Health Consultation

PESTICIDE MISAPPLICATION
IN A PRIVATE RESIDENCE

PARSONS, LABETTE COUNTY, KS 67357

November 17, 2010

Prepared by:

U.S. Department of Health and Human Services
Agency for Toxic Substances and Disease Registry

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.

Development of this document is being managed by ATSDR under the "Strike" process, which is a rapid-response focusing on a specific question. It does not include a comprehensive review of all technical memorandum, site contaminants, and potential exposure pathways. This concludes the 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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Statement of Issues

On October 28, 2010, the U.S. Environmental Protection Agency (EPA) Region 7 requested that the Agency for Toxic Substances and Disease Registry (ATSDR) review the results of wipe, soil, air, carpet, and drywall samples obtained from a home in Parsons, Kansas to determine if exposures to pesticide residues in the home could pose a potential health risk to occupants.

This EPA request is being managed by ATSDR under the "Strike" process, which is a rapid-response, focused effort that does not include comprehensive review of the technical memorandum, site contaminants, and exposure pathways.

Site Description and History

The home is a one-story house constructed in 1978 with a partially finished basement that contains an office. It has central air-conditioning and forced-air heating. The current owners purchased the home in 2008, and the house was treated for termites in July, 2009 by a professional exterminator. The exterminator, who is not licensed with the Kansas Department of Agriculture (KDA), applied pesticide through holes drilled into the exterior brick facade of the house. In April, 2010 the exterminator retreated the house for termites. The exterminator stated he treated the exterior of the house and the interior of the master bedroom and an office located in the basement with malathion. Following this pesticide application, the residents stated chemical odors in the master bedroom and basement office were so strong they closed the master bedroom door and air vents in the bedroom and quit using both rooms. Throughout the summer, visitors to the house commented on the strong odor in the home and the inability to stay in the home for prolonged periods of time. This indicates that pesticide residues may have been dispersed throughout the home by the air ventilation system.

The homeowners sought the assistance of the KDA, the state agency which regulates professional pesticide application in Kansas. KDA collected wipe samples at the residence August 6, 2010. Bifenthrin and malathion were detected on perimeter baseboard surfaces and in carpet and carpet pad samples in areas where the pesticides had been applied. Following the inspection, the homeowners removed materials that had been contaminated with pesticides from the house. The homeowners removed carpeting, drywall and insulation, as well as some ceiling tiles in the basement they thought had been contaminated.

Subsequent to the pesticide application, an adult female and a child in the house began to experience health effects. The adult stated she became fatigued, developed bruising and swelling, and experienced respiratory problems after being exposed to the pesticides. The child has had a history of nose bleeds that increased in frequency following the pesticide application. The homeowners contacted the University of Kansas Hospital's Association of Occupational and Environmental Clinics (AOEC) clinic for assistance in addressing their medical questions and concerns.

A physician affiliated with the AOEC ordered clinical lab tests that revealed depressed serum cholinesterase levels, especially in the adult. Cholinesterase levels for the other residents were not obtained. A reduction in cholinesterase activity is an indication of exposure to organophosphate pesticides, such as malathion (ATSDR 1994). The family moved out of the house in September 2010, and has not yet returned. The child's nosebleeds stopped and the adult female's symptoms improved upon moving out of the home; however, ATSDR is not aware if any follow-up testing of serum cholinesterase activity in these individuals has been performed.

The AOEC physician contacted ATSDR and EPA requesting assistance to further evaluate the house to determine if living in the residence poses a health hazard to residents. The EPA collected wipe, air, drywall, carpet pad, and soil samples on September 9, 2010, to assess pesticide contamination at the residence. EPA asked ATSDR to evaluate the results to determine if pesticide levels in the residence pose a health hazard.

Discussion

Analytical methods

Air samples were collected and analyzed in accordance with USEPA Method TO-10A for pesticides. Soil and interior surface samples were collected and analyzed in accordance with US EPA Method SW846 and EPA Region 7 RLAB Method 3240.2H. Details on collection and analysis of KDA samples were not available.

Sampling results

Sampling of indoor air, interior surfaces, contaminated carpet, and soil along the building perimeter detected several organochlorine, organophosphate and pyrethroid pesticides and their environmental degradation products. Results are presented in Tables 1-5.

