CHAPTER 3.C

PUBLIC HEALTH

A. INTRODUCTION

The primary purpose of the proposed Mosquito-Borne Disease Control Programs is to protect the public from outbreaks of mosquito-borne diseases, such as West Nile virus encephalitis. One means of adult mosquito population control is pesticide spraying, which in itself may pose a risk to public health. The analysis in this chapter examines the anticipated benefits to public health of adult mosquito control (reduction in the potential for an outbreak of a mosquito-borne disease such as encephalitis) versus the potential for a percentage of the City’s population to come into contact with a pesticide used for mosquito control and to react adversely to it following both short-term and long-term exposures.

This chapter first introduces the illnesses and adulticides that form the basis of the public health analysis and briefly describes the analysis methods. It then presents an assessment of current and future baseline conditions in the project’s Representative Areas without the proposed Adult Mosquito Control Programs (as per the CEQR process). (Detailed discussion of analyses can be found in Appendices A through D.) This chapter then addresses the potential for adverse public health impacts from the Proposed Action, including the potential risk to the City’s residents and visitors from the adulticides proposed for the program. The chapter ends with comparisons of the potential for illness, both mild and serious, with or without the proposed Mosquito-Borne Disease Control Program.

As mentioned in the beginning of this document, the EIS process requires agencies to disclose the potential significant adverse environmental impacts, if any, of a proposed program and examine, to an appropriate extent, how these impacts can be avoided or minimized. As part of this effort the lead agency must disclose whether significant adverse public health impacts may occur as a result of the project. Public health refers to the health of a population, rather than an individual. Issues to be considered when determining whether an impact would be considered “significant” to public health include the likelihood of occurrence, the time frame, seriousness of the potential health effect, duration, the number of people affected and reversibility of potential impacts.

The process of weighing risks and benefits of pesticide application is complex. It entails determining the likelihood and dose of the exposure and then reviewing the potential impacts on the general population and on sensitive members of the public, such as children and people with chronic illness. The public health impact of not spraying (i.e., the likelihood that some members of the public may become seriously ill or die as a result of a mosquito-borne illness) is evaluated as well.

In order to help make this determination, this EIS will combine information from a review of scientific literature, the Risk Assessment, Epidemiologic and Attributable Risk Analyses, as well as summary information from reports received by the New York City Poison Control Registry and New York State Department of Health (NYSDOH) Statewide Pesticide Poisoning Registry in determining whether potential adverse public health impacts would be significant.
B. DEFINITIONS
This section explains some of the key terms and issues that will be discussed in this chapter, and describes characteristics of the six active ingredients in the adulticide products that are being considered in this EIS.

MOSQUITOES AND THE TRANSMISSION OF VIRAL INFECTIONS
Mosquitoes are arthropod insects indigenous to the environment. There are approximately 3,100 mosquito species worldwide, and some 30 species live in New York City. As described in Chapter 1, “Description of the Proposed Action,” Table 1-1, some breed in salt or brackish water, others in fresh water. Some lay eggs that must survive through the winter in order to hatch; others reproduce up to seven times in a summer season; and others may be active in protected areas year-round. Many species feed primarily at dawn and dusk; others may feed throughout the day. In all cases, adult mosquitoes feed on plants, and only the female bites humans and other animals when she needs a blood meal in order to lay her eggs. If the mosquito has bitten an animal infected with a virus that can continue to live within the mosquito, then she will become a carrier of the virus and will be able to transmit the virus to other animals by means of a subsequent bite. Such a mosquito is called a “vector” for the transmission of the disease associated with the virus.

The mosquito-transmitted (“arboviral”) viruses at issue for this EIS are those that can result in encephalitis (inflammation of the brain) or meningitis (inflammation of the lining surrounding the brain and spinal cord). Traditionally, the five major types of arboviral encephalitis in North America have been: eastern equine encephalitis (EEE), western equine encephalitis (WEE), St. Louis encephalitis (SLE), LaCrosse encephalitis (LAC) and Venezuelan equine encephalitis (VEE). West Nile virus is a cause of a form of arboviral encephalitis new to the Western Hemisphere, although it has been long established in Europe, the Middle East and Africa. Because the most recent outbreak of arboviral encephalitis in New York City has been from the West Nile virus, this chapter focuses on that disease, including its characteristics and potential for harm to public health, using the Representative Areas as illustrative examples. The results of studies conducted by the New York City Department of Health (NYCDOH) and the Centers for Disease Control and Prevention (CDC) (see section C. below) suggest that most people who are bitten by a mosquito infected with the West Nile virus do not get sick. Of those who do respond to the virus, most experience flu-like symptoms, including fever, muscle pain, joint ache, headache, and gastrointestinal distress. However, a smaller percentage of people infected with the virus can develop encephalitis or meningitis, both of which can have serious consequences, including permanent neurological damage, coma, or death.

OVERVIEW OF INSECTICIDES EVALUATED
The 17 adulticides registered for use in New York State that are considered for application on a community-based scale in this EIS fall into two major categories: organophosphates and pyrethroids. Although all 17 adulticides could potentially be used by NYCDOH as part of the Proposed Action, five products, each containing one of the active ingredients of concern, were chosen for detailed technical analysis to assess public health risk. These five products contain a combination of the highest content of active ingredient and/or PBO, and the least amounts of inert. The exception to this was the choice of Fyfanon ULV (which contains a slightly lower percentage of the active ingredient malathion—see Chapter 2, “Pesticide Regulations and Usage,” Table 2-10), as this was the product used by the City in 1999. Two active ingredients found in the organophosphate group—malathion and naled—and three active ingredients in the pyrethroid group—permethrin, resmethrin and sumithrin—and a synergist were evaluated. The “active” ingredient is the chemical compound that is intended to
target and eradicate the adult mosquito. (See Chapter 2, “Pesticide Regulations and Usage.”) A
synergist is a chemical that enhances another chemical’s effectiveness; synergests are used with
pyrethroids to prevent insects from detoxifying pyrethroids. The synergist piperonyl butoxide (PBO),
which may also be considered an active ingredient on its own, and is typically added to pyrethroid
formulations, was evaluated. Further references in this chapter to the six “active ingredients” refer to
these six ingredients: malathion, naled, permethrin, resmethrin, sumithrin and the synergist PBO. For
purposes of this discussion, PBO is included in the list of the six “active ingredients,” even though it
is used primarily as a synergist. Adulticides also include “inert” ingredients, which are generally
solvents, to aid in the dispersion of the product. As discussed in Chapter 2, “Pesticide Regulations
and Usage,” information about the specific inert ingredients found in the adulticides was not disclosed
by the manufacturers to NYCDOH for the purposes of this EIS. Therefore, efforts have been made to
categorize the potential public health effects of these inerts from available information on the
general categories of these inerts and product test data found within the available literature.
USEPA groups adulticides into four classes according to their toxicity in mammalian species via
ingestion, inhalation, and skin contact: Class I, highly toxic; Class II, moderately toxic; Class III,
slightly toxic to practically non-toxic; and Class IV, practically non-toxic (USEPA, 1998f). Based on
the general toxicological results obtained from animal studies as outlined in Table 3.C-1 below,
USEPA uses this classification to determine the appropriate precautionary words for a product's label.

<table>
<thead>
<tr>
<th>Animal Study</th>
<th>Class I (highly toxic)</th>
<th>Class II (moderately toxic)</th>
<th>Class III (slightly toxic to practically non-toxic)</th>
<th>Class IV (practically non-toxic)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute ingestion</td>
<td>Up to and including 50 mg/kg</td>
<td>Greater than 50 mg/kg but less than 500 mg/kg</td>
<td>Greater than 500 mg/kg but less than 5000 mg/kg</td>
<td>Greater than 5000 mg/kg</td>
</tr>
<tr>
<td>Acute skin</td>
<td>Up to and including 200 mg/kg</td>
<td>Greater than 200 mg/kg but less than 2000 mg/kg</td>
<td>Greater than 2000 mg/kg but less than 5000 mg/kg</td>
<td>Greater than 5000 mg/kg</td>
</tr>
<tr>
<td>Acute inhalation</td>
<td>Up to and including 0.05 mg/L</td>
<td>Greater than 0.05 mg/L but less than 0.5 mg/L</td>
<td>Greater than 0.5 mg/L but less than 2 mg/L</td>
<td>Greater than 2 mg/L</td>
</tr>
<tr>
<td>Eye irritation</td>
<td>Corrosive (irreversible destruction to eye tissue) or</td>
<td>Involuntary closing of eye or irritation clearing in 8-21 days</td>
<td>Involuntary closing of eye or irritation clearing in 7 days or less</td>
<td>Minimal effects, clearing in less than 24 hours</td>
</tr>
<tr>
<td></td>
<td>involuntary closing of eye or irritation persisting for</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>more than 21 days</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Skin irritation</td>
<td>Corrosive (tissue destruction and/or scarring)</td>
<td>Severe irritation at 72 hours (severe inflammation or redness of skin or blistering)</td>
<td>Moderate irritation at 72 hours (moderate inflammation or redness)</td>
<td>Mild or slight irritation (slight inflammation or redness)</td>
</tr>
</tbody>
</table>

Source: USEPA, 1998f
For example, Class I would require the following precautionary wording on the label: DANGER – POISON; Class II would require the following statement: WARNING; Class III would require the following statement: CAUTION; and Class IV does not require any precautionary statement on the label. For example, if laboratory test animals can tolerate the ingestion of 2,500 mg/kg body weight (i.e., 2,500 mg of a chemical ingested per kilogram body weight of an animal) in an acute ingestion study, then the chemical is determined to be a Class III chemical (slightly toxic to practically non-toxic). It should be noted that this is an oversimplification. Typically two or more types of studies are used to determine the toxicity classification for a chemical.

**Types of Insecticides and Synergists**

**Organophosphates**

There is more than one type of organophosphate. About half of all organophosphate insecticides (including naled and malathion, the organophosphates being considered in this EIS), are in the dimethoxy organophosphate group (Gallo and Lawryk, 1991). The literature suggests that the dimethoxy compounds are the least toxic among organophosphate compounds (Gallo and Lawryk, 1991). Organophosphates are used in agriculture on a variety of food and feed crops, in the home, in gardens and in veterinary practice (Gallo and Lawryk, 1991). Organophosphate pesticides were first characterized for their adverse effects on living organisms in 1932, although related chemicals have been synthesized since 1820. Organophosphates are readily absorbed following inhalation and ingestion, or through skin contact. In insects, organophosphates such as malathion and naled work by interfering with the central nervous system. Specifically, this class of insecticide blocks an enzyme called acetylcholinesterase. This enzyme controls the degradation of a neuronal chemical called acetylcholine, which is responsible for communication between cells (e.g., between two nerve cells and/or between nerve cells and muscle cells). In the human body, the communication between these types of cells typically causes physical reactions, such as secretion of digestive juices in the stomach, or watering of the eyes due to irritation.

Organophosphates are considerably less toxic to mammals than to insects. Unlike insects, mammals are able to breakdown malathion into compounds that don't bind to acetylcholinesterase. Mammals possess specific enzymes (found primarily in the liver but also in many other mammalian tissues) that rapidly break down and detoxify organophosphates. This process minimizes their potential for causing adverse effects (Murphy, 1986). However, it is possible that excess exposure to malathion may overwhelm the detoxification mechanisms in mammals thus leading to acetylcholinesterase inhibition.

**Malathion**

USEPA has classified malathion as a Class III adulticide (slightly toxic to practically non-toxic in mammalian species). Malathion, a commonly used insecticide, is registered for use in the home or garden as well as for professional use. Malathion itself does very little to block acetylcholinesterase activity (Chambers and Dorough, 1994). However, once malathion has entered the body, it can be slightly altered to another organophosphate, malaoxon, which is approximately 1,000 times more effective at inhibiting acetylcholinesterase. Mammals, including humans, readily detoxify malathion using enzymes present in the liver. This greatly minimizes its potential for generating malaoxon. In contrast to mammals, insects cannot easily detoxify malathion, allowing for conversion to malaoxon (Klaassen, 1996; Costa, 1997). The literature suggests that due to these mammalian detoxification mechanisms, malathion is relatively less toxic to humans than many other organophosphates (Chambers and Dorough, 1994), and that exposures must be relatively high for toxicity to occur. Of considerable importance, however, is the fact that if malathion is stored over months improperly (i.e.,
open containers, fluctuation in temperature, etc.), there exists the potential for toxic impurities (such as malaoxon) to form, which can increase the toxicity to humans (Chambers and Dorough, 1994).

In addition to these detoxification mechanisms in humans, malathion is rapidly broken down and eliminated in human subjects exposed to a dose of malathion applied to skin (Dary et al., 1994 in USEPA, 2000b). In six human subjects, 50 percent of an initial dose of malathion, absorbed through the skin, was eliminated in an average of 7.5 hours (Dary et al., 1994 in USEPA, 2000b).

**Naled**

USEPA has classified naled as a Class II adulticide (moderately toxic in mammalian species). Naled is used to control adult mosquitoes and flies, on field crops, and in mushroom houses (Gallo and Lawryk, 1991). Short-term, immediate toxicity data, inhalation data and early reports of exposures in humans suggest that naled is not highly toxic, although it is considered slightly more toxic than malathion (ACGIH, 1998; Gosselin et al., 1984).

Naled is rapidly degraded to another organophosphate, dichlorvos, and shares many of the same physical and toxicological properties as dichlorvos (ACGIH, 1998). Due to its rapid degradation, most formulations of naled most likely contain some dichlorvos. Dichlorvos and naled are direct inhibitors of acetylcholinesterase and do not require further metabolic conversion to an active compound. The literature reports that dichlorvos and naled are more toxic to insects than to humans, partially due to the greater affinity of these organophosphates for the insect form of acetylcholinesterase (Gallo and Lawryk, 1991). Furthermore, as reported by Gallo and Lawryk, inhibition of the enzyme acetylcholinesterase by naled and dichlorvos is slowly reversible in mammals (mice) but is irreversible in insects (Gallo and Lawryk, 1991).

As with other organophosphates, the literature indicates that the absorption of naled in humans is rapid, through the skin and mucous membranes of the digestive and respiratory systems (Gallo and Lawryk, 1991). The literature indicates that naled is excreted in humans mainly *via* the kidneys (Gallo and Lawryk, 1991).

Both naled and dichlorvos are rapidly detoxified in humans by the liver, as well as in blood plasma (Gallo and Lawryk, 1991). Due to this rapid detoxification in multiple tissues, naled has a very short half-life (less than one hour) and does not accumulate to any measurable extent in the body (Gallo and Lawryk, 1991).

**Pyrethroids**

Pyrethroid compounds are synthetic chemicals manufactured to replicate the insecticidal properties of naturally occurring pyrethrins. Pyrethrins were first discovered in pyrethrum flowers such as chrysanthemums (daisy-like flowers), and are noted for their immediately noticeable effect on insects, as well as rapid degradation in the environment. The natural pyrethrins are now used mainly as the active ingredient in domestic insecticide products, such as over-the-counter spray used to control insects in gardens and households. As a chemical class, the synthetic pyrethroids were developed to improve insecticidal potency and to overcome pyrethrin’s inherent instability when exposed to sunlight. (Bowerman et al., 1987). For example, a common over-the-counter spray used to control ants and roaches contains two pyrethroids, cypermethrin and imiprothrin. Unlike the pyrethroids discussed in this EIS, cypermethrin and imiprothrin do not break down at all in sunlight (these two pyrethroids are not typically used for adult mosquito control) (Ware, 1999). Furthermore, based on toxicity values reported by the USEPA, as well as in the scientific literature, the pyrethroids discussed in this EIS are considered less toxic to mammals than both the naturally occurring pyrethrins, and the pyrethroids cypermethrin and imiporthrin, the two active ingredients found in a common over-the-

Unlike the organophosphates, pyrethroids do not inhibit the activity of acetylcholinesterase. Rather, pyrethroids work by preventing cells from building up opposing electrical charges on either side of the cell membrane in order to terminate the transmission of a nerve impulse. The differential in electrical charges is a fundamental physiological property of neural tissue, and its inhibition causes repetitive signal transmission along a nerve. The literature suggests that pyrethroids are broken down much more rapidly in mammals than in insects, and are thus less toxic to mammals than to insects (Lawrence and Casida 1982; Glickman and Casida, 1982). The literature also suggests that pyrethroids cause no long-term adverse effects in the central nervous system even after repeated exposures (Ray, 1991).

As reported in the literature, exposures to high doses of the three pyrethroids—permethrin, resmethrin and sumithrin—evaluated in this EIS can produce symptoms including excitability, exaggerated startle response, uncoordinated twitching of the back muscles, and whole body tremors (Ray, 1991).

Chemists group pyrethroids into two categories: Type I, and Type II. The Type I pyrethroids are the least toxic. The three pyrethroids – permethrin, resmethrin and sumithrin (phenothrin) – evaluated in this EIS are Type I pyrethroids (the least toxic pyrethroids) (Ray, 1991). No type II pyrethroids are considered for use by NYCDOH as part of the Proposed Action.

**Permethrin**

As described above, permethrin is classified as a Type I pyrethroid. Depending on its formulation, permethrin is classified by USEPA as either toxicity class II (moderately toxic) or III (practically non-toxic to slightly toxic) (USEPA, 1999b). It is used as a pesticide for a variety of agricultural crops and as a household pesticide to control cockroaches and flying insects. Permethrin is also used for the treatment of exoparasites (parasites on the surface of the body) such as lice living on humans. Due to its insecticidal efficacy and low incidence of allergic side effects (Ray, 1991), the literature suggests that it is considered to be of low toxicity to mammals (Haustein, 1991). As reported in the literature, only permethrin doses many times larger than levels expected from spraying have been found to produce toxic effects associated with skin, ingestion and inhalation exposures (Ray, 1991; Hartley and Kidd, 1987).

Studies in humans have shown that only a small amount of permethrin is absorbed through the skin into the body, where it is quickly broken down and eliminated. The American Medical Association reports that less than 2 percent of permethrin applied on the skin is absorbed in the body (AMA, 1991). In mammals, once absorbed into the bloodstream, permethrin is rapidly broken down by enzymes in the liver into relatively harmless inactive metabolites (i.e., carboxylic acids and alcohols that are naturally abundant in the human body). These metabolic products are quickly eliminated from the body through urine, feces and exhaled air and do not persist in tissues of the body. However, if permethrin present in the blood stream is not broken down by enzymes in the liver, it can be absorbed into fatty tissue (i.e., body fat and brain tissue) where it may persist with reported half-lives of 4 to 5 days (Hallenbeck and Cunningham-Burns, 1985).

**Resmethrin**

Resmethrin is classified by the USEPA in toxicity class III—slightly toxic to practically non-toxic (USEPA, 1999b). It has uses in household and agricultural pesticides as well as for mosquito control. The literature suggests that resmethrin is slightly toxic in humans by the inhalation exposure route, and even less toxic by oral ingestion and dermal absorption (USEPA, 1988; Hartley and Kidd, 1984).
Resmethrin is less likely to be absorbed into the body via dermal and inhalation exposure routes than via oral exposure. The literature suggests that like most pyrethroids, resmethrin is expected to be metabolized rapidly in the human body and does not persist in tissues (Murphy, 1986).

**Sumithrin**

Sumithrin is used for mosquito control in outdoor areas, as well as in shampoo for treatment of head lice (World Health Organization, 1990b). Unlike permethrin and resmethrin, USEPA has not classified sumithrin as to its toxicity class. While most pyrethroids are rapidly metabolized in mammals, Kaneko et al., (1981) found that 96 percent of sumithrin absorbed through the skin in rats in a single dose was excreted within 6 days. Residual sumithrin concentrations in fat tissues were slightly higher than in other tissues 7 days after a single oral dose of 10 mg/kg, suggesting that sumithrin may bioaccumulate in animals if they are exposed over a long period of time (Kaneko et al, 1981).

**Synergists**

The addition of synergistic compounds, such as PBO, improves the insecticidal efficacy of pyrethroids by blocking the enzymes responsible for breaking down pyrethroids in insects (Knowles, 1991). PBO also inhibits these enzymes in mammals, but only at doses much higher than doses that are effective in insects. As reported by Knowles (1991), PBO itself is considered minimally toxic, and is not considered likely to cause significant signs or symptoms of toxicity following short-term oral or skin exposures (Knowles, 1991). USEPA has not classified PBO as to its toxicity class.

PBO is poorly absorbed from the gastrointestinal tract. Once absorbed, it is excreted rapidly in the urine (Knowles, 1991). Because it is poorly absorbed from the gastrointestinal tract, PBO is largely excreted via the feces (Sarles and Vandegrift, 1952).

**Inert Ingredients**

In addition to active ingredients, the adulticide formulations contain inert ingredients. As discussed in Chapter 2, “Pesticide Regulations and Usage,” since information on the specific inert ingredients was not disclosed by the manufacturers to NYCDOH for the purposes of this EIS, efforts have been made to characterize the potential public health effects of these inert from available information on the general categories of these inerts and product test data found within the available literature.

Although these ingredients are inert in terms of insecticidal activity, they may have toxicological properties. Therefore, exposure to the inert ingredients must also be considered. The percentage of inert ingredients in the adulticide formulations varies, ranging from 3.2 percent for Fyfanon ULV (which contains malathion as the active ingredient), to 80 percent for Anvil 10+10 (which contains sumithrin as the active ingredient).

Because an adulticide formulation is considered classified business information, manufacturers are not required by law to provide information regarding the inerts to the public. However, information regarding inerts is required for Federal and State pesticide registration. Furthermore, the types and amounts of inerts are taken into account when establishing use restrictions, to ensure that health will not be adversely affected under conditions of proper use and handling.

In some cases, manufacturers actually do list the names and identities of at least some of the inerts, especially those associated with adverse health effects that may occur if the products containing the named inerts are not properly used and handled. Such information is provided on the labels and material safety data sheets (MSDSs) for adulticide formulations. For the adulticides containing pyrethroids considered in this EIS, information about the specific inert ingredients has not been
disclosed by the manufacturers; however, the MSDSs provide the general categories to which the inert ingredients belong. No information on the inerts for either of the organophosphates was available. Table 3.C-2 lists inerts and their amounts in the adulticide formulations discussed in this EIS.

<table>
<thead>
<tr>
<th>Product</th>
<th>Ingredient</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anvil 10+10</td>
<td>Aromatic Hydrocarbon (Petroleum distillate)</td>
<td>1-15%</td>
</tr>
<tr>
<td></td>
<td>White Mineral Oil</td>
<td>40-78%</td>
</tr>
<tr>
<td>Permethrin 57% OS</td>
<td>Naphthalene Depleted Aromatic 150 Solvent (Petroleum distillate)</td>
<td>&lt; 43%</td>
</tr>
<tr>
<td>Scourge</td>
<td>Aromatic Petroleum Solvent (Petroleum distillate)</td>
<td>20 - 28%</td>
</tr>
</tbody>
</table>

As is shown in Table 3.C-2, all of the pyrethroid formulations contain petroleum distillates of various types. USEPA has categorized most petroleum distillate inerts as potentially toxic (USEPA, 1987b). Aromatic petroleum solvent, which is an inert in Scourge, is a mixture of methylbenzene solvents (i.e., alkylbenzenes), including toluene, xylene, and other related compounds (Douglas et al., 1993). Although there is compelling evidence that benzene causes leukemia and other hematopoietic disorders (e.g., aplastic anemia) (IARC, 1982; Snyder and Kalf, 1994), the alkylbenzenes have not been associated with such effects, likely because they are metabolized in a completely different manner. On the other hand, workers repeatedly exposed to 200 to 300 parts per million (ppm) alkylbenzenes (Matsushita et al., 1975; Benignus, 1981), as well as repeatedly exposed solvent abusers (i.e., glue sniffers) (Morton, 1987), are known to suffer neurobehavioral effects and cerebellar damage. Moreover, in rats exposed to 333 ppm of aromatic petroleum solvent for 12 months (via inhalation), experienced significant increases in liver and kidney weights, although there were no other effects on blood chemistry, gross pathology (exterior appearance of test animals’ tissues and organs), or histopathology (microscopic appearance of cells in test animal’s tissues) (Clark et al., 1989).

Mineral oil, which is present in Anvil 10+10, is used therapeutically as a laxative, as well as to relieve symptoms associated with dry, itchy, scaly skin. Mineral oil is also a major ingredient in pharmaceutical preparations (intestinal lubricants) and cosmetics (cold creams and hair preparations) (IARC, 1984). Mineral oil is included in USEPA’s list of minimal risk inert ingredients which include substances that are ubiquitous in nature and not expected to present a hazard to human health or to the environment (USEPA, 1987b). This category includes food grade inert ingredients, many of which have been used for decades.

Although specific information regarding inert ingredients present in the adulticides were not available for this assessment, it was assumed that the likely composition of inerts would consist of chemicals such as mineral oils, mineral spirits, aromatic petroleum solvents, or Stoddard solvent. These chemicals are typically found in commercially available products such as paint thinner. Health effects associated with these compounds are discussed in more detail below in the Public Health Characteristics of Proposed Adulticides – Literature Review section.
Potential Public Health Effects of Insecticides

Insecticides are developed to kill insects, and they may contain toxic substances that have the potential to affect human health, either through their toxicity or because they irritate or exacerbate sensitivities and allergies, leading to a number of symptoms. Therefore, the assessment of the potential for impacts of the Proposed Action on public health from the use of insecticides and synergists examines a full range of possible effects, from relatively benign and short-lived skin and eye irritation to serious diseases, such as cancer. The toxicological information discussed for these signs and symptoms does not include data from suicides or willful exposure to pesticides. The public health issues are:

- Skin and eye irritation;
- Gastrointestinal distress;
- Respiratory problems (particularly asthma);
- Immunologic/allergic reactions;
- Multiple chemical sensitivity reactions;
- Acute neurologic effects;
- Cognitive developmental disabilities (including autism);
- Endocrine disruption;
- Developmental/reproductive effects, including birth defects; and
- Cancer.

C. CURRENT AND FUTURE CONDITIONS WITHOUT THE PROPOSED ACTION

INTRODUCTION

As described in Chapter 1, “Description of the Proposed Action,” and well-documented in the media at the time, in the summer of 1999, a mosquito-borne virus (ultimately identified as West Nile virus) was detected as the cause of an outbreak of mosquito-borne encephalitis in the City, centered in northern Queens. Although this virus was new to the Western Hemisphere, outbreaks of other types of mosquito-borne viral encephalitis have occurred from time to time in nearby areas of New York State, but there has never been a documented case in the City. NYCDOH has instituted a program of education, surveillance and control of mosquito larvae in an ongoing effort to limit or prevent future outbreaks of such viral infections. This effort plus the efforts of the private sector in controlling mosquitoes on a local basis constitute “current and future conditions without the Proposed Action.” The application of insecticides to control the proliferation of infected adult mosquitoes is the “Proposed Action.”

POTENTIAL PUBLIC HEALTH CHARACTERISTICS OF FUTURE OUTBREAKS WITHOUT THE PROPOSED ACTION

Public Health Characteristics of West Nile Virus Outbreaks

In considering conditions without the Proposed Action, the comparisons in this chapter focus on West Nile virus, primarily because it constitutes the most recent outbreak. The analysis in this section first addresses information on the virus assembled from the literature, then focuses on the public health characteristics of the 1999 outbreak in New York City. Finally, using the Representative Areas as
examples, this section estimates the potential for adverse effects on public health from future outbreaks, if infected adult mosquitoes are not controlled.

Until 1996 West Nile virus had not been considered a public health threat in Europe, except for a small outbreak in southern France in 1962. However, in the late 1990s there were important outbreaks in Romania and Russia. In these Eastern European outbreaks, the death rates were much higher than those that previously occurred due to West Nile virus. There were also important outbreaks in Israel, New York, and elsewhere in the late 1990’s and 2000. The number of cases of encephalitis and meningocencephalitis, an inflammation of the brain and the membranes covering the spinal cord and brain, caused by the virus, also increased dramatically.

The first large outbreak of West Nile virus reported in Europe occurred in 1996, when more than 500 cases were reported in Romania (Platonov et al., 2001). The true number may have been higher because surveillance was delayed and appropriate clinical samples were not available from many patients (Tsai et al., 1998). Seventeen people died, and hundreds more were admitted to hospitals with central nervous system infections. Researchers who studied the records of 393 of the people hospitalized with West Nile fever in southeastern Romania noted that the neurological diagnoses were meningitis (40 percent); meningocencephalitis (44 percent); and encephalitis (16 percent) (Tsai et al., 1998). The journal Lancet also mentioned that the epidemic affected an extensive area of southeastern Romania in 1996 and, from anecdotally reported cases in Bulgaria, an even larger area of the Danube delta (Tsai et al., 1998).

In southern Russia, 40 people died of acute aseptic meningocencephalitis in 1999 in an outbreak due to West Nile virus. Scientists and doctors estimated that 480 people hospitalized in the Volograd region of Russia suffering from aseptic meningocencephalitis, aseptic meningitis or acute fever had contracted West Nile virus. Again, the disease was more severe than in previous outbreaks there, with a higher proportion of the patients dying. Indeed, 40 of the 84 people hospitalized with acute aseptic meningocencephalitis died (Platanov et al., 2001). Approximately 1,000 cases of meningocencephalitis were reported altogether in the Volograd, Astrakhan and Krasnodar regions of southern Russia in 1999 (Lvov, 2000). While fewer data were available in journal articles on the cases in the Astrakhan and Krasnodar regions, researchers reported that clinical and epidemiological investigations indicated that the outbreak there, too, could be associated with West Nile virus.

The three large outbreaks in Volograd, Russia, Romania, and New York were caused by genetically similar West Nile virus strains (Platanov et al., 2001). The Russian strain however, was more similar to the Romanian strain of West Nile virus. Genetic sequencing of the virus responsible for the New York City outbreak in 1999 showed that it was most closely related to a strain of West Nile virus isolated from a goose in Israel in 1998. This suggests the wide circulation and emergence of potentially epidemic strains of the virus. These outbreaks were also noteworthy in that they occurred in regions where this disease had rarely (southern Russia and Romania) or never (New York) been reported before. The three cities—New York, Bucharest (Romania), and Volograd (Russia)—that were at the center of these virus outbreaks all are near large bodies of water and are on bird migration pathways. They also had unusually dry summers in the year of the major outbreak (Platanov et al., 2001).

Israel, one of the world’s major stopovers for migrating birds in the autumn and spring, between Eastern Europe and South Africa, experienced a widespread outbreak in 2000. Israel has approximately 2 million fewer residents than New York City. Yet, 439 confirmed cases of West Nile virus and 29 deaths (Ministry of Health, Israel, 2000) were caused by the disease, as compared with 62 confirmed cases and 7 deaths in the New York City metropolitan area in 1999.
The virus has been spreading geographically throughout the North East since it was first reported in New York City in 1999. Although West Nile encephalitis is not included in the list of nationally notifiable diseases, the CDC encourages states, especially those on the Eastern seaboard to conduct surveillance for West Nile. While encephalitis is already reportable to NYCDOH, the New York City Board of Health has recently proposed an amendment to the New York City Health Code to make acute arboviral infection also a reportable condition.

While 1 of the 2 fatalities and the majority (14) of last year’s reported U.S. cases of West Nile encephalitis were in New York City, seven other cases of West Nile encephalitis were reported to the CDC. Six of these occurred in New Jersey, and one in Connecticut. Nineteen of these patients were hospitalized.

Even though fewer Americans contracted West Nile virus last year than in 1999, the documented number and types of infected animals increased significantly. In 1999 scientists documented West Nile infections in birds and horses. With increased surveillance in 2000, infected raccoons, bats, rabbits and other mammals were found (NYSDOH; National Atlas USGS). West Nile-infected animals were also found over a larger geographic area last year than in 1999. Delaware, Massachusetts, Pennsylvania and Rhode Island each reported one infected mammal, and reports of infected birds were even more widespread. Dead birds infected with West Nile were found in most Northeastern and Central Atlantic states. Massachusetts reported 448 birds infected with West Nile; Rhode Island, 87 birds; Maryland, 50; Pennsylvania, 32; Virginia, 7; New Hampshire 7; Washington D.C, 5; and North Carolina, Delaware and Vermont reported 1 each. In New York City 185 infected birds were found last year; the total for all of New York State was 1,278 birds, including 10 live ones. Birds infected with West Nile were found in all but one of New York State’s counties in 2000. In New Jersey, 1,289 infected birds were reported; in Connecticut, 1,117. These numbers reflect only dead birds that were tested, not all potentially infected dead birds (USDA, APHIS, 2000).

Public Health Characteristics of the 1999 West Nile Virus Outbreak

When the outbreak of West Nile virus in the New York City metropolitan area came to light in the summer of 1999, a total of 59 hospitalized cases were detected. Seven of these people died. Of the 59 hospitalized patients, approximately 62 percent were age 65 and older. At the time, it was not known how many others had been exposed to the virus and how many of those people had become sick. To more fully understand the public health impact of the epidemic, clinical spectrum of illness and the possible risk factors for infection, a household-based survey of blood serum samples (“seroprevalence survey”) was conducted through the cooperative efforts of NYCDOH, CDC, the Public Health Service, the U.S. Department of Health and Human Services, and the National Center for Infectious Diseases.

The locale chosen for the survey was a 3-square-mile area of northern Queens, considered to be the epicenter of the outbreak, where 9 of the 59 hospitalized patients in 1999 lived. Within that area, cluster sampling was used to select a representative sample of households. All individuals 5 years and older were eligible. Serum samples were tested for antibodies to the West Nile virus. Of the 677 participants from 459 families, 19 (2.6 percent) were found to be positive for recent exposure to West Nile virus. (Statistical analysis found the 95 percent confidence interval—an interval within which a value would be expected to lie 95 percent of the time—ranging from 1.2 percent to 4.1 percent.) Seropositive individuals were more likely than seronegative individuals (29 percent vs. 11 percent) to

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1 The information contained in this section is entirely based on, “Epidemic West Nile Encephalitis, New York, 1999: Results of a Household-Based Seroprevalence Survey,” submitted for publication by Farzad Mostashari, et al.
report a recent illness with fever ("febrile" illness). All 6 of the Seropositive persons reporting a febrile illness reported muscle ache, 5 had headaches, 5 had fatigue, and 4 had joint pain. Three had consulted a doctor. Based on a population of 47,368 residents over five years old within the 3-square-mile area (from the U.S. Census, 1990), an estimated 219 febrile illnesses from infection with West Nile virus occurred in the study area, resulting in an estimated 123 outpatient visits. This compares with 9 cases originally diagnosed clinically in the area during the outbreak. Some 993 persons had asymptomatic West Nile virus infections. Extrapolating from the 59 hospitalized cases throughout the region, the study estimates that approximately 7,900 people in the region may have been infected, with 1,400 contracting mild febrile illnesses and 6,500 showing no symptoms.

As suspected, people who spent much time outdoors at dusk or dawn—peak biting periods for the Culex pipiens and several other types of mosquitoes—and people who never used DEET-containing insect repellant showed the highest risk of infection. The presence of dead birds in a neighborhood also signaled a higher risk of West Nile infection.

**Potential Characteristics of Future Outbreaks without the Proposed Action**

The 1999 outbreak, which occurred during the summer, was determined to be associated with West Nile virus. Beginning in early September, the City implemented a substantial emergency program to control the outbreak through public education efforts and the spraying of areas suspected to harbor infected mosquitoes.

Therefore, although the August-September 1999 outbreak is the closest experience New York City has to an uncontrolled, “No Action” condition (i.e., without adulticiding), it was not entirely without intervention. (Adulticide spraying did occur in September to control adult mosquitoes.) However, the Future No Action condition includes larviciding as part of the *Routine Program*. Since citywide larviciding actions were not undertaken in 1999 (the first year of the outbreak), data on the benefits of larviciding could not be included in this assessment of projected illness without the Proposed Action. Therefore, the projection of illnesses and hospitalizations in the Representative Areas may in fact be an overestimation. However, since the scenarios for the project’s Representative Areas rely on empirical data that are recent and come from New York City, it is possible, given the experience in Romania, Russia and Israel, where the outbreaks were not identified and dealt with as quickly as in New York City, that the illustrative scenarios could underestimate the extent and severity of the public health consequences associated with No Action larviciding and no adulticiding. Also, since it is probable that West Nile virus is here to stay (may become endemic to the area) and considering the virulence of the recent outbreaks in other developed nations, future outbreaks here could be considerably more severe than the one the City experienced in 1999 should preventive actions and the Proposed Action not be undertaken.

In order to estimate morbidity in each potentially affected community, the rates of infection, febrile illness, and hospitalization that were estimated from the October 1999 seroprevalence survey, and the rates of clinically diagnosed encephalitis in the summer of 1999 were applied to the populations in each Representative Area (See Table 3.C-3). These estimated rates were: infections in 2.6 percent of the population, febrile illness (fever) in 0.46 percent of the population (about 18 percent of those infected) and hospitalization in 0.02 percent of the population (about 0.8 percent of those infected). It should be noted that applying these infection, illness, and hospitalization rates to the Representative Areas assumes outbreak conditions in each area. That is, these rates assume that, without an adult.
mosquito control program, an outbreak similar to that which occurred in northern Queens in 1999 could potentially occur in any part of the City, as represented by the seven Representative Areas examined here.

Citywide figures assume an outbreak would occur across the entire City, which would be unlikely but not impossible without an adult mosquito control program. As discussed above, these are assumptions of infection rates that could be expected should outbreaks similar to that of 1999 occur in each Representative Area. The actual rates are likely to vary based on the demographic and land use characteristics for each study area. That is, in an area like Lemon Creek/Wolfe’s Pond, in Staten Island, it is possible that infection rates may be higher than in an area such as the Upper East Side of Manhattan, since an outbreak might be worse due to the greater number of mosquitoes in this part of Staten Island. Since there are too many factors to arrive at a reliable quantification of the difference in potential infection rates for each study area, the same infection rates are assumed for each study area. Additional information on each of the study areas can be found in Chapter 3.B, “Land Use, Community Facilities, Public Policy, and Zoning.”

In the absence of an adult mosquito control program, Representative Areas are projected to experience anywhere from 88 infections/mosquito season (in Lemon Creek/Wolfe’s Pond) to almost 1,900 infections/mosquito season (in the Upper East Side) in the future. For every 100 people infected, about 18 would be projected to come down with a febrile illness, and approximately one of those would be sick enough to require hospitalization. Judging by the rate of death among diagnosed, hospitalized cases in 1999 (7 of 59), 4 of the 33 people in these representative study areas projected to be hospitalized could die as a result of a mosquito borne disease outbreak in the future without an adult mosquito control program.

**RISK TO PUBLIC HEALTH FROM EXISTING ADULTICIDE USE**

To place in context the risks associated with spraying adulticides, it is useful to note that there is already a background concentration of insecticides in the everyday environment, and therefore New
Yorkers are already exposed to pesticides from a variety of sources (e.g., food, home use, lawn/garden use, etc.). As discussed in Chapter 2, “Pesticide Regulations and Usage,” commercial applicators reported using more than 13 million gallons and more than 20 million pounds of pesticide products in New York State in 1999. This included 6,668,786 gallons and 3,400,137 pounds used in New York City. Some applicators reported the figures in gallons; others reported in pounds. Because not all pesticide use is reported, the actual amounts used are likely to be greater, as discussed in Chapter 2, “Pesticide Regulations and Usage.” During the summer of 1999, New York City used 5,349 gallons of four pesticide products during its public health mosquito-spraying program (which represents less than 0.1 percent of the City’s total pesticide use). In the following year, 2000, New York City applied approximately 2,120 gallons of just one adulticide product. Of this amount, nearly 56 percent was applied in Staten Island. In 2000, Staten Island was the epicenter (i.e., location of the first human infection) of the West Nile virus outbreak. In 1999, however, Queens was considered to be the epicenter and therefore received the bulk of the adulticide applications (Mayor's Office Of Emergency Management; NYCDOH).

New Yorkers can come in contact with pesticides on food brought in from other states, as well as on food grown in New York State. Through its Pesticide Data Program, the U.S. Department of Agriculture keeps track of the amount of adulticides’ active ingredients found on randomly chosen food products normally sold in grocery stores and open-air markets across the United States. The New York State Department of Agriculture (USDA) and its Food Laboratory in Albany help to collect and process data about pesticide residue in food. The Pesticide Data Program searches for residues at the lowest detectable levels.

