Health Consultation

WA Department of Agriculture Pesticide Vulnerability Project

HEALTH BASED SCREENING LEVEL EVALUATION
AZINPHOS-METHYL, PENDIMETHALIN, and EPTC

APRIL 24, 2008

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Agency for Toxic Substances and Disease Registry
Division of Health Assessment and Consultation
Atlanta, Georgia 30333
Health Consultation: A Note of Explanation

An ATSDR health consultation is a verbal or written response from ATSDR to a specific request for information about health risks related to a specific site, a chemical release, or the presence of hazardous material. In order to prevent or mitigate exposures, a consultation may lead to specific actions, such as restricting use of or replacing water supplies; intensifying environmental sampling; restricting site access; or removing the contaminated material.

In addition, consultations may recommend additional public health actions, such as conducting health surveillance activities to evaluate exposure or trends in adverse health outcomes; conducting biological indicators of exposure studies to assess exposure; and providing health education for health care providers and community members. This concludes the health consultation process for this site, unless additional information is obtained by ATSDR which, in the Agency’s opinion, indicates a need to revise or append the conclusions previously issued.

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HEALTH CONSULTATION

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AZINPHOS-METHYL, PENDIMETHALIN, and EPTC

Prepared By:
The Washington State Department of Health
under cooperative agreement with the
Agency for Toxic Substances and Disease Registry
Foreword

The Washington State Department of Health (DOH) has prepared this health consultation in cooperation with the Agency for Toxic Substances and Disease Registry (ATSDR). ATSDR is part of the U.S. Department of Health and Human Services and is the principal federal public health agency responsible for health issues related to hazardous waste. This health consultation was prepared in accordance with methodologies and guidelines developed by ATSDR.

The purpose of this health consultation is to identify and prevent harmful human health effects resulting from exposure to hazardous substances in the environment. Health consultations focus on specific health issues so that DOH can respond to requests from concerned residents or agencies for health information on hazardous substances. DOH evaluates sampling data collected from a hazardous waste site, determines whether exposures have occurred or could occur, reports any potential harmful effects, and recommends actions to protect public health. The findings in this report are relevant to conditions at the site during the time of this health consultation, and should not necessarily be relied upon if site conditions or land use changes in the future.

For additional information or questions regarding DOH or the contents of this health consultation, please call the health advisor who prepared this document:

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For persons with disabilities this document is available on request in other formats. To submit a request, please call 1-800-525-0127 (voice) or 1-800-833-6388 (TTY/TDD).

For more information about ATSDR, contact the ATSDR Information Center at 1-888-422-8737 or visit the agency’s Web site: www.atsdr.cdc.gov/.
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<td><strong>Oral Reference Dose (RfD)</strong></td>
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<td><strong>Organic</strong></td>
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<td><strong>Parts per billion (ppb)/Parts per million (ppm)</strong></td>
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<td><strong>Reference Dose Media Evaluation Guide (RMEG)</strong></td>
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<td><strong>Route of exposure</strong></td>
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<td><strong>Surface Water</strong></td>
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Summary and Statement of Issues

The Washington Department of Agriculture (AG) requested that the Washington Department of Health (DOH) evaluate whether the United States Geological Survey (USGS) health-based water screening levels (HBSLs) for the pesticides azinphos methyl, pendimethalin, and s-ethyl dipropylthiocarbamate (EPTC) are appropriate benchmarks for identifying whether these three pesticides, if found in Washington groundwater or surface water, might pose a possible health risk. DOH agreed to do this evaluation by comparing the USGS HBSLs to standard health benchmarks for water, if they exist. DOH’s work was done in support of the Clean Water Fund contract between AG and the Washington Department of Ecology (Ecology).

DOH began its evaluation of the USGS HBSLs for azinphos methyl, EPTC, and pendimethalin after January 1, 2008, because of delays regarding the scope of work and contract language.(1) DOH conducts such evaluations in cooperation with the Agency for Toxic Substance and Disease Registry (ATSDR). Because of the short time frame available for DOH to do its evaluation and the time needed for ATSDR to review the document, only a draft health consultation has been completed to date. This document will be finalized, with some possible changes, after ATSDR completes its review.

Background

AG is considering using the USGS HBSLs for azinphos methyl, EPTC, and pendimethalin as part of its groundwater and surface water quality monitoring program. The HBSLs would be used as benchmark values that if exceeded in potable water would trigger contact with DOH, who would then be asked to assess the exposure and make a health determination. Before making a final decision about using such an approach, however, AG requested that DOH assess whether the USGS HBSLs for these three pesticides are suitable benchmarks (personal communication, phone conversation between Barbara Trejo, DOH, and Jim Cowles, AG, December 18, 2007).

Azinphos methyl, EPTC, and pendimethalin are part of a broad group of chemicals called pesticides. Table 1 and the following paragraphs provide some general information about these three pesticides.
Table 1: Pesticide Information – Azinphos methyl, Pendimethalin, and EPTC

<table>
<thead>
<tr>
<th>Chemical Name</th>
<th>CAS No.</th>
<th>Trade Name</th>
<th>EPA Cancer Class</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Azinphos methyl</td>
<td>86-50-0</td>
<td>Guthion</td>
<td>&quot;Not likely&quot; human carcinogen.</td>
<td>(2;3)</td>
</tr>
<tr>
<td>Pendimethalin (N-(1-ethylpropyl)-2,6-dinitro-3,4-xylidine.)</td>
<td>40487-42-1</td>
<td>Prowl; Pursuit</td>
<td>Group C (possible human carcinogen)</td>
<td>(4)</td>
</tr>
<tr>
<td>EPTC (S-Ethyl dipropylthiocarbamate)</td>
<td>759-94-4</td>
<td>EPTAM; Eradicane</td>
<td>No EPA carcinogenicity classification</td>
<td>(5)</td>
</tr>
</tbody>
</table>

