Appendix VI (b)
Malathion TOX Q & A Circular

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TOX Q & A Circular

MALATHION

This document provides information to public health practitioners on the potential adverse health effects of malathion, treatment, case definitions, severity index, and exposure standards; resource references are also included. Malathion may be used in mosquito control programs to prevent the spread of West Nile Virus. It is not expected to pose an unacceptable health risk to bystanders when applied according to label directions by trained licensed applicators.

What is malathion?

- Malathion (CAS number: 121-75-5) is broad-spectrum organophosphate insecticide registered in Canada for use in agriculture, home and garden, and for adult mosquito control programs. It has been used widely on a variety of agricultural crops since the 1950's in Canada and the US.

- It is a clear amber-colour liquid at room temperature with strong odour and low volatility, miscible in most organic solvents, but only slightly miscible in water. It is corrosive to some metals and may damage plastic, rubber and painted surfaces.

How does malathion exert its action?

- Malathion acts by inhibiting cholinesterase, the enzyme responsible for the destruction of the neurotransmitter acetylcholine. Inhibition of cholinesterase can cause accumulation of acetylcholine leading to disruption of normal physiological function. The dose required to kill adult mosquitoes, however, is much lower than that expected to produce adverse effects in humans.

- The cholinesterase inhibitory activity of malathion is primarily due to its metabolite malaxon.

How toxic is malathion?

- Malathion is readily absorbed into the body by ingestion, inhalation and through the skin.
- Malathion exhibits low acute toxicity via the oral, inhalation and dermal routes of exposure.
- Direct contact may cause skin and eye irritation.
- There is suggestive evidence of carcinogenicity of malathion in animal studies at high concentrations, but insufficient evidence to assess its carcinogenicity in humans.
- High doses of malathion in animal studies were found to result in developmental effect;

Does malathion use in mosquito control programs pose risk to public health?

- As with other chemical exposures, the risk of occurrence of adverse effects depends on the level of exposure to malathion and the susceptibility of the individual.
- Malathion is applied in mosquito control programs by truck-mounted or aircraft-mounted Ultra Low Volume (ULV) sprayers, dispensing very fine aerosol droplets that kill adult mosquitoes on contact. Very small amounts of malathion are used per unit area treated (up to a maximum of 60.8 g/hectare by ground application), minimizing the potential for exposure and risks to people.
- Malathion has been used safely in a number of large-scale pest control programs, including in the control of mosquitoes in Canada and the US, and in the control of Mediterranean fruit fly outbreaks in Florida and California.
- Health Canada has recently completed a risk assessment of public health uses of malathion, using most current scientific information and applying stringent safety factors, including special protection for children. It concluded that large-scale applications of malathion for adult mosquito control in residential areas do not pose unacceptable risk to bystanders and applicators, when applied by ULV equipment according to label directions. The exposure for a person who is outdoors during a spray application is estimated to be over a thousand times lower than the exposures that might pose a health concern.

- The risk assessment of malathion by the US Environmental Protection Agency has also indicated that health risks to bystanders from public health mosquito control programs are low and not of concern when used appropriately.

- Cases of significant malathion exposure may occur from accidental exposure.

- The public should be notified where and when pesticide application will take place (Regulation 914 under the Ontario Pesticide Act), so they can take measures to minimize exposure. Recommended precautions to minimize exposure include:
  - staying indoors during and immediately after spraying
  - Closing all windows and doors. Turning off air conditioning units and closing vents to circulate indoor air before spraying begins
  - Covering swimming pool surfaces
  - Covering outdoor furniture and play equipment or rinsing them off with water after spraying is finished.
  - Washing home-grown fruits and vegetables with water before cooking or eating them.
  - If eyes or skin come in contact with malathion spray, rinse immediately with water.
  - Wash clothes that come in direct contact with spray separately.

What are the signs and symptoms of malathion overexposure?

- Exposure to high doses of malathion, such as in the case of an accidental exposure, can cause short-term adverse health effects.

- As with all organophosphates, malathion poisoning is caused by the inhibition of cholinesterase. This results in elevated levels of acetylcholine and cholinergic over stimulation peripherally at neuroeffector junctions (muscarinic effects), at skeletal myoneural junctions and autonomic ganglia (nicotinic effects), and in the central nervous system.

- Depending on the level of exposure and susceptibility of the individual, a range of signs and symptoms of malathion overexposure may be experienced including:
  - **Exocrine glands:** Salivation, lacrimation, perspiration
  - **Eyes:** Miosis (pinpoint pupils), blurred vision
  - **Respiratory:** Rhinorrhea, coughing, wheezing, bronchial secretion, chest tightness, bronchoconstriction, respiratory depression. Respiratory failure is the most common cause of death in severe cases of malathion poisoning
  - **Cardiovascular:** Changes in heart rate and blood pressure. Bradycardia and hypotension are induced by muscarinic stimulation, but may be obscured by transient tachycardia and

hypertension due to nicotinic effects
  - **Gastrointestinal:** Nausea, vomiting, diarrhea, abdominal cramps
  - **Bladder:** Increased urination
  - **Skeletal Muscles:** Muscle twitching, cramps, and weakness
  - **Central Nervous System (CNS):** Headache, dizziness, drowsiness, fatigue, irritability, anxiety, confusion, tremor, convulsions, and coma. CNS effects are often the earliest manifestations of poisoning in adults and constitute the major signs and symptoms in children.

