assume resident lives at the same residence for the 50 year lifetime	50		Conservative screening assumption
Body weight	Adult female mean	60	kg	WHO (2004a) Generic Risk Assessment
	10-12 year old child	40		
Averaging time	For noncancer endpoints, assumes a chronic exposure	365	day	Assumption
	For cancer endpoints, assumes a 50 year lifetime	18,250		

Parameter	Explanation	Values	Units	Source
IVM concentration	IRS - See Calculation D-5 ITN -See Calculation D-6	Chemical specific data see Table D-17	mg ai/L	Assumption based on collected mass and volume data
DAF	Chemical-specific	Chemical specific data see Table D-17	Unitless	U.S. EPA (2002b) IWEM (DDT) Default from U.S. EPA (2002c) Guidance for SSLs

Disposal—Contaminated Groundwater

Table G-12. Resident's Chronic Dermal Exposure from Bathing

$$Absorbed\ Dose = \frac{Absorbed\ Dose * Surface\ area\ body * Exposure\ frequency * Exposure\ duration}{Body\ Weight * Averaging\ time}$$

Parameter	Explanation	Values	Units	Source
Absorbed dose		Calculated	mg ai/cm^2-event	See below, equation from U.S. EPA (2004) RAGS
Surface area body	Whole body; adult	16,900	cm^2	Exposure Factors Handbook (U.S. EPA, 1997b)
	Whole body; child	12,200		
Exposure frequency	Assumes 1 bath per week and daily body washing for 1 year; daily body washing is assumed to be the equivalent to 1 bathing event per week	104	events/yr	Provided by field worker (2005)
Exposure duration	For noncancer and cancer endpoints, assumes annual exposure	1	year	Typical assumption for chronic exposure – noncancer
	For cancer endpoints, assume resident lives at the same residence for the 50 year lifetime	50		Conservative screening assumption
Body weight	Adult female mean	60	kg	WHO (2004a) Generic Risk Assessment
	10-12 year old child	40		
Averaging time	For noncancer endpoints, assumes chronic exposure	365	day	Assumption
	For cancer endpoints, assumes a 50 year lifetime	18,250		

(continued)

Table G-12. (continued)

$$Absorbed\ Dose_{event} = (2 * Fraction\ absorbed) * Permeability\ coefficient * \left(\frac{Groundwater\ concentration}{1E+03}\right) * \sqrt{\frac{6 * \tau_{event} * t_{event}}{\pi}}$$

$$Groundwater\ concentration = \frac{IVM\ concentration}{DAF}$$

Parameter	Explanation	Values	Units	Source
Fraction absorbed	Chemical-specific	Chemical specific data see Table D-17	unitless	U.S. EPA (2004a) RAGS Dermal Risk Assessment
Permeability coefficient	Chemical-specific	Chemical specific data see Table D-17	cm/hr	Calculated, see below (from U.S. EPA, 2004a, RAGS)
IVM concentration	IRS - See Calculation D-5 ITN - See Calculation D-6	Chemical specific data see Table D-17	mg ai/L	Assumption based on collected mass and volume data
Groundwater concentration	Daily average insecticide concentration in the groundwater that is used for bathing	Calculated	mg ai/L	Calculated above
DAF	Chemical-specific	Chemical specific data see Table D-17	Unitless	U.S. EPA (2002b) IWEM (DDT) Default from U.S. EPA (2002c) Guidance for Soil Screening Levels
1E+03	Conversion factor from L to cm^3	----	cm^3/L	NA
τ_{event}	Chemical-specific	Chemical specific data see Table D-17	hr/event	Calculated, see below (from U.S. EPA, 2004a, RAGS)
t_{event}	Assumes a bath takes 10 minutes	0.17	hr/event	Provided by field worker (2005)

Table G-12. (continued)

$$Permeability\ \ Coefficient = 10\text{^}(-2.80 + 0.66 \log Kow - 0.0056 * MW)$$

$$\tau_{event} = 0.105 * 10^{(0\ 0056 * MW)}$$

Parameter	Explanation	Values	Units	Source
Kow	Octanol-Water Coefficient	Chemical specific data see Table D-17	Log (unitless)	Multiple sources, see Annex D, D-1
MW	Molecular Weight	Chemical specific data see Table D-17	g/mol	Multiple sources, see Annex D, D-1

Reuse of Insecticide Containers

Table G-13. Resident's Acute Ingestion Exposure

Parameter	Explanation	Values	Units	Source
IVM concentration	Assumes 20% emulsifiable concentrate	2.00E+05 (Methoprene)	mg ai/L	WHO (2001) WHOPES 4th meeting
	Assumes 50% emulsifiable concentrate	5.00E+05 (Temephos)		MSDS (Gharda Chemicals, 1999) (Temephos)
	IRS - See Calculation D-5 ITN - See Calculation D-6	Chemical specific data see Table D-17		Assumption based on collected mass and volume data
Dilution factor	1:20 volume by volume dilution; assumes 5% of insecticide remains in container	0.05	unitless	Assumes that economic value of pesticide will result in small amount remaining
Water ingestion rate	Adult	2	L/day	Exposure Factors Handbook (U.S. EPA, 1997b)
	Child	1		
Exposure duration	Assumes household uses one container of water (approximately 10 gallons) each day for drinking water, cooking, bathing, etc.	1	day	Provided by field worker (2005)
Body weight	Adult female mean	60	kg	WHO (2004a) Generic Risk Assessment
	10-12 year old child	40		
Averaging time	For noncancer endpoints, assumes an acute exposure	1	day	Provided by field worker (2005)
	For cancer endpoints, assumes a 50 year lifetime	18,250		Assumption

Storage—Spillage

Table G-14. Worker's Intermediate Inhalation Exposure

Parameter	Explanation	Values	Units	Source
Unit exposure	Assumes no PPE, open mixing/loading	0.0957 (WP)	mg ai/kg ai	SOPs (U.S. EPA, 1997a)
Application	Amount of insecticide on floor	Chemical specific data see Table D-17	kg ai/m^2-event	Najera and Zaim (2002) Criteria for use of insecticides
Area of spill	Contaminated surface is half the area of a small (12 m^2) storage shed	6	m^2	Provided by field worker (2005)
Exposure frequency	The number of trips a worker takes into the storage shed per day; assumes 1 trip in morning and 1 in evening	2	events/day	Assumption
Exposure duration	For noncancer endpoints, assumes 12 week spraying season working 6 days per week	72	day	Provided by field worker (2005)
	For cancer endpoints, assumes 2 spraying seasons per year, 72 days each	144		
Body weight	Adult female mean	60	kg	WHO (2004a) Generic Risk Assessment
Averaging time	For noncancer endpoints, 12 week spraying season, 7 days per week	84	day	Provided by field worker (2005)
	For cancer endpoints, assumes a 50 year lifetime	18,250		Assumption

Risk Estimate Non-cancer: Hazard Quotient and Hazard Index

Table G-15. Hazard Quotient and Hazard Index for Non-carcinogenic Insecticides

Hazard Quotient (HQ) Calculation

$$HQ = \frac{Predicted\ dose}{Noncancer\ Benchmark}$$

Hazard Index (HI) Aggregate Calculation

$$HI = HQ_{oral} + HQ_{Dermal} + HQ_{Inhalation}$$

Parameter	Explanation	Units	Source
Hazard Quotient	A comparison of a predicted insecticide dose to a reference dose level below which adverse health effects are unlikely; HQs greater than 1 are of concern	unitless	Calculated based on recommendation of U.S. EPA (1999a) OPP Guide for Risk Assessment
Predicted dose	May also refer to absorbed dose values found in Tables D-9 and D-11. Based on noncancer values for exposure duration and averaging time	mg/kg-day	Calculated (See G-1 to G-14)
Noncancer benchmark	The accepted amount of insecticide a receptor may be exposed to per unit body weight and time; Insecticide specific	mg/kg-day	Values presented in Annex D, D-3
Hazard Index	Aggregate risk calculation for a pesticide; exposures must be temporally similar; HIs greater than 1 are of concern	unitless	Calculated based on recommendation of U.S.EPA (1999a) OPP Guide for Risk Assessment

Risk Estimate: Cancer

Table G-16. Cancer Risk Estimates for Carcinogenic Insecticides (DDT, Permethrin)

Cancer Risk

$$Predicted\ Cancer\ Risk = LADD * Slope\ factor$$

Parameter	Explanation	Units	Source
Predicted cancer risk	The total risk of developing cancer from the lifetime exposure for a pathway	risk/lifetime	Calculated by above equation
LADD	Based on cancer exposure values for exposure duration and averaging time	mg/kg-day	Calculated (See D-1 to 14)
Slope factor	The cancer toxicological benchmark for DDT, Etofenprox, Permethrin, and Propoxur; dermal, ingestion, inhalation	per mg/kg-day	Values presented in Annex D, D-3

Pesticide-Specific Properties

Table G-17. Pesticide-Specific Properties for Exposure and Risk Calculations

Insecticide	IVM Method	Application IRS (kg ai/m^2)	IVM Concentration		DAF	Fraction Absorbed (FA)	Permeability Coefficient	τ_{event}	Octanol-Water Partition Coefficient (Kow)	Molecular Weight (MW) (g/mol)
			kg ai/L	mg ai/L						
Alpha-cypermethrin	IRS	3.00E-05	8.59E-05	8.59E+01	20	0.8	1.88E-02	22.5	5.16	416.3
	ITN	4.00E-05	6.00E-04	6.00E+02						
Bendiocarb	IRS	4.00E-04	1.15E-03	1.15E+03	20	1	1.18E-03	1.9	1.7	223.23
Bifenthrin	IRS	5.00E-05	1.43E-04	1.43E+02	20	0.7	6.19E-02	24.5	6	422.9
Cyfluthrin	IRS	5.00E-05	1.43E-04	1.43E+02	20	0.6	4.88E-02	28.4	5.94	434.29
	ITN	5.00E-05	7.50E-04	7.50E+02						
DDT	IRS	2.00E-03	5.73E-03	5.73E+03	1E+30	0.7	5.96E-01	10.1	6.91	354.49
Deltamethrin	IRS	2.50E-05	7.16E-05	7.16E+01	20	0.4	9.00E-03	70.9	5.43	505.24
	ITN	2.50E-05	3.75E-04	3.75E+02						
Etofenprox	IRS	3.00E-04	8.59E-04	8.59E+02	20	0.5	5.55E-01	13.5	7.05	376.5
	ITN	2.00E-04	3.00E-03	3.00E+03						
Fenitrothion	IRS	2.00E-03	5.73E-03	5.73E+03	20	1	5.41E-03	3.7	3.16	277.24
Lambda-cyhalothrin	IRS	3.00E-05	8.59E-05	8.59E+01	NA	0.3	2.00E-01	34.7	7	449.9
	ITN	1.50E-05	2.25E-04	2.25E+02						
Malathion	IRS	2.00E-03	5.73E-03	5.73E+03	20	0.9	1.46E-03	7.4	2.75	330.36

			IVM Concentration							
Methoprene	Growth regulator	4.00E-06	2.00E-01	2.00E+05	20	0.9	1.23E-01	5.8	5.5	310.48
Permethrin	ITN	5.00E-04	7.50E-03	7.50E+03	20	0.6	1.99E-01	16.3	6.5	391.3
Pirimiphos-methyl	IRS	2.00E-03	5.73E-03	5.73E+03	20	1	1.62E-02	5.4	4.12	305.3
Propoxur	IRS	2.00E-03	5.73E-03	5.73E+03	20	1	1.14E-03	1.6	1.56	209.25
Temephos	Larvicide	1.12E-05	5.00E-01	5.00E+05	NA	0.6	3.32E-02	43.0	5.96	466.48

Glossary

Absorbed dose (mg/kg-day)—The amount of pesticide a receptor is predicted to absorb per unit body weight and time.

Absorbed doseevent (mg ai/cm2-event)—The total amount (dose) of pesticide taken up by the skin at the end of exposure.

Adult—A person who is more than 12 years old

ai—Active ingredient (in a pesticide).

Amount of formulation used (L/event)—The volume of pesticide formulation required to fill a sprayer tank (for IRS) or treat a bed net (for ITN).

Application (kg ai/m2)—The mass of pesticide active ingredient sprayed or spilled per unit area.

Area (treated, spilled) (m2)—The area of the walls sprayed with insecticide per house or the total surface area of a spill within a pesticide storage shed.

Averaging time (days)—The period of time over which the dose is averaged.

Body weight (kg)—The body weight of the receptor (either a 10-year old child or an adult female).

DAF—Dilution-attenuation factor; the ratio used to represent the decrease in chemical concentration from source to groundwater due to natural environmental processes such as degradation, volumetric dilution, and sorption.

Daily food consumption rate (kcal/day)—The average per capita food consumption rate; assumes undernourishment of a portion of the population.

Daily volume of food eaten (m3)—The total volume of food consumed in one day.

Densitywater (kg/m3)—The mass per unit volume of water.

Dilution factor—The volumetric ratio of pesticide to water.

EC—Emulsifiable concentrate; a liquid pesticide formulation that forms an emulsion when added to water.

Energy value (kcal/kg)—The value of energy for carbohydrates that reach the colon per unit mass of food.

Exposure duration (days or year)—The period of time over which a receptor is exposed (via inhalation, ingestion, or dermal contact) to a pesticide.