During 1998, in various parts of the country, the Pesticide Data Program tested apple juice, cantaloupe, corn syrup, grape juice, canned and frozen green beans, whole milk, orange juice, pears, soybeans, canned spinach, fresh and frozen strawberries, sweet potatoes, tomatoes, and fresh and frozen winter squash (USDA, 1998). USDA chose these food items because they are the foods most often consumed by the American public, with emphasis on those foods consumed by infants and children (USDA, 1998). USEPA recommends monitoring for those pesticides whose toxicities and estimated dietary exposures indicate the need for more refined exposure estimates.

Of the approximately 8,500 samples collected and analyzed in 1998 by the Pesticide Data Program, 7,017 were fruit and vegetable commodities, 595 were whole milk, 590 soybean, and 298 corn syrup (USDA, 1998). Approximately 61 percent of the fruit and vegetable samples (domestic and imported) had detectable pesticide residues (USDA, 1998). Residues were also detected in 15 percent of the milk samples and 51 percent of the soybean samples. No residues were found in any of the corn syrup samples. Approximately 84 percent of all samples were domestic, and 15 percent were imports (less than 1 percent were of unknown origin) (USDA, 1998).

For fresh and processed fruit and vegetable samples, analysis was conducted for a total of 53 pesticides and 16 metabolites (breakdown products of the original pesticide compound). Forty-four pesticides and 25 metabolites were analyzed in milk samples, while 35 pesticides and 9 metabolites were analyzed in soybeans. High fructose corn syrup samples were analyzed for 83 pesticides and 26 metabolites.

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4 USDA, 1998 Annual Summary: p. 3.
The Pesticide Data Program only tested for three of the six active ingredients being considered in this EIS (malathion, permethrin, PBO). Naled, resmethrin and sumithrin were not among the list of pesticides tested in the program. The USDA occasionally found detectable levels of malathion in three items: pears (2 of a total of 712 samples), fresh strawberries (86 of a total of 610 samples) and frozen strawberries (9 of a total of 47 samples). The range of detected values for malathion was 0.012 to 0.015 ppm for pears; 0.003 to 0.3 ppm for fresh strawberries; and 0.003 to 0.04 ppm for frozen strawberries (USDA, 1998). Malathion was detected in 242 of a total of 590 soybean samples. The range of detected values was 0.003 to 0.191 ppm. These values are lower than USEPA Tolerance Level of 8 ppm for these commodities (USDA, 1998). A tolerance level is defined as the maximum quantity of a pesticide residue allowable on a raw agricultural commodity and is applicable to processed foods. Malathion was not detected in any milk samples or in any samples of high fructose corn syrup.

Permethrin was detected in three commodities: orange juice (1 of a total of 180 samples), canned spinach (141 of a total of 179 samples), and tomatoes (14 of a total of 180 samples). The detected concentrations for permethrin were 0.13 ppm in orange juice; 0.13 to 8.5 ppm in canned spinach, and 0.13 to 0.3 ppm in tomatoes. These values are lower than USEPA Tolerance Levels of 20 ppm and 2 ppm for canned spinach and tomatoes, respectively. A permethrin Tolerance Level has not been established for orange juice. Permethrin was not detected in samples of soybeans or in high fructose corn syrup.

PBO was detected in five commodities: canned spinach (1 of a total of 272 samples), fresh strawberries (6 of a total of 228 samples), sweet potatoes (5 of a total of 54 samples), tomatoes (3 of a total of 272 samples), and fresh winter squash (1 of a total of 55 samples). The detected concentrations for PBO were 0.099 ppm in canned spinach; 0.067 to 0.24 ppm in fresh strawberries; 0.067 ppm in sweet potatoes; 0.11 to 1.6 ppm in tomatoes; and 0.067 ppm in fresh winter squash. Detected values in sweet potatoes and tomatoes were lower than USEPA's Tolerance Levels of 0.25 and 8 ppm, respectively. PBO Tolerance Levels have not been established for canned spinach, fresh strawberries, and fresh winter squash. PBO was not analyzed in milk or soybean samples. In addition, PBO was not detected in any of the high fructose corn syrup samples.

In its Annual Water Quality Reports, the NYCDDEP has noted that it did not find malathion and permethrin in the City’s drinking water. (No tests are routinely conducted for resmethrin, sumithrin and PBO.) The New York State Department of Environmental Conservation operates a Water Quality Monitoring Program, which includes statewide testing for the presence of pesticides and pesticide residues (NYDEC, 2000). According to the 2000 Water Quality Monitoring For Pesticides Program (NYDEC, 2000), two key findings are:

1. *Many commonly used pesticides were detected:* however, “concentrations are generally well below all applicable health standards” (Section IV).

2. *Consumers are not likely to be exposed* to these contaminants via drinking water. “In all cases, public water-supply wells found to exceed State or Federal Maximum Contaminant Levels for Public Drinking Water Supplies (MCLs) are either not used, or are treated to prevent the contaminants from reaching consumers. No surface water intakes used for public water supply were found to exceed MCLs” (Section IV). Ninety-nine percent of New York City water is surface water.

Chapter 3.E contains a more extensive discussion of water, and Chapter 3.N discusses air quality.
REPRESENTATIVE AREA ASTHMA RATES
Of concern to residents in some communities are the effects of adulticide application on people with asthma, especially children with severe cases of asthma. To facilitate an analysis of the potential effects of adulticide application on asthma sufferers, this section presents baseline data on child asthma hospitalizations in each of the seven Representative Areas. It should be noted that child asthma hospitalization rates do not necessarily correlate to general asthma rates, nor do they necessarily reflect the overall incidence of asthma attacks in any given area (many of which may be self-medicated or medicated by doctors outside of hospitals). The seven Representative Areas have a range of child asthma hospitalization rates, with the highest rates corresponding to areas with the lowest incomes. Annual asthma hospitalization rates among children in the study areas in 1999 range from a low of 1.65 per 1,000 children aged 0 to 14, to a high of 14.28 per 1,000 children (see Table 3.C-4) in the Hunts Point/Soundview area. The Hunts Point/Soundview asthma rate is the highest among the study areas and is also among the highest in the City. The rate of asthma hospitalization among the general population is somewhat lower than in children—approximately 4.25 per 1,000 people in 1999 throughout New York City.

<table>
<thead>
<tr>
<th>Study Area</th>
<th>Nearest Zip Codes</th>
<th>Children Aged 0-14 in Nearest Zip Codes</th>
<th>Number of Asthma Hospitalizations</th>
<th>Asthma Hospitalization Rate (per 1,000 Aged 0-14)</th>
</tr>
</thead>
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<tr>
<td>College Point</td>
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<td>3,245</td>
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<td>8.32</td>
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<tr>
<td>Paerdegat Basin</td>
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<td>28,624</td>
<td>212</td>
<td>7.41</td>
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<tr>
<td>Edgemere/Far Rockaway</td>
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<td>134</td>
<td>7.71</td>
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<tr>
<td>Hunts Point/Soundview</td>
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<td>14,569</td>
<td>208</td>
<td>14.28</td>
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<tr>
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<td>302</td>
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<tr>
<td>Lemon Creek/Wolfe’s Pond</td>
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<td>New York City</td>
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<tr>
<td>New York City (All Ages)</td>
<td>7,422,564*</td>
<td>31,576*</td>
<td>4.25*</td>
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</tbody>
</table>

Notes: *Figures are for all ages. (NYCDOH Data)

D. PROBABLE IMPACTS OF THE PROPOSED ACTION
This section provides a brief description of the methods of analysis used to examine the potential adverse public health impacts from the Proposed Action. This section presents the information gathered in the literature review for each of the public health issues of concern, and attempts, in a risk assessment based on modeling techniques, to quantify the potential risks associated with the Proposed Action. This section also presents epidemiologic and attributable risk analyses that explore the past public health effects related to exposure to adulticide spraying activities.

METHODS OF ANALYSIS
To examine the potential for adverse public health impacts of the Proposed Action, the public health analysis employed three techniques: Literature Review, Risk Assessment, and Epidemiologic and Attributable Risk Analyses, as described below.
Literature Review

A literature search was conducted to assess potential human and animal effects of pesticide exposure based on peer-reviewed published articles as well as government documents. This literature search was performed in three major databases using the DIALOG information retrieval service. Two databases—MedLine and ToxLine—from the National Library of Medicine (NLM) were included in the DIALOG searches. NLM contains abstracts for thousands of scientific and medical publications. MedLine covers the medical and public health journals (including, among others, Journal of the American Medical Association, the New England Journal of Medicine, the CDC’s Morbidity and Mortality Weekly Report (MMWR), Environmental Health Perspectives, Environmental Research, Journal of Occupational and Environmental Health, and the American Journal of Epidemiology. ToxLine surveys broader toxicology literature, including some conference proceedings and international toxicology guidance documents. These two databases offer extensive and complete toxicological and health information on chemicals, including the six active ingredients evaluated in the EIS. Additionally, the DIALOG query searched the National Technical Information Service (NTIS) database, which contains Federal government documents and EPA reports. This DIALOG query was performed for all known adulticide active ingredients (malathion, naled, permethrin, resmethrin, sumithrin, and PBO), and the general categories of inert ingredients found in the adulticide products considered in this EIS, and all possible health effects they might cause. Searches were performed for the active ingredients, because toxicity information is generally reported for active ingredients rather than the products themselves. Furthermore, if there were any reports on toxicity effects associated with the products, they would be included in a search for the active ingredient.

The DIALOG literature search included parameters to search all human epidemiological and case study data resulting from exposure to one or more of the insecticides. Studies of toxicity in whole animals and isolated tissues under experimental conditions were also included in the literature search parameters. From the full list of search results, only those documents relevant to single compound exposures at common daily or occupational levels were reviewed. This excluded some studies (e.g., those examining exposure to multiple adulticides) that were unable to clearly implicate toxicity from the active ingredients under the exposure scenarios expected after spraying. The literature search also almost exclusively covered publications in English, although abstracts that had been translated into English from certain publications in other languages were also reviewed. The resulting body of literature discovered using these methods is as comprehensive and conclusive as possible for all important, scientific, peer-reviewed literature to date on the six active ingredients and their likely human health effects. More than 500 scientific articles were reviewed regarding the potential health effects associated with exposure to the active ingredients in the adulticides. From these reviewed articles, only those documents relevant to single compound exposures at common daily or occupational levels were reviewed. Approximately 150 documents are actively cited in this literature review.

In addition, articles and studies were gathered, to the extent possible, on the experience of communities in Europe, the Middle East and Africa with outbreaks of the West Nile virus.

5 While some of the effects were observed in tests conducted in whole organisms (in vivo), other effects were observed in tests conducted on individual organs or tissues (in vitro). Tests that were conducted in vitro generally do not take into account compensatory mechanisms for toxicity in the whole animal. For instance, the liver, which breaks down many toxins, may potentially greatly reduce the potency of a toxin in the whole organism. In vitro testing may at times overstate the potency of a chemical, depending upon how that chemical is further metabolized or changed by other systems in the organism.
**Risk Assessment**

The objective of the public health risk assessment in this EIS is to determine whether the application of adulticides to control the transmission of mosquito-borne pathogens in New York City may pose a significant human health risk. In a public health risk assessment, there are four steps, each of which is briefly described below:

- **Hazard Identification** identifies the chemicals of concern to be analyzed.
- **Exposure Analysis** determines how much of an adulticide people might be exposed to under various conditions during applications.
- **Toxicity Analysis** determines how much of an adulticide is required to cause a toxic effect, and predicts exposure levels at which risk is likely to be negligible or nonexistent.
- **Risk Characterization** integrates the relevant information from the preceding two steps to characterize the risks to the exposed population (i.e., the likelihood that there will be an increase in a particular health effect in the population exposed to a particular adulticide). The risk characterization also includes a description of the assumptions and uncertainties that go into the risk assessment, and an assessment of the overall confidence in the results of the analysis.

As discussed above and in Chapter 2, “Pesticides Regulations and Usage,” detailed information regarding the specific inert ingredients, and their amounts within the adulticides being analyzed, have not been disclosed by the manufacturers. Therefore, the risk assessment, which is a quantitative analysis, can be performed only for the active ingredients within the adulticides. This is a limitation of this analysis. However, the potential public health effects of the adulticide products as a whole (which include the inert ingredients) will be discussed qualitatively based on the information available in the literature regarding the general categories to which the inert ingredients belong.

In this analysis, the potential environmental health risk consequences from the proposed adulticide spraying are assessed based on the identification and examination of the potential health effects for each of the active ingredients in the New York State-approved adulticides included for study in the EIS and the potential exposure pathways. Because direct measurements of active ingredient concentrations for every adulticide following application are not available, the analysis relies on a range of estimates (i.e., concentrations and deposition levels from average to reasonable worst case conditions) provided by air dispersion and deposition modeling. Using air dispersion and deposition models for the active ingredients in the adulticide products, estimates of the resultant deposition and airborne concentrations and the potential for drift of insecticides from the proposed operations were developed. This information serves as the foundation for the public health risk assessment studies and the evaluation of alternatives.

**Epidemiologic and Attributable Risk Analyses**

**Epidemiologic Analysis**

To examine the possible impact of adulticiding on asthma exacerbations in New York City, the New York City Department of Health collaborated with the New York State Department of Health and the Centers for Disease Control and Prevention to develop analytic plans that would use existing data on emergency department/urgent care visits and hospitalizations and that would make best use of data available on adulticiding. The analyses were designed to determine whether the relative change in rates of asthma (i.e., emergency department/urgent care visits and hospitalizations for asthma) before (Pre-period) and after (Post-period) adulticiding occurred in 1999 was different from the change in the same time period in prior years, when no adulticiding occurred. While these analyses have been
designed to reduce some of the potential biases or confounding factors in the data, there are inherent limitations of the exposure and outcome data.

**Attributable Risk Analysis**

In addition to the epidemiologic analysis, an alternative approach was used to estimate the number of asthma hospitalizations that could potentially be attributed to adulticide application. This analysis made use of epidemiologic studies that report associations between changes in ambient air particulate concentrations and asthmatic events. In this approach, the number of asthma exacerbations that would be expected from the transient increment in airborne particulate concentrations caused by the spraying events are predicted.

Specifically, increases in asthma hospitalizations were predicted from increased concentrations of total particulate matter less than 10 microns in diameter (PM$_{10}$) resulting from both active and inert ingredients. The attributable risk calculation relied on conservative estimates (i.e., a worst case scenario) of population exposure to incremental PM$_{10}$ levels from the applied adulticides. That is, the assumptions that were made tended to overestimate the possible asthma impact of spraying events.

Based on the three analysis components mentioned above (Literature Review, Risk Assessment and Epidemiologic and Attributable Risk Analyses), estimating the potential for adverse impacts from the Proposed Action in the Representative Areas was examined.

**PUBLIC HEALTH CHARACTERISTICS OF PROPOSED ADULTICIDES – LITERATURE REVIEW**

A literature review of peer-reviewed medical and public health journals, toxicology literature, and other literature about public health issues related to spraying was conducted. The search was done in MedLine, NTIS, and ToxLine, and includes general literature for the major chemical groups of adulticides as well as the adulticide active ingredients, the inerts, and the synergist considered in this EIS. The most relevant findings of health effects that can be linked directly to exposure events to the active ingredients in the adulticides are described. For most of the conditions listed, more than 150 documents were reviewed. In addition, more than 250 documents were reviewed for possible evidence of hormonal effects (i.e., endocrine disruption) from adulticide exposure. The toxicological information discussed does not include data from suicides or willful exposure to large doses of pesticides.

**Skin and Eye Irritation**

**Review of Information**

Symptoms associated with skin and eye irritation include itching, redness, rashes and dryness. The organophosphate compounds as well as the pyrethroid compounds, particularly permethrin, have been found to cause both skin and eye irritation. The frequent occurrence of these skin and eye effects in the literature on permethrin may result in large part from its long history of effective use against insects, particularly head lice. The variation of the effect depends on the strength of the dose and the duration of the pyrethroid exposure.
**Organophosphates**

**Malathion**

**Evidence in Humans**

In an experimental study, malathion was found to cause a mild skin reaction (dosage not reported) in a high proportion of subjects (Gosselin, 1984). Following application of malathion to the skin, sweating and twitching in the area exposed may occur, usually within 15 minutes to four hours (Mackinson, 1981). Immediate reactions can also appear in people not previously reactive to malathion after sensitization has occurred following repeated exposures to other allergy-causing compounds. For example, thirty farmers with skin rashes were tested for skin reactions using distinct patches on the skin for each one of a series of locally used pesticides. Four farmers experienced skin reactions to malathion in particular, possibly as a result of prior sensitization to other pesticides. By contrast, farmers without skin rashes or prior exposures to malathion or other pesticides did not experience a skin reaction to malathion (Sharma and Kaur, 1990). This study suggests that skin exposure to malathion would have no effect for a population without preexisting skin rashes or sensitization to other organophosphates. At the same time, it suggests that malathion might cause a skin response in people who have – by whatever mechanism – previously been sensitized.

Eye irritation and visual effects are also occasionally seen after malathion exposure. In a human experiment in which four men were exposed for 1 hour daily, over 42 days, to 84.8 mg/m$^3$ (milligrams per cubic meter) malathion (which is approximately 1,485 times greater than the maximum predicted 1-hour airborne concentration calculated for this study), there was moderate irritation of the nose and eye membranes, but no other irritation signs or symptoms (Golz, 1959). Case studies have also documented suspected linkages between malathion spraying and visual impairment in children residing in an agricultural province of Japan where malathion was heavily and repeatedly used. Both symptoms and antidote treatments to restore proper vision are described by Ishikawa et al. (1993), but the omission of exposure concentrations in the report makes dose-response predictions based on these case reports impossible.

In 1976, skin and eye effects were found in case reports of malathion poisoning among pesticide applicators in Pakistan working in an anti-malaria campaign. The researchers noted that airborne malathion concentrations were very low (0.43 mg/m$^3$, less than the US standard for occupational standard of 15 mg/m$^3$), and they concluded that the poisoning cases were most likely resulting from direct skin contact with malathion. The authors of the report found that excessive skin contact associated with poor work practices (e.g., lack of protective clothing, inadequate training in pesticide mixing and application) was the primary path of exposure. Skin rashes and eye effects including constriction of pupils, aching in and behind the eyes, blurring of vision, and tearing were the most common, short-term indications of organophosphate poisoning caused by very high dose skin contact estimated to be 330 mg per 1.75 m$^2$ skin surface area, (i.e., roughly the equivalent of hands, forearms and lower legs) (Baker et al., 1978).

More recent data from the 1990's pesticide programs in California and Florida give conflicting reports on eye symptoms resulting from malathion exposure. Kahn et al. (1992), reviewed records of emergency department visits at a major hospital in Santa Clara, CA, and saw no significant increases in visits for dermatological or eye problems as a result of aerial spraying with malathion bait (a mixture of malathion and corn syrup for eradicating the Mediterranean fruit fly). Likewise, there was no increase in the prevalence of self-reported skin rash as a result of malathion spraying (Kahn et al., 1992). Of relevance to the proposed program, however, an emergency department at another hospital in Santa Clara reported 16 visits for skin or eye irritation associated with the same malathion-bait
spraying (USEPA, 1990). Similarly, in 1998, following the spraying in Florida, 23 cases of eye irritation were reported (CDC, 1999). Because these cases in both California and Florida were self-reported to local hospitals, they are unlikely to be fully representative of all possible skin and eye effects, as passive surveillance efforts are inherently limited by whether or not patients seek treatment. Differences in exposure levels may account for variations in reported effects within the California and Florida reports, but the reports do not include exposure data for comparison between the two states’ affected populations. In summary, the spraying of malathion in Florida and California has been associated with dozens of hospital visits for irritation of the eyes and skin. This is entirely consistent with what is known about the effects of malathion in other settings.

**Naled**

*Evidence in Humans*

Exposure of humans to naled has been associated with skin rashes, but not with eye effects or eye dysfunction (ACGIH, 1998). Naled poisonings have been diagnosed on the basis of burning rashes on the arms, face, neck, and abdomen (Edmundson and Davies, 1967). These effects were documented in one report detailing the symptoms of nine out of twelve women after working in a field that had been sprayed two hours beforehand with a mixture of pesticides, including naled. Four of these women were diagnosed with skin rashes developed from repeated exposure to pesticides. The results in three of the four patients gave strong evidence that naled had been the cause of the trouble (Hayes, 1982). Similar cases were found in tea growers who had developed rashes from repeated, prior exposures to pesticide mixtures including naled (Fujita, 1985). Direct irritation of the skin was also reported for an airplane pilot who was exposed to naled during loading and cleaning operations, through an unnoticed hole in his glove. Following loading and cleaning operations, naled was not washed off, and the exposed area became red with a burning sensation, and later became blistered (Mick et al., 1970).

**Pyrethroids**

Pyrethroids are associated with skin rashes and non-inflammatory irritation of the skin lasting up to 24 hours, and temporary numbness at very high concentrations. Pyrethroids appear to cause immediate irritation to the eye (NIOSH, 1997). Exposure to pyrethroids in the eyes may also result in blurred vision and damage to the cornea of the eye, which can vary in severity depending on exposure levels.

**Permethrin**

*Evidence in Humans*

In one study, people whose skin was exposed to permethrin, at 0.13 mg/cm², reported mild skin sensations lasting less than 24 hours (Flannigan and Tucker, 1985; Flannigan et al., 1985a,b). Another report following a skin application test found that 2 out of 17 volunteers developed mild rashes following a 9-day exposure to a 1 percent preparation of permethrin in paraffin (Pegam and Doughty, 1978, unpublished data cited in World Health Organization, 1990a). Mild and patchy rashes were also reported in 3 of 10 volunteers who were treated with a 1 percent preparation of permethrin for control of head lice (Farquar et al., 1981, unpublished data cited in WHO, 1990a). To systematically evaluate these findings with an experimental design, Kolmodin-Hedman et al. (1995) reported on 87 workers in a double-blind trial who were exposed to permethrin-treated botanical plants or untreated botanical plants in alternating weeks. The workers provided urine samples to be tested for traces of permethrin, and they also completed surveys describing their skin and eye symptoms. No correlations were evident linking any reported symptoms to contact with permethrin-treated plants. This was explained
by the workers’ proper use of protective clothing, which minimized the exposure levels to $1/1000^{th}$ of the exposure levels reported by Flannigan et al., in 1985.

Permethrin has been used in numerous commercial products for the control of mosquitoes and head lice with only limited reports of adverse side effects. For example, permethrin-impregnated uniforms, with concentrations ranging from 600 to 712 mg/m$^2$ of clothing, were issued to soldiers in Colombia to protect them from mosquitoes carrying malaria. (Soto et al., 1995) This study suggests that permethrin is relatively non-toxic in this form, as only 2 of the 229 soldiers reported mild skin irritation. In higher doses, and following direct application of permethrin to the skin, dermal effects are more common. Scalp and skin exposure to permethrin in shampoos and creams to combat head lice resulted in mild redness of the scalp (the U.S. National Library of Medicine’s Hazardous Substances Data Bank /WHO, 1990a). The temporary itching and mild redness was seen in only 1 percent of patients using a 1 percent permethrin shampoo. Furthermore, no adverse allergic reactions in the eyes and no neurological reactions were observed (Bowerman et al.). Another study found that none of the 230 in a group of volunteers using shampoos containing permethrin experienced a skin irritation reaction, which further suggests that permethrin is not expected to be harmful when used for treating lice (Lisi, 1992).

In the late 1980’s, a major public health study was undertaken to evaluate the safety of permethrin 1 percent cream rinse (commercially available as "Nix") for treatment of head lice. Thirty-seven local public health departments enrolled a total of 38,160 patients for 47,578 treatments with Nix from September 1, 1986, through January 31, 1988. Follow-up safety information was collected for 18,950 of these patients, between 7 and 14 days following treatment, via return visit or telephone contact. 103 adverse events were reported among the patients treated with permethrin. The rate of reported increased skin rashes and eye irritation was 2.2 per 1000 treatments among patients treated with permethrin. No serious, unexpected adverse events were detected in the 18,950 patients treated with permethrin. This study confirmed the safety profile of permethrin 1 percent in conditions of general use, as seen in clinical trials (Andrews et. al., 1992).

A smaller lice intervention study using permethrin also found mild itching as well as temporary burning or stinging of the skin in response to application of topical 5 percent permethrin-containing creams to treat scabies. (Schultz et al., 1990) As expected, these skin reactions were more common in patients with severe cases manifested by open sores, which are naturally more reactive to the ointment applications than unbroken skin. It should be noted that the cream contains higher concentrations than insecticidal shampoo and is not rinsed off (i.e., remains on the skin for a longer period of time).

Evidence in Animals

As in humans, skin redness was reported in rabbits exposed dermally to 0.13 mg/cm$^2$ permethrin (Flannigan et al., 1985a). However, skin irritation was not observed in two other studies with rabbits, using either a 25 percent preparation of permethrin or 100 percent permethrin (Metker et al., 1977, and Okuno et al., 1976, unpublished data cited in WHO, 1990a). Likewise, no skin irritation was observed in guinea pigs following a skin application of a 1 percent permethrin cream (Chesher and Malone, 1974, unpublished data cited in WHO, 1990a).

Reports of eye effects in animal testing of permethrin are also mixed. One study determined that redness, inflammation, and some tearing occurred in rabbits following application of undiluted permethrin to the eyes, whereas no eye irritation was observed in another study following a similar application (Okuno et al., 1976, and Parkinson et al., 1976, unpublished data cited in WHO, 1990a).
Animal studies regarding the skin and eye effects in animals directly exposed to permethrin are inconclusive.

**Resmethrin**

Symptoms associated with skin exposure to resmethrin were similar to those for permethrin exposure, and include itching, tingling, burning and numbness (Hartley and Kidd, 1987). No studies were located in the literature that reported whether exposure to resmethrin was associated with eye effects.

**Evidence in Humans**

There is limited evidence in humans of skin irritation from exposure to resmethrin. Only two people in a study of 230 volunteers experienced skin irritation reactions to resmethrin patch tests (Lisi, 1992). No other human studies of resmethrin exposure effects on the skin or eyes were found in the literature.

**Evidence in Animals**

There is limited evidence in rabbits of skin irritation from exposure to resmethrin. Skin irritation reactions were visible on rabbit ears following application of resmethrin for 72 hours (dose not specified) (Swentzel et. al., 1977, U.S. Army report cited in WHO, 1989). Although there were other animal studies of resmethrin exposure on the skin or eyes, these studies did not report adverse effects associated with resmethrin.

**Sumithrin**

Like other pyrethroids, there is limited evidence that exposure to sumithrin is associated with skin and eye effects. It should be noted that historically sumithrin has been the least frequently studied compound in the pyrethroid class. As a result, no animal evidence and only limited human evidence was available for the skin and eye effects of sumithrin.

**Evidence in Humans**

There is limited human evidence of skin or eye irritation caused by sumithrin. The only literature source available on this subject found no skin irritation among 8 volunteers treated with sumithrin doses between 0.44 – 0.67 mg/kg-day (milligrams per kilogram of body weight per day) for control of head lice (Hashimoto et al., 1981, as cited in WHO, 1990b). This limited evidence should not be interpreted as proof of safety.

**Evidence in Animals**

No animal studies of sumithrin exposure effects on the skin or eyes were found in the literature.

**Synergist**

No studies were located in the literature that reported whether exposure to PBO was associated with skin or eye effects in humans or animals.

**Inert Ingredients**

There is evidence that two of the inerts, aromatic petroleum solvent and mineral spirits, can cause skin and eye irritation in humans. However, based on the literature surveyed, it appears that skin irritation in humans is more common after direct contact with these compounds in the liquid form, and much less so if the exposure is to droplets or mists. Consequently, the literature suggests that concern for skin irritation would be greatest for pesticide applicators, due to improper handling, and would be much less for the general public following pesticide spraying. It should be noted, however,
that exposure to aerial or ground application of the adulticides with petroleum distillate inerts could result in direct deposition of droplets on skin or in the eyes. Therefore skin and eye effects must be considered to be plausible.

Evidence in Humans
The material safety data sheet (MSDS) for the aromatic petroleum solvent indicates that this chemical is slightly irritating to eyes, but does not cause eye injuries. The MSDS also indicates that skin irritation or dermatitis can result from frequent or prolonged contact with the aromatic petroleum solvent (Van Waters and Rogers, 1994).

According to Nethercott et al. (1980), severe skin irritation can occur when mineral spirits are applied directly to the skin (exposure concentrations not reported). Such effects are not expected following exposure to low concentrations of mineral spirits vapors. However, Carpenter et al. (1975) found that human volunteers exposed to mineral spirits vapors at a concentration of 2700 mg/m³ did cause eye irritation. Concentration of mineral spirits vapors expected due to spraying of adulticides to control mosquitoes are well below 2700 mg/m³. Carpenter et al. (1977a) reported that humans exposed to the aromatic petroleum solvent at either 190 or 410 mg/m³ for a period of 15 minutes noted irritation of the eyes, nose. At a lower concentration of 100 mg/m³, only one of six subjects reported mild nasal irritation, and no other effects were reported. The MSDS for mineral spirits states that they can cause eye irritation at vapor concentrations of at least 450 ppm (2362 mg/m³) (Mallinckrodt Baker, 1999), which is approximately 4,800 times greater than the maximum predicted 1-hour airborne concentration calculated in this EIS.

According to the MSDS for mineral oil, it is minimally irritating to the eye following direct contact, and is not expected to cause any skin irritation, even after prolonged direct contact (Penreco, 2000).

Evidence in Animals
The aromatic solvent can cause mild skin irritation in rabbits at doses greater than 8480 mg/kg (milligram solvent per kilogram animal weight) (RTECS, 1998). Carpenter et al. (1977a) observed both nasal and eye irritation following an eight-hour exposure to 8,700 mg/m³ (milligram solvent per cubic meter of air) of the aromatic solvent by rats.

Odorless mineral spirits were reported to be moderately irritating to rabbit eyes (RTECS, 2000).

The National Institute for Occupational Safety and Health (NIOSH) did not identify evidence of skin irritation in workers exposed to mineral oil mist at levels below 5 mg/m³ (ACGIH, 1998).

Summary/Conclusion
The most studied and tested compounds for skin and eye effects are malathion, naled, and permethrin, while less is known about the skin and eye effects of resmethrin and sumithrin. There was limited available information on the contribution of PBO to skin and eye irritation from the reviewed literature. Although there is some evidence that certain inerts can cause skin irritation in humans, skin irritation would more likely occur only after direct contact on the skin with liquid forms rather than from exposure associated with inert droplets and mists. Because all of the active adulticide ingredients have been linked to skin and eye irritation in humans, unnecessary exposure to workers and residents should be minimized to the greatest extent possible during the spraying intervals to reduce the potential for skin and eye effects.
Gastrointestinal

Review of Information

The intent of this section is to review the literature to determine possible gastrointestinal effects associated with exposure to the adulticides' active ingredients, synergist and the general categories of the inert ingredients.

Organophosphates

The literature suggests that gastrointestinal symptoms associated with exposure to low levels of organophosphates include loss of appetite, nausea, vomiting, abdominal pain, cramps and diarrhea. These effects are primarily associated with ingestion of organophosphates, but gastrointestinal effects can also be elicited from inhalation exposures to these chemicals.

Malathion

Evidence in Humans

A general description of the symptoms experienced within two hours after swallowing malathion includes loss of appetite, nausea, vomiting, abdominal cramps, and diarrhea (exposure concentrations not reported) (Mackison, 1981). A malathion impurity called isomalathion was linked to approximately 2,800 poisonings and five deaths after it was identified in improperly stored malathion (Aldridge et al. 1979). This occurred after over 7,500 sprayers were exposed to the isomalathion as part of a malaria eradication program in Pakistan in 1976.

Sixteen cases of nausea or vomiting, and 13 cases of abdominal pain or diarrhea, were reported at an emergency room in Santa Clara, CA, in association with aerial spraying of malathion bait for eradication of Mediterranean fruit flies (medflies) (USEPA, 1990). However, in another report of the Santa Clara spraying episode, the authors found no increase in the rate of self-reported upset stomach or nausea associated with the exposure to malathion (Kahn et al., 1992). Malathion sprayed to control medflies in Florida may have prompted 77 cases of gastrointestinal illness (CDC, 1999). Total malathion volume used during this spraying program in Florida was approximately 6,200 gallons between April and September (frequency of application not reported). The report suggests that approximately 132,000 persons resided in the areas treated with malathion. In a third study, malathion had been applied aerially in the San Francisco Bay Area to control an infestation by medflies (Thomas et al., 1992). The spray period under investigation occurred between July, 1981 and June, 1982; frequency of application and amount of malathion used were not reported. After adjusting for confounding variables (i.e., smoking, alcohol consumption, general fitness, age), gastrointestinal effects in 13 out of 7,450 pregnant women identified in the San Francisco Bay Area were shown to be significantly associated with second-trimester exposure to malathion. No formal relationship between the dose of malathion and gastrointestinal effects can be derived from this study.

Evidence in Animals

There are no documented incidents in the reviewed scientific literature of gastrointestinal effects in animals caused specifically by malathion.

Naled

Evidence in Humans

There were no documented incidents found in the scientific literature of gastrointestinal effects caused specifically by naled. However, short-term gastrointestinal effects are typical of many organophosphates – and this would be expected of naled as well. These short-term gastrointestinal...
Effects of organophosphates include abdominal cramps, nausea, vomiting and diarrhea, persisting for up to two days (ACGIH, 1998, WHO, 1986).

Evidence in Animals

Naled, which is used as a treatment for parasitic intestinal worms in dogs, can cause soft feces or diarrhea in dogs at doses greater than 35 mg/kg-day (Kobayashi et al., 1964). All dogs receiving naled treatment for intestinal parasites experienced this side effect.

Pyrethroids

There are no published examples of gastrointestinal effects in humans or animals caused by any of the pyrethroids discussed in the EIS.

Synergist

The reviewed scientific literature included no examples of or data about gastrointestinal effects in humans or animals caused by the synergist PBO.

Inert Ingredients

Only one report was found in the literature regarding gastrointestinal effects associated with exposure to inert ingredients.

Evidence in Humans

As reported by Haddad (1990, cited in NLM, 1996), gastrointestinal distress following ingestion of mineral spirits is generally mild and of short duration, and may include abdominal cramps, nausea, vomiting and diarrhea. It should be noted that mineral oil is often a major ingredient in laxatives.

Summary/Conclusion

From the data available, only the two organophosphate compounds, malathion and naled, appear to produce gastrointestinal symptoms. These effects occurred when people were exposed to levels far higher than would be expected from spraying in New York City. No reports were found linking either the pyrethroids, the synergist, or the inerts to these ailments.

Respiratory Effects Including Asthma

Review of Information

Asthma is a complex disease with multiple causes and substantial inter-individual variation in the severity of symptoms. Asthma is a chronic inflammatory disorder of the airways characterized by variable airflow obstruction and airway hyperresponsiveness in which prominent clinical manifestations include wheezing and shortness of breath (Sheffer et al., 1993). During an asthma “attack,” an individual experiences difficulty breathing which, if severe enough, and treatment is not rendered, may be fatal in rare instances (McFadden, 1998).

Although somewhat of a simplification, asthma can be categorized as having either an allergic or a non-allergic basis (Scadding, 1985; McFadden, 1987, Sears, 1997). Allergic asthma is usually associated with a family history of allergic disease, increased levels of certain immune system proteins, and/or positive responses to specific diagnostic tests. Although exercise, cold air, and respiratory infections may also exacerbate asthma for allergic asthmatics, allergen exposure may be most important for eliciting airway inflammation and hyper-responsiveness. About 75 percent of people suffering from asthma have allergic asthma (CDC, 1998). In contrast, people suffering from
non-allergic asthma, experience symptoms in their airways when confronted with such conditions as exercise, breathing cold air, or respiratory infections (McFadden, 1987).

Given concern that exposure to adulticides used for mosquito control could either aggravate pre-existing asthma or induce asthma in an individual with no prior history of the disease, and because urban populations, such as those in New York City are generally considered to have higher asthma rates than non-urban populations (Andrew et al., 2000), the potential for adulticide applications to precipitate onset of an exacerbation is examined in the following discussion. This discussion will include a review of the risk factors for asthma development and exacerbation; current prevalence, morbidity and mortality estimates of asthma; as well as an overview of the published scientific literature and product specific literature review, regarding the adulticides under consideration and their possible association with asthma onset and exacerbation.

Risk Factors for Development and Exacerbation of Asthma
Studies conducted to determine the etiology of asthma have linked several risk factors with the development of asthma. For instance, genetic susceptibility and family history may play a role in increased risk of development of asthma (Sears, 1997), as well as environmental factors such as in-utero exposure to maternal tobacco smoke (Gilliland et al., 2001). Other factors that have been implicated in increased risk of asthma development include low birth weight and preterm birth (Sears, 1997). Development of asthma is also linked to early exposure to allergens, such as house dust mites (microscopic organisms commonly found in the home) and tobacco smoke (Burney, 1992; Platts-Mills et al., 1997). However, though exposure to environmental tobacco smoke was strongly associated with asthma development in pre-school children, only one indoor exposure—dust mites—had “sufficient evidence of a causal relationship with asthma development” in these children (IOM, 2000). Other chemical and biological agents (e.g., respiratory infections and presence of cockroaches) had either a limited or suggestive evidence of an association with asthma development (IOM, 2000).

Estimates of Asthma Prevalence, Morbidity and Mortality

Prevalence of Asthma
In 1998, the CDC reported that the estimated self-reported prevalence among children was 7-10 percent among children (CDC, MMWR, 1998). According to the CDC report, over the last two decades the self-reported prevalence of asthma increased 75 percent among all persons of all ages and 160 percent in children 0-4 years of age. Another report estimated that asthma prevalence in Western countries doubled between 1977 and 1997 (Cookson & Moffat, 1997). Other parts of the world besides the West, have also reported an increase in asthma prevalence in urban areas. Though changes in infectious disease patterns (Cookson & Moffat, 1997), decreased physical activity, increasing prevalence of obesity (Platts-Mills, et al., 1999), and increased time spent indoors are hypothesized to be contributing factors to the increase in the prevalence of asthma, the subject is one of continuing research.

Asthma Morbidity and Mortality
While asthma morbidity and mortality rates have been rising throughout the United States over the last few decades (CDC, 1998), New York City has experienced a disproportionate increase. For instance, from 1982 to 1985, the number of deaths from asthma in New York City among individuals 5-34 years of age was three times the expected number of deaths based on national rates (Weiss et al., 1990).
In addition, asthma is the leading cause of hospitalization for children ages 0-14 and ranks among the leading causes of hospitalization for all age groups (NYCDOH, Stevenson et al., 1999). Between 1988 and 1997, the overall asthma hospitalization rate in New York City increased by 22 percent (Stevenson et al., 1999). This increase was most pronounced in children and in low-income populations (Stevenson et al., 1999). For example, the asthma hospitalization rate for preschool children from low income areas rose by 63 percent during the ten year period from 1988 to 1997 (Stevenson et al., 1999). In 1997, the hospitalization rate for asthma among children aged 0-4 was 16.0 per 1,000 children in NYC, compared to 6.1 per 1,000 in the United States, an almost three-fold difference (DHHS, Healthy People 2010, 2000). In 1998, however, asthma hospitalizations among children decreased approximately 27 percent in New York City compared with 1997 (NYCDOH).

Furthermore there are striking differences in the number of hospitalizations among New York City boroughs. Compared with the other boroughs, hospitalization and death rates are highest in the Bronx (Carr et al., 1992; de Palo et al., 1994). Neighborhood pockets of asthma are also apparent, with East Harlem reporting the highest rate of asthma hospitalizations—approximately 3,000 hospitalizations per 100,000 persons (Stevenson et al., 1999). The reasons for the borough and local disparities in asthma are not known, but may be due to differences in economic status and ethnicity; exposure to different asthma triggers; or access to medical care (Weiss et al., 1992; Platts-Mills et al., 1997).

