Task 3 Literature Review
Book 7: Ecotoxicity Review of Primary List Mosquito Control Agents

Prepared for:

Suffolk County Department of Public Works
Suffolk County Department of Health Services
Suffolk County, New York

CASHIN ASSOCIATES, P.C.
INTEGRAL CONSULTING, INC.
Annapolis, MD

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SUFFOLK COUNTY VECTOR CONTROL AND WETLANDS MANAGEMENT LONG - TERM PLAN AND ENVIRONMENTAL IMPACT STATEMENT

PROJECT SPONSOR

Steve Levy
Suffolk County Executive

Department of Public Works
Charles J. Bartha, P.E.
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Deputy Commissioner

Department of Health Services
Brian L. Harper, M.D., M.P.H.
Commissioner
Vito Minei, P.E.
Director, Division of Environmental Quality

PROJECT MANAGEMENT

Project Manager: Walter Dawydiak, P.E., J.D.
Chief Engineer, Division of Environmental Quality, Suffolk County Department of Health Services

Suffolk County Department of Public Works, Division of Vector Control
Dominick V. Ninivaggi
Superintendent
Tom Iwanejko
Entomologist
Mary E. Dempsey
Biologist

Suffolk County Department of Health Services, Office of Ecology
Martin Trent
Acting Chief
Kim Shaw
Bureau Supervisor
Robert M. Waters
Bureau Supervisor
Laura Bavaro
Senior Environmental Analyst
Erin Duffy
Environmental Analyst
Phil DeBlasi
Environmental Analyst
Jeanine Schlosser
Principal Clerk

SUFFOLK COUNTY LONG TERM PLAN CONSULTANT TEAM

Cashin Associates, P.C.	**Hauppauge, NY**
Subconsultants	
Cameron Engineering, L.L.P.	Syosset, NY
Integral Consulting	Annapolis, MD
Bowne Management Systems, Inc.	Mineola, NY
Kamazima Lwiza, PhD	Stony Brook University, Stony Brook, NY
Ducks Unlimited	Stony Brook, NY
Steven Goodbred, PhD & Laboratory	Stony Brook University, Stony Brook, NY
RTP Environmental	Westbury, NY
Sinnreich, Safar & Kosakoff	Central Islip, NY
Bruce Brownawell, PhD & Laboratory	Stony Brook University, Stony Brook, NY
Anne McElroy, PhD & Laboratory	Stony Brook University, Stony Brook, NY
Andrew Spielman, PhD	Harvard School of Public Health, Boston, MA
Richard Pollack, PhD	Harvard School of Public Health, Boston, MA
Wayne Crans, PhD	Rutgers University, New Brunswick, NJ
Susan Teitelbaum, PhD	Mount Sinai School of Medicine, NY
Zawicki Vector Management Consultants	Freehold, NJ
Michael Bottini, Turtle Researcher	East Hampton, NY
Robert Turner, PhD & Laboratory	Southampton College, NY
Christopher Gobler, PhD & Laboratory	Southampton College, NY
Jerome Goddard, PhD	Mississippi Department of Health, Jackson, MS
Sergio Sanudo, PhD & Laboratory	Stony Brook University, Stony Brook, NY
Suffolk County Department of Health Services, Division of Environmental Quality	Hauppauge, NY

Primary research for this report was conducted by Integral Consulting, Inc. (personnel including Judi Durda and Damian Preziosi). It was edited and revised in response to comments by Cashin Associates (personnel including David Tonjes, PhD) and Integral Consulting, Inc. (personnel including Judi Durda, Damian Preziosi, and Jim Lape). Review was provided by Cashin Associates (personnel including David J. Tonjes, PhD), Suffolk County Department of Public Works, Division of Vector Control, and Suffolk County Department of Health Services. Additional comments have been received from _____.

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AChE	Acetylcholinesterase
ACh	Acetylcholine
APHIS	Animal and Plant Health Inspection Service
ARS	Agricultural Research Station
ATSDR	Agency for Toxic Substances and Disease Registry
Bs	*Bacillus sphaericus*
Bt	*Bacillus thuringiensis*
Bti	*Bacillus thuringiensis israelensis*
CA	Cashin Associates, P.C.
CE	Cameron Engineering & Associates, LLP
CTDEP	Connecticut Department of Environmental Protection
CYP1A	Cytochrome P4501A
DEIS	New York City Adult Mosquito Control Program: Draft Environmental Impact Statement
DGEIS	Westchester County Comprehensive Mosquito-Borne Disease Surveillance and Control Plan: Draft Generic Environmental Impact Statement
EXTOXNET	Extension Toxicology Network
FAO	Food and Agriculture Organization of the United Nations
FCCMC	Florida Coordinating Council on Mosquito Control
FDA	Food and Drug Administration
FGEIS	Westchester County Comprehensive Mosquito-Borne Disease Surveillance and Control Plan: Final Generic Environmental Impact Statement
FIFRA	Federal Insecticide, Fungicide and Rodenticide Act
HSDB	Hazardous Substances Data Bank
IRIS	Integrated Risk Information System
kDa	Kilo Dalton
LC_{50}	Concentration which is lethal to 50% of a sample population
LD_{50}	Dose which is lethal to 50% of a sample population
LOAEC	Lowest observable adverse effect concentration
LOEC	Lowest observable effect concentration
LOAEL	Lowest observable adverse effect level
LOEL	Lowest observable effect level
NCIPM	National Center for Integrated Pest Management
NIH	National Institute of Health
NLM	National Library of Medicine
nm	Nanometer
NPIC	National Pesticide Information Center
NTIS	National Technical Information Services
NOAEC	No observable adverse effect concentration
NOEC	No observed effect concentrations
NOAEL	No observable adverse effect level
NOEL	No observable effect level
NYCDEP	New York City Department of Environmental Protection

NYSDEC	New York State Department of Environmental Conservation
OPP	USEPA Office of Pesticide Programs
PBO	Piperonyl butoxide
SCDHS	Suffolk County Department of Health Services
SCVC	Suffolk County Department of Public Works Division of Vector Control
PPDB	USDA Pesticide Properties Data Base
RED	Reregistration Eligibility Document
RSML	Remote Sensing and Modeling Laboratory
t-MA	Methoprenic acid
ULV	Ultra-low volume
WHO	World Health Organization
USDA	US Department of Agriculture
USEPA	US Environmental Protection Agency
USGS	US Geological Survey

Executive Summary

This document presents the results of a comprehensive review performed to evaluate the ecotoxicological characteristics of the primary list mosquito control agents selected by Cashin Associates, PC on behalf of and in consultation with the Suffolk County Department of Health Services and the Suffolk County Department of Public Works Division of Vector Control for detailed evaluation to support development of the *Suffolk County Vector Control and Wetlands Management Long-Term Plan* (the *Plan*). The ecotoxicological information provided in this document has been synthesized and summarized to support a subsequent ecological risk evaluation of mosquito control agent use in Suffolk County. This work is being conducted as part of the overall Impact Assessment being prepared as part of the *Plan*.

The primary list contains 11 mosquito control agents consisting of microbial pesticide and insect growth regulator larvicides, adulticides, a synergist, and a repellant. The larvicides examined in this report are:

- *Bacillus thuringiensis israelensis*
- *Bacillus sphaericus*
- methoprene.

The adulticides examined are:

- synthetic pyrethroids (i.e., permethrin, resmethrin, and sumithrin)
- organophosphate compounds (i.e., malathion and its chief metabolites/degradates malaoxon and isomalathion).

The synergist examined is piperonyl butoxide.

The repellant examined is garlic oil.

Information on the ecotoxicological characteristics of these control agents was primarily obtained from information previously compiled as part of the 2001 Westchester County *Comprehensive Mosquito-Borne Disease Surveillance and Control Plan: Draft Generic Environmental Impact Statement* and the 2001 New York City *Adult Mosquito Control Program: Draft Environmental Impact Statement*. Collectively, the Westchester County and New York City documents served as a comprehensive source of information available through 2001 on the ecotoxicological characteristics of mosquito control agents that are the focus of this study.

The data obtained from the Westchester and New York City documents were augmented by a separate comprehensive literature search to identify recent ecotoxicological information that has

been published since the time of these initial reports (2001 to June 2004). A number of scientific databases, including those from the US Environmental Protection Agency, US Department of Agriculture, and the National Library of Medicine, among others, were utilized. The collective body of scientific information within which the literature search was conducted is comprised of approximately 200 million records on scientific articles, regulatory and industry reports, gray literature, and scientific-based Internet web pages.

As part of the literature review and general information compilation effort, preliminary ecological receptor groups and corresponding measures of effect were identified. Measures of effect are measurable changes in an attribute of an ecological receptor or its surrogate in response to a stressor (e.g., a pesticide) to which it is exposed. Ecological receptor groups were preliminarily identified based on review of habitats and species present in Suffolk County. The preliminary ecological receptor groups for terrestrial species were identified as:

- mammals
- birds
- reptiles
- non target insects such as honeybees
- sensitive plants.

The preliminary ecological receptor groups for freshwater and estuarine aquatic life were identified as:

- fish
- amphibians
- crustaceans
- aquatic insects and larvae
- mollusks
- aquatic plants.

The principal measures of effect preliminarily selected for individuals of the terrestrial and aquatic ecological receptor groups were:

- growth
- survival
- reproduction.

Other measures of effect (i.e., biochemical changes in proteins, hormones, and enzymes), immunological effects, and behavioral or cognitive effects were additionally identified for consideration.

