GLOBAL PROGRAMMATIC INITIAL ENVIRONMENTAL EXAMINATION (P-IEE)[1] for Long Lasting Insecticidal Nets (LLINs) in DCHA/OFDA Humanitarian Assistance Programs

PROGRAM/ACTIVITY:
DCHA[2] Office: Office of Foreign Disaster Assistance **(**OFDA)

Country: Global

Title of Program: Procurement, Distribution or Use of LLINs in Humanitarian Settings

Grant Number(s): Various on Record with OFDA systems

Implementing Partner: Various Humanitarian Assistance NGOs

IEE Begin: August 15, 2011 **IEE End:** August 14, 2012 **Annual Amount:** Up to $2m

IEE Prepared by: Alexandr Kosyak, OFDA, Technical Assistance Group, Health;
Yene Belayneh, OFDA Technical Assistance Group, Pesticides

Date: August, 15, 2011

PIEE Amendment: Yes☐ No☒ If yes, date of original IEE: _____

ENVIRONMENTAL ACTION RECOMMENDED: (Place X where applicable)

☒ **Request for Categorical Exclusion(s):** activities have no adverse effect (i.e., training, technica assistance; not to include any infrastructure rehabilitation.)
☒ **Negative Determinatio**n: no significant adverse effects expected for activities which are well defined over life of the award.
☒ **with conditions** (mitigation measures specified)

☐ **Positive Determination:** potential for significant adverse effect of one or more activities. Appropriate environmental review needed/conducted.

SUMMARY OF FINDINGS:
The purpose of this Programmatic Initial Environment Examination (P-IEE) is to comprehensively review the activities undertaken by the OFDA LLIN program and provide threshold determinations of environmental impact and conditions for mitigation.

OFDA is often requested to support measures to control disaster related vector-borne diseases and other health risks through providing support for insecticide treated bed nets (ITNs), including long lasting insecticide treated nets (LLINs) to address vector borne

[1] This P-IEE is a supplement to the USAID Integrated Vector Management (IVM) Programmatic Environmental Assessment (PEA), 2011 meeting all requirements for environmental impact assessment per 22 CFR 216.
[2] The USAID functional Bureau of Democracy, Conflict and Humanitarian Assistance (DCHA).

diseases. The need for these materials has been on the rise and OFDA has been trying to address this issue on a case by case basis in an effort to reduce mortality and morbidity in humanitarian disaster settings among children under 5, the elderly, and pregnant and lactating mothers. The growing trend for increased natural disasters and more frequent man-made calamities, such as conflicts and civil strife, which drive large segments of populations into overcrowded IDPs or refugee camps are just a few signs of the likelihood of increased exposures to transmissible diseases. Given the potential upward trend in vector-borne diseases in the humanitarian sphere, OFDA will be faced with more requests for supporting intervention actions, including LLINs.

ENVIRONMENTAL THRESHOLD DETERMINATIONS

A **Categorical Exclusion** is recommended for activities involving provision of technical assistance, management and delivery of commodities, pursuant to 22 CFR 216.2(c)(2)(i), for activities involving education, training, technical assistance or training programs.

A **Negative Determination with Conditions**, per §216.3(a)(2)(iii), is recommended for activities that involve the procurement and/or use of insecticide-treated bednets procured directly by OFDA or by OFDA implementing partners such as NGOs and Public International Organizations (PIOs).

Conditions: OFDA AOTRs must ensure that Awardees comply with the conditions for the procurement and/or use of LLINs for OFDA programs as in Section 4.2 of the P-IEE. A brief summary of mitigation measures is below; (refer to Section 4.2 for a full description of required conditions).

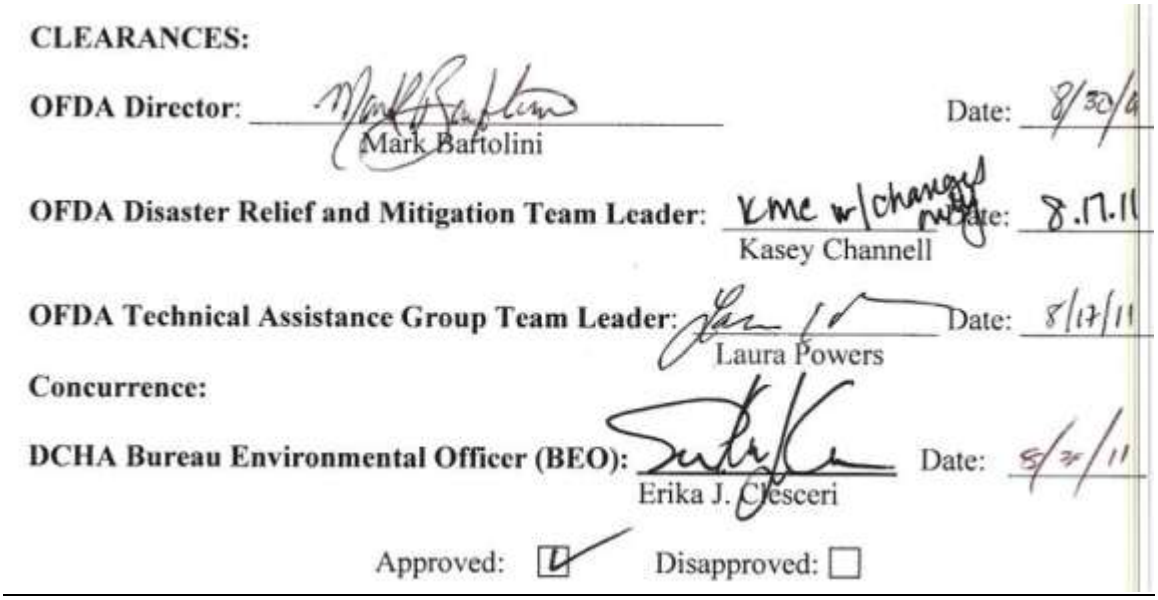
1. AOTR and AO shall include required environmental compliance language into each implementation instrument, and ensure that appropriate resources (budget), qualified staff, equipment, and reporting procedures are dedicated to this portion of the project.
2. Currently Permanet 2.0 and Olyset are recommended for OFDA programs. Other LLINs may be considered upon consultation with current USAID recommendations.
3. OFDA awardees must include training on the proper use, washing, acceptable re-use at end-of-life (EOL) and ultimate disposal of the LLINs to all beneficiaries as part of distribution campaign. At a minimum, OFDA awardees must include training i) on risks or LLINs for fisheries purposes amongst fishing communities and ii) local solutions to manage the long term solid waste of used nets on their EOL.
4. OFDA awardees must coordinate with Ministries of Health and/or UN Health Cluster entities to inform them of the LLINs introduced to the country for purposes of insecticide resistance monitoring at the country and/or regional level.
5. This P-IEE only pertains to LLINs activities for OFDA supported programs. Support for any other pesticide-related activity would necessitate the preparation of a PERSUAP, in accordance with 22 CFR 216 guidance and fulfilling all analytical elements required by 22 CFR 216.3(b), USAID's Pesticide Procedures.
6. OFDA awardee implementation will in all cases adhere to applicable host country environmental laws and policies.

Attachments:

Executive Summary: "Global Programmatic Initial Environmental Examination (P-IEE) for Long Lasting Insecticidal Nets (LLINs) in DCHA/OFDA Humanitarian Assistance Programs"

Full Text: "Global Programmatic Initial Environmental Examination (P-IEE) for Long Lasting Insecticidal Nets (LLINs) in DCHA/OFDA Humanitarian Assistance Programs"

USAID APPROVAL OF ENVIRONMENTAL ACTION(S):



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Archived in the Agency IEE Database:
http://www.usaid.gov/our_work/environment/compliance/database.html

GLOBAL PROGRAMMATIC INITIAL ENVIRONMENTAL EXAMINATION (P-IEE)[3] for Long Lasting Insecticidal Nets (LLINs) in DCHA/OFDA Humanitarian Assistance Programs

EXECUTIVE SUMMARY

This Programmatic Initial Environmental Examination (P-IEE) for Long Lasting Insecticide Nets (LLINs) was developed to provide details specific to the humanitarian assistance context for LLIN programs funded by the Office of Foreign Disaster Assistance (OFDA) in the Bureau for Democracy, Conflict and Humanitarian Assistance (DCHA). The P-IEE permits funding of OFDA humanitarian assistance for malaria management by LLIN for vulnerable populations receiving relief commodities and programs. This P-IEE is an extension into the humanitarian assistance space of the Programmatic Environmental Assessment (PEA) for Integrated Vector Management (IVM) for Malaria developed for the Agency by the Global Health Bureau (2011).