**Mechanism of Adulticide Exposure in Asthma Exacerbations**

Adulticide exposure could lead to an asthma exacerbation through several possible mechanisms. Though some epidemiologic studies have found an association between 24 hour average PM$_{10}$ (particulate matter, less than 10 microns in diameter) levels and asthma hospitalizations and emergency department visits others have not. (Norris et al., 1999; Schwartz et al., 1993; Sheppard et al., 1999; Tolbert et al., 2000; Henry et al., 1991; Hiltermann et al., 1997; Roemer et al., 1998; Roemer et al., 1999; Roemer et al., 2000). However, since adulticide spray is an aerosol, a proportion of which contains PM10 (see Attributable Risk Analysis), it is conceivable that the increase in PM10 might result in asthma exacerbations through an irritant effect. Exposure to adulticide spray might also precipitate an asthma exacerbation through an allergic mechanism among persons sensitized to the active or inert ingredients contained in adulticides, through prior exposure to these ingredients in the home, garden or workplace. Finally, adulticide use could contribute to emergency room visits or hospitalizations through psychological mechanisms. For some individuals with asthma, anxiety may exacerbate their asthma or influence their reaction to asthma symptoms. Thus, it is possible that concern about spraying in a community, if it created anxiety in persons with asthma, could contribute to some asthma attacks that might not otherwise have occurred or increase the severity of asthma attacks that would have occurred without spraying.

**Potential Role of Adulticides on Asthma Prevalence in New York City**

**Overview**

A review of the literature was conducted on the potential associations between adulticides and the development or exacerbation of asthma. For instance, in Durban, South Africa, use of (unspecified) pump insecticides was significantly associated with a higher prevalence of “doctor-diagnosed” asthma among adults not children (Nriagu et al., 1999). In addition, in a study conducted with seven participants, Newton and Breslin (1983) reported asthmatic-type reactions in people with asthma after exposure to pyrethrins as well as an insecticide containing pyrethroids and PBO. This study also demonstrated that asthma reactions can occur within minutes following exposure to these insecticides. There have also been several reports of people developing asthma following either prolonged or short-term exposure to organophosphate insecticides. (Bryant, 1985; Deschamps et al., 1994;
Fatal asthma following exposure to shampoos containing pyrethrins has also been reported (Wagner, 2000; Wax and Hoffman, 1994). However, the levels of pesticides used in the scenarios described in these reports, appear to be greater than the exposure levels expected with the use of adulticides for mosquito control to the population in New York City. The reactions reported by Newton and Breslin (1983), following exposure to the pyrethroid, tetramethrin and the synergist, PBO, and to pyrethrins, occurred at exposure concentrations ranging from 1,100 to a maximum of 6,700 mg/m$^3$ for the total product (including active ingredients and inerts) (Newton and Breslin, 1983). The concentrations for the active and synergist ingredients were approximately 13.1 mg/m$^3$, which is several orders of magnitude above the concentrations to which people in New York City would be exposed due to adulticide spraying (see estimates of expected adulticide exposures under Risk Assessment section below). Vandenplas (2000) reported a 47 year-old man who developed a sensitivity to the pyrethroid tetramethrin, which manifested as asthma. This sensitivity occurred following 6 years of employment as an exterminator of indoor pests, thus entailing prolonged exposure to high levels of insecticides. This occupational exposure scenario greatly contrasts with any predicted exposures to the general population due to adulticide spraying for mosquito control. Such spraying for mosquito control, as demonstrated in this EIS, would more likely entail relatively short exposure to relatively low levels of insecticides. Nevertheless, it points out that there may exist in New York City a susceptible sub-population who might have a pre-existing sensitization due to prior exposures due to occupation (e.g., exterminators), hobbies (e.g., gardening) or exposure to home use insecticides.

Exposure to organophosphate insecticides, though not specifically malathion or naled, has also been implicated in the development of asthma. It should be noted that there is no evidence documenting that people have become sensitized to either malathion or naled, specifically. *Fenthion, dichlorvos and tetramethrin are active ingredients which are not considered within this EIS; however, dichlorvos is present as a breakdown product of naled.* Deschamps et al., (1994) reported on a patient who developed asthma after working for 8 hours in a room that had been treated on the previous day with a large amount of the organophosphate dichlorvos, diluted in the solvent xylene (exposure concentration not reported). This lengthy exposure time to active ingredients would be much greater than the expected maximum exposure times to active ingredients from spraying in New York City. Sensitivity to organophosphates has also been reported, in one case to fenthion, and in another instances to dichlorvos (Bryant et al., 1985). The exposure to fenthion occurred in a packing shed at a slaughterhouse, where animal skins were sprayed with fenthion. The exposure to dichlorvos was from a flea collar on a pet. Although the exposure levels of fenthion and dichlorvos described for these patients were considered low as reported by Bryant et al. (1985), these exposures were much more persistent and prolonged than exposure to the adulticides used for mosquito control in New York City would be.

In accord with the lack of evidence that people can become sensitized to malathion specifically, a surveillance of acute health effects following a 1981 application of malathion bait for medfly eradication in California indicated no increase in prevalence of symptoms associated with asthma (Kahn et al., 1992). However, this type of study may not identify persons having asthma exacerbations as a result of spraying possibly because they were not aware that they were exposed and thus might not have recognized asthma exacerbations as being related to spraying. Studies of pyrethroids also suggested either no change, or a decrease in asthma symptoms, among children living in homes treated with a pesticide that kills mites and ticks containing the pyrethroid esdepallethin, and the synergist PBO (Bahir et al., 1997; Geller Bernstein et al., 1995).
There have been two case reports, in patients with previously diagnosed asthma, of fatal asthma following exposure to shampoo containing the natural product pyrethrin. (Wagner, 2000; Wax and Hoffman, 1994). Although the synthetic pyrethroids that New York City is evaluating for the EIS are similar to pyrethrins, they differ fundamentally in that the pyrethroids, unlike pyrethrins, do not contain impurities from the chrysanthemum flower. These impurities, such as oleoresin, are potentially allergenic, and are thought to be responsible for inducing fatal asthma (Wagner, 2000).

Solvents
In addition to the active ingredients contained in the adulticides already discussed in this EIS, the adulticide products may contain solvents, which also have the potential to either induce or aggravate asthma. Antti-Poika et al. (1992) studied 31 pairs of identical twins including some twins with asthma who had varying solvent exposure because of their different occupational exposures. Each twin pair had one twin with asthma and one twin with out asthma. The authors found that solvent exposure was exclusive to the asthmatic twin in each of 31 pairs. The twin without asthma did not report a history of solvent exposure. Solvents were also reported as a risk factor for developing occupational asthma (asthma associated with a workplace exposure) in a study in Sweden (Toren et al., 1999). Another study indicated that paints that contain solvents are more likely than water-based paints with reduced concentrations of solvents to cause asthma-type symptoms such as wheezing and breathlessness in people with asthma (Beach et al., 1997).

As with the active ingredients in adulticide products, the likelihood that an exposure to solvents would either induce or aggravate asthma is related to the level of solvent concentration. Harving et al. (1991) reported slight effects on the volume of air that could be exhaled in people with asthma exposed to a solvent mixture at a concentration of 25 mg/m³, while no effects were observed at 2.5 mg/m³. Likewise, a 1–3 mg/m³ solvent concentration caused no asthmatic reactions in a study involving painters (Wieslander et al., 1997). In comparison, the maximum solvent concentration expected from exposure to adulticides during spraying operations is about 0.03 mg/m³, or 100-fold lower than these no-effect levels⁶ (see estimates of expected adulticide exposures under Risk Assessment section below). These expected levels of solvents are much lower than the solvent levels that caused the asthmatic reactions reported in the aforementioned studies. Therefore, exposure to the solvents in the mosquito-control program is not likely to either induce or aggravate asthma.

Occupational Exposure to Adulticides and Asthma
Exposure to adulticides is not commonly associated with occupational asthma. The literature suggests that the incidence of reported occupational asthma is relatively low among agriculture and horticultural workers as compared to workers in other industries such as wood, rubber and plastic (Burge, 1991).

Organophosphates
Acute poisonings by organophosphate insecticides have produced dramatic respiratory effects including emphysema (abnormal air spaces in the lung tissue), pulmonary edema (fluid in the lungs), pink froth in the throat, and considerable congestion in the lungs (Gallo and Lawryk, 1991). Although some respiratory effects were noted following exposure to the two organophosphate active ingredients evaluated in this EIS, the severe acute effects listed above were not reported in the reviewed literature for malathion and naled.

⁶This is based on the concentration expected for Anvil, which has the highest proportion of inert ingredients (80%), which include solvents as well as other compounds.
3.C: PUBLIC HEALTH

Malathion

Evidence in Humans

The literature describes contradictory observations for the respiratory health of humans exposed to malathion. In one study, prevalence of self-reported shortness of breath or difficulty breathing was not associated with aerial spraying of bait for controlling medfly populations in Santa Clara, CA. In this instance, neither the number of hospital emergency department visits nor the specific rate of emergency department visits for asthma increased following the spraying of malathion (Kahn et al., 1992). In contrast, 10 persons with difficulty in breathing were reported at another emergency department in Santa Clara, CA, in association with some malathion spraying (USEPA, 1990). In another report, the spraying of malathion in Florida to control medflies was associated with 87 self-reported cases of respiratory illness (CDC, 1999). No definitive relationship between the dose of malathion and respiratory effects can be derived from these studies.

Evidence in Animals

There are no examples of respiratory or asthma effects in animals caused specifically by malathion found in the scientific literature.

Naled

Evidence in Humans

The literature contains no examples of respiratory or asthma effects caused specifically by accidental exposure to naled. However, at high doses, naled is known to cause short-term respiratory effects, including symptoms of excess phlegm, coughing, and perspiration, persisting for up to two days. These effects are described as being typical of organophosphate adulticides (ACGIH, 1998).

Evidence in Animals

There are no examples of respiratory or asthma effects in animals caused specifically by naled found in the scientific literature.

Pyrethroids

Symptoms of short-term exposures to pyrethroid insecticides are described as stuffy, runny nose, and scratchy throat, with wheezing, sneezing, shortness of breath and feelings of chest tightening in hypersensitive individuals (Rumack, 2000). There are no reports of asthma caused by the pyrethroids considered for use in New York City. There are no data on respiratory effects from chronic exposures to pyrethroids.

Permethrin

Evidence in Humans

Based on the literature review, there is little information available on the respiratory health of humans exposed to permethrin. In a survey of 87 plant nursery workers exposed to permethrin, Kolmodin-Hedman et al. (1982) reported that approximately 20 percent of workers reported either irritation of the throat, or increased mucus production. No formal relationship between the dose of permethrin and respiratory effects can be derived from this preliminary data. There are no published data on asthma caused by permethrin.
Evidence in Animals
A controlled laboratory experiment using beagle dogs was conducted to evaluate the effects of permethrin on lung function. The authors found there were no lung effects in dogs following long-term exposure to permethrin at concentrations up to 500 mg/m³, 6 hours per day, 5 days per week, for 13 weeks (Metker, 1978, unpublished data cited in WHO, 1990a). This was the only study in the scientific literature that reported respiratory effects of permethrin in animals.

Resmethrin
Evidence in Humans
The literature review found no observations about the respiratory health of humans exposed to resmethrin.

Evidence in Animals
Only one study was located which investigated respiratory health or asthma effects in animals exposed to resmethrin. This study, Miyamoto (1976) found no adverse respiratory effects in animals exposed to resmethrin.

Sumithrin
Evidence in Humans
There are no examples or data within the scientific literature of respiratory or asthma effects caused by sumithrin.

Evidence in Animals
Only one study was located which investigated respiratory health or asthma effects in animals exposed to sumithrin. This study, Miyamoto (1976) found no adverse respiratory effects in animals exposed to sumithrin.

Synergist
Evidence in Humans
There are no examples or data in the scientific literature of respiratory or asthma effects in humans caused by the synergist PBO.

Evidence in Animals
There are no examples or data of respiratory or asthma effects in animals caused by the synergist PBO available within the literature.

Inert Ingredients
Evidence in Humans
Aromatic petroleum solvent can cause irritation of the respiratory tract at concentrations greater than 1000 ppm (4,340 mg/m³), according to the MSDS (Van Waters and Rogers, 1994).

The MSDS for mineral spirits states that inhalation of its vapors can cause irritation of the respiratory tract, causing symptoms such as coughing, difficulty breathing, and chest pain (Mallinckrodt Baker, Inc., 1999).
Summary/Conclusion
Based on this review of the available literature, the application of adulticides is not expected to appreciably increase the occurrence of asthma attacks or other respiratory health effects due to the very low exposure concentrations. However, as mentioned earlier, there may exist in New York City a susceptible sub-population who might have a pre-existing sensitization due to prior exposures due to occupation (e.g., exterminators), hobbies (e.g., gardening) or home use of insecticides.

Presented below are the results of a study performed to assess the possible impact of adulticide spraying on asthma public and private hospitalizations, public hospital emergency department and urgent care visits in 1999. Also to further characterize the potential impact of adulticide use on asthma hospitalization, an attributable risk analysis was performed to estimate the proportion of asthma hospitalizations that might be attributed to adulticide spraying in “Response to Spraying Programs: Recent Experience.”

Immunologic/Allergic
Review of Information
The immune system is comprised of specialized cells that circulate throughout the body to protect it from infections and disease. Specialized cells originating in the thymus and bone marrow coordinate to develop recognition, and subsequent attack of foreign agents such as bacteria. The lymph nodes and various lymph tissues in the body, work with the immune system cells to eliminate the recognized disease and other foreign agents. Immunological dysfunction occurs when the immune system is either over-reactive (i.e., hypersensitive, as in patients with auto-immune diseases such as lupus or multiple sclerosis) or under-reactive (i.e., immune-suppressed, as with AIDS patients). Certain chemicals in the environment may trigger responses in the immune system that are far less severe than the over- or under-reactive immune diseases, but that may affect the body's ability to fight infection or react to allergens. There are numerous ways to measure immunological effects, all addressing some aspect of the body's ability to mount a defense against foreign agents that the body considers undesirable.

The most accurate tests of immunological and allergic effects in humans involve extensive blood and tissue analysis in a laboratory setting. For this reason, there tend to be very few studies that test for these effects when other health effects are more immediately visible and easily measured. Within human populations in particular, determining toxicity to the immune system is extremely difficult because it is not necessarily visibly manifest. For instance, it is very difficult to directly measure toxicity to the immune system, as evidenced by a rise in the rate of illness for a given population or community, because there are too many confounding factors that determine illness rates, including human variability in immune response. The most common indicator of immune system toxicity is an unusual rise in the frequency of allergic reaction, which is one type of immune response. Such a reaction could be associated with exposure to a substance that affects the immune system. Skin patch tests can also be used to determine if a particular individual has an allergic response to a specific chemical.

Organophosphates
A review by Zackov (1983) states that "most . . . organophosphorus pesticides elicit autoimmune reactions and suppress the production of antibodies against vaccines." However, Zackov did not indicate what doses or which specific organophosphates cause these effects. Therefore, it is not clear whether the reduced antibody production is due to an impaired immune system, or whether it results from a whole body toxic response (Zackov, 1983, cited in WHO, 1986).
Malathion

Evidence in Humans

Malathion exposure during the efforts in California to control the Mediterranean fruit fly population did not generate much evidence linking malathion to immunological or allergic effects. Kahn, et al., in 1992 reported that emergency room visits for allergic problems did not increase at the major hospital they studied in Santa Clara, CA. Furthermore, Schanker et al. (1992) studied ten people referred by local health departments for skin-related problems during the same malathion exposures in Southern California. These 10 had suspected allergic reactions to malathion and were referred out of a total of 298 people reporting general skin-related problems after malathion exposure. Because only one of these 10 in fact had an allergic reaction to malathion, it appears that allergic reactions to malathion are not very common. No other reports on malathion causing immune or allergic effects in humans were found.

Evidence in Animals

Rodgers et al. (1986a,b) are the only team of scientists found in the search of the scientific literature who have published animal studies of malathion's effects on the immune system. Their studies provide mixed results on malathion's toxicity to the various components of the immune systems. First, in mice exposed for 14 days to 143 mg/kg-day (milligram per kilogram of body weight per day) of malathion, they found decreased numbers of cells in the thymus, which suggested a decreased immune capacity. Second, in mice exposed for 5 days to 715 mg/kg-day of malathion they found an increased immune system response, which suggests a possible allergic, or over-immune reaction (Rodgers et al., 1986a). They conclude that malathion did not have an overall immune compromising effect on mice but that the immune system reduction effects are caused by malathion contaminants, such as O,O,S-trimethyl phosphorothioate, rather than malathion itself by suppressing the formation and response of antibodies (Rodgers et al., 1986b).

Additional 1997 findings demonstrated the link between malathion and immune response in rats and mice following acute oral and dermal contact with malathion (Rodgers and Xiong, 1997). In this acute exposure test, serum histamine levels indicating an allergic response were seen within four hours following doses that ranged from 10 mg/kg to 700 mg/kg. No effect levels were seen at doses of 0.1 mg/kg and 2 mg/kg for oral and dermal exposure routes, respectively.

Naled

The literature review found no observations of either immune or allergic reactions in humans or animals exposed to naled.

Pyrethroids

Some studies have suggested that pyrethroids may cause increased incidence of allergic response and hypersensitivity (Diel et al., 1999). However, Klaassen (1996) suggest that synthetic pyrethroids are less likely to cause respiratory allergic reactions than adulticides derived from natural pyrethrum. This is because people sensitive to ragweed pollen are also particularly prone to allergic reactions to the natural pyrethrum, which contains irritants that are missing from the synthetic form. Therefore, synthetic pyrethroids should be less likely to cause allergic reactions than are the preparations made from pyrethrum powder.

Regarding immune response, researchers have not observed an increased incidence of infections in laboratory animals during any of the long-term exposure studies of pyrethroids. The absence of
immune responses, even at high pyrethroid dose levels, suggests that pyrethroids likely do not cause immune system malfunction (Ray, 1991).

**Permethrin**

*Evidence in Humans*

Permethrin has been documented to cause only minor skin reddening as its only allergic effect. Abnormally red skin conditions were seen in two out of 17 volunteers following a 9-day exposure to a 1 percent preparation of permethrin in a skin allergy test (Pegum and Doughty, 1978, as cited in WHO, 1990a). Similar allergy-induced skin redness was also reported in 3 of 10 volunteers who were treated with a 1 percent preparation of permethrin for control of head lice (Farquhar et al., 1981, as cited in WHO, 1990a). More extensive discussion of other, non-allergic skin effects is found in the earlier section on skin and eye irritation.

*Evidence in Animals*

Permethrin did not cause any allergic reactions in a study involving an injection of a 0.1 percent solution of permethrin to guinea pigs (Metker et al., 1977; Metker, 1978, unpublished data cited in WHO, 1990a). Another animal study for harmful effects on the immune system from permethrin exposure found mixed results, with possible effects on the immune-system antibodies in mice (Stelzer and Gordon, 1984).

**Resmethrin**

*Evidence in Humans*

The literature review found no observations of either immune or allergic reactions in humans exposed to resmethrin.

*Evidence in Animals*

Resmethrin does not appear to cause allergic reactions in rabbits (Swentzel et al., 1977, U.S. Army Report cited in WHO, 1989). However, in other studies, resmethrin did cause a fast and higher than normal immune response in animals (animal species not specified) (Danliker et al., 1979, cited in WHO, 1989).

**Sumithrin**

The literature review found no observations of either immune or allergic reactions in humans or animals exposed to sumithrin.

**Synergist**

The literature review found no observations of either immune or allergic reactions in humans or animals exposed to the synergist, PBO.

**Inert Ingredients**

No information was found regarding immunological or allergic effects in relation to exposure to any of the inert ingredients.

**Summary/Conclusion**

Allergic reactions beyond irritation reactions have not been found to be commonly caused by any of the active ingredients reviewed in this report. The immune system-enhancing or -reducing health effects of the active ingredients are still poorly understood at this time. Malathion's mixed effects on
the immune system are thought to be caused by a common contaminant in malathion mixtures, generally associated with storage of malathion. Similarly, the data on permethrin and resmethrin are also inconclusive as to what effects, if any, they have on the immune system and illness rates in humans or animals. At this time it is not possible to conclude with certainty what impact, if any, the adulticides might have on the immune system.

**Multiple Chemical Sensitivity**

*Review of Information*

Multiple chemical sensitivity, or MCS, is generally considered to have many causes. It is considered to be an environmental illness causing fatigue, irritability, behavior problems, depression, confusion, and nervous tension. The scientific community remains divided as to whether psychological, toxicological, or some combination of both processes creates susceptibility to MCS. In their literature review published by the National Institutes of Health, Fiedler and Kipen (1997) write, “A growing debate has risen between those who regard chemical sensitivity as a disorder mediated by psychiatric factors in a manner similar to conditioned responses and those who see it as a genuine physical susceptibility to low-dose exposures presumed safe.”

Patients with MCS report a variety of chemical exposures, and many patients have medical histories that include asthma and nervous system symptoms such as depression. However, to date scientists have not been able to quantifiably link symptoms to specific levels of chemical exposures in a laboratory or field setting. This is largely due to a multitude of chemical exposures that can apparently trigger the hypersensitivity reactions of those suffering from MCS. Examples of exposure events that might cause hyper-sensitivity reactions include (but are not limited to): smelling perfumes and paints; exposure to new carpets, pressboard and plastic/vinyl furniture, natural gas used in stoves, cigarette smoke; consuming foods where agricultural adulticides are used; drinking chlorinated tap water; and wearing recently dry-cleaned clothing (Ziem and McTamney, 1997). Although MCS patients often report a link between their illness and common chemical exposures, including certain adulticides, the evidence to date is only from self-reports. Studies of particular compounds in the sprays that may worsen or cause MCS symptoms have not been performed or found in the reviewed scientific literature. Links, if any, between MCS and the active ingredients evaluated in this EIS, can only be determined through actual controlled clinical trials in humans, which currently do not exist in the literature reviewed.

**Organophosphates**

There are no animal or human examples or data of MCS caused by exposure to organophosphates (including malathion and naled) in the literature reviewed for this EIS.

**Pyrethroids**

*Permethrin, Resmethrin and Sumithrin*

There are no animal or human examples or data of MCS caused by exposure to pyrethroids (including permethrin, resmethrin, and sumithrin) in the literature reviewed for this EIS.

**Synergist**

There are no animal or human examples or data of MCS caused by exposures to synergists (including PBO) in the literature reviewed for this EIS.
Inert Ingredients
Ziem and McTamney (1997) report that numerous ingredient in products can potentially be associated or suspected of causing the onset of MCS and include, gasoline, kerosene, pesticides, solvents, new carpet, formaldehyde, carpet shampoo, adhesives/glues, fabric softener, cleaning products, and medications. Based on the list of products provided by Ziem and McTamney and self-reported MCS effects by 68 human test subjects, it is possible that certain ingredients in the listed products may also be present as inert ingredients in the adulticides. However, inert information was not available for the adulticides, therefore a causal association between inert ingredients in the adulticides and the incidence of MCS cannot be determined at this time.

Summary/Conclusion
There are conflicting reports found in the peer-reviewed scientific literature on possible links between the active ingredients and the synergist and MCS. One report provides a list of substances that may contain certain ingredients that are possibly in the adulticide products that can be suspected of causing the onset of MCS. Although people with MCS often do report a link between their illness and exposure to pesticides, to date no scientific studies in the available literature reviewed have definitively linked pesticide exposure with MCS. The controversy surrounding the cause of MCS may encourage researchers to explore more aggressively the causal links between the onset of the illness or development of symptoms and environmental factors. However, without a scientific consensus on the processes that create susceptibility to MCS, it is not possible to evaluate the role that adulticides or their chemical constituents might play in MCS reactions.

Neurological
Review of Information
Neurological effects (i.e., effects on the nervous system) in humans exposed to adulticides may be caused through either of two main pathways, both of which involve nerve cells. Nerve cells have the ability to generate electric signals and the ability to propagate these signals rapidly from one area of the body to another. The electric signal may initiate new electric signals in other nerve cells – a process where one nerve is essentially talking to another nerve. The cell-to-cell communication occurs by the action of chemical signals released from one nerve cell and received by the next nerve cell, enabling the electrical signal to be propagated. Nerve cells can also communicate with muscle cells in much the same way, via release of chemical signals that cause them to contract. In order to have normal nerve cell functioning, the chemical signal must be removed, by either being broken down by an enzyme, or re-sequestered by the nerve cell sending the signal, after the signal has been communicated between cells. The signaling is caused by chemicals called neurotransmitters. Acetylcholine is one such neurotransmitter, which is broken down by the enzyme acetylcholinesterase. Both are essential for normal functioning of the nervous system because they allow for clear communication between nerve cells themselves, or between the nerve cells and other body cells, such as muscles. Organophosphates, such as malathion and naled, interfere with proper function of the nervous system—particularly in insects—by reducing the action of the acetylcholinesterase enzyme; this causes a build-up of acetylcholine. The accumulation of this neurotransmitter prevents the effective transmission of nerve impulses from one nerve cell to the next, and from nerve cells muscles. As mentioned above, information is also relayed along the length of a nerve cell by a change in electrical charge on either side of the cell membrane. This change in electrical charge occurs via special channels in the cell membrane, which allow very small charged chemicals such as sodium, a component of table salt, to pass through the cell membrane. Some of the active ingredients, such as the pyrethroids discussed in this EIS, interfere with the proper functioning
of these special channels, thereby disrupting the relay of information along the length of the nerve cell. Effects of active ingredients on either neurotransmitters or membrane channels may produce harmful effects, including nervousness, shaking, convulsions, memory loss, fatigue, and other general central nervous system effects, including severe cognitive effects.

**Organophosphates**

As discussed above, exposure to organophosphate insecticides can result in the accumulation of acetylcholine, the chemical responsible for relaying information between nerve cells and between nerve cells and muscle cells. The impairment of nervous system function, which occurs due to the build-up of acetylcholine at nerve junctions, occurs very soon following exposure, and results from short-duration, or acute, exposure events. In other cases, there is a delay between the initial exposure to organophosphates, and the occurrence of readily observable neurological effects. In still other cases, neurological effects can remain dormant for years before appearing. All three types are discussed below, starting with the immediate and ending with the more rare dormant effects.

Immediate effects of organophosphate exposure on the human nervous system are extremely diverse as they can affect mental functioning, muscle control, and vision. The dose received in the exposure event typically determines the severity and duration of any adverse effects. Blurred vision and more serious visual effects have been reported in a few cases at higher exposure levels (Metcalf and Holmes, 1969). At sufficient doses of organophosphates, the accumulation of acetylcholine in the central nervous system can result in tension, anxiety, headache, giddiness, restlessness, nervousness, tremor, weakness, emotional instability, apathy, confusion, depression of breathing rate and heart beat, and convulsions (Gallo and Lawryl, 1991; Murphy, 1986). Other short-term neurological effects that have been noted following exposure to organophosphates include alterations in brainwave patterns, insomnia, excessive dreaming and nightmares (Metcalf and Holmes, 1969; Murphy, 1986).

For some organophosphates there is a delay between exposure, and the occurrence of readily observable symptoms. This delay, which is referred to as delayed neuropathy, can be as long as 4 weeks after the initial exposure to high concentrations. Initial symptoms primarily affect the legs, and include tingling and burning sensations, which can progress to weakness and the inability to coordinate voluntary muscular movements. Adults are more susceptible to developing delayed neuropathy than children. Currently, there are no reports of either malathion or naled causing delayed neuropathy in humans. Rather, other organophosphates have been associated with delayed neuropathy. Because of the low levels of exposure, the literature suggests that delayed nerve damage would not be expected to occur due to exposure to organophosphates following spray operations.

Long-term neurological effects of organophosphate pesticide poisoning that may go unnoticed until years after exposure were demonstrated in a survey of 100 “matched pairs.” One hundred individuals who had been exposed to organophosphates were compared with a control group of 100 individuals of similar age and racial, economic and educational backgrounds who had not been exposed (Savage, 1988). The authors calculated that a statistically significant number of individuals in the exposed group displayed abnormalities on measures of memory, mood, motor reflexes, intellectual functioning, academic skills, abstract thinking, flexibility of thinking, and simple motor skills. However, this study of exposure to high doses of organophosphates is of limited use in a risk assessment of exposure to organophosphates that is infrequent and at a dose level that the literature considers low, as would be the case for spraying of adulticides.
Malathion

Evidence in Humans

Central nervous system effects of malathion may include anxiety, restlessness, headache, and in more serious cases, tremors, confusion, drowsiness, slurred speech, coma, loss of reflexes, and convulsions (NIOSH, 1976). There are reports of nervous-system effects in humans following short-term, non-environmental long-term, and long-term environmental exposures to malathion.

There are two reported cases of neurological effects due to short-term exposures to malathion. The first report describes deliberate organophosphate poisonings with a commercial preparation of malathion in which the action on acetylcholine was followed by neurological manifestations (Dive et al., 1994). The authors hypothesize that more toxic malathion derivatives (including isopropylmalathion and O,O,S-trimethylphosphate) were formed after the preparation had been stored for a long period of time. The second report describes an accidental poisoning by food contaminated with malathion (Chaudhry, et al., 1998). Sixty men had consumed food prepared at a community kitchen that had been sprayed earlier that day with malathion. All of the men became temporarily ill with tremors and headache, and no other explanation for their symptoms was found. Chaudhry, et al. (1998) suggest that the neurological symptoms associated with this form of organophosphate poisoning can be differentiated from symptoms caused by other forms of poisoning.

Based on the literature review, two reports of chronic, long-term, exposure to malathion discuss different neurological effects. In the first report, exposure to malathion is suspected to have had a contributing role in the behavioral dysfunction of grain storage workers. These workers were also exposed to carbon disulfide, a substance known to be neurotoxic. Clinical signs from the occupational exposure to both of these fumigants included loss of consciousness and rigidity of muscles, tremors, loss of sensation in the limbs, loss of voluntary motor function, and transient cessation of respiration during sleep (Peters, 1982). In this case, exposure durations were estimated to range from 8 hours to 17 years, although the amount of exposure was not directly quantified in the study. Another study of chronic exposure to malathion indicated that clinical neurological effects include degeneration of the nerves connected to the eye. The study showed mainly nerve-eye impairments such as nerve degeneration, degeneration of the retina of the eye, the inability of an eye to follow an object smoothly from top to bottom, myopia, spasms, and mild general neurological impairments of the eyes. These symptoms were more severe among children than adults, who were exposed mainly to 3 percent malathion sprayed by helicopters multiple times each year over the course of three to five years (Ishikawa, 1993).

Three contradictory reports of chronic environmental exposure relate to aerial spraying with malathion bait to control the Medfly population. Kahn et al. (1992) conclude that the rate of self-reported nerve problems (including headache, blurred vision, tingling of extremities, irritability, forgetfulness, inability to concentrate, and dizziness) in a hospital emergency department did not increase as a result of aerial spraying with malathion in Santa Clara, CA. In contrast, there were 11 cases of headache, and 6 cases of dizziness recorded at another emergency department, that were thought to be associated with malathion spraying (USEPA, 1990). Malathion sprayed for medflies in Florida was associated with 74 self-reported cases of problems related to the nervous system (CDC, 1999). Unfortunately, there were no direct estimates of exposure for either the self-reported neurological problems or the emergency department visits. Therefore it is difficult to determine relevant exposure levels that would be likely to cause such effects. It should also be noted that the malathion-bait mixture is a different preparation than that used for adult mosquito control; the malathion-bait mixture remains for longer periods of time in the environment.
Evidence in Animals

There is one report of neurological effects in animals following various exposures to malathion. Dose-dependent changes in electroencephalogram and electromyogram patterns were observed in rats treated with malathion for 90 days at either 38 mg/kg-day or 75 mg/kg-day (Desi et al., 1975, 1976). However, the authors do not discuss the biological significance of these effects, either in rats or extrapolated to humans. These doses are significantly higher than those to which people would be exposed during adulticide spraying.

In another study which investigated the effects of organophosphate exposures (not defined) in the neonate mouse (10 days after birth), the authors suggested that irreversible changes occurred in the adult brain function in the mouse (Eriksson, 1997). The same exposures had no permanent effect when administered to the adult animal. The author suggested that neonatal exposure to a low dose can potentially lead to an increased susceptibility in adults to an agent having similar neurotoxic action, resulting in additional behavioral disturbances and learning disabilities.

In a recent USEPA review of malathion’s neurotoxicity, delayed responses were not observed in any studies of rats, and only in acute (short-term exposure) studies of hens (EPA HIARC, 1998b).

Naled

Short-term neurological effects of naled are typical of organophosphate adulticides. Effects such as abdominal cramps, nausea, cough, and excess perspiration persist for about two days; while anxiety, depression, vertigo, and rapid involuntary eye movement can persist for up to 4 months (ACGIH, 1998). Marked transient neurological effects such as convulsions, tremors, and muscle weakness are observed in rats following a single dose of 100 mg/kg. Effects are much less severe and observed in only a few animals at 25 mg/kg. There were no treatment-related effects within 7 days following treatment (USEPA, 1995). There are no reports of anecdotal or directly tested neurological effects in humans or animals following chronic exposures to naled.

Pyrethroids

As mentioned earlier, pyrethroids work by preventing cells from building up opposing electrical charges on either side of the cell membrane in order to terminate the transmission of a nerve impulse. The effects associated with pyrethroid exposures causes repetitive signal transmission along a nerve. Typical neurologic effects for pyrethroids include tremors, lack of coordination, hyperactivity, extreme mental or emotional depression, and paralysis (Ray, 1991). Pyrethroids alter the way information is relayed by changing the electrical charge on either side of the cell membrane. If these changes in electrical charges along the length of a nerve cell are altered, the cell will relay information poorly along the nerve, as well as between nerve cells.

Permethrin

Human Studies

Several studies describe a general lack of adverse effects to low doses of permethrin in humans. None of the patients using a 1 percent permethrin shampoo reported adverse effects to the central nervous system (Bowerman et al., 1987). Permethrin, when applied once at bedtime to treat scabies, was also shown to not have significant health impacts for patients suffering from pre-existing seizures and neurological complications (Haustein and Hlawa, 1989).

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6 Electroencephalogram – a recording from the scalp of brain electrical activity.
7 Electromyogram – a recording of electrical activity associated with functioning skeletal muscle used to diagnose neuromuscular disorders.
After dermal exposures, skin irritation was the most prevalent health effect, with no nervous-system effects appearing below the threshold dose of about 0.01 mg/cm² (0.01 milligrams per square centimeter) (Flannigan and Tucker, 1985b). Flannigan and Tucker report that above the lowest dose for permethrin that causes noticeable effects, irritant symptoms can progress into partial numbness in the body lasting from half an hour to a full day.

**Animal Studies**

Several studies in rats showed neurological effects resulting from oral exposure to high levels of permethrin. Short-term exposure in rats has been reported to cause aggressive fighting as well as agitated behavior; fine to whole-body tremors, including shaking of the head and forelimbs; decreased motor activity and grip strength; and increased resistance to capture and increased reactions to short sounds such as a bell’s ring (McDaniel and Moser, 1993). In another study, muscle tremors were noted for rats exposed to permethrin for 14 days at 432 mg/kg-day, but not at 216 mg/kg-day (Metker, 1977, unpublished data cited in WHO, 1990a). Likewise, exposure for 90 days at 500mg/kg-day caused tremors, which mainly subsided after the first week of treatment (Killeen and Rapp, 1976, unpublished data cited in WHO, 1990a). In another study, hyperexcitability was observed in rats exposed over 4 weeks to 1,000 mg/kg-day, but not at 500 mg/kg-day (Clapp, 1977, unpublished data cited in WHO, 1990a). And finally, in a 6-month dietary study, signs of hyperexcitability and tremors were only observed at 3,000 mg/kg-day, but not at 1,500 mg/kg-day (Kadota et al., 1975, unpublished data cited in WHO, 1990a). Agitation, tremors, and hyperexcitability in rats are therefore shown to clearly be associated with oral exposure to high levels of permethrin. These effects occurred at doses much higher than would be expected for humans exposed to permethrin during spraying of adulticides.

A more recent study of low dose administration of permethrin via a dermal dose of 0.13 mg/kg/day to rats produced some changes in the brain chemistry of rats. However, the dose did not produce behavioral effects in the rats until it was combined with other pesticides that are not included in adulticide formulations (Abou-Donia et al., 2001).

**Resmethrin**

**Human Studies**

There are no reports of neurological effects in humans following exposure to resmethrin.

**Animal Studies**

There are two studies that evaluated the nervous-system effects in rats following various exposures to resmethrin. According to several studies in the scientific literature, resmethrin did not have adverse effects on the nervous systems of laboratory animals when given to rats at 1,250 mg/kg-day for 32 weeks (Cox et al., 1979, and Schwartz et al., 1979; and unpublished data cited in WHO, 1989). Similarly, rats given smaller doses of 62.5 mg/kg-day for 32-weeks, 250 mg/kg-day for 20 days, or 632 mg/kg-day for 7 days also maintained healthy nervous system functioning (USEPA, 1983). Thus, these reports confirm the absence of neurological effects in rats exposed to relatively high levels of resmethrin.

**Sumithrin**

**Human Studies**

There are no examples or data of neurological effects in humans caused by sumithrin within the literature reviewed.
Animal Studies
There are three reports confirming the absence of neurological effects in rats following various high exposures to sumithrin. The literature suggests that sumithrin has low short-term toxicity, and sumithrin was not observed to produce tremors or more complex neurological symptoms, even at doses greater than 600 mg/kg-day when injected intravenously (WHO, 1990b). There were no signs of leg weakness or the inability to coordinate voluntary muscular movements in rats exposed to 5,000 mg/kg-day of sumithrin, for 5 days (Okuno et al., 1978, unpublished report cited in WHO, 1990b). Likewise, neurotoxic effects were not observed following a 4-hour inhalation exposure to 3,760 mg/m$^3$ (Kohda et al., 1977, unpublished data cited in WHO, 1990b). All three reports confirm the absence of neurological effects in rats exposed to relatively high levels of sumithrin.

Synergist
There are no examples or data of neurological effects in humans or animals caused by the synergist PBO available within the literature.

Inert Ingredients
Based on a review of the literature regarding neurological effects of the inert ingredients in humans and animals, it appears that these effects are likely to occur only at concentrations that are much, much greater than concentrations that the general public would be exposed to following spraying of adulticides for controlling mosquitoes.

Evidence in Humans
White et al. (1994), noted mild, transitory behavioral effects in automotive factory workers exposed to mineral spirits at vapor concentrations greater than 90 ppm (472 mg/m$^3$). There were no effects on other behavioral and psychological endpoints, such as mood states, delayed recognition, visual reproduction, pattern memory, vocabulary, and a card-sorting test.

Exposure to high vapor concentrations of mineral spirits can cause neurological effects such as headache, dizziness and nausea (Sullivan and Krieger, 1992, as cited in NLM, 1996). Other neurological effects, such as loss of appetite, muscle weakness, and impaired motor activity, have been reported in workers exposed to petroleum ethers for prolonged periods of time, indoors in areas with poor ventilation (Cavender, 1994).

Evidence in Animals
Aromatic solvent causes a general slowing of activity levels and changes in motor activity in laboratory animals following skin exposures at doses greater than 2 ml/kg (8,480 mg/kg) (RTECS, 1998). In adult rats exposed to 1,500 ppm (6,510 mg/m$^3$) for 90 days, there was no evidence of neurotoxicity or neuropathology (damage to nerves) (Douglas et al., 1993). A depression in the function and activity of the central nervous system in cats was observed by Carpenter et al. (1977a), following an 8-hour exposure to 8.7 mg/l (8,700 mg/m$^3$) of aromatic solvent. In another study with rats, Carpenter et al. (1977b) observed salivation, progressive loss of coordination, and mild tremors in rats exposed to the 4.5 mg/l of aromatic solvent for 6 hours/day, 5 days/week, for 9 weeks. No such treatment-related effects were observed at concentrations at or below 2.2 mg/l.

