FRONTIER CENTRE FOR PUBLIC POLICY
FRONTIER Backgrounder
BRIEF ANALYSIS

(FB037) AUGUST 2005

Mosquito Control With Malathion:
Are There Public Health Consequences?

Studies Prove Use of the Chemical Safe

By Rolf Penner, Agricultural Policy Fellow

Executive Summary

- The application of pesticides to control insect populations has occurred under a number of conditions, especially when insect-borne diseases become a threat.
- Malathion is the only pesticide recently evaluated for such use, and that evaluation determined that it poses no risk to human populations or the environment.
- Methods and rates of application and approved products have been thoroughly researched. Used as recommended, malathion is the safest product available.
- Animal testing has revealed very low toxic, reproductive or carcinogenic effects, even when fed at high doses.
- Monitoring for health effects on humans when malathion is ingested through the skin or by breathing indicates no cause for alarm.
- The damage inflicted on other insect species can be minimized.
- Extensive studies of malathion's effects on children and pregnant women have also proven that the risk is minimal.
- Authorities have concluded the risks of spraying malathion are negligible.
- Spraying of malathion to prevent spread of the West Nile virus is safe.

Introduction

Control of adult mosquito populations can be accomplished by the application of pesticides. In some situations—where a public health threat is considered imminent or immediate, for example, or when numbers are high enough to cause considerable nuisance and discomfort, mosquito adulticiding has been considered appropriate. That decision has usually depended on a number of factors: the gross numbers of adult mosquitoes, the time of season, the size of the geographic area, weather conditions, access, feasibility and, perhaps most importantly, the numbers of adult mosquitoes carrying infectious diseases that can be spread to humans.

Mosquito adulticides may be applied either by ground-based or aerial equipment. Adulticides typically are applied as an Ultra-Low-Volume (ULV) spray, with small amounts of insecticide dispersed either by truck-mounted equipment or from aircraft. The rates of active ingredient applied per acre or hectare are lower than those typically used to control pests on agricultural crops. The only registered product for adulticiding that has undergone a recent evaluation by the Pest Management Regulatory Agency (PMRA) is malathion.[1]

[1] *Re-evaluation of Malathion*, PMRA, September 5, 2003. For further information on malathion, visit the PMRA website at www.pmra-arla.gc.ca.

Malathion is a non-systemic, broad spectrum organophosphate insecticide and neurotoxin commonly used to control mosquitoes and other flying insects, especially during outbreaks of vector-borne diseases, to protect public health. It works by contact and ingestion action. Malathion degrades rapidly in the environment via hydrolysis, biodegradation, photochemical degradation, and photolysis.

The most common use of public health significance for this particular insecticide, as opposed to the rest of this class of chemicals, is the control of mosquitoes and other flying insects, especially during outbreaks of vector-borne diseases like West Nile encephalitis. This use usually involves ULV formulations because of the type of aerosol sprayer used to dispense the agent.[2]

Malathion has been used when necessary since 1956 by public health officials to control mosquito populations.[3] When applied in accordance with the rate of application and safety precautions specified on the label, malathion can be used to kill mosquitoes with virtually no risk to human health or the environment. Because of the very small amount of active ingredient released per hectare of ground, scientists have found that for all exposure scenarios considered, exposures to malathion were hundreds or even thousands of times below an amount that might pose a health concern.[4]

Methods and rates of application[5]

The PMRA has determined that large-scale applications of malathion in residential areas for control of adult mosquitoes do not pose an unacceptable risk to bystanders and operators (mixer/loaders and applicators) when used in the following manner:

- Ground applications are made with ULV equipment at the currently registered rate of up to 60.8 g a.i/ha or 6.08 mg\m2.
- Aerial applications are made with ULV equipment at a rate up to 260 g a.i/ha or 26 mg\ m2.
- In residential areas, rates must not exceed 260 g a.i./ha or 26mg\m2.
- Residential areas are defined as sites where bystanders including children may be potentially exposed during or after spraying. This includes around homes, school, parks, playgrounds, playing fields, public buildings or any other areas where the general public, including children, could be exposed.
- Operators wear long pants, long-sleeved shirts and chemical-resistant gloves during mixing/loading, application, clean-up and repair.