Under the National Environmental Policy Act (NEPA) statute, it is USAID regulation (per 22 CFR 216) and Automated Directives System (ADS) 204 policy to ensure that any negative environmental consequences of USAID activities involving the procurement and/or use of pesticides can be identified and mitigated prior to a final funding and implementation decision. This regulatory requirement is applicable for 1) OFDA direct procurement for pesticide containing material stockpiling, 2) NGOs proposals for LLIN procurement and/or use and 3) for the support of Public International Organizations (PIOs) procurement and/or use of LLINs, unless PIO demonstrates implementation of equivalent or superior safeguards. In particular, 22 CFR 216 mandates for the analytical elements of the USAID pesticide procedures, as in 22 CFR 216.3(b), for all programs, including for "international disaster assistance" programs.

This assessment covers specific environmental consequences involved with the procurement and/or use of the pesticide containing material found in Long Lasting Insecticidal Bednets or LLINs, and necessary safeguards and mitigation for humanitarian assistance programs funded by USAID. To meet 22 CFR 216 pesticide procedures and inform the AO and AOTR of the specific chemical hazards and risks, this examination contains detailed Pesticide Evaluation Report and Safer Use Action Plan (PERSUAP) and Pesticide Profiles Concerning Acute and Long-term Toxicological Hazards, either Human or Environmental for each of the three pesticides that could occur in an LLIN.

The information contained in this document is intended for use by OFDA decision makers and OFDA implementing partners in the field to guide environmentally sound LLIN programs supported by OFDA globally. As part of standard AOTR duties, OFDA will ensure that each proposal submitted in consideration for LLIN funding will have sufficient capacity to undertake the environmental safeguards associated to maximizes the effectiveness of this USAID program at the lowest possible impact to the underlying environmental resources.

[3] This P-IEE is a supplement to the USAID Integrated Vector Management (IVM) Programmatic Environmental Assessment (PEA), 2011 meeting all requirements for environmental impact assessment per 22 CFR 216.

GLOBAL PROGRAMMATIC INITIAL ENVIRONMENTAL EXAMINATION (P-IEE) for Long Lasting Insecticidal Nets (LLINs) in DCHA/OFDA Humanitarian Assistance Programs

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1.0 Background and Program Description

1.1 Background

Malaria problem in the humanitarian space

Vector born diseases are among the most serious life-threatening and debilitating diseases that continue affecting vulnerable populations in many developing countries. Malaria alone affects hundreds of millions of people globally causing nearly a million deaths annually. Half of the world's population is at risk of malaria, a disease endemic in more than 106 countries, mainly in the tropics with sub-Saharan Africa (SSA) being the hardest hit and parts of Asia and Latin America also prone to significant malaria epidemics. More than 40% of mortality of children under 5 is from malaria and over 85% of global mortality in many tropical African countries is attributed to the disease. It is estimated that the number of cases of malaria rose from 233 million in 2000 to 244 million in 2005 but decreased to 225 million in 2009. The number of deaths due to malaria is estimated to have decreased from 985,000 in 2000 to 781,000 in 2009 in some 106 countries. Although this may not directly apply to disaster settings, a decreased malaria burden has been observed in all WHO Regions, with the largest proportional decreases noted in the European Region, followed by the Region of Americas. The largest absolute decreases in deaths were observed in Africa.[4]

While disasters can significantly affect displaced people physically, psychologically, emotionally as well as economically, massive population displacements can also require both temporary and long-term resettlement often in camp settings or shelters. Such settlements are often overcrowded, with none to meager basic health care facilities and resources to practice even the most rudimentary hygiene and personal safety and security are often lacking. In most instances, displaced peoples' camp sites can create a very conducive environment for proliferation of vector-borne diseases such as malaria, dengue, typhus as well as other transmissible diseases. For instance, sleeping outside without protection (a behavior common among displaced people), lack of prevention and control strategies as well as migration of people to higher disease transmission areas can exacerbate the risk of vector-borne diseases, creating a further condition for additional humanitarian assistance.

OFDA's rationale for supporting LLINs

As the lead Agency for USG's response to international disasters, USAID through OFDA responds to different types of disasters, including but not limited to floods, earthquakes, volcanoes, tsunamis, hurricane and cyclones, pest and disease outbreaks, drought, extreme temperatures and fire, landslides, disasters caused by civil strife, conflicts, industrial accidents and nuclear power breakdown, etc. These events can have serious health, economic and social consequences on large numbers of vulnerable and affected populations and communities.

[4] http://www.who.int/malaria/world_malaria_report_2010/world_malaria_report_2010.pdf; http://www.fas.org-sgp-crs-misc-R41644.pdf;http://www.kff.org/globalhealth/upload/7882-03.pdf

When a disaster strikes in a country with an ongoing conflict the pre-existing health system can be adversely affected and impair health facilities through the loss of health staff, medical supplies, communication and transportation etc., and thereby significantly hinder access to primary health care and slow disease control programs. The risk of vector-borne diseases, such as malaria increases in disaster situations due to stagnant pooling of water resulting from floods, etc. Overcrowding, population movement to higher transmission areas and lack of personal protection can exacerbate the situation, all of which are characteristic features of disasters. In addition, flooding related disasters can also lead to overflow of toxic waste sites, or release of chemicals or human/industrial waste stored in the ground or in floodplains into river systems and significantly compromise safety and health of vulnerable populations and communities.

OFDA is often requested to support measures to control disaster related vector-borne diseases and other health risks. OFDA receives requests from implementing partners to provide support long-lasting insecticide treated nets (LLINs) to address vector borne diseases. The need for these materials has been on the rise and OFDA has been trying to address this issue on a case by case basis in an effort to reduce mortality and morbidity in humanitarian disaster settings among children under 5, the elderly, and pregnant and lactating mothers. In addition, OFDA also directly procures and distributes LLINs to communities in countries affected by disasters (Table 1).

The growing trend for increased natural disasters and more frequent man-made calamities, such as conflicts and civil strife, which drive large segments of populations into overcrowded IDPs or refugee camps are just a few signs of the likelihood of increased exposures to transmissible diseases. This situation requires donors and international organizations to respond to the needs of the displaced. Given the potential upward trend in vector-borne diseases in the humanitarian sphere, OFDA will be faced with more requests for supporting intervention actions, including LLINs. This means that providing wide-spread therapeutic interventions such as the distribution of malaria drugs will become very difficult in camp settings. The exception being pregnant women and other vulnerable populations that require critical and multiple interventions, not to mention the increasing malaria resistance to such drugs (refer Section 1.2., program description for further detail).

The efficacy of insecticide-treated nets for reducing the burden of malaria in sub-Saharan Africa has been repeatedly proven[5]. The WHO global malaria program has highlighted the public health benefits of insecticide treated nets (ITNs) and encourages large-scale implementation of ITNs throughout malaria prone and afflicted areas of the world through collaborations with bilateral and multilateral donors and host-country governments, particularly in SSA where 90% of malaria incidences occur. Both ITNs and LLINs can provide physical and chemical protection by preventing mosquito bites and reducing severe disease and mortality in malaria endemic regions when used in a community-wide setting. However, the need for re-treatment of the conventional ITNs every 6-12 months or more often, a rarity involving additional cost and potential health and environmental threats, will likely push OFDA to favor LLINs. In addition, LLINs also have a comparative advantage of remaining effective in providing protection throughout their lifecycle of 3 years or more.

[5] http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1142337/

With figures like these and the recent trend for malaria developing resistance to many of the curative drugs and to some extent pesticides, it is ever more logical to follow an integrated vector management approach in which the use of LLINs can play an important role.

OFDA's role in the larger Agency LLIN program

OFDA's support for LLINs becomes an essential ingredient in an effort to control and prevent malaria related mortality and morbidity, particularly in humanitarian settings, where in most instances, camp sites create an ideal condition for the proliferation of vector-borne diseases such as malaria, dengue, typhus and other transmissible diseases. These efforts can, undoubtedly save lives, reduce human sufferings and contribute to the overarching goals of the Presidential Malaria Initiative (PMI) and the Presidential Global Health Initiative (GHI).