Mineral spirits also cause a general slowing of activity levels in rats at oral doses greater than 5 g/kg, and inhalation doses greater than 5,500 mg/m$^3$ (RTECS, 2000).
Summary/Conclusion

The current peer-reviewed scientific literature indicates that exposure to some of the active ingredients of adulticides, as well as some of the inerts, is associated with neurological effects in humans and animals. The symptoms and durations of these effects vary widely, and may be caused by multiple biological mechanisms. It is noteworthy that malathion breakdown products more toxic than malathion itself can be formed after the preparation has been stored for a long period of time. Many of these studies demonstrate effects elicited under short-term, high-level exposure to the active and inert ingredients in adulticides. Examples of exposures that are more representative of the spraying of adulticides in New York City indicate that neurological effects would be either mild or completely absent in both humans and animals. For instance, some studies report that long-term, low-level exposure to organophosphates is generally thought to result in short-term effects on cognitive function, and neurological components of the eye. However, other studies of humans exposed to malathion are either complicated by simultaneous exposure to other chemicals, or present contradictory evidence of nervous-system effects in humans. The literature as cited in this section suggests that other adulticide ingredients such as permethrin are regarded as having negligible health effects at low levels of exposure, while available data on resmethrin and sumithrin show no neurological damage even at high levels of exposure.

Cognitive Developmental Disabilities Including Autism

Review of Information

Autism is a rare learning/behavioral disability affecting children. Many researchers suggest that a combination of genetic and environmental factors may play a role in this developmental disorder. Autism researchers estimate that 3 to 4 genes may play a role in autistic development observed in children, though other factors may amplify the genetic predisposition (Hollander, 1999). Broad population-based studies of disease incidence in identical twins reveal that autism has a 90 percent concordance rate (meaning that it occurs in both twins), while non-identical twins have only a 10-30 percent concordance rate (Goldman and Koduru, 2000). The role of environmental exposures is purely speculative at this time as no data exists supporting a linkage between exposure and autism. There are no reports of autism and learning disabilities in humans following exposures to any of the adulticides considered in the EIS. While NYCDOH has received reports of behavioral modification in autistic children following adulticide application, there were no published studies in the literature searched.

Organophosphates

No reports were found in the scientific literature of autism and learning disabilities in humans following exposures to either malathion or naled.

Pyrethroids

No reports were found in the scientific literature of autism and learning disabilities in humans following exposures to pyrethroids.

Synergist

No reports were found in the scientific literature of autism and learning disabilities in humans following exposures to the synergist PBO.
Inert Ingredients
No reports were found in the scientific literature of cognitive developmental disabilities in relation to exposure to any of the inert ingredients.

Summary/Conclusion
In general, the causes of learning disabilities ranging from autism to mild retardation are not well understood, and possible environmental causes of these developmental disorders are uncertain at this time. Many researchers and environmental health specialists agree that more neurologic and developmental toxicity research is needed on environmental contaminants, including pesticides. For example, age-dependent sensitivity and developmental periods of susceptibility need to be examined in pesticide developmental toxicity evaluations at all stages of development (Bruckner, 2000; Claudio et al., 1999). However, based on published studies, it is unlikely that pesticide exposures could be deemed responsible for either causing or exacerbating these conditions.

Endocrine Disruption
Review of Information
Certain chemicals in the environment may be acting as mimics of natural human hormones. Normal hormones are important agents of the body's control of growth, development, reproduction, and coordination of normal bodily functions. Foreign compounds, by altering the timing of signals ordinarily delivered by hormones, may lead to disruption of the body's control processes and to toxic outcomes such as developmental defects, reproductive failure, and cancer (Rhomberg, 1998). Endocrine disruptor compounds (EDCs) are difficult to study because it is nearly impossible to isolate the effects that one key chemical may have on the human endocrine system. Further complicating the issue is the fact that humans are exposed to a multitude of chemicals in daily life, from the air, water, food, and personal activities (i.e., smoking). Although long lists of potential/probable EDCs exist within the literature reviewed, there is no environmental agency or health agency that specifically lists chemicals causing endocrine disruption or regulatory limits based on the EDC's potential to disturb all hormone-based biological systems in the human body. This is indicative of the uncertainty and importance of the endocrine disruption issue. It appears that more scientific research is needed on the effects of the estrogenic effects of these compounds on, as the existing available data are very sparse. The literature review for the EIS focusing on the adulticides evaluated in this EIS found that the vast majority of the articles on endocrine disruption were available only to the already well-known endocrine disruptors such as DDT and DDE, persistent pesticides used from the 1940's to the 1970's.

Organophosphates
Organophosphates have been shown to have effects on chemical messengers (hormones) normally secreted directly into the blood by ductless glands (the endocrine system), which bring about a specific and adaptive physiologic response. In cases of organophosphate poisonings (such as malathion, diazinon, dichlorvos), the organophosphates themselves and the related inhibition of nerve cells can reduce pituitary gland function, which can alter body growth, milk production in women, metabolism, and sexual maturation (Guven et al., 1999). In the study by Guven et al., blood levels of some pituitary hormones (ACTH, cortisol, and PRL) returned to normal after recovery from poisoning, indicating that the hormonal effects of organophosphates are generally limited to very high one-time exposures. Studies of pesticide factory workers have suggested a correlation between increased exposure to organophosphates and decreased testosterone levels, with smaller effects on other male reproductive hormones (Padungtod, 1998).
Malathion

Human Studies
There are no examples or data available within the literature of endocrine disruption effects in humans caused by malathion.

Animal Studies
Malathion has been shown to interfere with luteinizing hormone and progesterone in animal studies; these effects are described in the next section on reproductive effects. Luteinizing hormone (LH) is an endocrine chemical that induces males to produce testosterone and that regulates the menstrual cycle in females. Progesterone is a steroid endocrine chemical secreted from ovaries in females that also regulates female menstrual cycle. Some animal studies of malathion suggest that it can have adverse effects on the reproductive capabilities of laboratory animals. Because it is often unclear if endocrine disruption is the cause of reproductive problems, these studies and effects will be described in the next section specifically addressing reproductive toxicity.

In another study, rats were given malathion (0.06 mg per rat) *via* ingestion for 21 days (Akhtar et al., 1996). Serum concentrations of three hormones secreted by the thyroid (triiodothyrorine (T3), thyroxine (T4), and thyrotrophin (TSP)) were measured in the exposed rats. For those rats exposed to malathion, T3 and T4 levels were decreased whereas TSP levels increased. The implications of these changes were not directly discussed; however, the authors of the study suggest that exposure to malathion may alter the secretory activity of endocrine glands.

There are no other examples or data of endocrine disruption effects in animals caused by malathion available within the literature.

Naled
There are no examples or data of endocrine disruption effects in humans or animals caused by naled available within the literature.

Pyrethroids

Permethrin

Human Studies
Permethrin has been shown to mimic some growth hormones and estrogens in an in vitro study (Go et al., 1999, Garey and Wolff, 1998). Hormones that influence growth include others, e.g., androgens, insulin, etc. Permethrin has, however, been shown to interrupt the ability of growth hormones (androgens) to send signals to specific cells, either by amplifying or reducing the hormone's intended effect. (Tyler et al., 2000). Landrigan et al. (1999) described their concerns about combined effects from exposure to multiple adulticides and already high background exposure levels for some common adulticide ingredients, including permethrin. Their measurements showed that background levels of permethrin in the residential environment are quite a small part of the total background levels of other common adulticide active ingredients, which are 20 µg/day in air and 170 µg/day in the diet (Landrigan et al., 1999).

Animal Studies
In a recent study, permethrin was applied to the skin of mice at doses ranging from 22 to 220 mg/kg-day every day or every other day for up to 30 days (Punareewattana et al., 2001). Antibody production decreased over the exposure period. The authors suggested that topical application of permethrin
may produce systemic immune effects. There were no other examples or data of endocrine disruption
effects in animals caused by permethrin available within the literature.

Resmethrin
There are no examples or data of endocrine disruption effects in humans or animals caused by
resmethrin available within the literature.

Sumithrin

**Human Studies**
Sumithrin has shown inhibitory effects on hormones in human cells (Go et al., 1999, Garey and
Wolff, 1998). In this particular experiment, human breast cancer tissue cells were used to evaluate the
effects on hormones associated with sumithrin.

**Animal Studies**
There are no examples or data of endocrine disruption effects in animals caused by sumithrin
available within the literature.

Synergist
There are no examples or data of endocrine disruption effects in humans or animals caused by the
synergist PBO available within the literature.

Inert Ingredients
No information was found regarding endocrine disruption in relation to exposure to any of the inert
ingredients.

**Summary/Conclusion**
In general, the identity and mechanisms of endocrine disruptors are not well understood at this time.
Many researchers and environmental health specialists agree that more laboratory screening and
testing are needed on potential endocrine disruptors, including pesticides, both individually and in
mixtures. However, based on the current evidence, of the compounds of interest, only malathion is a
suspected endocrine disruptor with serious reproductive effects. This is discussed in the next section.
It is uncertain whether two of the three pyrethroids considered in this EIS, permethrin and sumithrin,
may also have endocrine disruptive effects. In all cases, it is unlikely that insecticide exposure due to
spraying would be high enough to be deemed responsible for causing endocrine disruptive effects.

**Developmental/Reproductive Including Birth Defects**

**Review of Information**
Unlike the earlier section on cognitive developmental effects, this section discusses the initial
conception, development and birth of an organism, changes occurring in organisms at all stages of
growth, and the ability of organisms to produce offspring. These three major life processes are
encompassed in the heading “Developmental/Reproductive Effects.”

Reproductive toxicity is broadly characterized by harm caused to the reproductive organs of males
and females, impaired ability to produce eggs and sperm, and reduced fertility. These effects are
tested in laboratory animals using studies that follow multiple generations noting the number of pups
in those generations, and typically last several years. By contrast, developmental toxicity testing
requires observation of only one group of young animals during their maturity into adulthood,
following exposures that occur while these young animals are in the uterus (gestational exposures).
As part of the assessment of potential for exposure to occur via consumption of breast milk for infants, evidence that the active ingredients are found in breast milk and other factors affecting accumulation of the active ingredients in breast milk were considered. Such factors included rate of absorption from the gastrointestinal tract, rate of metabolism to compounds that are water soluble and can thus be eliminated via the urine, and subsequent elimination rate from the body. In general, chemicals, such as DDT, that tend to accumulate in breast milk, are generally fat soluble, thus facilitating their absorption. Once fat soluble chemicals are absorbed, they are not metabolized very rapidly, thus allowing them to accumulate in the body. An environmental exposure is specifically considered to be a developmental hazard if the young animal or person is found to be more vulnerable to harm than the older, full-grown animal or adult would be at the same dose level. Both reproductive and developmental toxicity will be discussed together in order to address the potential impacts of the adulticides on children and families to the fullest extent possible.

**Organophosphates**

For most organophosphates, no adverse developmental effects have been reported. The reproductive effects that have been reported in animal studies have not been seen in human exposure studies and generally occur only at elevated doses associated with significant toxicity to the mother (WHO, 1986). According to a recent USEPA committee report, a sufficient number of studies have investigated the reproductive effects of malathion and naled and have confirmed that they are not developmental or reproductive toxicants (USEPA HIARC, 1998b). Therefore, adverse developmental or reproductive health effects would not be expected at exposure concentrations that are already safe for adults by other toxicity standards. Reports from recent studies by the USEPA and independent researchers investigating the toxicity of malathion and naled are described in the sections that follow.

**Malathion**

**Evidence in Humans**

There is no evidence in human fetuses that exposure to malathion causes birth defects or other developmental abnormalities (Gallo and Lawryk, 1991). For example, Grether et al. (1987) reviewed hospital discharge records for newborns of mothers residing in areas adjacent to San Francisco Bay that were treated with malathion for controlling the medfly population. Exposure to malathion used for the control of the medfly population was not associated with the occurrence of birth defects or low birth weight. A more specific review of 7,450 pregnancies in the San Francisco Bay Area compared healthy births to those with complications such as physical deformities and stillbirths. All residences of the birth mothers were mapped with respect to where the various amounts of malathion spraying occurred. No significant associations could be found between physical deformities and/or stillbirths and the malathion treated areas. In this case, these data could not determine that malathion posed any developmental risk during pregnancy (Thomas et al., 1992).

**Evidence in Animals**

A number of toxicology studies in laboratory animals have been conducted to examine reproductive and developmental effects associated with malathion exposure (USEPA, 2000a, Manufacturers Research Identification Document [MRID] Numbers 41160901, 40812001, and 41583401). In 1998 the USEPA published the "Hazard Assessment of Organophosphates" which evaluated the animal evidence for malathion and naled (among others) for maternal and developmental toxicity in offspring (USEPA, 1998b). In rats and rabbits, no developmental effects were produced in the offspring and only the highest doses of malathion (200-800 mg/kg/day) yielded maternal toxicity signs such as decreases in body weight and food consumption. Overall, no developmental effects showing greater
sensitivity in pups than adults were observed in any of these studies. In addition, only high doses produced reproductive effects. For example, in male rats, a single, injected dose of 23 mg/kg of malathion reduced the rats’ ability to produce healthy sperm cells and caused drops in their sperm counts (Prakash and Venkatesh, 1996). As discussed in Hayes and Laws (1991), malathion is rapidly metabolized and eliminated from the body, with 92 percent of malathion eliminated via urine and feces within 24 hours, in rats. Within eight hours following administration, there is no unmetabolized malathion detected in the body, in rats. Therefore it is expected that little, if any, malathion would accumulate in the body, including in breast milk. Malathion has also been linked to reduced production of a hormone needed to start and sustain pregnancy, progesterone, in dairy cattle that received one dose of malathion at 1 mg/kg. As a result of this hormone drop, the malathion-exposed cattle experienced a reduced conception rate (16.6 percent), compared with the control group's rate of 50 percent (Prakash et al., 1992). It should be noted here that highest anticipated human doses of malathion from the spraying of adulticides would be at least 10,000 times lower than the 1 mg/kg daily doses that the cattle received. Therefore, the reproductive effects found in these animal studies are not likely to occur in any human populations.

**Naled**

*Evidence in Humans*
There were no studies available on reproductive or developmental effects of naled in humans.

*Evidence in Animals*
There is no evidence of developmental effects in the fetus following exposure to naled for either rats or rabbits. There was also no evidence of reproductive impairment in a reproductive study of rats followed for two generations (USEPA, 1998b). Naled is rapidly degraded to dichlorvos, and therefore elimination characteristics of dichlorvos should be similar to those of naled. Dichlorvos (and by analogy naled) is rapidly eliminated from the body, and has not been detected in the body, including milk from cows and rats given doses that cause severe poisoning (Hayes and Laws, 1991).

**Pyrethroids**

Of the three pyrethroids reviewed, only permethrin has been in commercial use long enough to develop a significant database of human health effects data. The studies of permethrin in the literature reviewed suggest that it is not harmful to either mothers or developing children at doses anticipated in humans from spraying of pyrethroids. For the other two pyrethroids, resmethrin and sumithrin, reproductive and developmental effects that were seen in animal studies described below also occurred only at doses that greatly exceed the comparable amounts of typical environmental human exposure. This lack of evidence for effects at low doses suggests that pyrethroids are unlikely to cause reproductive or developmental harm at typical environmental exposure levels resulting from adulticide spraying.

**Permethrin**

*Evidence in Humans*
Permethrin has been widely used to treat clothing to protect people from mosquitoes and ticks and to treat scabies and head lice in children. For example, permethrin-treated bed nets were effective against mosquitoes carrying malaria, and apparently harmless to both mother and child. No apparent adverse effects on the pregnancy or the infant’s development were seen (Dolan et al., 1993). Permethrin was also deemed to not have significant health impacts for nursing mothers, premature
infants, and small children when applied once at bedtime to treat scabies (Haustein and Hlawa, 1989).

_Evidence in Animals_

Several studies support the finding that permethrin exposure does not cause reproductive toxicity or birth defects in the fetus (WHO, 1990a). Lactating cows fed permethrin at doses 0.50 mg/kg for 28 days did not show an increase in mortality, and exhibited normal growth and milk production, and less than half of 1 percent (0.5 percent) of an administered dose was excreted via breast milk, in four lactating cows (WHO, 1990a). Also, a three-generation study of rats given daily doses of up to 180 mg/kg demonstrated no harmful reproductive effects. Reduced fertility was seen only at extremely high oral doses (greater than 2,500 mg/kg-day) administered during pregnancy (Wauchope et al., 1992). As mentioned in the previous introductory paragraph on pyrethroids, the anticipated doses of permethrin anticipated during spraying are far lower than the lowest animal doses in these reproductive studies. Therefore, any reproductive effects found in these animal studies are not likely to occur in any human populations.

_Resmethrin_

_Evidence in Humans_

There were no data available on reproductive or developmental toxicity effects caused by resmethrin in humans.

_Evidence in Animals_

Resmethrin has not been shown to have adverse effects on the developing fetus at doses below 80 mg/kg in laboratory animals. Developmental toxicity effects were observed in a three-generation study in rats, but only at doses greater than 500 mg/kg (Becci et al., 1979; Machi et al., 1979; Schwartz et al., 1979; Swentzel et al., 1977; and Waldron, 1969; unpublished data cited in WHO, 1989). The literature reported that rats exposed to resmethrin in utero did not exhibit any toxic effects on either the fetuses or the mothers at oral doses as high as 100 mg/kg-day (Miyamoto, 1976). The same report added that this was true for mice as well when they were exposed to doses as high as 50 mg/kg-day. Finally, a two-generation reproductive toxicity study in rats was conducted by Argus Research Labs in 1994 and summarized in the "Tox 1-liner" database for resmethrin (USEPA, 2000f). They also found that reproductive effects in the mother and developmental effects in the fetuses were not observed at doses below 71 mg/kg-day (Manufacturers Research Identification Document [MRID] Number 43189101). Resmethrin is rapidly eliminated from the body via the feces, with greater than 50 percent of an administered dose eliminated within 72 hours in rats (Miyamoto et al., 1971). In hens, 90 percent of an administered dose is eliminated within 24 hours (Christopher et al., 1985). Therefore, the percentage of an absorbed dose found in the breast milk is likely to be very low.

_Sumithrin_

_Evidence in Humans_

There were no data available on reproductive or developmental toxicity effects caused by sumithrin in humans.

_Evidence in Animals_

There is very limited evidence of reproductive and developmental toxicity caused by sumithrin exposure in laboratory animals. A study of pregnant rabbits conducted by WIL Research Labs in 1989 (Manufacturers Research Identification Document [MRID] Number 41230003) concluded that
decreased body weight and food consumption were likely in the mothers at doses of 100 mg/kg-day, while birth defects were seen only at doses exceeding 300 mg/kg-day. This suggests that developmental effects in the fetus occur only at doses of sumithrin greater than those that cause other toxic effects to the mother. The USEPA’s “Tox 1-liner” database for sumithrin (USEPA, 2000g) summarized the limited data and the high doses needed to produce poor outcomes by concluding that sumithrin has low reproductive and developmental toxicity. Sumithrin is rapidly eliminated from the body via both the urine and the feces, with 90-100 percent of an administered dose eliminated within 3 to 7 days, in rats. Therefore, the percentage of an absorbed dose found in the breast milk is likely to be very low.

Synergist

Evidence in Humans
There were no data available on reproductive or developmental toxicity effects caused by PBO in humans.

Evidence in Animals
There is evidence that PBO produces both reproductive and developmental effects in animals. Both reproductive and developmental effects were observed in mice receiving 0.8 percent (8,000 mg/kg) PBO in the diet, in a 2-generation study (Tanaka et al., 1992). Deformities were observed in mice born to mothers receiving 1,000-1,800 mg/kg PBO in olive oil force-fed to them on day 9 of their pregnancies (Tanaka et al., 1994). Additional deformities occurred with doses up to 5,000 mg/kg of PBO. However, no skeletal anomalies were observed in mice born to mothers receiving doses up to 600 mg/kg (Ogata et al., 1993). Similarly, birth defects were not observed in the offspring of rats treated with 300 or 1,000 mg/kg PBO. Therefore, it appears that the reproductive and developmental effects of PBO occur only at higher doses, at or above 1,000 mg/kg. As described for the other active adulticide ingredients in this section, this dose is far higher than the equivalent doses that human populations would be exposed to during adulticide spraying operations. Of the small amount of PBO absorbed, PBO is rapidly excreted via the urine (Hayes and Laws, 1991). Due to its poor absorption, and rapid elimination, PBO is not expected to accumulate in the body, including in breast milk.

Inert Ingredients

Evidence in Animals
Inhalation studies in pregnant mice indicate that the aromatic petroleum solvent is slightly toxic to fetuses at an air concentration of 500 ppm (2170 mg/m³), causing decreases in weight gain in fetuses. At the 500 ppm dose level, 27 of 30 female mice were pregnant compared with 26 of 30 for controls. The number of litters with viable pups were 23 at the 500 ppm dose level compared to 24 for controls. Fetal body weights were 1.16 grams on average compared with 1.25 grams on average for controls. There were no effects on either the fetuses or the mothers at air concentrations of 100 ppm (434 mg/m³) (McKee et al., 1990). In adult rats exposed to 1,500 ppm (6510 mg/m³) there were no effects on reproduction following a 12-week exposure period (McKee et al., 1990).

Summary/Conclusion
The scientific evidence suggests that for the adulticides’ active ingredients evaluated in this EIS, developmental effects are not likely to occur in the absence of other health effects in parents. By contrast, reproductive effects were found in animal tests for every adulticide, but the doses needed to produce those adverse reproductive effects varied widely. With regard to reproductive toxicity effects in animal tests, the lowest doses causing adverse effects were the following: malathion (1 mg/kg and
reduced conception rates), sumithrin (300 mg/kg and birth defects), and resmethrin (500 mg/kg and developmental toxicity in a 3-generation study). The literature suggests that the safest compounds in animal tests based on the doses needed for adverse effects were permethrin (greater than 2,500 mg/kg) and PBO (1,000 mg/kg). With very limited data available for naled it is not possible to determine safe doses of naled at this time. The adulticides’ active ingredients are not likely to be present at significant levels in breast milk. Furthermore, if the active ingredients are present in breast milk, exposures occurring via consumption of breast milk are expected to be much lower than exposures occurring via other pathways that are addressed in the risk assessment component of this study.

Each of the doses described in the animal studies summarized here correspond to human exposure levels much greater than those anticipated following the spraying of adulticides for mosquito control. For example, the anticipated exposure to malathion ranges from 0.000013 mg/kg to 0.244 mg/kg. Therefore, no reproductive adverse health effects are expected at the environmental doses following spraying. This expectation is confirmed by the human evidence citing a lack of reproductive harm in people in areas treated with adulticides for mosquito control. For malathion and permethrin, the limited human data from past pest-control efforts suggest that no adverse reproductive or developmental effects should be expected from the anticipated exposure levels of these ingredients.

Cancer

Review of Information

The intent of this literature search is to anticipate any possible carcinogenic effects from exposure to any of the adulticides discussed in the EIS. In the literature related more broadly to pesticides and cancer there are numerous studies relating exposure to commonly used household and agricultural pesticides to statistically increased rates of certain cancers. For instance, researchers Pogoda and Preston-Martin (1997) found increased risk of brain tumors among children whose mothers had used flea and tick products. Similarly, researchers Blair and Zahm (1995) suggest that farmers using commercial pesticides and herbicides experience higher rates of certain leukemias and lymphomas which merit further research and study. Several reviews of the literature on pesticides and cancer were examined for inclusion in our literature review (Daniels et al. 1997 and Zahm and Ward 1998). However, these studies all lack exposure assessments linking the specific adulticides to the cancer outcomes. Without these critical exposure or dose data, these articles cannot be further reviewed in the subsections that follow on the individual adulticides and carcinogenic effects.

Because cancer is the net result of a series of genetic changes affecting a cell's growth, division, and fate, the measurement of the ability of a pesticide to affect genes or gene expression is important in evaluating the carcinogenic (cancer-producing) process. Carcinogenic effects are sometimes measured in experiments by observing "key events" that serve as precursors in a sequence of events leading to carcinogenesis (the production of cancer). "Key events" can be either directly or indirectly related to the operation of specific genes involved in growth and differentiation of cells (differentiation is the process whereby cells acquire specific characteristics that distinguish them from other cells in the body, such as liver-specific, or kidney-specific characteristics). Carcinogenic effects can also be measured on a phenomenological basis by studying the rate of cancer occurrence in populations of animals or people exposed to a pesticide. Both types of measurements are considered in the literature review of carcinogenic effects of the pesticides discussed in the EIS.
Organophosphates

Malathion

The International Agency for Research on Cancer (IARC) of the World Health Organization classified malathion as a Group 3 carcinogen (not classifiable as to carcinogenicity based on inadequate or limited evidence), which means that no judgment has been made as to whether malathion is carcinogenic in humans (IARC, 1983). More recently, Based on a review of the available evidence, the USEPA’s Cancer Assessment Review Committee (CARC) concluded that a quantitative risk assessment for malathion was not necessary (hence the cancer criteria for malathion was withdrawn from USEPA’s toxicity criteria database, Integrated Risk Information System) (USEPA, 2000b). On Dec. 14, 2000, the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) Science Advisory Panel (SAP) agreed with the Cancer Assessment Review Committee’s conclusions.

As a result of animal studies, and in agreement with the International Agency for Research on Cancer’s decision on malathion, EPA is still considering downgrading malathion's cancer classification from “likely” to “suggestive” (USEPA 2000i – Malathion: Revisions to the Preliminary Risk Assessment and Registration Eligibility Decision [RED] Document). Classification as “suggestive” would indicate that although there is evidence that malathion is carcinogenic in animals, there is not sufficient evidence for assessing malathion's carcinogenic potential in humans. However, it should be noted that the proposal to downgrade malathion's classification does not have universal support within USEPA.

Despite the questionable results from USEPA's most recent cancer bioassays (tests in animals) regarding the carcinogenic potential of malathion in humans, this EIS is defining malathion cancer risks using a cancer slope factor (CSF) derived from an earlier cancer bioassay. A CSF is a quantitative estimate of risk from exposure to a chemical or compound. Cancer slope factors will be described in more detail in the risk assessment section of this chapter. In that bioassay, increased incidence of benign thyroid tumors was observed in male and female rats exposed to malathion. The cancer slope factor from that study was 1.52 x 10^{-3} (mg/kg-d)^{-1}, (or 0.00152 (mg/kg-d)^{-1})(USEPA, 1999b).

Human Studies

The literature review produced only one study relevant to the question of human cancers caused by malathion exposure. The one study available found no evidence of genetic damage (i.e. DNA breaks or anomalies) in certain cells of 14 farm workers occupationally exposed to malathion (van Bao, et al., 1974). The biomarker used for this study was the DNA of lymphocytes, which are among the many types of cells in the body where carcinogens can cause measurable effects.

Animal Studies

The majority of genotoxicity experiments that will be described below in representative tissues from animals suggest that malathion is not mutagenic. (Mutagenic means that a chemical can change the genetic material of cells, possibly causing cancer.) Tests for mutagenicity include those that measure permanent changes at a specific location of the genetic material (i.e., mutations), searches within cells for chromosomal breaks and defects as well as poor genetic functioning. Malathion's metabolite, malaoxon, also does not cause mutations in bacteria, or chromosomal aberrations in mammalian cells. However, malaoxon does cause mutations in mammalian cells in vitro (USEPA, 2000a).

There is limited evidence that malathion causes cancer in laboratory animals. In the most recent animal studies used by the USEPA for evaluating the carcinogenicity of malathion, the only treatment-related tumors were benign liver tumors in mice and rats, one benign nasal tumor in a
female rat, and a benign form of skin cancer, in a male rat (USEPA, 2000a). The significance of the liver adenomas (benign tumors) is not clear as they were only seen at relatively high doses (approximately 1,500 mg/kg-day in mice and 800 mg/kg-day in rats), where there was severe cholinesterase inhibition (in mice and rats) and high mortality due to non-cancer health effects (100 percent in male rats, 64 percent in female rats). The nasal tumors and skin cancer are potentially significant for several reasons. First, they were observed at doses that did not cause other signs of toxicity. Second, spontaneous occurrence of these types of tumors is relatively rare. And finally, there were no such tumors in the control group of animals.

In a recent study, investigators evaluated the potential for malathion to induce malignant transformation in mammary glands of rats (Cabello et al., 2001). The investigators found that cell proliferation was increased in rats that had previously received 340 mg malathion/kg-day for five days. After approximately 28 months, 24 percent of these rats (17/70), had developed carcinomas of the mammary gland. The authors suggest that malathion could induce changes in the epithelium of mammary glands influencing the process of carcinogenesis.

The recent carcinogenicity tests in animals reviewed by USEPA indicate that malaoxon (malathion's metabolite) is not carcinogenic in rats (USEPA, 2000b). Although there was a statistically significant increase in mononuclear cell leukemia (MCL) in male rats, this effect was only observed at a dose where there were other clear prior signs of toxicity. Furthermore, the incidence of MCL was within the testing laboratory’s historical control range, meaning that such results would be comparable to other groups of non-exposed rats.

**Naled**

USEPA has classified the carcinogenicity of naled as a group E, meaning there is sufficient evidence to suggest that naled is not carcinogenic (USEPA, 2000d).

**Human Studies**

There are no examples or data of cancer in humans caused by naled available within the literature.

**Animal Studies**

Evidence from an *in vitro* Ames test, which tracks changes in specific nutritional requirements of a bacteria as an indicator of the mutagenic potential, indicates that naled is mutagenic. Although naled does have mutagenic activity in bacterial cells, there was no increase in neoplastic (growing) lesions in treated animals vs. control animals in a 2-year study in rats (Braun et al., 1983; ACGIH, 1998). Another study did report an increase in benign mammary tumors in rats exposed to a breakdown product of naled called dichlorvos, but there was not a similar increase for malignant tumors (Gandhi and Snedeker 1999). Dichlorvos has been found to cause chromosome damage and neoplasms in other studies of mice and rats as well (Barrueco *et al.* 1994 and Chan *et al.* 1991). However, results from whole-animal DNA sensitivity studies (Braun et al., 1983; USEPA, 2000d) suggest that naled is not genotoxic (capable of altering genetic material) at exposure levels higher than would be expected from spraying naled in New York City. Furthermore, isolated cell tests reviewed by the USEPA (2000d) also suggest that naled exposure is not associated with chromosomal aberrations.

**Pyrethroids**

**Permethrin**

USEPA has classified permethrin as a group C carcinogen, meaning that it is a possible human carcinogen based on limited evidence of carcinogenicity in animals, and no data from human
population studies. The USEPA is also currently reviewing the use of its recommended cancer slope factor of $1.84 \times 10^{-2} \text{ (mg/kg-day)}^{-1}$, (or $0.0184 \text{ (mg/kg-day)}^{-1}$) for evaluating carcinogenic potential of permethrin (USEPA, 2000h). Cancer slope factors will be discussed in greater detail in the following section, “Risk to Public Health from Use of Proposed Insecticides.”

**Human Studies**

There are no examples of cancer in humans caused by permethrin available within the literature.

**Animal Studies**

Permethrin does not appear to be genotoxic because the literature indicates it is not mutagenic in either bacteria or mammalian cells, and it seems to have no effect on chromosomes or other genetic material (USEPA, 2000h; WHO, 1990a). In several studies, no carcinogenic effects were observed in either rats or mice at oral doses as high as 2,500 mg/kg-day (USEPA, 2000h; WHO, 1990a). However, in one study, permethrin caused increases in lung tumors in mice (doses were not specified for this study); and in another study, permethrin caused increases in benign liver tumors and both benign and malignant lung tumors (USEPA, 2000h). The cancer slope factor for human exposure is based on dose-related increases in both benign and malignant lung tumors observed in female mice (USEPA, 1999b; 2000h).

**Resmethrin**

USEPA has not yet evaluated the carcinogenic potential of resmethrin and the full evaluation of resmethrin may not occur until additional carcinogenicity data are submitted by the producers of resmethrin (USEPA, 2000f).

**Human Studies**

There are no examples of cancer in humans caused by resmethrin available within the literature.

**Animal Studies**

The literature search results suggest that resmethrin is not mutagenic in either bacteria or mammalian cells, and does not cause genetic damage (USEPA, 2000b; WHO, 1989). Tumors were not observed in animals exposed to resmethrin in two carcinogenicity studies summarized in USEPA's "Tox 1-liner" database for resmethrin (USEPA, 2000f). Increases in treatment-related tumors were not observed in rats at doses as high as 5,000 mg/kg-day, or in mice at doses up to approximately 200 mg/kg-day (USEPA, 2000f; WHO, 1989). However, one study reported that there was a statistically significant increase in malignant and benign liver cell tumors in a group of rats dosed with resmethrin at approximately 131 mg/kg-day (USEPA, 2000f).

**Sumithrin**

**Human Studies**

There are no examples of cancer in humans caused by sumithrin available within the literature. The literature reports that the likelihood of oncogenic (cancer-causing) effects in humans is generally regarded as extremely low or non-existent (WHO, 1990b).

**Animal Studies**

Sumithrin does not appear to be genotoxic, based on several lines of evidence. The literature suggests that sumithrin is not mutagenic either *in vitro* (isolated cells or tissues) or *in vivo* (using whole organisms, bacteria, yeast, or even mice). According to the literature, sumithrin does not cause chromosomal aberrations, either *in vitro* or *in vivo*; and it does not induce increases in abnormal
copying or repair of genetic material (unscheduled DNA synthesis, or DNA repair) (USEPA, 2000g, WHO, 1990b). Most of the in vivo animal tests suggest that sumithrin is carcinogenic only at doses (20,000 mg/kg diet or 1,116 mg/kg-day for the rat) inducing other non-cancer effects, which could increase an organism’s susceptibility to developing cancer. Increased incidence of cancer was not detected at doses as high as 450 mg/kg-day in several mouse and rat carcinogenicity tests summarized in USEPA’s "Tox 1-liners" for sumithrin (USEPA, 2000g). Additionally, sumithrin did not affect either the tumor burden or tumor profile in mice at doses up to 3,000 mg/kg for two years, and there was no evidence of cancer in rats receiving doses as high as 6,000 mg/kg, for two years (WHO, 1990b). These represent enormous doses.

Only one study found an increased incidence of malignant and benign liver cell cancer in male and female rats at 1,116 mg/kg-day (USEPA, 2000g). However, this dose was associated with excessive death of liver cells, suggesting that the increased incidence of cancer could have been a secondary manifestation of the liver damage, rather than a primary effect of sumithrin carcinogenic potential. Furthermore, this dose is approximately 10-fold greater than the level at which non-cancer effects are observed. Therefore, exposure levels that protect against non-cancer effects should offer a wide margin of safety against any possible cancer effects.

Synergist
PBO is classified by the International Agency for Research on Cancer as a Group 3 carcinogen, indicating it is not classifiable as to its carcinogenic potential in humans, due to inadequate evidence in either animals or humans (IARC, 1983). USEPA has classified piperonyl butoxide as to its carcinogenic potential as a Group C - possible human carcinogen, and recommended that for the purpose of risk characterization, the RfD and Margin of Exposure (MOE) approaches be used for quantification of human risk (USEPA, 2000e). The Group C classification was based on statistically significant increases in liver tumors in mice (adenomas and carcinomas). According to USEPA, the MOE and RfD approaches are appropriate for piperonyl butoxide based on observations of tumors only at doses where there is excessive toxicity, and based on what is considered a low mutagenic potential for piperonyl butoxide (USEPA, 2000e). The following section of this chapter, "Risk to Public Health from Use of Proposed Pesticides," will discuss and explain RfDs and MOE. The following section of this chapter, “Risk to Public Health from Use of Proposed Pesticides,” will discuss and explain RfDs and MOE.

Human Studies
There are no examples of cancer in humans caused by PBO available within the literature.

Animal Studies
There is inadequate data regarding carcinogenicity of PBO in animals. Dose-dependent increases in malignant and benign liver cell tumors were observed in male mice and rats given diets containing 1052 mg/kg-day PBO (Takahashi et al., 1994a,b). However, other tests for cancer in animals have provided evidence that PBO was not carcinogenic in either rats or mice at similar dose levels (NCI, 1978; Maekawa et al., 1985).

Inert Ingredients
Mineral oil is classified by IARC in Group 3, which means it is not classifiable as to its carcinogenicity in humans, due to inadequate evidence in either animals or humans (IARC, 1984).
Evidence in Humans
Excess cancers of the digestive or respiratory tract were not observed in 5,189 workers exposed to oil mist for at least one year (DeCoufle, 1976). No other human studies were found in the literature reviewed.

Summary/Conclusion
Numerous environmental health protection agencies at international, national, and state levels regulate compounds based on their known or suspected ability to cause cancer. Of the adulticide compounds considered in this EIS, only malathion and permethrin have been studied enough to be adequately classified by the IARC or the USEPA. Both of these are listed as suggestive or possible carcinogens. As seen in the review of the literature for all the adulticide compounds, the other three active ingredients (naled, resmethrin, and sumithrin) have very limited data and no final decision has been made regarding their carcinogenic potential. Similarly, the synergist PBO has too little data for classification as a carcinogen or non-carcinogen. This uncertainty in cancer potential will be handled in the risk assessment section that follows using either a cancer slope factor (CSF) approach for the suggested carcinogens (malathion and permethrin) or a margin of exposure (MOE) approach for the unknown or unlikely carcinogens. This combination of approaches should adequately describe the amount of cancer or non-cancer risk that people could be exposed to during the period following adulticide spraying.

RISK TO PUBLIC HEALTH FROM USE OF PROPOSED INSECTICIDES – RISK ASSESSMENT
This section of the EIS uses a modeling approach to assess the potential health effects on the public associated with the application of adulticides, in order to determine if they pose a significant human health risk. Risk assessment is a process by which scientists evaluate the potential for adverse health or environmental effects from exposure to naturally occurring or synthetic chemicals, including those in adulticides. The goal of this risk assessment is to provide a rational basis for making decisions about managing the use of adulticides in order to protect human health and the environment. Risk assessment is used as part of the decision-making process to ensure public protection against unacceptable risks and to allow the use of products whose benefits outweigh the risks associated with their use. A risk assessment approach uses existing methods and exposure factors developed by USEPA to estimate the risks. Because specific information regarding the inerts (i.e., chemical composition and concentration) was not available for this EIS, a quantitative assessment of the inert ingredients present in the adulticides was not performed in this risk assessment. Furthermore, a quantitative assessment of workers applying the adulticides was also not covered in this EIS. Workers applying the pesticides reviewed in this EIS must be appropriately certified and receive training in the proper handling of these pesticides. Recommendations for protection during mixing, loading or application are indicated on the adulticides' labels (i.e., use of personal protection equipment, use of masks and/or respirators if warranted, gloves, proper handling of adulticides). Recommendations for protection during mixing, loading or application are indicated on the adulticides' labels (i.e., use of personal protection equipment, use of masks and/or respirators if warranted, gloves, proper handling of adulticides). Furthermore, these workers fall under the guidelines outlined by the Occupational Safety and Health Administration (OSHA). OSHA concerns itself with the protection of workers health. It should be noted that if applicators don't follow recommendations on the adulticide label to limit their exposures (i.e., use the appropriate level of personal protective equipment, avoid direct exposure to spray drift, use application rates recommended by adulticide manufacturers), there is a potential for health effects.
Overview
If adulticides are used to kill adult mosquitoes, people might be exposed to these adulticides’ active ingredients in a variety of ways. During spraying, adulticides in the air could be inhaled; they could also settle and leave a residue on people’s skin and clothing. Such residues also may settle on non-targeted outdoor surfaces (such as lawns, gardens and swimming areas) and on surfaces within homes, which airborne insecticides could enter through open windows or ventilation systems. Therefore, the “exposure pathways” through which human exposure might occur include not only inhalation of airborne adulticides and skin contact with adulticide residue during spraying, but also accidental ingestion (eating) of adulticide residues because of hand-to-mouth behaviors; ingestion of contaminated produce and drinking water, and exposure due to participation in outdoor aquatic activities.

