



## ADDENDUM TO THE TOXICOLOGICAL PROFILE FOR CHLORDANE

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## ADDENDUM for CHLORDANE

### Supplement to the 1994 Toxicological Profile for Chlordane

#### Background Statement

*This addendum to the Toxicological Profile for Chlordane supplements the profile released in 1994.*

*Toxicological profiles are developed in response to the Superfund Amendments and Reauthorization Act (SARA) of 1986, which amended the Comprehensive Environmental Response, Compensation, and Liability Act of 1980 (CERCLA or Superfund). CERCLA mandates that the ATSDR Administrator prepare toxicological profiles on substances on the CERCLA Priority List of Hazardous Substances. ATSDR is also responsible for periodic updates to Toxicological Profiles. CERCLA further states that the Administrator will “establish and maintain inventory of literature, research, and studies on the health effects of toxic substances” [Title 42, Chapter 103, Subchapter I, § 9604 (i)(1)(B)].*

*The purpose of this addendum is to provide to the public and federal, state, and local agencies a non-peer reviewed supplement of the scientific data published in the open peer-reviewed literature since the profile’s 1994 release.*

*Chapter numbers in this addendum coincide with the [Toxicological Profile for Chlordane \(1994\)](#). This document should be used in conjunction with the profile. It does not replace it.*

## 2. HEALTH EFFECTS

### 2.2 DISCUSSION OF HEALTH EFFECTS BY ROUTE OF EXPOSURE

#### 2.2.1 Inhalation Exposure

##### 2.2.1.4 Neurological Effects

Kilburn and Thornton (1995) assessed measures of neurobehavioral function in a group of 216 adults who at an apartment complex in April of 1987 had been exposed to chlordane following application to external wood surfaces and soil. Later in 1987 and in 1988, the group was exposed to additional chlordane and chlorpyrifos applications. Tests for chlordane residue in 1990 and 1991 revealed concentrations  $\geq 0.5$   $\mu\text{g}/929$   $\text{cm}^2$  on 85% of 81 samples from external wood surfaces. Indoor concentrations as high as 13.6  $\mu\text{g}/929$   $\text{cm}^2$  were obtained on wipe samples, and 8-hour air samples taken from some of the apartments revealed chlorinated insecticide levels  $>0.5$   $\mu\text{g}/\text{m}^3$ . Eight subjects occupying the apartments had elevated blood levels of heptachlor (range 110–186 ppb), oxychlordane (70–150 ppm), and *trans*-nonachlor (76–200 ppm). During June–September 1994, each of the 216 subjects underwent a battery of neurophysiological and neuropsychological testing and provided information regarding the frequency of 35 respiratory, neurologic, and vegetative complaints. A referent group of 174 adults of similar age, educational level, weight, height, and sex ratio was likewise assessed. Compared to the referents, exposed subjects exhibited

- Significantly impaired performance of balance, reaction times, Culture Fair (measure of nonverbal nonarithmetical intelligence), digit symbol, verbal recall, and trail-making;
- Significantly elevated mood-state scores (tension, depression, anger, vigor, fatigue, confusion); and
- Elevated frequencies of respiratory, neurobehavioral, and rheumatic symptoms.

### 2.2.1.6 Developmental Effects

Fenster et al. (2006) studied a birth cohort of 385 low-income Latinas living in the agricultural community of Salinas Valley, California. Fenster and colleagues were looking for a possible association between exposure to 11 individual organochlorine pesticides, including oxychlordane and *trans*-nonachlor, and such outcomes as length of gestation, birth weight, and crown-heel length. Fenster and colleagues discovered no association between oxychlordane and *trans*-nonachlor exposure and developmental effects.

### 2.2.1.8 Cancer Effects

In a population-based, case-control study, Colt et al. (2006) examined non-Hodgkin's lymphoma (NHL) risk and use of insecticides in the home and garden. The study included 1,321 NHL cases and 1,057 controls from four areas of the country (Iowa, Los Angeles county, Detroit, and Seattle). Study subjects were given a questionnaire regarding the use of insecticides for eight specific types of pests including termites. Termite treatment was associated with a "modest", but not significant elevated risk (OR=1.3; 95% CI=1.0–1.6) for NHL in all areas except Seattle; and only if treatments were before 1988, when the use of chlordane for termite treatment was banned. Insecticide levels were measured in dust taken from used vacuum cleaner bags (682 cases and 513 controls). A significant trend for NHL was noted for increased levels of  $\alpha$ -chlordane residues in dust ( $p_{\text{trend}} = 0.04$ ), and a marginally significant trend was noted for increased levels of  $\gamma$ -chlordane ( $p_{\text{trend}} = 0.06$ ).