Information on ecotoxicological characteristics were reviewed and summarized for each of the 11 primary list mosquito control agents. Ecologically relevant routes of exposure for terrestrial and aquatic wildlife, namely for oral and inhalation exposures, were the focus of this evaluation. Emphasis was placed on information relevant to effects following acute and shorter-term exposures, rather than longer-term chronic exposures. This is because each of the control agents degrades fairly rapidly in the environment, and therefore, ecological exposures to single applications, or even repeated applications, are not anticipated to result in long-term, chronic exposure conditions for ecological receptors.

Approximately 100 articles and reports published since 2001 were reviewed. Based on this review and the collective evaluation, little new information is available on the ecotoxicological characteristics of the 11 primary control agents beyond that previously summarized in the Westchester and New York City documents. What new and ecologically relevant information does exist generally corroborates the previously summarized existing body of information.

Based on the collective evaluation, the ecotoxicological characteristics of each of the primary list control agents are briefly summarized below.[1]

Larvicides

- ***Bacillus thuringiensis israelensis*** **(Bti)** is a naturally occurring soil bacterium that produces toxins that are effective against mosquito and black fly larvae. These toxins disrupt digestion in the gut of target insect larvae, causing them to stop feeding. The toxins produced by Bti rapidly degrade in the environment. Bti is generally not considered a risk for non-target terrestrial and aquatic wildlife.

- ***Bacillus sphaericus*** **(Bs)** is a naturally occurring bacterium found in soil and aquatic environments that produces toxins that are effective against mosquito larvae. As in the case with Bti, the toxins in Bs disrupt digestion in the gut of mosquito larvae, causing them to stop feeding. The toxins in Bs degrade quickly in the environment. Bs is generally not considered a risk for non-target terrestrial and aquatic wildlife.

[1] The degree of toxicity (e.g., very low toxicity, low toxicity, moderate toxicity, high toxicity) used throughout this report to describe the relative toxicity of the primary list control agents is based upon the US Environmental Protection Agency classification procedures for pesticide labeling (USEPA 2003).

- **Methoprene** is a biochemical larvicide that acts as an insect growth regulator, initially preventing mosquito larvae from maturing and ultimately causing mosquito mortality. Methoprene generally degrades quickly in the environment. Methoprene is considered to be slightly to non-toxic to terrestrial wildlife, slightly to moderately toxic in fish, and highly to very highly toxic to aquatic invertebrates.

Pyrethroid Adulticides

Pyrethroids are synthetic chemical insecticides that act in a similar manner to pyrethrins, which are derived from chrysanthemum flowers. Pyrethroids disrupt nerve cell activity in insects, which ultimately leads to insect paralysis. To improve the efficacy of pyrethroid formulations, they are combined with chemical synergists (e.g., piperonyl butoxide). Permethrin, resmethrin, and sumithrin are pyrethroids included among the 11 primary list control agents.

- **Permethrin** is a broad spectrum pyrethroid used against a variety of pests, including adult mosquitoes. Permethrin generally degrades rapidly in the environment. Permethrin is considered to have limited toxicity to terrestrial wildlife, with the exception of bees, for which it is considered highly toxic. Permethrin is considered to be moderately to very highly toxic to aquatic life, most notably to invertebrates. Permethrin also exhibits a moderate tendency to accumulate in certain fish.

- **Resmethrin** is a broad spectrum pyrethroid used against a variety of pests, including adult mosquitoes. Resmethrin generally degrades rapidly in the environment. Resmethrin is considered slightly to practically non toxic to terrestrial wildlife, with the exception of bees, for which it is considered highly toxic. Resmethrin is considered to be moderately to very highly toxic to aquatic life.

- **Sumithrin** is a broad spectrum pyrethroid used against a variety of pests, including adult mosquitoes. Sumithrin generally degrades rapidly in the environment. Relatively few data are available on the ecotoxicological characteristics of sumithrin, but in general, it is considered nontoxic to terrestrial wildlife and slightly to highly toxic to aquatic life.

Organophosphate Adulticides

Organophosphate pesticides consist of a broad class of chemicals used primarily in insect and pest control. Organophosphates exert toxicity through the inhibition of

acetylcholinesterase. In insects, this inhibition interferes with the nerve-muscle communication, which ultimately causes paralysis of the insect. Malathion (including its breakdown products malaoxon and isomalathion) is the single primary list mosquito control agent belonging to the organophosphate class.

- **Malathion** is a nonsystemic broad-spectrum organophosphate chemical used against a variety of pests, including adult mosquitoes. Malathion generally degrades rapidly in the environment. A large amount of information is available on the ecotoxicological characteristics of malathion. In general, malathion exhibits low to moderate toxicity to terrestrial wildlife. Malathion is considered to be highly toxic to bees. Malathion is considered to be moderately to very highly toxic for both freshwater and estuarine/marine fish and invertebrates. Little information is available on the ecotoxicological characteristics of malathion's chief metabolites/degradates, malaoxon and isomalathion.

Synergists

A synergist is a chemical that enhances the potency of a pesticide. Pyrethroids are frequently used in combination with synergists. Synergists are added to pyrethroid formulations in order to slow down or prevent the metabolism of pyrethroids, thereby enabling a smaller amount of pyrethroids to have the same effectiveness. Piperonyl butoxide is the single primary list mosquito control agent belonging to the synergist class.

- **Piperonyl butoxide (PBO)** is utilized as a chemical synergist in pyrethroid formulations (namely in formulations with permethrin, resmethrin, and sumithrin as active ingredients). PBO generally degrades rapidly in the environment. PBO is generally considered to have limited toxicity to terrestrial wildlife. PBO is considered to be moderately to acutely toxic in fish and highly acutely toxic in aquatic invertebrates.

Repellants

Chemical repellants are pesticides that are used to prevent or limit insect and other pest activity. Repellants are used in a variety of applications, including those associated with the protection of humans, pets, livestock and plants. Repellants used against mosquitoes are typically applied as sprays in outdoor areas, or may be applied directly to the skin using aerosol, pump spray, and lotion formulations.

Garlic oil is the single primary list mosquito control agent belonging to the repellant class.

- **Garlic oil** is utilized as a repellant against mosquitoes. Garlic oil is non-persistent in the environment. Garlic oil is has a non-toxic mode of action for repelling mosquitoes, and it is generally regarded as safe to humans and the environment.

As seen from the preceding information, all of these compounds, with the exception of garlic oil, are considered toxic to non-target species to some degree. This does not mean, however, that these compounds will definitively cause ecological toxicity or injury when applied in the field. The ecological risks posed by these compounds can be evaluated only by combining the toxicity information presented here with estimates of environmental exposures. This type of evaluation will be presented in the ecological risk assessment to be subsequently conducted.

1. Introduction

This document presents the results of a comprehensive review performed to evaluate the ecotoxicological characteristics of the primary list mosquito control agents selected by Cashin Associates, PC (CA) on behalf of and in consultation with the Suffolk County Department of Health Services (SCDHS) and the Suffolk County Department Public Works Division of Vector Control (SCVC) for detailed evaluation to support development of the *Suffolk County Vector Control and Wetlands Management Long-Term Plan* (the *Plan*). The primary list consists of a total of 11 mosquito control agents representing larvicides, adulticides, synergists, and repellants. The information provided in this document is presented in preliminary support of the Literature Evaluation and Early Action Recommendation (Task 3) work currently being performed. The ecotoxicological information provided in this document also has been synthesized and summarized for use in the subsequent ecological risk evaluation that is being performed as part of the overall Impact Assessment (Task 8), and specifically that portion of which addresses potential ecological risks of mosquito control agents use in Suffolk County.

This summary of available ecotoxicological information is presented in four principal sections:

- **Overview of Primary List Mosquito Control Agents** - presents a summary of the primary list mosquito control agents for which ecotoxicological information was reviewed;
- **Ecotoxicity Data and Literature Sources** - provides an overview of the data and literature sources utilized in the identification and compilation of ecotoxicity data;
- **Ecological Receptor Groups and Measures of Effects** – presents a discussion and preliminary identification of potential ecological receptor groups and primary measures of effects considered to focus ecotoxicity data collection and review; and
- **Ecotoxicity Data Summary** – presents a summary of general background information, and information on the mode of action and ecological effects associated with each of the primary list mosquito control agents.

2. Overview of Primary List Mosquito Control Agents

As summarized in the 2004 draft report entitled, *"Mosquito Control Agents,"* CA and Cameron Engineering & Associates, LLP (CE) performed an extensive survey of mosquito control agencies outside Suffolk County to develop an inclusive list of agents and chemicals potentially used in Suffolk County to control mosquito populations. This survey placed particular emphasis on information pertaining to control agents utilized by regional mosquito control programs. The regional information was augmented by information from other areas of the country to identify control agents used under a broader range of environmental conditions (CA-CE 2004).

Based on this information, CA together with SCDHS and SCVC selected a primary list of 11 mosquito control agents for a detailed review of available ecotoxicological literature and data. The 11 control agents, consisting of microbial pesticide and insect growth regulator larvicides, pyrethroid adulticides, an organophospate adulticide (and degradates), a synergist, and a repellant, are presented below in **Table 1**.