Products registered for ULV application

Fyfanon ULV Ultra-Low Volume Concentrate Insecticide, Reg. No. 9337

Gardex Malathion ULV Concentrate, Reg. No. 16198

Malathion 95 ULV Insecticide, Reg. No. 25638

Wilson Malathion ULV Insecticide Concentrate, Reg. No. 14597

Definitions

NOAEL: No observed adverse effect level.

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[2] *Malathion Reregistration Eligibility Document*, U.S. Environmental Protection Agency, Washington, D.C., 2000

[3] *For Your Information. Malathion for Mosquito Control*, 735-F-00-001, U.S. Environmental Protection Agency, Washington, D.C., and *Questions and Answers. Pesticides and Mosquito Control*, 7506C, U.S. Environmental Protection Agency, Washington, D.C., both released in May, 2000.

[4] *Malathion: Revisions to the preliminary risk assessment for the reregistration eligibility decision document,* Office of Prevention, Pesticides and Toxic Substances, U.S. Environmental Protection Agency, Washington, D.C. April 28, 2000.

[5] PMRA, op. cit.

After first determining the minimum amount of pesticide required to make an animal sick, then reducing that dose slightly, one arrives at what is called the "no-effect level," or **NOEL**. To allow for the possibility that humans are more sensitive to the chemical than the test animals are, you divide NOEL by 10. Then you divide by 10 again to allow for especially sensitive humans. Reference doses have been set based on NOAELs for the most sensitive indicator of toxicity. These reference doses incorporate various uncertainty factors to account for extrapolating between rats and humans and for variability within human populations as well as additional uncertainty or safety factors to account for an extra level of protection that is warranted by the data.

LOAEL: Lowest observed adverse effect levels

MTD: Maximum tolerated dose

MOE: Margin of exposure

m2: Metres squared, a measurement of area (think of a piece of paper)

m3: Metres cubed, a measurement of volume (think of a box)

LD 50: Lethal Dose 50, the point at which 50% of the animals in the study died.

Toxicology summary

The toxicology database confirms that Malathion has anticholinesterase activity in various species including rats, mice, rabbits, dogs and hens. Although clinical signs of toxicity observed in laboratory animals are typical of the organophosphate class of chemicals, they occur at relatively much higher doses with malathion compared to other organophosphates.

Translation: Malathion is safer than other organophosphate insecticides.

Malathion did not accumulate in tissues following single or multiple exposures. There did not appear to be any dose-related or sex-related differences in the metabolism of malathion.

Malathion exhibits low acute toxicity via the oral, dermal and inhalation routes and exhibits slight eye and dermal irritation; it is not dermally sensitizing.

Results of the guideline genetic toxicology studies with malathion indicated that the test material did not cause gene mutations in bacteria or unscheduled DNA synthesis in cultured rat hepatocytes.

In chronic/oncogenicity studies performed with malathion in mice and rats, treatment related increased tumor incidences were observed in the liver (mouse, rat) and in the nasal/oral cavity (rat). Based on the weight of the evidence, the U.S. Environmental Protection Agency has classified malathion as having "suggestive evidence of carcinogenicity but not sufficient to assess human carcinogenic potential."[6]

The organophosphates as a chemical class are not, generally speaking, known to be carcinogenic.

PMRA has a concern that no carcinogenicity study via the inhalation route is available for evaluation. This lack of information is, however, taken into consideration in the risk assessment, particularly for workers who may be occupationally exposed to malathion, by implementation of a safety factor.

There was limited evidence in the database to suggest that malathion has an adverse effect on the endocrine system in mammals.

Toxicological Effects[7]

- **Acute toxicity:** Malathion is slightly toxic via the oral route, with reported oral LD50 values of 1000 mg/kg (of body weight) to greater than 10,000 mg/kg in the rat, and 400 mg/kg to

[6] *Overview of Malathion Risk Assessment,* U.S. Environmental Protection Agency, Washington, D.C., November 6, 2001.
[7] *Pesticide Information Profiles,* Extension Toxicology Network, June, 1996.

greater than 4000 mg/kg in the mouse. It is also slightly toxic via the dermal route, with reported dermal LD50 values of greater than 4000 mg/kg in rats. Effects of malathion are similar to those observed with other organophosphates, except that larger doses are required to produce them. The acute effects of malathion depend on product purity and the route of exposure. Numerous malathion poisoning incidents have occurred among pesticide workers and small children through accidental exposure.