**Azinphos methyl**

Azinphos methyl is a restricted use organophosphate insecticide that has been used on many crops including apples, pears, and cherries. EPA reports that there are no residential uses of azinphos methyl.(6) In Washington, azinphos methyl is applied to orchards (e.g., apple, pear) and various crops (e.g., potatoes, strawberries) with much of the application occurring in eastern Washington counties.(7) On November 16, 2006, EPA issued a determination that farm worker and ecological risks associated with azinphos methyl require the phase out of all remaining uses of this pesticide by 2012.(8)

Azinphos methyl is not considered a very persistent pesticide (half-lives of 10-40 days have been reported under field conditions).(2;9) It does not evaporate readily from soil or water (the estimated Henry's Law constant (2.4x10⁻⁸ atm-cu m/mole) suggesting that volatilization from water surfaces is not expected to be an important transport process, attaches strongly to soils, does not easily leach from the soil to groundwater, does not persist in the environment and can be degraded to many other compounds by microorganisms, sunlight, and water.(6;9) The only environmental degradation product of azinphos methyl of human health concern is reported to be the oxygen analog. This analog was reportedly found at a maximum of about 5% of the total amount of pesticide that was applied in a soil aerobic metabolism study.(6)

Azinphos methyl has been found in surface waters of Washington State.(6) It is rarely found in groundwater but it has been found at low levels in some areas where rapid groundwater recharge exists (e.g., karst terrain).(2;6;10) If it enters groundwater, azinphos methyl is not expected to persist.(6) DOH’s Office of Drinking Water reports that neither Group A nor B wells are tested for azinphos methyl so it is uncertain whether this pesticide exists in any Washington drinking water wells (personal communication; e-mail message from Donna Freir, DOH-Office of Drinking Water, to Barbara Trejo, DOH-Office of Environmental Health Assessments, February 1, 2008). ATSDR reports that azinphos methyl is rarely found in drinking water.(6)

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1 EPA proposed the cancellation of azinphos methyl for apples/crabapples, blueberries, cherries, pears, and parsley by 2012. Some uses of azinphos methyl were phase out in 2007 while others will be phase out in 2009.(8)
S-Ethyl dipropylthiocarbamate (EPTC)

EPTC is a thiocarbamate herbicide used to control the growth of germinating annual weeds such as broadleaves, grasses, and sedges. EPTC is applied by aerial or ground equipment or through chemigation (i.e., application of pesticides through an irrigation system). Because of its volatility it is incorporated into the soil immediately after it is applied to prevent volatilization. It is used across the U.S. in agricultural food production (e.g., corn, potatoes, dry beans, peas, alfalfa, and snap beans) and at parks and golf courses. EPTC is also available to the public for use in vegetable and ornamental gardens. It is unknown whether EPTC is widely used in Washington (personal communication; e-mail message from Jim Cowles, Washington Department of Agriculture to Barbara Trejo, Washington Department of Health, February 26, 2008). EPA reports that EPTC production and environmental release trends are anticipated to decrease. There do not appear to be plans to phase out the use of this chemical.

EPTC is not considered a persistent chemical. Laboratory tests suggest EPTC has a half life of 36 to 75 days. The estimated Henry's Law constant for EPTC (1.6X10^-5 atm-cu m/mole) indicates that volatilization of EPTC from water surfaces could be an important fate process. The primary (soil/water) degradation products of EPTC are EPTC-sulfoxide and dipropylamine. The limited data available suggest that these compounds are less persistent than the parent compound.

Monitoring data suggests that concentrations of EPTC in groundwater will likely be less than those found in surface water. However, the persistence of EPTC in groundwater might be greater than in surface water because losses due to volatilization would be expected to be much less. It is reported that EPTC has a low affinity for binding to soil and is water soluble, which indicates a potential for leaching but it is also reported that EPTC generally does not persist long in surface soils. Consequently, the potential to leach is greatly reduced. This is consistent with findings by California EPA Department of Pesticide Regulation and various EPA programs where EPTC has been tested but not detected. However, more recent testing by EPA suggests that EPTC might occur more frequently than previously detected. DOH’s Office of Drinking Water reports that EPTC has been found in only at a very low concentration (0.0600 micrograms per liter (ug/l)) in one of 5,177 tested samples from Group A or Group B wells (personal communication; e-mail message from Rhonda Leatherwood, DOH – Office of Drinking Water, to Donna Freir, DOH-Office of Drinking Water, dated February 15, 2008). Data collected by EPA indicates that EPTC has been found in surface waters.

In 2006, EPA’s Office of Water evaluated the health effects associated with EPTC to determine if it should be regulated under the federal Safe Drinking Water Act (SDWA). During that evaluation, EPA found that the available data on EPTC occurrence, exposure, and other factors suggested that it does not occur in public water systems at frequencies and levels of public health concern. As a result of that finding, EPA determined that regulating EPTC would not present “a meaningful opportunity to reduce health risk.”
**Pendimethalin**

Pendimethalin is a selective dinitroaniline herbicide used in agricultural (e.g., corn, alfalfa, soybeans) and non-agricultural areas to control broadleaf and grassy weeds. It is applied to soil with ground and aerial equipment at various times of the growing season (e.g., pre-plant, pre-emergence, and post-emergence). It is also used on residential lawns and ornamentals.(14) Pendimethalin is applied to orchards and various crops (e.g., beans, potatoes, strawberries) across Washington, with much of the application occurring in eastern Washington counties.(7)

Pendimethalin is considered a moderately persistent herbicide that can give rise to long-lasting metabolites. It contains dinitroanilines, which reportedly could result in the formation of nitrosamines.(14) Pendimethalin dissipates in the environment by binding to soil, microbial metabolism, and volatilization. It has been found in surface water as result of pendimethalin application and runoff. EPA reports that volatilization of pendimethalin from well-mixed surface waters may be an important transport process.(14) EPA reported in 1999 that pendimethalin was found infrequently in groundwater (i.e., found in only two states from 0.2 to 0.9 ug/l), which is consistent with information that suggests that it has low potential to leach into groundwater.(14) DOH’s Office of Drinking Water reports that neither Group A nor B wells are tested for pendimethalin so it is uncertain whether this pesticide exists in any Washington drinking water (personal communication; e-mail message from Donna Freir, DOH-Office of Drinking Water, to Barbara Trejo, DOH-Office of Environmental Health Assessments, February 1, 2008).