Mills and Yang (2005) performed a registry-based, case-control study of breast cancer in farm labor-union members in California (128 breast cancer cases diagnosed in 1988–2001 and 640 cancer-free controls matched by age and ethnicity). Using available records of pesticide applications between 1970 and 1999, exposures to selected pesticides—including chlordane—were estimated as no exposure, low

exposure, or high exposure. For chlordane, a significantly increased risk of breast cancer (OR=3.85; 95% CI=1.22–12.20) was noted in the high-use (compared with no use) breast cancer cases diagnosed between 1988 and 1994. No significant increased risk was seen in breast cancer cases diagnosed between 1995 and 2001. These results may reflect patterns of chlordane use, given that the pesticide was phased out in the 1980s.

Purdue et al. (2006) investigated relationships between cancer incidence and organochlorine insecticide use among pesticide applicators enrolled in the Agricultural Health Study of licensed applicators in Iowa and North Carolina between 1993 and 1997. Information on “ever use” (having ever used) of selected organochlorine pesticides—including chlordane—was collected from self-administered questionnaires at the time of enrollment. A total of 51,011 of the enrolled pesticide applicators reported “ever use” of the selected organochlorine pesticides; 7,244 of these pesticide applicators reported every use of chlordane. Through December 2002, among the chlordane-exposed subjects, 33 cases of rectal cancer had been diagnosed. Among the pesticide applicators with no reported chlordane use (n=43,767), 42 rectal cancer cases had been diagnosed. The study authors reported a significantly increased risk of rectal cancer for “ever use” of chlordane ( $\text{rr}=1.7$ ; 95% CI=1.0–2.8). However, they found no significant associations between “ever use” of chlordane and other cancers (prostate, lung, colon, bladder, non-Hodgkin’s lymphoma, leukemia, and melanoma) or all cancers combined.

## **2.2.2 Oral Exposure**

### **2.2.2.1 Death**

In a neurobehavioral screening study that employed female F344 rats, all rats died that during the course of a 14-day dosing period were repeatedly dosed with 52 or 156 mg chlordane/kg/day (Moser et al. 1995).

### 2.2.2.2 Systemic Effects

**Hematological Effects.** In another 90-day feeding study, observable and significant dose-related negative trends occurred in male Sprague-Dawley rats exposed to 0, 5, 13, or 50 ppm (0.25, 0.65, or 2.5 mg/kg/day) *trans*-nonachlor in food (Bondy et al. 2004). Negative trends included albumin/globulin ratio (A/G), blood urea nitrogen (BUN), calcium (Ca), chloride (Cl), phosphorus (PO<sub>4</sub>) triglycerides (TG), and thyroxine uptake (TU). In addition, a significant, dose-related positive trend of increased circulated erythrocytes, elevated total blood hemoglobin, mean corpuscular hemoglobin, and hematocrit were also observed. These significant, dose-related trends were not observed in female rats administered the same doses of *trans*-nonachlor. Significant, dose-related negative trends in alanine aminotransferase (ALT), A/G, and Cl, were observed for females Sprague-Dawley rats administered 0.25-2.5 mg/kg/day *trans*-nonachlor. A significant positive trend in the presence of thyroxine and PO<sub>4</sub> was observed in the same group of female rats administered 0.025-2.5 mg/kg/day.