Table 1. Interior surface sampling (microgram per square centimeter (µg/cm^2))

Sample # and Location	Matrix	Malathion	Isomalathion	Malaoxon	Heptachlor	Chlordane
EPA 1 Door trim between kitchen and TV room	Wipe	ND	ND	ND	ND	0.0026
EPA 2 Bedroom NW corner, studs and sheetrock	Wipe	0.322 J	0.20	0.16	ND	ND
EPA 3 Bedroom wall, behind bed	Wipe	0.046	ND	ND	0.0013	0.071
EPA 4 Dollhouse in playroom	Wipe	ND	ND	ND	ND	ND
EPA 5 Desk in downstairs office	Wipe	0.011 J	0.013	ND	ND	0.0067
EPA 5FD Sample 5 Field Duplicate	Wipe	0.0095 J	ND	ND	ND	0.0034

ND = non detect

J = estimated value

Table 2. Indoor air sampling (microgram per cubic meter (µg/m^3))

Sample # and Location	Matrix	Malathion	Chlorpyrifos	Diazinon	Heptachlor	Chlordane
PUF 743 Bedroom	Air	0.40	ND	ND	**0.12**	**0.38**
PUF 744 Bedroom	Air	0.48	ND	ND	**0.12**	**0.40**
PUF 745 Front hall	Air	ND	ND	ND	**0.12**	**1.1**
PUF 746 Basement office	Air	0.36	ND	ND	**0.14**	**1.9**
PUF 747 Basement	Air	ND	0.088	0.077	**0.12**	**1.3**
PUF 748 Game room	Air	ND	ND	ND	**0.15**	**1.4**

Bold text = concentrations exceeded comparison value

Table 3. Building foundation soil sampling (microgram per kilogram (µg/kg))

Sample #	Matrix	Malathion	Isomalathion	Malaoxon	Heptachlor	Heptachlor Epoxide
EPA 14	Soil	ND	ND	ND	ND	ND
EPA 15	Soil	ND	ND	ND	11 J	ND
EPA 16	Soil	ND	ND	ND	1.4	4.1 J
EPA 17	Soil	130 J	ND	ND	ND	ND
EPA 17FD	Soil	190 J	ND	ND	ND	ND
		Chlordane	**Endrin Ketone**	**p, p' - DDE**	**p, p' - Methoxychlor**	
EPA 14	Soil	27	ND	ND	ND	
EPA 15	Soil	11000	7.3 J	13J	8.8 J	
EPA 16	Soil	430	ND	ND	4.7 J	
EPA 17	Soil	53	ND	ND	ND	
EPA 17FD	Soil	32	ND	ND	6.8 J	

Table 4. Carpet and drywall samples (µg/kg)

Sample #	Matrix	Malathion	Heptachlor	Heptachlor Epoxide	Chlordane
EPA 9	Drywall	3500	ND	ND	120
EPA 12	Carpet pad	3200	420	110	4300

Table 5. KDA sample results (µg/swab)

Sample #	Matrix	Bifenthrin	Malathion
KDA 1	Carpet Pad	0.52	24.11
KDA 2	Swab	ND	0.09
KDA 3	Swab	ND	ND
KDA 4	Swab	ND	1.35
KDA 5	Swab	ND	6.68
KDA 6	Swab	ND	2.87
KDA 7	Swab	ND	2.79
KDA 8	Swab	1.57	ND

Data analysis

To evaluate potential health hazards, ATSDR first compares the sampling data to appropriate health-based screening levels. These comparison values include ATSDR Environmental Media Evaluation Guides (EMEGs), ATSDR Cancer Risk Evaluation Guides (CREG), and EPA regional screening levels, guidelines and environmental standards. Sample data that exceed these values are evaluated further.

EMEGs are environmental media-specific concentrations calculated from ATSDR's minimal risk levels (MRLs) that incorporate standard assumptions about bodyweight and intake estimates for children and adults. EMEGs are calculated for different durations of exposure: acute (1-14 days), intermediate (15-365 days), and chronic (more than 365 days).