This section assesses the potential health risks for each exposure pathway and each active adulticide ingredient. Mathematical models are used to predict how far a sprayed insecticide will travel from its source, how much of it will be remain in the air for a given time period, and how much of its residue will be deposited on surfaces (or people or fruit, etc.) with which it comes into contact. As discussed in Chapter 3.A, “Framework of the Analysis,” the ISC3ST dispersion model was used to predict the concentrations of adulticides in air, and surface deposition levels following an application. These conservative estimates (the concentrations and deposition levels of adulticides under average and reasonable maximum conditions) serve as the foundation for the public health risk assessment.

The risk assessment consists of four steps: hazard identification; an exposure analysis; a toxicity analysis; and a risk characterization, which characterizes the risks to the exposed population (e.g., the likelihood that there would be an increase in cancer in a population exposed to a particular active ingredient in adulticides). A complete discussion of these four steps is provided below. Also provided is a qualitative discussion of the significant sources of uncertainty and the conservative choices made in the risk assessment.

Hazard Identification
In this risk assessment, the chemicals of concern are the active ingredients in the adulticide products that could be applied as part of the Proposed Action.

Exposure Analysis
This is the second step in the public health risk assessment. The purpose of the exposure analysis in this EIS is to determine the amount of adulticides’ active ingredients to which people might be exposed under various conditions during and following spraying. This includes identifying human populations who would be potentially exposed in a particular geographical area (e.g., child and adult residents, city public workers, children and adults using parks and school playgrounds), “exposure pathways,” including those mentioned above (inhalation, skin, etc.), a range of values for exposure parameters (e.g., child and adult body weights, fruit and vegetable ingestion rates, amount of time spent indoors and outdoors), adulticide active ingredient concentrations predicted through dispersion and deposition modeling (e.g., concentrations and deposition levels of active ingredients in surface, water, soil, air), and estimates of the amount taken in by people during and following the spraying of adulticides.

The following guidance documents are used to develop a range of exposure parameters for the different groups of people identified in each geographical area:

*Risk Assessment Guidance for Superfund, Human Health Evaluation Manual* (USEPA, 1989a). This contains the general exposure equations used to estimate the amount of
adulticide taken in by people (see detailed discussion in the Calculation of Exposures section). This document, published in 1989, remains the standard guidance document for risk assessment for human health. As more information and refinements to risk assessment methodology have become available, supplemental guidance documents have been issued, including the following, which were also used in this risk assessment:

**Calculating the Concentration Term, Supplemental Guidance** (USEPA, 1992b). This supplemental guidance was developed specifically to provide a standardized approach to calculate chemical concentrations to which people may be exposed in various media, (e.g., soil, water, food, etc.).

**Exposure Factors Handbook - Volume 1. General Factors; Volume 2. Food Ingestion Factors; Volume 3. Activity Factors** (USEPA, 1997c,d,e). This three-volume set is a compilation of exposure data under a variety of exposure conditions. This information was used to determine the range of potential exposures for people in each of the geographical areas.

**Risk Assessment Guidance for Superfund, Volume 1: Human Health Evaluation Manual, Supplemental Guidance, Dermal Risk Assessment, Interim Guidance** (USEPA, 1999a). This guidance was developed specifically for skin exposures and provides recommended values to estimate skin exposures.

These documents are used because they represent the most current and complete knowledge for performing human health risk assessments. Most states that have available risk assessment guidance derive their information from these USEPA documents. Limitations associated with risk assessment guidance are addressed in the Alternative Assumptions Analysis section.

The Exposure Analysis section includes the following subsections:

- **Identification of Human Populations Potentially Exposed.**
- **Evaluation of Exposure Pathways**, which evaluates the routes by which people may come in contact with the adulticides.
- **Selection of Exposure Parameters**, which presents the rationale for the selection of exposure parameters for the human populations potentially exposed to adulticides.
- **Calculation of Exposure Concentrations**, which describes the approach used to estimate concentrations of active ingredients in air and deposition levels on surfaces based on dispersion and deposition modeling, in order to quantify potential human exposures to adulticide formulations.
- **Calculation of Exposures**, which integrates the information developed in the subsections described above, to estimate the amount of adulticides’ active ingredients taken in by people during and following applications.

**Identification of Human Populations Potentially Exposed**

Based on human activities and the various environment types (i.e., residential, commercial, industrial, institutional, and recreational) within the selected Representative Areas (College Point, Jamaica Bay/Paedergat Basin, Edgemere/Far Rockaway, Hunts Point/Soundview, Jerome Park/Van Cortlandt Park South, Manhattan’s Upper East Side, Lemon Creek/Wolfe’s Pond Park), several human populations which can potentially be exposed to adulticide spraying activities are identified for this EIS. To account for the variability in human populations (e.g., age, activity) resulting in the potential variability in exposures to the adulticides, the identified human populations were further broken down into specific age ranges and population subgroups. The following human populations and age groups address these issues:
Residents:
- Young Child (0-6 years)
- Older Child, Adolescent and Adult (7 years and older)

Workers:
- Commercial/Industrial
- Public Works (i.e., street sweepers, park employees, sanitation department)

Sensitive Groups:
- Hospitalized/In Nursing Homes
- Homeless
- Suffering from Asthma, Multiple Chemical Sensitivity, Autism and Learning Disabilities

School Populations:
- Older Child (7-12 years)
- Adolescent (13-18 years)
- Staff and Teachers (older than 18 years)

Park Visitors:
- Young Child (0-6 years)
- Older child (7-12 years)
- Adolescent (13-18 years)
- Adult (older than 18 years)
- Community Gardener (older than 18 years)

This risk assessment will evaluate the possible effects of adulticide exposure on all these population subgroups and their anticipated environmental settings. Thus, the possibility of various health risks are assessed for several potential age groups, including sensitive members of the population, under a broad range of exposure conditions and activities. While other individuals, in other settings, might be exposed, the groups being discussed here have the greatest potential for exposure. Therefore, if spraying adulticides does not pose a significant health risk to these people, it is not likely to pose a significant risk to others with lower potential for exposure.

USEPA (1991) recommended age ranges were used to characterize exposure for residents. Exposure duration is assumed to be 30 years, from ages 0 to 30 years, per USEPA (1991) guidance. Carcinogenic and noncarcinogenic risks were calculated separately for two age groups: 0 through 6 years (6 year period) and 7 through 30 (24 year period). USEPA considers children to be the most sensitive age group quantified in this EIS (i.e., greatest hand-to-mouth behavior, low body weight), therefore, exposures are expected to be higher in this age group than for an older children or adults.

Although not directly assessed as a specific group in this public health risk assessment, other human populations, such as developing fetuses and pregnant women, are accounted for by using USEPA-derived toxicity criteria. These criteria include safety factors to account for the variability in sensitivity in human populations. These safety factors account for sensitivity of pregnant women, the elderly, those suffering from chronic illnesses, as well as the developing fetus. This concept is more fully addressed in the subsequent “Toxicity Analysis” section.
As mentioned earlier, a quantitative assessment of workers applying the adulticides was not performed in this EIS. These adulticides must be applied by appropriately certified and trained applicators and these workers fall under the guidelines outlined by the OSHA.

**Evaluation of Exposure Pathways**

During adulticide application, there is the potential for the adulticide to drift from the spraying area due to wind and dispersion. Therefore, as discussed earlier in this section, there is the potential for exposure to adulticides in outdoor air and in indoor air, and to adulticide residue on skin, in swimming areas, gardens and any other surfaces where adulticide particles settle. In certain microenvironments within the spraying period, these deposition scenarios may allow for an adulticide to accumulate and persist for a longer time, depending on the particular adulticide’s breakdown rate.

The pathways by which people, animals, and plants can be exposed to an adulticide depend on when it is applied, and what medium (e.g., water, air, soil, surface) is affected. The airborne concentrations in people’s breathing zones may be affected by the spraying and also by the disturbance of “fugitive dust” containing the adulticides. (“Fugitive dust” would include, for example, dust generated by wind blowing or by people walking on unpaved paths, or by gardening or construction.) As described in Chapter 3.A, “Framework of the Analysis,” the public health risk analyses are based on the dispersion modeled results from ground-level (truck) spraying, as these resulted in the most conservative values (maximum amounts) for both concentrations in air and surface deposition levels. Table 3.C-5 presents the exposure pathways considered in this evaluation.

Exposure pathways identified in this EIS are determined by the activities that could potentially occur within the selected environment type (e.g., residential, commercial/industrial, community accessible/public parks). As indicated in Table 3.C-5, the most significant pathways are evaluated quantitatively (i.e., potential risks are calculated) while less significant pathways are discussed qualitatively (i.e., their risks are not calculated but are instead discussed in relation to the quantified pathways’ risks). A pathway is more likely to be discussed qualitatively if it describes a potential exposure to adulticides that is similar to or lower than (i.e., shorter exposure durations, lower contact rate with adulticides) the exposure for another pathway that is discussed quantitatively. For example, people living in nursing homes would have similar or lower exposures to adulticides than “adult residents.” In addition, the toxicity criteria (the level considered protective of human health) derived for the active ingredients in adulticides incorporate a safety factor to account for the variability in sensitivity in human populations (i.e., certain people are more sensitive than others to chemicals).

Certain pathways however, are not evaluated, as indicated in Table 3.C-5. This is because:

- The pathway is not considered a significant source of exposure for the population that is not evaluated when compared to another population that is evaluated. (For example, the ingestion of fruit and vegetables pathway is evaluated for child and adult residents rather than for child and adult recreators, except for community gardeners who consume their produce); or

- The pathway is considered not relevant or possible for the defined activity. (For example, it is not possible that park visitors would inhale indoor dust while pursuing outdoor activities.)

Acute (short-term) exposure pathways are defined in this EIS as those pathways with exposure durations of less than one day. As presented in Table 3.C-5, acute exposure pathways include those associated with exposure to adulticides immediately after application (i.e., inhalation of drift, skin contact with drift while spraying, and ingestion from hands of drift deposited on hands). Subchronic exposure pathways are defined as those pathways with exposure durations of half a year. This
assumes the selected adulticide ingredient would be used during only one spray season (during the active season for mosquitoes, from May to October). Chronic (long-term) exposure pathways are defined as those pathways with exposure durations to a maximum of 30 years. This assumes the selected adulticide ingredient would be used for mosquito control during each spray season for the entire 30 years. The selection of a 30-year exposure duration is based on two assumptions: 1) The typical upper-bound estimate for people living at the same location is approximately 30 years (USEPA, 1997e); and 2) different adulticides tend to be used over time, as insects may develop resistance to the adulticides’ active ingredients.

Selection of Exposure Parameters
Selection of exposure parameters (e.g., intake rate, exposure frequency, exposure duration, body weight) are consistent with current USEPA guidance. This multi-pathway exposure assessment is based on standard EPA exposure assumptions and risk assessment approaches. Consistent with USEPA guidance (1989a), both “central tendency” and “reasonable maximum exposure” (RME) values for the various pathways are evaluated. Central tendency exposure parameters are more typical of average exposure conditions, whereas RME values are defined as reasonable upper-bound exposure conditions. The central tendency and RME values are used to account for the variability in potential exposure for the various human populations evaluated in this assessment. The exposure parameters are presented in Appendix 3.C-1, along with reference citations and the rationale for the selection.

The risk assessment relies on standard USEPA default exposure and other assumptions contained in the Exposure Factors Handbook (USEPA, 1997c,d,e). A “default exposure” is a typical exposure number that is used when site-specific information is not available. The three-volume Exposure Factors Handbook presents information taken from surveys of U.S. populations regarding general factors (e.g., body weight, water ingestion rate) and activity factors (e.g., time spent indoors, time spent gardening).

Calculation of Exposure Point Concentrations
To quantify potential human exposures to adulticides, the concentrations and deposition levels of the adulticides’ active ingredients released from the applicator's truck are modeled in air and on surfaces. These modeled concentrations are called exposure point concentrations (EPCs). An EPC is the concentration of an active ingredient in soil, water, surfaces, food, and air with which people come in contact by the various exposure pathways (i.e., it is the amount of active ingredient that one is exposed to from a specific exposure pathway).

For acute (short-term) exposures (e.g., inhalation of drift or skin contact with drift during spraying; incidental ingestion of drift deposited or transferred onto hands), the EPCs are based on the maximum air-model results at a distance of 25 feet from the spray source during a single application of the adulticides. For subchronic and chronic exposures for the other pathways identified in Table 3.C-5 (e.g., skin absorption via soil and water; inhalation of vapors and particulates via water and via outdoor or indoor fugitive dust), the EPCs are derived from the deposition-model results. The deposition model results are used for subchronic and chronic exposures because all adulticides are assumed to settle out of the air within one week. (See Chapter 3.A, “Framework of the Analysis” for a detailed discussion on the dispersion modeling assumptions and results.)
Table 3.C-5: Relevant Exposure Pathways
For subchronic and chronic exposures, the EPCs are based on the average deposition level within a 300-foot swath (treatment area adjacent to the spray source), derived from the deposition modeling results (see Chapter 3.A, “Framework of the Analysis”). These deposition levels are modified according to the adulticide application schedule to account for both the accumulation and the degradation of the adulticide in the environment over the course of the selected 60-day spraying period. Based on the assumption for the frequency of application as described in Chapter 3.A, “Framework of the Analysis,” an adulticide could potentially be sprayed on days 1, 4, 14, 17, 27, 30, 40, 43, 53, and 56 (10 spray events in one season) in any given area. Over this time period, more and more of the adulticide would accumulate as more was applied, but some of the adulticide would also degrade, or break down.

The resulting EPCs in all media (air, water, surfaces, and soil) are determined by combining three things: the spraying schedule; the compound’s media-specific decay rates (i.e., how quickly the active ingredient breaks down or degrades in the environment), and the accumulated concentrations resulting from each additional spraying event. The resulting concentrations are averaged over 182 days (i.e., half a year). These derived 182-day average EPCs expected within 300 feet of the spraying locations are used for assessing subchronic and chronic exposures. A more detailed discussion of the approach used to estimate EPCs for soil, air, surfaces, and water is provided in Appendix 3.C-2. In addition, this Appendix presents the approach used to calculate the active ingredient concentrations in fish, fruit and vegetables, and in bathroom air (resulting from showering or bathing).

EPCs, as calculated using methods described in Appendix 3.C-2, are presented in Table 3.C-6 below. Table 3.C-6 shows, for example, that, at any vertical height, at a distance of 25 feet from a truck that sprayed an adulticide containing malathion, the amount of malathion in the air would be, at most, 57.1 micrograms per cubic meter of air.

The table also shows that (taking into account the accumulation and degradation of the adulticide) within a 300 foot swath adjacent to the spray source, the average deposition level of malathion—the amount of malathion that would settle onto a surface—would be, approximately 0.00002 milligram per square centimeter of surface area; and the average deposition of malathion on fruit would be, approximately 0.000128 milligram per kilogram of the fruit’s weight.

**Calculation of Exposures**

The following equations are used to estimate the amount of adulticides’ active ingredients to which people may be exposed during daily activities at home, at work, or at play following an application to control adult mosquitoes. The adulticides may enter the human body by one of the following exposure pathways, or by a combination of these pathways:

- Inhalation of adulticides in air;
- Ingestion of adulticides in soil, food, and water; and
- Skin contact with adulticides in soil, surfaces, and water.

The following equations, obtained from USEPA guidance (USEPA, 1989a), incorporate the exposure point concentrations described earlier and in Appendix 3.C-2 with the exposure parameters described in Appendix 3.C-1. The end result from combining all this information is an estimate of the amount of active ingredients to which a person may be exposed through daily activities. This amount is called the “effective concentration” (for inhalation) or the “average daily dose” (for ingestion and skin pathways).
Inhalation exposures are estimated using the following generalized equation:

\[
EC = \frac{EPC \cdot EF \cdot ED \cdot CF}{AT}
\]

Where:

- \( EC \) = Effective exposure concentration of an active ingredient in air (measured in \( mg/m^3 \); milligram of active ingredient per cubic meter of air)
- \( EPC \) = Exposure point concentration of an active ingredient in air (measured in \( ?g/m^3 \); microgram of active ingredient per cubic meter of air)
- \( EF \) = Exposure frequency (days per year); number of days within a year of exposure to an active ingredient
- \( ED \) = Exposure duration (in years); the number of years during which an exposure to an active ingredient is occurring
- \( CF \) = Conversion factor (0.001 \( mg/\mu g \); or 0.001 milligrams per microgram); this is required for the conversion of units from \( ?g/m^3 \) to \( mg/m^3 \)
- \( AT \) = Averaging Time; period over which exposure is averaged (measured in days). For noncarcinogens, the \( AT \) is a person’s ED (exposure duration in years) multiplied by 365 days per year. For carcinogens, the \( AT \) is a person’s average lifetime, 70 years (USEPA, 1997c) x 365 days per year.

Example—Inhalation exposure to malathion:

For an exposure point concentration (EPC) of 0.0000146 \( \mu g/m^3 \) (micrograms of malathion per cubic meter of air); an exposure frequency (EF) of 180 days of exposure per year; an exposure duration (ED) of 24 years, and an averaging time (AT) of 8,760 days (period over which exposure is averaged), the “effective exposure concentration” of malathion in air would be:

\[
EC_{\text{malathion}} = \frac{0.0000146 \cdot 180 \cdot 24 \cdot 0.001}{8760} = 0.000000007 \text{ mg/m}^3
\]

Therefore, in the above example, the estimate of the amount of malathion to which a person may be exposed through daily activities, or the “effective concentration” would be 0.000000007 milligrams of malathion per cubic meter of air. The approach used in this example for interpreting the calculations can be used for each exposure type given below.

Oral exposures are estimated using the following generalized equation:

\[
ADD = \frac{EPC \cdot IR \cdot EF \cdot ED \cdot CF}{BW \cdot AT}
\]
Table 3.C-6: Exposure Point Concentrations in Various Media
Skin exposures to adulticides’ active ingredients in soil are estimated using the following generalized equation:

$$\text{ADD} = \frac{\text{EPC} \times \text{SA} \times \text{AF} \times \text{EF} \times \text{ED} \times \text{ABS} \times \text{CF}}{\text{BW} \times \text{AT}}$$

Where:

- **ADD** = Average daily dose associated with skin contact (measured in mg/kg-day; milligram of active ingredient per kilogram of human body weight per day)
- **EPC** = Exposure point concentration in media, such as soil (in mg/kg; milligram of active ingredient per kilogram weight of media)
- **SA** = Skin surface area in contact with soil (measured in cm$^2$: square centimeters of skin)
- **AF** = Mass of soil adhered to the unit surface area of exposed skin (in mg/cm$^2$)
\[ \text{ADD} = \frac{EPC \times SA \times Kp \times EF \times ED \times ABS \times CF}{BW \times AT} \]

Where:

- \( \text{ADD} \) = Average daily dose associated with skin contact (measured in mg/kg-day; milligrams of adulticide per kilogram human body weight per day)
- \( EPC \) = Exposure point concentration in water (measured in mg/L; milligrams of adulticide active ingredient per liter of water)
- \( SA \) = Skin surface area in contact with water (measured in \( \text{cm}^2 \); square centimeters of skin)
- \( Kp \) = Permeability coefficient (measured in \( \text{cm/hr} \); centimeters per hour) is the rate at which a chemical seeps into the body through the skin.
- \( EF \) = Exposure frequency (days/year); number of days exposed to adulticide’s active ingredient
- \( ED \) = Exposure duration (years); number of years during which an exposure to an active ingredient is occurring
- \( ABS \) = Chemical-specific skin absorption factor
- \( CF \) = Conversion factor (0.001 L/cm\(^3\); liter per cubic centimeter); required to convert units from milligrams of active ingredient per liter of water over skin area to milligrams of active ingredient per kilogram human body weight per day
- \( BW \) = Body weight (in kg); the average human body weight over the exposure period
- \( AT \) = Averaging time; period over which exposure is averaged (in days)
See example given for inhalation exposure above, for the approach used in interpreting the calculations.

Appendix 3.C-3 presents these calculations for all the exposure pathways to the active ingredients by the identified population groups.

**Toxicity Analysis**

This section is the third step in the public health risk assessment. The purpose of the toxicity analysis is to determine how much of an adulticide is required to cause an adverse health effect, and to predict exposure levels at which those health effects are likely to be negligible or nonexistent. Those exposure levels are also called “toxicity criteria.” It should be noted that, where applicable, the toxicity effects of the breakdown products of the active ingredients are inherently accounted for in the toxicity tests performed for the active ingredient (i.e., the derivation of the toxicity test accounts for the presence of the active ingredient and the breakdown product). In this step, two general types of toxicity criteria are developed: the non-carcinogenic (or non-cancer) reference dose and concentration; and the carcinogenic slope factor and unit risk.

Before defining these terms, it should be noted that risks of harm are evaluated differently for cancer than for all other illnesses. For health effects other than cancer, scientists attempt to determine the maximum dose that is considered to have negligible health effects if a person is exposed on a daily basis. For cancer, however, risk is evaluated according to probability; specifically, the increased probability that an individual will, during his or her lifetime, develop cancer following a specific exposure to a chemical.

First, the toxicity criteria for health effects other than cancer will be discussed. A reference dose (RfD) or reference concentration (RfC) is defined by USEPA as a chemical-specific dose or concentration to which people, including sensitive individuals, can be exposed on a daily basis without adverse health effects (Barnes and Dourson, 1988; Dourson et al., 1989; USEPA, 1989a). “Chemical-specific” refers to the fact that RfDs and RfCs are unique to a particular chemical; each chemical has its own RfD and RfC. The difference between a reference “dose” and a reference “concentration” is that a reference “dose” refers to what individuals take into their bodies (e.g., through ingestion or through the skin), measured as a ratio of chemical ingested or absorbed to an individual’s body weight per day, whereas a reference “concentration” is the amount of a chemical that an individual is exposed to through breathing. Acute (short-term) and subchronic RfDs and RfCs are similar to chronic (long-term) RfDs or RfCs, except that the acute and subchronic RfDs and RfCs represent a daily exposure that is not likely to cause adverse health effects for exposures occurring during a shorter period of time (subchronic exposure) or a single day (acute exposure).

The second type of criteria is the cancer slope factor (CSF) and unit risk (UR). Like the cancer slope factor, the UR is the increased probability that an individual will develop cancer following a specific exposure to a chemical. This increased probability is in addition to everyone's probability of developing cancer from everyday exposures to a multitude of chemicals. The CSF parallels the RfD (it is used for ingestion exposures), while the UR parallels the RfC (it refers to concentrations in the air). It should be noted that not all chemicals can cause cancer.

The toxicity criteria used in this EIS were provided by the following sources:

- USEPA’s Hazard Identification Assessment Review Committee (HIARC) documents,
- USEPA's Integrated Risk Information System (IRIS) files,
- USEPA’s Office of Pesticide Programs (OPP), and
USEPA's “Tox 1-Liners,” which contain summaries of toxicology studies submitted to the Health Effects Division of USEPA’s Office of Pesticide Programs.

The Toxicity Analysis section includes the following two main subsections:

- Evaluation of Non-cancer Hazards and Cancer Risks: This subsection describes the approach used to derive noncarcinogenic and carcinogenic toxicity criteria.

- Toxicity Criteria: This subsection summarizes qualitative and quantitative toxicity information for the active ingredients and inert ingredients considered in this EIS. Quantitative information for the individual active ingredients includes toxicity criteria for evaluating both non-cancer health effects and carcinogenic potential. “Non-cancer” refers to all ailments other than cancer.

A more detailed description of the derivation of these toxicity criteria is provided in the following subsections. A summary of the non-cancer and cancer toxicity criteria used in this public health risk assessment is provided in a table following all the derivations for each active ingredient under consideration in the EIS.

**Evaluation of Non-Cancer Hazards and Cancer Risks**

**Non-Cancer Hazards**

Because adequate human data are not available for the adulticide ingredients evaluated in this public health risk assessment, toxicity values are all based on animal studies. In experimental animal studies, laboratory animals are exposed to a range of doses from which two critical “dose levels” are established. The first of these is the lowest dose that results in a toxic response, referred to as the Lowest-Observed-Adverse-Effect-Level (LOAEL). The second is the highest dose to which an animal can be exposed without experiencing any toxic response. This value is known as the No-Observed-Adverse-Effect-Level (NOAEL). It is assumed that any dose below the NOAEL can be safely tolerated by the animal for a period of time corresponding to the duration of exposure in the study. A “toxic response” is any observable and measurable harmful effect or ailment. The LOAEL usually corresponds to the most sensitive toxic effect in the most sensitive species of animal tested – the first observed effect. This effect could, for example, be a subtle change in an enzyme level in blood. As mentioned earlier, the most sensitive response determined in animal studies is used to develop toxicity criteria. These sensitive responses can be measured (e.g., by change in enzyme level in blood) but may not be observable. As generally defined by USEPA for animal studies, the duration of a study can range from one to seven days (for a short-term, or “acute,” study), from seven days to three months (for an intermediate, or “subchronic,” study), or from three months to the lifetime of the animal (a long-term, or “chronic,” study) (USEPA, 1989a). There are some slight variations of this definition depending on researchers; however, these time frames are more or less consistent across animal studies.

As discussed earlier, the USEPA has historically relied on toxicity values known as reference doses (RfDs) to evaluate non-carcinogenic effects associated with acute, subchronic and chronic low-dose oral and dermal exposures to humans. A “chronic RfD” is defined by USEPA as milligrams of a specific chemical per kilogram body weight of a person given on an daily basis (mg/kg-day) to which a population of sensitive humans can be exposed for a long period of time without detrimental effects occurring (Barnes and Dourson, 1988; Dourson et al., 1989; USEPA, 1989a). “Subchronic RfDs” and “acute RfDs” are similar to chronic RfDs, except that they represent a daily exposure that is not likely to cause detrimental effects for exposures occurring over a shorter period of time.
For inhalation exposures, the USEPA uses reference concentrations (RfCs) to evaluate non-cancer effects of chemicals. (As noted earlier, “non-cancer” refers to all ailments other than cancer.) The RfC is similar to the RfD, and represents an air concentration (measured in mg/L, or milligram of adulticide active ingredient per liter of air) to which a population can be exposed on a daily basis, that is not likely to be associated with an appreciable risk of adverse effects if the exposure is for a single day (for an acute RfC), or during either a portion of a lifetime (for a subchronic RfC) or for an entire lifetime (for a chronic RfC).

As mentioned above, because adequate human data are not available for the adulticide ingredients evaluated in this public health risk assessment, the RfDs and RfCs used to evaluate toxic effects to humans are conservatively derived from the animal-based NOAELs with various uncertainty factors (UFs) applied to them.

An RfD or RfC is calculated by dividing the NOAEL (usually corresponding to the most sensitive toxic effect in the most sensitive species of animal tested) by a series of uncertainty factors (UFs).

\[
\frac{RfD \text{ or } RfC}{NOAEL} = \frac{UFs}{\text{Dose or concentration to which people, including sensitive individuals, can be exposed on a daily basis without adverse health effects}}
\]

Where:

\[
RfD \text{ or } RfC = \text{Dose or concentration to which people, including sensitive individuals, can be exposed on a daily basis without adverse health effects}
\]

\[
NOAEL = \text{Highest dose to which an animal can be exposed without experiencing any toxic response}
\]

\[
UFs = \text{Uncertainty Factors}
\]

These uncertainty factors can also be considered as safety factors where the animal-based NOAEL is divided by safety factors to ensure adequate protection of the human population. These uncertainty factors or safety factors decrease the NOAEL that was selected based on animal studies to provide an additional margin of safety. For the active ingredients evaluated in this EIS, several types of uncertainty factors may be applied:

- An interspecies UF of 10 is used to account for the uncertainty associated with extrapolating from animal dose-response data to potential human responses. If a NOAEL is based upon a high quality study in humans, then this factor is unnecessary. For some chemicals (but not those evaluated in this EIS) a partial interspecies UF that is less than 10 can be used even when using a NOAEL based on animal data, if there is sufficient evidence that a lower UF will be adequately protective.

- The inter-individual UF of 10 addresses the variability in sensitivity among individuals in human populations (i.e., pre-disposing sensitivity to the chemical).

- The LOAEL to NOAEL uncertainty factor of 10 is used if the RfD is to be based upon a study for which a LOAEL but not a NOAEL was established. A UF is applied to address uncertainty in the difference between these two dose levels. A partial UF less than 10 can be used for some chemicals, for instance if the severity of adverse effects for the LOAEL is considered mild.

- The subchronic to chronic uncertainty factor of 10 is used when extrapolating from a subchronic exposure to a chronic exposure. If effects occurring following a sub-chronic
exposure are not expected to differ substantially from effects occurring following chronic exposure.

An additional safety factor of 10 is applied to ensure adequate protection of infants and children, if there is evidence to suggest that the developing fetus or newborns are particularly sensitive to effects of a chemical. This safety factor was not applied for the active ingredients evaluated in this EIS, as evidence from developmental and reproductive toxicity studies, as well as developmental neurotoxicity studies indicates that the developing fetus and newborns are either equally sensitive, or less sensitive, than adult animals to the effects of the active ingredients.

An additional modifying factor ranging from one to 10 may be applied to account for any residual additional uncertainty associated with the data.

Following the application of these uncertainty factors, the value of the RfD (the acceptable dose to which people may be exposed without incurring a health risk) is typically 10 to 10,000 times lower than the NOAEL to ensure adequate protection of the human population, including sensitive individuals (e.g., pregnant women, developing fetus, elderly, chronically sick). The use of these UFs provides an additional margin of safety in calculating these doses.

RfDs and RfCs for the six active ingredients evaluated in this EIS are based on studies using the appropriate exposure duration and route of exposure, wherever possible. If suitable route-specific studies are not available, criteria from other studies are used by applying route-to-route conversion factors. For instance, there are no EPA-derived toxicity criteria based specifically on toxicity studies involving long-term skin exposures. Therefore, oral toxicity factors are used, assuming that once a chemical is absorbed into the bloodstream, the health effects are similar regardless of whether the route of exposure is oral or through the skin.

Cancer Risks

Cancer risk, or carcinogenic potential, is represented by a cancer slope factor (CSF) for exposures to adulticides by ingestion, and by the unit risk factor (UR) for exposures to adulticides by inhalation. The CSF and unit risk are the probability of risk per unit dose of exposure. Depending on the amount of exposure (dose or concentration) to an active ingredient by an individual, the CSF or UR is multiplied by the exposure dose or concentration to determine the probability of developing cancer associated with a specific exposure.

To estimate an individual’s risk of developing cancer, scientists multiply the cancer slope factor for a particular active ingredient by the dose the individual receives. For example, if the resulting number is greater than 0.0001 (or 1 in 10,000), it is beyond the range considered protective of human health by USEPA of less than 0.000001 to 0.0001 (or 1 in 1,000,000 to 1 in 10,000). Again, the numbers chosen to calculate this cancer slope factor are for the most sensitive individuals, and use the most conservative (worst-case) estimates or scenarios (a detailed discussion is provided under the “Cancer Health Risks” subsection).

The CSF and UR are upper-bound estimates (the highest estimates) of the incremental probability that an individual will develop cancer in his or her lifetime per unit intake. For ingestion exposures, the CSF represents the probability of developing cancer per unit dose (unit dose is measured in mg/kg-day, or milligram of active insecticide ingredient per kilogram human body weight per day); for inhalation exposures, the UR represents the probability of developing cancer per unit concentration, (concentration is measured in g/m³ or micrograms of active ingredient per cubic meter of air). As with non-cancer toxicity criteria, the majority of CSFs and URs are derived from studies in animals.
For those active ingredients for which a CSF or UR has not been developed at this time but for which there is some evidence to support a threshold for carcinogenic effects, a margin of exposure (MOE) analysis can be used to evaluate cancer risks (USEPA, 1998e). This approach is explained in more detail in the MOE Analysis subsection in the following Risk Characterization step.

**Toxicity Criteria for Organophosphate Adulticides**

The toxicity studies used to derive the toxicity criteria for malathion and naled, the two active ingredients in the organophosphate adulticides that are being considered for control of the mosquito-borne viruses, are examined individually in the following subsections. Some information from the review of the scientific literature, which was presented in the earlier “Public Health Characteristics of Proposed Insecticides” section, is repeated below, as this information is used to derive the toxicity criteria. Each subsection below ends with the USEPA-recommended reference dose or concentration for the active ingredient being discussed.

**Malathion**

*Non-Cancer Toxicity Criteria—Ingestion*

To assess human risk associated with short-term (acute) dietary exposures to malathion, USEPA’s Hazard Identification Assessment Review Committee (HIARC) recommends the use of two rabbit studies (MRID # 00152569, 40812001) (USEPA, 1997b). In a preliminary range-finding study, pregnant rabbits received orally administered malathion in corn oil at doses of 1, 25, 50, 100, 200, or 400 mg/kg-day (milligrams of malathion per kilogram rabbit body weight per day) on gestation days 6 through 18. Signs of maternal toxicity, such as decreases in body weight and food consumption, and fetal mortality were observed at 200 and 400 mg/kg-day, while no maternal or fetal effects were observed at 0, 25, 50, or 100 mg/kg-day. Based on this study, a no-observed-adverse-effect-level (NOAEL) of 100 mg/kg-day was determined based on toxicity in pregnant rabbits. In a subsequent prenatal developmental toxicity study, pregnant rabbits were again used, and malathion doses of 1, 25, 50, or 100 mg/kg-day were orally administered on gestation days 6 through 18 (MRID #40812001). A reduction in maternal body weight gains and a slight increased incidence of resorptions (fetuses broken down and reabsorbed internally by the mother) per rabbit were observed at 50 mg/kg-day, while no effects were observed at lower doses. Based on this subsequent study, a NOAEL of 25 mg/kg-day was determined based on the endpoint of reduction in maternal body weight gain. Based on the evidence in these two studies an overall NOAEL of 50 mg/kg-day is recommended by HIARC for use in risk assessments for acute oral exposures to malathion. The Committee recommends a total uncertainty factor (UF) of 100 to be applied to the NOAEL, which means that the NOAEL is to be divided by a factor of 100. The 100 uncertainty factor is the product of a 10-fold UF for extrapolating from animal dose-response data to human response and a 10-fold UF for variability in sensitivity within the human population (USEPA, 1997a). An additional factor for infants and children is not needed because: (1) developmental toxicity studies in rats and rabbits show no increased fetal sensitivity to malathion compared to adults; (2) there was not an increased sensitivity in rat pup reproductive effects in a two generation reproduction toxicity study; and (3) the database for malathion toxicology is complete (very extensive). Therefore, a NOAEL of 50 mg/kg-day and a UF of 100 were used to calculate a USEPA-recommended acute reference dose (RfD) of 0.5 mg/kg-day (USEPA, 1997a). That is, based on USEPA guidance, a 70-kg person (approximately 155 pounds) could potentially ingest up to 35 milligrams of malathion per day every day for a short-term exposure duration without experiencing any acute adverse non-cancer health effects from it.

USEPA’s Hazard Identification Assessment Review Committee recommended subchronic and chronic oral RfD for malathion is based on a chronic 24-month study in which rats (90 male and 90
female rats per experimental dose) were fed diets containing malathion. Diets initially contained either 0, 100, 500, 600 or 1200 ppm (part per million) malathion. However, the low dose of 100 ppm was reduced to 50 ppm after 3 months due to inhibition of blood enzyme activity in female rats at 100 ppm. (“Inhibition of blood enzyme activity” means that the malathion interfered with the normal activity of the enzymes; very minor effects of an active ingredient are often first noticeable in blood enzymes.) Therefore, a NOAEL of 50 ppm (2.4 mg/kg-day or 2.4 milligram malathion per rat body weight per day) was identified, based on inhibition of blood enzyme activity at 50 ppm malathion in the diet. A total uncertainty factor (UF) of 100 (based on a 10-fold UF for extrapolating from animal dose-response data to human response and a 10-fold UF to account for variability in sensitivity within the human population) was applied to the NOAEL. This results in a USEPA-recommended sub-chronic and chronic reference dose (RfD) of 0.024 mg/kg-day (USEPA, 2000a).

Non-Cancer Toxicity Criteria—Inhalation

For evaluating inhalation exposure to malathion for any time period, USEPA’s Hazard Identification Assessment Review Committee recommends toxicity criteria (exposure levels at which non-cancer health effects are likely to be negligible or nonexistent), based on a 90-day inhalation study in rats (USEPA, 1997b). In this study, rats were exposed to a malathion aerosol at concentrations of 0.1, 0.45, or 2.01 mg/L (milligram of malathion per liter of air) for 6 hours per day, 5 days per week, for 13 weeks (MRID# 43266601). Effects on survival, body weight, and food consumption were not observed at any of the doses tested (USEPA, 1997b). In this study, a lowest-observed-adverse-effect-Level (LOAEL) air concentration of 0.1 mg/L was established based upon sores observed in the nose and throat and inhibition of blood enzyme activity. A no-observed-adverse-effect-level (NOAEL) air concentration was not determined.

For calculating the reference concentration (RfC) for any exposure duration, USEPA recommends the use of a total uncertainty factor of 1000 (based on a 10-fold UF for extrapolating from animal dose-response data to human response, a 10-fold UF for variability in sensitivity within the human population, and a 10-fold UF for extrapolating from a LOAEL to a NOAEL) (USEPA, 1998d). Therefore, based on a total uncertainty factor of 1,000 and the LOAEL of 0.1 mg/L, the resulting USEPA-recommended RfC for inhalation exposures is 0.0001 mg/L (USEPA, 1998a). That is, based on USEPA guidance, an individual can be exposed to an air concentration of 0.0001 mg/L without experiencing non-cancer health effects, for any exposure duration.

Non-Cancer Toxicity Criteria—Dermal (Skin) Exposures

To assess residential and occupational human risk associated with both short-term and subchronic dermal exposures to malathion, the Hazard Identification Assessment Review Committee (HIARC) recommends the use of a rabbit study (MRID# 41054201) (USEPA, 1997b). In the recommended study, rabbits received 15 skin applications of malathion in concentrations of 0, 50, 300, or 1,000 mg/kg-day. The doses were applied for 6 hours per day, 5 days per week for 3 weeks. The only significant treatment-related effect observed was the inhibition of blood enzyme activity in both male and female rabbits at 300 and 1,000 mg/kg-day doses. This inhibition was not associated with any observable changes in body weight or food consumption. The overall NOAEL was 50 mg/kg-day. A total uncertainty factor (UF) of 100 (based on a 10-fold UF for extrapolating from animal dose-response data to human response and a 10-fold UF for variability in sensitivity within the human population) recommended by HIARC was applied to the NOAEL (USEPA, 1997b). The acute and subchronic toxicity value was calculated by dividing the NOAEL value of 50 mg/kg-day by the UF of 100 to obtain a USEPA-recommended skin toxicity value of 0.5 mg/kg-day for short-term and...
intermediate (subchronic) skin exposures. That is, for skin exposure of 0.5 mg/kg-day, there should be no harmful non-cancer health effects for short-term and intermediate exposure durations.

As discussed earlier, there are no studies available for evaluating long-term skin exposure to malathion. Therefore, the chronic oral RfD was used to evaluate chronic skin exposures, using a skin-absorbed dose for malathion. Based on studies in humans, HIARC recommends a value of 10 percent for skin (“a value of 10 percent” means that HIARC recommends estimating that 10 percent of the deposits of malathion residue on the skin are absorbed) (USEPA, 1998b).

Cancer Potency – Ingestion

There is limited evidence that malathion causes cancer. In the most recent bioassays (animal tests) used by USEPA for evaluating the carcinogenicity of malathion, the only treatment-related effects were benign (i.e., not likely to spread to other tissues or organs) liver tumors in mice and rats, one benign tumor in the nose of a female rat, and a benign skin tumor in a male rat (USEPA, 2000a). The significance of the liver tumors is not clear as these are benign tumors, and they were only seen at relatively high doses (approximately 1,500 mg/kg-day in mice and 800 mg/kg-day in rats). The nasal and skin tumors may be potentially significant, because a) they were observed at doses which were not as high; b) spontaneous occurrence of these benign tumors is relatively rare; and c) there were no such tumors in the concurrent control group of animals (animals that did not receive malathion in their treatments).

