Malaria Indoors Residual Spraying (IRS)

Supplemental Environmental Assessment for Presidential Malaria Initiative—Indoor Residual Spraying (IRS) for Malaria Control in Mali

March 2008

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Supplemental Environmental Assessment for Presidential Malaria Initiative—Indoor Residual Spraying (IRS) for Malaria Control in Mali

Contract GH-I-00-06-00002-00

Prepared for
Global Health Bureau
United States Agency for International Development

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The author's views expressed in this publication do not necessarily reflect the views of the United States Agency for International Development or the United States Government.

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SUPPLEMENTAL ENVIRONMENTAL ASSESSMENT FOR
PRESIDENITAL MALARIA INITIAVE- INDOOR RESIDUAL SPRAYING (IRS) FOR MALARIA CONTROL IN MALI

PROGRAM/ACTIVITY DATA:

Program/Activity Number: GH-I-00-06-00002-00
Country/Region: Mali, Africa Bureau, West Africa (229-2130-4177 Room 325)

Program/Activity Title: Mali High Impact Health Services
SO6

Sub-activity: IRS Pilot Program for Malaria Control in Mali (Bla and Koulikoro Cercles)

Funding Begin: FY08 Funding End: FY08
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SEA Prepared By: Jeanne Chabrier and Tito Kodiaga, RTI International

Current Date: April 22nd , 2008

IEE Amendment (Y/N): Y

Filename & date of original IEE:

ENVIRONMENTAL ACTION RECOMMENDED: (Place X where applicable)

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

ADDITIONAL ELEMENTS: (Place X where applicable)

CONDITIONS: _X__ PVO/NGO: ____

Other Relevant Environmental Compliance Documentation: This IEE references the following USAID environmental compliance documentation that is already in effect for ongoing activities globally under USAID:

Integrated Vector Management for Malaria Vector Control: Programmatic Environmental Assessment: 03/2007

SUMMARY OF FINDINGS

In late June 2005, the United States Government (USG) announced a new five-year, $1.2 billion initiative to rapidly scale up malaria prevention and treatment interventions in high-burden countries in sub-Saharan Africa. The goal of this Initiative is to reduce malaria-related mortality by 50% after three years of full implementation in each country. This will be achieved by reaching 85% coverage of the most vulnerable groups---children under-five years of age, pregnant women, and people living with HIV/AIDS---with proven preventive and therapeutic interventions, including artemisinin-based combination therapies (ACTs), insecticide-treated bed nets (ITNs), Long Lasting Insecticide Nets (LLINs) intermittent preventive treatment of pregnant women (IPTp), and indoor residual spraying (IRS).

In implementing PMI, the U.S. Government is committed to working closely with host governments and within existing national malaria control plans. Efforts will be coordinated with other national and international partners, including the Global Fund to Fight AIDS, Tuberculosis, and Malaria (GFATM), Roll Back Malaria (RBM), the World Health Organization (WHO), United Nations Children's Fund (UNICEF) the World Bank Malaria Booster Program, and the non-governmental and private sectors, to ensure that investments are complementary and that RBM and Millennium Development goals are achieved. Country assessment and planning visits for PMI, as well as subsequent evaluations, will be highly consultative and held in collaboration with the PNLP and other partners.

As part of PMI, the United States Agency for International Development (USAID) proposes to implement a pilot Indoor Residual Spraying (IRS) program in Mali for malaria vector control during the 2008 spray season. USAID is obligated to comply with the Code of Federal Regulations Title 22 Section 216 (22 CFR 216). 22 CFR 216 mandates that detailed pesticide procedures are addressed prior to direct or indirect support of pesticide use. This document fulfills this legal obligation. Additionally, this document seeks to fulfill the Environmental Impact Assessment requirements of the government of Mali. This document relies heavily upon USAID's Integrated Vector Management for Malaria Vector Control: Programmatic Environmental Assessment (PEA), the primary resource for providing guidance for IRS implementation that maximizes the safety of workers and beneficiaries and minimizes environmental contamination. (PEA, 2007)

The pilot IRS program in Mali will use lambda-cyhalothrin, one of the World Health Organization (WHO) recommended IRS insecticides, but that is not yet registered for use by the Government of Mali. The insecticide is currently in the process of being registered by the Government of Mali through a request for a waiver from the Ministry of Health to the Ministry of Agriculture in order to fast track this matter. The IRS program will be targeted in the cercles (district) of Koulikoro and Bla. Approximately 430,000 persons comprise the target spray population in Mali. The malaria transmission season is dependent on when the rainy season starts, which is in June and can extend to October during the year. The spraying season intends to start shortly before the first rains start in mid June.

A negative determination with conditions is recommended for this project. The conditions are that USAID, USAID contractors, and the MOH implement the risk reduction actions outlined in the Environmental Management Plan (EMP). USAID will discuss the compulsory nature of EMP implementation with the MOH; and the development of a Memorandum of Understanding between RTI and MOH assigning roles and responsibilities for these risk reduction actions.

This SEA addresses two insecticides considered for IRS in Mali: Lambda-cyhalothrin (CS) commonly know as ICON and Ficum also known as Bendiocarb. However, through several small scale experiments conducted in Mali by the Ministry of Health and the Malaria Research Training Institute (MRTC). This study has recommended that Lambda-cyhalothrin will be the first choice for the first round of IRS, however during other consequent spray rounds other insecticides mentioned could be considered for use.

However, if pesticide not addressed in this document is proposed for use, USAID will require an additional SEA or SEA amendment that takes into account subsequent IRS campaigns of that pesticide.

As required by USAID's Automated Directives System (ADS) 204.5.4, the USAID/Mali Health Team will actively monitor ongoing mitigation and training activities for compliance with the recommendations in this SEA, and modify or end activities that are not in compliance.

APPROVAL OF ENVIRONMENTAL ACTION RECOMMENDED

CLEARANCE:
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List of Acronyms

ANC Antenatal care
AQ/SP Amodiaquine/sulfadoxine-pyrimethamine
ARV/ART Anti-retroviral/therapy
ASACO Association de santé Communautaire (Community health association)
ATN Assistance Technique Nationale (National Technical Asssistance)
BCC/IEC Behavior change communication/information education communication
CCM Country Coordinating Mechanism
CDC Centers for Disease Control and Prevention
CHV/*Relais* Community Health Volunteer
CILSS (Comité Inter-Etats de Lutte contre la Secheresse au Sahel)
CI Conseil Interministériel (Inter-Ministerial Consultation)
CC Comité Consultatif (Consulting Committee)
CNGPLe Comité National de Gestion des Pesticides (National Committee on the Management of Pesticides)
CSCOM Centre de santé communautaire (Community Health Center)
CSHGP Child Survival and Health Grants Program
CSREF Centre de santé de référence (Reference/District Health Center)
CropLife Mali - l'Association des Distributeurs de Produits Agropharmaceutiques
DDT Dichloro-diphenyl-trichloroethane DHS Demographic and Health Survey
DHPS Division Hygiène Publique et Salubrité (Division of Public Hygiene and Healthiness)
DNA - Direction Nationale de l'Agriculture
DNS Direction Nationale de la Santé (National Health Directorate)
DNACPN - Direction Nationale de l'Assainissement et Contrôle des Pollutions et des Nuisances (National Directive of Public Health and Pollution Prevention)
EIA l'Evaluation de l'Impact Environnemental (Environmental Impact Assessment)
EPI Expanded Program on Immunization (Programme Elargi de Vaccination)
ESR Epidemic Surveillance and Response
FENASCOM Fédération Nationale des Associations de Santé Communautaire (National Federation of Community Health Associations)
GFATM Global Fund to Fight AIDS, Tuberculosis, and Malaria
GOM Gouvernement du Mali (Government of Mali)
HBM Home-based management
INRSP Institut Nationale de Recherche en Santé Publique (National Institute of Public Health Research)
IPTp Intermittent preventive treatment of pregnant women
IRS Indoor residual spraying
ITN Insecticide-treated bed net
LBMA Laboratoire de Biologie Moléculaire Appliquée (Applied Molecular Biology Laboratory)
LLIN Long-lasting insecticide-treated bed net (Moustiquaires Imprégnées d'insecticide de longue duree)
LNS - Laboratoire National de la Santé
MCH Maternal and child health (Sante Maternelle et Infantile)
MOH Ministry of Health
MIP Malaria in pregnancy
OPV L'Office de la Protection des Végétaux (Bureau of the Protection of Vegetables)
ORIAM Réseau des Opérateurs d'Intrants Agricoles du Mali
PNPE - Politique Nationale de Protection de l'Environnement (National Agency for the Protection of the Environment)
PDDSS - Plan Décennal de Développement Socio Sanitaire
DPLM –Division Prévention et Lutte Contre la Maladie (Division of Prevention and Disease Control)
PRODIMAL - Société de Fabrication de Produits Insecticides
STP Secrétariat Technique Permanent

MS Ministère de la Santé
SODEMA- la Société de Détergent du Mali
SMPC Société malienne de Produits Chimiques
UEMOA- Union économique et monétaire ouest-africaine

Acknowledgements

The contents of this document was researched between the dates of the 1st of February to the 15th of February 2008, with the consultation and advice from many stakeholders in the IRS activities. The most prominent preoccupations existent during the time of research was:

- The necessity to follow national environmental regulation
- The impact on the agricultural practices in the region
- The impact on the flora and fauna of the River Niger and its tributaries

The following individuals and institutions have been consulted and their comments and preoccupations regarding IRS activities have been included in this document.

1. Mr. Farota , technical advisor , Ministry of Environment
2. Mr. Demba Sedibe, (focal point person for Ministry of Environment)
3. Mr. Sixte Zigirumugabe (PMI Country Coordinator /Malaria Advisor)
4. Christine Sow (Health Team Leader, USAID)
5. Dr. Sitan Traore, Entomologist PNLP, Ministry of Health
6. Dr. Mamadou Coulibaly, MRTC
7. Dr. Mamadou Diakite, MRTC
8. Mr. Abdramane Sidibe, Ministry of Agriculture, Legislative Division and Phytosanitary Monitoring
9. Mr. Sidi Sumare, technician, statistician, Direction of Planification/ Statistics, Koulikoro
10. Mr. Mohamed El Bechir Simpara, Regional Directive of Public Health and Pollution Prevention, Koulikoro
11. Mr. Gouro Samba Boko, Regional Directive of Public Health and Pollution Prevention of Bla
12. Dr. Moussa Traore, Chief Doctor, Cercle of Bla
13. African Program for the Elimination of Obsolete Pesticides (PASP-Mali)
14. Dr. Amadou Diarra, Departement of Agricultural Products and Regulations, Sahelian Committe on Pesticides, Permanent Secretary, Sahel Institute (INSAH)
15. Dr. Cheikh Hamallah SyllaSpecialist in the Management of Obsolete Pesticides, In charge of Operations, African Program for the Elimination of Obsolete Pesticides (PASP-Mali)
16. Dr. Massambou Sacko, Advisor in charge of the Program to combat Diseases, WHO, United Nations
17. Cheickne Sidibe, Agricultural Engineer, Director, Regional Directive of Public Health and Pollution Prevention, Ministry of the Environment and Public Health
18. Aliou Doumbia, Financial and Administrative Manager, African Program for the Elimination of Obsolete Pesticides (PASP-Mali)
19. Dr. Mamadou Camara, Specialist in Prevention and in charge of Communications, African Program for the Elimination of Obsolete Pesticides (PASP-Mali)
20. CILSS
21. National Directive of Public Health and Pollution Prevention Conservation de la Nature, Koulikoro

Executive Summary

This executive summary provides an overview of the Supplemental Environmental Assessment (SEA) for the proposed Indoor Residual Spraying (IRS) intervention to combat Malaria in Mali.

The SEA follows the Terms of Reference (ToR) developed by the RTI EA specialists and provided for review and approval by the Comite technique d'analyse environnementale (equivalent of a Malien Environmental Agency, part of the Ministry of Environment). The SEA was prepared by RTI staff from Washington DC with the public consultation process undertaken by the Malaria Research and Training Center (MRTC), based in Bamako Mali. Work on the SEA started in February 2008. The assessment considered baseline conditions, operation and closure phases for the project.

As required by the ToR, the SEA process included the following steps: (i) Identify the environmental and socio-economic resources potentially affected by the project; (ii) Predict positive and negative effects and the extent to which positive effects can be enhanced and negative effects mitigated; (iii) Quantify and assess the significance of effects where possible; (iv) Consider the need to compensate for any significant residual negative effects; and (v) Identify methods to mitigate and monitor resources that may be affected by the project.

Introduction and Study Objectives

The Government of Mali National Malaria Control Program (PNLP) and the President's Malaria Initiative (PMI) propose a pilot IRS program in the cercles of Bla and Koulikoro to determine the feasibility and desirability of IRS in Mali as a major public health intervention. Research Triangle Institute (RTI) International, a USAID contractor, is responsible for providing substantial technical assistance to the National Malaria Control Program (PNLP) and Koulikoro and Bla cercle's Community Health Centers (CSCOM) to plan and implement the pilot IRS program. Major components of program implementation that will be supported by PMI through RTI include:

- Purchase of insecticide, spraying equipment, and adequate amounts of personal protective clothing and equipment for staff;
- Financial support for trainers and spray teams;
- Technical advisors to plan the program, train field staff, and supervise field operations;
- Information, Education and Communication (IEC) campaigns to inform beneficiaries, raise public awareness, promote behavior change and promote cooperation;
- Financial support for renting a storage facility for the insecticide, empty sachets, spray and cleaning equipment; and
- Additional human health and environmental safety components as described in the Environmental Management Plan (EMP).

The pilot IRS program will utilize Lambda cyhalothrin, an insecticide recommended for IRS use in Malaria control by the World Health Organization (WHO), and currently in the process of being registered in Mali. The Programme National de la Lutte contre le Paludisme (PNLP) has requested that PMI support IRS in rural areas of Koulikoro and Bla cercles in the Southern parts of Mali, where malaria transmission is stable and endemic. It is expected that spray operations will cover a population of approximately 430 000.

Project Potential Adverse Impacts

The potential negative health impacts of the intervention include transitory, acute health impacts on the local population, targeted beneficiaries and spray operators including the entire spray team as a result of unintentional pesticide exposure. The acute health impacts could arise from ingestion, inhalation, dermal or eye exposure. Exposure leading to adverse human and environmental impacts could occur during the transportation, storage,

loading and unloading, spraying and after spray operations. This is what is commonly referred to as a pathway of exposure. Adverse impacts on the physical environment is anticipated and could occur due to accidental spills on water bodies, soil and vegetation, unintentional or intentional spraying of the physical environment, poor siting of pesticide storage facilities that could expose sensitive environment to contamination .

Potential adverse environmental impacts are expected to be minimal in most of the targeted spray areas, and the following mitigation measures will be pursued to minimize these potential adverse effects.