Exposure frequency (event/time or time/time)—The number of events in which a specific receptor is exposed per unit time, or the duration of contact (dermal or ingestion) per unit time.

Fraction absorbed—The fraction of the pesticide that is absorbed through the skin.

Groundwater concentration (mass ai/L)—The average pesticide concentration in groundwater that is used for drinking water.

IRS—Indoor residual spraying; an IVM process in which the walls of a house are sprayed with insecticide to kill mosquitoes inside the home.

ITN—Insecticide-treated nets, an IVM process in which bed nets are treated with insecticide to protect residents from mosquitoes.

IVM Concentration (mass ai/L)—The mass of active ingredient per unit volume for IRS and ITN.

Kow—Octanol-water partition coefficient; a chemical-specific property that characterizes a chemical's affinity for water or lipids.

LADD (mg/kg-day)—Lifetime average daily dose; a measure of dose that is used to assess cancer risk and is the amount of insecticide to which a receptor is exposed daily over her lifetime.

MW (g/mol)—Molecular weight; a chemical-specific property.

Permeability coefficient (cm/hr)—The rate at which a pesticide moves through the skin.

PPE—Personal protective equipment, such as gloves or masks.

Predicted dose (mg/kg-day)—The predicted amount of pesticide to which a receptor is exposed per unit body weight and time.

Surface area (body, hands, exposed) (cm2)—The total surface area of skin exposed to the pesticide.

Surface area of food (m2/day)—The total surface area of food inside a house sprayed by insecticide; the surface area represents the amount of food consumed in one day.

event (hr/event)—The lag time per event, which is the amount of time for the pesticide to diffuse through the skin.

tevent (hr/event)—The duration of an exposure event (e.g., a bath or treating a net).

Unit exposure (mg ai/kg ai)—The unit mass of active ingredient to which a receptor will be exposed via an exposure pathway (ingestion, inhalation, dermal) per unit mass of active ingredient from the process/practice (e.g., mixing).

Volume deposited onto skin (L)—The total volume of insecticide solution deposited onto the skin due to contact with a pesticide film present on surfaces and walls inside a residence after indoor spraying or from the immersion of hands into solution during the treatment of bed nets.

Water ingestion rate (L/day)—The volume of water a receptor consumes per day.

WP—Wettable powder; a fine powder pesticide formulation that must be mixed with water or another liquid before it is applied.

Annex G References

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Annex H: Screening Risk Results

Indoor Residual Spraying (IRS)

Preparing-Mixing

Table H-1. IRS – Adult Worker Intermediate Inhalation Exposure and Risk

Pesticide	Noncancer		Cancer	
	Predicted Dose (mg/kg-day)	HQ	LADD (mg/kg-day)	Cancer Risk
Alpha-cypermethrin	1.8E-05	4E-06	NA	NA
Bendiocarb	2.3E-04	1E-01	NA	NA
Bifenthrin	2.9E-05	4E-03	NA	NA
Cyfluthrin	2.9E-05	1E-01	NA	NA
DDT	1.2E-03	2E+00	1.1E-05	4E-06
Deltamethrin	1.5E-05	1E-03	NA	NA
Etofenprox	1.8E-04	2E-03	1.6E-06	8E-09
Fenitrothion	1.2E-03	3E+00	NA	NA
Lambda-cyhalothrin	1.8E-05	2E-02	NA	NA
Malathion	1.2E-03	5E-02	NA	NA
Pirimiphos-methyl	1.2E-03	2E+00	NA	NA
Propoxur	1.2E-03	3E-01	1.1E-05	4E-08

Table H-2. IRS – Adult Worker Intermediate Dermal Exposure and Risk

Pesticide	Noncancer		Cancer	
	Predicted Dose (mg/kg-day)	HQ	LADD (mg/kg-day)	Cancer Risk
Alpha-cypermethrin	1.8E-03	4E-04	NA	NA
Bendiocarb	2.4E-02	1E-01	NA	NA
Bifenthrin	3.0E-03	1E-02	NA	NA
Cyfluthrin	3.0E-03	1E-03	NA	NA
DDT	1.2E-01	2E+02	1.1E-03	4E-04
Deltamethrin	1.5E-03	1E-04	NA	NA
Etofenprox	1.8E-02	4E-02	1.6E-04	8E-07
Fenitrothion	1.2E-01	1E+01	NA	NA
Lambda-cyhalothrin	1.8E-03	2E-02	NA	NA
Malathion	1.2E-01	2E-01	NA	NA
Pirimiphos-methyl	1.2E-01	2E+02	NA	NA
Propoxur	1.2E-01	1E-02	1.1E-03	4E-06

Spraying

Table H-3. IRS – Adult Worker Intermediate Inhalation Exposure and Risk

Pesticide	Noncancer		Cancer	
	Predicted Dose (mg/kg-day)	HQ	LADD (mg/kg-day)	Cancer Risk
Alpha-cypermethrin	9.7E-04	2E-04	NA	NA
Bendiocarb	1.3E-02	6E+00	NA	NA
Bifenthrin	1.6E-03	2E-01	NA	NA
Cyfluthrin	1.6E-03	8E+00	NA	NA
DDT	6.5E-02	1E+02	6.0E-04	2E-04
Deltamethrin	8.1E-04	8E-02	NA	NA
Etofenprox	9.7E-03	1E-01	9.0E-05	5E-07
Fenitrothion	6.5E-02	2E+02	NA	NA
Lambda-cyhalothrin	9.7E-04	1E+00	NA	NA

Pesticide	Noncancer		Cancer	
	Predicted Dose (mg/kg-day)	HQ	LADD (mg/kg-day)	Cancer Risk
Malathion	6.5E-02	2E+00	NA	NA
Pirimiphos-methyl	6.5E-02	9E+01	NA	NA
Propoxur	6.5E-02	2E+01	6.0E-04	2E-06

Post-Application

Table H-4. IRS – Adult and Child Resident Acute Dermal Exposure and Risk

Pesticide	Receptor	Noncancer		Cancer	
		Absorbed Dose (mg/kg-day)	HQ	LADD (mg/kg-day)	Cancer Risk
Alpha-cypermethrin	Adult	1.1E-02	2E-03	NA	NA
	Child	1.7E-02	3E-03	NA	NA
Bendiocarb	Adult	1.5E-01	3E-01	NA	NA
	Child	2.3E-01	5E-01	NA	NA
Bifenthrin	Adult	1.9E-02	1E-01	NA	NA
	Child	2.9E-02	1E-01	NA	NA
Cyfluthrin	Adult	1.9E-02	6E-03	NA	NA
	Child	2.9E-02	1E-02	NA	NA
DDT	Adult	7.6E-01	2E+03	4.2E-05	1E-05
	Child	1.1E+00	2E+03	Not Calc	Not Calc
Deltamethrin	Adult	9.5E-03	1E-03	NA	NA
	Child	1.4E-02	1E-03	NA	NA
Etofenprox	Adult	1.1E-01	3E-01	6.3E-06	3E-08
	Child	1.7E-01	4E-01	Not Calc	Not Calc
Fenitrothion	Adult	7.6E-01	8E+01	NA	NA
	Child	1.1E+00	1E+02	NA	NA

Pesticide	Receptor	Noncancer		Cancer	
		Absorbed Dose (mg/kg-day)	HQ	LADD (mg/kg-day)	Cancer Risk
Lambda-cyhalothrin	Adult	1.1E-02	1E-01	NA	NA
	Child	1.7E-02	2E-01	NA	NA
Malathion	Adult	7.6E-01	2E+00	NA	NA
	Child	1.1E+00	2E+01	NA	NA
Pirimiphos-methyl	Adult	7.6E-01	5E+01	NA	NA
	Child	1.1E+00	8E+01	NA	NA
Propoxur	Adult	7.6E-01	8E-02	4.2E-05	2E-07
	Child	1.1E+00	1E-01	Not Calc	Not Calc

Table H-5. IRS – Adult and Child Resident Acute Ingestion Exposure and Risk

Pesticide	Receptor	Noncancer		Cancer	
		Absorbed Dose (mg/kg-day)	HQ	LADD (mg/kg-day)	Cancer Risk
Alpha-cypermethrin	Adult	5.3E-03	1E-03	NA	NA
	Child	8.0E-03	2E-03	NA	NA
Bendiocarb	Adult	7.1E-02	1E-01	NA	NA
	Child	1.1E-01	2E-01	NA	NA
Bifenthrin	Adult	8.9E-03	4E-02	NA	NA
	Child	1.3E-02	7E-02	NA	NA
Cyfluthrin	Adult	8.9E-03	3E-03	NA	NA
	Child	1.3E-02	4E-03	NA	NA
DDT	Adult	3.6E-01	7E+02	1.9E-05	6.6E-06
	Child	5.3E-01	1E+03	Not Calc	Not Calc
Deltamethrin	Adult	4.4E-03	4E-04	NA	NA
	Child	6.7E-03	7E-04	NA	NA

Pesticide	Receptor	Noncancer		Cancer	
		Absorbed Dose (mg/kg-day)	HQ	LADD (mg/kg-day)	Cancer Risk
Etofenprox	Adult	5.3E-02	1E-01	2.9E-06	1E-08
	Child	8.0E-02	2E-01	Not Calc	Not Calc
Fenitrothion	Adult	3.6E-01	4E+01	NA	NA
	Child	5.3E-01	5E+01	NA	NA
Lambda-cyhalothrin	Adult	5.3E-03	5E-02	NA	NA
	Child	8.0E-03	8E-02	NA	NA
Malathion	Adult	3.6E-01	7E-01	NA	NA
	Child	5.3E-01	1E+01	NA	NA
Pirimiphos-methyl	Adult	3.6E-01	2E+01	NA	NA
	Child	5.3E-01	4E+01	NA	NA
Propoxur	Adult	3.6E-01	4E-02	1.9E-05	7E-08
	Child	5.3E-01	5E-02	Not Calc	Not Calc

Insecticide-Treated Nets (ITNs)

Preparing-Mixing

Table H-6. ITNs – Adult Resident Acute Inhalation Exposure

Pesticide	Noncancer		Cancer	
	Predicted Dose (mg/kg-day)	HQ	LADD (mg/kg-day)	Cancer Risk
Alpha-cypermethrin	3.6E-10	9E-11	NA	NA
Cyfluthrin	4.6E-10	7E-07	NA	NA
Deltamethrin	2.3E-10	2E-08	NA	NA
Etofenprox	1.8E-09	2E-08	1.5E-11	8E-14
Lambda-cyhalothrin	1.4E-10	2E-07	NA	NA
Permethrin	4.6E-09	4E-08	3.8E-11	4E-13

Table H-7. ITNs – Adult Resident Acute Dermal Exposure

Pesticide	Noncancer		Cancer	
	Predicted Dose (mg/kg-day)	HQ	LADD (mg/kg-day)	Cancer Risk
Alpha-cypermethrin	9.0E-07	2E-07	NA	NA
Cyfluthrin	1.1E-06	4E-07	NA	NA
Deltamethrin	5.6E-07	6E-08	NA	NA
Etofenprox	4.5E-06	1E-05	3.7E-08	2E-10
Lambda-cyhalothrin	3.4E-07	3E-06	NA	NA
Permethrin	1.1E-05	2E-06	9.3E-08	9E-10

Treatment

Table H-8. ITNs – Adult Resident Acute Dermal Exposure

Pesticide	Receptor	Noncancer		Cancer	
		Absorbed Dose (mg/kg-day)	HQ	LADD (mg/kg-day)	Cancer Risk
Alpha-cypermethrin	Adult	2.4E-01	5E-02	NA	NA
	Child	3.6E-01	7E-02	NA	NA
Cyfluthrin	Adult	3.0E-01	1E-01	NA	NA
	Child	4.5E-01	2E-01	NA	NA
Deltamethrin	Adult	1.5E-01	2E-02	NA	NA
	Child	2.3E-01	2E-02	NA	NA
Etofenprox	Adult	1.2E+00	3E+00	6.6E-05	3E-07
	Child	1.8E+00	5E+00	Not Calc	Not Calc
Lambda-cyhalothrin	Adult	9.0E-02	9E-01	NA	NA
	Child	1.4E-01	1E+00	NA	NA
Permethrin	Adult	3.0E+00	6E-01	1.6E-04	2E-06
	Child	4.5E+00	9E-01	Not Calc	Not Calc

Disposal

Contaminated Groundwater—Drinking

Table H-9. Adult and Child Resident Chronic Ingestion Exposure and Risk

Pesticide	Receptor	Noncancer		Cancer	
		Absorbed Dose (mg/kg-day)	HQ	LADD (mg/kg-day)	Cancer Risk
Alpha-cypermethrin	Adult	1.4E-01	1E+01	NA	NA
	Child	1.1E-01	1E+01	NA	NA
Bendiocarb	Adult	1.9E+00	2E+03	NA	NA
	Child	1.4E+00	1E+03	NA	NA
Bifenthrin	Adult	2.4E-01	6E+01	NA	NA
	Child	1.8E-01	4E+01	NA	NA
Cyfluthrin	Adult	2.4E-01	1E+01	NA	NA
	Child	1.8E-01	7E+00	NA	NA
DDT	Adult	1.9E-28	4E-25	1.9E-28	6E-29
	Child	1.4E-28	3E-25	Not Calc	Not Calc
Deltamethrin	Adult	1.2E-01	1E+01	NA	NA
	Child	9.0E-02	9E+00	NA	NA
Etofenprox	Adult	1.4E+00	4E+01	1.4E+00	7E-03
	Child	1.1E+00	3E+01	Not Calc	Not Calc
Fenitrothion	Adult	9.5E+00	7E+03	NA	NA
	Child	7.2E+00	6E+03	NA	NA
Malathion	Adult	9.5E+00	3E+02	NA	NA
	Child	7.2E+00	2E+02	NA	NA
Methoprene	Adult	3.3E+02	8E+02	NA	NA
	Child	2.5E+02	6E+02	NA	NA