The launching of the PMI in 2005 by President George W. Bush, with a five-year plan and a $1.2 billion budget elevated the U.S. attention to malaria targeting a total of 17 countries in Africa. The goal of the initiative and a latter amendment was to half malaria-related deaths in these countries. In FY2008, Congress significantly increased funding for malaria and authorized the creation of U.S. Global Malaria Coordinator at USAID to oversee all U.S. malaria efforts[6]. In addition, malaria management efforts conducted by USAID and the CDC in three African countries, India, and in South America encourage OFDA's intervention actions in reducing malarial incidences in the humanitarian space.

In 2009, the Obama Administration launched the GHI, a new six-year (FY 2009–2014) effort to develop a comprehensive U.S. government strategy for global health. The GHI integrates the PMI into a larger global health portfolio and includes specific targets for malaria. U.S. bilateral funding commitments for malaria, which include PMI and other malaria efforts, totaled $2.8 billion between FY 2004 and 2010, and is approximately $733 million in FY 2011[7].

OFDA supports LLIN programs in countries historically not included in the PMI such as Sudan (Darfur, South Sudan), the DRC, Pakistan, Bolivia, Niger, and the Dominican Republic. OFDA also supports LLIN programs in PMI countries such as Ethiopia and Mozambique in structurally remote and shock-prone communities. The PMI provides support for malaria control beginning in 2006 in Angola, Tanzania and Uganda, and with a rapid scale-up underway in 15 countries by 2008 (Angola, Tanzania, Uganda, Malawi, Mozambique, Rwanda, Senegal, Benin, Ethiopia, Ghana, Kenya, Liberia, Madagascar, Mali and Zambia). The 2008 Lantos-Hyde Act authorized an expanded PMI program for 2009-2013 and in 2011, consistent with the USG Malaria Strategy, Nigeria and the DRC were added.

Considering the usefulness of LLINs for vector-borne disease control and prevention of acute malaria cases and given that LLINs contain pesticide (restricted goods) that invoke the Agency environmental regulations, it is even more urgent to prepare documentation that will enable OFDA to evaluate requests from its implementing partners and respond

[6] http--www.fas.org-sgp-crs-misc-R41644.pdf ; http://www.kff.org/globalhealth/upload/7882-03.pdf

[7] http://www.fas.org-sgp-crs-misc-R41644.pdf

accordingly. Therefore, it is critical that OFDA supports LLINs in countries where disasters heigthen the threat of malaria outbreaks, including those that are covered by the Presidential Initiatives. During the course of this process, OFDA will emphasize that adequate information and necessary training and communication materials are provided to the beneficiaries receiving the LLINs that specifically contain those nets containing the following insecticides: alpha-cypermethrin, deltamethrin, and permethrin.

1.2 Program Description

How LLINs fit into OFDA Health program

In the past, OFDA has supported activities that involved procurements, distributions, and use of hundreds of thousands of LLINs for the prevention and control of mosquito-borne diseases such as malaria, dengue and typhus in many countries where extensive flooding that resulted from heavy rains forced large numbers of people to abandon their villages and localities (see table below). For instance, heavy rainfall that began on July 22, 2010 resulted in subsequent flooding that affected nearly 17.6 million people in multiple regions of Pakistan causing more than 1,600 deaths nationwide in 79 of it 122 districts, according to Pakistan's National Disaster Management Agency (NDMA). As of September 21, 2010 the U.N. World Health Organization and Government of Pakistan Ministry of Health reported more than 163,000 suspected malaria cases in flood-affected provinces. At times, such a situation is further exacerbated by conflicts, civil strife and other causes pushing large segments of societies into IDP camps.

USAID/OFDA has developed a partnership with the Mentor Initiative to build the technical and operational capacity of Ministries of Health and NGO partners to respond to the burden of vector-borne diseases in crisis afflicted areas and improve vector-borne disease control in humanitarian space. This initiative aims to alleviate the burden of diseases such as malaria, dengue fever, leishmaniasis and others during periods of crisis in regions of the world most at risk. With USAID/OFDA support, Mentor will conduct targeted training courses for practitioners and stakeholders on malaria control in emergencies. These workshops emphasize the practical aspects of malaria control, including rapid diagnosis and treatment as well as the public health importance of establishing robust health sector infrastructure for dealing with malaria. Additionally, OFDA's partnership with Mentor will provide technical support for NGO field staff and national teams on improving case management while simultaneously providing policy guidance to Ministries of Health for streamlining malaria control programs with basic primary care and emergency response.

OFDA procured and/or distributed LLINs over the past five years

During the past several years, USAID/OFDA procured, distributed and/or stockpiled thousands of LLINs. In 2007, OFDA procured and distributed 50,000 LLINs to flood affected communities in Mozambique. The following year, it procured and distributed more than 27,700 LLINs to Bolivia, Burma and the Dominican Republic. In 2010, OFDA procured a strategic stockpile of 100,000 LLINs and in 2011, 1,000 LLINs from the stockpiles were distributed to Sri Lanka.

The main brand of LLINs OFDA procured and distributed is primarily PermaNet 2.0 which is manufactured by Vestergaard Frendsen (fee Table below for details). It is worth noting that both PermaNet 2.0 have received full UN WHO Pesticide Evaluation Scheme's approval and PermaNet 3.0 has received an interim approval. PermaNet 3.0 is manufactured by the same company and it is intended to be used in areas where mosquito resistance to pyrethroids has been detected. In addition, USAID/OFDA has also funded the procurement and distribution of LLINs to several malaria affected countries and camps through its implementing partners.

Table 1. USAID/OFDA and NGO directly procured and distributed/stockpiled LLINs (PermaNet 2.0) from 2007-2011, from Vestergaard Frandsen (source: OFDA Logistics).[8]

Year	*Quantity*		*Country Received*	*Cost of procurement in USD*	*Cost per bednet in USD*
	Procured	*Distributed*			
USAID/OFDA Directly Procured and Distributed/Stockpiled LLINs					
2007	50,000	50,000	Mozambique	384,500	7.69
2008	7,700	7,700	Bolivia	39,963	5.19
	15,000	15,000	Burma	75,150	5.01
	5,000	5,000	Dominican Republic	25,950	5.19
2010	100,000	0.00	Strategic stockpile in Miami and Dubai	570,000	5.7
2011	0	1,000 Dubai stock	Sri Lanka		
NGO Directly Procured LLINs					
2011	2,500		Yemen	25,000	10
	2,132		Ethiopia	10,660	5
	2,000		Sudan	14,280	7.14
	-		DRC	60,000	
	6,000		DRC	24,000	4
	6,000		Sudan	34,500	5.75
Total	**n=196,332**	**n=78,700**		**$1,264,003**	**Average: $6.07**

[8] Direct OFDA procurement, not procurement and/or use through implementing partner unsolicited proposals.

2.0 COUNTRY AND ENVIRONMENTAL INFORMATION (BASELINE INFORMATION)

2.1 Locations Affected

The OFDA LLIN Program is responsive yet unplanned due to the nature of the unsolicited proposal process under the humanitarian assistance context. The Program, as such, is broad by nature, and, as such, an adequate description of the diverse environments where OFDA will support malaria control interventions would be difficult to provide. It is required that the OFDA Implementing Partners that fall under the Global OFDA LLIN IEE should address the affected environment on a country-by-country basis.

2.2 National Environmental Policies and Procedures (host country both for environmental assessment and pertaining to the sector)

In many of the host countries where OFDA LLIN program are conducted, a regulatory framework for environmental impact assessment exists, often based upon US and European systems. However, as a result of prolonged internal conflict or civil war, little attention has been given to the implementation of environmental laws relating to environmental impact assessments (EIA). Many target host countries face many challenges such as lack of capacity, data, proper guidelines, enforcement, and most importantly awareness of the environment protection sector or its effectiveness.

Nevertheless, several NGOs and donor agencies have been developing administrative structures to address the needs of environmental protection and natural resources management. These structures require reviewing and tools improvements to produce effective environmental management of development and humanitarian assistance projects. Provision of detailed guidelines for environmental impact assessment can help to improve the practice in the management of environmental resources.