However, as noted earlier, USEPA is considering downgrading malathion’s cancer classification from likely to suggestive, which would indicate that although there is evidence that malathion is carcinogenic, there is not sufficient evidence for assessing malathion's carcinogenic potential in humans. However, it should be noted the proposal to downgrade malathion's classification does not have universal support within the EPA (USEPA, 2000b).

In spite of questionable results from USEPA's most recent cancer bioassays, this EIS evaluates malathion cancer risks via oral exposure using a CSF derived from an earlier cancer bioassay. In that bioassay, increased incidence of benign thyroid tumors was observed in male and female rats exposed to malathion. The cancer slope factor derived from this study was 0.00152 (mg/kg-d)^{-1}. As discussed above, to estimate an individual’s risk of developing cancer, the cancer slope factor for a particular active ingredient is multiplied by the dose the individual receives. If the resulting number is greater than 0.0001 (or 1 in 10,000), it is beyond the range that USEPA considers protective of human health. Therefore, in evaluating the cancer potency of malathion through the oral exposure pathway, if the CSF of 0.00152 (mg/kg-d)^{-1} (given above) is multiplied by the dose an individual receives (in mg/kg-d) and the result is less than 0.0001, it is within the range that USEPA considers protective of human health.

Cancer Potency—Inhalation

Although an inhalation unit risk (UR) was not derived for malathion by USEPA, this EIS conservatively evaluates malathion cancer risk via inhalation exposure by modifying the ingestion cancer slope factor (CSF). A unit risk estimate for inhalation can be calculated by dividing the oral cancer slope factor for malathion of 0.00152 (mg/kg-d)^{-1} by 70 kg (average human body weight), multiplying by the inhalation rate of 20 m³/day (cubic meters of air per day), and applying a unit correction factor of 0.001 mg?g (milligrams per micrograms) (USEPA, 1997b). The resulting unit risk for malathion is 0.000000434 (µg/m³)^{-1}.
**Naled**

**Non-Cancer Toxicity Criteria—Ingestion**

USEPA’s Hazard Identification Assessment Review Committee recommends using a 28-day study in rats as a basis for the acute reference dose (RfD). The critical effects in this study were inhibition of blood and brain enzyme activity. The **USEPA-recommended acute RfD of 0.01 mg/kg-day** is based on a no-observed-adverse-effect-level (NOAEL) of 1.0 mg/kg-day (milligrams naled per kilogram rat body weight per day) and a total UF of 100 (based on a 10-fold UF for extrapolating from animal dose-response data to human response and a 10-fold UF for variability in sensitivity within the human population) (USEPA, 1998c).

The subchronic and chronic RfDs for naled are based on a 2-year study where rats (55 animals per sex per dose) were fed diets containing naled at doses of 0, 0.2, 2, or 10 mg/kg-day. Brain enzyme activity was decreased by approximately 24 percent in both male and female rats, at 2 mg/kg-day. Therefore, the NOAEL was determined to be 0.2 mg/kg-day. **Applying the total UF of 100 (based on a 10-fold UF for extrapolating from animal dose-response data to human response and a 10-fold UF for variability in sensitivity within the human population)** (USEPA, 1998c), yields the USEPA-recommended subchronic and chronic RfD of 0.002 mg/kg-day. That is, an individual exposed (through ingestion) to less than 0.0002 mg/kg-day of naled on daily basis for a short-term exposure period, would not experience any non-cancer adverse health effects.

**Non-Cancer Toxicity Criteria—Inhalation**

USEPA’s Hazard Identification Assessment Review Committee recommends a 90-day inhalation study in rats for deriving the reference concentration (RfC) for naled. A NOAEL of 0.00023 mg/L (milligram naled per liter of air) was identified from this study, based on inhibition of blood enzyme activity (USEPA, 1998b). **This NOAEL is divided by a total UF of 100 (based on a 10-fold UF for extrapolating from animal dose-response data to human response and a 10-fold UF for variability in sensitivity within the human population)** resulting in a USEPA-recommended RfC of 0.0000023 (mg/L), for inhalation exposures of any exposure duration (USEPA, 1998c). Therefore, an individual exposed to a daily dose (through inhalation) of naled of up to 0.0000023 mg/L would not be expected to experience any non-cancer adverse health effects for any exposure duration.

**Non-Cancer Toxicity Criteria—Dermal (Skin) Exposures**

USEPA’s Hazard Identification Assessment Review Committee recommends use of a 28-day rat skin study for deriving the acute and subchronic skin reference dose (RfD) for naled. The critical effects in this study were inhibition of blood and brain enzyme activity. **The NOAEL of 1.0 mg/kg-day was divided by a total UF of 100 (based on a 10-fold UF for extrapolating from animal dose-response data to human response, and a 10-fold UF to account for variability in sensitivity within the human population)**, resulting in a USEPA-recommended acute and subchronic skin RfD of 0.01 mg/kg-day (USEPA, 1998b,c). Therefore, based on USEPA guidance, an individual’s daily exposure level for short-term and intermediate exposure durations through the skin should be below the RfD of 0.01 mg/kg-day in order for no acute or subchronic non-cancer effects to be experienced.

As with malathion, there are no studies available for evaluating long-term skin exposure to naled. **Therefore, the chronic oral RfD was used to evaluate chronic skin exposures.** A skin absorption value of 100 percent is considered appropriate by the USEPA, based on similarities in health responses for naled for oral and skin exposures (USEPA, 1999c).
Cancer Potency—Ingestion and Inhalation

Although naled does have mutagenic activity in bacterial cells, there was no increase in neoplastic (growing) lesions in treated animals vs. control animals in a 2-year study in rats (Braun et al., 1983; ACGIH, 1998).

Furthermore, results from whole-animal DNA sensitivity studies (Braun et al., 1983; USEPA, 2000d) suggest that that naled is not genotoxic (capable of altering genetic material) at exposure levels higher than would be expected from spraying of naled in New York City. Furthermore, isolated cell tests reviewed by the USEPA (2000d) also suggest that naled exposure is not associated with chromosomal aberrations. Furthermore, naled does not induce changes in chromosomes in cell culture studies (USEPA, 2000d).

Based on the lack of a carcinogenic response in these studies reviewed by USEPA, there is sufficient evidence to suggest that naled is not carcinogenic (USEPA, 2000d).

Toxicity Criteria for Pyrethroids Adulticides

The following subsections examine the toxicity studies used to derive the toxicity criteria for the three pyrethroid active ingredients—permethrin, resmethrin, and sumithrin—that are being considered for adult mosquito control as part of the Proposed Action. Each subsection below presents the USEPA-recommended toxicity criteria for the active ingredient being discussed. The toxicity criteria can be interpreted in the same manner as described in the “Toxicity Criteria for Organophosphate Adulticides” section above.

Permethrin

Non-Cancer Toxicity Criteria—Ingestion

The acute oral reference dose (RfD) was derived from an acute neurotoxicity study by McDaniel and Moser (1993) as summarized in the "Tox 1-liner" database (USEPA, 2000h). Rats were fed permethrin at single doses of 25, 75, or 150 mg/kg (milligrams permethrin per kilogram rat body weight) in corn oil. The low-observed-effect-level (LOEL)\(^8\) was determined to be 75 mg/kg based on increased excitability, aggressive behavior, abnormal coordination, decreased grip strength, decreased activity, and slight decreases in body weight. The NOEL was 25 mg/kg. A total UF of 100 (based on a 10-fold UF for extrapolating from animal dose-response data to human response and a 10-fold UF for variability in sensitivity within the human population) was applied to the NOEL, resulting in an acute RfD of 0.25 mg/kg-day.

The subchronic RfD was derived from a 13-week neurotoxicity study in rats conducted by the FMC Toxicology Lab in 1993, as summarized in the "Tox 1-liner" database (USEPA, 2000h). The rats were dosed at levels of 0-190 mg/kg-day (MRID #42933701). Neurological effects including tremors, abnormal posture, splayed limbs, and decreased grip strength were observed at doses of 91.51 mg/kg-day in males and 111.37 mg/kg-day in females. The NOEL for this study was 15.49 mg/kg-day (milligrams permethrin per kilogram rat body weight per day) in male rats. A total UF of 100 (based on a 10-fold UF for extrapolating from animal dose-response data to human response and a 10-fold UF for variability in sensitivity within the human population) was applied to the NOEL, resulting in a subchronic RfD of 0.155 mg/kg-day.

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\(^8\) The LOEL is different from the Lowest Observed Adverse Effect Level (LOAEL), which is the lowest level at which biologically significant adverse effects are observed and is therefore a more subjective criterion because there is no firm definition of an adverse effect. The LOEL may be a more conservative criterion than the
USEPA recommends the use of a chronic RfD of 0.05 mg/kg-day (USEPA, 1987a). This value is based on a 2-year study conducted by the FMC Corporation. The no-observed-adverse-effect-level (NOAEL) was established at 5 mg/kg-day. Increases in liver weights were observed at 25 mg/kg-day. A total UF of 100 (based on a 10-fold UF for extrapolating from animal dose-response data to human response and a 10-fold UF for variability in sensitivity within the human population) was applied in the RfD calculation.

Non-Cancer Toxicity Criteria—Inhalation

Inhalation criteria for all exposure durations were derived from a three-month inhalation study in rats identified from USEPA’s "Tox 1-liner" database for permethrin (USEPA, 2000h). Tremors, convulsions, and increases in liver enzyme activity were used to identify the LOEL at 0.5 mg/L (milligram of permethrin per liter of air) (MRID #00038415). The no-observed-effect-level (NOEL) for this study was determined to be 0.25 mg/L. For the acute and subchronic reference concentration (RfC), a total uncertainty factor (UF) of 100 (based on a 10-fold UF for extrapolating from animal dose-response data to human response and a 10-fold UF for variability in sensitivity within the human population) was applied to the NOEL resulting in a toxicity criterion of 0.0025 mg/L. An additional UF of 10 was used to extrapolate from subchronic to chronic exposures, resulting in a chronic RfC of 0.00025 mg/L.

Non-Cancer Toxicity Criteria—Dermal (Skin) Exposure

The acute and subchronic reference dose (RfD) for skin exposures is 1.5 mg/kg-day (milligrams permethrin per kilogram rat body weight per day), based on 3-week skin exposure study using rats (MRID# 41143801 and 42653301) from USEPA’s Tox 1-Liner database information for permethrin (USEPA, 2000h). The NOEL for this study was 150 mg/kg-day, based on increased liver weight in females at 500 mg/kg-day. A total UF of 100 (based on a 10-fold UF for extrapolating from animal dose-response data to human response and a 10-fold UF for variability in sensitivity within the human population) was applied in the RfD calculation.

There are no studies available for evaluating long-term skin exposure to permethrin. Therefore, the chronic oral RfD is used to evaluate chronic skin exposures, using a USEPA-recommended skin absorption factor of 50 percent (USEPA, 2000d).

Cancer Potency—Ingestion

USEPA has classified permethrin as a possible human carcinogen, based on limited evidence of carcinogenicity in animals (lung and liver tumors in female mice) but no data from human population studies. USEPA recommends using a cancer slope factor of 0.0184 (mg/kg-day)^{-1} for oral exposures (USEPA, 2000h). It should be noted that the USEPA is currently reviewing the use of the cancer slope factor of 0.0184 (mg/kg-day)^{-1}.

Cancer Potency—Inhalation

Although an inhalation unit risk (UR) was not derived for permethrin, this EIS conservatively evaluates the permethrin cancer risk via inhalation exposure by modifying the oral cancer slope factor. A unit risk estimate for inhalation can be calculated by dividing the oral slope factor for permethrin of 0.0184 (mg/kg-d)^{-1} by 70 kg (average human body weight), multiplying by the inhalation rate of 20 m³/day (cubic meters per day), and applying a unit correction factor of 0.001 LOAEL, as it considers effects that may not be considered adverse, such as changes in food consumption. A similar distinction exists between the NOEL and NOAEL.
mg/?g (milligram per microgram) (USEPA, 1997a). The resulting unit risk for permethrin is 0.00000526 (µg/m^3)^-1.

Resmethrin

Non-Cancer Toxicity Criteria—Ingestion

Both the acute and subchronic reference dose (RfD) for oral exposure were derived from a study conducted by the Food and Drug Research Laboratory (1980) as summarized in USEPA’s "Tox 1-liner" database (USEPA, 2000f). In this study, dogs were fed resmethrin at doses of 0, 10, 30, 100, and 300 mg/kg-day for six-months (MRID #00157961). Liver-weight increases in females occurred at 30 mg/kg-day. The no-observed-effect-level (NOEL) was determined to be 10 mg/kg-day. A total uncertainty factor (UF) of 100 (based on a 10-fold UF for extrapolating from animal dose-response data to human response and a 10-fold UF for variability in sensitivity within the human population) was applied to the NOEL, resulting in a RfD of 0.1 mg/kg-day.

For chronic human exposure scenarios, the USEPA recommends the use of an oral RfD of 0.03 mg/kg-day as the level at which resmethrin is not likely to cause adverse health effects. This value is based on a three-generation study in rats in which pup weight and viability were lowered at levels of 25 mg/kg-day. A NOAEL was not established from this study because this level was the lowest dose tested. A total UF of 1000 was applied in the RfD calculation (based on a 10-fold UF for extrapolating from animal dose-response data to human response, a 10-fold UF for variability in sensitivity within the human population, and a 10-fold UF to account for the lack of a definitive NOAEL value) (USEPA, 1989b, 2000f).

Non-Cancer Toxicity Criteria—Inhalation

Inhalation criteria for all exposure durations (acute, subchronic and chronic) were derived from a three month inhalation study in rats by the Huntingdon Research Corp (1985) as summarized in the USEPA’s "Tox 1-liner" database (USEPA, 2000f). This study was selected because it appeared to produce the most sensitive toxic effect in the most sensitive species. The low-observed-effect-level (LOEL) for this study was 0.1 mg/L (milligram resmethrin per liter of air). At this concentration, male rats exhibited behavioral effects and decreases in serum glucose (blood sugar levels); females exhibited decreased body weight gain and increases in ammonia in blood (MRID #00158476). A NOEL concentration was not established for this study.

To derive the acute and subchronic reference concentration (RfC), the LOEL of 0.1 mg/L was divided by a total UF of 1000 (based on a 10-fold UF for extrapolating from animal dose-response data to human response, a 10-fold UF for variability in sensitivity within the human population, and a 10-fold UF to account the lack of a definitive NOEL value) resulting in an RfC of 0.0001 mg/L. The chronic RfC is set at 0.00001 mg/L, with the addition of another UF (for a total uncertainty factor of 10,000) to account for extrapolating from a subchronic exposure to a chronic exposure.

Non-Cancer Toxicity Criteria—Dermal (Skin) Exposure

The acute and subchronic reference dose (RfD) for skin exposures is 10 mg/kg-day (milligram resmethrin per kilogram human body weight per day), based on a NOEL of 1,000 mg/kg-day (milligrams of resmethrin per kilogram of rabbit body weight per day) which was the highest dose at which there was no effect in a 3-week skin exposure study in rabbits (USEPA, 2000f, MRID# 42066901). A total UF of 100 (based on a 10-fold UF for extrapolating from animal dose-response data to human response and a 10-fold UF for variability in sensitivity within the human population) was applied in the RfD calculation.
There are no studies available for evaluating long-term dermal skin to resmethrin. Therefore, the chronic oral RfD for resmethrin is used to evaluate chronic skin exposures. A skin absorption value of 10 percent is considered appropriate by USEPA based on of the ratio of subchronic oral/skin RfD, with an additional uncertainty factor of 10 (USEPA, 1999a, 2000f).

Cancer Potency—Ingestion and Inhalation
The literature suggests that resmethrin is not mutagenic (i.e., that it does not cause mutations in genetic material in cells) in either bacteria or mammalian cells, and that it does not induce changes in chromosomes or unwanted formation of genetic material (USEPA, 2000b; WHO, 1989). However, there was a statistically significant increase in liver tumors in rats, at approximately 131 mg/kg-day in one reported study (USEPA, 2000f). In other studies reported in the literature, increases in treatment-related tumors were not observed in rats at doses as high as 5,000 mg/kg-day, or in mice at doses up to approximately 200 mg/kg-day (USEPA, 2000f; WHO, 1989.)

Although some information is available to evaluate the carcinogenic potential of resmethrin, USEPA has not yet undertaken this evaluation pending submission of additional carcinogenicity data by the manufacturers of resmethrin (USEPA, 2000f). Therefore, a cancer potency factor for resmethrin is not available at this time for use in this EIS risk assessment.

Sumithrin
Non-Cancer Toxicity Criteria—Ingestion
Both the acute and subchronic reference dose (RfD) were determined using a study performed by Life Science Research (1983) as summarized from the USEPA "Tox 1-liner" database for sumithrin (USEPA, 2000g). In this study, sumithrin was fed to rats for 13 weeks (MRID# 40998202). A LOEL was established at 216 mg/kg-day based on increases in liver weights and decreases in cholesterol in both male and female rats. A NOEL was established at 70 mg/kg-day. A total UF of 100 (based on a 10-fold UF for extrapolating from animal dose-response data to human response and a 10-fold UF for variability in sensitivity within the human population) was applied to the NOEL to derive an acute and subchronic RfD of 0.7 mg/kg-day.

The USEPA Office of Pesticide Programs recommends an oral chronic RfD of 0.071 mg/kg-day, as the exposure level at which no human health effects are expected to occur. This is based on a 1-year feeding study in dogs, in which liver effects were observed at levels of 26.8 mg/kg-day. The NOAEL was established at 7.1 mg/kg-day. A total uncertainty factor (UF) of 100 (based on a 10-fold UF for extrapolating from animal dose-response data to human response and a 10-fold UF for variability in sensitivity within the human population) was applied to the NOAEL to derive the RfD (USEPA, 1996).

Non-Cancer Toxicity Criteria—Inhalation
Inhalation criteria for all exposure durations were derived from a three-month inhalation study by Huntington Corporation (1989) in rats, as summarized in USEPA’s "Tox 1-liner" database for sumithrin (USEPA, 2000g). In this study, rats were exposed to sumithrin aerosols at concentrations of 0-1.066 mg/L (milligram sumithrin per liter of air) for 6 hours/day, 5 days/week for 13 weeks (MRID #41289201). Health effects observed in this study included increased liver and thyroid weights, slight changes of the thyroid, increased adrenal gland weights and minor lesions on adrenal glands. These effects were observed at concentrations of 1.1 mg/L, which is considered the LOAEL for the study. The NOAEL in this study is 0.291 mg/L. Using a total UF of 100 (based on a 10-fold UF for extrapolating from animal dose-response data to human response and a 10-fold UF for variability in
sensitivity within the human population), the acute and subchronic reference concentration are both 0.00291 mg/L. The chronic RfC is 0.000291 mg/L, using an additional UF of 10 to account for the extrapolating from a subchronic exposure to chronic exposure.

Non-Cancer Toxicity Criteria—Dermal (Skin) Exposure
The acute/subchronic RfD of 10 mg/kg-day for skin exposures is based on a no-observed-effect-level (NOEL) of 1000 mg/kg-day (highest dose tested) in a 3-week skin exposure study in rats (USEPA, 2000g, MRID# 4100971). A total UF of 100 (based on a 10-fold UF for extrapolating from animal dose-response data to human response and a 10-fold UF for variability in sensitivity within the human population) was applied in the RfD calculation.

There are no studies available for evaluating long-term skin exposure to sumithrin. Therefore, the chronic oral RfD for sumithrin is used to evaluate chronic skin exposures. A skin absorption value of 70 percent is considered appropriate by USEPA based on the ratio of acute-subchronic oral/skin RfD, with an additional uncertainty factor of 10 (USEPA, 1999a, 2000g).

Cancer Potency—Ingestion and Inhalation
The majority of cell culture bioassays suggest that sumithrin is carcinogenic only at doses where there is overt evidence of non-cancer adverse effects (USEPA, 2000g, WHO, 1990b). Increased incidence of cancer was not detected at doses as high as 450 mg/kg-day in several rat and mice studies as summarized in USEPA's tox-liners for sumithrin (USEPA, 2000g). Increased incidence of liver tumors was observed in male and female rats at 1,116 mg/kg-day (USEPA, 2000g). However, this dose was associated with excessive liver toxicity (excessive death of liver cells), suggesting that the increased incidence of cancer could be a secondary manifestation of liver toxicity, rather than a primary effect of sumithrin. Therefore, cancer potency factors for sumithrin are not available at this time for use in this risk assessment.

Toxicity Criteria for Synergist in Pyrethroids
The toxicity studies used to derive the toxicity criteria for the synergist, PBO (PBO), present in pyrethroid adulticides are examined below.

Piperonyl Butoxide
Non-Cancer Toxicity Criteria—Ingestion
The acute reference dose for oral exposures was derived from a developmental toxicity study in which pregnant rats were exposed to PBO during gestation days 6 through 15 (USEPA, 2000e, MRID # 42380801). A maternal no-observed-effect-level (NOEL) of 200 mg/kg-day was derived from this study. A total uncertainty factor (UF) of 100 (based on a 10-fold UF for extrapolating from animal dose-response data to human response and a 10-fold UF for variability in sensitivity within the human population) was applied to this NOEL, resulting in an acute oral RfD of 2 mg/kg-day.

The subchronic and chronic oral RfD for PBO recommended by USEPA's Office of Pesticide Programs is 0.0175 mg/kg-day. This RfD is based on a 1-year feeding study in dogs in which body and liver weight changes were observed at 75 mg/kg-day. The NOAEL from this study was 17.5 mg/kg-day. A total UF of 1000 (based on a 10-fold UF for extrapolating from animal dose-response data to human response, a 10-fold UF for variability in sensitivity within the human population, and a 10-fold UF for extrapolating from a subchronic exposure to a chronic exposure) was used to derive the RfD (USEPA, 1996).
Non-Cancer Toxicity Criteria—Inhalation

Inhalation toxicity criteria were derived from a 3-month inhalation study in rats, identified in USEPA’s “Tox 1-Liner” database for PBO (USEPA, 2000e). The NOAEL was 0.074 mg/L (milligram PBO per liter of air). A total UF of 100 (based on a 10-fold UF for extrapolating from animal dose-response data to human response and a 10-fold UF for variability in sensitivity within the human population) was applied to the NOAEL to derive a toxicity criterion of 0.00074 mg/L for acute and subchronic exposures. For chronic exposures an additional UF of 10 was used to extrapolate from a subchronic exposure to a chronic exposure, resulting in a chronic reference concentration (RfC) of 0.000074 mg/L.

Non-Cancer Toxicity Criteria—Dermal (Skin) Exposure

The acute and subchronic reference dose for skin exposures is 10 mg/kg-day, based on a NOEL of 1,000 mg/kg-day (highest dose tested) in a 3-week skin exposure study in rabbits (USEPA, 2000e, MRID# 42218201). A total UF of 100 (based on a 10-fold UF for extrapolating from animal dose-response data to human response and a 10-fold UF for extrapolating from subchronic to chronic exposures) was applied to the NOEL to derive the RfD.

There are no studies available for evaluating long-term skin exposure to PBO. Therefore, the chronic oral RfD for PBO is used to evaluate chronic skin exposures. A skin absorption value of 20 percent is considered appropriate by USEPA based on the ratio of acute oral/skin RfD (USEPA, 1999a, 2000e).

Cancer Potency—Ingestion and Inhalation

There is no evidence that PBO is mutagenic in bacteria, and PBO does not appear to induce either chromosomal aberrations or unscheduled DNA synthesis (USEPA, 2000e). Evidence regarding the carcinogenic potential of PBO in mammals is conflicting. Initial bioassays by the National Cancer Institute and Bioresearch Labs (Quebec, Canada) indicated that PBO was not carcinogenic in either rats or mice (NCI, 1978; USEPA, 2000e). However, treatment-related increases in both rats and mice were observed in several more recent studies (Takahashi et al., 1994a,b; USEPA, 2000e). Based on these data, USEPA has classified PBO as to its carcinogenic potential as a Group C - possible human carcinogen (USEPA, 2000e). The Group C classification was based on statistically significant increases in liver tumors in mice (adenomas and carcinomas).

At this point USEPA recommends using a RfD and Margin of Exposure (MOE) approach (discussed in the next section), rather than a cancer slope factor, for evaluating carcinogenic potential for PBO. According to USEPA, the MOE approach is appropriate for PBO based on observations of tumors only at very high doses and a low mutagenic potential for PBO (USEPA, 2000e).

Summary of Toxicity Criteria for the Active Ingredients Under Consideration

Table 3.C-7 presents a summary of the reference doses (RfDs), reference concentrations (RfCs), cancer slope factors (CSFs) and unit risks (URs) derived above for each of the active ingredients under consideration in the EIS.

As discussed above, an RfD or RfC is defined as a chemical-specific dose or concentration to which people, including sensitive individuals, can be exposed on a daily basis without adverse health effects over a duration of exposure.

The CSF and UR indicate the increased probability that an individual will develop cancer following a specific exposure to a chemical. This increased probability is in addition to everyone’s probability of
developing cancer due to variations in genetic risk factors and everyday exposures to a multitude of chemicals.

In Table 3.C-7, the values under the “Acute,” “Subchronic,” and “Chronic” headings represent thresholds—the amounts to which it has been determined, using USEPA guidance, that the most sensitive individuals can be exposed to over a specific exposure duration without experiencing any non-cancer adverse health effects (such as reproductive effects). If an individual is exposed to less than this amount, there should be no harmful effects. If the individual is exposed to more than this threshold amount, there is a possibility—but not a certainty—that the individual may experience harmful effects. For example, Table 3.C-7 indicates that, for chronic exposure to malathion through ingestion, if a person is exposed to a daily dose of up to 0.024 milligrams of malathion over a lifetime, there should be no non-cancer adverse health effects.

The information under “Cancer Risk” represents the additional probability of contracting cancer over a lifetime. As discussed earlier, to estimate an individual’s risk of developing cancer, the CSF for a particular active ingredient is multiplied by the dose the individual receives. If the resulting number is greater than 0.0001 (or 1 in 10,000), it is beyond the range that the USEPA considers protective of human health.

**Risk Characterization**

In this section, the information developed in the previous sections (“Exposure Analysis” and “Toxicity Analysis”) are combined to describe the likelihood and nature of potential health effects that human populations may experience following exposures to adulticides associated with New York City’s control of adult mosquitoes. The Risk Characterization Section contains the following subsections:

- **Evaluation of Non-cancer Health Risks**, which describes whether exposure to the active ingredients associated with the control of adult mosquitoes can be associated with any non-cancer health risks as described earlier in this public health risk assessment.

- **Evaluation of Cancer Risks**, which describes whether exposure to malathion and permethrin can be associated with a significant increase in cancer health risks. (For all other active ingredients in this study, there is either no evidence of carcinogenicity or limited evidence, with no established CSF as determined from the toxicity analysis.)

- **Margin of Exposure Analysis**, which evaluates cancer risks if there is sufficient evidence that there is a threshold dose for carcinogenic effects.

- **Evaluation of Acute Exposures**, which describes whether adverse health risks can be associated with exposure to adulticides immediately after application (i.e., contact with spray) or soon thereafter (i.e., in adulticide drift).

- **Alternative Assumptions Analysis**, which discusses the implications of the results of this public health risk assessment associated with the selection of exposure assumptions.

**Evaluation of Non-Cancer Health Risks**

Non-carcinogenic health risks are characterized as the increased likelihood (as opposed to incremental probability) that an individual will suffer adverse health effects (excluding cancer) as a result of chemical exposure. USEPA and other agencies have developed estimates of acceptable daily doses (the reference dose or concentration) over an exposure duration. USEPA defines the chronic reference dose (RfD) as an estimate of a daily exposure level for the human population, including sensitive individuals (e.g., elderly, fetus, pregnant women, chronically ill), that is likely not to create an appreciable risk of deleterious effects during a lifetime (USEPA, 1989a).
Table 3.C-7
USEPA Recommended Toxicity Criteria
To evaluate non-cancer risks, the ratio of the average daily dose associated with a particular exposure pathway to the acceptable daily dose is calculated, as shown below. This ratio, referred to as a “hazard quotient,” or HQ, indicates whether a specific exposure to an adulticide’s active ingredient (e.g., inhalation of malathion in air by a child resident) is likely to result in adverse health effects.

Therefore, if the ratio is equal to or less than one, no adverse health effects are expected from a daily exposure to the active ingredient (i.e., the exposure level is less than the amount to which people, including sensitive individuals, can be exposed on a daily basis without experiencing adverse non-cancer health effects).

An individual may be exposed to an adulticide through a variety of exposure pathways, as described earlier under the “Exposure Analysis” section. For each individual, the hazard quotients (HQs) for all the relevant pathways for a specific active ingredient are then summed to derive a hazard index (HI). This HI represents the sum of all potential exposures to a specific active ingredient. Thus, if the HI is less than or equal to 1.0, no adverse non-cancer health effects are expected. An HI greater than 1.0 does not mean that adverse human health effects will occur, but rather that further evaluation is required.

For all pathways, except inhalation, the HQ is calculated using the following equation:

\[ HQ \, ? \, \frac{ADD}{RfD} \]

Where:

- HQ = The Hazard Quotient associated with exposure to the chemical via the specified route of exposure (dimensionless – there are no units associated with the HQ)
- ADD = The estimated Average Daily Dose of the chemical via the specified exposure route (in mg/kg-day)
- RfD = The oral Reference Dose or appropriate substitute toxicity value identified for the chemical of concern (mg/kg-day); this is the dose to which people, including sensitive individuals, can be exposed on a daily basis without adverse health effects.

For inhalation exposures, the HQ was calculated using the following equation:

\[ HQ \, ? \, \frac{EPC_{air}}{RfC} \]

Where:

- HQ = The Hazard Quotient associated with exposure to the chemical (active ingredient) via the specified route of exposure (dimensionless—there are no units associated with the HQ).
- EPC_{air} = The Exposure Point Concentration of the constituent in air (µg/m³), meaning the amount of active ingredient to which people are exposed in the air.
The Reference Concentration or substitute toxicity value identified for the chemical of concern (mg/m³); this is concentration to which people, including sensitive individuals, can be exposed on a daily basis without adverse health effects.

The equations listed above are used to calculate an HQ for each pathway-individual active ingredient combination (e.g., inhalation by child resident of malathion in indoor air). The HQs are presented in extensive tables found in Appendix 3.C-3. Exposures to an adulticide’s active ingredient via all the possible exposure pathways for a specific population (e.g., exposure to malathion via all exposure pathways for a child resident) are grouped together, and the individual HQs are then added together to derive a Hazard Index (HI). An HI is the total of the individual HQs for each adulticide active ingredient for all pathways by a specific population group (e.g., young child resident). These HIs are presented in Appendix 3.C-4 and summarized in Tables 3.C-8 and 3.C-9. Table 3.C-8 presents the HIs for average exposures for each of the individual populations, and Table 3.C-9 presents the HIs for reasonable maximum exposures.

As shown in Tables 3.C-8 and 3.C-9, none of the evaluated human populations (i.e., child and adult residents, workers, homeless people, schoolchildren and teachers, and park visitors and community gardeners) have HIs exceeding a value of 1.0 for any of the six active ingredients evaluated in this assessment under average or reasonable maximum exposures. Therefore, the results indicate that non-cancer adverse health effects are not expected for any of these exposure scenarios. Although the HIs are still below 1.0 for naled, potential exposures to naled resulted in the highest ratio; whereas potential exposures to sumithrin resulted in the lowest ratios of all the six active ingredients in adulticides evaluated in this assessment. For example, Table 3.C–8 shows that for the most exposed group – adults exposed over 30 years under reasonable maximum-exposure conditions – the HI for naled is 0.51, whereas for the same group of adults, the HI for sumithrin is 0.0014. Because of the various safety factors incorporated into the derivation of the non-cancer health criteria to account for the variability in sensitivity of people, including pregnant women, the developing fetus, the elderly, and the chronically ill, non-cancer adverse health effects associated with potential exposures to any of the six active ingredients are not expected even for these sensitive individuals.

A limitation of this analysis relates to the fact that it does not consider the theoretical possibility that the simultaneous exposure to a mixture of several chemicals (i.e., adulticides, synergists and inerts) might result in synergistic adverse effects. This limitation is not unique to this EIS, but rather is due to the paucity of scientific knowledge concerning the effects of exposures to chemical mixtures.

**Evaluation of Cancer Health Risks**

Cancer risks for permethrin and malathion are evaluated using a cancer slope factor (CSF). Although there is some evidence that resmethrin, sumithrin, and PBO may be carcinogenic, cancer slope factors have not been derived for these compounds by USEPA. Therefore we evaluate cancer risks for resmethrin, sumithrin, and PBO using a Margin of Exposure (MOE) analysis, as discussed later in this section. As discussed above in the toxicity analysis, naled is not considered to be carcinogenic in humans. Therefore, cancer risks for naled are not evaluated.
Table 3.C-8
All Populations and Pathways - Summary of Non-Cancer Risks (Average Exposures)
| Table 8 cont |
Table 3.C-9
All Populations and Pathways - Summary of Non-Cancer Risks (Reasonable Maximum Exposures)
Carcinogenic risks are characterized as the upper-bound (highest estimated) incremental probability that an individual will develop cancer during his or her lifetime due to chemical exposure (USEPA, 1989a). It should be noted that this is a conservative model that may over-estimate the actual risks. The term "incremental" implies that this risk corresponds to the added probability of cancer above the background cancer risk typically experienced by all individuals in the course of daily life. Cancer risks are expressed as a unitless upper bound probability (e.g., one in a million, or $10^{-6}$) of an individual developing cancer over a lifetime, above the background risk, as a result of the exposure. USEPA has determined an acceptable target risk range of less than 0.000001 (i.e., one in a million) to 0.0001 (i.e., one in ten thousand).

\[ \text{Cancer Risk} = \text{ADD} \times \text{CSF} \]

Where:

- \( \text{CSF} \) = Cancer Slope Factor for the chemical, appropriate to the specific exposure pathway (measured in (mg/kg-day)$^{-1}$ – equivalent to (kg-day/mg))
- \( \text{ADD} \) =Average Daily Dose (measured in mg/kg-day).

For inhalation, cancer risk is the average daily exposure (ADE) concentration of the substance in air, multiplied by the unit risk factor (UR):

\[ \text{Cancer Risk} = \text{ADE} \times \text{UR} \]

The equations above are first used to calculate the cancer risk for each pathway-population combination. Total cancer risks for a given population are then determined by adding together the risks for each pathway for a given population.

The Total Excess Lifetime Cancer Risk for each population is determined by adding together the risks for each complete pathway for each population. A summary of total cancer risks for malathion and permethrin are presented in Table 3.C-10 for average exposures, and in Table 3.C-11 for reasonable maximum exposures. A further breakdown of the total cancer risks by pathway is presented in Appendix 3.C-4 for each of the population groups.

Carcinogenic risks characterized for the human populations listed above are within or below the USEPA-determined acceptable target risk range of less than 0.000001 to 0.0001. (Or from 1 in 1 million to 1 in 10,000.) Although still within an acceptable target risk range, the highest cancer risks for all human populations evaluated in this assessment are associated with exposures to permethrin. The highest estimated cancer risk of 0.00000489 (i.e. roughly 1 in 200,000) is for residents ("child and adult combined" to describe a child who grows up to be an adult during the spraying period) under reasonable maximum exposures to permethrin. This value is the added probability of getting cancer above the background cancer risk typically experienced by all individuals in the course of daily life. Unfortunately, taken all cancers together, cancer is a fairly common disease. In New York City alone, 30,000 new cases of cancer are diagnosed each year. Generally, the incidence of cancer increases with age and often varies by place of residence, racial/ethnic background and other demographic features of the population. Nationally, cancer is the third leading cause of death. For New York City residents, cancer has been the second leading cause of death for both men and women. The American Cancer Society has determined that the lifetime probability of developing cancer is 43.5 percent (0.435, or one chance in 2.3) in men and 38.3 percent (0.383, or one chance in 2.6) in women (Greenlee et. al., 2001). Cancer risks associated with exposures to malathion are approximately 10 to 100 times lower than risks associated with permethrin. For malathion, for example, Table 3.C-10 shows that a resident adult (including those belonging to a sensitive population group) who is potentially exposed to malathion under reasonable maximum exposure conditions over a lifetime would have a 0.0000000952—or approximately one in ten million—increased risk of developing cancer.
## Table 3.C-10
All Populations and Pathways—Summary of Cancer Risks (Average Exposures)

<table>
<thead>
<tr>
<th>Population</th>
<th>Total Chronic Cancer Risks</th>
<th>Malathion</th>
<th>Permethrin</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Resident</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Child</td>
<td></td>
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<td>0.0000012</td>
</tr>
<tr>
<td>Adult</td>
<td></td>
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<td>0.0000021</td>
</tr>
<tr>
<td>Sum for Lifetime</td>
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<td>0.0000033</td>
</tr>
<tr>
<td><strong>Worker</strong></td>
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<td></td>
<td></td>
</tr>
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<td>Commercial/Industrial</td>
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<td>0.00000018</td>
</tr>
<tr>
<td>Public Works</td>
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<td>0.0000002</td>
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<tr>
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<td></td>
<td></td>
</tr>
<tr>
<td>Adult</td>
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<td>0.00000045</td>
</tr>
<tr>
<td><strong>School</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Older Child (6-12)</td>
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<td>0.00000044</td>
</tr>
<tr>
<td>Adolescent (13-18)</td>
<td></td>
<td>0.00000001</td>
<td>0.00000039</td>
</tr>
<tr>
<td>Adult (&gt;18)</td>
<td></td>
<td>0.000000017</td>
<td>0.00000063</td>
</tr>
<tr>
<td><strong>Park Visitor</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Younger Child (0-6)</td>
<td></td>
<td>0.000000023</td>
<td>0.00000088</td>
</tr>
<tr>
<td>Older Child (7-12)</td>
<td></td>
<td>0.000000011</td>
<td>0.00000036</td>
</tr>
<tr>
<td>Adolescent (13-18)</td>
<td></td>
<td>0.000000083</td>
<td>0.00000024</td>
</tr>
<tr>
<td>Adult (&gt;18)</td>
<td></td>
<td>0.000000053</td>
<td>0.00000019</td>
</tr>
<tr>
<td>Community Gardener (&gt;18)</td>
<td></td>
<td>0.000000053</td>
<td>0.00000019</td>
</tr>
</tbody>
</table>
Table 3.C-11: All Populations and Pathways - Summary of Cancer Risks (Reasonable Maximum Exposures)

<table>
<thead>
<tr>
<th>Population</th>
<th>Total Chronic Cancer Risks</th>
<th>Malathion</th>
<th>Permethrin</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Total for Lifetime</td>
<td></td>
</tr>
<tr>
<td>Resident</td>
<td></td>
<td>0.0000000952</td>
<td>0.000000489</td>
</tr>
<tr>
<td>Child</td>
<td>0.00000000323</td>
<td>0.00000144</td>
<td></td>
</tr>
<tr>
<td>Adult</td>
<td>0.0000000629</td>
<td>0.00000346</td>
<td></td>
</tr>
<tr>
<td>Worker</td>
<td></td>
<td>0.0000000304</td>
<td>0.000000835</td>
</tr>
<tr>
<td>Commercial/Industrial</td>
<td></td>
<td>0.000000254</td>
<td>0.000000701</td>
</tr>
<tr>
<td>Public Works</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Homeless</td>
<td></td>
<td>0.000000014</td>
<td>0.000000469</td>
</tr>
<tr>
<td>Adult</td>
<td></td>
<td>0.00000014</td>
<td>0.000000469</td>
</tr>
<tr>
<td>School</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Older Child (6-12)</td>
<td>0.00000000159</td>
<td>0.000000474</td>
<td></td>
</tr>
<tr>
<td>Adolescent (13-18)</td>
<td>0.00000000116</td>
<td>0.000000404</td>
<td></td>
</tr>
<tr>
<td>Adult (&gt;18)</td>
<td>0.00000000518</td>
<td>0.00000017</td>
<td></td>
</tr>
<tr>
<td>Park Visitor</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Younger Child (0-6)</td>
<td>0.00000000255</td>
<td>0.000000909</td>
<td></td>
</tr>
<tr>
<td>Older Child (7-12)</td>
<td>0.0000000013</td>
<td>0.000000386</td>
<td></td>
</tr>
<tr>
<td>Adolescent (13-18)</td>
<td>0.00000000948</td>
<td>0.000000261</td>
<td></td>
</tr>
<tr>
<td>Adult (&gt;18)</td>
<td>0.00000000593</td>
<td>0.0000002</td>
<td></td>
</tr>
<tr>
<td>Community Gardener (&gt;18)</td>
<td>0.00000000592</td>
<td>0.0000002</td>
<td></td>
</tr>
</tbody>
</table>

**MOE Analysis**

According to USEPA's 1996 proposed revised Guidelines for Carcinogen Risk Assessment, a Margin of Exposure (MOE) analysis can be used to evaluate cancer risks if there is sufficient evidence to support that cancer will occur only if an individual is exposed to a dose level that is above what is known as a “threshold dose” (USEPA, 1998e). As long as exposures are below this threshold dose, there should not be any increased cancer risk. An MOE is calculated as the quotient of the threshold dose divided by the actual exposure dose, or:

\[
MOE = \frac{\text{ThresholdDose}}{\text{ExposureDose}}
\]

The Margin of Exposure, or MOE, is the ratio of the Point of Departure, divided by the actual exposure dose in humans above background. The Point of Departure is a dose, usually determined through animal studies, associated with a negligible increase in cancer. The MOE based on the Point of Departure can also be referred to as the calculated MOE. Because the actual human exposure dose is in the denominator of the ratio, lower exposure doses yield higher calculated MOEs. Higher
calculated MOEs suggest greater certainty that the exposure dose is sufficiently below the point of departure that the cancer risk is negligible. For some chemicals, such as PBO, USEPA has recommended “advisory” MOEs or “comparison” MOEs. Comparison MOEs take into account a number of factors that influence the certainty associated with the safety of the point of departure, and represent an MOE that provides sufficient certainty that cancer risks will be negligible at the actual human exposure dose. In general, higher comparison MOE values suggest there is greater uncertainty associated with the safety of the point of departure. As long as a calculated MOE is greater than a comparison MOE, there is little cause for concern regarding cancer. Likewise, a calculated MOE that is within the same order of magnitude of a comparison MOE also indicates that the exposure dose is sufficiently below the point of departure that cancer risks should be negligible. However a calculated MOE significantly below the comparison MOE would suggest a potential for increased cancer risks.