Pesticide	Receptor	Noncancer		Cancer	
		Absorbed Dose (mg/kg-day)	HQ	LADD (mg/kg-day)	Cancer Risk
Permethrin	Adult	1.3E+01	5E+01	1.3E+01	1E-01
	Child	9.4E+00	4E+01	Not Calc	Not Calc
Pirimiphos-methyl	Adult	9.5E+00	5E+04	NA	NA
	Child	7.2E+00	4E+04	NA	NA
Propoxur	Adult	9.5E+00	2E+03	9.5E+00	4E-02
	Child	7.2E+00	1E+03	Not Calc	Not Calc

Contaminated Groundwater—Bathing

Table H-10. Adult and Child Resident Chronic Dermal Exposure and Risk

Pesticide	Receptor	Noncancer		Cancer	
		Absorbed Dose (mg/kg-day)	HQ	LADD (mg/kg-day)	Cancer Risk
Alpha-cypermethrin	Adult	2.8E-02	6E-03	NA	NA
	Child	3.0E-02	6E-03	NA	NA
Bendiocarb	Adult	8.4E-03	7E+00	NA	NA
	Child	9.1E-03	7E+00	NA	NA
Bifenthrin	Adult	1.4E-01	7E-01	NA	NA
	Child	1.5E-01	8E-01	NA	NA
Cyfluthrin	Adult	1.0E-01	3E-02	NA	NA
	Child	1.1E-01	4E-02	NA	NA
DDT	Adult	7.0E-28	1E-24	7.0E-28	2E-28
	Child	7.5E-28	2E-24	Not Calc	Not Calc
Deltamethrin	Adult	9.9E-03	1E-03	NA	NA
	Child	1.1E-02	1E-03	NA	NA
Etofenprox	Adult	4.0E+00	1E+02	4.0E+00	2E-02
	Child	4.3E+00	1E+02	Not Calc	Not Calc

Pesticide	Receptor	Noncancer		Cancer	
		Absorbed Dose (mg/kg-day)	HQ	LADD (mg/kg-day)	Cancer Risk
Fenitrothion	Adult	2.7E-01	3E+01	NA	NA
	Child	3.0E-01	3E+01	NA	NA
Malathion	Adult	9.4E-02	2E-01	NA	NA
	Child	1.0E-01	2E+00	NA	NA
Methoprene	Adult	2.4E+02	2E+02	NA	NA
	Child	2.6E+02	3E+02	NA	NA
Permethrin	Adult	1.7E+01	3E+00	1.7E+01	2E-01
	Child	1.8E+01	4E+00	Not Calc	Not Calc
Pirimiphos-methyl	Adult	9.8E-01	1E+03	NA	NA
	Child	1.1E+00	2E+03	Not Calc	Not Calc
Propoxur	Adult	3.7E-02	4E-03	NA	NA
	Child	4.0E-02	4E-03	NA	NA

Reuse of Pesticide Containers

Table H-11. Adult and Child Resident Acute Ingestion Exposure and Risk

Pesticide	Receptor	Noncancer		Cancer	
		Absorbed Dose (mg/kg-day)	HQ	LADD (mg/kg-day)	Cancer Risk
Alpha-cypermethrin	Adult	1.0E+00	5E+01	NA	NA
	Child	7.5E-01	4E+01	NA	NA
Cyfluthrin	Adult	1.3E+00	6E+01	NA	NA
	Child	9.4E-01	5E+01	NA	NA
Deltamethrin	Adult	6.3E-01	6E+01	NA	NA
	Child	4.7E-01	5E+01	NA	NA
Etofenprox	Adult	5.0E+00	1E+02	2.7E-04	1E-06
	Child	3.8E+00	1E+02	Not Calc	Not Calc

Pesticide	Receptor	Noncancer		Cancer	
		Absorbed Dose (mg/kg-day)	HQ	LADD (mg/kg-day)	Cancer Risk
Methoprene	Adult	3.3E+02	8E+02	NA	NA
	Child	2.5E+02	6E+02	NA	NA
Permethrin	Adult	1.3E+01	5E+01	6.8E-04	7E-06
	Child	9.4E+00	4E+01	Not Calc	Not Calc
Pirimiphos-methyl	Adult	9.5E+00	6E+02	NA	NA
	Child	7.2E+00	5E+02	NA	NA
Temephos	Adult	8.3E+02	4E+03	NA	NA
	Child	6.3E+02	3E+03	NA	NA

Storage

Spillage

Table H-12. Adult Worker Intermediate Inhalation Exposure and Risk

Pesticide	Noncancer		Cancer	
	Predicted Dose (mg/kg-day)	HQ	LADD (mg/kg-day)	Cancer Risk
Alpha-cypermethrin	4.9E-07	1E-07	NA	NA
Bendiocarb	6.6E-06	3E-03	NA	NA
Bifenthrin	8.2E-07	1E-04	NA	NA
Cyfluthrin	8.2E-07	4E-03	NA	NA
DDT	3.3E-05	7E-02	3.0E-07	1E-07
Deltamethrin	4.1E-07	4E-05	NA	NA
Etofenprox	4.9E-06	5E-05	4.5E-08	2E-10
Fenitrothion	3.3E-05	8E-02	NA	NA
Malathion	3.3E-05	1E-03	NA	NA
Pirimiphos-methyl	3.3E-05	5E-02	NA	NA
Propoxur	3.3E-05	8E-03	3.0E-07	1E-09

Annex I: Treatment Guidelines for WHO-Recommended Insecticides for Indoor Residual Spraying

Section 1: Specific Treatment Guidelines for WHO-Recommended Insecticides for Indoor Residual Spraying (IRS) for Malaria

Organochlorines

DDT is the only insecticide of this chemical group which is still recommended for indoor residual spraying (IRS). Previously used organochlorines belonged to the cyclodiene sub-class, which included dieldrin and HCH. Dieldrin was abandoned because of its high acute toxicity to humans. Eventually, the whole subgroup became unusable because a mechanism common to all cyclodienes caused the rapid development of resistance.

DDT

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

The main danger of environmental contamination from using DDT as an indoor residual spray comes from diverting the insecticide from malaria control to agricultural use. A similar danger would occur if containers were inadequately disposed of or pumps indiscriminately washed in surface waters. These risks could be prevented by proper education and strict supervision.

Toxicology

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

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

Symptoms of poisoning

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

Emergency Treatment

Remove contaminated clothing and wash the affected skin with clean water and soap, and flush the affected area with large quantities of clean water. Keep the patient calm and in quiet, shaded conditions and seek medical assistance. Do not give the patient oils and fats.

Treatment by Medical Professional

1. **Observation**. Persons exposed to high levels of organochlorine pesticides by any route should be observed for sensory disturbances, incoordination, speech slurring, mental aberrations, and involuntary motor activity that would warn of imminent convulsions.
2. **Convulsions**. If convulsions occur, place the victim in the left lateral decubitus position with the head down. Move away furniture or other solid objects that could be a source of injury. If jaw movements are violent, place padded tongue blades between the teeth to protect the tongue. Whenever possible, remove dentures and other removable dental work. Aspirate oral and pharyngeal secretion, and when possible, insert an oropharyngeal airway to maintain an open passage unobstructed by the tongue. Minimize noise and any manipulation of the patient that may trigger seizure activity.

Dosage of Diazepam:

- *Adults*: 5-10 mg IV and repeat every 5-10 minutes to maximum of 30 mg.
- *Children*: 0.2 to 0.5 mg/kg every 5 minutes to maximum of 10 mg in children over 5 years, and maximum of 5 mg in children under 5 years.

Although lorazepam is widely accepted as a treatment of choice for status epilepticus, there are no reports of its use for organochlorine intoxication. Some cases have required aggressive management that included the addition of phenobarbital and induction

Seizures in patients caused by organochlorine toxicity are likely to be prolonged and difficult to control. Status epilepticus is common. For this reason, patients with seizures that do not respond immediately to anticonvulsants should be transferred as soon as possible to a trauma center and will generally require intensive care

admission until seizures are controlled and neurologic status is improved. Initial therapy with benzodiazepines should be instituted.

3. **Oxygen.** Administer oxygen by mask. Maintain pulmonary gas exchange by mechanically assisted ventilation whenever respiration is depressed.
4. **Skin decontamination.** Thoroughly decontaminate the skin.
5. **Gastrointestinal decontamination.** If organochlorine has been ingested in a quantity sufficient to cause poisoning and the patient presents within an hour, consider gastric decontamination procedures. If the patient presents more than an hour after ingestion, activated charcoal may still be beneficial. If the victim is convulsing, it is almost always necessary first to control seizures before attempting gastric decontamination. Activated charcoal administration has been advocated in such poisonings, but there is little human or experimental evidence to support it.
6. **Respiratory failure.** Particularly in poisonings by large doses of organochlorine, **monitor pulmonary ventilation** carefully to forestall respiratory failure. Assist pulmonary ventilation mechanically with oxygen whenever respiration is depressed. Since these compounds are often formulated in a hydrocarbon vehicle, hydrocarbon aspiration may occur with ingestion of these agents. The hydrocarbon aspiration should be managed in accordance with accepted medical practice as a case of acute respiratory distress syndrome, which will usually require intensive care management.
7. **Cardiac monitoring.** In severely poisoned patients, monitor cardiac status by continuous ECG recording to detect arrhythmia.
8. **Contraindications.** Do not give epinephrine, other adrenergic amines, or atropine unless absolutely necessary because of the enhanced myocardial irritability induced by chlorinated hydrocarbons, which predisposes to ventricular fibrillation. Do not give animal or vegetable oils or fats by mouth. They enhance gastrointestinal absorption of the lipophilic organochlorines.
9. **Phenobarbital.** To control seizures and myoclonic movements that sometimes persist for several days following acute poisoning by the more slowly excreted organochlorines, phenobarbital given orally is likely to be effective. Dosage should be based on manifestations in the individual case and on information contained in the package insert.
10. **Cholestryamine resin** accelerates the biliary-fecal excretion of the more slowly eliminated organochlorine compounds. It is usually administered in 4 g doses, 4 times a day, before meals and at bedtime. The usual dose for children is 240 mg/kg/24 hours, divided Q 8 hours. The dose may be mixed with a pulpy fruit or liquid. It should never be given in its dry form and must always be administered with water, other liquids, or a pulpy fruit. Prolonged treatment (several weeks or months) may be necessary.
11. **Convalescence.** During convalescence, enhance carbohydrate, protein, and vitamin intake by diet or parenteral therapy.

Organophosphates

Organophosphates, although rapidly metabolized and eliminated, produce prolonged inhibition of acetylcholinesterase, therefore disturbing the transmission of nerve impulses at the synapses. Organophosphates may thus produce a cumulative effect after repeated exposure, with recovery requiring the production of fresh acetylcholinesterase.

Toxicology

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

Malathion

Malathion is an organophosphate insecticide. The pure insecticidal compound (technical grade) of malathion is a liquid with relatively low vapor pressure, moderate water solubility, and relatively low toxicity.

Toxicology

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

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

Fenitrothion

Fenitrothion is an organophosphate insecticide. It has been used extensively as an indoor residual spray for malaria control since the 1970s. It is the most toxic to man of the insecticides approved for residual house spraying, and has a relatively low margin of safety.

Toxicology

Absorption route: Absorbed through the gastrointestinal tract as well as through intact skin and by inhalation.

Mode of action: A cholinesterase inhibitor.

Pirimiphos-methyl

Toxicology

Absorption route: Pirimiphos-methyl may be absorbed from the gastrointestinal tract, through the intact skin and less commonly, by inhaling fog, smoke, or spray mist.

Mode of action: A cholinesterase inhibitor. The degradation products desethyl pirimiphos-methyl and pirimiphos-methyloxon are also active but of transient stability, and have not figured significantly in mammalian studies.

Symptoms of poisoning

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

Emergency Treatment

Organophosphate poisoning is a medical emergency and requires immediate treatment. All supervisors and individual spraymen (in the case of dispersed operations) should be trained in first-aid and emergency treatment of organophosphate intoxication.

The affected person should stop work immediately, remove any contaminated clothing, wash the affected skin with soap and clean water and flush the skin with large quantities of clean water. Care must be taken not to contaminate others, including medical or paramedical workers.

Automatic injectors loaded with atropine sulfate and obidoxime chloride can be made available in the field whenever relatively toxic organophosphate insecticides are used in areas without easy access to medical care. Once given the emergency treatment, the patient should be rapidly referred to a hospital for full treatment.

Treatment by Medical Professional

Caution: Persons attending the victim should avoid direct contact with heavily contaminated clothing and vomitus. Wear rubber gloves while washing pesticide from skin and hair. Vinyl gloves provide no protection.