Mitigation Measures

Anticipated adverse impacts through pesticide exposure to the bio physical environment or human health including livestock will be avoided, minimized, mitigated, or compensated and corrected if possible before cumulative effects are experienced. Mechanisms to mitigate adverse impacts include; Provision of Personal Protective Equipment (PPE) of standards recommended by WHO for IRS activities to all the spray teams; Training of all the spray teams and drivers on good spraying techniques and how to respond in cases of emergency exposure to pesticides; Awareness creating and sensitization of all the targeted residents in the cercles on the do's and don't before the spraying and after the spraying to reduce exposure incidents; this will include instructions on not to enter the houses until 4 hours after the spraying; removal or covering of all furniture, curtains, food items etc from the houses; sweeping away into pit latrines or burning of any dead insects; tying up all livestock during the spray process; Undertaking pregnancy testing for all the female spray candidates and general physical testing for all the spray teams; Training of all the surrounding health care facility personnel on emergency response due to acute pesticide poisoning; Equipping all the health facilities with the recommended anti-dotes for pesticide poisoning; locating the storage facilities in environmentally sound sites including away from markets centers, hospitals, school, close to water sources etc,; Ensuring that the storage facilities are secured and double padlocked with security guards to avoid incidences of pilferage; Ensuring sound disposal of after spray pesticide residue through triple rinsing and then disposing the residue into soak pits; and ensuring that all the empty pesticide sachets and un-used pesticides are locked securely as recommended by WHO until such a time that an appropriate disposal mechanism will be arrived at and this could include shipping the sachets back to the manufacturer.

Significant adverse impact could occur in the fishing village of N'Togosso located in the cercle of Bla where the houses are located very close to the river which has a dam erected across it. Accidental spills when crossing the bridge or through unintentional or deliberate exposure while spraying to the external environment could end up contaminating this water body and on the fish, aquatic invertebrates, and the livelihoods of the largely dominant fisher folk.

For this reason, the SEA recommends that this particular village situated next to the dam be EXCLUDED from the IRS program and instead an alternative intervention including but not limited to the use of ITN be pursued. This is because the potential risk for contamination is too HIGH to mitigate effectively.

Compliance with measures described in the PERSUAP will be monitored on a regular basis by PNLP and DNACPN Mali. RTI International will also conduct an internal compliance inspection and submit a compliance report to major program stakeholders. Finally, USAID health and environment staff will visit the program site periodically to determine the progress of the IRS campaign as well as to assess compliance with this SEA.

A Safer Use Action Plan (SUAP) or Environmental Management Plan (EMP) has been prepared as part of this SEA and details the mitigation requirements for the pilot program to minimize these risks to human health and the bio-physical environment. Mitigation measures include substantial training for all individuals involved in implementation, community education, utilization of personal protective equipment, and best practices for re-use/disposal of contaminated water from operations.

Compliance with measures described in the EMP will be monitored on a regular basis by the Malian Environmental Ministry and relevant Koulikoro and Bla Officials. RTI International will also conduct an internal compliance inspection and submit a compliance report to major program stakeholders. Finally, USAID health and environment staff will visit the program site periodically to determine the progress of the IRS campaign as well as to assess compliance with this SEA.

The SUAP or EMP can be found at the end of the report and summarizes the required mitigation actions according to the time that the actions should be taken. Bolded indicators are those that are considered "minimum requirements" for all IRS programs, and are used to compare IRS programs funded through PMI through time; these indicators are also listed in the environmental compliance monitoring checklist in Appendix 1. USAID and *the Comite technique d'analyse environnementale* will discuss the compulsory nature of EMP implementation with the Ministry of Health; the Ministry of Health must be committed to the implementation of the EMP. Key institutions and collaborators who will assist in the implementation of the project include:

- Mali National Malaria Control Program (PNLP)
- Malaria Research and Training Center (MRTC)
- USAID Health Team
- RTI International
- Pharmaceutical Products Registration Committee (CNGP)
- Comite technique d'analyse environnementale (equivalent of a Malian Environnemental Agency)
- Direction Regionale de la Sante (Regional Health Center) of Segou (Bla) and Koulikoro
- Departmental Direction of Agriculture, Phytosanitary Studies and Protection of Vegetables of Bla and Koulikoro
- African Program for the Elimination of Obsolete Pesticides (PASP-Mali)

These institutions will be brought together in an IRS coordination committee to resolve program issues periodically and systematically. . This will be coordinated by the in country COP and or the country task manager to assign appropriate responsibilities. Roles played by each of these collaborating institutions are identified in the EMP table under "Implementation Responsibility."

This assessment is based on field visit and desk top research conducted in Mali from February 1st to February 22nd April, 2008, including consultations with several IRS program stakeholders. Additionally, government documents concerning pesticide use, the environment, and malaria control were reviewed and incorporated into this EA (see Bibliography).

Conclusion

Professionally IRS activities if undertaken well have minimal adverse impacts on the environment. The same can be assumed for this proposed IRS program in Mali if IRS activities when implemented properly can result in significant health benefits with minimal adverse effects on the environment. RTI International has a proven track history in implementing IRS activities in sub Saharan Africa and will employ the best practice elements that it has utilized in other countries to ensure sound environmental protection.

The pesticide for use-Lambda-cyhalothrin 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.

Lambda-cyhalothrin is not expected to be prevalent in surface or groundwater because it has extremely low water solubility and binds tightly to soil. 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

Recommendation

The following key recommendations are therefore proposed in view of the analysis and impacts identified. They include;

- Compliance to all the country regulations related to IRS including ensuring that the IRS activities do not occur until the pesticide is approved for use in the country.
- Training of the Mali environmental inspectors to build their capacity in undertaking inspection
- Ensure that the Information Education and Communication component of the project is accorded emphasis and occurs at the early stages of the project.
- Liaise with the African Program for the Elimination of Obsolete Pesticides (PASP-Mali) Director to ensure that they have capacity and support from us to ensure that the final disposal of the wastes occurs in a timely manner.
- RTI and PNLP should ensure that the EMP prepared is followed and that the responsibilities are clearly spelt out and understood by all the partners.

1.0 Background and Purpose

The Government of Mali through the Ministry of Health with funding from United States Agency for International Development (USAID) and with facilitation by Research Triangle Institute (RTI International) is proposing to undertake Indoor Residual Spraying (IRS) in Bla and Koulikoro Cercles to combat malaria spread that is transmitted during the rainy season.

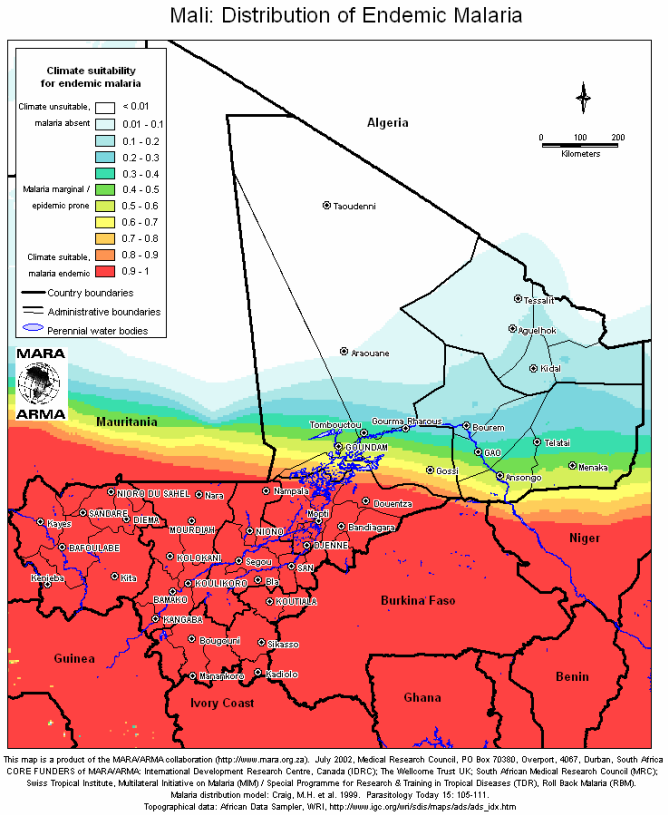
The objective of the study is to assess the environmental impacts associated with the proposed IRS spray activities Bla and Koulikoro including the pre spraying, spraying and post spraying phases of IRS.

PMI Background

Malaria is one of the major causes of morbidity and mortality in Mali, and is the primary cause of all outpatient visits for children less than five years of age (39%). One-third of all reported deaths are due to malaria, and 76% of these deaths occur in children less than five years of age.

In the 2005 annual statistical summary of the national health information system (*Système Local d'Information Sanitaire* or SLIS), health facilities reported 962,706 clinical cases of malaria, accounting for 36% of all outpatient visits (all ages).

Figure 1.



Distribution of Endemic Malaria and Climate suitability for endemic malaria

According to the SLIS, the reported incidence of suspected cases of malaria in 2005 was 82 per 1,000 population nationally, with regional incidence ranging from 52/1,000 in Mopti to 115/1,000 in Bamako. Infants had the highest reported incidence of 247/1,000, followed by children ages 1-4 years at 135/1,000. Actual malaria incidence may be much higher, since many patients with malaria do not seek care from health facilities. In fact, only an estimated 15-20% of 10 febrile children present to health facilities. In 2004, WHO estimated a rate of 450/1,000 confirmed cases among the population while the PNLP reported an annual incidence of presumed malaria cases of 70/1,000 (Source: J.O. Guintran, WHO). Overall, geographic coverage of the total population is estimated at 50% within 5km and 75% within 15 km radius from the health facility.

Malaria generally is endemic to the central and southern regions (with >90% of Mali's population), and epidemic in the north. Malaria transmission varies in the five geo-climatic zones. It occurs year-round in the Sudano-Guinean zone in the south, with a seasonal peak between June and November. The peak transmission season is shorter in the Sahelian Zone, lasting approximately 3 months from August to October. Epidemics occur in the north and in parts of Koulikoro and Kayes regions.

Malaria transmission is endemic in the Niger River delta and areas around dams and with rice cultivation, and is endemic with low transmission in urban areas including Bamako and Mopti.

Malaria Vector Species and Mlaria Transmission

Plasmodium falciparum (85-90%) accounts for most malaria infections while P. malariae (10 - 14%) and P. ovale (1%) make up the remaining infections. There is also recent evidence of P. vivax in epidemic-prone regions of the north.

Climatic zones in Mali range from desert regions in the North with less than one month of rainfall to Sudano-Guinean Zone in the far south with 6-7 months of rainfall. Malaria transmission in the three northernmost regions and the northernmost districts of Kayes, Kouikoro, Segou and Mopti are considered zones of epidemic risk and will not be considered for IRS at present.

IRS is potentially a cost-effective option in much of the remainder of the country where malaria transmission is perennial but with seasonal peaks that vary in duration from 3 to 6 months. In Year 1, IRS will not be considered in rice growing areas and zones of irrigation and around the Niger River Delta where transmission is holoendemic or in the urban areas of Bamako and Mopti, where malaria is endemic with limited transmission. Depending on the duration of the insecticide effectiveness on the walls, areas with 6-7 months of rain may require a second round of spraying before the end of the rainy season and thus will not be considered in the first year of IRS.

1.2 History of Malaria Control in Mali and Intervention Target Areas

Insecticide-treated nets (ITN): The promotion and use of ITNs has been a priority intervention for the MOH. The PNLP strategy aims to achieve 80% ITN use among children under five and pregnant women by 2011. Although there is moderately high coverage of non LLINs through various distribution channels, massive efforts will be necessary through PMI and partner support to scale-up LLIN activities and achieve the objective of 85% ownership and use. PMI will contribute through the procurement of more than 660,000 LLINs targeting children under five and pregnant women. PMI will also support the distribution of free LLINs in the public sector and support an assessment of the management and logistics system related to the distribution of LLINs. In addition, PMI will help to examine net preferences, determinants and barriers to net use and relevant messaging to target populations. The results will help to define clear messages regarding correct and consistent use of LLINs for communities and PMI will support multichannel strategies to communicate this information.

Indoor residual spraying (IRS):
No systematic program for IRS is currently operational, and the country does not have experience in large-scale IRS programs. The DHPS carries out campaigns for mosquito and rat reduction. The district government may provide the insecticides, spray personnel and per diem for the sprayers. In other instances, communities or individuals may purchase the insecticide and the agents will carry out the spraying either as part of a campaign or at the request of an individual. IRS is conducted in a consistent manner in the gold mine areas of Sadioloa, Yatela, Loulou, Morila and Kalana, but is limited to the mines. PMI will encourage mining companies to expand spraying activities to villages surrounding mines. No Global Fund activities or private sector activities other than in the mines are currently underway.

PMI will support IRS in at least two endemic districts to cover a population of about 430,000 in the Bla and Koulikoro Cercles. PMI will support the PNLP's focus on larviciding to assess the impact of this approach in conjunction with IRS. PMI will expand the work of MRTC/NIH in its efforts to assess the impact of spraying in hamlets near the Niger River on neighboring villages approximately 3-5 km away from the river; it is a possibility that the mosquitoes of the river habitats are the source of mosquitoes for villages during rainy season. Lastly, PMI will work with partners to ensure that tariffs on insecticides for IRS and larviciding are reduced or eliminated.

Malaria in Pregnancy including intermittent preventive treatment (IPTp): Utilization of antenatal care (ANC) by pregnant women has been low in Mali, and although IPTp has been a national policy since 2005, national coverage is still very low. Preliminary data from the 2006 DHS indicates that only 6% of pregnant women reported receiving any Sulphadoxine Pyrimethamine (SP) during an ANC visit, and only 4% receive two doses. To improve these statistics, PMI will procure SP with UNICEF to ensure universal coverage. PMI will also work closely with the MOH and other partners to strengthen ANC services through the support of in-service trainings and health policy/financing and treatment guideline revisions.

Case management: Malaria diagnosis in most facilities is based on clinical grounds and fewer than 10% of suspected cases of malaria are laboratory confirmed. The PNLP wants to strengthen microscopic diagnosis where it already exists and implement rapid diagnostic tests (RDT) where microscopy is not available. To support these goals, PMI will procure microscopes and other supplies to support laboratories nationwide, and work with the PNLP and other partners to strengthen in-service training and quality control for malaria diagnosis.

The overwhelming issue with malaria treatment in Mali is poor geographic and economic access to care. According to the 2006 DHS, only 31.4% of children younger than five years of age with fever received any antimalarial, and only 15.1% were treated within 24 hours. Ensuring prompt, effective and safe ACT treatment to 85% of patients with confirmed or suspected malaria in Mali will represent one of the greatest challenges for the PNLP. Global Fund Round 6 has committed around $4.3 million for financing ACTs in Mali from 2007-2009. PMI will support a comprehensive approach to improving ACT implementation through training, supportive supervision, policy revision for severe malaria, community-based ACT implementation and communication strategies that promote care-seeking for febrile children and compliance with treatment regimens. PMI will also procure needed ACTs and drugs for severe malaria, as well as support the logistics and distribution system, drug quality control and pharmacovigilance.

Environmental Management
There have been no public government efforts to pursue this intervention in Malaria control within the PNLP to date. However, within the National Malaria Strategic Plan for the Ministry of Health environmental management is identified and mentioned as part of the integrated vector management strategy and as an intervention that is under consideration for implementation in mosquito control especially in urban settings in Mali.

Larviciding

The PNLP has plans to undertake trials and research in larviciding as an intervention for mosquito control. At present, a pilot aimed at using larvicides is under consideration in 8 villages' in Koulikoro. The MRTC will provide leadership in undertaking trials in this study to find out the effectiveness of larviciding as an intervention before scale up is considered. This will be supported by USAID and is expected to begin in June 2008.