- Malathion poisoning is not known to cause delayed or long-term health effects.

- An "Intermediate Syndrome" has been reported with other organophoshates. It consists of respiratory and skeletal muscle weakness beginning 1 to 4 days after initial recovery from the acute cholinergic poisoning and may last up to 15 days.

- Rarely, the occurrence of "Organophosphate-Induced Delayed Neuropathy" (OPIDN), a distal sensory-motor polyneuropathy that may begin 6 to 21 days after exposure, has been described with other organophoshates

How is overexposure to malathion treated?

- As with other organophosphates, the treatment acute poisoning consists of supportive measures and repeated administration of antidotes.

- If breathing is depressed or stopped, artificial respiration should be applied. Contaminated clothing and shoes should be removed and isolated. Where direct contact with the substance occurred, skin and/or eyes should be flushed immediately with water.

- Two drugs that are used to treat organophosphate toxicity are:
  - **Atropine** is the classical antidote, a cholinergic receptor antagonist which is extremely effective in blocking the effects of excess acetylcholine at peripheral muscarinic sites.
  - **Pralidoxime** (2-PAM), a cholinesterase re-activator which is used in conjunction with atropine to relief both nicotinic and muscarinic effects. It is administered in severe poisoning cases only, and as early in poisoning as possible to be efficacious.

- Early administration of diazepam, in addition to atropine and pralidoxime, may help prevent the onset of seizures and potential brain and cardiac morphologic damage.

Are there laboratory tests to evaluate malathion exposure?

- Blood is drawn to determine the levels of plasma cholinesterase and red blood cells (RBC) acetylcholinesterase levels. Depressions of plasma cholinesterase and/or RBC acetylcholinesterase are generally available biochemical indicators of organophosphate exposure, but are not specific to malathion. If the measured levels are lower than the lower limits of the normal activities of these enzymes, this usually indicates excessive absorption of cholinesterase-inhibiting chemicals. The absence of individual's baseline enzyme levels and other factors, including liver damage, may affect the interpretation of the results.

- Measurement of the alkyl phosphate metabolites of malathion in urine is a better indicator of exposure, but it is not normally used due to lack of qualified laboratories that can perform this analysis.

How to investigate an incident of malathion exposure?

- The "Control of West Nile Virus" regulation (199/03) under the Ontario Health Protection and Promotion Act requires the local Medical Officer of Health to "maintain a means to record, investigate, and report any confirmed or likely adverse or unintended human health effects attributed to mosquito control actions".

- Data collection on the exposure, health effects and relationship between exposure and effect is required. This includes date and location of exposure, route of exposure, date of the illness event, signs and symptoms, and laboratory test results.

- To determine causality between exposure and health effects, the criteria for exposure, health effects, and causality between exposure and effect that are used by the US national public health pesticide surveillance system to define cases of pesticide-related illness can be applied. Based on that, the following are three reportable case classifications for malathion:
  1) **Definite case**
     a) Exposure criteria: Laboratory/clinical/environmental corroborate exposure
     b) Health effects criteria: two or more new post-exposure abnormal signs and/or laboratory findings reported by a licensed health care professional.
     c) Causality criteria: there is evidence supporting causal relationship between exposure and health effect (health effects consistent with malathion and temporal relationship between exposure and health are plausible).
  2) **Probable case**

a) Criteria for exposure and causality are the same as for definite case (above), and two or more new post-exposure abnormal symptoms were reported; or
b) Criteria for health effects and causality are same as for definite case (above), but evidence of exposure is based solely upon written or verbal report.

3) Possible case

a) Exposure criteria: evidence of exposure is based solely upon written or verbal report
b) Health effects criteria: two or more new post-exposure abnormal symptoms reported
c) Causality criteria: Same as for definite case

- The severity index of the US "State-Based Surveillance of Acute Pesticide Illness and Injury" can then be used in conjunction with the case definitions for malathion related illness. The four severity categories are:
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  - **S-1 Death**

  - **S-2 High severity**
    - life threatening and typically requires treatment and hospitalization
    - signs and symptoms include coma, cardiac arrest, renal failure, and respiratory depression.
    - individual sustains substantial loss of time from work or other activities (>5days)
    - individual may sustain permanent functional impairment

  - **S-3 Moderate severity**
    - severe illness often involving systemic manifestations, and treatment provided
    - no residual impairment is present

  - **S-4 Low severity**
    - often manifested by skin, eye or upper respiratory irritation. It may also include fever, headache, dizziness or fatigue.
    - typically resolved without treatment
    - minimal lost time (<3days) from work or normal activities

What are the maximum allowable concentrations of malathion in air and drinking water in Ontario?