MRLs are an estimate of daily human exposure to a hazardous substance that is likely to be without an appreciable risk of adverse noncancer health effects. MRLs are based on the most sensitive chemical-induced effect relevant to humans and are intended to protect sensitive individuals. Reference doses (RfDs) and reference concentrations (RfCs) are developed by EPA and used like the health-based guidelines developed by ATSDR.

CREGs are media-specific comparison values that are used to identify concentrations of cancer-causing substances that may result in an increase of background cancer rates in an exposed population.

MRLs, EMEGs and CREGs are used as screening tools to help public health professionals decide if additional evaluation is needed. Exposure to a level above an EMEG or MRL does not mean that adverse effects will occur. Comparison values used in this evaluation are presented in Table 6.

Exposure pathway evaluation

Based on the historical indoor application of pesticides, the primary pathways of exposure to the occupants would be from direct dermal contact with contaminated surfaces, inhalation of pesticide particulates, and incidental ingestion of pesticide residues in house dust.

Wipe samples – No comparison values were identified for surface wipes in a non-occupational setting. Several wipe samples were collected from areas where typically there would not be significant and frequent contact (e.g., wall behind bed) so it is difficult to interpret the significance of these data. Two areas with relevance for human contact were sampled, including a dollhouse and a desk. The dollhouse sample was negative, however malathion residue was found on the surface of the desk. These data imply that pesticide residues on interior surfaces could be a source of exposure to building occupants.

As part of the American Healthy Homes Survey, the EPA and the U.S. Department of Housing and Urban Development jointly funded a study of pesticide residues in a randomly selected nationally representative sample. Interior wipe samples were analyzed for 24 insecticides. This study identified the most commonly detected insecticides were permethrin, chlorpyrifos, chlordane, piperonyl butoxide, cypermethrin and fipronil (Stout 2009).

A comparison of the levels of pesticides detected in wipe samples in this property with the levels in the national sample revealed that the concentrations in the Parsons site were above the 75th percentile for chlordane, above the 95th percentile for heptachlor, and 24

times greater than the maximum detected concentration of malathion in the study. The results clearly show that pesticide residues exist in this home above national averages (Stout 2009).

Soil - Soil concentrations did not exceed comparison values and do not require further analysis.

Air – Indoor air samples for chlordane and heptachlor exceeded comparison values indicating there may be a concern for long-term exposures. Air data require further analysis to determine the potential public health impact of exposure. Details of this analysis are in appendix A.

Table 6. Environmental media comparison values

Analyte	**Media Screening Value**	
	Air (µg/m^3)	Soil (µg/kg)
Bifenthrin	None	None
Malathion	200 – Acute EMEG 20 – Intermediate EMEG No chronic EMEG for malathion	1,000,000 µg/kg – child chronic EMEG 10,000,000 µg/kg – adult chronic EMEG
Isomalathion	5 – derived from Malathion Intermediate EMEG of 10 µg/m^3 and relative potency factor of 4 for Isomalathion.[1]	None
Malaoxon	0.3 – derived from Malathion Intermediate EMEG of 10 µg/m^3 and relative potency factor of 64 for Malaoxon.[1]	None
Chlorpyrifos	None	50,000 µg/kg – child chronic EMEG
Diazinon	10 – Intermediate EMEG	40,000 µg/kg – child chronic EMEG 500,000 µg/kg – adult chronic EMEG
Heptachor	0.0008 - CREG	5,000 µg/kg – child intermediate EMEG 70,000 µg/kg – adult intermediate EMEG 200 µg/kg - CREG
Heptachlor Epoxide	0.0004 – CREG	700 µg/kg - child RMEG 9,000 µg/kg – adult RMEG 80 µg/kg - CREG
Chlordane	0.2 Intermediate EMEG 0.02 – Chronic EMEG 0.01 - CREG	30,000 µg/kg – child chronic EMEG 400,000 µg/kg – adult chronic EMEG
Endrin Ketone	None	None
p, p'- DDE	0.025 – EPA Regional Screening Level Residential Air	1,400 – EPA Regional Screening Level Residential Soil
p, p'-Methoxychlor	None	310,000 – EPA Regional Screening Level Residential Soil

[1] There are no health-based comparison values for the evaluation of inhalation exposure to the malathion breakdown products, isomalathion and malaoxon. However, USEPA has conducted a relative toxicity analysis of isomalathion and malaoxon, indicating that they both have greater toxicity than malathion. The relative potency for isomalathion is 4 and for malaoxon is 62 (USEPA 2009). Based on these relative potency factors, the estimated comparison values are isomalathion: 5 ug/m^3 and malaoxon: 0.3 ug/m^3.