PMI will support the PNLP's focus on larviciding to assess the impact of this approach in conjunction with IRS. PMI will expand the work of MRTC/NIH in its efforts to assess the impact of spraying in hamlets near the Niger River on neighboring villages approximately 3-5 km away from the river; it is a possibility that the mosquitoes of the river habitats are the source of mosquitoes for villages during rainy season. Lastly, PMI will work with partners to ensure that tariffs on insecticides for IRS and larviciding are reduced or eliminated.

1.3 CURRENT STATUS OF MALARIA CONTROL INCLUDING POLICIES IN MALI

In late June 2005, the United States Government (USG) announced a new five-year, $1.2 billion initiative to rapidly scale up malaria prevention and treatment interventions in high-burden countries in sub-Saharan Africa. The goal of this Initiative is to reduce malaria-related mortality by 50% after three years of full implementation in each country. This will be achieved by reaching 85% coverage of the most vulnerable groups---children under-five years of age, pregnant women, and people living with HIV/AIDS---with proven preventive and therapeutic interventions, including artemisinin-based combination therapies (ACTs), insecticide-treated bed nets (ITNs), intermittent preventive treatment of pregnant women (IPTp), and indoor residual spraying (IRS).

The President's Malaria Initiative (PMI) began in three countries in 2006: Angola, Tanzania, and Uganda. In 2007, four countries were added: Malawi, Mozambique, Senegal, and Rwanda. In 2008, eight additional countries, including Mali, were added to reach a total of 15 countries covered under the PMI. Funding began with $30 million in Fiscal Year (FY) 06 for the initial three countries, $160 million in FY 07, and will increase to $300 million in FY 08, and reach $500 million in FY 10 in 15 countries.

In implementing PMI, the U.S. Government is committed to working closely with host governments and within existing national malaria control plans. Efforts will be coordinated with other national and international partners, including the Global Fund to Fight AIDS, Tuberculosis, and Malaria (GFATM), Roll Back Malaria (RBM), the World Health Organization (WHO), United Nations Children's Fund (UNICEF) the World Bank Malaria Booster Program, and the non-governmental and private sectors, to ensure that investments are complementary and that RBM and Millennium Development goals are achieved. Country assessment and planning visits for PMI, as well as subsequent evaluations and environmental management, will be highly consultative and held in collaboration with the PNLP and other partners.

The PNLP's Strategic Plan 2007-2011 envisions an integrated vector control program that includes ITNs, indoor and outdoor spraying, and destruction of larval habitats, larviciding, and environmental cleanup in urban zones. In the proposed PNLP budget, indoor residual spraying appears to be limited to epidemic response in the 17 northern districts. The proposed budget for IRS for 2007 includes $33,000 for equipment, $89,000 for insecticide and $35,000 for campaign organization. Additionally, in the PRODESS, the GOM proposes to conduct a small IRS pilot project in selected districts of Kayes and Koulikoro with funds from Organisation Pour la Mise on Valeur du Fleuve Sénégal (OMVS) (about $42,000 USD).

In every district, the agents of *Division Hygiène Publique et Salubrité* (DHPS) are equipped with at least one sprayer and in every region at least one fumigator. In 2004, 100 sprayers were purchased and 20 more were purchased yearly thereafter. Brand names for equipment include Shogun, Matabe and Roxy, each with a capacity of 16-18 liters; there are no Hudson sprayers in country.

PMI will support IRS to cover a population of approximately 431,000. The specific areas to be covered include Bla Cercle with a population of around 259,000 and Koulikoro Cercle with around 172,000 people. Criteria for district selection included high seasonal malaria transmission (assumed from high infant mortality in DHS), seasons of less than 6 months, relatively high population density, and poor coverage with other interventions. Selection of the district was done in consultation with the MOH and scientists from MRTC and CDC. Baseline entomology assessment was conducted during the rainy season of 2007. PMI will procure materials including insecticide, spraying equipment, and personal protective clothing and equipment for spray operators and supervisors, and will cover expenses for trainers and spray teams and rental of insecticide storage facilities. Training at the regional, district and community level will be provided, with supervision provided jointly by PMI and DHPS. IEC to inform beneficiaries, raise public awareness, promote behavior change (including environmental management and sanitation) and promote cooperation will provided by PMI with assistance of DHPS. PMI will also provide technical support for the spraying and entomology assessment.

The local CSCOM and CSREF will ensure additional human health and environmental safety components of IRS, with PMI assistance. MRTC will provide entomological training and will assist PNLP and DHPS with entomologic monitoring and wall bioassays to determine the residual effect of pesticides. Selection of IRS and larviciding sites by PNLP, MRTC and CDC as well as monthly vector monitoring activities including indoor and outdoor landing catches and pyrethroid spray catches should take place in 2007 in preparation of 2008 spraying.

While current PNLP policy encourages IRS in epidemic-prone areas, PMI does not support wide use of IRS in epidemic prone areas. PMI encourages the use of IRS in areas of seasonal malaria transmission where it can dramatically reduce malaria transmission and mortality. In addition to the following USG support, PMI will work with partners to ensure that tariffs on insecticides for IRS and larviciding are reduced or eliminated.

Larviciding: ($110,000) The GOM has strongly voiced a desire for an integrated vector control program that includes larviciding and environmental management. USAID and RTI will support this initiative with appropriate environmental management. Larval source reduction will be included in the IEC/BCC of IRS activities. In addition, PMI proposes to fund an operational research project in a small subset of houses included in the IRS program, to determine if there is an added benefit to larviciding of water sources surrounding sprayed homes. RTI and MRTC will carry out activities. This will be a separate study from the IRS expansion near the Niger River described below.

Expansion of IRS near the Niger River: ($80,000) MRTC/NIH has been studying mosquito activity in small hamlets located on the Niger River and in the neighboring villages approximately 3-5 km away from the river. During the dry season, *Anopheles gambiae* is present in high numbers in riverine hamlets due to larval habitats formed by the receding river, but in the nearby villages, mosquitoes are almost undetectable and when found are in houses on the side of the village closest to the river. MRTC/NIH hypothesizes that the mosquitoes of the river habitats are the source of mosquitoes for villages during rainy season. MRTC/NIH plans to carry out a small study aiming to reduce or eliminate mosquitoes with IRS (and perhaps larviciding) in one hamlet during the dry season and to measure mosquito activity in nearby villages as rainy season begins. PMI has added operational research funds to allow the MRTC to expand this activity to 5-10 additional hamlets along the river. Each hamlet is a small village with 20-50 houses. USAID and RTI will support these activities and ensure proper environmental management.

IRS for Epidemic Response: ($50,000) Sprayers, PPE, and insecticide will be pre-positioned in a central location for the epidemic prone North. This will help support WHO's plan for epidemic preparedness and response which is updated annually.

Entomological Monitoring: ($100,000) In the height of the rainy season (September) of 2007, insecticide susceptibility will be conducted in two districts targeted for IRS. In 2008, immediately after spraying is implemented, cone bioassays using colony-reared mosquitoes will be carried out on the walls for a predetermined number of houses for two months after spraying to assess the quality of spraying. A subset of these houses will be monitored

monthly thereafter to determine the duration of insecticidal activity on the wall. In addition, vector activity studies will be conducted in selected villages within the two districts from May until November. These studies will include monthly indoor and outdoor landing catches, pyrethroid spray catches (PSC), and insecticide susceptibility assays. Mosquitoes will be identified to strain level by polymerase chain reaction (PCR) and sporozooite levels will be determined by enzyme-linked immunosorbent assay (ELISA).

1.4 NATIONAL MALARIA CONTROL PLAN AND STRATEGY

Through the MOH, the Government of Mali (GOM) guides and coordinates all interventions in malaria control. The PNLP was first established in 1993 and was till very recently within the Disease Control Division of the National Health Directorate (DNS). The PNLP mandate is to propose policies and guidelines, draft strategic orientation for all malaria interventions and support decentralized regional and district health teams through training and supervision. In March 2008, the PNLP was raised at a Directorate level, reporting to the Ministry's Secretary General. In the past, due to its lower positioning in the MOH organizational structure the PNLP was not able to participate in crucial meetings where key malaria control decisions were made (e.g. annual plan projections, budgets, etc.).

The PNLP National Strategic Plan for the period 2007 – 2011 is influenced by RBM and the April 2000 Abuja Declaration. The national strategy aims to achieve the following:

- Reduce malaria mortality by at least 50 % as compared to year 2000 levels;
- Reduce health facility recorded malaria case-fatality rates by at least 80 %, as compared to year 2005 levels; and
- Reduce malaria morbidity by at least 50 % as compared to year 2000 levels.

To achieve these objectives, the PNLP has defined four major strategies: 1) improved case management, 2) intermittent preventive treatment of malaria in pregnancy (IPTp), 3) vector control through the use and distribution of ITNs, destruction of mosquitoes breeding sites using larvicides, and targeted indoor residual spraying, and 4) malaria epidemic preparedness.

Three strategic approaches have been adopted to support this including community mobilization and behavior change communication, operations research and monitoring and evaluation. In 2006, the MOH decreed that ITNs should be distributed free-of-charge through public health facilities for children under five and pregnant women, as should treatment for children under five with ACTs. The PNLP has recently established six working groups including: drugs and case management, communication and social mobilization, vector control, ITNs, operations research, monitoring and evaluation, and capacity reinforcement. These working groups will further develop national policies, guidelines, and training materials for policy implementation.

Based on proposed activities, in Year 1 of the PMI program, the following results are expected:
Prevention:

- Approximately 2 million long-lasting ITNs (LLINs) (of which PMI will provide 660,000) will have been distributed to children under five and pregnant women;
- Approximately 86,000 houses, housing a total of 430,000 residents, in the two districts targeted by the MOH and PMI for IRS will have been sprayed; and
- Intermittent preventive treatment with SP in pregnant women will have been implemented in all health facilities nationwide.
- Malaria treatment with ACTs will have been implemented in all government health facilities.

- The following paragraphs describe the proposed approach for each of the major interventions:

Building PNLP capacity: To help the PNLP reach its coverage targets for the key malaria interventions, RTI will collaborate with other partners to strengthen the capacity of PNLP staff and others at the national, regional, district and community levels to plan, implement, supervise, monitor and evaluate malaria control activities including environmental management. In addition, RTI will work with the MOH and partners to help identify additional staffing resources to support the PNLP's activities. Key contributions will be made in training health workers and developing and strengthening capacity for supportive supervision and ensuring sound environmental management.

Monitoring and evaluation: RTI, along with USAID, will play a major role in helping the PNLP establish a comprehensive vision and plan for monitoring and evaluation of malaria activities. The evaluation approaches will provide essential data to measure national coverage and process indicators. PMI will build upon the PNLP's existing activities within their framework and ensure that PMI M&E approach complements that of other partners. Activities will include support to the development and implementation of a comprehensive M&E plan for the national program, strengthening of sentinel sites, M&E for indoor residual spraying and other areas

1.5 Administration of Malaria Control Activities

Mali is divided into eight administrative regions (Kayes, Koulikoro, Sikasso, Ségou, Mopti, Gao, Tombouctou and Kidal) plus the capital Bamako. The eight regions are subdivided into 49 administrative "Cercles" comprising 53 health districts. Bamako is divided into six urban communes that serve as six urban health districts. Governance is decentralized into 703 communes, each commune being administered by a local council and mayor. The health system has four levels:

- Central level: four national reference hospitals
- Regional level: six regional hospitals
- District level: 59 district referral health centers (Centres de Santé de Référence or SREF)
- Community level: 753 community health centers (Centres de Santé Communautaire or CSCOM); not all are functional. CSCOMs are controlled by a community health association (ASACO)

Health financing through cost recovery

Mali has a strong cost recovery system in place which is based on the "Bamako Initiative". At the district level, communities can establish CSCOMs based on the following criteria: a minimum of 10% contribution to the construction or renovation of the health facility; the hiring and support of health personnel; and the establishment of an ASACO (community health association, referred to hereafter as "ASACO"). All CSCOMs are supposed to deliver the national minimum package of services – antenatal care, immunizations, and curative services. Once authorized by the District Medical Officer, the MOH provides an initial stock of medicines; in principle communes provide 15% of their national allocations for social services, a proportion of which should support the CSCOMs.

Three forms of revenue generation exist at CSCOMs including membership fees, the sale of essential drugs and fees for services, which are managed by the CSCOM's ASACO. Service fees vary by health area and are set by the ASACO after consultation with the population. Membership fees allow for reduced service charges at some CSCOMs. Funds derived from the sale of medications are kept in a separate account to prevent providers from overprescribing to generate revenue. This also prevents decapitalization of pharmacy stock. The ASACO purchases replacement drugs for the CSCOM through the national pharmacy system or in the private sector based on availability. Selected drugs (e.g. vitamin A, ORS) are provided free by donors. CSCOMs are required to finance the transportation of their drugs from CSREFs. Due to small profit margins, loss or use of revenues for non-pharmaceutical purposes, CSCOM drug stores often become decapitalized.

National financial planning for malaria and health/social development

The PNLP receives annual budget support from PRODESS II (the 2nd National Health and Social Development Program, 2005-9). The Comité de Suivi (evaluation committee) approves the annual PRODESS operating plan, which includes funding gaps expected to be covered by donors. Several partners (Netherlands, Sweden and Canada) provide direct budget support on an annual basis. All other donor funds are targeted to sub-sectors and programs. The Government of Mali (GOM) contributes to mostly salaries and other operating costs in PRODESS annual budgets. The GOM also uses HIPC funds t4o pay some MOH salaries, especially at the CSCOM level. Overall, the GOM has steadily increased the contribution of the national budget devoted to health from about 6% in 2000 to about 8% in 2005, with commitments for additional increases in the future. The GOM-approved fiscal year 2007 Operating Plan for PRODESS includes budget line items totaling about $1 million for activities to be conducted by the PNLP. This does not include staffing of the PNLP, which is funded separately. Some of the highlights include LLIN procurement and distribution, surveillance, IRS, IPTp and training. Only a portion of these activities will be funded by the PRODESS budget (including resources from countries providing direct budget support); the remainder will depend on other donor funding.

1.6 Need for Action and the Preferred Alternative

The IRS program in Mali is associated with the U.S. President's Initiative on Malaria in Africa, which was announced 30 June, 2005, and seeks to reduce malaria mortality by 50% in up to 15 countries (total population: 175 million) in sub-Saharan Africa in five years. This will be accomplished by rapidly scaling up the following proven malaria prevention and treatment interventions in each country to reach 85% coverage of vulnerable groups (children under five, pregnant women, and people living with HIV/AIDS):

- treatment of malarial illnesses with artemisinin-based combination therapies (ACTs);
- intermittent preventive treatment (IPT) of pregnant women with effective antimalarial drugs, currently sulfadoxine-pyrimethamine;
- distribution of insecticide-treated bed nets (ITNs); and
- Indoor residual spraying (IRS).

In implementing these interventions, the United States, through USAID and CDC, will work in partnership with the Government of Mali and build on existing national malaria control plans, policies and resources. The Initiative will support and complement efforts of the Global Fund (GFATM), the World Bank, and other members of the Roll Back Malaria (RBM) Partnership. The Initiative will include detailed reporting on inputs, outputs, and results.

2.0 Alternatives Including the Proposed Action

2.1 Alternative Intervention to Malaria Control

This study considered the following interventions for combating malaria as alternatives.