**USGS HBSL Approach**

Historically, USGS compared results from water quality testing to federal drinking water standards and other guidelines. However, drinking water standards and guidelines (e.g., maximum contaminant levels (MCLs)) do not exist for many chemicals. To address this problem, USGS developed HBSLs for these chemicals, including pesticides such as azinphos methyl, pendimethalin, and EPTC (Table 2), so it can assess and communicate the significance of its water quality findings.

Table 2 – USGS HBSLs, Cancer Class, and Oral Reference Dose for Azinphos Methyl, Pendimethalin, and EPTC(15)

<table>
<thead>
<tr>
<th>Chemical Name</th>
<th>HBSL* (ug/l)</th>
<th>USGS Cancer Class Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Azinphos methyl</td>
<td>10</td>
<td>Not likely</td>
</tr>
<tr>
<td>Pendimethalin</td>
<td>70</td>
<td>Cancer Class C*</td>
</tr>
<tr>
<td>EPTC</td>
<td>200</td>
<td>Not carcinogenic</td>
</tr>
</tbody>
</table>

* USGS rounds the HBSLs to one significant figure.(16) Consequently, the HBSL values presented in Table 2 could be different than the actual calculated values. For example, the calculated EPTC HBSL is 175 ug/l but is rounded to 200 ug/l.

** Cancer Class C – possible human carcinogen
HBSLs, like MCLs, are maximum contaminant concentrations that are not expected to cause adverse health effects over a lifetime of exposure to drinking water. They are considered non-enforceable water quality benchmarks that, like other health benchmarks, if exceeded, indicate a potential human health concern, which would need to be further evaluated. (16) Such an evaluation might include a risk assessment, which generally includes evaluating other additional factors like multiple exposures pathways, or weight-of-evidence evaluations.

The USGS developed the HBSLs in cooperation with the U.S. Environmental Protection Agency (EPA) and others using EPA methodologies for establishing drinking water guidelines. They also used EPA peer-reviewed, publicly available human health toxicity information. Neither cost nor technical limitations were considered when developing the HBSLs. (16) The first USGS HBSL methodology was developed in 2001. Since then, the methodology has been revised with the latest revisions published in 2007. USGS reports that the most recent revisions reflected changes in EPA policies and allow the use of the most recent toxicity information. (16)

HBSLs are calculated using standard EPA - Office of Water equations for establishing drinking water guideline values (i.e., lifetime non-cancer and cancer risk concentration values) for the protection of human health (Appendix A). USGS also adopted EPA Office of Water assumptions for establishing drinking-water guidelines: lifetime ingestion of 2 liters of water per day by a 70-kilogram adult. For non-carcinogens, USGS typically assumes that 20 percent of the total contaminant exposure comes from drinking water sources (i.e., relative source contribution (RSC)) and 80 percent comes from non-water sources of exposure (e.g., residuals in food and ambient air). (16) It should be noted, however, that it is uncertain whether the RSC used by USGS during HBSL development is meant to take into account exposures to groundwater or surface water contaminants via the inhalation or dermal routes of exposure.

For carcinogenic chemicals, USGS calculates an HBSL range, which represents the contaminant concentration in drinking water that corresponds to an excess estimated lifetime cancer risk of 1 chance in 1 million (1E-06) to 1 chance in 10 thousand (1E-04). For non-carcinogens, the HBSL represents the maximum contaminant concentration in drinking water that is not expected to cause any non-cancer adverse effects over a lifetime of exposure. (16)

USGS indicates that “... contaminant concentrations or concentration statistics indicative of long-term exposure are most appropriate to compare to MCLs or HBSLs in most applications.” USGS also suggests that because contaminant concentrations tend to change slowly over time in ground water, it is appropriate for the purpose of screening level assessments to compare groundwater contaminant concentrations measured in individual well samples to MCLs or HBSLs. For surface waters, however, USGS suggests “[f]or screening-level assessments of surface water, annual or long-term mean (average) concentrations (determined from multiple samples over a period of time and time-weighted) generally are most appropriate for comparison to MCLs or HBSLs because mean concentrations provide a more reliable indication of long-term exposure than concentrations from individual samples.” If insufficient surface water data is...
available, however, USGS does suggest comparing the limited results to the HBSLS if “caution is exercised”.(16)

Discussion

The use of health benchmarks as an initial step for evaluating possible health risks associated with exposure to specific environmental contaminants is a common practice. Health benchmarks are developed for single chemicals only. They do not take into account that mixtures of contaminants may exist. In addition, many benchmarks are developed for only one route of exposure, such as ingestion of drinking water, although other routes of exposure are possible. Before using health benchmarks, it is important to determine what possible routes of exposure might exist for the chemicals of interest.

Health Concerns and Possible Routes of Exposure – Azinphos methyl, EPTC, and Pendimethalin

DOH reviewed relevant literature to determine possible health concerns and routes of exposure for azinphos methyl, pendimethalin, and EPTC if found in potable groundwater or surface water. Brief summaries of possible health concerns and routes of exposure are provided below and in Table 3. As noted in Table 3, ingestion is only one of the possible routes of exposure for these three pesticides.

Table 3: Possible Routes of Exposure - Drinking Water

<table>
<thead>
<tr>
<th>Chemical Name</th>
<th>Ingestion</th>
<th>Inhalation</th>
<th>Dermal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Azinphos methyl</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pendimethalin</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>EPTC</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
</tbody>
</table>

Azinphos Methyl

Azinphos methyl is a low volatility pesticide. The primary exposure pathway for azinphos methyl is through ingestion of food treated with this pesticide.(2) However, EPA reports that both acute and chronic dietary risk from food is not of concern for the general population or for any population subgroup.(6) Exposures as a result of ingestion of contaminated drinking water, inhalation exposure, and dermal exposure to azinphos methyl are expected to be low for the general population.(2) However, this may not be the case for people working and/or living in agricultural areas where this pesticide is applied.