Chemical and physical properties

Chlordane

Chlordane is a cyclodiene organochlorine (OC) pesticide used in the past as soil insecticides for the control of termites and soil-borne insects whose larval stages feed on the roots of plants. The cyclodienes were the most effective, long-lasting and economical termiticides ever developed. Because of their persistence in the environment, resistance that developed in several soil insect pests, and in some instances biomagnification in wildlife food chains, most agricultural uses of cyclodienes were canceled by the EPA between 1975 and 1980, and their use as termiticides canceled in 1984-88 (Ware 2004).

Malathion

Malathion is an organophosphorous (OP) insecticide that is used to kill insects on agricultural crops, on stored products, on golf courses, in home gardens, and in outdoor sites where trees and shrubs are grown at home; it is also used to kill mosquitoes and Mediterranean fruit flies (medflies) in large outdoor areas. Malathion is used to kill fleas on pets and to treat head lice on humans. Malathion comes in two forms: a pure form of a colorless liquid and a technical-grade solution (brownish-yellow liquid), which contains malathion (greater than 90%) and impurities in a solvent. The technical-grade malathion smells like garlic.

Malathion is a manufactured chemical, so it is only found in the environment as a result of its manufacture or use. Malathion has been manufactured in the United States since 1950 and has been used to kill insects on many types of crops since this time. Because malathion can be dangerous to humans, the EPA requires that a certain amount of time must pass between the time of application of the insecticide and entry by a worker into a field where the chemical has been applied. Usually, at least 12 hours must pass between application and entry, but in some cases, such as when workers are entering a field to hand harvest or hand prune the crops, time periods as long as 6 days must pass between application and entry into the field. In this way, exposure to malathion can be controlled and accidental exposures can be prevented.

Heptachlor

Heptachlor is an insecticide of the organochlorine class. Pure heptachlor is a white powder that smells like camphor (mothballs). The less pure grade is tan. Trade names include Heptagran®, Basaklor®, Drinox®, Soleptax®, Termide®, Gold Crest H-60®, and Velsicol 104®.

Heptachlor was used extensively in the past for killing insects in homes, buildings, and on food crops. These uses stopped in 1988. Currently it can only be used for fire ant control in underground power transformers.

Health effects of concern for exposure

Chlordane

Acute exposure of humans to high levels is characterized by gastrointestinal upset and neurological signs, including tremors and convulsions. Death may ensue, often preceded by convulsions. Neurological signs have been consistently observed in animal poisoning as well, firmly establishing chlordane as a neurotoxicant. Longer term exposure of humans to lower levels also caused neurological signs, including grand-mal seizures and altered EEG, but levels of exposure were not quantified. The occurrence of jaundice in persons living in chlordane treated homes and the alteration of serum enzyme levels in persons working as pesticide applicators suggest that the liver is an important target organ in humans (ATSDR 1994).

Inhalation exposure for the general population arises chiefly from living in homes treated with chlordane, because chlordane volatilizes from the treated soil and accumulates in indoor air. Although levels at which adverse effects occur are not definitely known, neurological symptoms and jaundice have been associated with chlordane in treated homes (ATSDR 1994).

With relevance to symptoms reported in one of the residents (nosebleeds, bruising), the toxicological profile for chlordane cites anecdotal reports of blood dyscrasias associated with organochlorine pesticides (chlordane, lindane, DDT). This suggests that there may be individuals who are unusually susceptible to the effects of chlordane exposure that might affect normal platelet function and blood clotting (ATSDR 1994).

Liver function tests were normal for 15 workers at a chlordane manufacturing plant, 14 of whom had been employed 9-16 years (Fishbein et. al. 1964). Air exposures of 1.2-1.7 $\mu g/m^3$ were cited in this report. Similar levels of 1.9 $\mu g/m^3$ were detected in the basement office of the Parsons home.

Data were not located regarding reproductive or developmental effects in humans.