3.0 Evaluation of Program with Respect to Environmental Impact Potential

Potential environmental impacts of long lasting insecticide treated nets (LLINs) are examined pertaining to the activity, including the procurement, storage, transportation, and management of LLINs, specifically those nets wherein the following insecticides are coated on or impregnated into netting: Deltamethrin (Permanet 2.0), and Permethrin (Olyset). The environmental impact associated with the manufacturing of LLINs is not within the scope of this examination.

From 2008 to 2010: nearly 290 million LLINs were delivered to sub Saharan Africa through various donor programs. There is growing awareness of the potential environmental impact that the millions of insecticide-treated nets pose during their

lifecycle; that is, from use as a public health tool or to their various alternative re-uses and their final disposal. Potential environmental risks and/or health impacts may arise from either exposure to pesticide active ingredients (AI) and/or to mis-management related to the physical and structural properties of the nets.

First, during their use for public health and malaria control purposes, there is a potential risk of exposure to pesticide residues in LLINs by lactating mothers to infants, who breast-feed for up to 2 years in developing countries. Unfortunately, very little is known of the exposure route of pesticides in to breast milk from the prolonged minimal exposure to LLINs or the health risk this poses to infants. This is an issue that has recently come to the attention of WHOPES. Present evidence suggests that potential neurologic and endocrine effects are associated with pyrethroids at levels equal or below known levels in breast milk[9]. Because mothers are exposed to insecticides via various routes and for extended periods of time, accumulated residues are transferred to infants via breast milk, in some cases exceeding recommended intake levels. Using or washing LLINs pose a less of a threat via dermal or oral ingestion of pyrethroids than during treatment of ITNs that has shown to be within acceptable exposure levels. Even with such a risk, the benefits of using ITNs in reducing morbidity and mortality from malaria outweigh the risks[10].

Second, an additional potential impact exists to aquatic species due to pesticide AI exposure since pyrethroid insecticides are toxic to fish and other aquatic organisms (e.g., frogs, insects, crayfish, etc.). Aquatic or surface water ecosystems can be exposed to the LLIN pesticides through washing of nets in rivers. Nets used for young children are often washed more frequently due to soiling with feces and urine.

Third, LLINs have a limited lifespan. After the useable life for public health purposes, millions of nets will be re-used in some manner by resource-limited communities. Some evidence has shown LLINs used preferentially to non-LLINs as fishing nets in coastal fishing villages due to higher tensile strength[11], availability and cost (free) following distribution programs by health ministries or NGOs. Small mesh sizes of LLINs results in fishing nets that scour aquatic systems for juvenile, under-sized fish, causing disruptions in food chains and reducing future population growth.

Fourth, after nets are damaged and otherwise unable to be re-used, millions of nets eventually accumulate as solid waste in regions without functioning landfills or semi-regulated open dump sites. Currently WHO Global Malaria Program is piloting a

[9] "Malaria Control Insecticide Residues in Breast Milk: The Need to Consider Infant Health Risks", Hindrik Bouwman and Henrik Kylin, *Environ Health Perspectives*, 117:1477–1480 (2009).

[10] "Risk Assessment of the Use of Deltamethrin on Bednets for the Prevention of Malaria", S.M. Barlow, F.M. Sullivan, and J. Lines, *Food and Chemical Toxicology*, 39:407 – 422 (2001).

[11] "Unforeseen misuses of bed nets in fishing villages along Lake Victoria", Noboru Minakawa, Gabriel O Dida, Gorge O Sonye, Kyoko Futami, and Satoshi Kaneko, *Malar J*. 2008; 7: 165. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2532690/?tool=pubmed

study project on sustainable management of LLINs throughout their life cycle to assess alternatives for what to do with nets at the end of their useable life[12].

4.0 RECOMMENDED MITIGATION ACTIONS (INCLUDING MONITORING AND EVALUATION)

4.1 Recommended IEE Determination

As a pesticide-containing material, Long Lasting Insecticidal Mosquito Nets (LLINs) are a restricted USAID good/commodity. Support for the acquisition, distribution, marketing and /or use of LLINs can only be conducted in accordance with USAID environmental compliance pesticide procedures 22 CFR 216.3(b)(1).

A **Negative Determination with Conditions** is recommended herein for malaria control programs involving the use of insecticide-treated bed nets per §216.3(a)(2)(iii).

As discussed in the Programmatic Environmental Assessment for Insecticide-Treated Materials in USAID Activities in Sub-Saharan Africa (ITM PEA) (available online at http://www.afr-sd.org/documents/iee/32AFR2_ITM_PEA.pdf), the choice to use WHO-recommended brands of LLINs rather than nets requiring retreatment is the most effective risk mitigation measure available.

4.2 Mitigation, Monitoring, and Evaluation

As required by ADS 204.3.4, the OFDA Agreement Officer's Technical Representative (AOTR) will ensure that provisions of the IEE concerning mitigation measures and the conditions specified herein are met. The AOTR is responsible for assuring that implementing partners have the human capacity and budget necessary to incorporate environmental considerations into program planning and implementation. The following 6 conditions will be included in OFDA solicitations and awards.

To procure and/or use LLINs, the OFDA AOTR will ensure compliance with the following:

Conditions:

1. **Contracting**: The AOTR and Agreement Officer (AO) shall ensure the inclusion of required environmental compliance and reporting language into each implementation

[12] Alliance for Malaria Prevention: http://www.allianceformalariaprevention.com/resources/Sustainable%20management%20of%20nets%20life-cycle%20-%20Aurelie%20Bottelin.pdf

instrument, and ensure that appropriate resources (budget), qualified staff, equipment, and reporting procedures are dedicated to this portion of the project.

2. **Procurement**: Currently Permanet 2.0 and Olyset are recommended for OFDA programs[13], based upon status as:
    a. Full or interim approval by WHOPES[14] and
    b. Recommendation by USAID Global Health Bureau due to analysis of efficacy and manufacturing reliability through the President's Malaria Initiative (PMI).
3. **Use and Disposal**: Environmentally preferred options for LLINs and LLIN packaging include: 1. Use the net as long as possible; 2. Re-use the net for other purposes not harmful to the environment and health; 3. Recycle; 4. Dispose safely. Beneficiary training must include aspects of environmental impact as in following:
    a. **Washing**: When training on how to determine the useful life of the LLIN, frequency of washing and formation of holes must be addressed[15]. Training must emphasize that that nets be washed inland, away from biologically sensitive ecosystems like rivers, lakes, or marshes to reduce risk of pyrethroid contamination.
    b. **Avoidance of Misuse**: Recipient users must be informed that LLINs are not to be used for any fishing purposes, including as fishing nets in ponds, lakes, rivers, estuaries or the ocean. The use of a LLIN as a fishing net is an indiscriminate fishing technique which has been widely documented to have serious implications for fisheries sustainability and ecosystem function[16,17]. The LLIN's mesh holes are small enough to catch juvenile fish and larval populations en masse that could devastate fishery productivity[18].
    c. **Opportunities for Re-Use**: Ecologically and public health safe alternatives for re-use of LLINs at this end-of-life might include for non-food packaging, ropes, non-food storage purposes within the home, window screening, fencing and especially continued use as a bed net until a newly treated bed net is available as nets have a protection factor even without chemical treatment.
    d. **Disposal or Recycling of Nets**: WHO recommends universal coverage, yet LLINs have a limited lifespan. The options for disposal of nets at their end-of-life (EOL) will need to take into account the environmental impacts of both

[13] Other LLINs can be discussed on a case by case basis, subject to further review.

[14]World Health Organization Pesticides Evaluation Scheme (WHOPES) approved LLINs http://www.who.int/whopes/Long_lasting_insecticidal_nets_Apr_2011.pdf.

[15] Smith et al. (2007), Am. J. Trop. Med. Hyg., 77(6_Suppl), pp. 243-248, "Evaluation of Bednets After 38 Months of Household Use in Northwest Ghana", **http://www.ajtmh.org/cgi/content/full/77/6_Suppl/243.**

[16] Dalzell P. (1996), "Catch rates, selectivity and yields of reef fishing." In: N.V.C. Polunin & C.M. Roberts (eds) Reef Fisheries. London: Chapman & Hall, pp. 161–192.

[17] McClanahan, T.R., and Mangi, S.C., (2004), "Gear based management of a tropical artisanal fishery based on species selectivity and capture size." *Fisheries Management and Ecology* 11; 51-60.