1. **Airway protection**. Ensure that a clear airway exists. Intubate the patient and aspirate the secretions with a large-bore suction device if necessary. Administer oxygen by mechanically assisted pulmonary ventilation if respiration is depressed. Improve tissue oxygenation as much as possible before administering atropine, so as to minimize the risk of ventricular fibrillation. In severe poisonings, it may be necessary to support pulmonary ventilation mechanically for several days.
2. **Atropine sulfate**. Administer atropine sulfate intravenously or intramuscularly if intravenous injection is not possible. Remember that atropine can be administered through an endotracheal tube if initial IV access is difficult to obtain. Depending on

the severity of poisoning, doses of atropine ranging from very low to as high as 300 mg per day may be required, or even a continuous infusion.

The objective of atropine antidotal therapy is to antagonize the effects of excessive concentrations of acetylcholine at end-organs having muscarinic receptors. Atropine does not reactivate the cholinesterase enzyme or accelerate disposition of organophosphate. Recrudescence of poisoning may occur if tissue concentrations of organophosphate remain high when the effect of atropine wears off. Atropine is effective against muscarinic manifestations, but it is ineffective against nicotinic actions, specifically muscle weakness and twitching, and respiratory depression.

Despite these limitations, atropine is often a life-saving agent in organophosphate poisonings. Favorable response to a test dose of atropine (1 mg in adults, 0.01 mg/kg in children under 12 years) can help differentiate poisoning by anticholinesterase agents from other conditions. However, lack of response, with no evidence of atropinization (atropine refractoriness) is typical of more severe poisonings. The adjunctive use of nebulized atropine has been reported to improve respiratory distress, decrease bronchial secretions, and increase oxygenation.

3. **Glycopyrolate** has been studied as an alternative to atropine and found to have similar outcomes using continuous infusion. Ampules of 7.5 mg of glycopyrolate were added to 200 mL of saline and this infusion was titrated to the desired effects of dry mucous membranes and heart rate above 60 beats/min. During this study, atropine was used as a bolus for a heart rate less than 60 beats/min. The other apparent advantage to this regimen was a decreased number of respiratory infections. This may represent an alternative when there is a concern for respiratory infection due to excessive and difficult-to-control secretions, and in the presence of an altered level of consciousness where the distinction between atropine toxicity or relapse of organophosphate poisoning is unclear.

4. **Pralidoxime**. Before administering pralidoxime, draw a blood sample (heparinized) for cholinesterase analysis (since pralidoxime tends to reverse the cholinesterase depression). Administer pralidoxime (Protopam, 2-PAM, a cholinesterase reactivator) in cases of severe poisoning by organophosphate pesticides in which respiratory depression, muscle weakness, and/or twitching are severe. When administered early (usually less than 48 hours after poisoning), pralidoxime relieves the nicotinic as well as the muscarinic effects of poisoning. Pralidoxime works by reactivating the cholinesterase and also by slowing the “aging” process of phosphorylated cholinesterase to a non-reactivatable form.

   Note: Pralidoxime is of limited value and may actually be hazardous in poisonings caused by the cholinesterase-inhibiting carbamate compounds.

Dosage of Atropine:

In ***moderately severe poisoning*** (hypersecretion and other end-organ manifestations without central nervous system depression), the following dosage schedules have been used:

• *Adults and children over 12 years:* 2.0-4.0 mg, repeated every 15 minutes until pulmonary secretions are controlled, which may be accompanied by other signs of atropinization, including flushing, dry mouth, dilated pupils, and tachycardia (pulse of 140 per minute). **Warning:** In cases of ingestion of liquid concentrates of organophosphate pesticides, hydrocarbon aspiration may complicate these poisonings. Pulmonary edema and poor oxygenation in these cases will not respond to atropine and should be treated as a case of acute respiratory distress syndrome.

•*Children under 12 years:* 0.05-0.1 mg/kg body weight, repeated every 15 minutes until atropinization is achieved. There is a minimum dose of 0.1 mg in children. Maintain atropinization by repeated doses based on recurrence of symptoms for 2-12 hours or longer, depending on severity of poisoning. Maintain atropinization with repeated dosing as indicated by clinical status. Crackles in the lung bases nearly always indicate inadequate atropinization. Pulmonary improvement may not parallel other signs of atropinization. Continuation of, or return of, cholinergic signs indicates the need for more atropine. When symptoms are stable for as much as six hours, the dosing may be decreased.

Severely poisoned individuals may exhibit remarkable tolerance to atropine; two or more times the dosages suggested above may be needed. The dose of atropine may be increased and the dosing interval decreased as needed to control symptoms. Continuous intravenous infusion of atropine may be necessary when atropine requirements are massive. **The desired end-point is the reversal of muscarinic symptoms and signs with improvement in pulmonary status and oxygenation,** without an arbitrary dose limit. Preservative-free atropine products should be used whenever possible.

Note: Persons not poisoned or only slightly poisoned by organophosphates may develop signs of atropine toxicity from such large doses. Fever, muscle fibrillations, and delirium are the main signs of atropine toxicity. If these appear while the patient is fully atropinized, atropine administration should be discontinued, at least temporarily, while the severity of poisoning is reevaluated.

Dosage of Pralidoxime:

- *Adults and children over 12 years:* 1.0-2.0 g by intravenous infusion at a rate of no more than 0.2 g per minute. Slow administration of pralidoxime is strongly recommended and may be achieved by administering the total dose in 100 mL of normal saline over 30 minutes, or longer.
- *Children under 12 years:* 20-50 mg/kg body weight (depending on severity of poisoning) intravenously, mixed in 100 mL of normal saline and infused over 30 minutes.

Dosage of pralidoxime may be repeated in 1-2 hours, then at 10-12 hour intervals if needed. In very severe poisonings, dosage rates may be doubled. Repeated doses of pralidoxime are usually required. In cases that involve continuing absorption of organophosphate (as after ingestion of large amount), or continuing transfer of highly lipophilic organophosphate from fat into blood, it may be necessary to continue administration of pralidoxime for several days beyond the 48 hour post-exposure

interval usually cited as the limit of its effectiveness. Pralidoxime may also be given as a continuous infusion of approximately 500 mg/hour, based on animal case studies and adult patient reports.

Monitor blood pressure during administration because of the occasional occurrence of hypertensive crisis. Slow or stop administration if blood pressure rises to hazardous levels. Be prepared to assist pulmonary ventilation mechanically if respiration is depressed during or after pralidoxime administration. If intravenous injection is not possible, pralidoxime may be given by deep intramuscular injection.

5. **Skin decontamination**. In patients who have been poisoned by organophosphate contamination of skin, clothing, hair, and/or eyes, decontamination must proceed concurrently with whatever resuscitative and antidotal measures are necessary to preserve life. Flush the chemical from the eyes with copious amounts of clean water. If no symptoms are evident in a patient who remains alert and physically stable, a prompt shower and shampoo may be appropriate, provided the patient is carefully observed to insure against any sudden appearance of poisoning. If there are any indications of weakness, ataxia, or other neurologic impairment, remove the victim's clothing, have the victim lie down, and give the victim a complete bath and shampoo using copious amounts of soap and water. Surgical green soap is excellent for this purpose, but ordinary soap is about as good. Wash the chemical from skin folds and from under fingernails. Contaminated clothing should be promptly removed, bagged, and laundered before returning. Contaminated leather shoes should be discarded. Note that the pesticide can contaminate the inside surfaces of gloves, boots, and headgear. Attendants should wear rubber gloves, because vinyl provides no protection against skin absorption.
6. **Gastrointestinal decontamination**. If organophosphate has been ingested in quantity probably sufficient to cause poisoning, consider giving gastrointestinal (GI) decontamination. If the patient has already vomited, which is most likely in serious exposures, further efforts at GI decontamination may not be indicated. In significant ingestions, diarrhea and/or vomiting are so constant that charcoal adsorption and catharsis are not indicated.
7. **Observation**. Observe the patient closely for at least 72 hours to ensure that symptoms (sweating, visual disturbances, vomiting, diarrhea, chest and abdominal distress, and sometimes pulmonary edema) do not recur as atropinization is withdrawn. In very severe poisonings by ingested organophosphates, particularly the more lipophilic and slowly hydrolyzed compounds, metabolic disposition of toxicant may require as many as 5-14 days. In some cases, this slow elimination may combine with profound cholinesterase inhibition to require atropinization for several days or even weeks. As dosage is reduced, the lung bases should be checked frequently for crackles. If crackles are heard, or if there is a return of miosis, bradycardia, sweating, or other cholinergic signs, atropinization must be re-established promptly.
8. **Furosemide** may be considered if pulmonary edema persists in the lungs even after full atropinization. It should not be used until the maximum benefit of atropine has been realized. Consult package insert for dosage and administration.

9. **Pulmonary ventilation**. Monitor pulmonary ventilation carefully to forestall respiratory failure even after the patient recovers from muscarinic symptomatology, particularly in poisonings by large ingested doses of organophosphate. In some cases, respiratory failure has developed several days following organophosphate ingestion, and has persisted for days to weeks.
10. **Hydrocarbon aspiration** may complicate poisonings that involve ingestion of liquid concentrates of organophosphate pesticides. Pulmonary edema and poor oxygenation in these cases will not respond to atropine and should be treated as a case of acute respiratory distress syndrome.
11. **Cardiopulmonary monitoring**. In severely poisoned patients, monitor cardiac status by continuous ECG recording. Some organophosphates have significant cardiac toxicity.
12. **Seizure control**. Though rare, convulsions occur despite therapy with atropine and pralidoxime in severe organophosphate poisonings. Make sure that causes unrelated to pesticide toxicity are not responsible, including head trauma, cerebral anoxia, or mixed poisoning. The benzodiazepines (diazepam or lorazepam) are the agents of choice as initial therapy to control convulsions.
13. **Contraindications**. The following drugs are contraindicated in nearly all organophosphate poisoning cases: morphine, succinylcholine, theophylline, phenothiazines, and reserpine. Adrenergic amines should be given only if there is a specific indication, such as marked hypotension.
14. **Re-exposures**. Persons who have been clinically poisoned by organophosphate pesticides should not be re-exposed to cholinesterase-inhibiting chemicals until symptoms and signs have resolved completely and blood cholinesterase activities have returned to at least 80 percent of pre-poisoning levels. If blood cholinesterase was not measured prior to poisoning, blood enzyme activities should reach at least minimum normal levels before the patient is returned to a pesticide-contaminated environment.
15. **Prophylaxis.** Do not administer atropine or pralidoxime prophylactically to workers exposed to organophosphate pesticides. Prophylactic dosage with either atropine or pralidoxime may mask early signs and symptoms of organophosphate poisoning and thus allow the worker to continue exposure and possibly progress to more severe poisoning. Atropine itself may increase the health hazards of an agricultural work setting by causing impaired heat loss due to reduced sweating and impaired ability to operate mechanical equipment due to blurred vision (mydriasis).

Carbamates

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

Toxicology

The inhibition of AchE induced by carbamates is relatively labile. As a result, although symptoms may occur during operational exposure, the patient recovers normally follows once exposure stops. Specific toxicology information on the approved carbamates is as follows:

Bendiocarb

Bendiocarb is a carbamate insecticide with low vapor pressure, low odor and no corrosive and staining properties. This makes it acceptable to most householders. It is rapidly hydrolyzesd in alkaline media (such as whitewash) and rapidly degraded in soil. Like other N-methylcarbamates, bendiocarb is a fast-acting anticholinesterase compound, with high acute oral toxicity.

Toxicology

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

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

Propoxur

Toxicology

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

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

Symptoms of poisoning

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

Emergency Treatment

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

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

Treatment by Medical Professional

Caution: Persons attending the victim should avoid direct contact with heavily contaminated clothing and vomitus. Wear rubber gloves while washing pesticide from skin and hair. Vinyl gloves provide no protection.

1. **Airway protection**. Ensure that a clear airway exists. Intubate the patient and aspirate the secretions with a large-bore suction device if necessary. Administer oxygen by mechanically assisted pulmonary ventilation if respiration is depressed. Improve tissue oxygenation as much as possible before administering atropine to minimize the risk of ventricular fibrillation. In severe poisonings, it may be necessary to support pulmonary ventilation mechanically for several days.
2. **Atropine**. Administer atropine sulfate intravenously or intramuscularly if intravenous injection is not possible. Remember that atropine can be administered through an endotracheal tube if initial IV access is difficult to obtain. Carbamates usually reverse with much smaller dosages of atropine than those required to reverse organophosphates. (See dosage on next page.)

   The objective of atropine antidotal therapy is to antagonize the effects of excessive concentrations of acetylcholine at end-organs having muscarinic receptors. Atropine does not reactivate the cholinesterase enzyme or accelerate excretion or breakdown of carbamate. Recrudescence of poisoning may occur if tissue concentrations of toxicant remain high when the effect of atropine wears off. Atropine is effective against muscarinic manifestations, but is ineffective against nicotinic actions, specifically, muscle weakness and twitching, and respiratory depression.

   Despite these limitations, atropine is often a life-saving agent in N-methyl carbamate poisonings. Favorable response to a test dose of atropine (1 mg in adults, 0.01 mg/kg in children under 12 years) given intravenously can help differentiate poisoning by anticholinesterase agents from other conditions such as cardiogenic pulmonary edema and hydrocarbon ingestion. However, lack of response to the test dose, indicating no atropinization (atropine refractoriness), is characteristic of moderately severe to severe poisoning and indicates a need for further atropine. If the test dose does not result in mydriasis and drying of secretions, the patient can be considered atropine refractory.