2.2.0 Insecticide Treated Nets (ITNs)

The promotion and use of ITNs has been a priority intervention for the MOH. The PNLP strategy aims to achieve 80% ITN use among children under five and pregnant women by 2011. Although there is moderately high coverage of non LLINs through various distribution channels, massive efforts will be necessary through PMI and partner support to scale-up LLIN activities and achieve the objective of 85% ownership and use. PMI will contribute through the procurement of more than 660,000 LLINs targeting children under five and pregnant women. PMI will also support the distribution of free LLINs in the public sector and support an assessment of the management and logistics system related to the distribution of LLINs. In addition, PMI will help to examine net preferences, determinants and barriers to net use and relevant messaging to target populations. The results will help to define clear messages regarding correct and consistent use of LLINs for communities and PMI will support multichannel strategies to communicate this information.

The use of ITN/LLN was not rejected as an alternative and is mentioned here with the sole purpose of highlighting the fact that as part of the IVM strategy, ITN/LLN use will still be pursued alongside with IRS in the 2 districts as part of the wider integrated approach to malaria control.

2.2.1 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).

This study did not consider environmental management as an alternative primarily because the National Malaria Control strategy does not factor this as an effective intervention in its plans. Further to this, environmental

management would not be a suitable approach for pursuit in the two cercles because these are mainly rural areas in terms of setting thus limiting the effectiveness of environmental management as a possible strategy.

2.2.2 Larviciding:

GOM strongly voiced a desire for an integrated vector control program that includes larviciding and environmental management. Larval source reduction will be included in the IEC/BCC of IRS activities. In addition, PMI proposes to fund an operational research project in a small subset of houses included in the IRS program, to determine if there is an added benefit to larviciding of water sources surrounding sprayed homes. RTI and MOH will carry out activities. This will be a separate study from the IRS expansion near the Niger River described below.

2.3 Alternative IRS Pesticides or Chemical

The Maria Research Training Centre (MRTC) in collaboration with the PNLP (National Malaria Control Program), was delegated the responsibility to produce experiments on the effectiveness of other alternative chemicals other than Lambda-Cyhalothrin ICON.

The following alternative chemical was considered as possible for use in spraying;

- Ficam M (bendiocarb 800g/kg),

The chemical was evaluated by MRTC using the following criteria namely

- Toxicity to human health and Environment
- Resistance level
- Effectiveness to last on the wall for a long time after the spraying

As far as the insecticide resistance testing went there was no resistance to any of the two insecticides used when the operational dosages were used. This was true in both districts (Koulikoro and Bla). However the kdr genotyping results call for attention as homozygote and heterozygote resistant individuals are found in the vector population. That definitely rings a bell for the resistance monitoring in the intervention areas by using more samples.

Since one of the goals of this study is to identify insecticides to be used for the up-coming IRS intervention the following recommendations can be made:

- the use of lambda-cyhalothrin at the dosage of 30mg/m2 since it is clear from the Malian legislations that this molecule can be used,
- the use of bendiocarb as back-up since more information is needed on its registration in Mali.
- The actual intervention could start and since there will be monitoring of the resistance, there is time to register the bendiocarb if need be before a probable appearance of resistance to the lambda-cyhalothrin.

2.4 Alternative Spray Site

This was not considered as an alternative and the main reason for this being the fact that these 2 cercles were identified as the zones with a high epidemic for Malaria spread based on studies conducted by the MRTC and PNLP. IRS activities are only conducted in areas where malaria incidences and epidemics have been studied over a long period of time and data is available to indicate that these are malaria endemic and epidemic areas.

2.5 No Project Alternatives

A no project scenario was also looked into in this study. USAID's direct support of IRS activities in the 2 cercles is bound to translate to a certain degree into direct efforts for malaria vector control in Mali. Intervention through IRS to

reduce the spread of Malaria is undoubtedly going to lead to providing protection against malaria for the approximately 430,000 targeted populations.

Targeted intervention to combat malaria in the cercles is expected to lead into reduced incidence of adult morbidity, miscarriages, low birth-weight, and adverse effects on fetal neurodevelopment. It will also reduce incidence of malaria-related childhood anemia, complications, organ failure, and death.

The no-project scenario will mean the status quo of the area remains and no occurrence of adverse impacts as well as positive impacts posed by the project implementation. The no project option will have the forgone costs and benefits highlighted above. The table 2 below describes the alternatives in a summary form.

Alternatives Considered and Preferred		
	IRS Campaign using registered and non registered insecticides including: Bendiocarb Lambda-cyhalothrin Bifenthrin Cyfluthrin Deltamethrin Alphacypermethrin	USAID support would include the following components: • Purchase of Insecticide, spraying equipment, and adequate amounts of personal protective clothing and equipment for staff • Financial support for trainers and spray teams • Technical advisors to plan the program, train field staff, and supervise field operations • IEC to inform beneficiaries, raise public awareness, promote behavior change and promote cooperation • Financial support for renting storage facilities for insecticide, spraying equipment, personal protective clothing and empty insecticide sachets • Financial support and technical assistance for additional human health and environmental safety components, including infrastructure for responsible disposal of contaminated wash-water (e.g., Evaporation tank, ablution block and/or soak pit) • Financial support for empty sachets disposal as needed The pesticides listed on the left are the pesticides which will be considered for IRS activities in Mali. Although in this year's pilot activities only one will be chosen. Out of these six pesticides, there are two classes of pesticides which can be identified: Carbamate (Bendiocarb) and Pyrethroid (Lambda-cyhalothrin, Bifenthrin, Cyfluthrin, Deltamethrin, Alphacypermethrin). The Government of Mali, the Malaria Research and Training Center, has considered the two of the six pesticides (Bendiocarb and Lambda-cyhalothrin) listed in the column on the left, however has preferred to use only Lambda-cyhalothrin for Round 1 of the pilot project, for reasons of effectiveness, mortality to resistant mosquitoes and relatively low level of toxicity to the environment and affected population. Partially, due to previous registration of Lambda-cyhalotrin in Mali (which is not the case for Bendiocarb), it was chosen as the best fit for this pilot IRS Project. In future rounds of spraying, it may be decided that one of the other mentioned insecticides will be used. For this reason, this SEA intends to include all considered pesticides (all in the Pyrethroid class, instead of just one) in this analysis.
Alternatives Considered		
	ITN/LLIN Program	USAID is committed to continuing support for ITN and LLIN scale-up activities within Mali. Malaria prevention through scaling up the use of treated mosquito nets (ITN, LLIN) is a key strategy of the PNLP. USAID /PMI supported a national campaign along with other partners in December 2007 where over 2.2 million LLINs were distributed to families with children under

		five. During FY 08, PMI will procure over 600,000 LLINs for distribution at health facilities to pregnant women attending ANC visits and to children on completion of their routine vaccinations.
	Larviciding	This alternative was considered and it was found out that the PNLP and the National Malaria Strategic Plan plans to undertake trials in 8 villages of Koulikoro as pilot for testing the efficacy of larviciding as a mosquito control intervention.
	Alternatives Considered and Rejected	
	Environmental Management	Environmental Management was considered and rejected because the target area for IRS is in a rural setting. For Environmental Management to be effective it requires an urban setting. This ruled out the implementation of this consideration.
	Alternatives Not Considered	
	No Action	According to USAID's *Integrated Vector Management for Malaria Vector Control: Programmatic Environmental Assessment*, the no action alternative will not be considered; the risks posed by IRS are acceptable to USAID in light of the risks posed by malaria.

2.6 Human Health and Environmental Effects of Preferred Alternative

As a consequence of implementing the Preferred Alternative, approximately 430,000 people in the cercles of Bla and Koulikoro will be covered by this vector control program. This protection will reduce the incidence of adult morbidity, miscarriages, low birth weight, and adverse effects on fetal development due to malaria. It will also reduce the incidence of malaria-related childhood anemia, complications, organ failure and death.

Few adverse human health or environmental effects are anticipated as result of occupational, residential, and/or environmental exposure to pyrethroids and carbamates due to mitigation efforts.

During the use of pyrethroids, notably the ones mentioned in the preferred alternative, effects from occupational exposure could include eye, skin and respiratory irritation, although personal protective equipment should minimize such effects. These acute effects can also occur in the resident population up to 24 hours after spraying; however, residents typically do not experience these effects if they re-enter their residences four hours after spraying.

During the use of Bendiocarb, effects from occupational exposure are fast acting, but reversible, particularly with cholinesterase inhibition. After carbamate exposure, cholinesterase recovery may take from several hours to several weeks, depending on the degree of exposure. The poisonous effects of carbamate pesticides come about through the inhibition of cholinesterase, an enzyme produced in the liver. Cholinesterase, is an enzyme that catalyzes the hydrolysis of the neurotransmitter acetylcholine into chorine and acetic acid, a reaction necessary to allow a

cholinergic neuron to return to its resting state after activation. 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.

3.0 AFFECTED ENVIRONMENT

Refer to section H.

See pesticide procedure H

4.0 ENVIRONMENTAL CONSEQUENCES

4.1 Unavoidable Adverse Effects

Road Accidents

Following the procurement of the pesticide and eventual shipping to Mali, this consignment must then be transported from the place of arrival to the main warehouse and subsequently to the satellite warehouses in the spray sites of the cercles of Koulikoro and Bla. This activity of transportation thus presents the risk of vehicle accidents and consequent insecticide spillage. Such spillage could expose both humans and aquatic environments to the insecticide which could lead to adverse human health and ecological consequences.

Fetal Exposure

It is also possible that the impacts of normal residential exposure of pregnant women could include neurological effects on unborn fetuses, but further research is necessary to test this hypothesis (Berkowitz, et al. 2003). This fetal exposure in the home would be an unavoidable risk of the IRS operation.

Accidental Warehouse Fires

Human inhalation of toxic fumes in the event of a storehouse fire is also an unavoidable risk. Information on the combustion byproducts of pyrethroids can be found in below (taken from USAID's *Integrated Vector Management Programs for Malaria Vector Control: Programmatic Environmental Assessment* (IVM PEA), pages 57-58) as well as fire-fighting instructions from Material Safety Data Sheets.

Table 2.Insecticide, Combustion Byproduct, and Extinguishing Instructions

Pesticide	Combustion Byproduct	Extinguishing Instructions
Alpha-cypermethrine	Open burning of lambda-cyhalothrin creates nitrogen oxides, hydrogen chloride, and hydrogen fluoride (WHO, 1997)	Extinguishing media: For small fires use water spray, alcohol-resistant foam, dry chemical or carbon dioxide. For large fires, use Alcohol-resistant foam, Water spray. Extinguishing media which must not be used for safety reasons: Do not use solid water stream as it may scatter and spread fire. Specific hazards during fire fighting: As the product contains combustible organic components, fire will produce dense black smoke containing hazardous products of combustion. Exposure to decomposition products may be a hazard to health. Special protective equipment for firefighters: Wear full protective clothing and self contained breathing apparatus. Further information: Do not allow run-

Pesticide	Combustion Byproduct	Extinguishing Instructions
		off from fire fighting to enter drains or water courses. Cool closed containers exposed to fire with water spray.
Bendiocarb	Fine dust may form explosive mixtures in air. The product is not flammable, but when heated above 125º C will evolve toxic fumes of methyl isocyanate. Water is the preferred extinguishing medium as it decomposes any methyl isocyanate.	Water fog or fine spray, carbon dioxide, dry chemical, foam. Fire fighters should wear full protective gear, including self-contained breathing apparatus (AS/NZS 1715/1716). Keep unnecessary people away and move all other personnel to windward side of fire. Bund area with sand or earth to prevent contamination of drains or waterways. Dispose of fire control water or other extinguishing agent and spillage safely later.
Delta-methrine	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)	Suitable extinguishing media: Water spray jet, carbon dioxide (CO2), dry powder, foam. Extinguishing media which should Product itself is non-combustible not be used for safety reasons: Fire extinguishing measures to suit surroundings.
Bifenthrin	Not available	Suitable extinguishing media: Carbon dioxide (CO2), Foam; Powders Not suitable extinguishing media: Water (the product is hazardous for the environment - do not dilute it) Specific fire fighting methods: Isolate fire area. Evacuate downwind. Contain the extinguishing fluids by bunding (the product is hazardous for the environment). Do not attempt to fight the fire without suitable protective equipment. Do not breathe fumes Protection of fire-fighters: Self-contained breathing apparatus and complete protective clothing
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 to-date.

(Source: IVM PEA, USAID, Jan 2007)

4.2 Irreversible or irretrievable commitments of resources

Financial related costs for the spraying in the cercles of Koulikoro and Bla once committed and used will hence become irretrievable. Financial costs related to the IRS activities will involve the procurement of new spray pumps that could be used in future IRS interventions not necessarily supported by the US government and the required environmental analysis. The storage facilities will also contain barrels or tubs used for rinsing sprayers and cleaning overalls, face shields, gloves, and boots. If not secured, these barrels or tubs may be pilfered and used for drinking water or food storage.

4.3 Environmental impacts of the proposed action

The proposed action of applying pesticide through IRS in the cercles of Koulikoro and Bla to combat Malaria like any other intervention is bound to pose potential adverse impacts on the environment both in terms of social, biophysical and health related negative consequences.

Both the cercles of Koulikoro and Bla have areas in which there are flood plains present, caused by the River Niger and the River Bani (actually a tributary to the River Niger in Bla) during the rainy seasons. Any contamination of the watershed will not only affect the fisheries and ecological status of the ecosystem but the livelihood of the wide fisher folk communities whose lives thrive on fishing.

Eliminating communities that are close to the dam in N'togosso in the cercle of Bla from IRS and training and supervision of spray personnel according to best practices should adequately address this risk.

4.4 Direct and indirect effects and their significance

Direct Effects

USAID's direct support of IRS activities in the cercles of Bla and Koulioro are bound to translate to a certain degree into direct efforts for malaria vector control in Mali. Intervention through IRS to reduce the spread of malaria is undoubtedly going to lead to providing protection against malaria for the approximately 430,000 targeted populations.

Targeted intervention to combat malaria in the cercles of Bla and Koulikoro is expected to lead into reduced incidence of adult morbidity, miscarriages, low birth-weight, and adverse effects on fetal neurodevelopment. It will also reduce incidence of malaria-related childhood anemia, complications, organ failure, and death.

Expected negative impacts include possible contamination of the natural environment from accidental spills of the insecticide, as well as human health exposure owing to poor handling, negligence or accidents.

Indirect Effects

Through this action, USAID will be providing the CSCOMs with backpack compression sprayers. Upon completion of this program, USAID will no longer supervise the use of this capital.

4.5 Complementary and Conflicting Policies, Plans or Controls for the Areas under Consideration

Malian Constitution: The constitution recognizes to all citizens the "right to a healthy environment" and stipulates in article 15 that the "protection of the environment and the assurance of quality of life is the purpose and responsibility of the state".
RTI will ensure to its greatest capacity that norms regarding the protection of the environment will be respected.

Decree 03-594/PRM of the 31st of December 2003 refers to the Environmental Impact Assessment, which outlines the rules, regulations and procedures that a private or public project must include.
RTI has completed this requirement for the Government of Mali, to do an in-country environmental assessment. It is reviewed and approved by the DNACPN (the National Public health and Pollution Prevention Ministry)

Decree 02-305 overviews the protection of Vegetables
RTI is obliged to respect the protection of agricultural practices in the areas where IRS will be conducted. This decree enforces the protection of crop production.