Malathion

Effects of malathion on human health and the environment depend on how much malathion is present and the length and frequency of exposure. Effects also depend on the health of a person and/or certain environmental factors.

Malathion interferes with the normal function of the nervous system. Because the nervous system controls many other organs, malathion indirectly can affect many additional organs and functions. Exposure to high amounts of malathion in the air, water, or food may cause difficulty breathing, chest tightness, vomiting, cramps, diarrhea, watery eyes, blurred vision, salivation, sweating, headaches, dizziness, loss of consciousness, and death. If persons who are exposed accidentally or intentionally to high

amounts of malathion are rapidly given appropriate treatment, there may be no long-term harmful effects (ATSDR 2003).

If people are exposed to levels of malathion below those that affect the function of the nervous system, few or no health problems seem to occur. This has been shown in studies with volunteers who inhaled or swallowed small known amounts of malathion. Twelve male volunteers inhaled malathion products at 5,300 µg/m^3, 21,000 µg/m^3, or 85,000 µg/m^3 for one hour per exposure, two exposures per day for 42 consecutive days. The test subjects reported nasal and eye irritation at the highest dose during the first 5-10 minutes of each exposure. The authors concluded that no effects on cholinesterase activity occurred, but noted that one subject in each of the two highest dose groups exhibited reduced plasma cholinesterase activity (Golz 1959).

There is no evidence that malathion affects the ability of humans to reproduce. There is also no conclusive proof that malathion causes cancer in humans, although some studies have found increased incidence of some cancers in people who are regularly exposed to pesticides, such as farmers and pesticide applicators. The International Agency for Research on Cancer (IARC) has determined that malathion is unclassifiable as to carcinogenicity to humans (ATSDR 2003).

Heptachlor

Heptachlor exceeded ATSDR cancer risk screening levels but was below levels of concern for non-cancer health effects.

The carcinogenicity of heptachlor and heptachlor epoxide has been evaluated in a number of human studies. In general, these studies have examined possible associations between heptachlor and/or heptachlor epoxide tissue levels or a surrogate of heptachlor exposure and the prevalence of cancer. Mixed results have been reported across tumor types and within tumor types.

The EPA has classified heptachlor and heptachlor epoxide as a probable human carcinogen and the International Agency for Research on Cancer (IARC) considers heptachlor possibly carcinogenic to humans (ATSDR 2007).

Public health implications

All samples detected pesticide residues below their respective health screening guidelines with the exception of chlordane and heptachlor in indoor air. All air samples detected chlordane, ranging from 1.9 µg/m^3 in the basement office (PUF 746) to 0.38 µg/m^3 in the bedroom (PUF 744). The average chlordane concentration was 1.08 µg/m^3. Heptachlor was detected in all samples ranging from a high of 0.15 µg/m^3 in the basement game room (PUF 748) to 0.12 µg/m^3 in bedroom samples. The average value of heptachlor was 0.13 µg/m^3.

Since chlordane and heptachlor levels exceeded screening guidelines the data were evaluated further (see Appendix A).

Noncancer health effects

Analysis of the chlordane air sampling data indicated that the levels of chlordane exposure exceeded the ATSDR MRL; however exposure estimates were over 600 times below the lowest level identified in a study where no adverse effects on the liver were seen in rodents during a 90-day inhalation study (Kasawinah and Clark 1989). The no adverse effect level (NOAEL) identified in the study was converted by EPA using dosimetric exposure models into a human equivalent concentration of 650 $\mu g/m^3$ (USEPA 1998). This NOAEL for liver effects (enlarged liver) was the most sensitive effect identified in test animals.

In a human study, liver function tests were normal for 15 workers at a chlordane manufacturing plant, 14 of whom had been employed 9-16 years (Fishbein et. al. 1964). Air exposures of 1.2-1.7 $\mu g/m^3$ were cited in this report. Similar levels of 1.9 $\mu g/m^3$ were detected in the basement office of the Parsons home. Although there is the potential for exposure above ATSDR's minimal risk level, the levels of chlordane in air are below levels where long term adverse health effects were seen in human and animal studies.

Cancer concerns

The measured levels of chlordane and heptachlor in air exceeded their respective cancer screening values.