Occupational exposures to azinphos methyl can be high for workers who mix, load and apply azinphos-methyl at agricultural sites. In these situations, azinphos methyl is considered highly toxic by inhalation, dermal absorption, ingestion, and eye contact.(10) Risk to field workers who re-enter azinphos methyl treated sites to harvest, thin, prune and perform other post-application activities is a concern. (6)
A handful of cases of illness related to azinphos methyl exposure are reported every year in Washington. These exposures usually occur to pesticide handlers during application of azinphos methyl to fruit trees but there have also been reports of illness from pesticide drift (personal communication; e-mail message from Barb Morrissey, DOH – Pesticide Program to Barbara Trejo, DOH – Site Assessment Section, February 25, 2008).

At high levels, azinphos methyl affects the normal function of the nervous system by interfering with an enzyme called acetylcholinesterase, which is found in the brain and nerves, and is important to the normal functioning of muscles and many organs. Exposure to high levels of azinphos methyl can cause muscle twitching, watery eyes, diarrhea, salivation, and death. The available human and animal data suggest that reductions in acetylcholinesterase (AChE) activity are the most sensitive end points of the toxicity of azinphos methyl. It can also affect other cholinesterase enzymes (e.g., butyrylcholinesterase). If people are exposed to levels of azinphos methyl below those that affect nerve function, few or no health problems appear to occur. No studies have looked at whether azinphos methyl could cause cancer in humans. However, long-term studies with rats and mice did not indicate that azinphos methyl is a cancer-causing chemical.(2)

Apples, pears, cherries, and peaches are crops most likely to contain azinphos methyl residues. Since children have more fruit in their diets, their exposure to azinphos methyl may be higher than for adults. It is unknown whether children are more susceptible than adults to the health effects of azinphos methyl and it is also unknown whether this pesticide can cause birth defects or other damage to developing children.(2)

EPTC

The primary route of exposure to EPTC appears to be through ingestion of residues of the herbicide in food and drinking water. It is reported that dermal and inhalation exposure, may occur in occupational or residential settings during handling activities such as mixing, loading, or applying EPTC.(11,12,12) It has been found in acute toxicity studies that EPTC is most toxic when inhaled and moderately toxic via the oral and dermal routes of exposure (11) EPTC is a volatile chemical so it could pose an inhalation risk if found at elevated levels in groundwater or surface water used as a potable water source. Dermal exposure to EPTC contaminated water is also possible. Illness associated with EPTC exposure is only reported occasionally in Washington (personal communication: e-mail message from Barb Morrissey, DOH – Pesticide Program to Barbara Trejo, DOH – Site Assessment Section, February 25, 2008).

EPTC is considered a reversible acetylcholinesterase (AChE) inhibitor. Also, an increase in the incidence and severity of cardiomyopathy was reportedly observed in sub-chronic and chronic studies performed on both rats and dogs. The central and peripheral nervous systems also are affected by EPTC exposure with rats and dogs exhibiting an increase in the incidence and severity of degenerative effects (neuronal and/or necrotic degeneration).(12) The neurotoxic effects of EPTC (neuronal necrosis/degeneration) are reportedly consistent with effects seen in other thiocarbamates.(11) In addition to
neurotoxic effects, EPTC has the ability to induce maternal and reproductive toxicity and secondary developmental toxicity in exposed rats and rabbits. There is also there is some concern that children may be a sensitive population for EPTC exposure. (12)

The EPA Office of Water used long-term studies in mice and rats and short-term studies of mutagenicity to evaluate the potential for carcinogenicity. Based on these data and using EPA’s 2005 guidelines for carcinogen risk assessment, EPTC was not considered likely to be carcinogenic to humans. (12)

**Pendimethalin**

The greatest risk of exposure to pendimethalin occurs via dermal contact, inhalation and ingestion primarily during mixing and application of pendimethalin in agricultural and residential settings and through contact with treated plants and soil. (9,14) Exposure to pendimethalin residues in foods is reportedly extremely low. (14,17) The general population is most likely to be exposed through ingestion and dermal contact with contaminated water. (9) Because pendimethalin is considered a volatile chemical, it could pose an inhalation risk if found in potable water.

Pendimethalin is reported to be of low acute toxicity. However, it has been found to cause thyroid follicular cell adenomas in male and female rats and has been classified by EPA as a Group C, possible human carcinogen. (14,17)

Illness associated with pendimethalin exposure is only reported occasionally in Washington (E-mail message from Barb Morrissey, DOH – Pesticide Program to Barbara Trejo, DOH – Site Assessment Section, February 25, 2008).

**Benchmarks**

Only a few standard drinking water benchmarks exist for azinphos methyl, pendimethalin, and EPTC (ATSDR water comparison values, EPA Region 9 preliminary remediation goals for tap water, and/or Ecology MTCA groundwater (potable) Method B cleanup levels (Table 4). (18-20) Two less common drinking water benchmarks were also found and included in Table 4: EPA’s Office of Water developed a contaminant candidate list health reference level (HRL) for EPTC in drinking water and EPA’s Office of EPA’s Office Of Prevention, Pesticides, and Toxic Substances developed drinking water levels of concern (DWLOCs) for azinphos methyl and EPTC. (11,12) No carcinogenic benchmarks were available for pendimethalin although it is considered a potential carcinogen. Appendix B contains the equations used to derive these benchmarks along with the exposure parameters.