- **Chronic toxicity:** Human volunteers fed very low doses of malathion for 1½ months showed no significant effects on blood cholinesterase activity. Rats fed dietary doses of 5 mg/kg/day to 25 mg/kg/day over 2 years showed no symptoms apart from depressed cholinesterase activity. When small amounts of the compound were administered for 8 weeks, rats showed no adverse effects on whole-blood cholinesterase activity.

- **Reproductive effects:** Several studies have documented developmental and reproductive effects due to high doses of malathion in test animals. Rats fed high doses of 240 mg/kg/day during pregnancy showed an increased rate of newborn mortality. However, malathion fed to rats at low dosages caused no reproductive effects. It is not likely that malathion will cause reproductive effects in humans under normal circumstances.

- **Teratogenic effects:** Rats fed high doses (240 mg/kg/day) showed no teratogenic effects. Malathion and its metabolites can cross the placenta of the goat and depress cholinesterase activity of the fetus. Chickens fed diets at low doses for two years showed no adverse effects on egg hatching. Current evidence indicates that malathion is not teratogenic.

- **Mutagenic effects:** Malathion produced detectable mutations in three different types of cultured human cells, including white blood cells and lymph cells. It is not clear what the implications of these results are for humans.

- **Carcinogenic effects:** Female rats on dietary doses of approximately 500 mg/kg/day of malathion for two years did not develop tumors. Adrenal tumors developed in the males at low doses, but not at the high doses, suggesting that malathion was not the cause. Three of five studies that have investigated the carcinogenicity of malathion have found that the compound does not produce tumors in the test animals. The two other studies have been determined to be unacceptable studies and the results discounted. Available evidence suggests that malathion is not carcinogenic but the data are not conclusive.

- **Organ toxicity:** The pesticide has been shown in animal testing and from use experience to affect the central nervous system, immune system, adrenal glands, liver and blood.

Human data[8]

Various studies referenced by the U.S. Centers for Disease Control and Prevention have looked at malathion's effects on humans. (The specific studies are indicated in brackets. Some text has been transcribed directly.)

Workers exposed to initial concentrations up to 85 mg/m^3 for one hour (that may have declined rapidly) over 42 consecutive days suffered no adverse effects [Golz 1959]. Workers exposed to concentrations that peaked at 56 mg/m^3 and averaged 3.3 mg/m^3 for 5 hours had normal cholinesterase levels [Culver et al. 1956]. A lethal oral dose of 246 to 471 mg/kg has been reported [Farago 1967; Jusic and Milic 1978]. [Note: An oral dose of 246 to 471 mg/kg is equivalent to a 70kg worker being exposed to about 11,500 to 22,100 mg/m^3 for 30 minutes, assuming a breathing rate of 50 liters per minute and 100% absorption.]

In a study to quantify potential human exposure to malathion via dermal contact from ground ULV mosquito sprays, deposition was monitored on body surfaces of three human subjects during

[8] *Malathion, IDLH Documentation*, Centers for Disease Control and Prevention, at http://www.cdc.gov/niosh/idlh/121755.html. The CDC's specific study references are indicated in brackets.

malathion spraying using a truck-mounted ULV aerosol generator.[9] Two of the subjects stood at stationary positions for five minutes downwind at 7.6 m and 15.2 m, facing the path of the spray vehicle; the other subject jogged in the same direction and immediately downwind at 1.5 m of the vehicle. The amount of time the jogger was exposed was not specified. Deposition of malathion droplets on the skin surfaces was determined from analysis of gauze patches that were placed on various locations. From the results, the investigators determined that total deposition varied from 0.18 mg (0.0026 mg/kg) for a stationary 70-kg man wearing long pants and a long-sleeved shirt to the worst case scenario of 7.8 mg (1.1 mg/kg) for a shirtless 70 kg jogger in short pants.

However, these doses represent dermal deposition rather than dermal absorption.