[18] "Unforeseen misuses of bed nets in fishing villages along Lake Victoria", Noboru Minakawa, Gabriel O Dida, Gorge O Sonye, Kyoko Futami, and Satoshi Kaneko, *Malar J*. 2008; 7: 165. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2532690/?tool=pubmed.

the disposal of plastic net material and the residual pesticide contained within. Experience demonstrates that at the end of the LLIN useful life, community members will use nets in manners that are not recommended, i.e., fishing/seine nets, bridal garments, and infant swaddling. Preferred disposal is safe recycling or incineration in accordance with FAO/WHO and Basel Convention guidelines[11].

e. **Disposal or Recycling of Packaging**: Packaging for LLIN contains pesticide residues that must be handled properly. Assess the locally existing options for the safe recycling/disposal of bags. Do NOT burn LLIN bags in open air; Do NOT incinerate LLIN bags unless the proper incineration conditions are available; Do NOT re-use LLIN bags for any other purpose. Preferred methods include: Burn LLIN bags according to FAO/WHO and Basel Convention guidelines; Investigate local recycling options for safe applications; Store LLIN packaging only if safe incineration or recycling is expected in the near future; If recycling or incineration is not possible; Bury locally. (WHO/ Global Malaria Programme).

f. **Communications**: For all of these potential environmental impacts, printed insert materials will be distributed to all beneficiaries receiving LLINs. These materials will contain the basic components of the safe and effective use of the LLINs in the simplest language and pictoral representation to address different languages and literacy/numeracy competencies.

4. **Insecticide Resistance**: The OFDA awardee must coordinate with Ministries of Health and/or UN Health Cluster entities to inform them of the number of LLINs introduced to a sub-region of the country to determine the level of insecticide resistance monitoring at the country and/or regional level. To date, pyrethroids are the only class of chemical approved by the WHO for use on mosquito nets. The development of pyrethroid resistance in *Anopheles gambiae* has been highlighted in recent years due to the increased reliance on pyrethroid treated nets for malaria prevention and control.
5. **Coordination**: OFDA grantees are expected to coordinate with local health entities at the central or municipal government level, and/or UN Health Clusters.
6. **Host Country Regulations**: OFDA awardee implementation will in all cases adhere to applicable host country environmental laws and policies.

ANNEX A: Pesticide Evaluation Report, Safer for Use Action Plan (PERSUAP)

The following information meets the requirements of the USAID Pesticide Procedures section of the environmental compliance regulation, 22 CFR 216.3 (b)(1) and contains specific information regarding the toxicity, use and disposal of LLINs embedded with alpha-cypermethrin, deltamethrin and permethrin.

Pesticide procedures element: As part of the evaluation to determine the potential environmental impact the planned use of pesticides by a project may have, an SEA must address the environmental impact. This assessment shall include but not be limited to the following considerations:

a. The USEPA registration status of the requested pesticide[19]. There are three pesticides, all pyrethroids, currently used in the production of LLINs: alpha-cypermethrin, deltamethrin and permethrin. The OFDA programs procure nets with each of these pesticides. Of these, deltamethrin and permethrin are both registered by the Environmental Protection Agency (EPA). Alpha-cypermethrin, although not registered for use in the United States today by the EPA, it is approved for use by the WHO as an agent for use in LLINs for mosquito vector control.

b. The basis for selection of the requested pesticide. Established in 1960 to promote and coordinate testing and evaluation of pesticides employed for use in public health, the WHO Pesticide Evaluation Scheme (WHOPES) meets annually to review selected compounds, formulations and/or products. USAID adheres to the WHOPES recommendations. These three pyrethroid insecticides are recommended for use as vector control agents when incorporated into a polymer net because they are considered safe for humans in close contact settings and are efficacious at lower concentrations, and have both a rapid and persistent effect (http://www.who.int/whopes/recommendations/wgm/en/). At present, pyrethroids are the only class of insecticides recommended for the treatment of nets (http://www.who.int/whopes/Insecticides_ITN_Malaria_ok3.pdf). Should that change during the life of the OFDA project and other insecticides become available for the treatment of nets, the appropriate amendments to the SEA would be made. The decision for specific nets and individual pesticides, due to similar low to moderate acute impacts is made based on country preference, cost and availability. Pyrethroids are the only class of pesticides currently used in LLINs.

[19] It is important to note that the United States, where EPA registration is effective, does not have a malaria problem, does not perform indoor residual spraying, and has little market for pesticides with important health uses (and where it does use them, generally uses small amounts). Therein lays one of the issues with relying heavily on EPA registration. Many markets are too small for manufacturers to attempt to gain registration status. Therefore, many products which might receive active registration status for the small amounts of insecticide used in health programs, had the US had a problem with malaria and performed wall spraying, never do. Likewise the EPA will not have user risk data for IRS applications, because they are not performed in the United States.

c. The extent to which the proposed pesticide use is part of an integrated pest management program. OFDA programs typically support only the use of LLINs in absence of an integrated vector management strategy. Resistance monitoring by Ministries of Health or WHO may indicate resistance to pyrethroids. But at this time no no other class of insecticide is available in LLINs. Because mosquito knock down rates, at this time, may be decreased, the nets continue to provide both barrier protection, repellant and knock down protection.

d. The proposed method or methods of application, including bioavailability of appropriate application and safety equipment. The pyrethroid insecticides used in the manufacture of nets intended for use as a protective barrier against mosquitoes are at relatively low doses and considered safe when applied in LLINS. The low to moderate toxicity of these pyrethroids have been shown, via WHOPES evaluations, to be relatively safe in the given settings. Nets are distributed in plastic packaging to ensure handlers and distributors are not exposed to the pesticide during distribution as repeated pesticide exposure increases the chance of dermal reactions. At the same time it is critical that the distribution of these nets include flyers that describe the safe use and disposal techniques required to provide safe exposure limits to human health and the environment.

e. Any acute and long-term toxicological hazards, either human or environmental, associated with the proposed use and measures available to minimize such hazards. Please see attached Annex A for complete chemical and toxicological profile on each of the three pesticides.

f. The effectiveness of the requested pesticide for the proposed use. Please refer to parts b and c above as well as Annex A for detailed information on the efficacy and utility of the three pyrethroids used in the LLIN products.

g. Compatibility of the proposed pesticide with target and non-target ecosystems. The environmental behavior of the pesticides used in the nets. Additional details for alpha-cypermethrin, deltamethrin and permethrin are provided in 'Annex A Pesticide Profiles' section.

Alpha-cypermethrin. Alpha-cypermethrin is a broad spectrum, nonsystemic, synthetic pyrethroid insecticide used on field crops, fruits, vegetables, and livestock, and in residential applications. It is also commonly used as an insecticide to kill mosquitoes to control malaria transmission.

In the air, alpha-cypermethrin exists in both vapor and particulate phases. As a vapor, it is broken down by reactions with hydroxyl radicals and ozone. The half-life for these reactions is estimated at 18 hours to 49 days. As a particulate, alpha-cypermethrin is removed from the atmosphere by wet and dry deposition. Once in the terrestrial environment, alpha-cypermethrin binds tightly to soil. Volatilization is the major fate process in moist soils; however, the tight bond of alpha-cypermethrin to soil attenuates the volatilization. In non-sterile soil, alpha-cypermethrin is biodegraded by environmental organisms and sunlight. It does not build up in surface soils nor leach to subsurface soils. In aquatic environments, alpha-cypermethrin bonds tightly to

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

Deltamethrin. Deltamethrin is a broad spectrum synthetic pyrethroid insecticide first marketed in 1977 for use in agricultural and public health applications. It is considered the most powerful synthetic pyrethroid. For mosquito control, bed nets and other materials are treated with deltamethrin to protect the user. Deltamethrin is typically formulated as emulsifiable concentrates, wettable powders, ultra-light-volume and flowable formulations, and granules (either alone or combined with other pesticides). A dispersible tablet is also used to treat mosquito nets. In terrestrial environments, deltamethrin is not expected to be mobile, because it binds tightly to soil particles. It is insoluble in water, and recommended application rates are low. Volatilization from moist soils and biodegradation are major fate processes. However, volatilization is lessened by deltamethrin's tendency to adsorb to soil particles. As with other synthetic pyrethroids, deltamethrin degrades rapidly in soil and plants. It does not bioaccumulate in terrestrial systems. Very little leaching to groundwater is expected, because deltamethrin binds tightly to soil and is practically insoluble in water. Volatilization is a major environmental fate process in surface waters, but is lessened by soil adsorption. Deltamethrin breaks down quickly in water, with reported half-lives of 2 to 4 hours. It has a high potential to bioconcentrate in aquatic organisms.