3. **Skin decontamination**. In patients with contaminated skin, clothing, hair, and/or eyes, decontamination must proceed concurrently with whatever resuscitative and antidotal measures are needed to preserve life. Flush the chemical from eyes with copious amounts of clean water. For asymptomatic individuals who are alert and physically able, a prompt shower and shampoo may be appropriate for thorough skin decontamination, provided the patient is carefully observed to insure against sudden appearance of poisoning. If there are any indications of weakness, ataxia, or other neurologic impairment, remove the victim's clothing, have the victim lie down, and give the victim a complete bath and shampoo using copious amounts of soap and water. Wash the chemical from skin folds and from under fingernails. Attendants should wear rubber gloves, as vinyl provides no protection against skin absorption.

   Contaminated clothing should be promptly removed, bagged, and laundered before returning. Contaminated leather shoes should be discarded. Note that the pesticide can contaminate the inside surfaces of gloves, boots, and headgear.

Dosage of Atropine:

In ***moderately severe poisoning*** (hypersecretion and other end-organ manifestations without central nervous system depression), the following dosage schedules have proven effective:

- *Adults and children over 12 years:* 2.0-4.0 mg, repeated every 15 minutes until pulmonary secretions are controlled, which may be accompanied by other signs of atropinization, including flushing, dry mouth, dilated pupils, and tachycardia (pulse of 140 per minute). **Warning:** In cases of ingestion of liquid concentrates of carbamate pesticides, hydrocarbon aspiration may complicate these poisonings. Pulmonary edema and poor oxygenation in these cases will not respond to atropine and should be treated as a case of acute respiratory distress syndrome.
- *Children under 12 years:* 0.05-0.1 mg/kg body weight, repeated every 15 minutes until pulmonary secretions are controlled, which may be accompanied by other signs of atropinization as above (heart rates vary depending on age of child with young toddlers having a rate approaching 200). There is a minimum dose of 0.1 mg in children.

Maintain atropinization by repeated doses based on recurrence of symptoms for 2-12 hours or longer depending on severity of poisoning. Crackles in the lung bases nearly always indicate inadequate atropinization and pulmonary improvement may not parallel other signs. Continuation or return of cholinergic signs indicates the need for more atropine.

Severely poisoned individuals may exhibit remarkable tolerance to atropine; two or more times the dosages suggested above may be needed. Reversal of muscarinic manifestations, rather than a specific dosage, is the object of atropine therapy. However, prolonged intensive intravenous administration of atropine sometimes required in organophosphate poisonings is rarely needed in treating carbamate poisoning.

Note: Persons not poisoned or only slightly poisoned by N-methyl carbamates may develop signs of atropine toxicity from such large doses. Fever, muscle fibrillations, and delirium are the main signs of atropine toxicity. If these signs appear while the patient is fully atropinized, atropine administration should be discontinued, at least temporarily, while the severity of poisoning is reevaluated.

4. **Gastrointestinal decontamination**. If N-methyl carbamate has been ingested in a quantity probably sufficient to cause poisoning, consider giving gastrointestinal decontamination as outlined in Chapter 2. If the patient has presented with a recent ingestion and is still asymptomatic, adsorption of poison with activated charcoal may be beneficial. In significant ingestions, diarrhea and/or vomiting are so constant that charcoal adsorption and catharsis are not indicated. Attention should be given to oxygen, airway management, and atropine.
5. **Urine sample**. Save a urine sample for metabolite analysis if there is need to identify the agent responsible for the poisoning.
6. **Pralidoxime** is probably of little value in N-methyl carbamate poisonings because atropine alone is effective. Although not indicated in isolated carbamate poisoning, pralidoxime appears to be useful in cases of mixed carbamate/organophosphate poisonings and cases of an unknown pesticide that present with muscarinic symptoms.
7. **Observation**. Observe patient closely for at least 24 hours to ensure that symptoms (sweating, visual disturbances, vomiting, diarrhea, chest and abdominal distress, and sometimes pulmonary edema) do not recur as atropinization is withdrawn. The observation period should be longer in the case of mixed pesticide ingestion, because of the prolonged and delayed symptoms associated with organophosphate poisoning. As the dosage of atropine is reduced over time, check the lung bases frequently for crackles. Atropinization must be re-established promptly, if crackles are heard, or if there is a return of miosis, sweating, or other signs of poisoning.
8. **Furosemide** may be considered for relief of pulmonary edema if crackles persist in the lungs even after full atropinization. Furosemide should not be considered until the maximum effect of atropine has been achieved. Consult package insert for dosage and administration.
9. **Pulmonary ventilation**. Particularly in poisonings by large doses of N-methyl carbamates, monitor pulmonary ventilation carefully to forestall respiratory failure, even after the patient recovers from muscarinic symptomatology.
10. **Cardiopulmonary monitoring**. In severely poisoned patients, monitor cardiac status by continuous ECG recording.
11. **Contraindications**. The following drugs are probably contraindicated in nearly all N-methyl carbamate poisoning cases: morphine, succinlycholine, theophylline, phenothiazines, and reserpine. Adrenergic amines should be given only if there is a specific indication, such as marked hypotension.
12. **Hydrocarbon** aspiration may complicate poisonings that involve ingestion of liquid concentrates of some carbamates formulated in a petroleum product base. Pulmonary edema and poor oxygenation in these cases will not respond to atropine and should be treated as cases of acute respiratory distress syndrome.
13. **Prophylaxis**. Do not administer atropine prophylactically to workers exposed to N-methyl carbamate pesticides. Prophylactic dosage may mask early symptoms and

signs of carbamate poisoning and thus allow the worker to continue exposure and possibly progress to more severe poisoning. Atropine itself may increase the health hazards of the agricultural work setting, including impaired heat loss due to reduced sweating and impaired ability to operate mechanical equipment due to blurred vision (mydriasis).

Pyrethroids

These modern synthetic insecticides are similar chemically to natural pyrethrins, but modified to increase stability in the natural environment. They are now widely used in agriculture, in homes and gardens, and to treat ectoparasitic disease.

Pyrethroids are formulated as emulsifiable concentrates, wettable powders, granules, and concentrates for ultra low volume application. They may be combined with additional pesticides (sometimes highly toxic) in the technical product or tank-mixed with other pesticides at the time of application.

Toxicology

Certain pyrethroids exhibit striking neurotoxicity in laboratory animals when administered by intravenous injection, and some are toxic when ingested orally. 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. Fatalities have occurred rarely after pyrethroid exposure, usually following ingestion (He et al., 1989).

The most severe toxicity is to the central nervous system, although more uncommon. Seizures have been reported in severe cases of pyrethroid intoxication. 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 paresthesia 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 hands, forearms, and neck are sometimes involved. Sweating, exposure to sun or heat, and applying water increase the disagreeable sensations. Sometimes the effect is noted within minutes of exposure, but a 1-2 hour delay in the appearance of symptoms is more common. Sensations rarely persist more than 24 hours. Little or no inflammatory reaction is apparent where the paresthesia is reported; the effect is presumed to result from pyrethroid contact with sensory nerve endings in the skin. The paraesthesia is not allergic in nature, although sensitization and allergic responses have been reported as an

independent phenomenon with pyrethroid exposure. Race, skin type, or disposition to allergic disease does not affect 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 paraesthesia described above.

Other signs and symptoms of toxicity include abnormal facial sensations, 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.

Specific toxicology for the 5 recommended pyrethroids is described below.

Alpha-cypermethrin

Alpha-cypermethrin is a synthetic pyrethroid.

Toxicology

Absorption may occur to some extent after inhalation or dermal exposure but, as with other pyrethroids, alpha-cypermethrin is rapidly metabolized and excreted from the body.

Mode of action: Neurotoxicity through disruption of nerve fiber impulse transmission.

Cyfluthrin

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

Toxicology

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

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

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

Deltamethrin

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

Deltamethrin is used at dosages of 10-25 mg/m^2 giving a residual effect of 3-6 months. Protective clothing for spraymen should consist of overalls (washed daily), canvas or rubber boots, and hats.

Toxicology

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

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

Etofenprox

Etofenprox is a synthetic non-ester pyrethroid with high vapor pressure and low water solubility. Etofenprox is the insecticide with lowest acute toxicity to mammals of those recommended for indoor residual spraying. It is used as a WP 20 percent formulation, at a dosage of 100-300 mg/m^2 giving a residual effect of 3-6 months.

Toxicology

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

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

Lambda-cyhalothrin

Lambda-cyhalothrin is a synthetic pyrethroid, of the alpha-cyano group, with a core (-CCOOCHCN-), as in alpha-cypermethrin and deltamethrin. Lambda-cyhalothrin has low vapor pressure, is essentially insoluble in water, and has low volatility. It is available in WP formulation and is used at a dosage of 20-30 mg/m^2 giving a residual effect of 3-6 months.

Toxicology

Absorption route: Lambda-cyhalothrin may be absorbed through the gastrointestinal tract, by inhalation, or through the skin. Skin absorption of lambda-cyhalothrin is very low and no systemic effects from skin absorption have been described. Dermal and inhalational exposures usually have mild or no adverse effects. Following substantial ingestion,

patients may develop coma, convulsions, and severe muscle fasciculations, and may take several days and occasionally weeks to recover. No known fatalities have been reported after lambda-cyhalothrin exposure.

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

Symptoms of poisoning

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

Nevertheless, if ingested, these products may produce nausea, vomiting, cough, respiratory distress, and convulsions.

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

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

Treatment by Medical Professional

1. **Skin decontamination.** Wash skin promptly with soap and water. If irritant or paresthesia occurs, 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 paresthesia. They are safe to apply 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 makes the reaction worse.

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. 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.
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.
5. **Seizures.** Any seizures should be treated as outlined in the general principles for management of acute poisoning.

Section 2: General Principles in the Management of Acute 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, remove the victim's clothing, have the victim lie down, and give the victim a complete bath and shampoo using copious amounts of soap and water. Check for pesticide sequestered under fingernails or in skin folds and wash these areas.

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 to the patient. 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 do not provide adequate protection from pesticide contamination.

Airway Protection

Ensure that a clear airway exists. Suction any oral secretions using a large bore suction device if necessary. Intubate the trachea if the patient has respiratory depression or if the patient appears obtunded or otherwise neurologically impaired. Administer oxygen as necessary to maintain adequate tissue oxygenation. In severe poisonings, mechanically supporting pulmonary ventilation for several days may be necessary.

Note on Specific Pesticides: There are several special considerations with regard to certain pesticides. In **organophosphate** and **carbamate** poisoning, adequate tissue oxygenation is essential prior to administering atropine.

Gastrointestinal Decontamination

A joint position statement has recently been released by the American Academy of Clinical Toxicology and the European Association of Poisons Centres and Clinical Toxicologists on various methods of gastrointestinal decontamination. A summary of the position statement accompanies the description of each procedure.

1. **Gastric Lavage.** If the patient presents within 60 minutes of ingestion, lavage may be **considered**. Insert an orogastric tube and follow with fluid, usually normal saline. Aspirate back the fluid in an attempt to remove any toxicant. If the patient is neurologically impaired, airway protection with a cuffed endotracheal tube is indicated prior to gastric lavage. Lavage performed more than 60 minutes after ingestion has not proven to be beneficial and runs the risk of inducing bleeding, perforation, or scarring due to additional trauma to already traumatized tissues. It is almost always necessary first to control seizures before attempting gastric lavage or any other method of GI decontamination. Studies of poison recovery have been performed mainly with solid material such as pills. There are no controlled studies of pesticide recovery by these methods. Reported recovery of material at 60 minutes in several studies was 8 percent to 32 percent. There is further evidence that lavage may propel the material into the small bowel, thus increasing absorption.

Note on Specific Pesticides: Lavage is contraindicated in hydrocarbon ingestion, a common vehicle in many pesticide formulations.

Position Statement: Gastric lavage should not be routinely used in the management of poisons. Lavage is indicated only when a patient has ingested a potentially life-threatening amount of poison and the procedure can be done within 60 minutes of ingestion. Even then, clinical benefit has not been confirmed in controlled studies.

2. **Activated Charcoal Adsorption**. Activated charcoal is an effective absorbent for many poisonings. Volunteer studies suggest that it will reduce the amount of poison absorbed if given within 60 minutes. There are insufficient data to support or exclude its use if time from ingestion is prolonged, although some poisons that are less soluble may be adsorbed beyond 60 minutes. Clinical trials with charcoal have been done with poisons other than pesticides. There is some evidence that paraquat is well adsorbed by activated charcoal. Charcoal has been anecdotally successful with other pesticides.

Dosage of Activated Charcoal:

- *Adults and children over 12 years:* 25-100 g in 300-800 mL water.
- *Children under 12 years:* 25-50 g per dose.
- *Infants and toddlers under 20 kg*: 1 g per kg body weight.