In a dermal absorption study in humans,[10] C-radio-labeled malathion (dissolved in acetone) was applied to a 13 cm^2 circular area on the ventral surface of the forearms of seven subjects at a rate of 4 ug/cm^2. The skin sites were not protected. Dermal penetration of malathion through the skin was estimated by calculating the total amount of radioactivity excreted in the urine in five days. A mean of 7.84% ± 2.71% (S.D.) of the applied dose of radioactivity was recovered in the five-day urine.

That indicates a dermal absorption rate of approximately 5% to 10% over a five-day period. Feldman and Maibach concluded that the dermal absorption rate is about 10%.

The California Department of Health Services conducted indirect assessments and symptom prevalence surveys to determine whether aerial application of malathion bait used to eradicate the Mediterranean fruit fly in Santa Clara County, California posed a health hazard to the public.[11] In one indirect assessment, the records of a major hospital emergency department were compared during the first five weeks of spraying, the two weeks before spraying, and a corresponding seven-week period the year before. No significant differences in the number of visits were found, and none of the hospital emergency rooms in the county reported cases of pesticide poisoning. Another assessment of the frequency of ambulance calls in the same periods also showed no significant differences, but this assessment was relatively insensitive. An assessment for an increase in cases of asthma at a medical school hospital showed no increase, but the number of cases in this study was too small for definitive conclusions. In the symptom prevalence surveys, an on-site home visit study, the other a telephone survey, there was no evidence the aerial spraying of malathion caused any detectable increase in symptoms.

Studies to determine whether an increase in fetal loss, low birth weight, and birth defects occurred in the same malathion program in Santa Clara County, California were negative [Grether et al. 1987; Thomas et al. 1990].

Toxicity to Pets, Livestock, and Wildlife[12]

Fortunately, malathion has relatively low toxicity for birds and mammals, and low potential for bioaccumulation [EPA 2000b, c; Humphreys 1988; Osweiller 1996; USDOI 1975]. The use of malathion is approved for direct application on livestock, cats and dogs to control for fleas and ticks.

The PMRA has determined that malathion degrades rapidly in the environment, especially in moist soil, and it displays low toxicity to birds and mammals. Malathion is highly toxic to insects, including beneficial ones such as honeybees. Because adult mosquito programs are typically carried

[9] *Guidelines for Arbovirus Surveillance Programs in the United States*, by C.G. Moore, R.G. McLean, C.J. Mitchell, R.S. Nasci, T.F. Tsai, C.H. Calisher, A.A. Marfin, P.S. Moore, and D.J. Gubler, U.S. Centers for Disease Control and Prevention, 1993.
[10] *Absorption of some organic compounds through the skin in man*, by R.J.Feldman and H.I. Maibach, Journal of Investigative Dermatology, 1970.
[11] *Assessment of acute health effects from the medfly eradication project in Santa Clara County, California*, by E. Kahn, M.Berlin, M.Deane, R.J. Jackson, J.W. Stratton, Archives of Environmental Health 47:279-284.
[12] Ibid.

out at night or early morning, the impact on honeybees is minimal since this is when they are least active.

Malathion is also highly toxic to fish and aquatic insects. To minimize exposure to aquatic organisms, care should be taken to avoid overspray or drift to aquatic environments like sloughs, ponds, prairie potholes, lakes, rivers, streams and wetlands when applying malathion or when cleaning and rinsing spray equipment or containers.

Residential (bystander) exposure and risk assessment

Residential risk assessment is concerned with estimating risks to the general population, including children, during or after pesticide application. Residential risk is estimated by comparing the amount of pesticide to which an individual may be exposed to endpoints from the most relevant toxicology studies with respect to route and duration to estimate a margin of exposure (MOE)**.** This is compared to a target MOE that incorporates safety factors protective of the most sensitive populations. If the MOE is less than the target

MOE, it does not necessarily mean exposure will result in adverse effects. However, mitigation measures will be necessary to reduce exposure.

Malathion does not persist in the environment and would not accumulate between applications

For short- and intermediate-term dermal risk assessment for adults**,** the assessment was driven by the most sensitive adult subpopulation of pregnant women. The oral NOAEL *of 25 mg/kg bw/day* from a rabbit developmental study was selected based on the increased incidence of dose with resorptions in the presence of maternal toxicity (reduced mean body weight gain) at 50 mg/kg bw/day. The target MOE selected when using this study is 300; this accounts for standard uncertainty factors of 10 for interspecies extrapolation and 10 for intraspecies variability. In addition, an additional 3× safety factor is warranted due to the severity of the endpoint (resorptions = embryofetal deaths). This target MOE would, therefore, be considered protective of pregnant women and their unborn children.