Permethrin. Permethrin [(3-phenoxyphenyl)methyl 3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropane carboxylate] is a broad spectrum, nonsystemic, synthetic pyrethroid insecticide registered for use on numerous food/feed crops, livestock and livestock housing, modes of transportation, structures, and buildings (including food handling establishments), and for residential uses. It is also commonly used as an insecticide to kill mosquitoes to control malaria transmission. Permethrin enters the atmosphere when it is sprayed in malaria control operations. Like all pyrethroids, permethrin is broken down and degraded rapidly by sunlight and other compounds found in the atmosphere. Often, permethrin lasts only 1 or 2 days in the atmosphere before being degraded. Any remaining permethrin will be removed by precipitation and deposited in terrestrial and aquatic environments. Once in the terrestrial environment, permethrin appears to dissipate primarily by binding to the soil and by soil microbial degradation. It is moderately persistent in soil, but due to its hydrophobicity, permethrin is also extremely immobile in soil and stays in the surface layers. Permethrin is not very soluble in water, resulting in little concern for groundwater contamination. Permethrin is likely to enter aquatic environments either through direct application or as result of runoff. Once in a waterbody, permethrin has a very high affinity for soils and sediment in aqueous systems, and will bind quickly to sediment in the water column (Imgrund, 2003).

h. The conditions under which the pesticide is to be used, including climate, flora, fauna, geography, hydrology, and soils. The pyrethroid pesticides are incorporated into polymer fiber nets, which are then sealed in bags for transport. Once at the point of destination, these LLINs are taken out of their bags and hung over sleeping spaces. Given proper use of the LLIN, the net pyrethroid will not escape to groundwater, surface water or soils. However, if the nets are misused these nets may leach in water and to soil via washing, and inappropriate fishing and disposal.

OFDA can supply LLINs for any countries to any target countries requiring humanitarian assistance. The dominant climate for LLIN is warm, and can be either arid or humid. The general climate in which the nets will be hung has some diversity but is the same climate conducive to the propagation of the *Anopheles* mosquito. In all cases the nets are to be used within the dry interior of structures over beds etc.

i. The availability and effectiveness of other pesticides or nonchemical control methods. While the current technology for LLINs supports only pyrethroids, there is research to create a LLIN product incorporating both pyrethroid and non-pyrethroid insecticide as a mosaic or mixture. New contact insecticides may become available in the future but are not yet available (http://www.who.int/malaria/publications/atoz/itnspospaperfinal.pdf).

j. The requesting country's ability to regulate or control the distribution, storage, use and disposal of the requested pesticide. All nets procured through the OFDA project must be registered in the country in which the nets are distributed, as is common practice with the USG President's Malaria Initiative (PMI). There may be host-country or UN Health Cluster systems in place to respond to the supply chain needs and to the handling of LLINs.

k. The provisions made for training of users and applicators. Each OFDA LLIN program, regardless of the size, will include training on the safe/effective use and ultimate disposal including recommended and not recommended options for re-use of the nets for alternative purposes.

l. The provisions made for monitoring the use and effectiveness of the pesticide. As required under ADS 204.3.4, the AOTR of the project will actively monitor and evaluate whether environmental consequences unforeseen under activities described herein arise during implementation, and modify or end activities as appropriate. Any grants or monetary transfers of USAID funds (e.g., subgrants) to support this program's activities must incorporate provisions that the activities to be undertaken will comply with the environmental determinations and recommendations of this SEA. This includes assurance that the activities conducted with USAID funds fit within those described in the approved SEA and that any mitigating measures required for those activities be followed.

3) Activities that directly or indirectly result in the generation and disposal of hazardous or highly hazardous medical waste or in techniques that have a direct or indirect environmental impact.

References for this section include:
http://www.who.int/water_sanitation_health/medicalwaste/167to180.pdf
http://www.bchealthguide.org/healthfiles/hfile29.stm
Safe management of wastes from health-care activities, edited by A. Prüss, E. Giroult and P. Rushbrook. Geneva, WHO, 1999, http://www.who.int/water_sanitation_health/Environmental_sanit/MHCWHanbook.htm. English
EGSSAA Chapter 8, "Healthcare Waste: Generation, Handling, Treatment and Disposal" (http://www.encapafrica.org/EGSSAA/Word_English/medwaste.doc) for additional guidance on proper handling and disposal of medical waste.

ANNEX B: Pesticide Profiles Concerning Acute and Long-term Toxicological Hazards, Either Human or Environmental

1. Profile for Alpha-Cypermethrin:

CAS Registry Number 67375-30-8

Summary of Insecticide

Chemical History

Alpha-cypermethrin is a highly active synthetic pyrethroid insecticide used to control a wide variety of pests in agricultural and public health applications. It is similar to the natural insecticide pyrethrum, which comes from chrysanthemums; however, it is more effective and longer lasting (ATSDR, 2003; IPCS, 1992). Alpha-cypermethrin is available in technical grade formulation, emulsifiable concentrate, ultra-low-volume formulation, suspension concentrate, and in mixtures with other insecticides (HSDB, 2005; IPCS, 1992). For mosquito control, it is used in bed nets and other materials that are dipped in alpha-cypermethrin to protect the user (WHO, 1997, 1998). It is considered one of the best insecticides for impregnation of traps and screens (WHO, 1997). Alpha-cypermethrin is not currently registered for use in the United States (HSDB, 2005), but cypermethrin is.

Alpha-cypermethrin is of low risk to humans when used at levels recommended for its designed purpose (HSDB, 2005; ATSDR, 2003). However, as a synthetic pyrethroid, alpha-cypermethrin exhibits its toxic effects by interfering with the way the nerves and brain normally function (HSDB, 2005; ATSDR, 2003). It has moderate acute toxicity and is a suspected endocrine disruptor but does not inhibit cholinesterase (PAN, 2005). 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 paraesthesias or a burning, tingling, or stinging. However, these effects are generally reversible and disappear within a day of removal from exposure (HSDB, 2005; ATSDR, 2003; 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)[20] was identified for neurological and respiratory effects in rats exposed to alpha-cypermethrin via inhalation for 4 hours (IPCS, 1992). An uncertainty factor of 100 to account for intra- and interspecies variation was applied, for an inhalation benchmark of 4 mg/kg/day. This value is appropriate for all exposure durations.

Due to limited low-dose oral data for alpha-cypermethrin, health benchmarks for cypermethrin were used and are expected to be protective of human health. The acute oral MRL for cypermethrin of 0.02 mg/kg/day is based on a LOAEL of 20 mg/kg for neurological effects (altered gait and decreased motor activity) in rats with an uncertainty factor of 1,000 applied. Long-Evans rats were given single gavage doses of up to 120 mg/kg cypermethrin. Motor activity and FOB were assessed at 2 and 4 hours post-dosing. A NOAEL was not identified (ATSDR, 2003). The chronic oral RfD for cypermethrin of 0.01 mg/kg/day is based on a NOEL of 1 mg/kg/day for systemic effects with an 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

[20] 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).

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 hydrolyses 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. 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).

2. Profile for Deltamethrin (Active Ingredient for LLIN Permanet):

CAS Registry Number 52918-63-5

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-low-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 it 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 interfering with the way the nerves and brain normally function. 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 macroinvetebrates 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)

3. Profile for Permethrin (Active Ingredient for LLIN Olyset):

CAS Registry Number 52645-53-1

Summary

Chemical History

Permethrin is a synthetic pyrethroid insecticide used in agricultural and human health applications. It is similar to the natural insecticide pyrethrum, which comes from chrysanthemums; however, it is more effective and longer lasting (WHO/FAO, 1984; IPCS, 1990). For mosquito control, it is used in bed nets and other materials that are dipped in permethrin to protect the user (EXTOXNET, 1996; WHO/FAO, 1984). Permethrin is of low risk to humans when used at levels recommended for its designed purpose (ATSDR, 2003a). However, as a synthetic pyrethroid, permethrin exhibits its toxic effects by interfering with the way the nerves and brain normally function. Typical symptoms of acute exposure are irritation of skin and eyes, headaches, dizziness, nausea, vomiting, diarrhea, and excessive salivation and fatigue. Inhaled permethrin has been shown to cause cutaneous paresthesias or a burning, tingling, or stinging. However, these effects are generally reversible and disappear within a day of removal from exposure (ATSDR, 2003a).