The MOE tells us by how much the actual exposure dose is below the threshold dose. The magnitude of an acceptable MOE depends on the data that were used for identifying a threshold dose, as well as relevant information regarding variability within animal species (e.g., variability within human sensitivity) and between species (e.g., variability between laboratory test animals and humans). An acceptable comparison MOE can range anywhere from 1 to 10,000. For some chemicals, there is sufficient understanding of the biological processes leading to cancer, as well as differences between animals and humans regarding these processes, to know with a fair amount of certainty that any dose at or below the threshold dose would not be associated with an increased cancer risk. Therefore, for these chemicals, under USEPA guidance, an acceptable MOE is 1.0. For other chemicals, either the biological processes leading to cancer, and/or the differences between animals and humans regarding these processes, are not fully understood. Therefore, USEPA recommends that actual exposures for these chemicals be well below the threshold dose, resulting in an MOE greater than 1.0, to provide an added margin of safety.

The magnitude of the comparison MOE depends on the data and information available for defining the threshold dose, as well as the degree of uncertainty regarding these data and information. If the data are sufficient, and there is little uncertainty regarding these data, then the comparison MOE will be low (e.g., 10). On the other hand, if there are significant gaps in the database, or information regarding a chemical, and/or some uncertainty regarding these data and information, then the comparison MOE will be higher (e.g., 100 or more). For example, if the reference dose (RfD) for non-cancer hazards is also considered to be a threshold dose for cancer, USEPA generally recommends a comparison MOE of 10.

Although there is some evidence that resmethrin, sumithrin, and PBO may be carcinogenic, CSFs have not been derived for these compounds by the USEPA. As noted earlier, this is why cancer risks for resmethrin, sumithrin, and PBO are evaluated using a MOE analysis.

For PBO, USEPA specifically recommends using the RfD as the threshold dose, with a comparison MOE of 10. USEPA has not quantified carcinogenic potential of sumithrin or resmethrin, nor has it recommended a threshold dose and comparison MOE. There is sufficient evidence indicating that sumithrin is not genotoxic (harmful to genetic material), and that sumithrin causes cancer only at very high doses (far greater than one would experience following spraying). Therefore, using sumithrin's RfD as the threshold dose, a comparison MOE of 10 should be adequately protective. Although there is no evidence in the literature that resmethrin is genotoxic, carcinogenic effects are observed at lower doses in animal studies. Therefore, resmethrin's RfD was used as the threshold dose, with a comparison MOE of 100. Table 3.C-12 presents the MOEs for sumithrin, resmethrin, and PBO. The calculated MOE is compared to the comparison MOE to determine the potential for increased cancer
risk. A calculated MOE greater than the comparison MOE implies that exposure to the particular active ingredient is low enough to not be of concern. A calculated MOE less than the comparison MOE could indicate a potential health risk.

<table>
<thead>
<tr>
<th>Active Ingredient</th>
<th>Dose (mg/kg-day)</th>
<th>RfD (mg/kg-day)</th>
<th>Calculated MOE</th>
<th>Comparison MOE</th>
<th>Calculated MOE &gt; Comparison MOE?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sumithrin</td>
<td>0.0000633</td>
<td>0.071</td>
<td>1121</td>
<td>10</td>
<td>Yes</td>
</tr>
<tr>
<td>Resmethrin</td>
<td>0.00000514</td>
<td>0.03</td>
<td>5835</td>
<td>100</td>
<td>Yes</td>
</tr>
<tr>
<td>Piperonyl Butoxide (PBO)</td>
<td>0.00211</td>
<td>0.0175</td>
<td>8</td>
<td>10</td>
<td>No*</td>
</tr>
</tbody>
</table>

*As described earlier under “Calculation of Exposure Point Concentration,” this calculated MOE is based on the assumption that the same individual (for this analysis, a child and adult resident) would be directly exposed to 10 spray events in one season.

As shown in Table 3.C-12, for resmethrin and sumithrin, the MOE analysis indicates that potential exposures to these two chemicals by resident children, the most sensitive individuals quantified in this EIS, and resident adults, is low enough to be of no concern. However, for PBO the calculated MOE is slightly lower than the comparison MOE, which would imply that potential exposures to PBO may not be low enough to ensure adequate protection for human health. However, it should be noted that the MOE analysis for PBO was based on the concentration of PBO found in the pyrethroid product Scourge Insecticide, which contains the highest concentration of PBO (54 percent) of all the pyrethroid products registered for use. In comparison, Anvil 10+10 (which contains the active ingredient sumithrin) contains 10 percent PBO, and Aqua-Reslin (which contains the active ingredient permethrin) contains a maximum of 20 percent PBO. Also, although the MOE analysis for this concentration of PBO shows a calculated MOE lower than the comparison MOE, when considering the various conservative assumptions that the calculated MOE are based on, this difference can be considered to be negligible. It should also be noted that the reference dose for PBO, which is based on a NOAEL level for changes in liver weight in animals, is more than 1,000 times lower than a dose in animals at which no increases in any types of cancer were observed. As an added measure of protection, USEPA recommends an advisory or comparison MOE of 10, such that recommended exposures would be 10,000 times lower than a non-carcinogenic dose in animals. Again, for PBO, the calculated MOE was 8 as compared with the comparison MOE of 10, which is essentially close enough that there should be no concern for excess cancer risk.

**Evaluation of Acute Exposures**

Acute exposures—those occurring within 24 hours of adulticide spraying—are evaluated using risk-based concentrations (RBCs). RBCs are the concentrations in air that are associated with no adverse health effects. RBCs are calculated using acute (one-day, immediate) toxicity criteria (acute RfCs and RfDs), and represent a maximum exposure level, below which no adverse health effects are expected. Because children are the most sensitive population group quantified in this EIS, RBCs for children were calculated under the residential scenario. Therefore, RBCs for children are lower, and thus more conservative, than RBCs for other population groups. RBCs were calculated according to the following equation:
Where:

- **RBC** = Risk Based Concentration measured in micrograms of active ingredient per cubic meter of air
- **BW** = Body weight for child (15 kg)
- **AT** = Averaging time period over which exposure is averaged (1 day)
- **ET** = Exposure time (6.1 hours)
- **24** = 24 hrs/day
- **CF₁** = Conversion factor \((10^6 \text{ g-L/m}^3 - 1,000,000 \text{ microgram — Liter per milligram – cubic meter})\)
- **CF₂** = Conversion factor for air deposition to air concentration \((0.4387 \text{ mg-m/g})\)
- **CF₃** = Conversion factor \((0.0001 \text{ m}^2/\text{cm}^2 — \text{ meter square per centimeter square})\)
- **SA_{hand}** = Surface area of child hand \((450 \text{ cm}^2 — \text{square centimeters})\)
- **SA_{body}** = Surface area of exposed body \((2800 \text{ cm}^2 — \text{square centimeters})\)
- **RfC_{acute}** = Reference concentration to which a person, including sensitive individuals, can be exposed on daily basis without adverse health effects for short-term, inhalation exposure
- **RfD_{oral-acute}** = Reference dose to which a person, including sensitive individuals, can be exposed on daily basis without adverse health effects for short-term, oral exposure
- **RfD_{dermal-acute}** = Reference dose to which a person, including sensitive individuals, can be exposed on daily basis without adverse health effects for short-term skin exposure

The RBCs calculated for children in the residential scenario are presented in Table 3C-13. RBCs are compared to the acute exposure concentrations. As long as the acute exposure concentrations are less than or equal to the RBCs, adverse health effects resulting from acute exposure to the active ingredients being studied are not expected to occur.

As shown in Table 3C-13, results from this approach indicate that the maximum modeled air concentrations for sumithrin, permethrin, resmethrin, and PBO occurring within 24 hours of adulticide spraying are lower (up to 10 times lower) than the calculated RBCs. This would imply that acute exposures to these active ingredients would not result in adverse acute health effects. The results also show that the maximum short-term modeled air concentrations for malathion, and naled are higher than the calculated RBCs, which would imply that immediate health effects could potentially result from malathion, and naled exposures.
### Table 3.C-13
Evaluation of Acute Exposures

<table>
<thead>
<tr>
<th>Active Ingredient</th>
<th>Acute RfCs\textsubscript{air} (mg/L)</th>
<th>Acute RfD\textsubscript{ingestion} (mg/kg-day)</th>
<th>Acute RfD\textsubscript{dermal} (mg/kg-day)</th>
<th>RBC\textsubscript{air} (g/m\textsuperscript{3})</th>
<th>Max Air Conc. (g/m\textsuperscript{3})</th>
<th>Max &gt; RBC ?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sumithrin</td>
<td>0.0029</td>
<td>0.5</td>
<td>10</td>
<td>358.9</td>
<td>3.8</td>
<td>No</td>
</tr>
<tr>
<td>Permethrin</td>
<td>0.0025</td>
<td>0.25</td>
<td>1.5</td>
<td>92.4</td>
<td>22.1</td>
<td>No</td>
</tr>
<tr>
<td>Resmethrin</td>
<td>0.0001</td>
<td>0.1</td>
<td>10</td>
<td>60.54</td>
<td>7.4</td>
<td>No</td>
</tr>
<tr>
<td>PBO</td>
<td>0.00074</td>
<td>2</td>
<td>10</td>
<td>549.4</td>
<td>22.1</td>
<td>No</td>
</tr>
<tr>
<td>Naled</td>
<td>0.000023</td>
<td>0.01</td>
<td>0.01</td>
<td>0.94</td>
<td>18.4</td>
<td>Yes</td>
</tr>
<tr>
<td>Malathion</td>
<td>0.0001</td>
<td>0.5</td>
<td>0.5</td>
<td>50.6</td>
<td>57.1</td>
<td>Yes</td>
</tr>
</tbody>
</table>

**Alternative Assumptions Analysis**

The process of evaluating human health risks involves multiple steps. Inherent in each step are uncertainties that ultimately affect the final risk estimates. Uncertainties may exist in numerous areas, including environmental sampling data, derivation of toxicity values, and estimation of potential site exposures. However, where uncertainties exist, conservative inputs or approaches were generally used so that potential risks would be overestimated. This section presents a qualitative discussion of the significant sources of uncertainty and the conservative choices made in the risk assessment. General sources of uncertainty that are common to most risk assessments are described first, followed by a discussion of specific sources of uncertainty in this particular risk characterization. Overall, despite the inherent uncertainties, the risk estimates calculated in this assessment are conservative, and are likely to over-predict actual risks.

**Exposure Analysis**

The exposure assumptions used to estimate chemical intakes also contribute to the uncertainty in the risk characterization. This analysis uses a range of conservative values for exposure parameters that represent average or central tendency to reasonable “worst-case” estimates. The conservative inputs selected for some of the more important exposure parameters are discussed below.

**Soil vs. Dust Concentrations**

Typically, outdoor soil is a major component of indoor house dust. However, the concentrations of contaminants in indoor dust are typically lower than contaminant concentrations measured in outdoor soil. USEPA’s lead guidance assumes that the ratio of indoor dust concentrations of lead to outdoor soil concentrations of lead is about 70 percent (USEPA, 1994). Other studies indicate that the ratio of interior dust to outdoor soil concentrations is likely to range from 30 percent to 45 percent (Fergusson et al., 1986; Fergusson and Kim, 1991; Calabrese and Stanek, 1992). For the residential scenario in this risk characterization, it is assumed that interior dust concentrations are 100 percent of the outdoor soil concentrations (i.e., that contaminant concentrations in indoor dust are the same as the contaminant concentrations in site soils).

**Fraction of Inhalable Soil Particulates**

To calculate the fraction of soil particles that is re-suspended and subsequently inhaled, a particulate matter of size 10 microns or less (also known as PM10) was used to estimate ambient particulate concentrations. A value of 60 µg/m\textsuperscript{3} was used to calculate the ambient particulate concentrations. This PM10 value is derived from the average 24-hour concentrations measured at NYSDEC Region 2 monitoring stations (NYSDEC, 1996). The use of the PM10 of 60 µg/m\textsuperscript{3} is conservative considering...
that the annual average PM10 for the same monitoring stations in New York City is approximately 27 µg/m3 (NYSDEC, 1996). This assumption is likely to overestimate exposures.

**Water Exposure Point Concentrations**

Degradation and dilution of the adulticides in surface water were not assumed in the derivation of the EPCs for water. This is a conservative assumption in that the adulticides are likely to break down in surface water and become diluted due to the mixing effects in the reservoir. This assumption is likely to overestimate exposures.

**Soil Ingestion Rate**

Because incidental soil ingestion is associated with soil activities (e.g., gardening), USEPA's default incidental soil ingestion rates for children overstate typical intake estimates reported by investigators and are thus conservative. Specifically, the risk assessment uses USEPA's estimated soil ingestion rate of 100 to 200 mg soil/day for 1-6 year olds, and 50 to 100 mg soil/day for children older than 6 years old and adults. However, literature published since 1994 suggests that 100 to 200 mg/day and 50 to 100 mg/day estimates of the soil ingestion rate may overstate empirical values. For example, Stanek and Calabrese (1995) reported a reanalysis of the 1989 Calabrese et al. and 1990 Davis et al. studies of soil ingestion rates. The reanalysis calculated a median soil ingestion rate of 37 mg/day for children in both the Calabrese et al. and Davis et al. data sets. The soil ingestion rates used in the risk assessment are conservative and are likely to overestimate exposures.

**Soil/skin Adherence Factor**

This factor represents the amount of soil that adheres to skin and is available for dermal exposure. Because this value is likely to vary based on an individual's activity, the values used for this parameter are somewhat uncertain. However, this EIS used values that are likely to overestimate exposure and risk. The reasonable maximum exposure (RME) soil/skin adherence factor of 0.2 mg/cm² is based on exposure to wet soil, which adheres much more than dry soil particles. (RME is the upper-bound estimate in a range of possible values; for example, soil adherence factors can range from 0.02 mg soil per cm² skin surface area to 0.2 mg soil per cm² skin surface area.) USEPA-recommended values for child and adult individuals were used. It is likely that these values overestimate exposure on a yearly basis, because while individuals may engage in similar activities for some period of time, it is unlikely that they will have such direct contact with soil every day. This assumption is conservative and is likely to overestimate exposures.

**Relative Absorption Factors for Dermal Contact**

Because dermal absorption of soil contaminants is a complicated issue, there is considerable uncertainty associated with dermal absorption rates. Various factors affect the efficiency of dermal absorption, for example the duration of skin contact. Since most individuals bathe at least once each day (USEPA, 1997c), washing may remove any soil residues adhering to the skin before much absorption occurs. Therefore, skin absorption rates based on studies with long exposure durations may tend to overestimate actual absorption, which, the literature suggests, generally occurs in shorter time periods. However, soil loadings have also been shown to affect skin absorption rates; the percentage of dermal absorption may increase as soil loadings decrease. The use of various testing methods also introduces uncertainties: In vivo animal studies introduce uncertainties regarding animal-to-human extrapolation, while in vitro studies using human skin introduce uncertainties regarding in vitro to in vivo extrapolations.
The amount of chemical absorbed from soil is dependent on several chemical, physical, and biological factors of both the soil and the receptor. Examples of factors in soil which determine the amount of chemical available for absorption include soil type, organic carbon content, cation exchange capacity, particle size, temperature, and pH. Chemical factors affecting absorption include lipid solubility, chemical speciation, and stability of the chemical. Physical factors impacting absorption are soil loading rate, surface area exposed to soil, soil contact time, and soil adherence. Biological factors would include skin condition, skin absorption, skin blood flow, and age of individual. The exact relationship of all these factors to dermal absorption is not known resulting in some level of uncertainty. It is not possible to make a general statement about the direction or magnitude of this uncertainty.

**Kp Values for Dermal Absorption via Water**

In the assessment of dermal exposures to chemicals in water, permeability coefficients (Kp) have been identified as major parameters contributing uncertainty. Measuring or predicting Kp is fairly uncertain for most compounds, especially those with high or low K\textsubscript{ow} and molecular weight. Predicted Kps are highly dependent on their associated K\textsubscript{ow} values. The accuracy and experimental design vary greatly in experiments to measure Kp so that all K\textsubscript{ow}s are not of equal value. Because information is not available in determining how K\textsubscript{ow}s were measured, it is not possible to determine whether exposures doses would have been underestimated or overestimated.

**Relative Absorption Factors for Inhalation and Ingestion**

The relative absorption factor for inhalation and oral values used in this risk assessment was conservatively assumed to be 100 percent based on recommended USEPA guidance (USEPA, 1989a). Actual absorption is likely to be lower than 100 percent. This assumption is conservative and is likely to overestimate exposures.

**Toxicity Analysis**

In general, USEPA uses conservative approaches to develop toxicity criteria. USEPA uses uncertainty factors of up to 10,000 in deriving reference doses (RfDs).\textsuperscript{9} Cancer slope factors (CSFs) are typically derived using conservative dose-response models, which assume that cancer risks at high doses are proportional to cancer risks at low doses. However, this is often not the case, such that at low doses cancer risks are proportionally much lower than cancer risks at high doses. These approaches are likely to overestimate cancer and non-cancer risks. Specifically for malathion, it should be noted that this EIS is evaluating cancer risks for malathion, even though USEPA has withdrawn its CSF for malathion, and is expected to downgrade malathion’s cancer classification from a “likely human carcinogen,” to “suggestive evidence of carcinogenicity, but not sufficient to assess human carcinogenic potential.” Furthermore, nearly half of USEPA’s Scientific Advisory Panel (SAP) which has reviewed the scientific evidence regarding the carcinogenic potency of malathion thought that malathion is “not likely to be carcinogenic to humans.” Only one SAP member thinks malathion is a “likely” human carcinogen (USEPA, 2000c).

Another source of uncertainty is the toxicological information used in the risk characterization. The development of toxicity factors (e.g., RfDs and CSFs) involves extrapolation of results from animal studies to predict potential adverse health effects and the level at which they would occur in humans. Animal studies usually involve very high doses of chemicals, while human exposures to chemicals in

\textsuperscript{9} Uncertainty factors are safety factors that are applied to account for issues such as species-to-species extrapolation, protection of sensitive human subpopulations, study duration, study deficiencies, incomplete databases, etc.
the environment are typically very low. Animal studies also usually involve a homogeneous population, a very consistent exposure regimen, and a distinct period of exposure; while humans have a wide range of sensitivities and potential exposures. In addition, there may be important differences in chemical uptake, metabolism, and distribution between animal species and humans. Each of these variables contributes uncertainty to the predicted adverse health effects in humans. Toxicological uncertainty may result in either over- or under-estimates of the potential health risks. USEPA uses conservative assumptions, however, in developing its toxicity factors, so these factors likely overestimate potential health risks.

The lack of dermal toxicity criteria also contributes to uncertainty in the risk estimates. Because toxicity criteria are not available for the dermal route of exposure, following USEPA guidance (USEPA, 1989a), dermal toxicity criteria were extrapolated based on oral toxicity criteria. The dermal route of exposure can result in different patterns of distribution, metabolism, and excretion than occur from the oral route. When oral toxicity values are applied to dermal exposures, uncertainty in the risk assessment is introduced because these differences are not taken into account in the risk assessment. Since any differences between the oral and dermal pathways would depend on the specific chemical, use of the oral toxicity factors can result in the over or underestimation of risk. It is not possible to make a general statement about the direction or magnitude of this uncertainty.

**Summary/Conclusions**

The potential environmental health risk consequences from the Proposed Action were assessed for each of the active ingredients of concern. As discussed above in the Methods of Analysis section, since the risk assessment is a quantitative analysis and the specific inert ingredients and their amounts were not available, the risk assessment was performed only for the active ingredients found within the adulticide products. Summaries of the potential public health effects as a whole (which include the inert ingredients), are discussed in the Literature Search section of this chapter. Of the 17 adulticides that could potentially be used by NYCDOH as part of the Proposed Action, five products (containing the five active ingredients and synergist of concern) were chosen for technical analysis based on composition and likelihood of use by NYCDOH for future adult mosquito control.

As described in the Risk Characterization section above, non-cancer risks were evaluated using a hazard index (HI) approach. For a particular population group, an HI below 1.0 would indicate that non-cancer adverse health effects would not be expected. Table 3.C-14 below characterizes the non-cancer risks for all evaluated population groups. Therefore, an “X” indicates that no expected potential risk from exposure to the active ingredient was found for any of the evaluated population groups, whereas a “?” indicates a there could be a potential risk from exposure to the active ingredient.

Potential cancer risks for malathion and permethrin were calculated using a cancer slope factor (CSF) analysis, for each population group and exposure pathway. An “X” in Table 3.C-14 for cancer risks represents a carcinogenic risk within or below the USEPA-determined acceptable target risk range, whereas a “?” would indicate a carcinogenic risk outside of or above the USEPA-determined acceptable range.
Table 3.C-14: Risk Assessment Summary
Potential cancer risks for sumithrin, permethrin and PBO were calculated using a margin of exposure (MOE) analysis, for resident children, the most sensitive population group quantified in this risk assessment. For exposure to these three active ingredients, An “X” in Table 3.C-14 would imply that exposure to the active ingredient of concern for resident children would be low enough not to be of concern. A “?” would indicate that potential exposure to the active ingredient may not be low enough to ensure adequate protection for human health.

Acute exposures were calculated using risk-based concentrations (RBC), which are the concentrations in air that are associated with no adverse health effects. For this analysis, resident children were again used as the most sensitive population group quantified in this EIS, and therefore the results were more conservative than for other population groups. An “X” in Table 3.C-14 indicates no adverse health effects expected, whereas a “?” indicates potential adverse health effects.

As shown in Table 3.C-13, exposure to the six active ingredients indicate that non-cancer adverse health effects are not expected for any evaluated human population group, through any exposure pathway (i.e., inhalation, dermal, ingestion). Cancer risks are within USEPA acceptable ranges, for malathion and permethrin, and cancer risks for exposure to resmethrin and sumithrin would be low enough to be of no concern. Based on the risk assessment modeling results, acute adverse health effects would be unlikely to occur with exposures to the active ingredients in the pyrethroid products including PBO.

For malathion and naled, based on the conservative assumptions used in this risk assessment, the RBCs for these active ingredients were exceeded. As discussed earlier, RBCs are calculated using acute toxicity criteria and represent a maximum exposure level. However, conservative assumptions are used both in the exposure analyses (in the development of exposure concentrations) and toxicity analyses (in the development of toxicity criteria). Therefore, although the modeled air concentrations for these two active ingredients exceed the RBCs, actual dose absorbed through inhalation is likely to be lower than 100 percent (one of the conservative assumptions used), and therefore this calculation is likely to overestimate exposures. Given the low likelihood for acute health effects to occur, acute exposures to malathion and naled would not constitute a significant adverse public health impact.

For PBO, as there is no cancer slope factor derived for this compound by USEPA, the more conservative MOE approach was applied to determine possible cancer risk. As explained previously, the MOE for PBO (at a concentration of 54 percent, the highest found among the pyrethroid products) was slightly lower than the comparison MOE, indicating that potential exposures to PBO may not be low enough to ensure adequate protection for human health. However, as discussed earlier when considering the various conservative assumptions used both within the exposure analyses and toxicity analysis, the cancer risk for PBO is most likely overestimated in the MOE analysis. The difference between the calculated MOE and comparison MOE is minimal. Therefore, there should be no concern for excess cancer risk, and no significant adverse public health impact would be expected.

**PUBLIC HEALTH RESPONSE TO SPRAYING PROGRAMS: RECENT EXPERIENCE – EPIDEMIOLOGIC AND ATTRIBUTABLE RISK ANALYSES**

Presented below are the results of a study performed to assess the possible impact of adulticide spraying on asthma public and private hospitalizations, and public hospital emergency department and urgent care visits in 1999. Also, to further characterize the potential impact of adulticide use on asthma hospitalization, an attributable risk analysis was performed to estimate the proportion of asthma hospitalizations that might be attributed to adulticide spraying.
**Epidemiologic Analysis**

**Introduction**

The potential for human respiratory health effects from exposure to pesticides used for control of adult mosquitoes (adulticides) include both short- and long-term illness. Asthma exacerbations in relation to the use of mosquito adulticides in response to West Nile virus in New York City have been of considerable concern due in part to high rates of asthma in some New York City communities. To address this concern, the analyses described below, focused on short-term effects, specifically, attacks or worsening of asthma. Stimulation of an inflammatory response and bronchospasm following inhalation, mediated by an immune reaction or an irritant effect, is one possible mechanism by which exposure to such pesticides could trigger an episode of asthma. A severe clinical response prompting an emergency department/urgent care visit or hospitalization might be expected to occur within hours to days following this type of exposure.

**Asthma Seasonal Patterns and Variability**

Asthma exacerbations are known to increase as a result of exposure to numerous factors including pollen levels and respiratory infections. As a result, general seasonal patterns in asthma hospitalizations have been well-established (New York City Asthma Fact Book). In New York City, asthma hospitalization rates generally rise in the fall and winter and also in May (New York City Asthma Fact Book). Figure 3.C-1, which shows asthma hospitalizations from July through December, depicts some of the seasonal patterns in asthma hospitalizations in New York City.

Although there is a general seasonal trend, asthma hospitalizations have been shown to exhibit considerable day-to-day or week-to-week variability. For example, in Figure 3.C-2 in 1996 “week 2” had fewer asthma admissions than the other years (1995, 1997, 1998, 1999), while “week 4” had more asthma events than the other years. Similar effects can be seen in Figure 3.C-3 for asthma emergency department and urgent care submissions. The inherent variability in daily or weekly asthma hospitalizations or emergency visits is extremely important in attempting to interpret findings of asthma events in relation to possible environmental exposure.

To examine the possible impact of adulticiding on such asthma exacerbations in New York City, the New York City Department of Health collaborated with the New York State Department of Health and the Centers for Disease Control and Prevention to develop analytic plans that would use existing data on emergency department/urgent care visits and hospitalizations and that would make best use of data available on adulticiding. The analyses were designed to determine whether the relative change in rates of asthma (i.e., emergency department/urgent care visits and hospitalizations for asthma) before (Pre-period) and after (Post-period) adulticiding occurred in 1999 was different from the change in the same time period in prior years, when no adulticiding occurred. While these analyses have been designed to reduce some of the potential biases or confounding factors in the data, there are inherent limitations of the exposure and outcome data. The following provides an overview of the data, analytic plan, results, limitations and conclusions of these investigations.

**Exposure Data**

In 1999, aerial (using malathion) and ground (using pyrethroids) spraying was performed intermittently, citywide, for approximately 5 weeks (September through the first three days in October). Boundaries for spraying in 1999 did not correspond to geocoded areas (e.g., zip codes, census tracts, etc).
Outcome Data

The outcome information used in these investigations included hospitalization data from all New York City hospitals (obtained from the Statewide Planning and Research Cooperative System (SPARCS) and emergency department and urgent care visits from New York City public hospitals only (obtained from NYC Health and Hospital Corporation [HHC]). Only New York City residents were included in the analysis, given an assumption that exposure to adulticides occurred in the borough of residence. An event was defined as a primary diagnosis of asthma (ICD, 9: 493). A visit or admission in which asthma was a secondary diagnosis was not included as an event since it is presumed that an asthma exacerbation was not the primary reason for the visit or admission. Therefore, for these investigations, persons who were New York City residents in 1999 and had a primary diagnosis of asthma were included in the analysis. For analyses using HHC data, Staten Island could not be included since there are no public acute care facilities in Staten Island.

Synopsis of Analytic Plan

The analyses examined whether asthma emergency department/urgent care visits or hospitalizations were increased after spraying in 1999 for WNV. Since the entire City was sprayed in many areas at least twice during the month of September, there were no non-exposed areas to use as a control to compare the sprayed areas with non-sprayed areas in 1999. Therefore, data from the same months in past years were used as comparisons. Thus, since adulticiding began in September, when hospital admissions and emergency department visits for asthma normally increase, we compared the increase between August (the unexposed period) and September (the exposed period) in 1999 to the increase in asthma between August and September in prior years. Since rates can change over years and between months, examining the rates of change within a year is an attempt to control for between year influences.

For the monthly analysis, the relative increase was examined by comparing the number of asthma hospitalizations in September to the number in August 1999 to the same time period in each year from 1989-1998 in the monthly hospitalization analyses. Both the “weekly hospitalization analyses” and the “weekly emergency department/urgent care analyses” for each year compared each of the five weeks post Labor Day (to control for school openings when an increase in asthma hospitalizations and emergency department or urgent care visits normally increase) to the average weekly events in August for each year. For the hospitalization data, information on the day of event was available for 1989 through 1999. For the emergency care and urgent care data information was available for the day of the event for the years 1995-1999, however only the weekly analysis was performed (the monthly analysis is currently being conducted).

Comparisons were made by calculating a rate ratio which compared September to August asthma events in each year. The objective was to determine how the rate ratio in 1999 compared with previous years. A rate ratio of 1 suggests that there was no increase between August and September. A rate ratio of greater than 1 suggests that the number of asthma events was greater in September than in August. A rate ratio of less than 1 would indicate that the number of asthma events was less in September than in August. Since asthma events increase in September compared to August, rate ratios are generally greater than 1 for each year.

These analyses assume that any differences in hospital admission policies and practices would have a similar affect on August and September emergency department/urgent care visits and hospital admissions within a year.
Results

Asthma exacerbations in relation to the use of adulticides in New York City have been of considerable concern due to the high rates of asthma in some New York City communities. This section as well as Figures 3.C-1 to 3.C-3 and Tables 3.C-15 to 3.C-20 present a summary of the results of the asthma analyses.

Monthly Hospitalization Analyses

Citywide

Based on Figure 3.C-1 and Table 3.C-15, asthma hospitalization events do not appear to have been substantially higher in September relative to August in 1999 compared to the other eleven years that were investigated (1989-98). As can be seen in Table 3.C-15, the rate ratios ranged from 1.41 to 2.03 over the 11-year period. For 1999, there was a 79 percent increase (rate ratio=1.79) in asthma hospitalizations between August and September. This was not substantially different from the median rate ratio of 1.72 which occurred in 1991. Additionally, the increases from August to Citywide asthma admissions in both September 1993 and 1995 were greater than in 1999 and the increase in 1997 was fairly similar to that in 1999.

Borough

Within boroughs, while the increases in asthma hospitalizations between August and September in 1999 were among the highest in the 11 years studied (See Table 3.C-15), in no borough was the increase highest in 1999. In 1999, compared to previous years, the rate ratio was sixth highest in Brooklyn (rate ratio=1.64) while the range was 1.32 to 1.97 in previous years to second highest in Manhattan (rate ratio=1.93) where the rate ratio ranged from 1.27 to 2.11 in previous years.

Age

Age specific analyses (Table 3.C-16) revealed that for those under 20 years of age, the August to September increase was lower in 1999 for more than half the other years. For example, among children 0-4 years of age, there was about a 2 ¼ fold (rate ratio=2.22) increase between August and September in 1999 compared to almost a 3 fold increase in 1991 (rate ratio=2.91), the year with the highest rate ratio. Among children 5-14 years of age, the rate ratio was 2.86 in 1999 compared with a high of 5.16 in 1993. For individuals 20 years of age and above, the rate ratio for 1999 was among the highest (rate ratio=1.56, range 1.11-1.58). Those individuals 40 years of age and older, the rate ratios were highest in 1993 and 1999 (both rate ratios=1.24).

Weekly Hospitalization Analyses

Citywide

Asthma weekly hospitalization analyses are shown in Figure 3.C-2 and Tables 3.C-17. The analysis of asthma hospitalizations by week revealed variations in 1999 by week. For example, citywide in 1999 there was a 30 percent higher (rate ratio=1.30, range 1.03-1.43) asthma hospitalization rate in the first week of spraying compared to the average weekly asthma hospitalization rate in August. In the second week in 1999, the rate ratio was the highest for that 11-year period (rate ratio=1.92, range

10 In the Results section, note that the range given for the rate ratio appears as presented in the data. No statistical significance should be inferred.

11 Persons of unknown age were included in the monthly citywide and borough analysis using hospitalization data.

12 Persons of unknown age were included in the weekly hospitalization citywide and borough analysis.
### Table 3.C-15
Rate Ratios* of Monthly Public and Private Hospital Asthma Admissions in the Five Boroughs (1989-99)

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Notes: *Rate Ratio=Number of monthly asthma admissions in a particular month of a year/Number of admissions in August of that same year.

### Table 3.C-16
Rate Ratios* of Monthly Public and Private Hospital Asthma Admissions in the Five Boroughs by Age Group (1989-99)

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Notes: *Rate Ratio=Number of monthly asthma admissions in a particular month of a year/Number of admissions in August of that same year.
1.16-1.92). Yet asthma hospitalizations in the third, fourth and fifth weeks after Labor Day were near or below the average weekly rate ratio for those same weeks in prior years.

**Borough**

The citywide findings (Table 3.C-17) showing that 1999 had the largest rate ratios in the second week in September compared to August relative to other years were reflected in the Bronx and New York counties. However, in no other county or week were the highest rate ratios found in 1999.

**Age**

When stratified by age (Table 3.C-18), the rate ratio observed for each age group in a given week in 1999 between August and September was for the most part considerably lower than the greatest increase observed for that week in prior years (Table 3.C-18). For instance, in 1999, the rate ratio in the first week for young children (0-4 years) was 1.30. The range for the first week over the 11 years was 1.03-1.88. A similar pattern emerged for older children (5-14 years) as well as those in the 15-19 years & the 20-39 year age groups. Older adults (40 years & over) were the only group where 1999 had the highest rate ratio for any week or age group and this occurred in the third week only (rate ratio=1.44, range 1.05-1.44).

**Weekly Emergency Department/Urgent Care Analyses (New York City Public Hospitals)**

**City Wide**

As shown in Table 3.C-19, citywide, 1999 had the highest rate ratio for the second week (rate ratio=1.83, range 1.39-1.83) which was, however, very similar to the next highest rate ratio in 1997 (rate ratio=1.82). The increases seen in Week 3 (rate ratio=1.99, range 1.62- 2.10), Week 4 (rate ratio=1.95, range 1.73-2.36) and Week 5= (1.77, range 1.70-2.25) were similar to those of other years.

**Borough**

Kings and New York counties reflected the citywide results for the most part with largest increase relative to other years occurring by the end of the second week (Table 3.C-19). For instance, New York County had the highest percentage increase from August to September in the first two weeks of 1999 (Week 1: rate ratio=1.72, range 0.95-1.72; Week 2: (rate ratio=1.72, range 0.96-1.72) while Kings County experienced the highest in Week 2 (rate ratio=1.69, range 1.28-1.69). Both the Bronx and Queens counties exhibited smaller rate ratios for each week in 1999 relative to all other years.

**Age**

The results of the analysis when stratified by age are presented by in Table 3.C-20. Among older teenagers (15-19 years), 1999 had the largest increase from August to September in Week 1 only, (Week 1: rate ratio=1.47, range 0.96-1.47). However, children 04 years of age saw the largest increase from August to September in the 1st and 2nd week of 1999 relative to prior years (Week 1: rate ratio=1.66, range 0.84-1.66) and (Week 2: rate ratio=2.37, range 0.99-2.37). Older children (5-14 years) had the largest increase only in Week 2 of 1999 relative to prior years (rate ratio=3.46, range 1.81-3.46) as did those persons 20-39 years (rate ratio=1.32, range 0.96-1.32). Among older adults, 40 years and over, rate ratios for all five weeks in 1999 were lower than 1997 (the year with the greatest increases from August to September for all weeks but Week 1).

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13 Person of unknown age were not included in the public hospital emergency department and urgent care analysis for either citywide or borough analysis.
### Table 3.C-17
Rate Ratios* of Weekly Public & Private Hospital Asthma Admissions in the Five Boroughs (1989-99)

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**Notes:** *Rate Ratio=Number of weekly asthma admissions in a particular week of a year/Average number of weekly admissions in August of that same year.*
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**Notes:** *Rate Ratio=Number of weekly asthma admissions in a particular week of a year/Average number of weekly admissions in August of that same year.*
### Table 3.C-19
**Rate Ratio*, Weekly Public Hospital ED & Urgent Care Asthma Visits By Borough, September-August, 1995-1999**

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**Note:** *Rate Ratio=Number of weekly asthma admissions in a particular week of a year/Average number of weekly admissions in August of that same year.*
Limitations

While these analyses provide an initial attempt to investigate the relationship between use of adulticides and asthma events, the available data have many limitations that could not be addressed in this analysis. Additionally, control or unexposed communities could not be identified since the entire city was sprayed twice in approximately five weeks. Thus, the exposure of interest was measured “ecologically”; that is, the entire New York City population was assumed to be equally exposed to the adulticide. All three of these analyses are subject to the primary limitation of all ecological studies, namely associations found at the population level will not necessarily mirror that which happens at the level of the individual. For example, a person who was exposed may not have been one of the people who had an asthma event and, similarly, a person not exposed may have been one of the people who had an asthma event.

Additionally, the outcome data that were available were somewhat crude in that unique patient information was unavailable and thus re-admissions and re-visits could not be identified. Therefore it is not known whether the number of asthma visits or hospitalizations may include several visits or admissions of the same person. Also, emergency and urgent care visits, unlike hospital admission data, could only be obtained from public hospitals and are therefore not necessarily representative of possible effects in the general population. Further, information regarding hospital admission practices, access to emergency and urgent medical care, or changes in coding procedures were not available, all of which could greatly influence the number of admissions and visits for certain illnesses.

Moreover, the analytic method that was used which was limited to borough level analyses and did not provide for control of confounding factors (such as the influence of weather conditions, like rain, that might impact adulticide use and the number of asthma visits or hospitalizations)\(^\text{14}\) provides little sensitivity to detect small to moderately large increases in asthma events due to exposure to adulticides. In addition, this method does not provide for direct assessment of the temporal relationship between adulticide use and an increase in asthma exacerbations because the time frames between the exposure and the outcome could not be determined. Finally, due to the insufficient number of years of data available and therefore few data points, statistical testing was not performed.