Pesticide Regulation

Order 01-046/PRM of the 20th of the September 2001 authorizes the ratification of the Communal Regulation of member states of the CILSS (Inter-State Committee for Drought Control in the Sahel) on the registration of pesticides signed in Djamena the 16th of December 1999.
RTI will not be permitted to import and or procure any pesticide without the documentation that its exact composition is registered in country. A waiver drafted by the Ministry of Health to the Ministry of Agriculture has been sent and registration is in process for Lambda-cyhalothrin.

Law 89-61/AN-RM of the 2nd of September 1989 states that the importation of toxic waste will be prohibited.
RTI will not be involved in the importation trade of toxic waste.

Law 02-14/AN-PR of the 3rd of June 2002 instituting the registration and the management of pesticides in the Republic of Mali. It states overall general principles on matters surrounding their importation, their chemical composition, packaging and repackaging and of the storage of pesticides.
After the pesticide sachets are used RTI will transfer these materials to the DNACPN, in charge on the inter-state African Program for the disposal of Obsolete Pesticides (Program is part of the United Nations) for removal.

Law 01-20/AN-RM of the 26th of April 2001 relative to pollution and harmful substances that chemical substances " which can "pose a danger to man or his environment are subject to tight regulation and inspections by Ministries in charge of Environment and Public Safety"
With respect to this law, RTI will ensure that all personnel hired to conduct IRS and will handle the pesticides will abide by the most stringent of safety rules and will have the proper protective equipment to prevent and mitigate exposure. (This is explained in greater depth in the following chapters)

Hydrology Regulations

Order 02-049/P-RM of the 29th of March 2002 on the Creation of the Niger Bassin Agency- outlines the roles and responsibilities of the Niger River Basin Agency, which includes the "preservation of the River, including the protection of terrestrial and aquatic ecosystems."

Through the proper compliance of this SEA and proper training of spray teams, RTI will respect and comply with the demands of the River Niger Basin Agency, and will respect basin environments to ensure there is no contamination of its flora and fauna.

Law 02-006 of the 31st of January 2002, Water Law: this law gives the general outline that the conservation, protection and management of water resources is obligatory by the Ministry of Environment and must be respected by all. Article 14 states that it is strictly prohibited to spill and contaminate the water bodies and their flora and fauna.

RTI must respect this law, and has taken precautionary measures to avoid spraying in areas where contamination risk is high, such as near the dam in N'Togosso, in the cercle of Bla. Contamination of the River Niger and its tributaries would be detrimental to the local economies.

5.0 USAID Pesticide Procedures, 22 CFR Part 216.3(b)

A. The USEPA registration status of the requested pesticide

The section below provides brief background information about ICON the pesticide of choice for IRS activities in Mali. The annex section of the report has a detailed profile analysis of this chemical for further reference.

A. The USEPA registration status of the requested pesticide

Table 3: Registration Status in Mali of selected pesticides

Is the pesticide…	Bendiocarb	Lambda-Cyhalothrin	Bifenthrin	Cyfluthrin	Deltamethrin	Alpha-cypermethrin
Registered by the host country (for public health use)?	NO	No- but MOH in Mali has requested a waiver for its use. Still pending,	YES	YES	YES	YES
Registered by EPA for "same or similar use"?	NO- registration was voluntarily cancelled in 1999	NO	YES	YES	YES	Not Registered— but other forms of cypermethrin registered for residential uses
WHO-recommended?	YES	YES	YES	YES	YES	YES

B. The basis for selection of the requested pesticide

The chemicals used in IRS 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:

- **Pesticide Registration in host country**

As it stands, none of the proposed pesticides used for IRS listed above are currently registered for use in Mali, except for Bifenthrin. This is a concern; however the National Malaria Control Program (PNLP) is taking action to be granted a waiver for the chosen pesticide, lambda-cyhalothrin. PNLP under the auspices of the Ministry of Health is engaged in discussions with the Ministry of Agriculture to get a ministerial decree to use ICON for the IRS activities.

- **Acceptability of the pesticide to the National Malaria Control Program (PNLP) in Mali**

According to the studies by MRTC, both Bendiocarb and Lambda – Cyhalothrin are acceptable for use in IRS activities in Mali because they all give the same results in terms of effectiveness to killing mosquitoes. Bifenthrin on the other hand, is not as appropriate for the surface as the lambda-cyhalothrin or the bendiocarb.

- 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*

The following table illustrates the potential for exposure above levels of concern based on results from a screening risk assessment conducted for *USAID's Programmatic Environmental Assessment for Integrated Vector Management*. The screening risk assessment was a conservative assessment of chemicals used in IRS, examining worst-case scenarios of occupational and residential exposure. The assessment compared estimated exposures to US EPA human health benchmarks for each chemical. Additional details can be found in Chapter 5 of the *PEA for IVM*.

Table 4: Risk Levels of Exposure: Occupational and Residential

Occupational Exposure				**Residential Exposure**			
Risk Below Levels of Concern	**Low Risk**	**Moderate Risk**	**High Risk**	**Risk Below Levels of Concern**	**Low Risk**	**Moderate Risk**	**High Risk**
Alpha-cypermethrin	Bendiocarb			Alpha-cypermethrin			
Deltamethrin	Lambda-cyhalothrin			Bendiocarb			
Bifenthrin	Cyflurin			Lambda-cyhalothrin			
				Cyfluthrin			
				Bifenthrin			
				Deltamethrin			

- **Risk to environment, livestock and/or agricultural trade**

Table 5: Toxicity of IRS Insecticides to Non Target Organisms, showing those considered in this EIA (taken from page 106 form PEA) ranking is WHO I suppose

Proposed IRS Pesticide	**Mammal**	**Bird**	**Fish**	**Other Aquatic**	**Bee**	**Persistence**	**Bioaccumulate**
Lambda-Cyhalothrin	High Toxicity	Low Toxicity	High Toxicity	High Toxicity	High Toxicity	Medium Toxicity	High Toxicity
Bendiocarb	Medium Toxicity	Medium Toxicity	Medium to High Toxicity	Medium Toxicity	High Toxicity	Medium Toxicity	Medium Toxicity

Proposed IRS Pesticide	Mammal	Bird	Fish	Other Aquatic	Bee	Persistence	Bioaccumulate
Deltamethrin	Medium Toxicity	Low Toxicity	High Toxicity	High Toxicity	High Toxicity	Medium Toxicity	High Toxicity
Cyfluthrin	Medium Toxicity	Low Toxicity	High Toxicity	High Toxicity	High Toxicity	High Toxicity	Medium to High Toxicity
Alpha-cypermethrin	Low Toxicity	Low Toxicity	High Toxicity	High Toxicity	High Toxicity	Medium Toxicity	High Toxicity
Bifenthrin	Medium Toxicity	Medium Toxicity	High Toxicity	High Toxicity	High Toxicity	No data	Low Toxicity

Toxicity ; The only 2 remaining chemicals that were considered were Ficam M (bendiocarb 800g/kg) and Lambda-Cyhalothrin. In spite of all of them being able to effectively perform well in killing the mosquito vector, Lambda-Cyhalothrin is considered a much more toxic chemical to the environment than Bendiocarb. However, the Ministry of Health has a preference to Lambda-Cyhalothrin than to Bendiocarb and this eventually guided the selection of the pesticide for use.

Vector resistance
According to MRTC data emerging from 2007 sentinel site susceptibility testing, malaria vectors do not express a resistance to pyrethroids. In fact, the vector mortality was the same between bendiocarb and lambda-cyhalothrin.

Secondary factors include:
Appropriateness of surface for spraying
Lambda-cyhalothrin and bendiocarb are appropriate for household surfaces where they will be sprayed. The households both in Koulikoro and Bla are made of mud and hold the pesticides on the walls effectively.

Duration of effectiveness (and implications for cost)
According to WHO, all pyrethroids listed are expected to have duration of 3 to 6 months; however, the duration of effectiveness varies under different climatic conditions as well as surfaces. Technical information on duration of effectiveness on the primary wall surface types in Koulikoro and Bla will be considered when selecting insecticides during the procurement process.

Cost of insecticide
The cost of pyrethroids is approximately 8-12 USD per sachet. Additional cost considerations, taking into account in-kind product support, will be considered during the procurement process.

Table 6: Costs of Insecticides

Cost of Insecticide	
Pesticides considered	**Cost per sachet ($)**
Bendiocarb (Ficam)	9.00
Alpha-cypermethrine (Fendona)	12.00
Deltamethrine	9.90
Lambda-cyhalothrin	7.40

Source : http://www.who.int/medicinedocs/

When determining the best choice of pesticide for IRS in Mali, cost was not a large factor in this decision process. However, when observing the chart above, Bendiocarb appears to be the second cheapest of all the four choices.

Tertiary factors include:

The need for an insecticide of a different class to prevent resistance
If IRS is pursued by the MRTC in the medium to long term, Mali will need to develop and implement a resistance management program; however, for a one-time pilot program, exclusive use of pyrethroids is an acceptable course of action as it is not expected to stimulate additional vector resistance in the cercles of Koulikoro and Bla. The use of Bendiocarb, which is a carbamate, is also an acceptable substitute which will help manage resistance in this area.

Major classes of insecticides used in other vector control interventions that could promote resistance
RTI has been informed by the Regional Ministry of Agriculture in Koulikoro that lambda-cyhalothrin has been used in the past to control pests in the cultivation of cotton.

Major classes of insecticides used in the agricultural sector that could promote resistance
RTI has been informed that pyrethroids have been used in the cercles of Koulikoro and Bla. If the program is expanded and expected to continue for several years, it is advisable to take into account agricultural pesticide use in the development of a resistance management scheme for malaria vector control.

Host-country capacity to prevent pilferage
Compared to most countries where IRS is being implemented, Mali has substantial capacity to prevent pilferage of insecticide in an IRS program, provided that the appropriate infrastructure and personnel for pesticide storage is provided. District officials and the PNLP can benefit from the knowledge and expertise of the DNACPN and their African Program to eliminate Obsolete Pesticides.

C. The extent to which the proposed pesticide use is part of an integrated vector management program

Currently the PNLP exclusively uses ITNs and LLINs in malaria vector management. The proposed pesticide use is intended to examine the possibility of expanding this one-dimensional approach to encompass two complementary vector-control measures. To-date, the PNLP has not included larviciding or environmental management in its strategy for malaria vector management.

D. The proposed method or methods of application, including availability of appropriate application and safety equipment

The proposed method of application is Indoor Residual Spraying, or IRS. IRS is a commonly-used malaria vector control method that is particularly effective in preventing malaria epidemics. It is implemented by the application of residual insecticides, to which *Anopheles* female 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 on human victims. Several formulations of insecticides are available for this purpose; those that may be used in Mali's IRS program include: Deltamethrine, Bendiocarb, Alpha cypermethrin, Lambda-cyhalothrin, Bifenthrin and cyfluthrin.

The residual effect of the aforementioned insecticides are sufficient to kill resting mosquitoes for a period ranging from 2 to 6 months depending on the insecticide and its formulation, the surface on which it is applied (mud, cement or thatch), and local conditions. (see MRTC study 2008) 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 seasons, as heavy rains prompt increases in the *Anopheles* vector population. To be effective, IRS must attain coverage rates of at least 85% of the houses in a target area.

The spray operators who implement IRS use compression sprayers to apply a measured amount of insecticide on the interior walls of houses and structures. A water-soluble insecticide is added to the sprayer containing a pre-measured amount of water, the prayer is pressurized, and the material is then applied to the interior walls of targeted homes and structures. After the day's spraying is complete, spray operators must clean the sprayer following the manufacturer's recommendations to ensure their proper operation and calibration.

The spray equipment used for IRS will be manufactured according to WHO specifications for compression sprayers for IRS operations. Cercles of Bla and Koulikoro CSCOMs and National PNLP Health Officials will determine mechanisms by which potential spray operators will be chosen. Spray operators will initially be chosen based on their completion of primary school, their ability to read, write and make calculations, as well as a medical exam to determine fitness for implementation of the activity. Pregnancy tests will be conducted as part of the medical exam to ensure that pregnant women are not included on the spray teams. The MOU between GOM/MOH and USAID will place the responsibility on MOH to ensure commitment and enforcement.

The individuals recruited for IRS campaigns will receive intensive training on the use, operation, calibration and repair of the sprayer and practical exercises during a 5-day period prior to the beginning of the spraying campaign. They will also receive training to understand proper hygiene, to recognize the signs and symptoms of exposure, and to understand the referral procedure for any incidents involving exposure. This training will be conducted in accordance with WHO's "Manual for Indoor Residual Spraying" (WHO 2002). Potential spray operators must also pass written and practical tests at the end of training. In this way, spray operators will be prepared to conduct appropriate application of the insecticide.

Each spray team will consist of six spray operators. Each spray operator will be provided with the following safety equipment, in accordance with WHO and FAO specifications:

- Broad-rimmed hat/helmet
- Face shield or goggles (face shield preferable)
- Dust mask or filtered mask
- 2 or 3 cotton overalls
- Nitrile rubber, neoprene, PVC or butyl rubber gloves, without inside lining, long enough to cover forearm
- Rubber boots

Supervisors will observe two spray teams to ensure spraying occurs according to best practices. Supervisors will travel between spray teams and will observe spray operators and team leaders in the preparation, spray technique, and sprayer and PPE cleanup during the IRS campaign, as well as compile all data collected by their respective teams. Supervisors and additional district and national malaria program personnel will receive a 5-day "training of trainers course" according to WHO best professional practices, and will also receive additional training on personnel management, environmental aspects, entomological monitoring, geographical reconnaissance, and data recording and analysis. After each day's spray activities, storekeepers should collect sachet packing material from spray operators to track the amount of insecticide used, and the supervisor should ensure that spray operators practice proper personal hygiene to avoid prolonged insecticide exposure. The insecticide is packaged in water-soluble sachets, minimizing pesticide exposure to spray operators during sprayer preparation.

Scrupulous attention to personal hygiene is an essential component of the safe use of pesticides. For spray operators, safety precautions will depend largely on personal hygiene, including washing and changing clothes. A

schedule for carrying out and supervising personal hygiene, regular washing of protective clothes and cleaning of equipment will be organized along the following lines (WHO 2006):
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—in circumstances where a full-body shower or bath is not feasible, face/neck and hands must be washed with soap and water.

- Working clothes must be washed regularly.
- 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.
- A drop-cloth and overalls wash-person will be hired and provided with his/her own protective gear. Wash persons will wash overalls at a central location in tubs used exclusively for overall washing. Spray operators must also wash themselves (at least face/neck, and hands) after each day's operations using wash basins specifically procured for that purpose or in a shower or bathing area. Spray operators should never wash themselves, their overalls, or their PPE in any water bodies. All wash-water should be disposed of in a concrete evaporation tank covered with a locked grate, an ablution block, or a soak pit, and improvement of existing infrastructure at Illovo for proper disposal of contaminated water (see Pesticide Procedures J for more detail on wash-water disposal options).