Description of Data Quality and Quantity

Several comprehensive reviews on the toxicity of permethrin have been prepared or updated in recent years:

- Toxicological Profile for Pyrethrin and Pyrethroids (ATSDR, 2003a)
- An EPA risk assessment for the Reregistration Eligibility Decision (RED) document (U.S. EPA, 2005f)
- IRIS summary review (U.S. EPA, 2005g).

EPA and ATSDR have developed quantitative oral human health benchmarks (EPA's acute and chronic RfDs, short-, intermediate-, and long-term inhalation and dermal benchmarks and ATSDR's acute and intermediate oral MRLs). Other relevant references include

- Environmental Health Criteria 94: Permethrin (IPCS, 1990)
- Specifications for Permethrin (WHO, 1999a).

Summary Table

Duration	Route	Benchmark Value	Units	Endpoint	Reference
Acute, Intermediate, Chronic	Inhalation	0.11	mg/kg/day	Inhalation NOAEL of 0.042 mg/L (11 mg/kg/day) for neurological effects in rats with UF of 100 applied	U.S. EPA (2005f)
Acute, Intermediate, Chronic	Oral	0.25	mg/kg/day	Acute and chronic RfD based on clinical effects in rats	U.S. EPA (2005f)
Acute, Intermediate, Chronic	Dermal	5	mg/kg/day	Dermal NOAEL of 500 mg/kg/day in rats with a UF of 100 applied	U.S. EPA (2005f)
Cancer	Inhalation, Oral, Dermal	0.009567	per mg/kg/day	CSF for lung tumors in female mice	U.S. EPA (2005f)

For inhalation exposure, a NOAEL of 0.042 mg/L (11 mg/kg/day) was identified for neurological effects in rats exposed via inhalation and an uncertainty factor of 100 was applied. This value is appropriate for short- (1–30 days), intermediate- (1–6 months), and long-term (>6 months) inhalation exposures (U.S. EPA, 2005f).

For oral exposure, an acute and chronic oral RfD of 0.25 mg/kg/day was derived based on a NOAEL of 25 mg/kg/day for clinical signs (i.e., aggression, abnormal and/or decreased movement) and increased body temperature observed in rats, with an uncertainty factor of 100 applied (U.S. EPA, 2005f). The acute and chronic RfD was adopted to also represent intermediate exposures.

For dermal exposure, a NOAEL of 500 mg/kg/day was identified in rats dermally exposed for 21 days and an uncertainty factor of 100 was applied. This value is appropriate for all exposure durations (U.S. EPA, 2005f).

To assess potential carcinogenic risks, a cancer slope factor (CSF) of 9.567×10^{-3} per mg/kg/day was derived based on lung tumors in female mice chronically exposed to permethrin in the diet (U.S. EPA, 2005f).

Insecticide Background

CASRN: 52645-53-1

Synonyms: 3-Phenoxyphenyl)methyl3-(2,2-dichloroehenyl)-2,2-dimethylcyclopropanecarboxylate (ATSDR, 2003a)

Chemical Group: pyrethroid

Registered Trade Names: Ambush, BW-21-Z, Cellutec, Dragnet, Ectiban, Eksmin, Exmin, FMC 33297, Indothrin, Kafil, Kestrel, NRDC 143,

Pounce, PP 557, Pramex, Qamlin, and Torpedo (EXTOXNET, 1996), Acion, AI3, AMbushfog, BW-21-7, CO-Opex, Matadon, NIA 33297, Outflank, OMS-1821, Perthrine, Picket G, Perigen, PP557, R86557, Stockade, Stomoxin, S-3151, SBP-1513, Talcord, WL43479 (WHO/FAO, 1984)

Usage

Permethrin is used as a broad spectrum insecticide to combat pests on a variety of crops. It is also used to control ectoparasites in animals, biting flies, and cockroaches and is used in greenhouses, gardens, and for termite control (EXTOXNET, 1996). It belongs to the pyrethroid class of insecticides, which have long been used to control mosquitoes, human lice, beetles, and flies (ATSDR, 2003a). For mosquito protection, it is used in bed nets and other materials that are dipped into the permethrin to protect the user. Permethrin for agricultural use is restricted by EPA due to its potential toxicity to aquatic organisms, and it may only be purchased and used by certified applicators (ATSDR, 2003a).

Formulations and Concentrations

Permethrin is available in technical grade, emulsifiable concentrates, dusts, smokes, ultra-low volume (UVL), and wettable powder formulations (EXTOXNET, 1996). Technical grade permethrin may be mixed with carriers or solvents resulting in the commercial formulations. These commercial formulations may also include ingredients that may potentiate the toxicity compared to technical grade permethrin. These ingredients must be identified on the label. WHO indicated that the content of permethrin in the formulated products must be declared and shall not exceed the listed standards. For impregnated mosquito netting, the permissible permethrin content is 20 +/- 3 mg/kg (WHO, 2002). Technical grade permethrin must have no less than 900 g/kg permethrin. The emulsifiable concentrate should contain > 25–100 g/kg +/- 10% of the declared content, 100–250 g/kg +/- 6% of the declared content, or > 250–500 g/kg +/- 5% of the declared content (WHO, 1999a). Permethrin that is used for bed nets comes in the emulsifiable concentrations ranging from 10 to 55 percent active ingredient. The 55 percent emulsifiable concentration is only for professional use (WHO, 1999a).

Shelf Life

Permethrin is stable for 2 years or longer at 50^{o}C. It is most stable in acidic environments and optimal stability is at pH 4. Photochemical degradation occurs in laboratory studies but not in field data. Pyrethrins, in general, are stable for a long time in water-based aerosols (HSDB, 2005).

Degradation Products

Pyrethroid insecticides are often formulated with synergists that act to prevent the breakdown of enzymes and thus enhance the activity of the pyrethroid (ATSDR, 2003a).

Permethrin needs to be stored in a dry, cool, well-ventilated location to prevent the risk of it breaking down prior to use. Permethrin's breakdown products include 3-phenoxybenzyl(1RS)-cis, trans-3-(2,2-dichloroviny)-2-2dimethylcyclopropanecarboxylate (PAN, 2005).

Environmental Behavior

Fate and Transport in Terrestrial Systems

Permethrin is moderately stable in the environment (WHO/FAO, 1984). It binds tightly to soil making it almost immobile in most soil types. Studies have shown that permethrin is immobile in clay and loamy sands, while its degradation products have some mobility. As a result, it is not easily taken up by plants or leached into groundwater (ATSDR, 2003a).

In soil, permethrin is of low to moderate persistence (EXTOXNET, 1996). The reported half-life ranges from 30 to 38 days in soil (EXTOXNET, 1996) and < 2.5 days in a sediment and seawater solution. The U.S. Department of Agriculture (USDA) Pesticide Database lists the half-life of permethrin as 4–40 days in aerobic soils. It is broken down largely by microorganisms in nonsterile soil and may also be broken down by sunlight at the surface of soil (ATSDR, 2003a).

Fate and Transport in Aquatic Systems

Permethrin is not expected to be released in large quantities into water because it is generally applied to crops and vegetation aerially or on the ground from sprayers. Nearby waters, however, might be affected by spray drift. Permethrin is prohibited from being applied for mosquito control within 100 feet of lakes, rivers, or streams due to its aquatic toxicity (ATSDR, 2003a). Because permethrin binds tightly to soil and is practically insoluble in water, very little leaching into groundwater has been reported (EXTOXNET, 1996). Due to its low vapor pressure and Henry's law constant, permethrin volatilizes slowly from water. When permethrin is released into water, it rapidly partitions to suspended solids and sediments, which further mitigates volatilization. Studies have shown that greater than 95 percent of permethrin applied directly onto lake sediment was absorbed.

Permethrin breaks down quickly in water. Studies have reported a half-life of < 2.5 days near estuarine areas (EXTOXNET, 1996). Additionally, permethrin undergoes photolysis in sunlit surface waters, with a reported half-life of 14 days in seawater exposed to light (ATSDR, 2003a). In water, a loss of toxicity was observed for permethrin that had aged for 48 hours in sunlight (EXTOXNET, 1996).