Table 1 – Primary List of Mosquito Control Agents Identified for Detailed Review

Agent	Pesticide Category	Class	Trade Name (TM)/®
*Bacillus thuringiensis israelensis (*Bti)	Microbial pesticide	Larvicide	Vectobac, Teknar
Bacillus sphaericus (Bs)	Microbial pesticide	Larvicide	Vectolex
Methoprene	Insect growth regulator	Larvicide	Altosid
Malathion	Organophosphate	Adulticide	Fyfanon, Atrapa
Malaoxon	--	Metabolite/degradate	--
Isomalathion	--	Degradate	--
Permethrin	Pyrethroid	Adulticide	Permanone
Resmethrin	Pyrethroid	Adulticide	Scourge
Sumithrin	Pyrethroid	Adulticide	Anvil
Piperonyl butoxide	Microsomal enzyme inhibitor	Synergist	--
Garlic oil	Biochemical pesticide	Repellant	Garlic Barrier

Provided below is a summary of the sources of information utilized to perform the detailed ecotoxicological data and literature review for these 11 agents.

3. Ecotoxicity Data and Information Sources

Information on the ecotoxicological characteristics of the 11 primary control agents was primarily obtained from information previously compiled as part of the Westchester County *Comprehensive Mosquito-Borne Disease Surveillance and Control Plan: Draft Generic Environmental Impact Statement* (DGEIS) (Westchester County Board of Health 2001) and the New York City *Adult Mosquito Control Program: Draft Environmental Impact Statement* (DEIS) (New York City Department of Health 2001).

Collectively, the Westchester County DGEIS and New York City DEIS represent an extremely thorough and comprehensive source of information on the ecotoxicological characteristics of mosquito control agents. The sources of ecotoxicological information relied upon in the development of these documents included the following:

- US Environmental Protection Agency (USEPA) Integrated Risk Information System (IRIS);
- USEPA Hazardous Substances Database (HSDB);
- USEPA Office of Pesticide Programs (OPP) website;
- USEPA Pesticide One-liners Database;
- US Geological Survey (USGS) Acute Toxicity Database;
- US Department of Agriculture (USDA) Agricultural Research Station (ARS) and Remote Sensing and Modeling Laboratory (RSML);
- USDA Pesticide Properties Data Base (PPDB);
- Extension Toxicology Network (EXTOXNET);
- National Institute of Health (NIH);
- World Health Organization (WHO) Environmental Health Criteria documents;
- National Technical Information Services (NTIS);
- Primary scientific literature identified through the National Library of Medicine (NLM) TOXNET database (which provides access to over 3 million scientific articles); and
- A variety of miscellaneous sources, including those from academia and the larger scientific community, manufacturers and commercial vendors, regulatory agencies, and mosquito control agencies.

The ecotoxicological information presented in the Westchester County DGEIS and New York City DEIS is nonetheless somewhat incomplete, since they only contained information generated until 2001. As part of the current data and literature review, additional research was conducted on the ecotoxicological characteristics of the 11 priority list agents to identify new information generated since 2001 to the present time (June 2004). This was accomplished by updating searches in many of the above sources, with particular emphasis on conducting searches in the primary scientific literature to identify new and emerging research information. An updated search of primary scientific literature was performed using the following bibliographic sources:

- Scirus Scientific Search Engine (with access to over 18 million scientific articles and reports and over 167 million scientific-related Web pages);
- APT Online (with access to over 150 natural science specialty journals);
- USEPA ECOTOX database (Internet accessible ecotoxicity database, containing over 400,000 records) (USEPA 2002a); and
- NLM TOXNET database.

Based on this revised search, approximately 500 scientific articles published between 2001 through June 2004 were identified.

4. Ecological Receptor Groups and Measures of Effects

In order to identify relevant, recent literature for review, as well as to evaluate retrospectively the ecotoxicity information previously presented in the Westchester County DGEIS and New York City DEIS, it was necessary to identify preliminary ecological receptor groups and corresponding measures of effects. Measures of effect are measurable changes in an attribute of an ecological receptor (or its surrogate) in response to a stressor (e.g., a pesticide) to which it is exposed. It was necessary to define each of these because

1) ecotoxicological data and literature are available for a host of wildlife and laboratory species, some of which may not be representative of the types of wildlife present and of interest in Suffolk County; and
2) various measures of effects may be reported that are not directly applicable to assessing ecological risks.

By first identifying ecological receptor groups and corresponding measures of effects, it was possible to identify the most relevant ecotoxicological information for review.

4.1. Ecological Receptor Groups

Based on a preliminary review of habitats and species present in Suffolk County, terrestrial wildlife species potentially impacted by mosquito control agents include the following ecological receptor groups:

- Mammals (e.g., deer, raccoon, mice);
- Birds (e.g., insectivorous songbirds, waterfowl and other water-associated birds);
- Reptiles (e.g., turtles, snakes);
- Non-target insects (e.g., honeybees, butterflies); and
- Sensitive plants.

Aquatic life species potentially impacted by mosquito control agents include the following ecological receptor groups in both freshwater and estuarine/marine environments:

- Fish (e.g., bluegill, rainbow trout, mummichog);
- Amphibians (e.g., frogs);
- Crustaceans (e.g, crayfish, crabs, lobster);
- Aquatic insects and larvae (e.g., benthic organisms, stoneflies);

- Mollusks (e.g., snails, clams, oysters); and
- Aquatic plants (e.g., algae).

4.2. Measures of Effect

The principal measures of effect selected to assist in ecotoxicity data collection and review included growth, survival, and reproduction in individuals of the terrestrial and aquatic ecological receptor groups identified above in Section 4.1. Other measures of effect, such as those based on biochemical changes in proteins, hormones, and enzymes (i.e., induction of cytochrome P4501A [CYP1A], hormesis, endocrine disruption), immunological effects, and behavioral or cognitive effects are additionally important, and were considered to support the synthesis of a collective weight-of-evidence regarding the ecotoxicological characteristics of each chemical.

5. Ecotoxicity Summary

A summary of the ecotoxicological data and other information relevant to potential adverse effects to the ecological receptor groups is provided below for the 11 primary list control agents. This summary is based on a synthesis of collective information gathered from the Westchester DGEIS, the New York City DEIS, and the review of approximately 100 relevant scientific articles and reports (of the approximately 500 identified) published since 2001. A complete bibliographic listing of these recent, reviewed references is provided in **Appendix A** of this report.

For each of the 11 control agents, general background information on use, mode of toxicity, and environmental persistence is provided, along with specific information on acute and chronic effects to wildlife or relevant surrogate species.

For the purposes of these summaries, acute effects are those considered to occur within hours of a single dose administration. Lethality is the most common toxicological endpoint reported in the acute toxicity literature, although a variety of sub-lethal responses can occur. Chronic effects are those that occur following longer-term, multiple exposures over a significant portion of an animal's lifetime or during a critical life stage. Sub-chronic effects are those that occur following exposures intermediate between acute and chronic. Chronic and sub-chronic toxicological endpoints can include growth, reproduction, and survival, as well as a variety of other sub-lethal responses.

Efforts have been taken throughout this review to acknowledge the potential limitations associated with translating the results of longer term chronic laboratory studies to potential ecological impacts under natural conditions in the field. Complex and often inter-connected degradation and sorption mechanisms which naturally occur in the field are generally not reproducible in the laboratory. Such mechanisms are important considerations, however, because they have the potential to preclude continual sublethal exposures to ecological receptors.

The discussions of toxic effects are accompanied by toxicity data summary tables for each of the 11 control agents. In the case of terrestrial wildlife, receptors may experience direct exposure to aerially or ground applied control agents. Possible routes of exposure include dermal absorption, inhalation, and ingestion of residues in food, water, and soil. In the case of mammals and birds, emphasis is placed on the compilation and summary of oral toxicity data, given that these data are most readily available and because they are particularly relevant to assessing direct ingestion and residue-related exposures. Because short-term exposures to aerially applied control agents are additionally relevant, inhalation toxicity data has also been compiled and summarized, although this data is typically limited to longer-term, laboratory studies in rats, rather than

wildlife species. Data on dermal toxicity is generally limited, and what data does exist suggests that this route of exposure is far less important than the oral and inhalation routes of exposures. In addition, birds and mammals are largely protected from dermal exposure by feathers and fur, respectively. Therefore, no dermal toxicity data are summarized. Aquatic wildlife may be exposed to control agents following application through drift and/or runoff to surrounding water bodies. Under such scenarios, aquatic wildlife are expected to come into direct contact with water. Aquatic toxicity data are generally based upon aqueous exposure conditions, and these data are of focus in the data summary tables.

In certain instances, a single toxicity value for acute effects and a single value for chronic effects are presented for each of the receptor groups. These values represent the values that will most likely be considered in the subsequent ecological risk assessment. Multiple values, or a range of values, may also be presented for a given species or across multiple species. This is done to permit an explicit examination of the potential uncertainty associated with toxicity values in the ecological risk assessment.

The descriptors used to describe the degree of toxicity (e.g., very low toxicity, low toxicity, moderate toxicity, highly toxicity) used throughout the summaries to describe the relative toxicity of the primary list control agents are based upon the general descriptors used by USEPA in their classification procedures for pesticide labeling (USEPA 2003).

Although some of the 11 control agent formulations include inert ingredients (that is, ingredients other than the registered active ingredients) and synergists, this section focuses on the primary active ingredients because most available toxicological information is for those chemicals individually.