For short- and intermediate-term inhalation risk assessment for adults, the LOAEL of 25.8 mg/kg bw/day (0.1 mg/L) was selected from a 90-day inhalation toxicity study in rats. The LOAEL was established based on the observation of lesions in the nasal respiratory epithelium. The NOAEL for erythrocyte and brain cholinesterase depression occurred at this dose. The target MOE selected when using this study is 1000; this accounts for standard uncertainty factors of 10 for interspecies extrapolation and 10 for intraspecies variability, with an additional uncertainty/safety factor of 10 because a NOAEL was not identified and because of the severity of the nasal lesions also observed at the LOAEL in a 2-week range-finding study and concern for the potential for development of nasal cavity tumours with chronic exposure via the inhalation route. This would provide an intrinsic margin of safety of >960 to the developmental NOAEL of 25 mg/kg bw/day. This target MOE would therefore be considered protective of pregnant women and their unborn children.

For short- and intermediate-term dermal, inhalation and non-dietary oral ingestion by children, the oral LOAEL of 5 mg/kg bw/day from the comparative cholinesterase study in rats was selected based on inhibition of erythrocyte cholinesterase in PND 11 or PND 21 pups following single or repeated dosing. The target MOE selected when using this study is 1000; this accounts for the standard uncertainty factors of 10 for interspecies extrapolation and 10 for intraspecies variability, as well as an additional 10× uncertainty/safety factor due to the use of a LOAEL and for the potential increased sensitivity of younger populations. As in the adult assessment, a dermal absorption value of 10% was incorporated for exposure by the dermal route.

Bystander exposure and risk assessment during and after application

Exposure estimates were generated for a 62 kg adult, 39 kg child (adolescent) and a 15 kg toddler.

Two general exposure scenarios were considered: 1) exposure to adults and toddlers while on turf during or immediately after application, and 2) exposure to adults and adolescents while gardening during or immediately after application.

Dermal exposure was assessed for all population groups. Non-dietary oral exposure, resulting from hand-to-mouth transfer and direct ingestion of soil or turf was also assessed for toddlers. Finally, inhalation exposure was assessed for all population groups.

Bystander risk estimates are above the target MOE for all exposure routes and scenarios associated with either ground ULV or aerial ULV applications. The MOEs that were attained were sufficiently large and thus are anticipated to provide further accommodation for those with environmental sensitivities. The MOEs would be further enhanced through measures such as remaining indoors during and immediately after spraying.

Aggregate risk assessment

As a commitment to ensuring protection of human health, the PMRA assesses risk on the basis of aggregate exposure from all non-occupational sources. Aggregate exposure is the total exposure to a single pesticide that may occur from all sources and routes of exposure, including food, drinking water, residential, and any other exposures.

Standards and Guidelines for the Protection of Human Health

The U.S. Agency for Toxic Substances and Disease Registry has not developed minimal risk levels (MRLs) for malathion, but the EPA[13] has proposed several risk assessment values. A proposed acute oral RfD of 0.5 mg/kg for 1-day exposure is based on a dose of 50 mg/kg/day, which resulted in decreased body weight in rabbits that were exposed on gestation days 6 to 18 in the study by Siglin (1985). Although the 50 mg/kg/day dose was a LOAEL for decreased body weight during the 13 days of exposure, EPA considered this dose to be a NOAEL for decreased body weight for 1 day of exposure and applied an uncertainty factor of 100 (10 for interspecies extrapolation and 10 for human variability). EPA also proposed using an air concentration LOAEL of 100 mg/m^3, 6 hours/day, 5 days/week, for 13 weeks in the study by Beattie (1994), converted to a dose of 25.8 mg/kg/day, for short, intermediate, and long term inhalation risk assessment. The uncertainty factor was 1000 (10 for use of LOAEL, 10 for interspecies extrapolation, and 10 for human variability) to yield a risk assessment value of 0.03 mg/kg/day. A short term and intermediate dermal risk assessment value of 0.5 mg/kg/day was also proposed by EPA, based on a NOAEL of 50 mg/kg/day for cholinesterase inhibition in rabbits exposed dermally for 6 hours/day, 5 days/week for 3 weeks in the study by Moreno (1989).