- 24hr time-weighted average ambient air standard: 120ug/m3 (Regulation 337 under the Environmental Protection Act).
- 8hr time-weighted average occupational exposure limit in air: 1 mg/m3 inhalable vapour and aerosol
- (Regulation 833 amended to 70/5 respecting Control of Biological and Chemical Agents under the Occupational Health and Safety Act)
  - Maximum concentration in drinking water: 0.19 mg/liter (Regulation 169/03 under the Safe Drinking water Act)

References

Agency for Toxic Substances and Disease Registry (ATSDR). ToxFAQs™ for Malathion, Sept 2001. http://www.atsdr.cdc.gov/tfacts154.html

ATSDR. Medical Management Guidelines (MMGs) for Malathion, June 16, 2003. http://www.atsdr.cdc.gov/MHMI/mmg154.html

Center for Disease Control (CDC). Surveillance for Acute Insecticide – Related Illness Associated with Mosquito-Control Efforts --- Nine States, 1999—2002;

MMWR, July 11, 2003.
http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5227a1.htm

CDC. Case definition for acute pesticide-related illness and injury cases reportable to the National Public Health Surveillance System, Jan 31, 2000.
http://www.cdc.gov/niosh/pestsurv/pdfs/pest-casedef2000.pdf

CDC. Severity index for use in state-based surveillance of acute pesticide-related illness and injury, Nov 01, 2003.
http://www.cdc.gov/niosh/pestsurv/pdfs/pest-sevindexv6.pdf

US National Pesticide Information Center (NPIC). Malathion Technical Fact Sheet, February 2001. http://npic.orst.edu/factsheets/malatech.pdf

Extension Toxicology Network (EXTOXNET). Pesticide Information Profiles, Malathion, June 1996. http://ace.orst.edu/info/extoxnet/pips/malathio.htm

New York State Department of Health. Malathion and Mosquito Control Information Sheet, June 2002.
http://www.health.state.ny.us/nysdoh/pest/malathio.htm

New York State Department of Health. Health Advisory: Tick and Insect Repellents, Information related to insecticide use for preventing the spread of west Nile virus, June 2002.
http://www.health.state.ny.us/nysdoh/pest/hlthWNV.htm

US Environmental Protection Agency (EPA). Recognition and Management of Pesticide Poisonings, 5th edition, January 27, 2003.
http://www.epa.gov/oppfead1/safety/healthcare/handbook/handbook.htm

US EPA. Pesticides: Topical & Chemical Fact Sheets, Malathion for Mosquito control, April 17, 2002.
http://www.epa.gov/pesticides/factsheets/malathion4mosquitos.htm

US EPA. Questions & Answers, Malathion Preliminary Risk Assessment, May 11, 2000. http://www.epa.gov/pesticides/op/malathion/malathionq&a.pdf

US EPA. Office of pesticide Programs, Overview of Malathion Risk Assessment, November 6, 2000. http://www.epa.gov/pesticides/op/malathion/overview.htm

US EPA. Office of Pesticides Programs, Malathion Summary, November 3, 2000. http://www.epa.gov/pesticides/op/malathion/summary.htm

Health Canada. Fact Sheet on the use of Malathion in Mosquito Control Programs, April 2003.

Health Canada Pest Management Regulatory Agency (PMRA). Draft Malathion Re-evaluation Document, July 2003.

B. Mokhlesi et al. Critical Care Review, Adult Toxicology in Critical Care, Part II: Specific Poisonings, CHEST 123:897-922, 2003.

American Conference of Governmental Industrial Hygienists (ACGIH). Documentation for Biological Exposure Index of Acetylcholinesterase Inhibiting Pesticides, 2001.

D. J. Ecobichon. Toxic Effects of Pesticides. In C.D. Klaassen, ed., Casarett and Doull's Toxicology: The Basic Science of Poisons, McGraw-Hill, New York, 1996, pg. 643-689.

H. Kalant and W.H.E. Roschlau, eds., Principles of Medical Pharmacology, 6th ed., Oxford University Press, New York, 1998, Pg. 130-147.

California Environmental Protection Agency. Office of Environmental Health Hazard Assessment (OEHHA), Guidelines for Physicians who supervise workers exposed to cholinesterase-inhibiting pesticides, 4th edition, 2002. http://www.oehha.ca.gov/pesticides/pdf/docguide2002.pdf

California Environmental Protection Agency. OEHHA, Pesticide Illness Surveillance (pesticide illness reporting), 2000. http://www.oehha.ca.gov/pesticides/programs/Pestrpt.html

New York State Department of Health. New York State West Nile Virus Responsible Plan – Guidance Document, May 2001.

Ontario Ministry of the Environment. Malathion Best Practices Document, July 2003.