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2 EPA developed a range of DWLOCs for various populations. However, only the lowest DWLOCs for azinphos methyl and EPTC are presented in Table 4.
Table 4: Drinking Water Health Benchmarks Derived by ATSDR, EPA and Ecology

<table>
<thead>
<tr>
<th>Chemical Name</th>
<th>USGS HBSL (ug/l)</th>
<th>ATSDR Chronic EMEG (ug/l)</th>
<th>ATSDR Intermediate EMEG (ug/l)</th>
<th>ATSDR Intermediate RMEG (ug/l)</th>
<th>EPA R9 Chronic PRG (ug/l)</th>
<th>MTCA B Chronic GW cleanup level (ug/l)</th>
<th>EPA Chronic HRL (ug/l)</th>
<th>EPA Chronic DWLOC (ug/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Azinphos methyl</td>
<td>10</td>
<td>30 (child)</td>
<td>30 (child)</td>
<td>NA*</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>7 (child)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>100 (adult)</td>
<td>100 (adult)</td>
<td>NA*</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>40 (adult)</td>
</tr>
<tr>
<td>Pendimethalin</td>
<td>70</td>
<td>NA</td>
<td>NA</td>
<td>400 (child)</td>
<td>1500</td>
<td>640 (20)</td>
<td>NA</td>
<td>NA</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>1000 (adult)</td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>EPTC</td>
<td>200</td>
<td>NA</td>
<td>NA</td>
<td>300 (child)</td>
<td>910</td>
<td>200 (20)</td>
<td>175</td>
<td>20 (child)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>900 (adult)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>68 (adult female)</td>
</tr>
</tbody>
</table>

*NA – not available

Table 5: Routes of Exposure addressed by ATSDR, EPA, and Ecology Azinphos Methyl, EPTC, and Pendimethalin Benchmarks

<table>
<thead>
<tr>
<th>Route of Exposure covered by Benchmarks</th>
<th>USGS HBSL (ug/l)</th>
<th>ATSDR Chronic EMEG (ug/l)</th>
<th>ATSDR Intermediate EMEG (ug/l)</th>
<th>ATSDR Intermediate RMEG (ug/l)</th>
<th>EPA R9 Chronic PRG (ug/l)</th>
<th>MTCA B Chronic GW cleanup level (ug/l)</th>
<th>EPA Chronic HRL (ug/l)</th>
<th>EPA Chronic DWLOC (ug/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ingestion</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RSC*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Inhalaional</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>X –EPTC only</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dermal</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*RSC = relative source fraction
Exposures to pesticides would be expected to be higher in agricultural areas, where people are exposed via other sources then drinking water. It appears that the health benchmarks noted above likely do not take into account maximally exposed populations such as people who apply pesticides and/or live near fruit orchards or other crops that have been treated with pesticides although their exposures may be significantly higher than the average person. People who work in agricultural occupations could also have higher exposures. It is reported that families of agricultural workers might also be exposed to higher levels of these pesticides than average because the chemical can be carried home on personal items (e.g., clothes, vehicles).(2)

The routes of exposure addressed by each benchmark are summarized in Table 5. None of the benchmarks included in Table 4 addressed all the routes of exposure identified by DOH for azinphos methyl, EPTC, and pendimethalin in potable water (Table 3). The following summarizes DOH’s findings about the use of the USGS HBSLs as health benchmarks:

**Azinphos Methyl Benchmark Comparison**

Only three health benchmarks were found for azinphos methyl (Table 4): ATSDR intermediate (i.e., 15 days to 1 year exposure) and chronic environmental media evaluation guidelines (EMEGs) and an EPA drinking water level of concern (DWLOC). As noted in Table 3, azinphos methyl poses a possible health risk via ingestion and dermal contact. However, none of the available benchmarks addressed both possible routes of exposure. The following bullets summarize DOH’s findings regarding the azinphos methyl health benchmarks:

- The ATSDR azinphos methyl EMEGs are slightly higher than the USGS HBSL (Table 4). However, the EMEGs only address ingestion of azinphos methyl (via cooking, drinking, and food preparation).³
- The EPA chronic DWLOC addresses ingestion of drinking water containing azinphos methyl and also considers residual azinphos methyl levels found in food. The EPA DWLOC for child exposures is slightly less than the USGS HBSL (Table 4).

It is uncertain whether dermal contact with azinphos methyl in groundwater is a significant route of exposure.⁴ Given this fact and the above findings regarding the azinphos methyl benchmarks, DOH cannot currently determine whether the USGS azinphos methyl HBSLs is an acceptable benchmark.

**EPTC Benchmark Comparison**

Four health benchmarks were found for EPTC (Table 4): ATSDR intermediate EMEG, EPA Region 9 preliminary remediation goal (PRG) for chronic exposures, Washington

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³ EMEGs are not derived to take into account dermal exposures that might occur via showering.
⁴ Determining the significance of the dermal route of exposure for azinphos methyl, EPTC, and pendimethalin is beyond the scope of this health consultation. DOH can evaluate this further in the future, if requested by AG.
Model Toxics Control Act (MTCA) method B groundwater cleanup level for chronic exposures, and EPA chronic health reference level (HRL). As noted in Table 3, EPTC poses a possible health risk via ingestion, inhalation, and dermal contact. However, none of the available benchmarks addressed the three possible routes of exposure. The following bullets summarize DOH’s findings regarding the EPTC health benchmarks:

- The ATSDR intermediate EMEG is a little higher than the USGS HBSL (Table 4). However, the EMEG only address ingestion of EPTC (via cooking, drinking, and food preparation). It does not take into account dermal contact with or inhalation of EPTC vapors associated with contaminated water.
- The EPA Region 9 PRG for EPTC only addresses ingestion of drinking water and is higher than the USGS HBSL.
- The MTCA method B groundwater cleanup level for EPTC was derived to be protective if EPTC contaminated groundwater is ingested and inhaled. Although the MTCA level is equal to the USGS HBSL, it is uncertain whether that level would be lower if the dermal route of exposure was also considered.
- The EPA HRL is less than the USGS HBSLs. Like the USGS, EPA applied a 20% relative source fraction to account for drinking water usage. It is unknown if the USGS or EPA relative source fraction takes into account ingestion, inhalation, and dermal contact.