Many activated charcoal formulations come premixed with sorbitol. Avoid giving more than one dose of sorbitol as a cathartic in infants and children due to the risk of rapid shifts of intravascular fluid. Encourage the victim to swallow the adsorbent even though spontaneous vomiting continues. Antiemetic therapy may help control vomiting in adults or older children. As an alternative, activated charcoal may be administered through an orogastric tube or diluted with water and administered slowly through a nasogastric tube. Repeated administration of charcoal or other absorbent every 2-4 hours may be beneficial

in both children and adults, but use of a cathartic such as sorbitol should be avoided after the first dose. Repeated doses of activated charcoal should not be administered if the gut is atonic. The use of charcoal without airway protection is contraindicated in the neurologically impaired patient.

Note on Specific Pesticides: The use of charcoal without airway protection should be used with caution in poisons such as organophosphates, carbamates, and organochlorines if they are prepared in a hydrocarbon solution.

Position Statement: Single-dose activated charcoal should not be used routinely in the management of poisoned patients. Charcoal appears to be most effective within 60 minutes of ingestion and may be considered for use for this time period. Although it may be considered 60 minutes after ingestion, there is insufficient evidence to support or deny its use for this time period. Despite improved binding of poisons within 60 minutes, only one study suggests that there is improved clinical outcome. Activated charcoal is contraindicated in an unprotected airway, a GI tract not anatomically intact, and when charcoal therapy may increase the risk of **aspiration** of a hydrocarbon-based pesticide.

Seizures: Lorazepam is increasingly being recognized as the drug of choice for status epilepticus, although there are few reports of its use with certain pesticides. Emergency personnel must be prepared to assist ventilation with lorazepam and any other medication used to control seizures. See dosage table below. For organochlorine compounds, use of lorazepam has not been reported in the literature. Diazepam is often used for this, and is still used in other pesticide poisonings.

Dosage of Diazepam:

- *Adults*: 5-10 mg IV and repeat every 5-10 minutes to maximum of 30 mg.
- *Children*: 0.2 to 0.5 mg/kg every 5 minutes to maximum of 10 mg in children over 5 years, and maximum of 5 mg in children under 5 years.

Dosage of Lorazepam:

- Adults: 2-4 mg/dose given IV over 2-5 minutes. Repeat if necessary to a maximum of 8 mg in a 12 hour period.
- Adolescents: Same as adult dose, except maximum dose is 4 mg.
- Children under 12 years: 0.05-0.10 mg/kg IV over 2-5 minutes. Repeat if necessary .05 mg/kg 10-15 minutes after first dose, with a maximum dose of 4 mg.

Caution: Be prepared to assist pulmonary ventilation mechanically if respiration is depressed, to intubate the trachea if laryngospasm occurs, and to counteract hypotensive reactions.

Phenobarbital is an additional treatment option for seizure control. Dosage for **infants, children, and adults** is 15-20 mg/kg as an IV loading dose. An additional 5 mg/kg IV

may be given every 15-30 minutes to a maximum of 30 mg/kg. The drug should be pushed no faster than 1 mg/kg/minute.

For seizure management, most patients respond well to usual management consisting of benzodiazepines, or phenytoin and phenobarbital.

Section 3: References

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Annex J: CODEX Maximum Residue Limits

Insecticide use in IRS	Commodity	MRL or EMRL (mg/kg)	Additional Information		Footnote
BENDIOCARB					No MRLs established or prior MRLs revoked
BIFENTHRIN					Residues are not expected to exceed 0.01 mg/kg.
	Barley	0.05	(*)		
	Barley straw and fodder, Dry	0.5			
	Cattle fat	0.5			
	Cattle kidney	0.05	(*)		
	Cattle liver	0.05	(*)		
	Cattle meat	0.5		(fat)	
	Cattle milk	0.05	(*)		
	Chicken eggs	0.01	(*)		
	Chicken fat	0.05	(*)		
	Chicken meat	0.05	(*)	(fat)	
	Chicken, Edible offal of	0.05	(*)		
	Grapefruit	0.05	(*)		Residues are not expected to exceed 0.01 mg/kg.
	Hops, Dry	10			
	Lemon	0.05	(*)		Residues may occur near this level.
	Maize	0.05	(*)		Residues are not

Insecticide use in IRS	Commodity	MRL or EMRL (mg/kg)	Additional Information	Footnote
				expected to exceed 0.01 mg/kg.
	Maize fodder	0.2		
	Maize forage	0.05	(*)	
	Orange, Sweet	0.05	(*)	Residues may occur near this level.
	Pear	0.5		
	Potato	0.05	(*)	Residues are not expected to exceed 0.01 mg/kg.
	Strawberry	1		
	Wheat	0.5	Po	
	Wheat bran, Unprocessed	2	PoP	
	Wheat flour	0.2	PoP	
	Wheat forage (whole plant)	0.2		
	Wheat straw and fodder, Dry	0.5		
	Wheat wholemeal	0.5	PoP	
CYFLUTHRIN	Apple	0.5		
	Cattle milk	0.01	F	The MRL accommodates external animal treatment.
	Cotton seed	0.05		
	Maize	0.05		
	Peppers, Sweet	0.2		
	Rape seed	0.05		

Insecticide use in IRS	Commodity	MRL or EMRL (mg/kg)	Additional Information		Footnote
	Tomato	0.5			
CYHALOTHRIN	Cabbages, Head	0.2			
	Cotton seed	0.02	(*)		
	Cotton seed oil, Crude	0.02	(*)		
	Cotton seed oil, Edible	0.02	(*)		
	Pome fruits	0.2			
	Potato	0.02	(*)		
CYPERMETHRIN	Alfalfa forage (green)	5		dry wt	
	Barley	0.5			
	Beans, Shelled	0.05	(*)		
	Berries and other small fruits	0.5			
	Brassica vegetables	1			
	Cherries	1			
	Citrus fruits	2			
	Coffee beans	0.05	(*)		
	Common bean (pods and/or immature seeds)	0.5			
	Cucumber	0.2			
	Edible offal (mammalian)	0.05	(*)		The MRL accommodates external animal treatment.
	Egg plant	0.2			
	Eggs	0.05	(*)		

Insecticide use in IRS	Commodity	MRL or EMRL (mg/kg)	Additional Information		Footnote
	Kale	1			
	Leek	0.5			
	Lettuce, Head	2			
	Maize	0.05	(*)		
	Maize fodder	5		dry wt	
	Meat (from mammals other than marine mammals)	0.2	(fat)		The MRL accommodates external animal treatment.
	Milks	0.05	F		The MRL accommodates external animal treatment.
	Mushrooms	0.05	(*)		
	Nectarine	2			
	Oilseed, except peanut	0.2			
	Onion, Bulb	0.1			
	Peach	2			
	Peanut	0.05	(*)		
	Peas (pods and succulent=immature seeds)	0.05	(*)		
	Peppers	0.5			
	Plums (including prunes)	1			
	Pome fruits	2			
	Poultry meat	0.05	(*)		
	Root and tuber	0.05	(*)		

Insecticide use in IRS	Commodity	MRL or EMRL (mg/kg)	Additional Information	Footnote
	vegetables			
	Sorghum straw and fodder, Dry	5		
	Soya bean (dry)	0.05	(*)	
	Spinach	2		
	Sweet corn (corn-on-the-cob)	0.05	(*)	
	Tea, Green, Black	20		
	Tomato	0.5		
	Vegetable oils, Edible	0.5		
	Wheat	0.2		
	Wheat straw and fodder, Dry	5		
DDT	Carrot	0.2		
	Cereal grains	0.1		
	Eggs	0.1		
	Meat (from mammals other than marine mammals)	5	(fat)	T
	Milks	0.02	F	
	Poultry meat	0.3		
DELTAMETHRIN	Apple	0.2		
	Beans (dry)	1	Po	
	Brassica vegetables	0.1		
	Bulb vegetables, except fennel, bulb	0.1		
	Carrot	0.02		

Insecticide use in IRS	Commodity	MRL or EMRL (mg/kg)		Additional Information	Footnote
	Cereal grains	2		Po	
	Citrus fruits	0.02			
	Eggs	0.02	(*)		
	Field pea (dry)	1		Po	
	Flowerhead brassicas	0.1			
	Fruiting vegetables, Cucurbits	0.2			
	Grapes	0.2			
	Hazelnuts	0.02	(*)		
	Kidney of cattle, goats, pigs & sheep	0.03	(*)		
	Leafy vegetables	0.5			
	Leek	0.2			
	Legume vegetables	0.2			
	Lentil (dry)	1		Po	
	Liver of cattle, goats, pigs & sheep	0.03	(*)		
	Mandarins	0.02			
	Meat (from mammals other than marine mammals)	0.5		(fat)	The MRL accommodates external animal treatment.
	Milks	0.05		F	
	Mushrooms	0.05			
	Nectarine	0.05			
	Olives	1			

Insecticide use in IRS	Commodity	MRL or EMRL (mg/kg)	Additional Information	Footnote
	Onion, Bulb	0.05		
	Oranges, Sweet, Sour	0.02		
	Peach	0.05		
	Plums (including prunes)	0.05		
	Potato	0.01	(*)	
	Poultry meat	0.1	(fat)	
	Poultry, Edible offal of	0.02	(*)	
	Pulses	1	Po	
	Radish	0.01	(*)	
	Stone fruits	0.05		
	Strawberry	0.2		
	Sunflower seed	0.05	(*)	
	Sweet corn (corn-on-the-cob)	0.02	(*)	
	Tea, Green, Black	5		
	Tomato	0.3		
	Walnuts	0.02	(*)	
	Wheat bran, Unprocessed	5	PoP	
	Wheat flour	0.3	PoP	
	Wheat wholemeal	2	PoP	
ETOFENPROX	Pome fruits	1		
	Potato	0.01	(*)	

Insecticide use in IRS	Commodity	MRL or EMRL (mg/kg)		Additional Information		Footnote
FENITROTHION	Cereal grains	10		Po		
	Meat (from mammals other than marine mammals)	0.05	(*)	(fat)	E	
	Milks	0.002	(*)		E	
	Rice bran, Unprocessed	20		PoP		
	Rice, Polished	1		PoP		
	Wheat bran, Processed	2		PoP		
	Wheat bran, Unprocessed	20		PoP		
	Wheat flour	2		PoP		
	Wheat wholemeal	5		PoP		
MALATHION	Apple	2				
	Asparagus	1				
	Beans (dry)	2				
	Beans, except broad bean and soya bean	1				
	Blueberries	10				
	Broccoli	5				
	Cabbages, Head	8				
	Cereal grains	8		Po		
	Citrus fruits	4				
	Cucumber	0.2				
	Grapes	8				
	Mustard greens	2				

Insecticide use in IRS	Commodity	MRL or EMRL (mg/kg)	Additional Information	Footnote
	Onion, Bulb	1		
	Peach	6		
	Peppers	0.1		
	Raspberries, Red, Black	8		
	Root and tuber vegetables	0.5		
	Spinach	3		
	Spring onion	5		
	Strawberry	1		
	Sweet corn (corn-on-the-cob)	0.02		
	Tomato	0.5		
	Tomato juice	0.01		
	Turnip greens	5		
	Turnip, Garden	0.2		
	Wheat flour	2	PoP	
PIRIMIPHOS-METHYL	Apple	2		
	Brussels sprouts	2		
	Cabbages, Head	2		
	Carrot	1		
	Cauliflower	2		
	Cereal grains	10	Po	
	Cherries	2		
	Citrus fruits	2		

Insecticide use in IRS	Commodity	MRL or EMRL (mg/kg)	Additional Information	Footnote
	Common bean (pods and/or immature seeds)	0.5		
	Cucumber	1		
	Currant, Black	1		
	Dates, Dried or dried & candied	0.5	Po	
	Dried fish	8	Po	
	Eggs	0.05	(*)	
	Gooseberry	1		
	Kiwifruit	2		
	Lettuce, Head	5		
	Meat (from mammals other than marine mammals)	0.05	(*)	
	Milks	0.05	(*)	
	Mushrooms	5		
	Olives	5		
	Peanut	2	Po	
	Peanut oil, Crude	15	PoP	
	Peanut oil, Edible	15	PoP	
	Peanut, whole	25	Po	
	Pear	2		
	Peas (pods and succulent=immature seeds)	0.05	(*)	
	Peppers	1		

Insecticide use in IRS	Commodity	MRL or EMRL (mg/kg)	Additional Information	Footnote
	Plums (including prunes)	2		
	Potato	0.05	(*)	
	Raspberries, Red, Black	1		
	Rice bran, Unprocessed	20	PoP	
	Rice, Husked	2	PoP	
	Rice, Polished	1	PoP	
	Rye wholemeal	5	PoP	
	Spinach	5		
	Spring onion	1		
	Strawberry	1		
	Tomato	1		
	Wheat bran, Unprocessed	20	PoP	
	Wheat flour	2	PoP	
	Wheat wholemeal	5	PoP	
	White bread	0.5	PoP	
	Wholemeal bread	1	PoP	
PROPOXUR				No MRLs established or prior MRLs revoked

Larvicide	Commodity	MRL (mg/kg)	Additional Information		Footnote
METHOPRENE					The MRL accommodates external animal treatment.
	Cattle milk	0.05		F	

Larvicide	Commodity	MRL (mg/kg)	Additional Information		Footnote
	Cereal grains	5		Po	
	Edible offal (mammalian)	0.1			
	Eggs	0.05			
	Maize oil, Edible	0.2	(*)	PoP	
	Meat (from mammals other than marine mammals)	0.2		(fat)	The MRL accommodates external animal treatment.
	Wheat bran, Unprocessed	10		PoP	
	Wheat flour	2		PoP	
	Wheat wholemeal	5		PoP	

Key	
MRL	Maximum Residue Limit
EMRL	Extraneous Maximum Residue Limit
(*)	At or about the limit of determination.
E (only for MRLs)	The MRL based on extraneous residues.
F (for milks)	The residue is fat soluble and MRLs for milk products are derived as explained in "Codex Maximum Residue Limits/Extraneous Maximum Residue Limits for Milk and Milk Products".
(fat) (for meat)	The MRL/EMRL applies to the fat of meat.
Po	The MRL accommodates post-harvest treatment of the commodity.
PoP (for processed foods)	The MRL accommodates post-harvest treatment of the primary food commodity.
T	The MRL/EMRL is temporary, irrespective of the status of the ADI, until required information has been provided and evaluated.
V (for products of animal origin)	The MRL accommodates veterinary uses.