5.1. Larvicides

Larvicides are insecticide formulations that can be applied, by ground or aerial application, to target specific insect groups in their larval or pupal development stages. *Bacillus thuringiensis israelensis* (Bti), *Bacillus sphaericus* (Bs), and methoprene are the three larvicides included in the primary list.

5.1.1. *Bacillus thuringiensis israelensis* (Bti)

General Background Information

Bti is a naturally occurring soil bacterium used as a microbial pesticide. Microbial pesticides are comprised of microscopic living organisms (e.g., bacteria, fungi, protozoa) or the toxins produced by these organisms. Bti is used to control the filter feeding stages of mosquito, black fly, midge, and fungus gnat larvae (Valent Biosciences Corp. undated,

USEPA 1998, NCIPM 2004a, Glare and O'Callaghan 1998). Granular and liquid formulated products can be applied through ground or aerial application (Valent Biosciences Corp. undated). Bti is commonly registered under the trade name VectoBac® and Teknar®.

Bti is produced commercially in large fermentation tanks. As bacteria live and multiply in the right conditions, each cell produces an asexual reproductive spore and a crystalline structure containing protein toxins called endotoxins (specifically delta-endotoxins) (Weinzierl et al. 1997, Mittal 2003). Commercial products containing Bti may consist of the endotoxins and spores (USEPA 2000a), or just the endotoxins (NCIPM 2004a). The endotoxins associated with the Bti spore must be ingested by larvae before they act as poisons (and are therefore referred to as "stomach" poisons). After ingesting Bti, enzyme activity and alkaline conditions in the larvae's gut break down the crystalline structures, and activate the endotoxins (Mittal 2003, Weinzierl et al. 1997). Once the endotoxins are activated, they rapidly bind to the cells lining the midgut membrane and create pores in the membrane, upsetting the gut's ion balance. This results in paralysis of the gut, thus interfering with normal digestion and feeding (Brown 1998, Weinzierl et al. 1997, Lacey and Merritt 2003, Dale and Hulsman 1990).

Bti's selectivity in terms of its ability to target the larvae of certain insect species, particularly mosquito and black fly larvae, is attributable to a variety of factors. Bti produces five distinct types of endotoxins ranging in size from 27 to 138 kilo Daltons (kDa) (Mittal 2003, FCCMC 1998).[2] Alkaline conditions in the larvae's gut, generally corresponding to a pH of 7 or greater, are required to activate these endotoxins. Specific enzymes must also be present in the gut to cause activation. In addition, distinct chemical receptors must be present in the plasma membrane of the gut to encourage binding of the endotoxins (Mittal 2003, Weinzierl et al. 1997). Mosquitoes that are most susceptible to Bti include species in the genera *Aedes* and *Psorophora*. *Anopheles* and *Culex* are also susceptible to Bti, but generally higher than normal application rates are required (Weinzierl et al. 1997).

Because Bti is not considered a risk to non-target organisms, USEPA does not require formal environmental fate data for registration. However, the behavior of Bti, and *Bacillus thuringiensis* (Bt) strains in general, has been fairly well studied (USEPA 1998). The length of time that Bti remains effective against insect larvae varies, depending primarily on the species and behavior of the larvae, environmental conditions, and water quality. In

[2] Targeted insects are less likely to build up resistance to Bti because each of the five produced toxins varies to some degree in its mode of toxicity (FCCMC 1998).

general, Bti is effective from one to seven days after application. Because Bti is used predominantly in aquatic settings, its response to light has not been extensively studied. However, UV light in the range of 300 – 400 nanometers (nm), falling within the wavelength range of sunlight, has been shown to inactivate both spores and endotoxins of Bt (Gelernter 2001). Bti toxin can last for a few months in the soil and has an above-ground half-life of 1-4 days on plant surfaces. As a result, exposure to most above-ground nontargets organisms is expected to be minimal (USEPA 1998). In aquatic environments, Bti has a tendency to bind to particulate matter in the water column and settle out on the bottom. When adsorbed to particulates in the water column, Bti is too large to be ingested by insect larvae (Gelernter 2001). Once settled on the bottom, Bti is not available for consumption by targeted mosquito and black fly larvae which reside in the open water column or at the water's surface. Thus, the efficacy of Bti may be limited in aquatic systems with a large amount of particulate matter (Yousten et al. 1992, Weinzierl et al. 1997).

Bti, as is the case with Bt strains in general, does not colonize or cycle (reproduce and persist to infect subsequent generations of pests) in the magnitude necessary to provide continuing control of target pests (Weinzierl et al. 1997). The bacteria may multiply in the infected host, but bacterial multiplication in the insect does not result in the production of abundant spores or endotoxins (Weinzierl et al. 1997, USEPA 1998). Once larvae die, few or no infective units are released into the environment (Weinzierl et al. 1997).

Ecotoxicity

Bti is generally not considered a risk for non-target organisms (USEPA 1998). There is some evidence of Bti effects to nontarget aquatic dipterans that include midges (Chironomidae), biting midges (Ceratopogodinae), and dixid midges (Dixidae), which are commonly associated with mosquitoes within the aquatic environment. These organisms are taxonomically similar to mosquitoes and black flies and can possess the gut pHs and enzymes necessary to activate Bti's delta-endotoxins. Adverse effects to these groups, however, have only been noted at dosages 10 - 1,000 times greater than the application rate specified for mosquito control (FCCMC 1998).

Overall, USEPA has concluded that Bti does not pose significant adverse risks to non-target organisms or the environment, especially since rates higher than those used for vector control are needed to produce any adverse effects (USEPA 1998). Recent literature confirms Bti's limited overall toxicity to wildlife (Brown et al. 2002, Russell et al. 2003, Lacey and Merritt 2003).

Table 2 (in the rear of the report) presents a summary of ecotoxicity data for Bti by ecologic al receptor group.

5.1.2. *Bacillus sphaericus* (Bs)

General Background Information

Bs, like Bti, is a naturally occurring bacterium used as a microbial pesticide. Bs is found naturally in soil and aquatic environments. Commercial formulations utilizing Bs (e.g., VectoLex®) consist of living bacterium that produce spores (NCIPM 2004b). Granules that contain the Bs are mixed with water and other substances, and then sprayed from the air or from the ground (Valent Biosciences Corp. undated).

Bs spores produce two delta-endotoxins that are toxic specifically to mosquito larvae upon ingestion (Valent Biosciences Corp. undated, Weinzierl et al. 1997, Lacey and Merritt 2003, Mittal 2003). Similar to the mode of action of Bti, Bs exerts toxicity through the release of the endotoxins upon ingestion by mosquito larvae, which results in the disruption of gut activity and ultimately leads to death. The selectivity of Bs is attributable to the fact that certain gut conditions (i.e., pH, enzymes, chemical receptors) unique to mosquito larvae must be present to result in toxicity. Bs has been shown to be effective against many mosquito genera. All species of *Culex* larvae are considered susceptible to Bs, and many species of *Aedes*, *Psorophora*, *Coquillettidia*, *Mansonia* and *Anopheles* are also very susceptible. However, susceptibility of species within these genera is variable (FCCMC 1998, Valent Biosciences, undated).

USEPA does not require formal environmental fate data for Bs given its nontoxic nature to non-target organisms (USEPA 1999a, NYSDEC 1996). The length of time that Bs remains effective against mosquitoes varies, depending primarily on the species and behavior of mosquito larvae, environmental conditions, and water quality (USEPA 1999a, Lacey and Merritt 2003, Gelernter 2001). In general, Bs is effective for one to four weeks after application (Abbott Lab. undated, USEPA 1999a), though measures of effectiveness range from as little as 2.5 hours to more than 60 days. UV light in the range of 300 – 400 nm, falling within the wavelength range of sunlight, has been shown to inactivate both spores and endotoxins of Bs (Gelernter 2001). Bs is less likely than Bti to adsorb to particulate matter and settle out of the water column. Therefore, it is considered to have generally higher efficacy against mosquito larvae in waters with a higher degree of particulates (Yousten et al 1992, Weinzierl et al. 1997, FCCMC 1998). As it occurs naturally, Bs does cycle and maintain itself in the environment (Lacey 1990); however, the

insecticidal formulations currently in use do not cycle in water to infect subsequent generations of mosquito larvae (Weinzierl et al. 1997).

Ecotoxicity

Bs is generally not considered a risk for non-target organisms. The commercially available form of *Bs*, VectoLex®, has been extensively tested and is considered non-toxic to nontarget organisms (Westchester County Board of Health 2001, NYSDEC 1996). USEPA concluded that Bs does not pose any significant risk to non-target organisms or the environment (USEPA 2000a). No additional recent information has been identified for Bs to contradict these general findings.

Table 3 (in the rear of the report) presents a summary of ecotoxicity data for Bs by ecological receptor group.

5.1.3. Methoprene

General Background Information

Methoprene is a biochemical pesticide found in two formulations (methoprene and methoprene sustained release formula) and is registered under the Altosid™ trade name line. Methoprene is used to control mosquitoes, beetles, horn flies, tobacco moths, sciarid flies, fleas (eggs and larvae), fire ants, pharoah ants, midge flies, and Indian meal moths. It is also registered for use on a number of foods including meat, milk, eggs, mushrooms, peanuts, rice, and cereals (USEPA 1991, USEPA 2001, USEPA 2002b). There are also uses in food processing plants and eating establishments; along with non-food uses such as for tobacco, ornamentals, golf courses, pet products, uses in and around the home, and boxcars (USEPA 2002b).