Given the information above regarding EPTC, it is uncertain whether the USGS HBSL is a suitable benchmark.

**Pendimethalin Health Benchmark Comparison**

Three health benchmarks were found for pendimethalin (Table 4): ATSDR intermediate EMEG, EPA Region 9 preliminary remediation goal (PRG) for chronic exposures, and Washington Model Toxics Control Act (MTCA) method B groundwater cleanup level for chronic exposures. As noted in Table 3, pendimethalin poses a possible health risk via ingestion, inhalation, and dermal contact. However, none of the available benchmarks addressed the three possible routes of exposure. The following bullets summarize DOH’s findings regarding the EPTC health benchmarks:

- The ATSDR intermediate EMEG is higher than the USGS HBSL (Table 4). However, the EMEG only address ingestion of pendimethalin (via cooking, drinking, and food preparation).
- The EPA Region 9 PRG for pendimethalin is higher than the USGS HBSLs but only addresses ingestion of drinking water.
- The MTCA method B groundwater cleanup level for pendimethalin is higher than the USGS HBSL but only addresses ingestion of drinking water.

It is unknown, whether the HBSL for pendimethalin, a Class C carcinogen, which was calculated using a non-standard approach, is appropriately protective. In addition, none of the pendimethalin non-carcinogen health benchmarks take into account dermal contact with EPTC or inhalation of EPTC vapors although these appear to be possible exposure
pathways. Consequently, it is uncertain whether the USGS HBSL for pendimethalin is an appropriate benchmark.

**Children’s Health Concerns**

Children can be uniquely vulnerable to the hazardous effects of environmental contaminants. When compared to adults, pound for pound of body weight, children drink more water, eat more food, and breathe more air, which can lead to increased exposure to contaminants. Additionally, the fetus is highly sensitive to many chemicals, particularly with respect to potential impacts on childhood development. For these reasons, the specific impacts that contaminants like azinphos methyl, EPTC, and pendimethalin might have on children, as well as other sensitive populations, exposed to these chemicals in potable water was considered in this health consultation. Sensitive populations include occupational or agricultural workers who may be applying these azinphos methyl, EPTC and pendimethalin, and their families who may be exposed to high levels of these chemicals. Children and sensitive subpopulations should continue to be considered during future work.

**Conclusions**

- Based on a comparison with available health benchmarks for azinphos methyl, EPTC, and pendimethalin, it is uncertain whether the USGS HBSLs are suitable health benchmarks. Most of the existing health benchmarks were derived to address ingestion of these three pesticides via drinking water. However, other possible routes of exposure exist for these pesticides in drinking water including inhalation and/or dermal contact. The significance of the inhalation and dermal exposures is unknown at this time.
- Azinphos methyl, EPTC, and pendimethalin would likely be found in groundwater and surface water in agricultural and other areas where they are being applied. People who apply these chemicals and their families as well as people who live near these areas could be exposed to these chemicals via other exposure pathways. The USGS HBSLs do not appear to take into account these occupational or other high exposures.
- The literature suggests that breakdown products and contaminants are associated with azinphos methyl, EPTC, and pendimethalin. It is unknown if these chemicals would might also pose a possible drinking water health risk.

**Recommendations**

The Washington Department of Agriculture should not make decisions about the use of the USGS HBSLs for azinphos methyl, EPTC, and pendimethalin as health benchmarks until further evaluation is completed.

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5 Consequently, the use of the USGS HBSL for these pesticides at this time would result in an indeterminate public health hazard conclusion.
Action Plan

- If the Washington Department of Agriculture decides to continue evaluating whether the USGS HBSLs for azinphos methyl, EPTC, and pendimethalin are suitable benchmarks, the following tasks should be undertaken:
  - Determine whether the inhalation and dermal risks associated with azinphos methyl, EPTC, and pendimethalin are significant. If they are significant, determine whether the RSC used by USGS during HBSL development adequately takes into account exposures to groundwater or surface water contaminants via the inhalation or dermal routes of exposure.
  - Evaluate whether the HBSLs are suitable for agricultural workers who are applying these pesticides, and their families, or other people with high exposures.
  - Identify breakdown products and contaminants associated with azinphos methyl, EPTC, and pendimethalin and include them in future potable water monitoring if they could pose a health risk.
Appendices
Appendix A  
USGS HBSLs Formula
USGS uses the following formula for calculating carcinogenic, possible carcinogenic and non-carcinogenic HBSLs:

### Carcinogens (except possible (Group C) carcinogens or contaminants with suggestive evidence of carcinogenic potential):

**Carcinogenic HBSL (ug/l) = \((70 \text{ kg body wt}) \times (\text{risk level})\) \(\frac{2 \text{ l/day}}{2 \text{ l/day}}\) \times (\text{SF}) \times (\text{mg/1,000 ug})\)**

Where:
- mg = milligrams;
- \(\mu\text{g} = \text{micrograms}\)
- l = liter
- \(\text{ug/l} = \text{micrograms per liter}\);
- kg body wt = kilograms of body weight = 70
- risk level = 10^-6 to 10^-4 cancer risk range
- SF = cancer slope factor [mg/kg/day]^{-1}

### Possible Carcinogen (Group C) or chemical with suggestive carcinogenic potential:

For possible (Group C) carcinogens or contaminants with suggestive evidence of carcinogenic potential, HBSLs are calculated using the EPA Office of Water equation for calculating Lifetime HA values for Group C carcinogens. This approach uses an Rfd, rather than a slope factor, and includes relative source contribution and a risk management factor (RMF)

**Possible Carcinogen HBSL (ug/L) = (\text{Rfd x }) \times (70 \text{ kg body wt}) \times (1,000 \text{ ug/mg}) \times \text{RSC} \times (2 \text{ L water consumed/day}) \times \text{RMF}\)**

Where:
- Rfd = reference dose (mg/kg/day)
- RSC = relative source contribution (defaults to 20 percent in absence of other data)
- RMF = Risk Management Factor (defaults to 10 in the absence of other data)

### Non-Carcinogens

**Non-carcinogenic HBSL (ug/l) = (\text{Rfd}) \times (70 \text{ kg body wt}) \times (1,000 \text{ ug/mg}) \times \text{RSC} \times (2 \text{ L water consumed per day})\)**
Appendix B
Health Based Screening Level Equations and Exposure Parameters
The equations and RfDs (or MRLs) (Table B-1) used to derive the health benchmarks presented in this health consultation report are summarized below.