**Musculoskeletal Effects.** In 115 men from the general Swedish male population, persistent organochlorine serum concentrations, including oxychlordanes and *trans*-nonachlor, were not associated with bone mineral density (Glynn et al. 2000)

**Hepatic Effects.** In a 90-day feeding study (Bondy et al. 2004), significant, dose-related positive trends in microsomal protein levels, P450 levels, benzyloxyresorufin, and BFC dealkylase activity were observed for male Sprague-Dawley rats exposed to 0, 5, 13, or 50 ppm in food (0.25, 0.65, 2.5 mg/kg/day) *trans*-nonachlor. Significant, dose-related positive trends in microsomal protein levels, aminopyrine, and BFC dealkylase activity were observed for female Sprague-Dawley rats administered 0.25-2.5 mg/kg/day *trans*-nonachlor in the same study. In female rats at all administered doses, ethoxyresorufin and BFC dealkylase activities were both elevated. Male and female rats had a significant, dose-related positive trend of hypertrophy of zone 3 or zones 2 and 3 hepatocytes with

increasing *trans*-nonachlor doses. For both male and female rats, these changes were significantly different from controls at 2.5 mg/kg/day *trans*-nonachlor. In male and female rats, *trans*-nonachlor and oxychlordane accumulated equally in the kidneys and liver, though the concentration of *trans*-nonachlor was about 2.8-fold higher than that of oxychlordane in adipose tissue.

Bondy et al. (2000) observed significantly increased mean absolute and relative liver weights in male (73 and 87%, respectively) and female (59 and 70%, respectively) rats administered technical chlordane by daily gavage at 25 mg/kg/day for 28 days. Significantly increased relative, but not absolute, liver weight (13% higher than controls) was also noted in male, but not female, rats of the 2.5 mg/kg/day dose group. Bondy and colleagues observed no significant effects on liver weight at the low dose (0.25 mg/kg/day). Histopathological examinations of livers revealed treatment-related effects at the 25 mg/kg/day dose level that included significant incidences of hypertrophy and changes in the appearance of cytoplasm of each male and female rat (7/7 of each sex, no incidences in controls) and anisokaryosis in female rats (7/7 vs. 0/7 in controls). These effects are considered to represent an adaptive response associated with increased microsomal enzyme activity.

Malarkey et al. (1995) reported chlordane-induced hepatocellular centrilobular hypertrophy, frequent micronucleate hepatocytes, and hepatoproliferative lesions composed predominantly of acidophilic hepatocytes in nearly 100% of male B6C3F1 and B6D2F1 mice administered technical chlordane in the diet at 55 ppm continuously for up to a lifetime (estimated intake of 9.4 mg chlordane/kg/day).

Centrilobular hypertrophy was detected within 50 days after the initiation of treatment, persisted in virtually all treated mice, and declined in prevalence and severity as tumor development progressed.

Barrass et al. (1993) reported chlordane-induced hepatocellular hypertrophy in male C57B1/10J mice that received chlordane in the diet at a concentration of 50 ppm for up to 2 years (estimated intake of 8.6 mg chlordane/kg/day).

**Renal Effects.** Bondy et al. (2000) also observed significantly increased mean-absolute, but not relative, kidney weight in male, but not female, rats administered technical chlordane by gavage at 25 mg/kg/day and *cis*-nonachlor by gavage at  $\geq 2.5$  mg/kg/day for 28 days. In the serum of male rats exposed to 25 mg/kg/day, clinical chemistry revealed significantly increased blood urea nitrogen (BUN) and significantly decreased creatine kinase. All male rats in this group also exhibited histopathologic kidney lesions consisting of various degrees of hyperplasia and sloughing of epithelial cells in tubule segments and proteinaceous material or cell debris in tubule luminae. Control rats did not exhibit these lesions. A later study found that in male and female rats, *trans*-nonachlor and oxychlordane accumulated equally in the kidneys and liver, though the concentration of *trans*-nonachlor was about 2.8-fold higher than that of oxychlordane in adipose tissue a doses of 0.25, 0.65, 2.5 mg/kg/day in food during a 90-day study (Bondy et al. 2004).