Using these proposed values for the risk assessments for public health mosquito uses, EPA[14] concluded that adult and the toddler risk estimates for combined dermal and inhalation exposure did not exceed the levels of the EPA's concern for residential bystander inhalation and dermal exposure from truck fogger and aerial ULV mosquito control applications. This assessment included incidental oral ingestion for hand-to-mouth activities. Given the low levels of malathion used for the control of mosquito-borne diseases, ATSDR finds this assessment reasonable.

[13] *Malathion: Revisions to the preliminary risk assessment for the reregistration eligibility decision document,* op. cit.
[14] Ibid.

Conclusion

The relevant studies by Canada's PMRA, the U.S.'s EPA and CDC reach the same conclusions—that the use of malathion to control mosquitoes at the recommended rates in urban areas poses little risk to the population. Further to this, while scientists are reluctant to give absolute assurances the data presented above strongly suggests that there is actually no risk to the population at large.

The maximum allowed rate of application of 26 mg\m2 results in exposure levels far lower than is known to cause harm from animal and human testing. Rats, for example, fed dietary doses of 5 mg/kg of body weight/day to 25 mg/kg/day over 2 years showed no symptoms.

Exposure to urban residents would predominantly be through absorption of the active ingredient through the skin. Studies with rats have reported that the dermal LD50 value which is the point at which 50% of the experiment animals died was greater than 4000 mg\kg of body weight. Testing done on humans who stood in the direct path of malathion spraying, truck mounted ULV (ultra-low-volume) aerosol generators resulted in total depositions ranging from .0026 mg\kg of body weight for a stationary 70kg man wearing long pants and a long sleeved shirt to the worst case scenario of 1.1mg\kg for a shirtless 70kg jogger in short pants. It must be noted that this does not factor in the amount of actual ingredient which is absorbed into the skin, other studies indicate that the maximum absorption rate through the skin would be 10% which lowers this exposure level to a range of .00026 to.11mg\kg of body weight. Further reducing the exposure level is the fact that virtually no one would actively be trying to ride along side a spray truck and the fact that spraying is done predominantly in the very early hours of the morning.

Inhalation of malathion while spraying is going on is another concern to the public. A study done on workers who where exposed to initial concentrations up to 85 mg\ m^3 for one hour over 42 days suffered no adverse effects. This is of course a far higher concentration for a much longer duration than the general public would ever have to inhale since the maximum allowable spray rate is 26 mg\m2.

It is now common for public officials to cite the threat of West Nile virus as the need to spray for mosquitoes in urban areas and that that threat outweighs the so-called danger of spraying malathion. While West Nile is a public health threat that should be taken seriously, spraying malathion poses no such similar but lesser threat. It is not the lesser of two evils and should not be described as such to placate the demands of anti-chemical political correctness. The public is not well served when they are mislead into believing something that has been shown to be safe, when properly used, is not safe.

ABOUT THE AUTHOR

Rolf Penner is Canada's most "hands-on" think-tank-based farm policy commentator. He is a successful third generation farmer who operates an 1800- acre mixed farm near Morris, Manitoba. He has been working with pesticides for 20 years now and has been actively researching scientific studies on them for the last five. Rolf believes that science is not just for people with PhDs, and strives to bring the knowledge gained from scientific studies down to an everyday level of understanding. He is fond of saying that farming is really the practical application of thousands of years of scientific theory. He graduated from the University of Manitoba with a diploma in Agriculture in 1988. Rolf is a frequent media commentator on agriculture issues and writes frequently in a range of daily, weekly and monthly local, regional and national newspapers.

Other Recommended Reading

1.http://dsp-psd.pwgsc.gc.ca/Collection/H113-18-2003-10E.pdf#search='Malathion%20for%20ultra%20low%20volume%20(ULV)%20applications,toxicology'

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11. http://www.cdc.gov/niosh/idlh/121755.html

12. http://www.atsdr.cdc.gov/NEWS/malathion-consult_10-14.htm

13.http://www.winnipeg.ca/cms/bugline/forcast/pmra%20malathion%20fact%20sheet%20april%202003.pdf