Table B-1: RfDs (or MRLs) for Azinphos Methyl, EPTC, and Pendimethalin

<table>
<thead>
<tr>
<th>Benchmark</th>
<th>MRL/RfD (mg/kg/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Azinphos methyl</td>
</tr>
<tr>
<td>USGS HBSL</td>
<td>0.00149</td>
</tr>
<tr>
<td>ATSDR EMEG/RMEG</td>
<td>0.003 (MRL)</td>
</tr>
<tr>
<td>EPA Region 9</td>
<td>NA</td>
</tr>
<tr>
<td>Ecology MTCA B Groundwater</td>
<td>NA</td>
</tr>
<tr>
<td>EPA HRL</td>
<td>NA</td>
</tr>
<tr>
<td>EPA DWLOC</td>
<td>0.00149</td>
</tr>
</tbody>
</table>

* EPA re-registration document for pendimethalin indicates the RfD is 0.10 mg/kg/day
** EPA’s Office of Prevention, Pesticides, and Toxic Substances applied a 10-fold safety factor, known as the Food Quality Protection Act (FQPA) safety factor, to the chronic EPTC RfD (0.025 mg/kg/day) resulting in a chronic level, which they refer to as a chronic population adjusted (cPAD) of 0.0025 mg/kg/day. The chronic PAD (0.0025) represents a 10-fold safety factor, known as the Food Quality Protection Act (FQPA) safety factor, applied to the chronic EPTC RfD (0.025 mg/kg/day). EPA’s FQPA Safety Factor Committee recommended that the 10x FQPA safety factor be retained for all population subgroups for acute, chronic and residential exposure assessments because of the neuronal necrosis/degeneration effects and the potential for residential exposure to infants and children from use of EPTC.(11;21)

**ATSDR – EMEG/RMEG (Water)**

Environmental Media Evaluation Guidelines (EMEGs) represent concentrations in environmental media (e.g., water) to which people may be exposed during a specified time period (e.g., acute, intermediate, chronic) without experience adverse health effects. They are derived used ATSDR minimal risk levels (MRLs). If no MRLs are available, Reference Dose Evaluation Guidelines (RMEGs) are developed using EPA’s reference doses (RfDs)

\[
\text{EMEG (mg/l)} = \frac{(\text{MRL} \times \text{BW})}{\text{IR}}
\]

\[
\text{RMEG (mg/l)} = \frac{(\text{RfD} \times \text{BW})}{\text{IR}}
\]

Where:
- MRL = minimal risk level (mg/kg/day) (see table)
- RfD = oral reference dose (mg/kg/day)
- mg/l = milligram/liter
- BW = body weight: Child = 10 kg; Adult = 70 kg
- IR = ingestion rate: Child = 1 liter/day; Adult = 2 liters/day
**EPA Region 9 – Preliminary Remediation Goals (Tap Water) Ingestion and Inhalation Exposures to Non-carcinogenic Contaminants in Water**

EPA Region 9 considers ingestion of drinking water an appropriate pathway for all chemicals. However, inhalation of volatile chemicals from water is only considered routinely when EPA considers the chemical volatile (i.e., chemicals with a Henry’s Law constant of $1 \times 10^{-5}$ atm-m$^3$/mole or greater and with a molecular weight of less than 200 grams per mole).(22) Neither pendimethalin nor EPTC were considered volatile by the EPA Region 9 definition.(19)

$$[\text{Non Carcinogenic}] \ C (\text{ug/l}) = \frac{\text{THQ} \times \text{BW}_a \times \text{AT}_n \times 1000 \text{ug/mg}}{\text{EF}_r \times \text{ED}_d \times (((\text{IRW}_a/ \text{RfD}_o))}$$

Where:
- THQ = target Hazard Quotient = 1 [unitless]
- BW$_a$ = adult body weight = 70 kg
- AT$_n$ = averaging time = ED*365 days
- EF$_r$ = residential exposure frequency = 350 days/year
- EF$_d$ = residential duration = 30 years
- IRW$_a$ = adult drinking water ingestion = 2 liters/day
- RfD$_o$ = oral reference dose (mg/kg/day)

**Ecology Method B Groundwater Cleanup Levels**

Under the Model Toxics Control Act Cleanup Regulation Method B groundwater cleanup levels are established based on estimates of groundwater as a source of drinking water the highest beneficial use and the reasonable maximum exposure expected to occur under both current and potential future site use conditions and that exposure to hazardous substances through ingestion of drinking water and other domestic is the primary route of exposure. When volatile chemicals are found in groundwater an inhalation correction factor is used to adjust exposure estimates based on ingestion of drinking water to take into account exposure to hazardous substances that are volatilized and inhaled during use of the water.(23)

$$\text{Ground water cleanup level (ug/l)} = \frac{\text{RfD} \times \text{ABW} \times \text{UCF} \times \text{HQ} \times \text{AT} \times \text{DWIR} \times \text{INH} \times \text{DWF} \times \text{ED}}{\text{RfD}_o}$$

Where:
- RfD = reference dose
- ABW = average body weight during the exposure duration = 16 kg
- UCF = unit conversion factor = 1,000 ug/mg
- HQ = hazard quotient = 1 (unitless)
- AT = averaging time = 6 years
- DWIR = drinking water ingestion rate = 1.0 liter/day
- INH = inhalation correction factor = 2 (unitless) for VOCs otherwise 1 (unitless)
- DWF = drinking water fraction = 1.0 (unitless)
- ED = exposure duration = 6 years