**Endocrine Effects.** Everett and Matheson (2010) used the National Health and Nutrition Examination Survey (NHANES), 1999–2004 to evaluate the associations of total diabetes and prediabetes (glycohemoglobin 5.7-6.4%) with eight pesticide and pesticide metabolites, including oxychlordane (a metabolite of chlordane), *trans*-nonachlor (a major component of technical chlordane), and heptachlor epoxide (a metabolite of heptachlor, a component of technical chlordane). In separate adjusted logistic regressions, oxychlordane (age-adjusted odds ratio [OR] = 2.9; 95% confidence interval [CI] = 1.78-4.71), *trans*-nonachlor (OR=2.36; 95% CI= 1.48-3.76), and heptachlor epoxide (OR=2.09; 95% CI = 1.46-3.00) were associated with total diabetes. In a combined logistic regression oxychlordane (OR = 1.90; 95% CI = 1.09-3.32) and heptachlor epoxide (OR= 1.70; 95 % CI = 1.16-2.49) were associated with total diabetes. Heptachlor epoxide was associated with prediabetes in both the separate (OR=1.45, 95% CI =1.04-2.01) and combined (OR=1.40; 95% CI=1.00-1.95) models.

Lee et al. (2010) reported a nonlinear association between type 2 diabetes and serum levels of both *trans*-nonachlor and oxychlordan in a nested case-control study that included 90 cases and 90 controls enrolled in a Coronary Artery Risk Development in Young Adults (CARDIA) cohort.

Montgomery et al. (2008) reported an increased risk of diabetes (OR=1.25; 95% CI=1.09–1.43) among chlordan-using licensed pesticide applicators enrolled in an Agricultural Health Study between 1993 and 2003. The study included assessments for other pesticides as well, including six other organochlorine insecticides (aldrin, DDT, dieldrin, heptachlor, lindane, and toxaphene). Among those who self-reported ever using chlordan were 372 diabetics and 7,365 nondiabetics.

In a study that included 1,303 Mexican Americans 20–74 years of age from the Hispanic Health and Nutrition Examination Survey, 1982–1984, Cox et al. (2007) reported significant associations between self-reported diabetes and serum levels of both *trans*-nonachlor and oxychlordan.

Nagayama et al. (2007) reported approximately 2-fold higher concentrations of selected organochlorine substances (PCBs, dioxin-like compounds, DDT, hexachlorocyclohexanes, chlordan, and hexachlorobenzene) in the breast milk of Japanese mothers who gave birth to neonates with cretinism (n=22) compared with a group of 102 mothers who gave birth to normal neonates. After adjustments for parity and mother's age, calculated ORs yielding significant results were 22 for hexachlorobenzene, 10 for DDT, 6.6 for chlordan, and 2.8 for hexachlorocyclohexanes. Using these results, the study authors suggested that such compounds may play a role in cretinism.

Significant dose-related changes of the epithelial in small, medium, and large follicles of the thyroid were observed for male and female and Sprague-Dawley rats administered 0, 5, 13, or 50ppm *trans*-nonachlor in a 90-day feeding study (Bondy et al. 2004). Additionally, male rats administered 5–50 ppm *trans*-

nonachlor had significant dose-related cytoplasmic vacuolation in small to medium follicles of the thyroid.

### **2.2.2.3 Immunological Effects**

Tryphonas et al. (2003) administered technical chlordane, *trans*-nonachlor, or *cis*-nonachlor to male and female Sprague-Dawley rats by gavage at doses of 0, 0.25, 2.5, or 25 mg/kg/day for 28 days and assessed immune system treatment effects. Significantly increased serum IgM was observed in high-dose female rats. In addition, both the *trans*- and *cis*-nonachlor treated groups exhibited more pronounced immunological effects than did those treated with technical chlordane.

### **2.2.2.4 Neurological Effects**

Single-dose oral administration of chlordane to groups of female, F344 rats (8/group) resulted in significantly increased excitability at  $\geq 156$  mg/kg (doses ranged from 16 – 291 mg/kg) (Moser et al. 1995). Significantly increased grip strength was noted at 291 mg/kg. Clonic-tonic convulsions were also observed in some of the rats in this group. Moser and colleagues also observed significant effects following repeated oral dosing (5–156 mg/kg/day for up to 14 days). Effects included decreased motor activity after 4 days at 156 mg/kg/day, increased excitability after 9 days at 156 mg/kg/day and 4 days at 52 mg/kg/day, increased urination after 14 days at 16 mg/kg/day, and increased touch response after 4 days at 156 mg/kg/day.