If USAID does not continue its support for the IRS program, program materials must be distributed or destroyed accordingly. All personal protective equipment (PPE), spray equipment, and environmental compliance equipment would be provided to the CSComs for its use in future spray programs. Insecticide would have to be provided to the PNLP. Rented warehouses would be decontaminated with water and detergent and revert to their owners. There are two options once the empty sachets are returned to the district storage facility. First, the empty sachets may be returned to the manufacturer for disposal. This proposal will be included in tender documents. If manufacturer recapture is not feasible, then RTI will be obligated to store the empty sachets in sealed drums until such time that the Pesticides Control Board (within the *Ministere d'Agriculture, Etudes Phytosanitaires et produits agricoles* Ministry of Agriculture, Study of Phytosanitary agricultural products) and through the supervision and authorization of the CNAC (The National Accreditation and Control Committee, *Comite National d'Agrement et de Controle)* and through the DNACPN (the African Program for the Elimination of Obsolete Pesticides) can arrange proper incineration of the sachets and obsolete pesticide stocks. Non-contaminated 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). Plastic barrels, on the other hand should be punctured and rendered unusable and disposed of in a landfill and not burned or incinerated. 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.

E. Any acute and long-term toxicological hazards, either human or environmental, associated with the proposed use and measures available to minimize such hazards

For acute and long-term toxicological hazards, see the toxicological profiles for Bendiocarb, DeltaMethrine, Alphacypermethrine, Bifenthrin, cyflurin and Lambda-cyhalothrin from USAID's *Integrated Vector Management for Malaria Vector Control: Programmatic Environmental Assessment* that can be found on USAID's Environmental Health Project website: http://www.ehproject.org/PDF/ehkm/ivm-env_assessment.pdf

Residential Exposure. The steps to mitigate, to the fullest extent possible, occupational exposure to Lambda-cyhalothrin is mentioned in the preceding section and described fully in the WHO's "Manual for Indoor Residual Spraying" (WHO 2002). However, as in all IRS operations, the risk of residential exposure is also present. District authorities and program staff will work with relevant boards, committees, and non-governmental organizations to carry out an IEC campaign to sensitize residents to IRS activities, in accordance with WHO guidelines. The IEC campaign (as well as IRS Program team leaders and supervisors who will also instruct residents on best practices prior to spraying) should focus on the following elements of residential safety during an IRS program:

- clear homes of mats or rugs, furniture, cooking implements and foodstuffs prior to spraying
- if furniture cannot be moved out of the home, then move it to the center of the room if possible and cover with drop-cloth
- stay outside the home during spraying and for four hours after spraying
- move and keep all animals outside the home during spraying, and for four hours after spraying
- sweep up any insects killed from the spraying and drop them in latrine pits
- sweep floors free of any residual insecticide that may remain from the spraying
- do not replaster or paint over the sprayed walls after spraying
- keep using bednets for protection against malaria
- if skin itches after re-entrance into home, wash with soap and water; for eye irritation, flush eyes with water; for respiratory irritation, leave the home for fresh air; for ingestion, if soap and water are unavailable, or if symptoms persist, contact program staff or go to nearest health facility.

The IEC component for IRS will coordinate closely with other PMI IEC initiatives.

Pesticide Exposure and Treatment. USAID will work with the DNACPN of Mali and District Health Officials to ensure that the medicines necessary for treatment are available in all relevant Koulikoro and Bla cercles CSCOM and CSREF health facilities, hospitals and health centers. In the following section this will be elaborated in greater detail.

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 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 hydrolyzed 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.

All the public hospitals in the spray sites will be stocked up with all or part of the following recommended drugs to use when cases of poisoning occurs to the spray team members or residents. The health officers will also receive training (refresher) on treatment for emergency cases of critical exposure and poisoning before the spraying occurs.

Finally, all the sprayers will also during the general IRS training receive training and first aid measures to take if exposure occurs.

Table 7: Drugs Recommended for Treatment of Pyrethroid Exposure

Name of drug	Active ingredients
Promethazine	Promethazine Hydrocloride
Panadol	Paracetamol
Diazepam	Benzodiazapine/Diazapam
Lorazepam	Lorazepam
Calamine cream	Calamine, zinc oxide, glycerol, phenol, purified water, sodium citrate, betonite,
Vit E	Tocopherol, fragrance, mineral oil, deionized water, sodium hydroxide, stearic acid
Hydrocortisone cream	1% hydrocortisone
Salbutamol	Salbutamol 100 mcg, suspended inert aerosol
Salbutamol tablets	Salbutamol sulphate 4 mg
Activated Charcoal	Activated Charcoal

Safe Pesticide Transport.
Prior to long-distance transport of the insecticide from the customs warehouse/central storage facility to the District, drivers will be informed about general issues surrounding the insecticide and how to handle emergency situations (e.g. road accidents). Training for long-distance transport from the distributorship to the district storage facilities will include the following information:

- For what use the insecticide is intended
- Toxicity of the insecticide
- Understanding security issues, implications of the insecticide getting into the public
- Handling an accident or emergency (according to FAO standards)
- Combustibility and combustion byproducts of insecticide

- Drivers hired specifically for the two-month spray campaign period will receive:
- Training provided to spray operators (with the exception of sprayer operation and spray practice)
- Handling an accident or emergency (according to FAO standards)
- Handling vehicle contamination (see below)

Because vehicles will be rented for 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). To prevent pesticide runoff from vehicle washing, drivers will also be responsible for wiping the vehicle bed with a damp cloth prior to washing the exterior of the vehicle. Finally, drivers will be responsible for cleaning and decontaminating the interior of the vehicle and exterior bed at the end of the spray campaign. Drivers will 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.

Acute and Toxicological Hazards to Outside Environment

Carbamates

The risk of vehicle accidents and consequent insecticide spillage is always present. Such spillage could expose humans, birds (e.g. chickens) and aquatic environments to carbamates with adverse consequences. It is also possible that the impacts of normal residential exposure of pregnant women could include neurological effects on unborn fetuses, but further research is necessary to test this hypothesis (Berkowitz, et al. 2003). Information on the combustion byproducts of carbamates can be found in USAID's Integrated Vector Management Programs for Malaria Vector Control: Programmatic Environmental Assessment (IVM PEA), pages 57-58.

Pyrethroids

The risk of vehicle accidents and consequent insecticide spillage is always present. Such spillage could expose both humans and aquatic environments to pyrethroids with adverse consequences. It is also possible that the impacts of normal residential exposure of pregnant women could include neurological effects on unborn fetuses, but further research is necessary to test this hypothesis (Berkowitz, et al. 2003). This fetal exposure in the home would be an unavoidable risk of the IRS operation. Human inhalation of toxic fumes in the event of a storehouse fire is also an unavoidable risk. Information on the combustion byproducts of pyrethroids can be found in USAID's Integrated Vector Management Programs for Malaria Vector Control: Programmatic Environmental Assessment (IVM PEA), pages 57-58.

Aquaculture

The cercles of Koulikoro and Bla have rivers and tributaries all forming part of the River Niger. Fishing is a vibrant economic way of life among the local communities that operate in this region. IRS activities in this area definitely pose a high risk factor in relation to possible contamination of the water bodies and the ecosystems dependent on it. The following mitigation scenarios will be followed;

- Release of sprayer rinse-water into water bodies. Sprayer rinse-water will be re-used for the next day's operations.

- Spray operators washing themselves, overalls and PPE in water bodies. Spray operators should wash themselves, and wash persons should wash overalls and PPE at the local or central meeting point for IRS operations. No washing will be allowed in the Lake.

- Households that are within 50m from the River shore will not be sprayed to minimize chances of contamination

- The fisher folk will be asked to remove all the fishing nets from their houses during the spraying to avoid contamination of the net which would then be introduced into the lake and hence cause pollution of the water and the fisheries. This will be done through extensive IEC by RTI staff and the PNLP.

Livestock

Pyrethroids are generally considered the safest insecticides that can be used in IRS, although individual pyrethroids impacts on mammals range from low to high toxicity. ICON as indicated in the table below shows a high toxicity to large mammal. As a general precaution, all livestock must exit the house for four hours after spraying. After re-entering the home, dead insects from home should be collected and thrown into a pit latrine to prevent pets and livestock (particularly chickens and guinea-fowl) from eating them.

Pesticide residue is also known to remain on the wall surfaces and sometimes drip on the ground after the spray activity and in effect could end up causing harm to livestock including chicken, goats, and cows if they get in contact with surfaces that have been sprayed immediately after the spraying. Further more if chicken or other fowls including ducks feed on dead insects not targeted by the IRS they could be at risk through poisoning. The cercles all keep livestock and include cows, goats, ducks, and chicken among others. This impact can be avoided if the mitigation measures proposed are pursued. However, in terms of significance and magnitude, it could lead to loss of life by livestock if poisoning were to occur.

Table 8. Toxicity of IRS Insecticides to Non Target Organisms, showing those considered in this EIA (taken from page 106 form PEA)

Proposed IRS Pesticide	Mammal	Bird	Fish	Other Aquatic	Bee	Persistence	Bioaccumulate
Lambda-Cyhalothrin	High Toxicity	Low Toxicity	High Toxicity	High Toxicity	High Toxicity	Medium Toxicity	High Toxicity
Bifethrin	Medium Toxicity	Medium Toxicity	High Toxicity	High Toxicity	High Toxicity	No data	Low Toxicity
Deltamethrin	Medium Toxicity	Low Toxicity	High Toxicity	High Toxicity	High Toxicity	Medium Toxicity	High Toxicity

F. The effectiveness of the requested pesticide for the proposed use

Vector Resistance

Insecticide Quality

USAID support for IRS will require that insecticide procurements will be accompanied by a Certificate of Analysis, assuring that the formulation was tested and that the appropriate amount of active ingredient is present in the formulation.

G. Compatibility of the proposed pesticide with target and non-target ecosystems

See pesticide Procedure section E

H. The conditions under which the pesticide is to be used, including climate, flora, fauna, geography, hydrology, and soils

6.1 Overview of Bla

The cercle of Bla is located in the south part of the Region of Segou, which lies north east of the capital of Mali, Bamako. The Bla has a surface area of 6,200 km2 and is predominately composed of plains and shoals. There are generally three types of soils: silty, lateritic, and silty-sandy. The average rainfall varies between 600 and 1000 mm per year (PSP 1981-1990 DNPPSS). The climate is Sudano-Sahelian, which is a semi arid climate, bushy savannah. The vegetation is composed of large bushes and trees. A few locally named examples include: Nere, Karite, Tamarind, Chao and Lenge trees.

Hydrology

Table 9 Rainfall Data

Last ten Years Rainfall in Bla										
Year	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007
rainfall in mm	798.4	1058.4	607	566.7	547	932.7	638.5	664	974	762
days of rainfall	56	68	53	42	33	51	36	48	54	47

There are three main water systems in the *cercle* of Bla: the Bani (which is the most important and the main tributary to the greater River Niver) flows from West to East through Mali towards Niger, the Koni that flows from Burkina Faso in the East, and the Madani that takes its source in the West in Cote d'Ivoire. These rivers are important for the irrigation of the agricultural fields and also for fishing.

Agriculture

The main food crops are millet, sorghum, maize, and rice often grown in rotation with legumes such as niébé, and groundnut. The main cash crop, known in Mali as "white gold", is cotton and its production is currently increasing. Additionally, there has been increasingly more cultivation of watermelon and peanuts; however calabash remains as the most profitable crop during the seasonal rainfalls.

Livestock and Fishing activities

Cattle, sheep and poultry are widespread and raised by almost all households. Fishing is also an important source of income by the communities bordering riverbeds of the Bani River, and more substantial during the rainy seasons when the river beds expand and the wetlands are filled.

Protected Areas and Natural Environment

There is one community forest called the Falo forest that is protected. It is located in the south-western part of the *cercle*. There are no important fauna within the forest, however according to the Local Direction of Protection and Conservation of Nature, this forest is foraged by locals for forest products.

Fauna has become increasingly rare in the last few years, however, it has been reported that gazelles still exist as well as pheasants. However, in the last twenty years with the introduction of cotton plantations, there has been a lot of habitat destruction which has made a lot of the endemic fauna flee. Furthermore, according to Local Direction of Protection and Conservation of Nature, lambda-cyhalothrin was used all over the region for agricultural purposes and did have an impact on the environment. At one time, there was honey production and apiculture, however, due to the pesticide, these populations were greatly reduced.

Table 10: Malaria Prevalence in Bla 2007

	Cercle Bla		
	Cerebral Malaria	Malaria	Total Population
Beguene	167	254	10340
Eskef	554	1108	n/a
Bla Central	403	1053	36391
Bogoni	25	1234	5055
Diaramona	39	2089	10121
Diedala	24	69	4013
Diena	58	240	10100
Dougouolo	35	850	10340
Foulo	293	363	18481
Fani	205	1197	12767
Kagoukasso	14	229	8705
Kemeni	3	1008	10198
Koulanoulougou	237	643	3937
Koukienbo	362	3548	6686
Morela	25	1087	8265
Namposso	444	1413	1064
Niala	0	666	7501
Niamalha	53	264	7904
Tenesso	136	444	4579
Samabougo	39	417	5376
Sambola	26	95	5271
Somasso	126	1707	10726
Tienabougou	25	624	6686
Tonto	11	512	9983
Touna	168	1796	20184
Yankasso	280	1840	11441
			255217

Source: PNLP and CSREF Bla, 2007

6.2 Overview of Koulikoro Cercle

The Cercle of Koulikoro is divided into 10 communes (among them are Dinandougou, Koula, Meguetan, Nyamina, Sirakorola, Tienfela, and Tougouni) and has a population of 172,000 inhabitants.

Koulikoro, the city, is the capital of the Region of Koulikoro, which in it, includes the cercle of Koulikoro. The capital of the Koulikoro Region, Koulikoro is located on banks of the Niger River, 59 kilometres (37 mi) from Mali's capital Bamako.

Koulikoro, the city (and parts of the cercle), is very industrialized and is the terminus of the Dakar-Niger Railway. Between August and November, at the end of the rainy season, the Niger River can be used to transport goods to other important cities in Mali including: Ségou, Mopti, Tombouctou and Gao.

Protected Areas and Natural Environment
There are three protected areas in the cercle of Koulikoro, Tienfala (3,000 ha), Nyamina (5,996 ha), and Kenenkou (6,065 ha).

In terms of fauna there are not many species in the cercle of Koulikoro. In areas closer to the Niger River, the fauna is much richer and includes: hippopotami, crocodiles and manatees. In the hunting zones, there are partridges, pheasants, monkeys, warthogs, hyenas, antelopes.