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**EPA HRL – Drinking Water**

The Safe Drinking Water Act (SDWA) requires EPA to make regulatory determinations for no fewer than five contaminants beginning in August 2001 and continuing every five years thereafter. One of the criteria used to determine whether or not to regulate a chemical on the contaminant candidate list is determining whether the contaminant may have an adverse effect on the health of persons. This is done by calculating a health reference level (HRL).

\[
\text{HRL} = \frac{(\text{RfD} \times \text{BW})}{\text{IR} \times \text{RSC}}
\]

Where:
- \( \text{RfD} \) = reference dose (mg/kg/day)
- \( \text{BW} \) = body weight = 70 kg
- \( \text{IR} \) = ingestion rate = 2 liters/day
- \( \text{RSC} \) = relative source fraction = 20%. 

**EPA DWLOC**

EPA’s Office Of Prevention, Pesticides, and Toxic Substances uses drinking water levels of concern (DWLOCs) to assess risk associated with exposure from pesticides in drinking water. EPA defines a DWLOC as “the maximum concentration in drinking water which, when considered together with dietary exposure, does not exceed a level of concern.” DWLOCs are establish for each population subgroup (adult and child scenarios) and compared to actual or modeled groundwater levels. A level below the DWLOC indicates the pesticide is not a drinking water risk. (11) DWLOC values are not considered regulatory standards.

\[
\text{DWLOC chronic} = \frac{[\text{chronic water exposure (mg/kg/day) \times (body weight)}]}{[\text{consumption () \times 10^{-3} mg/ug}]} \\
\text{Where:}
\]

Chronic water exposure (mg/kg/day) = [cPAD - (chronic food (mg/kg/day)] (see Tables B-2 and B-3 for values for EPTC and azinphos methyl) body weights and water consumption values: 70kg/2L (adult male), 60 kg/2L (adult female), and 10 kg/1L (child).
Table B-2: Input parameters and Chronic DWLOWs for Azinphos Methyl

<table>
<thead>
<tr>
<th>Population subgroup</th>
<th>Chronic PAD (mg/kg/day)</th>
<th>Food exposure (mg/kg/day)</th>
<th>Allowable water exposure (mg/kg/day)</th>
<th>DWLOC (ppb)</th>
</tr>
</thead>
<tbody>
<tr>
<td>U.S. Population</td>
<td>0.0015</td>
<td>0.000195</td>
<td>0.001305</td>
<td>46</td>
</tr>
<tr>
<td>Nursing infants (&lt;1 year)</td>
<td>0.0015</td>
<td>0.000194</td>
<td>0.001306</td>
<td>13</td>
</tr>
<tr>
<td>Non-nursing infants (&lt;1 year)</td>
<td>0.0015</td>
<td>0.000803</td>
<td>0.000697</td>
<td>7</td>
</tr>
<tr>
<td>Children (1-6 years)</td>
<td>0.0015</td>
<td>0.000495</td>
<td>0.001005</td>
<td>10</td>
</tr>
<tr>
<td>Children (7-12 years)</td>
<td>0.0015</td>
<td>0.000329</td>
<td>0.001171</td>
<td>12</td>
</tr>
<tr>
<td>Females (13-19 years)</td>
<td>0.0015</td>
<td>0.000172</td>
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<td>40</td>
</tr>
<tr>
<td>Females (20+ years)</td>
<td>0.0015</td>
<td>0.000114</td>
<td>0.001386</td>
<td>42</td>
</tr>
<tr>
<td>Males (13-19 years)</td>
<td>0.0015</td>
<td>0.000205</td>
<td>0.001295</td>
<td>45</td>
</tr>
<tr>
<td>Males (20+ years)</td>
<td>0.0015</td>
<td>0.000121</td>
<td>0.001379</td>
<td>48</td>
</tr>
</tbody>
</table>

PAD = population adjusted dosage

Table B-3: Input parameters Chronic DWLOWs for EPTC

<table>
<thead>
<tr>
<th>Population Subgroup</th>
<th>Chronic PAD (mg/kg/day)</th>
<th>Food Exposure (mg/kg/day)</th>
<th>Maximum Water Exposure (mg/kg/day)</th>
<th>Chronic DWLOC (ug/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adult male</td>
<td>0.0025</td>
<td>0.000231</td>
<td>0.00227</td>
<td>78</td>
</tr>
<tr>
<td>Adult Female</td>
<td>0.0025</td>
<td>0.000229</td>
<td>0.00227</td>
<td>68</td>
</tr>
<tr>
<td>Infants &lt;1 yr</td>
<td>0.0025</td>
<td>0.000281</td>
<td>0.00222</td>
<td>20</td>
</tr>
<tr>
<td>Children 1-6</td>
<td>0.0025</td>
<td>0.000435</td>
<td>0.00207</td>
<td>20</td>
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<tr>
<td>Non-Hispanic Black</td>
<td>0.0025</td>
<td>0.000271</td>
<td>0.00223</td>
<td>76</td>
</tr>
</tbody>
</table>

PAD = population adjusted dosage
Certification

This draft Health Based Screening Level Evaluation Azinphos-methyl, Pendimethalin, and EPTC WA Department of Agriculture Pesticide Vulnerability Project health consultation was prepared by the Washington State Department of Health under a cooperative agreement with the federal Agency for Toxic Substances and Disease Registry (ATSDR). It was completed in accordance with approved methodologies and procedures existing at the time the health consultation was initiated. Editorial review was completed by the Cooperative Agreement partner.

[Signature]
Technical Project Officer, CAT, CAEB, DHAC

The Division of Health Assessment and Consultation (DHAC) ATSDR, has reviewed this health consultation and concurs with the findings.

[Signature]
Team Lead, CAT, CAEB, DHAC, ATSDR