### **2.2.2.5 Reproductive Effects**

To investigate a possible erectile dysfunction association, Polsky et al. (2007) assessed exposure in 335 males to individual PCB congeners and chlorinated pesticides. Polsky and colleagues measured plasma

levels of these compounds in the 335 males who visited a group of five urologists for various conditions from 1997 through 1999 in Kingston, Canada. No participant had a history of prostate cancer nor had an abnormal serum prostate-specific antigen measurement and digital rectal exam within 1 year of enrollment. Oxychlordan (OR = 0.47, 95% CI 0.23-0.96) and *trans*-nonachlor (OR = 0.47, 95% CI 0.23-0.95) were associated with a reduced risk of erectile dysfunction, but the authors could not rule out the role of chance in these findings. Results did not support an association between exposure to PCB congeners, chlorinated pesticides, and erectile dysfunction.

Al-Omar et al. (2000) administered commercial chlordan (75% active ingredient) to groups of male BALB-C mice (10 per group) by gavage at doses of 0, 75, or 275 mg/kg/day for 35 days and assessed treatment-related effects on reproductive tissues. During treatment weeks 3–5, Al-Omar and colleagues observed significantly increased mean body weight gain in both groups, relative to controls. Significantly decreased mean testicular weight was observed in both groups beginning at treatment week 3, and by week 5 mean testicular weight was more than 20% lower than controls. Results of histopathologic examinations for treatment weeks 2–5, at both dose levels, revealed treatment-related, significant decreases in mean diameter of seminiferous tubules and numbers of Sertoli cells, spermatogonia, primary and secondary spermatocytes, and spermatids.

#### **2.2.2.6 Developmental Effects**

Trabert et al. (2012) assessed the association between exposure *in utero* to chlordan and cryptorchidism and hypospadias. Levels of *trans*-chlordan and oxychlordan were measured among pregnant women enrolled in the Collaborative Perinatal Project (CPP) from 1959 to 1965 who delivered sons with cryptorchidism or hypospadias and sons without either condition. Results did not support an association between chlordan levels and cryptorchidism and hypospadias (*p*-trend all >0.45).

Gladen et al. (2003) assessed whether weight at birth is associated with prenatal exposure to persistent organochlorine compounds, including *trans*-nonachlor and oxychlordane. From 1993 to 1994, organochlorine compounds were measured in breast milk 4–5 days after birth and were used as the index for prenatal exposure for 197 singleton infants selected from the at-large population in two Ukrainian cities. Infants within the upper tertile of oxychlordane (82 ng/g milk fat) and *trans*-nonachlor (73 ng/g milk fat) had slightly smaller, though statistically insignificant, mean birthweights compared with the lower tertile. Seven of eight preterm infants were in the upper oxychlordane tertile. But the small number of preterm births in this study prevented the authors from drawing any conclusions. The authors reported that prenatal exposure to the concentrations of chemicals studied did not affect weight at birth.

Narotsky and Kavlock (1995) administered technical chlordane to groups of timed-pregnant Fischer 344 rats (19–23/group) by gavage on gestation days 6–19 at doses of 0, 21, or 28 mg/kg/day and assessed maternal and developmental effects. Both chlordane groups exhibited initial maternal weight loss (gestation days 6–8) and significantly depressed gestational weight gain (gestation days 6–20; approximately 30 and 55%, respectively, less than controls). No clinical signs of maternal toxicity were reported. No significant, treatment-related effects appeared in numbers of implants, resorptions, or live litters at birth. Both chlordane groups exhibited significantly decreased mean numbers of live pups at 6 days postpartum (5.2 and 1.5 pups/litter for the 21 and 28 mg/kg/day groups, respectively, compared with 7.9 pups/litter in controls). No gross signs of treatment-related malformations were observed.