Annex K: Stockholm Convention Questionnaire for Reporting on Production and Use of DDT for Disease Vector Control

Annex III to decision SC-1/25

Format for reporting by each Party that uses DDT for disease vector control pursuant to paragraph 4 of part II of Annex B to the Stockholm Convention on Persistent Organic Pollutants and questionnaire for reporting other information relevant to the evaluation of the continued need for DDT for disease vector control

COUNTRY: _____ **3-year reporting period:**_____ **-** _____

Name of principal reporting official	
Designation	
Agency name and address	
Fax:	
E-mail	
Signature of official	_____ Date: _____

SECTION A: PRODUCTION AND USE OF DDT

A.I. SOURCES OF DDT

In-country production

1. Is DDT produced in your country? YES ☐ NO ☐ (If NO, proceed to question # 4)

2. If YES, please list the DDT production facilities in the country:

No.	Production Facility and Location	Total production capacity (kg)	Net output/yr (kg) Yr. 1	Yr. 2	Yr. 3	Formulation (type & % of active ingredient [a.i.])	% for in-country use
i.							
ii.							
iii.							

3. For each of the production facilities listed above, provide the following:

No.	Facility	Export information				
		Destination country(s)	Quantity/yr (kg) Yr. 1	Yr. 2	Yr. 3	Formulation (type and % a.i.)
i.						
ii.						
iii.						

Import

4. Has DDT been imported into your country over the reporting period? YES ☐ NO ☐. (if NO, proceed to question 6.)

5. If DDT is imported please provide the following:

Country of export	Name of manufacturer	Total net wt of import/yr for the reporting period (kg) Yr. 1	Yr. 2	Yr. 3	Formulation (type & % of a.i.)

Stock information

6. Is DDT repackaged/reformulated in the country? YES ☐ NO ☐ (If NO, please proceed to question 8)

7. If YES, please complete the following table:

Repackaging/ reformulation agency	Description of repackaging (boxed, polythene bagged; description of labeling, etc.)	Formulation (type and % of active ingredient)	Intended end-use	Average annual amount (kg)

8. Please provide the following information on the usable stocks of DDT in your country.

Location	Total amount in storage (kg)	Formulation (type and % a.i.)	Managing authority of facility	Conditions of storage (e.g., storage capacity; access)

A.II. DDT DISPOSAL

9. Do you have obsolete DDT stocks in the country? YES ☐ NO ☐ (If NO, proceed to question 13)

10. If YES, what is the total weight of obsolete DDT stock in the country? (kg):_____
Please tick here ☐ if amount is unknown.

11. Please provide the following information on facilities where obsolete DDT is stored.

Facility and location	Total capacity of storage (kg)	Total amount (kg) of obsolete pesticides in storage at the facility	Amount (kg) and approximate age (yrs) of obsolete DDT component

12. For each storage facility storing obsolete DDT listed in question 11, please complete the following on the storage conditions.

Facility	Storage conditions					
	Housed or open?	Regular inspection? (yes/no). If yes how often?	Adequate security? (yes/no)	Leaky roof? (yes/no)	DDT leaking into environment (yes/no)	Any other comment on human and environmental safety (e.g., need for repackaging)

13. Which agency is directly responsible for DDT disposal? _____

14. Is DDT disposed of in-country? YES ☐ NO ☐

15. If the answer to question 14 is NO, is the obsolete DDT exported? YES ☐ NO ☐. If exported, then indicate destination and intent of export

_____

16. If obsolete DDT is disposed of in-country, then please complete the following table:

Disposal method (Electro-chemical, incineration, etc.)	Facilities using method	Years method has been in use	Disposal capacity/yr (kg)	Amount disposed of/yr (kg)	Cost of disposal (per kg)

A.III. DDT USE

17. What is the total amount of DDT used annually for disease vector control (kg)?

Yr 1:_____ , formulation (type & % a.i.)_____

Yr 2_____ , formulation (type & % a.i.)_____

Yr 3_____, formulation (type & % a.i.)_____

18. Please complete the following table for each disease for which DDT is used:

Disease	Total national population at risk of disease	Disease burden: prevalence rate (a) & mortality rate (b) a	b	% Total national population at risk that is covered by DDT use Yr1	Yr2	Yr3	Main vector species targeted	DDT resistance in target species (Yes, no)	Year resistance was first reported

19. Complete the following table for each disease for which DDT is used (please use additional page as necessary):

Disease	Local areas where DDT is used (e.g., district)	Population size in targeted areas	Disease transmission classification in targeted areas (stable or unstable; if stable, indicate if holo-, hyper-, meso- or hypo-endemic)[a]	Coverage in targeted areas (% of houses) Yr1	Yr2	Yr3	Annual amount of DDT used (kg) Yr1	Yr2	Yr3

[a] See instructions for definitions of endemicity.

A.IV. REGULATION AND CONTROL:

20. Are there laws and/or regulations governing or restricting the purchase and/or use of DDT?

YES ☐ No ☐. If NO, go to question 29

21. If YES, please complete the following table (use additional sheets if need).

Title of relevant law or regulation on DDT	Year it was passed or enacted	List the main objectives of the law or regulation (e.g., Prohibits the use of public transport for transporting of DDT)

22. Please indicate the major limitations with the effective enforcement of existing regulations. (Tick all that apply.)

Inadequate enforcement resources/facilities	Regulations not well understood by enforcement agencies	Inadequate number of trained personnel	Other (please specify)

23. Name the overall managing authority for DDT in the country._____

24. Which agency actually authorizes the use of DDT for disease vector control purposes?
_____

25. Please clarify if the authorizing agency (check all that apply):

- ☐ is directly involved in vector control application of DDT
- ☐ performs supervisory roles
- ☐ has district offices in charge of DDT application in local areas
- ☐ trains field staff (spray operators, inspectors etc.)
- ☐ is involved in public education on safe use of pesticides

26. Please list any other agencies with specialized management roles for DDT:

Agency	Description of role in DDT management

End-use information

27. Do local municipalities use DDT for disease vector control purposes? YES ☐ NO ☐

28. Are there any other agencies (e.g., private agencies, NGOs) involved in using DDT for disease vector control purposes? YES ☐ NO ☐. (If NO, go to question 31).

29. If the answer to question 28 is YES, please complete the following table.

Name of agency	Areas where agency uses DDT (e.g., districts)	Population size covered by agency	Annual amount of DDT used (kg active ingredient)	DDT use related activities carried out by agency		
				Training of sprayers (yes/no)	Community education/ awareness?	Other (specify)

30. For the agencies listed in question 29, provide the following additional information:

Agency	DDT application budget (as % of overall vector control budget)	Total personnel & person hours expended per application cycle			Annual population coverage		
		Yr.1	Yr. 2	Yr. 3	Yr. 1	Yr. 2	Yr.3

31. What is the average cost per house sprayed with DDT (including labor and other operational costs)?
Local currency _____ current equivalent in US$_____

32. How would you rate the general acceptance / refusal of DDT for indoor-application by the households (please tick as appropriate)?

	Provide calculated rate if available	Estimated rate (if calculated rate is not available)				
		Very Low (1)	Low (2)	(3)	High (4)	Very high (5)
Refusal rate						
Re-plastering rate						

33. If the acceptability of indoor application of DDT is low, what are the reasons given for the lack of acceptance by the households (please tick all that apply)?

Inconvenient - moving furniture etc.	Unpleasant smell of DDT	Dislike for white residues on walls	Reluctance to provide access to strangers (sprayers)	Timing of spraying inappropriate	Other (specify)

34. Is DDT application limited to certain house types or households? YES: ☐ NO: ☐. If YES, please indicate the house types targeted (e.g., traditional houses, western-type houses)

_____

35. What are the criteria for selecting a geographical area or community for DDT indoor application?

_____

_____

36. Who determines the timing of DDT application at the local level?

_____

37. What factors determine the timing of the DDT application cycle? _____

_____

38. How many DDT application cycles are there in a year? ONE ☐_ TWO ☐ OTHER?

_____

39. How long does an application cycle take (time – in days or hrs)? _____

Resistance monitoring

40. What bioassay test procedure(s) is used for detecting DDT resistance? _____

_____

41. Please complete the following table on vector susceptibility to DDT according to WHO susceptibility test[22].

Disease	Main vector species	Minimum mortality %	Maximum mortality %	Year last tested	Specific geographical areas associated with test, if any

42. Please provide the following information on insecticide residual efficacy according to the WHO standard bioassay test).[23] (If no information is available for the reporting period, please provide the most recent data.)

(a) DDT bioassay results by month: yr1

Month 1_____

Month 4_____

Month 8_____

Month 12_____

(b) DDT bioassay results by month: yr2

Month 1_____

Month 4_____

Month 8_____

Month 12_____

[22] Mortality after 24-hour holding period of mosquito specimens exposed to diagnostic concentration (4 per cent DDT) for 1 hour

[23] 24-hour holding period mortality of vector strains of known DDT susceptibility exposed for 1 hour to a DDT-sprayed surface (75 per cent WP)

(c) DDT bioassay results by month: yr3

Month 1_____

Month 4_____

Month 8_____

Month 12_____

43. Briefly describe the surveillance mechanism(s) in the country for monitoring DDT resistance (Include the number & location of sentinel sites, if any):

_____

_____

_____

_____

_____

_____

SECTION B: DDT ALTERNATIVES (INSECTICIDES, METHODS, AND STRATEGIES)

B.I.: DDT ALTERNATIVES

44. Please complete the following tables for DDT alternatives that are in use:

Alternative control category	Method or chemical used	Disease targeted	Annual use (kg of active ingredient or quantity as applicable)	Target population (%)	Accept-ability[a]	Annual budget (US$) (and as % of vector control)	Unit cost[b]
Biological control (e.g., bacteria)							
Chemical control & related strategies (e.g., insecticide-treated nets, pyrethroids)							
Environ-mental control (e.g., source reduction)							

[a]End-user refusal rate (Rt) and/or use rate (Ut), indicate as appropriate

[b] As appropriate. e.g., unit cost of ITN or cost of chemical application per house

45. Complete the following table on sources of the alternative options listed above, as applicable:

Alternative category	Biological or chemical product used	Source (Import/local)	Formulations (as applicable)	Annual import (kg active ingredient)	Managing authority
Biological control					
Chemical control					

46. Complete the following table on the disposal relating to the alternative options listed:

Alternative category	Biological or chemical product used	Total national stock (kg or quantity, as applicable)	Total obsolete stock (kg or quantity, as applicable)	Disposal method used	Annual disposal cost (US$)	Agency responsible for disposal
Biological control						
Chemical control						

47. Provide information on vector resistance to any of the insecticides listed previously as DDT alternatives in use:

Disease	Vector species	Insecticide tolerance or resistance reported in the country (indicate region/area of country associated with report)	Year of first report

48. Complete the table on other DDT alternative(s) that have been considered for use or have been used in the country in the past but are not used any more:

Alternative control category	Method or product used & mode of application	Disease targeted	Reason why the use of the method/product was rejected or stopped
Biological control			
Chemical control & related strategies (e.g., insecticide-treated nets)			
Environmental control			

Main vector(s) susceptibility to insecticide (DDT alternatives listed)

49. For the alternative insecticides in use, please indicate for the targeted vector species, the minimum & maximum mortality rates using the standard (discriminating/diagnostic) insecticide concentration.

Disease	Vector species	Insecticide 1: …… …… Mortality		Insecticide 2: …… …… Mortality		Insecticide 3 …… Mortality		Insecticide 4: …… …… Mortality		Insecticide 5: …… …… Mortality	
		Min %	Max %	Min %	Max %	Min %	Max %	Min %	Max %	Min %	Max %
Year last tested											

Insecticide residual efficacy (for each insecticide listed above) Please provide information on insecticide residual efficacy according to the WHO bioassay test.[24] (If no information is available for the reporting period, please provide the most recent data.)

50. Insecticide name: _____

Please provide the following information on insecticide efficacy:

(a) Insecticide bioassay results by month: yr1

Month 1_____

Month 4_____

Month 8_____

Month 12_____

[24] 24-hour holding period mortality of vector strains of known susceptibility exposed for 1 hour to an insecticide-sprayed surface.