Methoprene is an insect growth regulator that acts by interfering with maturation and reproduction in insects by mimicking the activity of natural juvenile insect hormone, also referred to as ecdysone. Ecdysone is a hormone in insects, secreted by glands near the brain, that controls the retention of juvenile characteristics in larval stages (Antunes-Kenyon and Kennedy 2001). If present, ecdysone (or methoprene acting as an insect growth regulator controlling ecdysone) leads to a suppression of adult characteristics. Although applied at the larval stage, response to methoprene usually occurs in the last instars of the larval or nymph form, or pupae form. In the case of mosquitoes, larvae are the target stage, but the effect is not seen until lack of adult emergence (Antunes-Kenyon and Kennedy. 2001).

Methoprene degrades rapidly in sunlight, both in water and on inert surfaces. Within three days of application, 90 percent will degrade via photolysis and microbial metabolism; without microbial metabolism, photolysis will degrade 80 percent in 13 days (USEPA 1991, USEPA 2001, USEPA 2002b). Overall, methoprene has a half-life ranging from 30 hours to 14 days, depending on environmental conditions. Higher temperatures and salinity lead to higher degradation rates (Glare and O'Callaghan 1999). The effects of methoprene last up to a week, but it reaches undetectable levels in ponds within 48 hours of application (Madder 1980, Schaefer and Dupras 1973). After four days, only 1 percent of the original application concentration will persist in the top two inches of soil. Methoprene is tightly adsorbed to soil and is rapidly broken down, therefore it is not likely to be transported to ground water (USEPA 1991, USEPA 2001, USEPA 2002b). Methoprene sustained release formulation does not produce residual concentrations greater than those produced with the application of a liquid formulation (Westchester County Board of Health 2001).

Ecotoxicity

Methoprene is generally considered to be slightly to non-toxic to terrestrial wildlife. The oral LD_{50} for rats is greater than 10,000 mg/kg (USEPA 2002b). Methoprene is considered slightly toxic to birds (Extoxnet 1996a). In mallards, an acute oral LD_{50} of greater than 2,000 mg/kg in the diet was determined. Dietary no observed effect concentrations (NOECs) (based on reproductive impairment) range from 3 ppm for mallard ducks to 30 ppm for bobwhite quail (USEPA 2002b).

Recent work by Schulz et al. suggest that methoprene may have some impact on honeybee foraging, though definitive data are pending (Schulz et al. 2002).

Methoprene is considered moderately toxic to warm water, freshwater fish (bluegill 96-hour LC_{50} of 1.52 ppm), and is slightly toxic to cold water, freshwater fish (rainbow trout 96-hour LC_{50} is greater than 50 ppm) (Extoxnet 1996a, USEPA 2002b). Methoprene is considered highly toxic to freshwater invertebrates, (daphnid 42-day no observable adverse effect concentration [NOAEC] of 27 ppb, lowest observable adverse effect concentration [LOAEC] of 51 ppb) (USEPA 2002b).

For amphibians, mortality has not been observed at concentrations up to 1.3 ppm (leopard frog). However, adverse effects such as reduced body weight and developmental delays at 720 ppb (leopard frog) were observed (USEPA 2002b). In recent years, methoprene has received considerable attention as a possible causative agent of the increase in amphibian malformations (Ankley et al. 1998, Henrick et al. 2002). The theory that methoprene might mimic the action of retinoids and cause malformations in amphibian populations is

partially supported by research on how methoprenic acid (t-MA) can stimulate gene transcription in vertebrates, particularly amphibians during metamorphosis. Much of this theory, however, remains largely supported by ancillary information and anecdotal reports, as well as contradictory findings within and outside of the taxon (Degitz et al. 2001, Degitz et al. 2003, Oberdorster et al. 2000, Smith et al. 2003). Research in this area is considered ongoing and future experimental findings and other developments warrant attention.

Methoprene can be very highly acutely toxic to estuarine and marine invertebrates, as seen in studies with grass shrimp and mud-crabs (USEPA 2002b). Marine organisms are not likely to be exposed to methoprene, but estuarine organisms are likely to be exposed as a result of application within estuarine habitats. Methoprene degrades rapidly in water so the use of most formulations in estuaries is generally not of concern (Extoxnet 1996a). However, concern has in fact been raised in recent years with respect to methoprene's potential impact on shrimp, crabs and lobsters (Antunes-Kenyon and Kennedy 2001). These concerns stem from the fact that a shared evolutionary past, as well as resultant similarities in biology, exist between crustaceans and dipteran species (including mosquitoes). These concerns have been additionally heightened by events such as the widely-publicized 1999 Long Island lobster die-off (Logomasini undated). Most of the recent studies of estuarine invertebrates have used shrimp, Atlantic oysters, amphipods, copepods, and mud crab. In generally, concern for these species is not anticipated to occur at expected environmental concentrations (Antunes-Kenyon and Kennedy 2001).

Table 4 (in the rear of the report) presents a summary of ecotoxicity data for methoprene by ecological receptor group.

5.2. Pyrethroid Adulticides

The pyrethroids are synthetic pyrethrin-like materials widely used for insect control. Pyrethrins are natural pesticides harvested from some chrysanthemum plants (mainly *Chrysanthemum cinerarnaefolium*) (USEPA 2002e, Westchester County Board of Health 2001). Chemically, pyrethroids are esters of specific acids (e.g., chrysanthemic acid, halo-substituted chrysanthemic acid, 2-(4-chlorophenyl)-3-methylbutyric acid) and alcohols (e.g., allethrolone, 3-phenoxybenzyl alcohol) (WHO-FAO 1990).

Permethrin, resmethrin, and sumithrin are pyrethroids commonly used in mosquito control programs to kill adult mosquitoes**.** Pyrethrins and pyrethroids have a similar mode of action — they work on the nerve axons by keeping open sodium channels used to propagate signals along a nerve cell. Initially, they cause nerve cells to discharge repetitively; later, they cause paralysis. These pesticides affect both the peripheral and the

central nervous systems. When applied alone, pyrethroids may be swiftly detoxified by enzymes in the insect. Thus, some pests will recover. To delay the enzyme action so a lethal dose is accomplished for pest control, a synergist (e.g., piperonyl butoxide) is generally added to pyrethroid formulations to improve efficacy (USEPA 2002e, Westchester County Board of Health 2001).

Pyrethroids used in mosquito control programs generally do not pose unreasonable risks to wildlife or the environment (USEPA 2002e). Pyrethroids, when applied at mosquito control rates, are low in toxicity to mammals, and are practically nontoxic to birds. Mosquito control formulations of pyrethroids break down in the environment, and high temperatures and sunlight accelerate this process. However, pyrethroids are toxic to aquatic life and non-target insects, including honeybees (USEPA 2002e, Westchester County Board of Health 2001). For that reason, USEPA has established specific precautions on the pyrethroid product labels to reduce such risks, including restrictions that prohibit the direct application of products to open water or within 100 feet of lakes, streams, rivers or bays (USEPA 2002e).

Pyrethroids are generally metabolized in mammals through ester hydrolysis, oxidation, and conjugation, and there is little tendency to accumulate in tissues. Metabolization in other species is generally less well studied (ATSDR 2003a). In the environment, pyrethroids are fairly rapidly degraded in soil and in plants. Ester hydrolysis and oxidation at various sites on the molecule are the major degradation processes. As a chemical class, pyrethroids have very low volatility, are all very poorly soluble in water, and have a tendency to bind very tightly to organic particles in soil (New York City Department of Health 2001). Given these characteristics, pyrethroids are not expected to leach to groundwater or surface water bodies. In aquatic settings, pyrethroids strongly adsorb on sediments, and once adsorbed, are difficult to remove with water (WHO-FAO 1990).

Provided below are general background information and ecotoxicity summaries for the three pyrethroid adulticides, permethrin, resmethrin, and sumithrin, selected as primary control agents.

5.2.1. Permethrin

General Background Information

Permethrin is a broad spectrum pyrethroid insecticide which is used against a variety of insect pests. It is used in greenhouses, home gardens, and for termite control. It also controls animal ectoparasites, biting flies, and cockroaches. Permethrin is additionally used to control insects on a variety of food and non-food products, including on nut, fruit,

vegetable, cotton, ornamental, mushroom, potato, and cereal crops (Extoxnet 1996b). Permethrin is the also the active ingredient in several topical anti-parasitic formulations used in human and veterinary medicine.

There are four isomeric forms, two cis- and two trans-, of technical permethrin. Product formulations can vary greatly in isomeric content (Extoxnet 1996b). Permethrin commonly appears under the trade names Permanone™, Pounce™, Nix™, Torpedo™, and Dragnet™.

Permethrin is readily degraded in most soils (except highly organic types). Field dissipation studies performed for permethrin indicate a half-life of 42 days in soil.[3] Degradation in soil is largely attributable to microbial biodegradation (Westchester County Board of Health 2001, Extoxnet 1996b). On surfaces, permethrin is degraded by sunlight, but may remain insecticidally active for up to 26 days. Half-life in water has been reported to be less than 2.5 days, and half-life in sediment has been reported to be 2.5 days. Permethrin has also been found to bioaccumulate to a low to moderate degree in aquatic organisms, most notably in aquatic insect larvae, aquatic plants (e.g., duckweed), and some fish (see below) (Westchester County Board of Health 2001).