Cassidy et al. (1994) assessed the pre- and postnatal effects of technical chlordane in Sprague-Dawley rats. The study included oral administration of chlordane to groups of pregnant rats (5/group) from gestation day 4 throughout gestation, parturition, and lactation at doses of 0, 0.1, 0.5, or 5.0 mg/kg/day and oral dosing of the offspring on postnatal days 22–80. In tests conducted between postnatal days 77 and 85, the chlordane-exposed offspring exhibited sex- and dose-related effects on testosterone levels, selected behavioral tests of spatial abilities, and body weight. Female, but not male, offspring exhibited

significant increases in body weight, decreases in testosterone levels, improved spatial abilities, and increases in auditory startle-evoked responses. Chlordane-exposed male rats exhibited significant increases in male-typical mating behaviors and decreases in Cl<sup>-</sup> uptake in brain microsacs. Male rats did not show a significant decrease in testosterone levels at any dose, though a 10% decrease in testosterone was observed in male rats doses with 5.0 mg/kg/day. The authors interpreted these results as indicative of chlordane-induced masculinization of sexually dimorphic functions and behaviors by mimicking sex steroids, by limiting their levels, or both.

Blyler et al. (1994) administered analytical grade chlordane to groups of pregnant BALB/c mice (number per group not specified) at doses of 0 or 80 mg/kg/day on gestation days 1–18. Myeloid hemopoietic activity of bone marrow cells from 6-week-old offspring was evaluated for *in vitro* colony-forming units-in-culture in response to exogenously added recombinant forms of the cytokines granulocyte/macrophage-colony stimulating factor (CSF), macrophage-CSF, and interleukin 3 (IL-3). Female, but not male, offspring exhibited a significant depression of the numbers of bone marrow colony forming units-granulocyte/macrophage (CFU-GM), CFU-IL-3, and CFU-M. Chlordane treatment did not significantly affect the number of recoverable, viable bone marrow cells in male or female offspring.

#### **2.2.2.8 Cancer Effects**

A number of case-control studies examined possible associations between risk of selected cancer endpoints and levels of chlordane or chlordane-related substances such as *cis*- and *trans*-nonachlor (major components of technical chlordane) or oxychlordane (a metabolite of chlordane) in plasma or serum samples (Table 2-1) or in adipose tissue (Table 2-2). Because the study populations were not selected to be representative of occupational exposure, these studies are summarized under oral exposure; the assumption was that the diet was the major source of blood or adipose tissue levels.

Several case-control studies found no significant associations between risk of breast cancer and plasma or serum levels of chlordane or chlordane-related compounds (Table 2-1) (Demers et al. 2000; Gammon et al. 2002; Ward et al. 2000; Wolff et al. 2000).

McGlynn et al. (2008) found significant associations between risk of testicular germ cell tumors and serum levels of *cis*-nonachlor, *trans*-nonachlor, and total chlordanes. Similar analysis for seminoma (i.e., testicular tumors arising from sperm-forming tissues) revealed significant associations between seminoma and levels of *cis*-nonachlor, *trans*-nonachlor, oxychlordanes, and total chlordanes. Cook et al. (2011) also found significant associations between exposure to p,p'-DDE, *cis*-nonachlor and *trans*-nonachlor with testicular germ-cell tumors. Hardell et al. (2003) reported significant association between risk of testicular cancer and lipid-adjusted plasma *cis*-nonachlor levels. Hardell et al. (2003) also found significant associations between risk of testicular cancer and plasma levels of *trans*-nonachlor and *cis*-nonachlor in the serum of mothers of the testicular cancer cases. Assessment according to testicular tumor type resulted in significant associations between risk of seminoma and maternal plasma *cis*-chlordanes levels and between risk of nonseminoma and maternal plasma *trans*- and *cis*-nonachlor levels.

**Table 2-1. Selected Results from Case-Control Studies in which Possible Associations Between Risk of Selected Cancer Endpoints and Blood Levels of Chlordane or Chlordane-Associated Compounds Were Assessed**

Study group	Compound	Serum/plasma levels in ng/g lipid	Result	Reference
<b>Breast cancer</b>				
586 cases, 390 controls	Chlordane	<62.47 (Q1 <sup>a</sup> ) to ≥473.08 (Q5)	No significant association	Gammon et al. 2002
150 cases, 150 controls	Oxychlordanes	10.9 (cases), 10.1 (controls) <sup>a</sup>	No significant association	Ward et al. 2000
	<i>trans</i> -Nonachlor	11.7 (cases), 10.4 (controls) <sup>a</sup>	No significant association	
315 cases, 219 hospital- and 307 population-based controls	Oxychlordanes	<8.4 (Q1 <sup>a</sup> ) to ≥16.3 (Q5)	No significant association	Demers et al. 2000
	<i>trans</i> -Nonachlor	<10.6 (Q1) to ≥20.7 (Q5)	No significant association	