(b) Insecticide bioassay results by month: yr2

Month 1_____

Month 4_____

Month 8_____

Month 12_____

(c) Insecticide bioassay results by month: yr3

Month 1_____

Month 4_____

Month 8_____

Month 12_____

B.II. DISEASE MANAGEMENT STRATEGIES

51. Is there a national vector control policy? YES ☐ NO ☐

52. Is the country implementing an integrated vector management (IVM) strategy? YES ☐ NO ☐

53. If yes, please list the component parts of the IVM for the diseases listed in this report:

Disease	Annual budget (US$)	Vector control component	% of overall budget	Major limitation to implementation

54. Please indicate the vector resistance management strategy employed. _____
_____
_____

55. Provide any information on the entomology laboratories available in country. For each laboratory, indicate if it is adequately equipped to carry out insect resistance testing and related functions. If not, please indicate (quantify if possible) the limitations faced. _____
_____
_____

56. Is there research into the development of locally appropriate alternative intervention options to DDT?
YES ☐ NO ☐

57. If the answer to question 56 is YES, please complete the following table

Type of research on DDT alternative	Institution leading the research	Year initiated

SECTION C: GENERAL HUMAN AND ENVIRONMENTAL SAFETY ISSUES

58. Has there been any insecticide incident(s) in relation to vector control with generalized human exposure &/or environmental release of INSECTICIDES in the country (e.g., road accidents, spills)? YES ☐ NO ☐

59. If the answer to question 58 is yes, please complete the following table:

Incident Number	Insecticide (DDT & other)	Details of exposure or environmental release			
		Date	Place	Quantity released	Estimated number of people exposed
I					
ii					
iii					
iv					

60. Please complete the following table for the incidents listed in question 59.

Incident number (Question 59)	Details of exposure or environmental release			
	Caused of incident (e.g., Road accident during transport)	Remedial actions taken	Agency undertaking remedial action	Safeguards employed to prevent future incidents
i				
ii				
iii				
iv				

61. Which agency(ies) is(are) responsible for assessing the risks posed by the use of insecticides for public health?

_____

_____

62. Is there a program to raise awareness among communities and households on safety issues relating to insecticide use in disease vector control? YES ☐ NO ☐

63. If YES, who implements the program and what public education method(s) are used?

_____

_____

SECTION D: SYSTEMS STRENGTHENING IN DISEASE VECTOR CONTROL

64. Targets for relevant trained personnel in the national disease vector control program (by category):

Category of personnel	Level of training (PhD, Master, Bachelor)	Present staffing levels (number)	Targeted staffing level
Technical (e.g., management, planners)			
Operational (e.g., sprayers, sanitarians, mosquito collectors)			
Other (please list)			

65. What is the overall budget for disease vector control_____ (US$). Also indicate as a percentage of the national health budget_____

66. What is the budget shortfall (US$) for vector control (percentage)? Yr.1_____ Yr. 2_____ Yr. 3_____

67. Give the proportion of the annual budget mobilized in-country _____and externally_____.

68. List the facilities in the country providing training in disease vector control.

Training facility	Specialization (vector biology, entomology etc.)	Training level provided (degree or other)	Annual output

69. Provide details on the in-service training programs available, especially at the regional and district levels.

_____
_____
_____

70. Do formal mechanisms exist for inter-sectoral collaboration in disease vector control?
YES ☐ NO ☐

If the answer is YES, please complete the following table (tick as appropriate).

Policy on inter-sectoral collaboration	Inter-sectoral committee/board at national level	Inter-sectoral committee at district level	Joint planning (indicate if national, provincial, district etc.)	Joint implementation of activities

71. If the answer to question 70 is NO, what are the limitations to developing such mechanisms?

_____
_____
_____
_____

72. What are the limitations to the monitoring and evaluation of vector control programs?

_____
_____
_____

and how can they be best overcome?

_____
_____
_____
_____

73. Please provide any other general information relevant to your country's situation with regards to vector borne diseases and their control:

_____
_____
_____

Annex L: Public Comments Received

Michael Macdonald

Lusaka

22 March 2006

Dear Colleagues,

I did a quick read through the PEA and made some specific comments as listed below.

But overall I feel I am missing a discussion on some important strategic issues such as resource allocation between rural malaria control and treatment services and urban IRS; about the intense systems support needed for IRS (there is one way to do IRS correctly and a thousand ways it can go wrong); and the relation between IRS and ITNs (I see ITNs as a 'safety net' for when the IRS does not deliver and as an 'exit strategy', i.e., with IRS as the malaria transmission rates go down, and ITN coverage goes up, and surveillance systems are strengthened, there will come a point, hopefully sooner than later, that IRS can be withdrawn in favor of IVM (ITNs and environmental management).

I don't have my books with me here, but you should look at the Kampala conference from the mid 1950s. They feared implementing IRS in endemic areas because of the loss of immunity and potential for subsequent epidemics. They did not have ITNs; we do.

And so I think it very important to highlight – as we have been trying to do for a couple of years now, that ITNs and IRS are not an 'either/or' decision. Both must be used. So these are just some general comments on the substance of the PEA.

In terms of formatting it is very, very long and I wonder if some of the sections could be combined (e.g., individual insecticides are discussed in at least three different sections) or shortened.

Specific Comments

Page 14. I would remove the phrase "with hopes diminished that ITNs alone could solve the malaria problem." Sometimes "ITNs alone" are the only measure possible: it is not a question of 'hopes diminished.' I think there is a basic misunderstanding of the meaning of IVM. To me the cardinal point of IVM is to "build capacity at the operational level (the district or municipality) to plan, implement, monitor and evaluate vector control and its epidemiological and entomological impact." To that end, I would elevate the third bullet " methods bases on local knowledge" to the top, and rephrase it something like I have just written, rather than 'based on local knowledge of factors influencing vector

biology, disease transmission, and morbidity" (what about mortality?). This also points to IVM as a 'systems' issue and not just a 'commodity' issue. I see later on Page 15 you do talk about the 'management' aspect – but I think that should be highlighted in the bullets for those who just skim the document!

"Engagement with Local Communities" is a bit vapid. I would just expand the "collaboration with other public and commercial sector organizations, civil society groups, and the communities themselves (such as those involved with irrigated agriculture and urban development) to reduce vector breeding, and to adopt more rational and cost effective control measures.

Pg 32. The alphacypermethrin question. I understood that the reason alphacyperemethrin was not registered in the US was that it was off-patent and nobody (including BASF, the maker of Fendona) wanted to spend the money to register it. Maybe ask John Thomas at BASF to comment. Although not as 'user friendly' as the other pyrethroids, Fendona is widely used.

Bendiocarb – Can you explain why registration was lost? Was it just that the manufacturer did not want to 'renew the subscription' or were there new toxicology findings?

Cyfluthrin – I don't know if we want to get into the commercial aspects, but my understanding is that BAYER is no longer promoting Cyfluthrin for mosquito control (as their Deltamethrin is a superior product).

Pg. 38 Deltamethrin - Check the typos, I think you want to say "ultra-low" not "ultra-light" (sounds like one of them yuppie beers).

Pg. 40 Permethrin – Why this is the only one to have a chemical name? I would delete to be consistent with the others. Also, as with all the chemical names in this section – do you also want to include the more common trade names?

Pg. 43. The document states: "Alpha-cypermethrin interferes with the way the nerves and brain normally function." So does yuppie beer. I just did a quick PubMed and found this recent paper:

Toxicol Appl Pharmacol. 2005 Jul 25; "Structure-activity relationships for the action of 11 pyrethroid insecticides on rat Na(v)1.8 sodium channels expressed in *Xenopus* oocytes." Choi JS, Soderlund DM., Department of Entomology, New York State Agricultural Experiment Station, Cornell University, P. O. Box 462, Geneva, NY 14456, USA.

Pyrethroid insecticides bind to voltage-sensitive sodium channels and modify their gating kinetics, thereby disrupting nerve function. This paper describes the action of 11 structurally diverse commercial pyrethroid insecticides on the rat Na(v)1.8 sodium channel isoform, the principal carrier of the tetrodotoxin-resistant, pyrethroid-sensitive sodium current of sensory neurons, expressed in *Xenopus laevis* oocytes. All 11 compounds produced characteristic sodium tail currents following a depolarizing pulse

that ranged from rapidly-decaying monoexponential currents (allethrin, cismethrin and permethrin) to persistent biexponential currents (cyfluthrin, cyhalothrin, cypermethrin and deltamethrin). Tail currents for the remaining compounds (bifenthrin, fenpropathrin, fenvalerate, and tefluthrin) were monoexponential and decayed with kinetics intermediate between these extremes. Reconstruction of currents carried solely by the pyrethroid-modified subpopulation of channels revealed two types of pyrethroid-modified currents. The first type, found with cismethrin, allethrin, permethrin and tefluthrin, activated relatively rapidly and inactivated partially during a 40-ms depolarization. The second type, found with cypermethrin, cyfluthrin, cyhalothrin, deltamethrin, fenpropathrin and fenvalerate, activated more slowly and did not detectably inactivate during a 40-ms depolarization. Only bifenthrin did not produce modified currents that fit clearly into either of these categories. In all cases, the rate of activation of modified channels was strongly correlated with the rate of tail current decay following repolarization. Modification of Na(v)1.8 sodium channels by cyfluthrin, cyhalothrin, cypermethrin and deltamethrin was enhanced 2.3- to 3.4-fold by repetitive stimulation; this effect appeared to result from the accumulation of persistently open channels rather than preferential binding to open channel states. Fenpropathrin was the most effective compound against Na(v)1.8 sodium channels from the perspective of either resting or use-dependent modification. When use dependence is taken into account, cypermethrin, deltamethrin and tefluthrin approached the effectiveness of fenpropathrin. The selective expression of Na(v)1.8 sodium channels in nociceptive neurons suggests that these channels may be important targets for pyrethroids in the production of paresthesia following dermal exposure.

Pg. 43. DDT “banned… mainly due to its persistence in the environment” I would add the phrase “ and enormous volumes used in agriculture.” Also explain better “except in accidental exposures” this is ambiguous – you mean like eating a kilogram? Better explain how much was the accidental exposure

Pg. 45 Fenitrothion – The PEA states: “At sufficient exposure levels, typical symptoms of cholinergic poisoning may occur.” Again this is ambiguous. It is my understanding that IRS programs using fenitrothion (and to a lesser extent malathion) should conduct weekly cholinesterase levels on the spraymen.

Pg 54 Disposal. Also include incineration of unused pesticide and empty containers

Pg. 55 Storage – Maybe this comes later in the document, but there are very specific guidelines for storage facilities.

Page 58 The PEA states “…estimates of exposure to pesticides based on common or projected IVM practices in African countries.” I think you could rather say “experiences in countries where IRS has been conducted” – we have a lot experience from the Americas, South and Southeast Asia on pesticide exposure in both public health and agriculture

Pg 61 Typo – left out the year for the ITN PEA.

Pg 64. Not sure if this will make a difference in the later calculations, but the 35.8 m2 of sprayable surface is extremely low. In Zambia we calculate 90m2 for "informal" houses and 180m2 for "formal."

Pg 96 Effect on non-target organisms. This is good, but could be more direct. When we talk about "birds" a major concern is domestic chickens who may eat insects killed by the spraying, and when we talk of "animals" we often think of domestic cats who rub against the walls and then lick themselves clean.

Pg 106 Can we insert "and IRS" into the phrase "environmental management generally has greater impact and costs less per person in urban than in rural areas."

Pg. 108: The Pakistan case study. Great you are using this. Maybe you could call Richard Baker or some else directly involved with this to get more information (Andy?). As I recall, the malathion 'cracked' to become iso-malathion, which could not be detoxified by the liver. For me, one of the lessons was that the malathion purchased was generic and possibly of substandard quality to begin with. I don't think the severe poisoning and deaths would have happened with regular malathion – likewise I don't think we can claim: "Had the mitigation practices recommended in this PEA been planned for and implemented during the program, the poisoning would have been avoided." They were spraying, unknowingly, a very toxic chemical.

Pg 111 I would be cautious in saying that IRS is operationally homogenous. Some chemicals are more problematic than others: e.g., DDT or the O.P.s I am surprised there is nothing about cholinesterase monitoring.

Pg. 114 "Transport of rinsed packaging materials to power plant or cement kiln"—This is a very important element—I hope there are more details later in the PEA.

Pg 132 Organizations: do you want to add groups such as 'Croplife' http://www.croplife.org/ who may be beneficial in applicator training and pesticide storage? And no offense, but I would not include GFATM in this list of technical support agencies – rather someone like FAO or UNEP.

Pg 133. The one-day training of contractors and two-day training for senior officials: is there anything currently available? If so, please reference.

Pg. 136. There has been some confusion recently on the European Union MRLs – check on this to see who has the responsibility of testing – is it the importing country in Europe, or the malaria endemic country with the IRS program?

Pg. 137. Mosquito resistance. I think you could give much more specific (and interesting) information on resistance – request a couple of paragraphs from WHO, Liverpool, or MRC in Durban. A couple of important points. First, there is a nascent resistance-monitoring network through WHOPES. Second, ITNs may still be effective in the presence of KDr resistance in west Africa, but IRS failed in the presence of mono-oxygenase in South Africa. Finally, maybe say a word about pesticide resistance management.

Pg 139 Prevention vs. treatment. This section seems out of place and I would just drop it or blend it in somewhere near the beginning of the document. The term “coordination-challenged” is a new one, and rather offensive. I would just drop the entire section.

Pg. 141 – Check those dates

That’s all for now.

All the best for the next steps in completing this important document.