IARC and the EPA have classified chlordane as a possible human carcinogen. EPA has established an Inhalation Unit Risk of 1E-04 per $\mu g/m^3$. This theoretical risk estimate equates to one additional tumor in a population of 10,000 after a lifetime of exposure to 1 $\mu g/m^3$. The average level of chlordane in the home was measured at 1.08 $\mu g/m^3$, slightly exceeding the 1E-04 risk level.

EPA has established an Inhalation Unit Risk for heptachlor of 1.3E-03 per $\mu g/m^3$. The average level of heptachlor in the home was measured at 0.13 $\mu g/m^3$, which exceeds the 1E-04 risk level.

Total combined excess lifetime cancer risk estimates equate to 3 E-04. Elevated cancer risk estimates do not imply that the levels of chlordane and heptachlor in the home will cause cancer in the occupants. Rather, the USEPA uses cancer risk estimates as a support tool to make decision on when to take action, with risk estimates exceeding 1E-04 typically supporting some kind of response.

Conclusions and Recommendations

ATSDR believes that the available evidence suggests that living in this house could pose a potential long-term health risk from exposure to pesticide residues. This conclusion is based on the following: 1) There is evidence that family members experienced health complaints that stopped once they moved out; 2) the AOEC physician's report indicated that acetylcholinesterase levels were depressed in family members living in the home; and 3) air sampling data exceed health-based screening levels, with an excess lifetime cancer risk estimate exceeding EPA's acceptable risk range.

ATSDR recommends further action be taken to reduce pesticide residues in the home before it is reoccupied. Specific recommendations to EPA (or the appropriate response authority include):

1. Sample the air filter to determine if pesticide residues are circulating through the home air ventilation system. If the filter is not present, then a swab of the plenum before and after the filter stage could indicate contamination. If contamination of the ventilation system is detected, clean the HVAC system and associated ductwork.
2. Clean and/or treat contaminated interior surfaces sufficiently to mitigate exposure to pesticide residues.
3. Collect additional air samples after cleaning the interior to determine if pesticide concentrations are within acceptable limits. Prior to sampling, the heat should be on and windows closed to represent worst-case conditions during cold-weather seasons.

Additional considerations:

Petroleum distillates are used as carriers in pesticide applications and may contribute to excess volatile organic compound (VOC) concentrations in indoor air.

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Appendix A: Air sampling data evaluation

Air sample # and Location	Chlordane (µg/m^3)	Heptachlor (µg/m^3)
PUF 743 Bedroom	0.38	0.12
PUF 744 Bedroom	0.40	0.12
PUF 745 Front hall	1.1	0.12
PUF 746 Basement office	1.9	0.14
PUF 747 Basement	1.3	0.12
PUF 748 Game room	1.4	0.15
Average	**1.08**	**0.13**

Chlordane	
Chronic EMEG/MRL	0.02 µg/m^3
Intermed EMEG/MRL	0.2 µg/m^3
Acute EMEG/MRL	None
CREG	0.01 µg/m^3
RfC	0.7 µg/m^3
NOAEL human equivalent concentration (HEC)	650 µg/m^3
EPA's Inhalation Unit Risk	1E-04 per µg/m^3
IARC Cancer Class	2B: Possibly carcinogenic to humans (limited human evidence, less than sufficient evidence in animals)
EPA Cancer class (Based on 1996 cancer assessment guidelines)	KL - Known/Likely human carcinogen

Heptachlor	
Chronic EMEG/MRL	None. The available inhalation data are considered inadequate for the development of MRLs for heptachlor and heptachlor epoxide.
Interm EMEG/MRL	
Acute EMEG/MRL	
CREG	0.0008 µg/m^3
EPA's Inhalation Unit Risk	1.0E-03 per µg/m^3
IARC Cancer Class	2B: Possibly carcinogenic to humans (limited human evidence, less than sufficient evidence in animals)
EPA Cancer class (Based on 1986 cancer assessment guidelines)	B2 :Probably human carcinogen (inadequate human, sufficient animal studies)

Excess lifetime cancer risk (ELCR) = air concentration (µg/m^3) x inhalation unit risk (µg/m^3)$^{-1}$