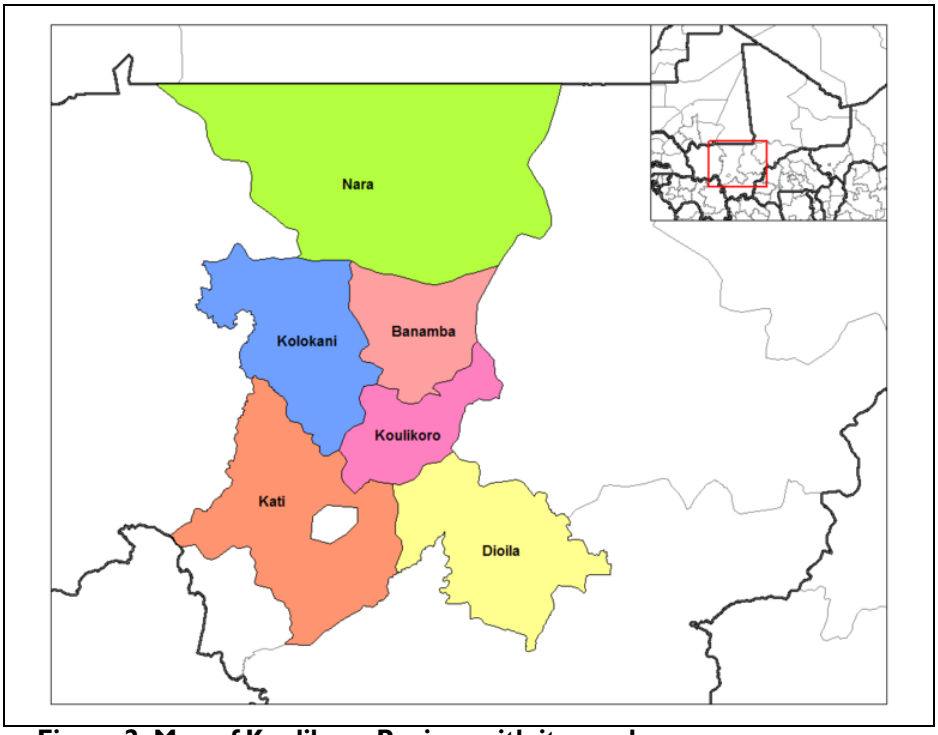


Figure 2; Map of Koulikoro Region, with its cercles

I. The availability and effectiveness of other pesticides or non-chemical control methods

DDT could be used as another possible pesticide but the sensitivity of handling this pesticide presents a challenge as well as country capacity to use this chemical and thus is not a preferred option. Furthermore, likewise to pyrethroids, the predominant malaria vector, Anopheles Gambiae, has developed a resistance to DDT.

Environmental management may also be difficult to implement in the cercles of Koulikoro and Bla due to its adjacency to River Niger and its tributaries; however, during the course of the IRS pilot program, the potential to utilize environmental management and larviciding will be investigated by the PNLP and MRTC. ITNs/LLINs are currently being distributed in Koulikor and Bla and this is a strategy which will be expanded.

J. The requesting country's ability to regulate or control the distribution, storage, use and disposal of the requested pesticide

All facilities used for storage, distribution and transportation of insecticide products should comply with relevant requirements of the Workers Health and Safety of Mali. To that end, the following sections and the EMP describe the program requirements for storage, distribution and transportation.

Supply Chain and Disposal Options

Mali has substantial ability to control the distribution, storage and use, but not disposal of pyrethroids in this case Lambda-cyhalothrin. The supply chain of insecticide will be as follows:

Manufacturer (Pesticide)
▼
Customs (Pesticide)
▼
Distributor Storage (Pesticide)
▼
District Storage (Storekeeper and Supervisor) (Pesticide)
▼
At the end of the spray round, unused pesticide will be kept under lock and seal until such a time that can be re-used for further IRS and if expired they can be disposed in accordance to international disposal requirements for obsolete pesticides.
▼
Spray Operators (spray operators must sign out all pesticide received daily and return empty sachets at the end of the day, see *Distribution*)
▼
District Storage (empties)
▼

There are two options once the empty sachets are returned to the district storage facility. First, the empty sachets may be returned to the manufacturer for disposal. This proposal will be included in tender documents. If manufacturer recapture is not feasible, then USAID will be obligated to store the empty sachets in sealed drums until such time that the Government of Mali, (with the African Program for the Elimination of Obsolete Pesticides) can arrange for proper incineration along with obsolete pesticide stocks. Burning or burial of empty sachets are not an acceptable form of disposal.

Distribution

Currently there are no courses provided to drivers on insecticide transport on a regular basis. Drivers transporting insecticide will be trained according to the guidelines listed in *Pesticide Procedures E* of this document and USAID's *Integrated Vector Management for Malaria Vector Control: Programmatic Environmental Assessment*, through the auspices of the distributor.

Distribution of insecticide sachets within the program must be conducted in the following manner:

- At reception at provincial warehouse lot numbers of insecticide and quantities are registered on shelf inventory card.
- District requisitions are approved at the program (provincial) office where copies are maintained.
- Requisition goes to provincial warehouse where distribution takes place and signed for, based on sachet numbers.
- On reception at district office, all sachets are counted and stamped with the relevant district stamp and registered on stock card.
- 5-6 can refills/day are issued to each spray operator, with their code written on the sachet.
- At the end of the day, empty and full sachets are returned and number checked against what was signed for.

- The next day all previously signed but unused sachets are re-issued and *again signed for by the relevant spray operator*.
- Spray operator performance, number of structures sprayed versus can refills used is calculated to see if there is an over or under application.
- At the end of the spray round, stock remaining = stock at start - no of sachets distributed. No. sachets distributed should be equal to no. can refills used.

Storage

Storage of the pesticides upon entry of the country remains a key activity in the IRS project that requires maximum supervision to guard against pilferage. It is required that a feasible, safe and acceptable warehouse be identified for storage of the pesticide and an evaluation be undertaken by the environmental specialists to determine the suitability of the storage site in accordance with the WHO guidelines for transportation and stock control including storage.

At the time of undertaking this Environmental Assessment possible storage sites for the pesticides had not been identified, however, personnel later identified a site, which will be further discussed in a later section

Temporary storage facilities must follow the minimum standards:

- Presence of a dedicated and trained storekeeper
- Thermometer installed/temperature recorded
- Insecticide stored separately from food and medicine
- Stock records up-to-date
- First-in, first-out pesticide use established
- Facility double-padlocked and guarded
- Soap and clean water available at all times
- Shower/bathing facilities available for spray operators (designated wash basins at a minimum)

USAID will fund the renovation of storage facilities, training of storekeepers to fulfill not only the minimum standards listed above, but best practices, as well as the commodities required for safety and security required in the facilities (see Environmental Compliance Budget Items and Procurement List).

USAID will fund the renovation of storage facilities and training of storekeepers to fulfill not only the minimum standards listed above, but best practices, as well as the commodities required for safety and security required in the facilities (see Appendix 2: Environmental Compliance Budget Items and Procurement List).

Rinse-Water Re-Use and Wash-Water Disposal

Water used to rinse out sprayers at the end of each day must be re-used at the beginning of the next day's work to save water and reduce the potential for pollution from contaminated rinse-water. The best practice for rinse-water re-use is called "progressive rinse." With this rinse method, seven barrels/drums/containers of approximately 200-litres each are placed in a line. Every other container is filled with water (e.g. the first container is empty, the second is filled with water, the third is empty, and so on; the seventh container is empty).

During the end-of-day cleanup, the remnants of a pump charge from the field are emptied into the first container. This will be a limited volume, which should be much less than half of this container, as most sprayers will be returned empty from the field (the uncommon situations where more insecticide returns is where the distance to the new site makes it difficult for the team to reach to empty their sprayers. Even then, the amount coming back will be less than a full drum or 220 liters). The spray operator will then fill the sprayer less than half-full with a cup of water from the

second container, close and shake the sprayer, and dump the sprayer water in the third container. The spray operator will repeat those steps with the fourth and fifth containers, then with the sixth and seventh containers, making sure to rinse the outside of the sprayer only at the sixth container (although not *in* the sixth container).

The following day, spray pumps are filled with liquid from containers in the same sequential order: container one, then container three, then container five. Any remaining liquid in the fifth and seventh containers are quite dilute and can be disposed in (a) an evaporation tank (b) an ablution block, or (c) a soak pit.

(a) Evaporation Tank. An impervious evaporation tank is repaired or constructed and covered by a locked grate. This can allow the insecticide to settle out and the water to evaporate. This disposal method works well if the tank has the appropriate capacity and if the rains do not cause it to overflow. See the figure below.

Figure 3. Soak Pit Surrounded by Wooden and Mesh Fencing

Evaporation Tank Construction

The Evaporation Tank should be:

- constructed with concrete and cement
- sunk into the ground and the sides raised about 20-30cm
- sited down slope from the wash area where you do triple rinse
- 3 meters long, 2 meters wide and 20-30 centimeters deep

The Evaporation Tank should have:

- A top covered by chicken wire or fencing wire mesh
- A drain which is kept open in the rain season and when IRS is not taking place (this is to get rid of rains and to clean it easily at the start of the IRS cycle)

Key Requirements:

- Remember the evaporation tank should be constructed in such a way that it is an extension of the triple rinse arrangement so that the drips and run off and soil can be pushed to the tank

- Don't forget that the important thing is only a minimum of water should be reaching the tank. This way evaporation will not be a problem
- In places where spraying will occur in the rain season, the progressive rinse site/wash area should be protected from rainfall
- After the spraying round, all the small amount of sand that would have ended into the evaporation pan and the insecticide residue should be scooped out (during cleaning process) and placed into a bag and placed together with empty sachets
- Remember that PPE should be worn to carry contaminated water to the evaporation tank—this activity still constitutes handling of insecticide

Figure 4. Evaporation Tank in Zambia

(b) Ablution Block. Repair or construction of an impervious ablution block that drains to a pit latrine. Although pouring the water directly into a pit latrine can work, this process makes it a little easier and lessens the risk of spillage and human exposure.

(c) Soak Pit. The site for the soak pit may be selected by the environmental authority (soak pits are usually sited at the highest point at the IRS depot/storage site and away from the natural path of run-off water). Depending on the size of the operation, you can construct a small or large pit. Usually an area of three meters by three meters (or nine square meters) is excavated to a depth of one meter. The bottom of the pit is packed with hard coal or charcoal. This is followed by saw dust (where this is feasible) and stone aggregates. The area is then fenced off to keep domestic animals and children out of the soak pit area. Because there is no loose soil, it serves as a nice area where washing of overalls can be done. The soak pit is also good for drying overalls, laying them either on top of the stones or over the fencing. The figure below shows a soak pit with partially-constructed fencing (the bottom piece of mesh was still being fitted for attachment in this picture).

K. The provisions made for training of users and applicators

Provisions made for training of users and applicators are described under Pesticide Procedures D. Training for spray operators and supervisors will be conducted over a 1- 2 week period. Training will be compliant with WHO's "Manual for Indoor Residual Spraying" (WHO 2002).

L. The provisions made for monitoring the use and effectiveness of the pesticide and ENVIRONMENTAL MANAGEMENT TABLE

Monitoring Use

Monitoring appropriate use of the insecticide will be carried out in multiple ways. First, RTI will provide training to district environmental officials or other select authorities such that they are capable of evaluating the quality of spraying activities and associated environmental compliance actions within the program. RTI will work with USAID to determine appropriate reporting mechanisms for these managers. RTI itself will also conduct an inspection to assess

compliance with this Environmental Management Plan and develop a plan of action to achieve complete compliance if deficiencies are found. RTI is already conducting inspections in IRS programs in PMI countries. Beyond the capacity building for environmental managers and the RTI inspection, the Chief of Party and other program staff will be responsible for documenting and reporting safety and environmental compliance issues to RTI to acquire technical assistance as needed and address compliance issues in a timely fashion. The objective of these activities is not only to ensure environmental compliance in the short term, but also to integrate safety and environmental standards into the program such that those standards carry forward beyond the timeframe for USAID support of IRS. Results of environmental compliance monitoring and subsequent mitigation activities from these three sources—district environmental managers, RTI environmental compliance staff, and Mali program staff—will be summarized in each final project report submitted to USAID. Finally, USAID's Automated Directives System (ADS) 204.5.4 requires that the Strategic Objective (SO) team actively monitor ongoing activities for compliance with the recommendations in this EA, and modify or end activities that are not in compliance.

Monitoring Effectiveness

The primary function of entomological monitoring associated with vector management is to assure that interventions are effective. Such monitoring is essential for IRS as well as in areas where only ITNs have been deployed. The monitoring program for Mali will be administered by MRTC and will include the following elements:

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 adulticides used in both IRS and on ITNs, susceptibility studies can be carried out using WHO test strips or CDC bottle assays on wild-caught adults or adults reared from immatures. While 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.

Furthermore, WHO susceptibility kits have been used in the past by the Mali PNLP and will be used as part of a nationwide monitoring program funded through the IVCC so Mali should continue to rely primarily on the WHO susceptibility kits. However, where possible, both should be done as the bottle bioassay tends to be more sensitive to small changes in insecticide susceptibility. 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 coding for pesticide resistance in the local vector population.

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 if 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 houses with mud walls that are sprayed under the IRS program, small punches can be made into the wall and tested for insecticide levels using High Performance Liquid Chromatography (HPLC).

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 to be used in Mali will include window exit traps and pyrethrum spray catches (PSCs).

ENVIRONMENTAL MANAGEMENT PLAN
PRE Spray Phase

Activity	Impact	Mitigation Measure/ Action Required	Monitoring Indicator	Responsible Party
Transportation of Pesticides from the port of entry to the storage facility	Accidental Spills of Insecticides during Road Transportation to warehouse and spray sites **(Human Health and Environmental impacts)**	Ensure that the drivers identified to haul the insecticide to the spray sites are well trained on the FAO standards and guidelines for the storage, transport and stock control for pesticides	Number of Road Accidents and spills reported Number of Drivers trained from records showing Drivers Training	RTI –Team responsible for IEC
	Possible environmental contamination caused by warehouse exposure due to poor siting of warehouses, Pilferage and vermin attack of the stored pesticides before spraying	Ensure the selected warehouse is sited away from a flood plain area, water course, wells, schools, markets	Number of storage facilities located inside of floodplain, nearby schools, hospitals, water courses	RTI –
		Secure the selected warehouse and apply all the guidelines for Storage and Stock Control manual by FAO.	Number of secured storage facilities as per the FAO Storage and Stock Control Manual	RTI –
Storage of Pesticides before spraying activities in the warehouse	Accidental Fires and injuries in the Warehouses	All warehouses must be equipped with a fire extinguisher, thermometer, exit doors and warning signs, and proper stacking position and height as stipulated in the FAO Storage and Stock Control Manual.	Presence of firefighting equipment, thermometers, warning signs and at least 3 exits access in the warehouse	RTI –
		All the workers handling pesticides or other products and equipment in the storage facilities must all have PPE including goggles, gloves, boots, overall, dust masks etc.	Number of workers that have access to PPE (to ensure the availability of PPE to all the workers)	RTI –Team responsible for IEC
		All spray operators and store managers must be trained on how to operate the fire extinguishers and what to do in case of fire outbreaks.	Number of workers trained in fire prevention and fighting	RTI –Team responsible for IEC