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\(^{14}\)Weekly weather and air pollutant data from 1995 through 1998, for the five boroughs combined, were compared to 1999 data to identify any differences that may partially account for the variations of weekly hospitalizations or ED visits due to respiratory [i.e., asthma] illness. The data were plotted by time for barometric pressure, relative humidity, temperature, total nitrogen oxides, ozone, precipitation, and sulfur dioxide. The results were variable from week to week, with no general pattern during the pre- and post-spraying periods for 1999 that could explain the observed hospitalization data compared to earlier years.
### Chapter 3.C: Public Health

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### Notes:

*Rate Ratio=Number of weekly asthma admissions in a particular week of a year/Average number of weekly admissions in August of that same year.*
During the summer of 2000, NYCDOH recommended that all persons who experience adverse reactions to pesticides should call their doctor or the PCC. Doctors were advised to call the PCC for consultation and to report if a patient presented any suspected or confirmed pesticide-related illness. Doctors were also advised to report suspected and confirmed cases to the New York State Department of Health Pesticide Poisoning Registry (NYSPPR).

In 2000, PCC received calls from the public related to possible infection with West Nile virus, as well as reports of mosquito bites and reports of exposures to adulticides both human and animal. All reports related to adulticide exposure were forwarded to the Disease Intervention Unit at NYCDOH. NYCDOH then forwarded these reports to NYSPPR for additional review and follow-up.

There were 339 reports to the PCC related to adulticide exposures in 2000. Of these, 157 persons reported some type of symptom. As would be expected with the type of exposure that the general public would experience related to mosquito control, the majority of these symptoms were short term and minor in nature.

NYSDOH's NYSPPR has preliminarily determined that approximately 15 of these persons could be possible or probable cases to be included in their registry. NYCDOH also analyzed hospital data to assess the possible impact of spraying on human health.

**Conclusions**

No conclusions about the potential relationship between adulticide use and asthma exacerbations can be made from the results of the analyses described in this section. Asthma hospitalizations and emergency department visits in 1999 did not appear to be greatly higher than those in earlier years when adulticides were not used. However, in some subgroups or boroughs increases were found. An important criterion in epidemiology is whether results are consistent across groups and in different studies. Additionally, the more analyses that are performed, the more likely it is to identify a positive finding. While our analyses have revealed some findings that may be suggestive of higher asthma rates after spraying, these findings were not consistently found and must, therefore, be interpreted with caution. However, because analyses at the zip code level were not possible for 1999 or at the individual level (i.e., exposed individuals only), only gross population changes can be detected. As a result, this analysis cannot rule out the possibility that use of adulticides precipitated an increase in asthma or respiratory exacerbations in subgroups of New York City’s population.

The analyses described are an attempt at investigating the effects of adulticides on asthma exacerbations. Due to the many limitations of these investigations, these analyses should be viewed as a first step in describing asthma exacerbations during pre and post spraying periods. These analyses should not be considered conclusive of a finding of an effect or non-effect. Clearly, analytic approaches need to be developed to determine if any potential effect on asthma exacerbations is the result of adulticide use. Additional epidemiologic research utilizing more sensitive exposure and outcome as well as measures of potential confounders need to be developed.

**Attributable Risk Analysis**

*Estimation of the Attributable Risk for Asthma Hospitalization from Particulate Matter Generated by Adulticide Spraying*

The epidemiologic studies discussed above analyze the potential observed impacts on asthma exacerbations from the application of adulticides by examining existing data on emergency department/urgent care visits and hospitalizations. This approach utilized observed relative changes in rates of asthma that were based on recorded hospital data for the periods before and after adulticides
were applied in various portions of the City in 1999 and 2000. Numerous limitations exist with these analyses and thus an alternative approach was also used to estimate the number of asthma hospitalizations that could potentially be attributed to adulticide application. This analysis made use of epidemiologic studies that report associations between changes in ambient air particulate concentrations and asthmatic events. In this approach, the number of asthma exacerbations that would be expected from the transient increment in airborne particulate concentrations caused by the spraying events are predicted. Such an analysis is referred to an attributable risk analysis.

In this analysis, the entire population in all of the zip codes of the Representative Areas (as defined in Chapter 3.A “Framework of the Analysis”), were assumed to be exposed to additional airborne particulate matter levels resulting from the spraying of adulticides. The particulate matter levels were calculated by the application of an air dispersion model from the source, i.e., the spray trucks. The predicted increases in air particulate exposure were combined with descriptive data on the prevalence of asthma as well as on the number and rates of asthma hospitalizations to estimate the theoretical percentage increase in asthma hospitalizations that could occur. The percentage increase above baseline levels is called the “attributable risk” of asthma exacerbation caused by adulticide application. Using data specific to New York City, the actual number of additional asthma hospitalizations that may be attributable to the adulticiding actions that would be undertaken as part of the Proposed Action, were estimated.

Specifically, increases in asthma hospitalizations were predicted from increased concentrations of total particulate matter less than 10 microns in diameter (PM$_{10}$) resulting from both active and inert ingredients. The attributable risk calculation relied on conservative estimates (i.e., a worst case scenario) of population exposure to incremental PM$_{10}$ levels from the applied adulticides. That is, the assumptions that were made tended to overestimate the possible asthma impact of spraying events.

**Scientific Literature on How PM$_{10}$ Concentrations Induce Asthma Hospitalizations**

Some studies in the epidemiologic literature show associations between daily PM$_{10}$ levels and either hospital admissions or emergency room visits for asthma (Norris et al., 1999; Schwartz et al., 1993; Sheppard et al., 1999; Tolbert et al., 2000). Others do not (Henry et al., 1991; Hiltermann et al., 1997; Roemer et al., 1998; Roemer et al., 1999; Roemer et al., 2000). For the studies that report associations, it has not been established whether the associations are causal, and even if causal, it is unclear if the whole increment is attributable to PM$_{10}$, as opposed to other air pollutants that co-vary with PM$_{10}$ (Koren, 1997; Koren and Utell, 1997). Exposure of asthmatics in clinical chamber studies does not show exacerbation of asthma at ambient PM$_{10}$ levels (Utell et al., 1983). Also, asthma hospitalizations vary geographically in a pattern unrelated to the pattern of PM$_{10}$ concentrations (Carr et al., 1992; de Palo et al., 1994; Claudio et al., 1999). Moreover, asthma hospitalizations have a seasonal pattern different from PM$_{10}$ seasonal patterns (Thomas and Whitman, 1999). Finally, time trends in PM$_{10}$ concentrations over the recent decade are in a direction opposite to time trends in asthma hospitalizations over the same period (Mannino et al., 1998).

For the purposes of these asthma risk calculations, relationships from studies showing a positive association with PM$_{10}$ were employed. The associations were assumed to be causal, and the reported associations were assumed to be entirely due to PM$_{10}$, and not to other pollutants (e.g., SO$_2$, CO, O$_3$) and/or weather and stress conditions that may co-vary with PM$_{10}$. The epidemiologic associations reported in the literature have been developed from monitors that track generic, ambient PM$_{10}$, which is composed of diverse constituents including waste combustion particulate, hydrocarbon smog, fugitive dust, vehicle emissions, bioaerosols, wood smoke, sulfates, nitrates, etc. For the purposes of
our attributable asthma risk calculations, associations reported for ambient PM$_{10}$ were assumed to apply equally well to PM$_{10}$ generated by adulticide spraying.

**Assumptions for the Attributable Risk Analysis**

The epidemiologic associations on how PM$_{10}$ may affect asthma hospitalizations have used data on PM$_{10}$ 24-hour-average concentrations. The relevant exposure for this analysis is, therefore, the potential for an increased lung dose of inhaled particulate over a 24-hour time period. The epidemiologic studies examine whether any impact is detectable in asthma hospitalization statistics in the days after an increment in 24-hour-average PM$_{10}$ levels.

Thus, a key factor included in the projection is the maximum 24-hour-average increment in PM$_{10}$ concentration due to a single spraying event. For a single spraying event, the maximum 1-hour-average PM$_{10}$ concentrations for total aerosol (active+inert ingredients) at a distance of 25 ft laterally away from the route of the spraying truck have been predicted to range from a low of 2.5 µg/m$^3$ (for the product Dibrom Concentrate Insecticide which contains the active ingredient naled) to a high of 59 µg/m$^3$ (for the product Biomist 1.5+7.5 ULV which contains the active ingredient permethrin) (see Appendix 3.A-3). For the remaining 23 hours of the day, the increment contributed by the spraying would decrease to negligible levels.

Therefore, the maximum 24-hour-average PM$_{10}$ concentration was derived by dividing the above maximum 1-hour-concentrations by 24. Based on the calculation, the maximum 24-hour-average PM$_{10}$ concentration increment (above background PM$_{10}$ levels) due to spraying can range from a low of 0.11 µg/m$^3$ up to 2.5 µg/m$^3$. This represents a 23-fold range in incremental 24-hr-average PM$_{10}$ concentrations.

In any of the Representative Areas, given that the applications would occur in the evening, the percentage of the population actually exposed to spray would be significantly less than the total population. For this analysis, it was assumed that the whole zip code would be exposed (i.e., 100 percent of the population). The maximum number of spraying events expected per year for any Representative Area was assumed to be 10. To ensure a conservative analysis (i.e., most protective of human health), 10 spraying events per year per zip code were assumed in the calculations.

Asthma statistics for New York City represent another key set of factors included in this analysis to project the number of excess asthma hospitalizations due to spraying of adulticides. Asthma prevalence is likely to vary across the zip codes in the Representative Areas. Since asthma prevalence data are not available for New York City populations, national estimates of prevalence were included in our calculations. Thus, 7.4 percent used for was the prevalence of asthma in New York City children and 4.74 percent was used for adults (MMWR, 1998). These rates are likely to underestimate the rates in urban areas, especially in some areas of New York City where rates are known to be high. An NYCDHO survey in three public schools in the Hunts Point section of the Bronx revealed a prevalence (as defined by self-report of every being diagnosed with asthma and having symptoms in the last year) of 22 percent. A similar survey in 2 schools in East Harlem revealed a prevalence of 21 percent. The one zip code in a Representative Area for which data were available from the prevalence survey was 10474 (Hunts Point). For this zip code the prevalence rate of 22 percent was used to calculate the attributable risk.

The health outcome of interest, asthma hospitalizations, varies across the zip codes in the Representative Areas. Baseline asthma hospitalization rates range from a high of 14.3 per 1,000 per year for ages 0-14 (Hunts Point, zip code 10474) to a low of 0.90 per 1,000 per year for ages 15+ (Upper East side, zip code 10128, and Wolfe’s Pond West, zip code 10309). This represents a 16-fold
range in asthma hospitalization rates. For 1999, the total number of baseline asthma hospitalizations for children in all the Representative Areas in the EIS was 938 (ages 0-14). For 1999, the total number of baseline asthma hospitalizations for adults in all the Representative Areas was 1,299 (ages 15+). For the entire City as a whole, the number of asthma hospitalizations in year 1999 was 12,782 for ages 0-14, and 18,794 for ages 15+ (NYCDOH data).

**Estimation of Increases in Asthma Hospitalizations**

The generic aerosol component of the spraying, i.e., the total PM$_{10}$ concentration from the products, was assumed to be the relevant factor in increasing the risk of asthma hospitalizations, and the relationship between PM$_{10}$ concentrations and increased asthma hospitalizations was assumed to be a linear, non-threshold relationship that did not depend on the nature or level of the pre-existing, background PM$_{10}$.

The following effect functions, reported in the epidemiologic literature (and developed using data from Seattle and Atlanta) were utilized. It was assumed that the results represented associations that could be applied to New York City, and could serve as the basis of a relationship between PM$_{10}$ increments and potential for exacerbation of asthma hospitalization rate:

For Children:
- Norris et al, 1999: 15 percent increase per 11 µg/m$^3$, or 0.0136 per 1 µg/m$^3$
- Tolbert et al, 2000: 4 percent increase per 15 µg/m$^3$, or 0.0027 per 1 µg/m$^3$

For Adults:
- Schwartz et al, 1993: 12 percent increase per 30 µg/m$^3$, or 0.0040 per 1 µg/m$^3$
- Sheppard et al, 1999: 5 percent increase per 19 µg/m$^3$, or 0.0026 per 1 µg/m$^3$

The effect functions represent the fractional increment in daily asthma hospitalizations predicted to result from a daily increment in PM$_{10}$ concentrations. Thus, the incremental effect on annual asthma hospitalizations depends on the number of days per year that are affected by spraying events, which was estimated to be a maximum of 10. Using the maximum and minimum PM$_{10}$ increments and the maximum and minimum effect functions, the following ranges for the potential effect of spraying events on increasing the number of annual asthma hospitalizations for children and adults were derived:

**Fractional Increase for Children:**
- Upper range of effect: \( \frac{10}{365} \times 0.0136 \times 2.5 \) = 0.000932
- Lower range of effect: \( \frac{10}{365} \times 0.0027 \times 0.11 \) = 0.000008

**Fractional Increase for Adults:**
- Upper range of effect: \( \frac{10}{365} \times 0.0040 \times 2.5 \) = 0.000274
- Lower range of effect: \( \frac{10}{365} \times 0.0026 \times 0.11 \) = 0.000008

These estimates show that the maximum effect predicted for children would be about 1 asthma hospitalization per 1,000 baseline annual asthma hospitalizations. The maximum effect predicted for adults would be about 0.27 hospitalizations per 1,000 baseline annual asthma hospitalizations.
For 1999, the total number of baseline asthma hospitalizations for children aged 0-14 in the Representative Areas was 938. Hence, a maximum effect of about 1 of the asthma hospitalizations per year would be predicted as a result of the spraying. For 1999, the total number of baseline asthma hospitalizations for adults aged 15+ in the Representative Areas was 1,299. Hence a maximum effect of about 1 of the asthma hospitalization every three years would be predicted as a result of the spraying.

For the entire City, the number of 1999 asthma hospitalizations was 12,782 for ages 0-14, and 18,794 for ages 15+. Hence, if the entire City was subjected to 10 applications of adulticides and 100 percent of the population was directly exposed to the adulticide spraying, the above methodology would predict a maximum annual impact of 12 hospitalizations for ages 0-14 and 5 hospitalizations for ages 15+ that would occur as a result of the spraying.

Limitations to the PM$_{10}$ Approach for Estimating Attributable Risk

As discussed earlier, one of the major uncertainties with the PM approach is the assumption that the correlations reported in the epidemiologic literature reflect a causal relationship between PM and exacerbation of asthma. A number of lines of evidence that mitigate against a causal link have already been noted. Even with the assumption that the associations are causal, there is uncertainty as to whether the PM produced by spraying will cause effects similar to those linked to ambient PM. The spraying event is of short time duration, and the composition of the PM produced is different from that encountered in the ambient environment. The epidemiologic associations utilize 24-hour-average PM$_{10}$ concentrations, but the PM produced by spraying builds up and decays to zero over a much shorter time frame. In this analysis, the PM exposure from spraying was converted to its 24-hour-average equivalent, because no acceptable epidemiologic data are available for the impact on asthma of PM excursions of shorter duration.

The attributable risk estimates have relied on the assumption that any asthma impact is related to inhalation exposure of airborne spray ingredients in particulates that have an aerodynamic diameter of 10 micrometers or less (this is the definition of “PM$_{10}$”). It was estimated that PM$_{10}$ represents about 12 percent of the airborne particulate produced by spraying, and the possibility that the material in the larger particle sizes may have an effect cannot be ruled out. However, the larger particle sizes settle out of the air more quickly, and even if inhaled, do not penetrate as deeply into the respiratory tract as the PM$_{10}$ fraction. The PM approach also assumes that exposure is via inhalation of PM$_{10}$, and this methodology does not account for any effects via dermal exposure or ingestion exposure due to contact with material deposited on surfaces.

The PM$_{10}$ approach assumes that asthma impact is related to the mass of inhaled particle and not specifically to its allergic or antigenic potential. No numeric estimates are available that would allow calculation of attributable risk due to the allergic potential of the adulticide products. However, the PM$_{10}$ analysis does not rule out the possibility that some asthmatics may be allergic to some component in one of the products. None of the evidence available to date support allergenicity for the spray products. Finally, it should be acknowledged that stress may trigger an asthma attack, and the mere fact of witnessing or anticipating a spraying event could be stressful for some individuals.

As noted in the above discussion, the aerosolized adulticides differ substantially from ambient PM10 in terms of chemical composition and physical characteristics. Consequently, their disposition in the respiratory tract, as well as their ultimate effects, may also differ. For example, whereas insoluble ambient PM10 particles may be taken up by pulmonary macrophages and cleared from the respiratory tract via the mucociliary escalator, the aerosolized adulticides may dissolve in the mucus lining of the respiratory tract, with subsequent absorption into the systemic circulation. Once dissolved in the
mucous lining, the aerosolized adulticides may also elicit local reactions contributing to airway hyper-responsiveness. These include the ability of pyrethroids to irritate sensory nerves, the ability of malathion to stimulate mast cell de-granulation and histamine release, and the ability of petroleum distillates to function as mucous membrane irritants. However, as discussed in the toxicology section, the estimated inhaled dose is not expected to be sufficient to elicit these airway effects. The attributable risk analysis focused on PM, because it is only for ambient PM10 that correlative evidence suggests the possibility of effects on asthma at very low PM concentrations. Clinical and toxicologic data do not support asthma effects at such extremely low doses. The analysis provides a conservative estimate of possible effects.

Another limitation of the analysis is that attributable risks were based on 24-hour average aerosolized adulticide concentrations. It is possible that short-term exposures of duration less than 24 hours (e.g., several minutes) may be more relevant for evaluating effects of inhalation exposure on airway responsiveness. However, the correlative data used for estimating risks associated with exposure to ambient PM10 are only available for 24-hour average exposures. Therefore, the attributable risks based on 24-hour average aerosolized adulticide concentrations may underestimate actual risks.

E. CONCLUSIONS

The public health analyses indicate that the potential for illness, both mild and serious, without a program to control the adult mosquito population would be greater than the risk of adverse reaction to the chemical ingredients in the adulticides proposed for the Mosquito-Borne Disease Control Program. The conclusions from each public health analysis (Literature Review, Risk Assessment and Epidemiologic and Attributable Risk Analyses) are discussed below.

Literature Review

Skin and Eye Irritation

Although there is some evidence that certain inerts can cause skin irritation in humans, skin irritation would more likely occur only after direct contact on the skin with liquid forms rather than from exposure associated with inert droplets and mists. Because all of the active adulticide ingredients have been linked to skin and eye irritation in humans, unnecessary exposure to workers and residents should be minimized to the greatest extent possible during the spraying intervals to reduce the potential for skin and eye effects.

Gastrointestinal

From the data available, only the two organophosphate compounds, malathion and naled, appear to produce gastrointestinal symptoms. These effects occurred when people were exposed to levels far higher than would be expected from spraying in New York City. No reports were found linking either the pyrethroids, the synergist, or the inerts to these ailments.

Respiratory Effects Including Asthma

Based on this review of the available literature, the application of adulticides is not expected to appreciably increase the occurrence of asthma attacks or other respiratory health effects due to the very low exposure concentrations. However, as mentioned earlier, there may exist in New York City a susceptible sub-population who might have a pre-existing sensitization due to prior exposures due to occupation (e.g., exterminators), hobbies (e.g., gardening) or home use of insecticides.
Immunologic/Allergic
Allergic reactions beyond irritation reactions have not been found to be commonly caused by any of the active ingredients reviewed in this report. The immune system-enhancing or -reducing health effects of the active ingredients are still poorly understood at this time. Malathion's mixed effects on the immune system are thought to be caused by a common contaminant in malathion mixtures, generally associated with storage of malathion. Similarly, the data on permethrin and resmethrin are also inconclusive as to what effects, if any, they have on the immune system and illness rates in humans or animals. At this time it is not possible to conclude with certainty what impact, if any, the adulticides might have on the immune system.

Multiple Chemical Sensitivity
There are conflicting reports found in the peer-reviewed scientific literature on the possible links between the active ingredients and the synergist and MCS. One report provides a list of substances that may contain certain ingredients that are possibly in the adulticide products that can be suspected of causing the onset of MCS. Although people with MCS often do report a link between their illness and exposure to pesticides, to date no scientific studies in the available literature reviewed have definitively linked pesticide exposure with MCS. The controversy surrounding the cause of MCS may encourage researchers to explore more aggressively the causal links between the onset of the illness or development of symptoms and environmental factors. However, without a scientific consensus on the processes that create susceptibility to MCS, it is not possible to evaluate the role that adulticides or their chemical constituents might play in MCS reactions.

Neurological
The current peer-reviewed scientific literature indicates that exposure to some of the active ingredients of adulticides, as well as some of the inerts, is associated with neurological effects in humans and animals. The symptoms and durations of these effects vary widely, and may be caused by multiple biological mechanisms. It is noteworthy that malathion breakdown products more toxic than malathion itself can be formed after the preparation has been stored for a long period of time. Many of these studies demonstrate effects elicited under short-term, high-level exposure to the active and inert ingredients in adulticides. Examples of exposures that are more representative of the spraying of adulticides in New York City indicate that neurological effects would be either mild or completely absent in both humans and animals. For instance, some studies report that long-term, low-level exposure to organophosphates is generally thought to result in short-term effects on cognitive function, and neurological components of the eye. However, other studies of humans exposed to malathion are either complicated by simultaneous exposure to other chemicals, or present contradictory evidence of nervous-system effects in humans. The literature as cited in this section suggests that other adulticide ingredients such as permethrin are regarded as having negligible health effects at low levels of exposure, while available data on resmethrin and sumithrin show no neurological damage even at high levels of exposure.

Cognitive Developmental Disabilities Including Autism
In general, the causes of learning disabilities ranging from autism to mild retardation are not well understood, and possible environmental causes of these developmental disorders are uncertain at this time. Many researchers and environmental health specialists agree that more neurologic and developmental toxicity research is needed on environmental contaminants, including pesticides. For example, age-dependent sensitivity and developmental periods of susceptibility need to be examined in pesticide developmental toxicity evaluations at all stages of development (Bruckner, 2000; Claudio
et al., 1999). However, based on published studies, it is unlikely that pesticide exposures could be deemed responsible for either causing or exacerbating these conditions.

**Endocrine Disruption**

In general, the identity and mechanisms of endocrine disruptors are not well understood at this time. Many researchers and environmental health specialists agree that more laboratory screening and testing are needed on potential endocrine disruptors, including pesticides, both individually and in mixtures. However, based on the current evidence, of the compounds of interest, only malathion is a suspected endocrine disruptor with serious reproductive effects. It is uncertain whether two of the three pyrethroids considered in this EIS, permethrin and sumithrin, may also have endocrine disruptive effects. In all cases, it is unlikely that insecticide exposure due to spraying would be high enough to be deemed responsible for causing endocrine disruptive effects.

**Developmental/Reproductive Including Birth Defects**

The scientific evidence suggests that for the adulticides’ active ingredients evaluated in this EIS, developmental effects are not likely to occur in the absence of other health effects in parents. By contrast, reproductive effects were found in animal tests for every adulticide, but the doses needed to produce those adverse reproductive effects varied widely. With regard to reproductive toxicity effects in animal tests, the lowest doses causing adverse effects were the following: malathion (1 mg/kg and reduced conception rates), sumithrin (300 mg/kg and birth defects), and resmethrin (500 mg/kg and developmental toxicity in a 3-generation study). The literature suggests that the safest compounds in animal tests based on the doses needed for adverse effects were permethrin (greater than 2,500 mg/kg) and PBO (1,000 mg/kg). With very limited data available for naled it is not possible to determine safe doses of naled at this time. The adulticides’ active ingredients are not likely to be present at significant levels in breast milk. Furthermore, if the active ingredients are present in breast milk, exposures occurring via consumption of breast milk are expected to be much lower than exposures occurring via other pathways that are addressed in the risk assessment component of this study.

Each of the doses described in the animal studies summarized here correspond to human exposure levels much greater than those anticipated following the spraying of adulticides for mosquito control. For example, the anticipated exposure to malathion ranges from 0.000013 mg/kg to 0.244 mg/kg. Therefore, no reproductive adverse health effects are expected at the environmental doses following spraying. This expectation is confirmed by the human evidence citing a lack of reproductive harm in people in areas treated with adulticides for mosquito control. For malathion and permethrin, the limited human data from past pest-control efforts suggest that no adverse reproductive or developmental effects should be expected from the anticipated exposure levels of these ingredients.

**Cancer**

Numerous environmental health protection agencies at international, national, and state levels regulate compounds based on their known or suspected ability to cause cancer. Of the adulticide compounds considered in this EIS, only malathion and permethrin have been studied enough to be adequately classified by the IARC or the USEPA. Both of these are listed as suggestive or possible carcinogens. As seen the review of the literature for all the adulticide compounds, the other three active ingredients (naled, resmethrin, and sumithrin) have very limited data and no final decision has been made regarding their carcinogenic potential. Similarly, the synergist PBO has too little data for classification as a carcinogen or non-carcinogen.
**Risk Assessment**

According to the public health Risk Assessment, none of the evaluated human populations (i.e., child and adult resident, workers, homeless people, school children and teacher, and park visitors and community gardeners) have HIs (ratios of exposures over non-cancer health criteria) exceeding a value of 1.0 for all active ingredients evaluated in this assessment under average or reasonable maximum exposures. Thus, non-cancer adverse health effects are not expected. Although the HIs are still below a value of 1.0 for naled, potential exposures to naled resulted in the highest ratios; whereas, potential exposures to sumithrin resulted in the lowest ratios for all active ingredients evaluated in this assessment. Because of the various safety factors incorporated in the derivation of the non-cancer health criteria to account for the variability in sensitivity of people, including pregnant women, the developing fetus, the elderly, and the chronically ill, non-cancer adverse health effects associated with potential exposures to the active ingredients are not expected for these individuals.

Carcinogenic risks characterized for the human populations evaluated above are within or below the USEPA-determined acceptable target risk range of less than one in one million to one in ten thousand. The highest cancer risk of roughly 1 in 200,000 estimated in this assessment is for residents (child and adult combined) under reasonable maximum exposures to permethrin. This value represents the added probability of getting cancer above the background cancer risk typically experienced by all individuals in the course of daily life. As discussed earlier, taken all cancers together, cancer is a fairly common disease. In New York City alone, 30,000 new cases of cancer are diagnosed each year. Generally, the incidence of cancer increases with age and often varies by place of residence, racial/ethnic background and other demographic features of the population. Nationally, cancer is the third leading cause of death. For New York City residents, cancer has been the second leading cause of death for both men and women. The American Cancer Society has determined that the lifetime probability of developing cancer is 43.5 percent (or one chance in 2.3) in men and 38.3 percent (or one chance in 2.6) in women. Although still within acceptable target risk range, the highest risks for all human populations evaluated in this assessment are associated with exposures to permethrin. Cancer risks associated with exposures to malathion are approximately 10 to 100 times lower than risks associated with permethrin.

Although toxicity criteria for cancer are not available for resmethrin, sumithrin, and PBO, there is some limited evidence that these active ingredients may be carcinogenic. A margin of exposure (MOE) analysis was performed for resmethrin, sumithrin, and PBO for the child resident (considered to be the most sensitive group evaluated in this risk assessment), and for resident adults. In this analysis, to ensure adequate protection for human health, a calculated MOE should be greater than the comparison MOE. The comparison MOE was selected as an additional safety factor to ensure adequate protection for human health. The calculated MOEs (i.e., reference dose divided by exposure dose) for resmethrin and sumithrin are greater than the comparison MOEs for these two chemicals, which indicates that potential exposures to these two chemicals by resident children is low enough not to be of concern. The calculated MOE for PBO (at the highest concentration found in pyrethroid products—54 percent), is slightly lower than the comparison MOE. Although this would imply that potential exposures to PBO present in an adulticide product may not be low enough to ensure adequate protection for human health, it is not considered a significant adverse public health impact due to the likelihood of overestimation in the calculations.

Finally, results from the risk-based concentration (RBC) approach to evaluate acute exposures (e.g., inhalation of drift, skin contact with drift while spraying, and ingestion of drift deposited on hands) by resident children indicate that the maximum modeled air concentration for sumithrin, resmethrin, permethrin and PBO occurring within 24 hours of adulticide spraying are lower (up to 10 times...
lower) than the calculated RBCs. However, the maximum modeled air concentrations for malathion and naled are greater than the calculated RBCs, which would imply that immediate health effects could potentially result from malathion and naled exposures. However, given the conservative assumptions used in this calculation, exposures are likely overestimated. Therefore, considering the conservative assumptions, and the short-term (acute) nature of the exposure, exposures to malathion and naled would not constitute a significant adverse public health impact.

Uncertainties in this public health risk assessment exist in numerous areas, including derivation of toxicity values, and estimation of potential exposures to adulticides by human populations. However, where uncertainties exist, conservative inputs or approaches were used so that potential risks would be overestimated.

**Epidemiologic and Attributable Risk Analyses**

**Epidemiologic Analysis**

No conclusions about the potential relationship between adulticide use and asthma exacerbations can be made from the results of the epidemiologic analyses. For the most part, the data indicated that, overall, the use of adulticides did not appear to appreciably increase asthma hospital admissions or emergency department/urgent care visits in 1999 at the population level relative to prior years. However, in some subgroups or boroughs increases were found. An important criterion in epidemiology is whether results are consistent across groups and in different studies. Additionally, the more analyses that are performed, the more likely it is to identify a positive finding. While our analyses have revealed some findings that may be suggestive of higher asthma rates after spraying, these findings were not consistently found and must, therefore, be interpreted with caution. However, because analyses at the zip code level were not possible for 1999 or at the individual level (i.e., exposed individuals only), only gross population changes can be detected. As a result, this analysis cannot rule out the possibility that use of adulticides precipitated an increase in asthma or respiratory exacerbations in subgroups of New York City’s population.

The epidemiologic analyses are an attempt at investigating the effects of adulticides on asthma exacerbations. Due to the many limitations of these investigations, these analyses should be viewed as a first step in describing asthma exacerbations during pre and post spraying periods. These analyses should not be considered conclusive of a finding of an effect or non-effect. Clearly, analytic approaches need to be developed to determine if any potential effect on asthma exacerbations is the result of adulticide use. Additional epidemiologic research utilizing more sensitive exposure and outcome as well as measures of potential confounders need to be developed.

**Attributable Risk Calculation**

The results of the attributable risk calculation show that the maximum effect predicted for children would be about 1 asthma hospitalization per 1,000 baseline annual asthma hospitalizations. The maximum effect predicted for adults would be about 0.27 hospitalizations per 1,000 baseline annual asthma hospitalizations.

For 1999, the total number of baseline asthma hospitalizations for children aged 0-14 in the Representative Areas was 938. Hence, a maximum effect of about 1 of the asthma hospitalizations per year would be predicted as a result of the spraying. For 1999, the total number of baseline asthma hospitalizations for adults aged 15+ in the Representative Areas was 1,299. Hence a maximum effect of about 1 of the asthma hospitalization every three years would be predicted as a result of the spraying.
For the entire City, the number of 1999 asthma hospitalizations was 12,782 for ages 0-14, and 18,794 for ages 15+. Hence, if the entire City was subjected to 10 applications of adulticides and 100 percent of the population was directly exposed to the adulticide spraying, the above methodology would predict a maximum annual impact of 12 hospitalizations for ages 0-14 and 5 hospitalizations for ages 15+ that would occur as a result of the spraying.

**Overall Conclusions**

For this EIS, potential public health impacts in New York City from the implementation of the *Mosquito-Borne Disease Control Program* were evaluated using three major approaches: Scientific Literature Review; Risk Assessment; and Epidemiologic and Attributable Risk Analyses. Each of these three approaches can provide some of the necessary information required in evaluating these potential impacts. Likewise, each has its limitations. However, when these elements are reviewed together, they each contribute to providing a more complete assessment. This can be used to weigh the existing evidence.

Based on the literature reviewed, adverse health impacts from potential exposure to adulticides at the levels associated with mosquito control, are not expected for such public health issues as gastrointestinal distress, neurological effects, cognitive developmental disabilities, endocrine disruption and developmental/reproductive effects. At this time, it is not possible to determine solely from the literature, the potential effects of the adulticides on the immune system and MSC reactions. However, based on the Risk Assessment, exposures to the adulticides at levels expected from application for mosquito control indicate no adverse health impacts for all non-cancer public health issues.

As discussed above in the Conclusion sections of the Literature Review, all six of the active ingredients and certain inert ingredients have been linked to skin and eye irritation in humans upon direct exposure. However, the risk assessment conducted for this EIS indicated that for only two active ingredients (malathion and naled), a one-time exposure (i.e., exposure through inhalation, direct skin contact or ingestion) could result in short-term health effects (e.g., skin irritation or respiratory effects) for some individuals. It should be noted however, that risk assessment calculations were based on conservative exposure assumptions (e.g., direct exposure occurring at 25 feet from the spray truck) and, therefore, these exposures are not the exposures anticipated for the general population. However, there may be more highly susceptible subpopulations (e.g., exterminators, gardeners), some of whom have pre-existing sensitizations. Also, although naled was modeled in the risk assessment in the same manner as the other active ingredients (i.e., to yield conservative results, the risk assessment results were based on concentration and deposition values from ground application), ground application of naled is not considered for the Proposed Action. A review of the scientific literature suggested that the application of adulticides is not expected to significantly increase the occurrence of asthma events or other respiratory health effects at the low exposure concentrations associated with mosquito control. The epidemiologic analysis of short-term respiratory events found that no conclusions about the potential relationship between adulticide use and asthma exacerbations can be drawn. The attributable risk calculation predicted that the increase in asthma hospitalizations potentially related to the application of adulticides as part of the Proposed Action would be relatively low among both adults and children with existing asthma. The analyses described are an attempt at investigating the effects of adulticides on asthma exacerbations. Due to the many limitations of these investigations, these analyses should be viewed as a first step in describing asthma exacerbations during pre and post spraying periods. These analyses should not be considered conclusive of a finding of an effect or non-effect. Clearly, analytic approaches need to be developed...
to determine if any potential effect on asthma exacerbations is the result of adulticide use. Additional epidemiologic research utilizing more sensitive exposure and outcome as well as measures of potential confounders need to be developed.

The potential impacts from spraying adulticides should be compared with the potential public health impacts if adulticide spraying were not conducted. The West Nile virus outbreaks in New York City in both 1999 and 2000 demonstrated that West Nile virus infection can result in serious illnesses, including encephalitis and meningitis, and deaths. In other countries that had not experienced large outbreaks of the virus, recent outbreaks have been surprisingly severe. Since 1996, there have been significant West Nile virus outbreaks in southern Russia (40 deaths, approximately 1,000 diagnosed cases) and Romania (17 deaths, approximately 500 diagnosed cases). Less severe illnesses associated with West Nile virus infection could affect New York City residents, as demonstrated by the results of the serosurveys conducted in Queens and Staten Island. While there is a possibility that some sensitive individuals may experience health effects within a short period of time following application of adulticides for control of mosquitoes, it is likely that such impacts would be short-term in nature.

For PBO, because there is less cancer risk information available, a very conservative USEPA cancer model was used. This model employs a comparison number to which a calculated cancer risk number is compared. The calculated risk number should equal or exceed the comparison number. The NYCDOH EIS Risk Assessment assumed a long-term exposure for an individual to be exposed to 10-spray events in a 2-month period, occurring every year over 30 years to the maximum concentration of PBO found in any of the pyrethroid products evaluated. The calculated cancer risk number (8) was very close to the comparison cancer risk number of 10. Given the very conservative exposure assumptions made and the conservative modeling used, the cancer risk from PBO is in all likelihood overpredicted.

Among a minority of persons in the general population, exposure to the adulticides evaluated in this EIS could result in minor, short-term, self-limiting symptoms including eye and nose irritation and/or respiratory symptoms from the Proposed Action. Long-term non-cancer health effects were determined to be unlikely, and the risk associated with long-term exposure to PBO is considered to be negligible from the Proposed Action.

The likelihood of symptom occurrence would be increased for people who are directly exposed, such as those individuals who are accidentally directly sprayed. As with other exposures that could potentially have adverse effects, reducing exposure is of prime importance. Every precaution would be taken to prevent such occurrences. NYCDOH would make every reasonable effort to keep the public informed with respect to the schedule for applying the pesticides, so that sensitive persons and the general public can take appropriate precautions to prevent exposure. Spraying would generally be applied in the late evening hours, and announcements would be made preceding the vehicles as a warning to people who may be in the immediate area.

Therefore, from evaluation of the results of the three public health analyses mentioned above, it was determined that no significant adverse public health impacts would be expected from exposure to the adulticides when applied for the purposes of the Mosquito-Borne Disease Control Program and that any effects would likely be less than those of West Nile virus.

The analysis relies on the universe of information available (such as the literature review, the results of the risk assessment and the epidemiologic and attributable risk analyses), and the precautions that would be undertaken by NYCDOH. NYCDOH is aware that the experiencing of symptoms by particular individuals even if for a relatively short period of time, may be considered “significant” to those affected persons. However, in determining the significance of the potential adverse impact of
the Proposed Action on public health, NYCDOH has determined that the potential adverse effects to the population from applying pesticides would not be considered significant when they are outweighed by the potential risk to the public health if the Proposed Action were not taken.

NYCDOH may need to use adulticides to prevent serious illness and deaths from West Nile virus in future years. The results of this EIS will help inform the department’s decision in selecting which chemical or chemicals to use in adulticiding efforts.
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CHAPTER 3.C: PUBLIC HEALTH


3.C-137 July 2001


Table 3.C-3 Projected* West Nile Infections: Future Without an Adult Mosquito Control Program** ........3.C-13
Table 3.C-4 1999 Child Asthma Hospitalizations ...........................................................................3.C-16
Table 3.C-5: Relevant Exposure Pathways .....................................................................................3.C-62
Table 3.C-6: Exposure Point Concentrations in Various Media Where: ........................................3.C-65
Where: ..............................................................................................................................................3.C-66
Table 3.C-7 USEPA Recommended Toxicity Criteria .................................................................3.C-83
Table 3.C-8 All Populations and Pathways - Summary of Non-Cancer Risks (Average Exposures) table 8
 contTable 3.C-9 All Populations and Pathways - Summary of Non-Cancer Risks (Reasonable Maximum
 Exposures) ........................................................................................................................................3.C-86
Table 3.C-9 All Populations and Pathways - Summary of Non-Cancer Risks (Reasonable Maximum Exposures)
 ...........................................................................................................................................3.C-88
Table 3.C-10 All Populations and Pathways—Summary of Cancer Risks (Average Exposures) ........3.C-91
Table 3.C-11: All Populations and Pathways - Summary of Cancer Risks (Reasonable Maximum Exposures)
 ..................................................................................................................................................3.C-92
Table 3.C-12 Margin of Exposure Analysis (based on resident children) ........................................3.C-94
Table 3.C-13 Evaluation of Acute Exposures ................................................................................3.C-96
Table 3.C-14: Risk Assessment Summary .....................................................................................3.C-100
Table 3.C-15 Rate Ratios* of Monthly Public and Private Hospital Asthma Admissions in the Five Boroughs
 (1989-99) ........................................................................................................................................3.C-105
Table 3.C-16 Rate Ratios* of Monthly Public and Private Hospital Asthma Admissions in the Five Boroughs by
 Age Group (1989-99) ......................................................................................................................3.C-105
Table 3.C-17 Rate Ratios* of Weekly Public & Private Hospital Asthma Admissions in the Five Boroughs
 (1989-99) ........................................................................................................................................3.C-107
Table 3.C-18 Rate Ratios* of Weekly Public & Private Hospital Asthma Admissions in the Five Boroughs by
 Age Group (1989-99) ......................................................................................................................3.C-107
Table 3.C-19 Rate Ratio*, Weekly Public Hospital ED & Urgent Care Asthma Visits By Borough, September-
Table 3.C-20 Rate Ratio, Weekly Public Hospital ED & Urgent Care Asthma Visits By Age Group, September-
 August, 1995-1999 ........................................................................................................................3.C-110