Chlordane ELCR: 1.08 µg/m^3 x 0.0001 (µg/m^3)$^{-1}$ = 1 E-04

Heptachlor ELCR: 0.13 µg/m^3 x 0.0013 (µg/m^3)$^{-1}$ = 2 E-04

Total combined ECLR: 3E-04

Supporting information

1. Chlordane is classified by EPA as B2; probable human carcinogen, using the 1986 Guidelines for Carcinogen Risk Assessment. Under the 1996 Proposed Guidelines, it would be characterized as a likely carcinogen by all routes of exposure. These characterizations are based on the following summaries of the evidence available: (1) human epidemiology studies showing non-Hodgkin's lymphoma in farmers exposed to chlordane and case reports of aplastic anemia, chlordane associated with home use are inadequate to demonstrate carcinogenicity; (2) animal studies in which benign and malignant liver tumors were induced in both sexes of four strains of mice and occurred with an elevated, but not statistically significant, incidence in a fifth strain, as well as liver toxicity but no tumors in rats of two strains; and (3) structural similarity to other rodent liver carcinogens (USEPA 1998).

2. Heptachlor is classified by EPA as B2: probable human carcinogen, using the 1986 Guidelines for Carcinogen Risk Assessment. There were three epidemiologic studies of workers exposed to chlordane and/or heptachlor. One retrospective cohort study of pesticide applicators showed marginal statistically significant increased mortality from bladder cancer. The other two studies were retrospective cohort studies of pesticide manufacturing workers. Neither of them showed any statistically significant increased cancer mortality (USEPA 1993). Both these populations also had confounding exposures from other chemicals.

   Long-term carcinogenicity bioassays with heptachlor have been performed in rats and mice, with the latter showing a statistically significant increase in liver carcinomas in the treated male and female groups by comparison to controls. The NCI (1977) reported a significant dose-related increase of hepatocellular carcinomas in male and female B6C3F1 mice (USEPA 1993).

3. Human occupational study

   Fishbein, W.I., J.V. White, and H.J. Isaacs. 1964. Survey of workers exposed to chlordane. Ind. Med. Surg. 33: 726-727.

   Liver function tests were normal for 15 workers at a chlordane manufacturing plant, 14 of whom had been employed 9-16 years. Air exposures of 1.2-1.7 $\mu g/m^3$ were cited in this report.

4. Principal study: ATSDR inhalation MRL (1994) and EPA Inhalation RfC 1998) for chlordane

Kasawinah, A., C. Hardy, and G. Clark. 1989a. Comparative inhalation toxicity of technical chlordane in rats and monkeys. J. Toxicol. Environ. Health 28(3): 327-347.

Wistar rats (35 47/sex/group) were exposed to 0, 0.1, 1.0, or 10 mg/m^3 technical chlordane, 8 hours/day, 5 days/week, for 13 weeks, followed by a 13-week recovery period. Blood chemistry and urinalysis were performed before and at 5 and 13 weeks of exposure. Histopathology was performed on all major tissues, including nasal passages. At the end of the exposure period, increased liver weights ($p < 0.01$) were observed for male and female rats exposed to 10 mg/m^3 at weeks 9 and 14. Analysis of blood chemistry results gave indications of hepatic functional alteration, but only among rats exposed to the highest concentration. Alterations included a significant decrease in glucose (83% of control for females), increased globulins (114% of control for males), increased total protein (104% of control for males), decreased albumin (95% of control for males), an increase in cholesterol (158% of control for females), and an altered albumin/globulin (A/G) ratio in males. This pattern of alterations in blood chemistry is indicative of changes in the functioning of the liver, the major site of synthesis of plasma proteins. In view of what is known about the progression of liver effects with increasing concentrations of chlordane, this pattern of changes is considered an adverse effect, with a LOAEL of 10 mg/m^3 and a NOAEL of 1 mg/m^3.

To derive the EPA RfC, EPA converted the study NOAEL into a human equivalent concentration. The NOAEL(HEC) is calculated for a particle: extra-respiratory effect (liver). The estimated RDDR(ER) is 2.7 for an MMAD of 1.8 um and sigma g of 3.1, based on dosimetric modeling. NOAEL(HEC) = NOAEL(ADJ) x RDDR(ER) = 0.24 mg/m^3 x 2.7 = 0.65 mg/m^3. An uncertainty factor of 1,000 was applied to derive the RfC.