Ecotoxicity

Permethrin is generally considered to have limited toxicity to terrestrial wildlife (USEPA 2002e). Permethrin has been described as moderately to practically non-toxic in mammals. In rats, LD_{50}s range from 430 to 4,000 mg/kg in the diet (Extoxnet 1996b). Very high dietary concentrations of permethrin (e.g., 500 mg/kg [~18,000 mg/kg body weight [bw] day [d] as LOAEC) were shown to cause increased liver weights, body tremors, salivation, hyperactivity, hyperexcitability, urination, defecation, incoordination, and death over the course of a two-year rat study (Westchester County Board of Health 2001). Fertility of rats was affected when they received very high doses of permethrin during pregnancy (250 mg/kg bw d of permethrin during the sixth to 15th day of pregnancy) (Extoxnet 1996b, Westchester County Board of Health 2001). Metabolic breakdown products of permethrin are quickly excreted in mammals and do not persist significantly in body tissues. There are no methods for chemical identification of metabolites in the urine (Extoxnet 1996b).

[3] Field dissipation studies determine how fast a pesticide disappears from the upper soil layers after the pesticide is applied to bare soil at a known application rate. Such studies simulate the disappearance of the pesticide under naturally-occurring environmental conditions. Disappearance can be due to any or all of the following: degradation due to water, sunlight and/or microbial activity, leaching from soil due to downward movement of rain water, and evaporation into the air.

Permethrin has been described as practically non-toxic to birds (chronic dietary lowest observable adverse effect concentrations [LOAECs] greater than 9,900 mg/kg in mallard ducks, greater than 13,500 mg/kg in pheasants, and greater than 15,500 mg/kg in Japanese quail; acute oral LD_{50} for starling of 43,000 mg/kg bw d), although chronic low doses have been reported to suppress the immune system activity of young chickens (Extoxnet 1996b, Westchester County Board of Health 2001).

As with other pyrethroids, permethrin kills insects that eat or come in contact with it by paralyzing the nervous system, but, at low concentrations, permethrin also repels insects (Westchester County Board of Health 2001). Permethrin has been shown to be extremely toxic to bees at the time of treatment and a day after treatment (on surfaces) (Extoxnet 1996b, Moncharmont et al. 2003, Westchester County Board of Health 2001). Permethrin is not phytotoxic to most plants when used as directed, although some injury to ornamental plants has been reported (Extoxnet 1996b).

Aquatic wildlife are particularly vulnerable to the impact of permethrin (Baser et al. 2003, Crosa et al. 2001, Extoxnet 1996b, Gonzalez-Doncel et al. 2003, Westchester County Board of Health 2001). The 48-hour LC_{50} for rainbow trout is 0.0125 mg/L for 24 hours, and 0.0054 mg/L for 48 hours. The 48-hour LC_{50} in bluegill sunfish and salmon is 0.0018 mg/L (Extoxnet 1996b). In general, there is little data available in the literature regarding the chronic toxicity of pyrethroids, particularly of permethrin, to aquatic wildlife (Rand undated).

Permethrin is toxic to young oysters, but at much higher concentrations than for fish and crustaceans (Westchester County Board of Health 2001). Recent studies have provided preliminary evidence that permethrin may induce certain biomarkers, such cytochrome P450, (Fisher et al. 2003) as well as cause immunosuppressive effects in a variety of aquatic organisms, including fish and aquatic insects (Nayak et al. 2004).

The bioconcentration factor for permethrin in bluefish is 715 times the concentrations in water; the bioconcentration factor is 703 in catfish. This indicates that the compound has a low to moderate potential to accumulate in these organisms (Extoxnet 1996b).

Table 5 (in the rear of the report) presents a summary of ecotoxicity data for permethrin by ecological receptor group.

5.2.2. Resmethrin

General Background Information

Resmethrin is a broad spectrum pyrethroid insecticide used for control of flying and crawling insects in homes, greenhouses, indoor landscapes, mushroom houses, and industrial sites, insects that infest stored products, and for mosquito control (Extoxnet 1996c). It is also used for fabric protection, pet sprays, and shampoos, and it is applied to horses and in horse stables (Extoxnet 1996c, WHO-FAO 1996c). Resmethrin commonly appears under the trade name Scourge™, which is used to control adult mosquitoes.

Resmethrin is classified as relatively insoluble in water, but it is highly soluble in organic solvents (Westchester County Board of Health 2001). It binds tightly to soil and is not expected to be mobile in soil or to contaminate ground water (Extoxnet 1996c). In addition to binding to soil, resmethrin may sorb to sediments, suspended particles, and plants. Biodegradation, hydrolysis, and photodegradation are the rapid degradation pathways for resmethrin, with environmental half-lives ranging from 15 minutes to just over a month, depending on the environmental setting (Extoxnet 1996c, WHO-FAO 1996). Resmethrin's photodegradation half-life on surfaces is approximately three hours, while half-lives in soil and sediment have been reported to be 30 and 36.5 days, respectively (Westchester County Board of Health 2001). Environmental degradation products reported for resmethrin are chrysanthemic acid, benzaldehyde, benzyl alcohol, benzoic acid, phenylacetic acid, and various esters (Extoxnet 1996c).

Ecotoxicity

Resmethrin is considered slightly to practically non-toxic to terrestrial wildlife. For mammals, the oral LD_{50} for technical resmethrin in rats is variously reported as 1,244 mg/kg bw d or greater than 2,500 mg/kg bw d. Resmethrin is slightly toxic via inhalation, with a four-hour inhalation LC_{50} in rats of greater than 9.49 mg/L (Extoxnet 1996c). Chronic studies in rats have shown that the administration of resmethrin can result in an increase in stillborns and lower weight of pups. Additionally, a delay in fetal rat skeleton formation has been observed. Resmethrin is practically nontoxic to birds. Its LD_{50} in California quail is greater than 2,000 mg/kg bw d, and for Japanese quail, the five-day dietary LC_{50} is greater than 5,000 ppm (Extoxnet 1996c, Westchester County Board of Health 2001).

As is the case with the other pyrethroids, resmethrin is considered highly toxic to bees (Extoxnet 1996c, WHO-FAO 1996).

Aquatic wildlife are particularly vulnerable to the impact of resmethrin. Studies have shown that resmethrin can be highly toxic to fish with LC_{50}s generally ranging from less than 1 to 7 µg/L, and highly toxic to aquatic crustaceans (LC_{50}s generally ranging from approximately 1 to 200 µg/L), and oysters, with oysters being the least sensitive (LC_{50} of

up to 1,800 µg/L (Extoxnet 1996c, Rand 2002, Rand undated, Westchester County Board of Health 2001). In general, there is little data available in the literature regarding the chronic toxicity of pyrethroids to aquatic wildlife (Rand undated).

Table 6 (in the rear of the report) presents a summary of ecotoxicity data for resmethrin by ecological receptor group.

5.2.3. Sumithrin

General Background Information

Sumithrin (also called phenothrin) is a broad spectrum pyrethroid insecticide registered for use against mosquitoes in swamps, marshes, and recreational areas. Sumithrin can also be used to kill pests in transport vehicles such as aircraft, ships, railroad cars, and truck trailers, and for institutional non-food use, use in homes, gardens, and greenhouses, and on pets (USEPA 2002e). Sumithrin is the active ingredient in the product Anvil 10 + 10™.

Sumithrin degrades readily, with a half-life of less than one day, on plants and other surfaces. In soil, sumithrin degrades rapidly, with a half-life of 1-2 days under dry, sunny conditions. Under flooded conditions, the half-life increases to 2-4 weeks for the trans isomer and 1-2 months for the cis isomer (WHO-FAO 1990). Half-life is longer in the absence of light — sumithrin has been found to remain almost intact on grains stored in the dark for up to 12 months (WHO-FAO 1990, Westchester County Board of Health 2001) In general, the degradative processes that occur in the environment lead to less toxic products (WHO-FAO 1990).

Ecotoxicity

Less data are available regarding the toxicity of sumithrin to non-target species than for the other evaluated pyrethroids. For terrestrial wildlife, sumithrin is generally considered to be nontoxic. In mammals (e.g., mice, rats, dogs), acute toxicities are all extremely low (i.e., acute rat LD_{50} greater than 5,000 mg/kg bw d), and few chronic effects have been noted (Westchester County Board of Health 2001). Sumithrin appears to be relatively nontoxic to birds (i.e., acute bobwhite quail LD_{50} of 2,500 mg/kg bw d).

No data have been identified on the toxicity of sumithrin to bees (Westchester County Board of Health 2001).

For aquatic wildlife, sumithrin has been shown to exhibit low to very high toxicity to fish (LC_{50}s ranging from approximately 1 to 66 µg/L) and very high toxicity in crustaceans (LC_{50} less than 1 µg/L) (WHO-FAO 1990).

No additional research based on recently published articles and reports was identified to augment the above general findings.

Table 7 (in the rear of the report) presents a summary of ecotoxicity data for sumithrin by ecological receptor group.

5.3. Organophosphate Adulticides

Organophosphate pesticides consist of a broad class of chemicals used primarily in insect and pest control. These pesticides cover a wide variety of use categories, such as forests and woodlands, greenhouse food and non-food crops, livestock, seed treatments, oilseed and fiber crops, stored food and feed, terrestrial feed and food crops, structural uses, outdoor ornamentals and indoor plants, plantscapes, and turf (ATSDR 2003b, USEPA 1999b, USEPA 2000b, USEPA 2002d).