**Table 2-1. Selected Results from Case-Control Studies in which Possible Associations Between Risk of Selected Cancer Endpoints and Blood Levels of Chlordane or Chlordane-Associated Compounds Were Assessed**

Study group	Compound	Serum/plasma levels in ng/g lipid	Result	Reference
175 cases, 355 controls	<i>trans</i> -Nonachlor	≤25 (T1) to ≥693 (T3)	No significant association	Wolff et al. 2000
<b><u>Endometrial Cancer</u></b>				
154 cases, 205 controls	Oxychlordane	16.6 (cases), 14.3 (controls) <sup>b</sup>	No significant association	Weiderpass et al. 2000
	<i>trans</i> -Nonachlor	27.4 (cases), 25.1 (controls) <sup>b</sup>	No significant association	
<b><u>Testicular cancer</u></b>				
All testicular cancer (754 cases, 928 controls)	<i>trans</i> -Nonachlor	≤2.18 (Q1) to >3.86 (Q4)	RR=1.46; 95% CI=1.07–2.00 (Q1 vs. Q4)	McGlynn et al. 2008
	<i>cis</i> -Nonachlor	≤10.5 (Q1) to >24.5 (Q4)	RR=1.56; 95% CI=1.11–2.18 (Q1 vs. Q4)	
	Oxychlordane	≤8.05 (Q1) to >17.1 (Q4)	No significant association	
Seminoma cases only <sup>c</sup> (313 cases, 913 controls)	Total chlordanes	Not stated	RR=1.51; 95% CI=1.09–2.10 (Q1 vs. Q4)	
	<i>trans</i> -Nonachlor	≤2.18 (Q1) to >3.86 (Q4)	RR=1.72; 95% CI=1.11–2.67 (Q1 vs. Q4)	
	<i>cis</i> -Nonachlor	≤10.5 (Q1) to >24.5 (Q4)	RR=1.93; 95% CI=1.27–2.93 (Q1 vs. Q4)	
	Oxychlordane	≤8.05 (Q1) to >17.1 (Q4)	RR=1.64; 95% CI=1.04–2.60 (Q1 vs. Q4)	
	Total chlordanes	Not given	RR=1.90; 95% CI=1.20–3.00	

**Table 2-1. Selected Results from Case-Control Studies in which Possible Associations Between Risk of Selected Cancer Endpoints and Blood Levels of Chlordane or Chlordane-Associated Compounds Were Assessed**

Study group	Compound	Serum/plasma levels in ng/g lipid	Result	Reference
All testicular cancer (58 cases, 61 controls)	<i>cis</i> -chlordane	0.1–4.6 (cases), 0.2–2.6 (controls)	No significant association	Hardell et al. 2003
	<i>trans</i> -Nonachlor	1.6–28 (cases), 0.9–26 (controls)	No significant association	
	<i>cis</i> -Nonachlor	0.4–7.6 (cases), 0.3–7.8 (controls)	OR=2.6; 95% CI=1.2–5.7 <sup>d</sup>	
	Oxychlordane	0.9–33 (cases), 2.0–32 (controls)	No significant association	
	Sum of chlordanes	8.0–72 (cases), 8.2–70 (controls)	OR=1.3; 95% CI=0.6–2.8 <sup>d</sup>	
Seminoma cases only <sup>c</sup>	<i>cis</i> -Nonachlor	Not stated	OR=4.8; 95% CI=1.4–16 <sup>d,e</sup>	
All testicular cancer based on plasma levels of mothers of cases	<i>cis</i> -chlordane	0.2–7.9 (cases), 0.2–1.5 (controls)	No significant association	
	<i>trans</i> -Nonachlor	2.4–64 (cases), 0.6–42 (controls)	OR=4.1 95% CI=1.5–11 <sup>f</sup>	
	<i>cis</i> -Nonachlor	0.4–9.2 (cases), 0.4–2.8 (controls)	OR=3.1; 95% CI=1.2–7.8 <sup>f</sup>	
	Oxychlordane	1.9–50 (cases), 1.4–32 (controls)	No significant association	
	Sum of chlordanes	14–131 (cases), 5.8–76 (controls)	No significant association	
Seminoma cases only	<i>cis</i> -chlordane	Not given	OR=4.3; 95% CI=1.1–17 <sup>f,g</sup>	
Nonseminoma cases only	<i>trans</i> -Nonachlor	Not given	OR=5.6; 95% CI=1.7–19 <sup>f,g</sup>	
	<i>cis</i> -Nonachlor	Not given	OR=2.8; 95% CI=1.01–7.8 <sup>f,g</sup>	