Human Health Effects

Acute Exposure

Effects/Symptoms

There are limited data on the acute toxicity of permethrin in humans. Acute effects observed from occupational exposure include burning and itching of the skin of the periorbital area within a few hours of inhalation exposure to permethrin. Ingestion of permethrin causes nausea and vomiting. As a Type I pyrethroid, its primary target is the nervous system (U.S. EPA, 2005f). Typical effects seen following acute exposure to higher levels of permethrin are almost all related to the action of it on the nervous system, as pyrethroids prolong the open phase of the sodium channel during nerve cell excitation. Animal studies have indicated that effects may be caused by repetitive activity in sensory motor nerves (IPCS, 1990; WHO/FAO, 1984). These symptoms of permethrin exposure are transitory and disappear anywhere within a few hours to a few of days once the exposure is discontinued (EXTOXNET, 1996).

In animals, oral and inhalation exposures to permethrin are almost nontoxic. Reported LD_{50} values for technical permethrin range from 430 to 4,000 mg/kg in rats, while a 4-hour LC_{50} of 23.5 mg/L is reported in rats. Permethrin is slightly toxic through dermal contact, with dermal LD_{50}s of over 4,000 mg/kg in rats and over 2,000 mg/kg in rabbits. The toxicity depends on the ratio of cis and trans isomers, with cis being more toxic, and the solvent used (EXTOXNET, 1996; WHO/FAO, 1984). Reported dermal LD_{50} values include > 4,000 mg/kg (no solvent) in rabbits, > 2,500 mg/kg (no solvent) in rats and mice, and 750 mg/kg (in xylene) in rats (WHO/FAO, 1984). Dermal exposure to permethrin has caused mild irritation to both intact and abraded skin of rabbits (EXTOXNET, 1996).

Treatment

Permethrin and its metabolites can be detected in blood and urine; however the methods are not practical given how quickly these compounds are broken down in the body (ATSDR, 2003a; WHO/FAO, 1984). Levels of the degradation product 3-phenoxybenzyl in urine may be useful indicators of exposure (WHO/FAO, 1984).

There are no antidotes for permethrin exposure. Treatment depends on the symptoms of the exposed person. If a person exhibits signs of typical pyrethroid toxicity following permethrin exposure (nausea, vomiting, shortness of breath, tremors, hypersensitivity, weakness, burning, or itching), they should immediately remove any contaminated clothing. Any liquid contaminant on the skin should be soaked up and the affected skin areas cleaned with alkaline soap and warm water. Eye exposures should be treated by rinsing with copious amounts of 4 percent sodium bicarbonate or water. Contact lenses should be removed. Vomiting should not be induced following ingestion exposures, but the mouth should be rinsed. The person should be kept calm and medical attention should be sought as quickly as possible (PAN, 2005; WHO/FAO, 1984). Medical personnel will treat severe intoxications with a sedative and anticonvulsant. Ingestion of large amounts of permethrin should be treated with gastric lavage using a 5 percent bicarbonate solution followed by powdered activated charcoal. Skin irritation may be treated with a soothing agent and exposure to light should be avoided.

Chronic Exposure

Noncancer Endpoints

Little data are available for humans following chronic exposures to permethrin, though it is not likely to cause long-term problems when used under normal conditions (EXTOXNET, 1996). Chronic occupational exposure to permethrin caused skin and eye irritation in 33 percent of exposed Swedish workers. However, no complaints were reported in volunteers exposed to 0.5 mg/m^3 from an indoor application (WHO/FAO, 1984).

Data in animals indicate that oral exposure to permethrin is not highly toxic, but effects reported are largely neurological. Doses of 5 mg/kg/day for 90 days did not produce effects in dogs (EXTOXNET, 1996) while higher oral doses of 500 mg/kg and greater for 3 months caused transient clinical signs. Mice and rats chronically exposed to dietary levels up to 5,000 mg/kg (mice) and 2,500 mg/kg (rats) exhibited no consistent effects on growth or food consumption (WHO/FAO, 1984). Inhalation and dermal studies in animals indicate that permethrin is nontoxic or minimally toxic. No effects were observed in rats exposed to up to 500 mg/m^3, 6 hours per day, for 13 weeks. Additionally, rabbits dermally exposed to 1.0 g/kg/day on abraded skin for 21 days showed no effects other than moderate skin irritation (WHO/FAO, 1984). Based on the lack of reproductive effects in animals exposed to high oral does of permethrin, human reproductive toxicity is not expected. Additionally, permethrin shows no teratogenic or mutagenic activity (EXTOXNET, 1996; WHO/FAO, 1984).

Cancer Endpoints

EPA has classified permethrin as "likely to be carcinogenic to humans" by the oral route. A long-term, high dose dietary exposure study reported an increased incidence of benign lung and liver tumors in mice. This is supported by equivocal evidence in one strain of rats and structure-activity relationship information (U.S. EPA, 2005f).

Toxicokinetics

Permethrin is readily absorbed via the gastrointestinal tract, inhalation, and less so through intact skin (WHO/FAO, 1984). In mammals, permethrin is rapidly metabolized in the liver (EXTOXNET, 1996). The trans isomer is metabolized by hydrolysis and the cis isomer is not as easily hydrolyzed and is thus more toxic (WHO/FAO, 1984). The hydroysis and oxidation products of permethrin metabolism are quickly excreted in urine and feces with the trans isomers more rapidly excreted than the cis isomers. The primary excretion products of both isomers in most species studied include 4'-HO-3-PBA sulfate (in rats), 4'-HO-3-PBA (trans) and 6-HO-3-PBA (cis) sulfates (in mice), N-(3-phenoxybenzoyl) glutamate (in cows), and cyclopropane-carboxylic acid glucuronides and 3-PBA glucuronides products in most of the species studied (WHO/FAO, 1984). Permethrin may persist in fatty tissues. The reported half-life in the brain and body fat is 4–5 days (EXTOXNET, 1996).

Ecological Effects

Acute Exposure

Toxicity in Non-Targeted Terrestrial Organisms

Permethrin, like other pyrethroids, is very unlikely to harm terrestrial organisms other than its targets, such as mosquitoes and other pests (EXTOXNET, 1996). Permethrin has a very low toxicity in birds (WHO/FAO, 1984; EXTOXNET, 1996). Oral LD_{50} values range from 9,900 mg/kg for the formulation Pramex in mallard ducks to over 15,500 mg/kg in Japanese quail (EXTOXNET, 1996), while the acute oral LD_{50} for the technical material was >11,275 mg/kg in mallard ducks and >32,000 mg/kg in starlings. Subacute LD_{50}s were >23,000 mg/kg for all bird species tested. No adverse effects or significant accumulation in tissues or eggs were seen in hens exposed to a spray mist of 3.77–11.94 mg/bird (WHO/FAO, 1984). As with other pyrethroid insecticides, permethrin is extremely toxic to honey bees (EXTOXNET, 1996).

Toxicity in Non-Targeted Aquatic Systems

Permethrin is very toxic to fish (EXTOXNET, 1996); however, because it is rapidly absorbed and degraded in the aquatic environment, the risk is of short duration (WHO/FAO, 1984). The high toxicity in fish is illustrated by the low exposures that cause mortality. The reported 48-hour LC_{50} for rainbow trout is 0.0054 mg/L, while in bluegill sunfish and salmon it is 0.0018 mg/L (EXTOXNET, 1996). The 96-hour LC_{50}s range from 0.1–0.5 µg/L in rainbow trout to 15 µg/L in mosquito fish (WHO/FAO, 1984). Permethrin has a low to moderate potential to accumulate in fish, with reported bioconcentration factors of over 700 times the concentrations in water for bluefish and catfish (EXTOXNET, 1996). A bioconcentration factor of 1,900 was reported in eastern oysters following a 28-day incubation (ATSDR, 2003a). Permethrin is also known to be toxic to some aquatic invertebrates, amphibians in larval form, aquatic insects, and crustaceans (WHO/FAO, 1984). A disruption in growth and development of tadpoles has been reported (EXTOXNET, 1996).

Chronic Exposure

Due to low rate of application and low persistence of permethrin in both terrestrial and aquatic environments, serious adverse effects are not anticipated from chronic exposures (HSDB, 2005)