Organophosphates exert toxicity through the inhibition of acetylcholinesterase (AChE) at cholinergic junctions of the nervous system of organisms. These junctions include postganglionic parasympathetic neuroeffector junctions (sites of muscarinic activity), autonomic ganglia and the neuromuscular junctions (sites of nicotinic activity) and certain synapses in the central nervous system (ATSDR 2003b, USEPA 2002d). Acetylcholine (ACh) is the neurohumoral mediator at these junctions. Since AChE is the enzyme that degrades ACh following stimulation of a nerve, its inhibition allows ACh to accumulate and result in initial excessive stimulation followed by depression (ATSDR 2003b, USEPA 1999b, USEPA 2000b, USEPA 2002d). In insects, this inhibition interferes with the nerve-muscle communication at neuromuscular junctions, and that ultimately causes paralysis of the insect (ATSDR 2003b, USEPA 1999b, USEPA 2000b). Organophosphate compounds vary greatly in their toxic capabilities. They are often selected for use because they produce little or no tissue residues (ATSDR 2003b, USEPA 1999b, USEPA 2000b, USEPA 2002d).

Malathion (including its breakdown products malaoxon and isomalathion) is the single primary list mosquito control agent belonging to the organophosphate class.

5.3.1. Malathion

General Background Information

Malathion is a nonsystemic broad-spectrum organophosphate chemical that is used in agriculture and horticulture applications (ATSDR 2003b, USEPA 1999b, USEPA 2000b). Malathion has been widely used since the 1950s on raw agricultural products including edible grains, fruits, nuts, forage crops, cotton, and tobacco (ATSDR 2003b). Malathion

has also been used to control parasites of livestock and domestic animals, through aerial applications in and around livestock barns, dairies, poultry houses, and food processing plants. Malathion has widespread use as a ground and aerial spray to control Mediterranean fruit fly and mosquito populations. Malathion is used as a pediculicide in shampoos to treat head lice on children and adults (ATSDR 2003b, Westchester County Board of Health 2001).

Malathion is the active ingredient in mosquito control products including Fyfanon™ and Atrapa™. These products contain over 95 percent malathion and are often applied undiluted. However, they may be diluted with a petroleum solvent similar to kerosene before application, in which case the petroleum solvent will make up most of the pesticide solution (ATSDR 2003b).

Malathion contains approximately 5 percent impurities consisting largely of reaction byproducts and degradation products (ATSDR 2003b). As many as 14 impurities have been identified in technical-grade malathion. The identities of the impurities and their percent in technical grade malathion were found to be as follows (ATSDR 2003b):

- S-1,2-ethyl-O,S-dimethyl phosphorodithioate (isomalathion; 0.2 percent)
- S-1,2-bis(ethoxycarbonyl)-ethyl-O,O-dimethyl phosphorothioate (malaxon; 0.1 percent)
- diethylfumarate (0.9 percent)
- O,S,S-trimethyl phosphorodithioate (0.003–1.2 percent)
- O,O,S-trimethyl phosphorothioate (0.04 percent)
- O,O,S-trimethyl phosphorodithioate (1.2 percent)
- O,O,O-trimethyl phosphorothioate (0.45 percent)
- diethylhydroxysuccinate (0.05 percent)
- ethyl nitrite (0.03 percent)
- diethyl mercaptosuccinate (0.15 percent)
- diethyl methylthiosuccinate (1.0 percent)
- O,O-dimethylphosphorothioate (0.05 percent)
- diethyl ethylthiosuccinate (0.1 percent)
- sulfuric acid (0.05 percent)

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Malathion possesses a relatively low acute toxicity compared to other organophosphates. Signs and symptoms of acute toxicity are typical of those induced by organophosphate insecticides as a group. Almost all of the systemic effects observed following exposure to malathion are due to the action of its active metabolite, malaoxon, on the nervous system, or are secondary to this primary action. Malathion must be oxidized before it causes inhibitory potency and toxicity. Oxidation occurs via cytochrome P450 and results in the conversion malathion to malaoxon. Malaoxon inhibits the enzyme AChE at the various sites where the enzyme is present in the nervous system, (i.e., the central nervous system, the sympathetic and parasympathetic divisions of the autonomic nervous system, and the neuromuscular junction). In general, acute toxicity of malathion is considered predominantly attributable to the presence of its chief degradate, malaoxon (ATSDR 2003b, USEPA 2000b).

Malathion is degraded in the environment through three main pathways, activation, degradation, and isomerization. Activation of the compound involves oxidative desulfuration, yielding malaoxon (ATSDR 2003b, USEPA 2000b). Activation may be achieved by photo-oxidation, chemical oxidation, or biological activation, the latter of which occurs enzymatically through the activity of mixed function oxidases. Degradation of malathion occurs through both chemical and biological means, with hydrolysis being the most important pathway for each (ATSDR 2003b, USEPA 2000b). Malathion can be broken down via microbial and photodegradation under various settings. Its half-lives can range from five hours to 25 days, depending on the medium (i.e. water, soil, air) (Westchester County Board of Health 2001). Isomerization results in the formation of isomalathion (ATSDR 2003b).

Limited data exists with respect to the environmental fate of malaoxon and isomalathion (ATSDR 2003b, USEPA 2000b). USEPA has identified the environmental fate data gap for each of these chemicals, with special attention on the need for data development with respect to malaoxon. According to USEPA, "Acceptable environmental fate studies specifically for malaoxon; including degradation, metabolism, mobility, dissipation, and solubility data; would be very useful for future assessments." In the interim, USEPA has defaulted to evaluating the environmental fate of malaoxon based on the characteristics of malathion (USEPA 2000b).

The majority of the data available on the bioaccumulation of malathion suggest that, while malathion may be bioconcentrated, it is rapidly metabolized or depurated from the tissue of aquatic organisms and is, therefore, not likely to be biomagnified in an aquatic-based food

chain. In the USEPA 2000 Reregistration Eligibility Document (RED) for malathion, bioconcentration factors values ranging from 23 to 135 were reported for whole bluegill sunfish, while a range of 4.2 – 18 was reported for the edible tissue of the fish (USEPA 2000b). These results and those reported in Howard (1991) do not clearly indicate whether bioconcentration in aquatic organisms is an important fate process for malathion that would allow for the potential for biomagnification of malathion in the food chain. However, it was also reported to USEPA that 96 and 73 percent of the malathion residues depurated from the whole and edible fish tissues, respectively, during a 14-day depuration period (USEPA 2000b). Additionally, residue analysis indicated that the parent compound was partially metabolized in the fish, with 33.3 – 35.9 percent of the residues present as the degradate malathion monocarboxylic acid and 5.7 percent of the residues present as one of 22 other compounds including malathion dicarboxylic acid, malaoxon, demethyl malathion, monoethylfumarate, and oxalacetic acid (ATSDR 2003b, USEPA 2000b). Additionally, in a review paper, Niimi (1987) reported that the half-life of malathion in the muscle tissue of carp was one day. These data indicate, despite the apparent tendency of malathion to partition into the tissues of aquatic organisms, that the potential for biomagnification in the food chain is likely to be low because malathion appears to be metabolized by aquatic organisms (ATSDR 2003b, USEPA 2000b).

Ecotoxicity

Of the primary mosquito control agents evaluated as part of this review, malathion has by far the largest amount of information available regarding its ecotoxicological characteristics. This summary represents a distillation of the vast amount of toxicological information available, and relies to a large degree on the previous summaries provided in the New York City DEIS and Westchester DGEIS, as well as on the USEPA 2000 RED document for malathion. Where relevant, additional information from recent research published since 2001 is additionally discussed.

In general, malathion exhibits generally low to moderate toxicity to terrestrial wildlife (USEPA 2000b, USEPA 2002c).

Malathion has been shown to result in slight toxicity to mammals (USEPA 2000b). High acute doses (e.g., acute oral LD_{50}s ranging from 150 – 2,100 mg/kg bw d) may cause death. While adverse effects of malathion on mammals have often been widely documented in acute studies, fewer studies are available with respect to chronic effects. In mammals, malathion can affect the central nervous system, the immune system, adrenal glands, liver and blood. Rats fed high doses during pregnancy had an increased number of stillborn and pups with low birth weight; there were no adverse effects at low doses.

During a two-year chronic study in rats, there were observed decreases in brain cholinesterase levels and body weights. An eight-week study showed no effects on whole-blood cholinesterase activity when small amounts were administered (Westchester County Board of Health 2001). In general, sublethal effects may occur at concentrations as low as 100 mg/kg for certain mammalian species. Reproductive effects are not expected unless concentrations remain at 500-1000 mg/kg for extended periods of time (USEPA 2000b).

Malathion has been shown to result in slight to moderate toxicity to birds (USEPA 2000b, Westchester County Board of Health 2001). High doses (e.g., 14-day LD_{50} for pheasants of 167 mg/kg bw d) can cause death. Yet, chronic, low doses show little to no effects. For example, chickens fed low doses for two years showed no adverse effects in egg hatching. A study using ultra-low volume (ULV) malathion applied at two or more times the application rate for mosquito control showed no effect on insectivorous birds as measured by loss of food source (e.g., non-target insects), fledgling success, adult bird weight, and nestling weight (Westchester County Board of Health 2001).

Some limited toxicity data for reptiles is available. For Carolina anoles, an acute oral LD_{50} was reported to be 2,324 mg/kg (Hall and Clark 1982). Mitchell and Yutema (1973) observed abnormal development in embryos of the common snapping turtle exposed to malathion.