		Develop an Emergency Response Plan	Develop an Emergency Response Plan	

Spraying Phase

Activity	Impact	Mitigation Measure/ Action Required	Monitoring Indicator	Responsible Party
IRS Spraying of Women	Foetal Exposure	Pregnancy tests to ensure pregnant women are not on the spray teams; prohibition of breastfeeding women on spray teams; Education of women regarding risk and presentation of consent forms	**Percentage female spray operators who took pregnancy tests**	RTI and Ministry of Health/PNLP
			Percentage female spray operators who indicated they were not breastfeeding	
			Percentage female spray operators who have signed consent forms	
		Reassign women spray operators who become pregnant the campaign to tasks that minimize occupational exposure to insecticides	Number of females reassigned	RTI and Ministry of Health- PNLP
IRS Spraying men and women, transport of spray operators to and from site	Spray Operators, Drivers and storekeepers Exposure due to negligence or lack of PPEs, or un-intentional exposure caused by	Training of spray operators, team leaders and supervisors according to WHO and EA guidelines; training of storekeepers, drivers and health workers	● All outlines for training exercises include components described in the text of this EA, as well as the EMP ● **Number of vehicle accidents** ● **Number of major spill during insecticide transport**	RTI – and Ministry of Health- PNLP

	accidents	Provide PPEs to all the workers, supervisors, team leaders and store managers. Train the team leaders, sprayers, supervisors and store keepers on emergency procedures to take if exposure occurs accidentally i.e. dermal, eye or ingestion emergencies.	● **Number of Health workers trained** ● **Number of Storekeepers trained** ● **Number of Drivers trained** (see guidelines in Pesticide Procedures E) Spray Operators conduct the following activities during spraying: ● **Frequently agitate spray can** ● **Hold pump such that compression gauge can be seen** ● **Stands parallel to wall being sprayed** ● **Stands 45 cm from wall** ● **1m/2.5 sec spray rate** ● **75 cm swatch width and 5 cm overlap** ● **Nozzle not dripping** ● **All house wall surfaces sprayed** ● No eating, drinking or smoking witnessed during operations (previously mentioned)	
		Ensure that each Team Leader and Supervisors effectively monitor the spray operations diligently and take		
		Procurement of sprayers manufactured according to WHO specifications; procurement and proper use of PPE by spray operators, team leaders and supervisors (cotton overalls, face shield, dust mask, broad-rimmed hat, rubber gloves, gum boots) procurement of PPE for wash persons.		
		Prohibition of eating, drinking and smoking during work; prohibition of eating before washing		
IRS Spraying in Households in the two cercles: Bla and Koulikoro	Residential Exposure and possible health effects from exposure to the pesticide through dermal contact, ingestion (direct	IEC Campaign, instruct residents to: Clear homes of mats or rugs, furniture, cooking implements and foodstuffs prior to spraying	Number of Households cleared and well prepared before the spraying	RTI and Ministry of Health- PNLP

	or indirect) or inhalation	Move all furniture out of the house and for immovable ones, take to the centre of the house and cover accordingly	Furniture covered and or moved to the centre of the houses	RTI and Ministry of Health- PNLP
		Advise residents to stay outside the home during spraying and for two to four hours after spraying	Number of hours residents stay outside of the house until the recommended time lapse	
		Move and keep all animals outside the home during spraying, and for four hours after spraying. Sweep up any insects killed from the spraying and drop them in latrine pits Sweep floors free of any residual insecticide that may remain from the spraying	Animals kept away from the houses until the recommended time after spraying	
		Advise not to re-plaster or paint over the sprayed walls after spraying and keep using bed nets for protection against malaria	Number of houses not plastered or painted after the spraying period	
		If skin itches after re-entrance into home, wash with soap and water; for eye irritation, flush eyes with water; for respiratory irritation, leave the home for fresh air; for ingestion, if soap and water are unavailable, or if symptoms persist, contact program staff or go to nearest health facility	Cases of reported exposures to the health facilities/ CSCOMs	
IRS Spraying, Pilferage, Storage and Handling of Pesticide	Acute Exposure of Pesticide that goes untreated through ingestion, inhalation, eye and dermal contact could	Ensuring treatment medicines for insecticide exposure listed in EA mitigation section are available at the CSCOM level.	**Percentage of treatment medicines available at health facilities** Availability of first aid kits in storage facilities and hired vehicles	RTI and Ministry of Health- PNLP

	cause serious human health effects	Ensure first Aid kits are available in the storage facilities and the transport vehicles		
IRS Spraying, Accidental Release, Pilferage, during the spray rounds	Aquaculture Contamination	IEC Campaign, informing fisher folk involved in aquaculture in the target areas in the Koulikoro and Bla cercles to clean any aquaculture equipment stored in their home before use in the River Niger, tributaries or other main water bodies, and to ensure disposal of floor residue and dead insects as a result of IRS in pit latrines or a hole especially dug for the purpose of disposal	Number of post-spraying complaints from fisher folk involved in aquaculture in target area	RTI, Ministry of Livestock and Fisheries, Ministry of Water, Ministry of Environment, Sanitation and Pollution Prevention
IRS Spraying in Households in the cercles of Koulikoro and Bla	Community Exposure from ingestion, inhalation, eye and dermal contact could cause serious human health effects	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 4 hours after spraying Prohibition of spraying in homes where food, utensils and flooring have not been removed from the house, and where furniture has not been removed outside *or* moved to the middle of the room and covered with a cloth by the spray operator	Residents outside house during spraying (previously mentioned) Residents stay outside for four hours after spraying (previously mentioned) Occurrence of skin/eye/throat irritation (previously mentioned Food and goods outside house during spraying (previously mentioned	RTI Supervisors, Team Leaders
Negligence in securing of the storage facility, and lack of monitoring and supervision of the spray operators	Pilferage that could lead to Community Exposure and Environmental Contamination	Daily tracking of insecticide sachets used, spray-operator sign-out of sachets, return of empty sachets to supervisors, etc. (Indicators are equivalent to procedures listed in Pesticide Procedures)	At reception at provincial warehouse lot numbers of insecticide and quantities are registered on shelf inventory card Regional requisitions are approved at the program office where copies are	Storekeepers, Team Leaders, Supervisors, RTI,

		Ensure that the storage facilities meet all the security criteria listed in the FAO Storage and Stock Control Manual	maintained Requisition goes to provincial warehouse where distribution takes place and signed for, based on sachet numbers (if provincial warehouse present) On reception at district office, all sachets are counted and stamped with the relevant district stamp and registered on stock card.	
Storage of extra unused pesticide	Potential Exposure without Impact on Vector	Collection of insecticide samples and lab-testing of insecticide to ensure quality control	● Moisture content ● 75% active ingredient present	RTI
	Potential Exposure without Impact on Vector	Entomological monitoring	● Monitoring results presented in end-of-round report and monitoring reports submitted after end-of-round report	RTI

Post Spraying Phase

Activity	Impact	Mitigation Measure/ Action Required	Monitoring Indicator	Responsible Party
Transportation of Insecticides back to warehouse	Accidental Spills of Insecticides during Road Transportation to from spray sites to warehouse **(Human Health and Environmental impacts)**	Ensure that the drivers identified to haul the insecticide to the spray sites are well trained on the FAO standards and guidelines for the storage, transport and stock control for pesticides	Number of Road Accidents Records showing Drivers Training	RTI –Team responsible for IEC
Negligence in securing storage facilities and poor monitoring of spray operators and storekeepers	Pilferage and Community Exposure, Environmental Contamination	Keep storage facilities up to standards described in Pesticide Procedures J; Storage of all insecticides, empty packaging, barrels and tubs in storage facilities, reducing use of contaminated goods domestically	Presence of a dedicated and trained storekeeper ● Insecticide stored separately from food and medicine (previously mentioned) ● Stock records up-to-date (previously mentioned) **● Facility double-padlocked and guarded** **● Facility physically secure** ● 5-6 can refills/day are issued to each spray operator, with their code written on the sachet. These sachets are signed out buy the spray operator ● At the end of the day, empty and full sachets are returned and number checked against what was signed for	RTI- PNLP

			● The next day all previously signed but unused sachets are re-issued and again signed for by the relevant spray operator ● **Spray operator performance, number of structures sprayed versus can refills used is calculated to see if there is an over or under application** ● At the end of the spray round, [stock remaining] = [stock at start] - [no of sachets distributed]. No. sachets distributed should be equal Stock records up-to-date (previously mentioned)	
Negligence in proper storage rules, securing storage facilities and poor monitoring of spray operators and storekeepers	Accidental Fires and injuries in the Warehouses	All warehouses must be equipped with a fire extinguisher, thermometer, exit doors and warning signs, and proper stacking position and height as stipulated in the FAO Storage and Stock Control Manual.	Presence of firefighting equipment, thermometers, warning signs and at least 3 exits access in the warehouse	RTI – PNLP
		All the workers handling pesticides or other products and equipment in the storage facilities must all have PPE including goggles, gloves, boots, overall, dust masks etc.	Availability of PPE to all the workers.	RTI – PNLP

		All spray operators and store managers must be trained on how to operate the fire extinguishers and what to do in case of fire outbreaks. Develop an Emergency Response Plan	Training in fire prevention and fighting Develop an Emergency Response Plan	RTI - PNLP
Negligence of Safety and Clean Up Protocol	Residents' Exposure by using public vehicles used to transport pesticides	End-of-program cleaning/decontamination of interior and exterior of vehicles	Interiors and exteriors of vehicles cleaned	Drivers/Rental company
Negligence of Safety and Clean Up Protocol of Spray operators and Supervisors	Environmental Contamination and Resident Exposure from post spray disposal activities	Daily sprayer maintenance, sprayer progressive rinse, spray operator bathing, washing of overalls, PPE and cloths used to cover furniture, latrine disposal of laundry wash-water Ensure that a soak pit is constructed for disposing residual water after clean up Storage of empty sachets until manufacturer recapture or disposal option selected by the country. Procurement and distribution of barrels for progressive rinse, and wash-tubs for personal hygiene; inscription of program barrels and tubs as District Health Office property to deter sale and domestic use in event of pilferage	Evidence of progressive rinsing during all post spray clean ups Evidence of soak pits in all the return sites for clean up designed and constructed in the acceptable format Evidence of empty sachets stored in sealed barrels awaiting recapture by manufacture Availability of wash barrels and tubs with program inscription	RTI - PNLP

	Spray Operator and Community Exposure, Environmental Contamination continue unnoticed	Train district and/or national environmental compliance inspectors in Training of Trainers (TOT) and spray operator training course	National Directive of Public Health and Pollution Prevention - Environmental Compliance Inspectors trained on IRS	RTI, National Directive of Public Health and Pollution Prevention
Spray Operators Post Spray Cleanup activities	Spray operator exposure due to lack of washing after spraying	Ensure all spray sites have washrooms with adequate water and soap for washing	Soap and clean water available at all times (previously mentioned) ● Adequate numbers of shower/bathing facilities available for spray operators (designated wash basins at a minimum) (previously mentioned)	RTI- PNLP
Spray Operators Post Spray Cleanup activities	Spray Operator Exposure due to sprayer negligence during progressive rinse	Ensure supervision by Team Leaders ad Supervisor during progressive rinse. Ensure that progressive rinse occurs when sprayers are still dressed up in their full PPE		RTI- PNLP
Post Spray Storage and Lock Up	Environmental Contamination and residential exposure due to unused pesticide and empty sachets getting access to the local environment	Storage of empty sachets until manufacturer recapture or disposal option selected by host country Ensure that the warehouse is well secure and accountability of all stock is available by the store keepers.	Empty sachets collected and counted, stored in sealed drums	RTI, Supplier, National Directive of Public Health and Pollution Prevention

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APPENDIX 1 : Environmental Compliance Budget Items and Procurement List

Storage

Training for storekeepers

Physical Maintenance

- Materials/labor for store-house renovation
- Locks and keys for storage facilities
- Pallets for stacking insecticide and other equipment
- Construction of securable boxes for pesticide if storehouses cannot be properly secured

Emergency Kit

- 2 bags sawdust/sand
- Empty container to contain spillage residues
- Spade
- Brush
- Fire extinguisher

Health Kit

- Container of water or tap (inside)
- Bar of soap
- Eyewash set— *Ensure instructions are in host country language*
- Medical/first-aid kit— *Ensure instructions are in host country language*

Stock Management Kit

- Stock-book
- Bin cards
- Thermometer
- Pens

Storekeeper PPE

- Nitrile rubber, neoprene, PVC or butyl rubber gloves, without inside lining, long enough to cover forearm
- Rubber boots
- Overalls
- Goggles/face-shield
- Vapor masks for half-face respirators with organic vapor cartridges

Health Centers (should be provided by MOH if possible)

Health Worker training in pesticide poisoning

Poisoning treatment meds—*Ensure instructions are in host country language*

Pregnancy test kits — *Ensure instructions are in host country language*

Transport

Training for drivers (see your SEA or PEA for guidance)

For vehicle washing, nitrile rubber, neoprene, PVC or butyl rubber gloves, without inside lining, long enough to cover forearm

Washing
For each central meeting area for spray teams (usually storage facilities, either temporary or permanent):

- Basins for face and hand washing *or* materials to construct temporary bathing facilities *or* materials to renovate existing facilities to accommodate the size and number of spray teams meeting for daily clean-up
- Basins for washing overalls *separate from basins for face/hand washing*
- Materials for wash area demarcation (hard coal/charcoal, saw dust, stone aggregates/gravel, fencing and wire mesh), *or* budget for construction/renovation of ablution block, *or* budget for construction/renovation of evaporation tank with locked grate
- 7 barrels/drums for progressive rinse (this is enough to triple-rinse)—often it is helpful if they are wide enough or deep enough to submerge the entire spray can
- 3 plastic cups to pour rinse-water into spray can
- Detergent for washing overalls
- For each Wash Person, PPE:
    - Chemical apron
    - Nitrile rubber, neoprene, PVC or butyl rubber gloves, without inside lining, long enough to cover forearm
    - Rubber boots
    - Goggles
    - Dust mask

Operations
For each Spray Operator, PPE:

- Broad-rimmed hat/helmet
- Face shield or goggles (face shield preferable)
- Dust mask or filtered mask
- 2 or 3 cotton overalls/spray operator
- Nitrile rubber, neoprene, PVC or butyl rubber gloves, without inside lining, long enough to cover forearm
- Rubber boots (in appropriate sizes that don't cause blisters; keep in mind in several countries the spray teams are composed of 50% women, so smaller boot sizes may be warranted; other shoes/boots will absorb the chemical and is not safe)
- Extra PPE in the event gloves get torn, face shields break, dust masks get contaminated (all this *will* happen)

For each Spray Operator, additional field equipment:

- 1 drop-cloth (can be a bed sheet or something similar) to cover household furniture
- Plastic cover, small handbag or something to prevent spray card from being impregnated with insecticide in the field

Non EC-Related Procurement Suggestions
Funnel with strainer (to easily rid debris out of water used in pump charge) for each spray operator

Identification Cards including name and picture for all program staff (including supervisors, team leaders and spray operators)

APPENDIX 2 : Toxicological Profile for Lambda-Cyhalothrin (from USAID PEA for IVM)

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 The shelf life of Lambda-cyhalothrin is usually 2 years (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

Non cancer 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).

APPENDIX 3 : Toxicological Profile for Alpha-Cypermethrin (from USAID PEA for IVM)

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)[1] 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

[1] *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).*

0.01 mg/kg/day is based on a NOEL of 1 mg/kg/day for systemic effects with an 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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APPENDIX 4 : Toxicological Profile for Bifenthrin (from USAID PEA for IVM)

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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APPENDIX 5 : Toxicological Profile for Cyfluthrin (from USAID PEA for IVM)

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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APPENDIX 6 : Toxicological Profile for Deltamethrin (from USAID PEA for IVM)

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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APPENDIX 7 : Pyrethroids and Pyrethroid Poisoning Treatment (from USAID PEA for IVM)

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 decontamination.** 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.

Appendix 8: 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 absorbed beyond 60 minutes. Clinical trials with charcoal have been done with poisons other than pesticides. There is some evidence that paraquat is well absorbed 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.