Malathion is considered to be highly toxic to bees on an acute contact basis either through exposure to direct spray or through foliar residue contact within eight hours after spray is applied. Field incidents of extensive honeybee mortality following malathion application have also been documented (USEPA 2000b).

In general, aquatic life exhibits greater toxicant sensitivity to malathion than terrestrial wildlife. USEPA has reviewed extensive data and has classified malathion as very highly to moderately toxic for both freshwater and estuarine/marine fish species. These collective findings are generally supported by recently published research (Brewer et al. 2001, Brown et al. 2004, Fulton and Key 2001, Singh et al. 2004)

Malathion use has been implicated as the possible or probable cause of fish kills in local areas where it has been applied (USEPA 2000b, Westchester County Board of Health 2001). The USDA Animal and Plant Health Inspection Service (APHIS) has concluded, however, that in certain instances fish mortality can not be attributed solely to malathion, but is likely due to a combination of conditions including: stress of malathion, low dissolved oxygen, and high water temperature (APHIS 1997). In addition, the application of malathion for mosquito control has also been suspected of causing a large-scale lobster die-off in the Long Island Sound in 1999. Based upon information provided in February

2001 by the Connecticut Department of Environmental Protection (CTDEP), the die-off was unlikely the result of adulticide application, but was more likely the result of a combination of environmental factors including high temperatures, low dissolved oxygen and a parasitic protozoan (*Paramoeba ssp.*) (CTDEP 1999). Recent findings by De Guise et al. (2004) suggest acute mortality for lobsters may occur at concentrations of malathion in seawater at 38 µg/L, while concentrations as low as 5 µg/L may result in sublethal effects, most notably immunotoxic effects (De Guise et al. 2004). However, such sublethal effects did not exhibit a consistent dose response relationship (De Guise et al. 2004). The issue of mosquito control pesticides and lobster mortality is discussed extensively elsewhere in the Literature Search (see Book 8, Part 2).

USEPA has determined that sufficient data exists to suggest that malathion may have teratogenic effects to early life stages of some frog species if environmental concentrations exceed 1 ppm (USEPA 2000b, Pawar et al. 1983). Acute effects occur generally within the range of 200-400 µg/L, which USEPA considers to be "highly toxic" (USEPA 2000b). Other effects, such as behavioral and immunosuppressive effects have also recently been documented (Fordham et al. 2001, Gilbertson et al. 2003).

Malathion is considered to be moderately to very highly toxic to freshwater and estuarine and marine invertebrates, such as daphnids, crayfish, oysters, shrimp and blue crab. Based on the data reviewed to date for aquatic early life stages of terrestrial non-target insects, USEPA has additionally classified malathion as highly to very highly toxic to aquatic larvae of these species (USEPA 2000b). Malathion has also been classified as highly toxic to benthic invertebrates (Westchester County Board of Health 2001). These collective findings are generally consistent with recently published research (Barata et al. 2004, DeLorenzo et al. 2001, Fulton and Key. 2001, Jimenez et al. 2003, Lehtonen et al. 2003)

Limited data exists regarding the ecotoxicity of malathion's two primary degradates, malaoxon and isomalathion. Malaoxon is commonly believed to be the neuroactive toxic agent of malathion after oxidation *in vivo* and toxicity data show it to have higher acute toxicity than malathion (USEPA 2000b). Acute oral toxicity of malaoxon has been reported in rats (LD_{50} of 158 mg/kg), and acute toxicity data is also available for one fish species (LC_{50} for medaka of 365 µg/L) and aquatic midge (24 hour LC_{50} of 5.4 ppb) (HSDB 2003b, USEPA 2002a). No data were identified of ecological relevance for isomalathion. In addition, a number of data gaps persist with respect to the transformation and general environmental fate characteristics of each of these chemicals. Given these considerations, evaluations of potential ecological impacts associated with malaoxon and isomalathion are most appropriate within a qualitative discussion framework relative to

impacts delineated for malathion. This is generally the approach that has been adopted by USEPA in the ecological hazard and risk assessment sections of the 2000 RED document for malathion (USEPA 2000b).

5.4. Synergists

A synergist is a chemical that enhances the potency of a pesticide. Pyrethroids are frequently used in combination with synergists, including piperonyl butoxide (PBO) and n-octylbicycloheptene dicarboximide (ATSDR 2003a, NPIC 2000). When applied alone, pyrethroids may be swiftly detoxified by enzymes in the insect (thereby enabling some pests to recover). Synergists such as PBO are added to pyrethroid formulations in order to slow down or prevent the metabolism of pyrethroids, thereby enabling a smaller amount of pyrethroids to have the same effectiveness. Many formulations of permethrin, resmethrin, and sumithrin, including Scourge™ and Anvil™, used along the East Coast for mosquito control, contain the synergist PBO (USEPA 2002e, Westchester County Board of Health 2001).

PBO was identified in the primary list of mosquito control agents. Provided below are general background information and ecotoxicity summaries for PBO.

5.4.1. Piperonyl Butoxide (PBO)

General Background Information

PBO is a derivative of piperic acid and, as discussed, is generally utilized as a chemical synergist in pyrethroid formulations. Pyrethroid products containing PBO are used to control mosquitoes in outdoor residential and recreational areas, as well as indoors to control insects such as fleas, ticks, and ants. Formulations of pyrethrins containing PBO are also used as a pediculicide to control body, head and crab lice (HSDB 2003a).

PBO prevents metabolic enzyme activity (specifically that of Cytochrome P450 enzymes), through microsomal enzyme inhibition in insects, thereby allowing the active ingredients to remain available and cause enhanced toxic effects (HSDB 2003a, Klaasen et al. 1986, NPIC 2000). PBO's effect on Cytochrome P450 enzymes is biphasic; it both inhibits and induces enzymatic activity. The inhibition of Cytochrome P450 enzymes occurs rapidly, followed by a slow induction process (NPIC 2000).

PBO is rapidly degraded in soil with a half-life of 14 days in aerobic soils. If released to soil, PBO is expected to have moderate to low mobility. If released into water, PBO is expected to adsorb to suspended solids and sediment. Although stable to hydrolysis under sterile, dark conditions, PBO is degraded by sunlight in aqueous solution (HSDB 2003a).

The potential for piperonyl butoxide to bioaccumulate in aquatic organisms is considered low to moderate (HSDB 2003a, NPIC 2000).

Ecotoxicity

PBO is generally considered to have limited toxicity to terrestrial wildlife (USEPA 2002e). PBO has been described as low to very low in toxicity to mammals. In rats, acute oral LD_{50}s range from 4,570 to 12,00 mg/kg bw d. PBO is similarly low in toxicity via inhalation exposures (NPIC 2000). PBO has limited reproductive and teratogenic effects in laboratory rats and rabbits (NPIC 2000, WHO-FAO 1995). Toxicity to birds is also considered to be low to very low (i.e., LD_{50}s generally higher than 2,500 mg/kg bw d). Relative to the other evaluated control agents, PBO exhibits limited toxicity to bees (Westchester County Board of Health 2001).

PBO is considered to be moderately to acutely toxic in fish and highly acutely toxic in aquatic invertebrates (NPIC 2000).

No additional research based on recently published articles and reports was identified to augment the above general findings.

Table 9 (in the rear of the report) presents a summary of ecotoxicity data for PBO by ecological receptor group.

5.5. Repellants

Repellants are chemicals that are used to prevent or limit insect activity. Repellants are used in a variety of applications, including applications for the protection humans, pets, livestock and plants. Repellants used to prevent mosquito bites are typically applied as sprays in outdoor areas, or may be applied directly to the skin using aerosol, pump spray, and lotion formulations.

Garlic oil was identified as the single repellant in the primary list of mosquito control agents. Provided below are general background information and ecotoxicity summaries for garlic oil.

5.5.1. Garlic Oil

General Background Information

Garlic is a naturally occurring substance that is widely distributed and commercially available for flavoring and seasoning. It is a "generally recognized as safe," or GRAS, substance under US Food and Drug Administration (FDA) regulations.[4]

Garlic is also used as a biochemical pesticide under certain agricultural, ornamental and residential conditions to repel insects, particularly mosquitoes, as well as target birds, deer, rodents, armadillos, and other pests (USEPA 1992, Garlic Research Labs undated). In these formulations, garlic is present as either a powder or a distilled extract from the fresh or dehydrated bulb or cloves obtained from *Allium sativum*. Garlic is dispersible in water (polar carriers) and oil (non-polar carriers) with agitation (USEPA 1992). Garlic oil is the active ingredient in the spray products Garlic Barrier AG+™ and Mosquito Barrier™.

Garlic is considered to be non-persistent in the environment (USEPA 1992).

Ecotoxicity

Used as a pesticide, garlic has a non-toxic mode of action for repelling target birds and insects. USEPA has determined that no significant adverse effects to humans or the environment are associated with the use of garlic as a pesticide, and data on its ecotoxicity are not required for its registration as a pesticide (USEPA 1992)[5]. As part of this review, no relevant data were identified on the ecotoxicological characteristics of garlic.

[4] See 21 CFR 182.10, 182.20 and 184.1317

[5] Garlic is currently on the USEPA's exempted products list as stipulated under the USEPA Federal Insecticide, Fungicide and Rodenticide Act (FIFRA), Section Sec 25(b). This list contains "minimum risk" pesticides which may be used freely without regulation owing to their demonstrated safety.

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Appendix A
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