**Table 2-1. Selected Results from Case-Control Studies in which Possible Associations Between Risk of Selected Cancer Endpoints and Blood Levels of Chlordane or Chlordane-Associated Compounds Were Assessed**

Study group	Compound	Serum/plasma levels in ng/g lipid	Result	Reference
<b>Non-Hodgkin's lymphoma</b>				
422 cases, 460 controls	Oxychlordane	≤6.07 (Q1) to >13.7 (Q4)	OR=2.68; 95% CI=1.69–4.24	Spinelli et al. 2007
	<i>trans</i> -Nonachlor	≤8.97 (Q1) to >20.83 (Q4)	OR=1.70; 95% CI=1.11–2.60	
74 cases, 147 controls	Oxychlordane	≤86.5 (Q1) to ≥181.3 (Q4)	No significant association	Cantor et al. 2003
	<i>trans</i> -Nonachlor	≤53.8(Q1) to ≥109.8 (Q4)	No significant association	

<sup>a</sup>Quintile

<sup>b</sup>Mean serum concentrations, ranges for quartiles not specified.

<sup>c</sup>No significant associations between risk of nonseminoma and serum levels of any of the chlordane-related compounds.

<sup>d</sup>ORs calculated by comparing cases and controls with plasma levels below the control median value to cases and controls with plasma levels above the control median value.

<sup>e</sup>No significant associations between risk of seminoma and serum levels of other chlordane-related compounds or risk of nonseminoma and serum levels of any of the chlordane-related compounds.

<sup>f</sup>ORs calculated by comparing cases and controls whose mothers had plasma levels below the median value to cases and controls whose mothers had plasma levels above the control median value.

<sup>g</sup>No significant associations between risk of seminoma or nonseminoma and serum levels of other chlordane-related compounds.

**Table 2-2. Selected Results from Case-Control Studies in which Possible Associations Between Risk of Selected Cancer Endpoints and Levels of Chlordane or Chlordane-Associated Compounds in Adipose Tissues were Assessed**

Study group	Compound	Adipose tissue levels in ng/g lipid	Result	Reference
<b>Prostate Cancer</b>				
58 Prostate cancer cases, 20 controls	<i>trans</i> -chlordane	0.06–1.2 (cases), 0.11–0.84 (controls)	OR=3.49; 95% CI=1.08–11.2 <sup>a</sup>	Hardell et al. 2006
	Oxychlordane	5.9–72 (cases), 6.9–73 (controls)	No significant association	
	<i>trans</i> -Nonachlor	4.7–131 (cases), 16–110 (controls)	No significant association	
	<i>cis</i> -Nonachlor	0.57–13 (cases), 0.97–14 (controls)	No significant association	
	Sum of chlordanes	21–234 (cases), 29–192 (controls)	No significant association	
54 Prostate cancer cases, 99 controls	<i>Trans</i> -chlordane	≤ 25 (Q1)	No significant association	Ritchie et al. 2003
		26–43 (Q2)	No significant association	
		>43 (Q3)	No significant association	
	Oxychlordane	≤25 (Q1)	No significant association	
		25–32 (Q2)	OR=3.11; Wald CI=1.27–7.63	
		>32 (Q3)	No significant association	
<b>Non-Hodgkin's lymphoma</b>				
175 non-Hodgkin's lymphoma cases, 481 controls	Oxychlordane	≤90 (T1) to >150 (T3) <sup>b</sup>	OR=1.79; 95% CI=1.04–3.08	Quintana et al. 2004
	<i>trans</i> -Nonachlor	≤150 and >150 <sup>b</sup>	No significant association	
27 non-Hodgkin's lymphoma cases, 17 controls	<i>cis</i> -chlordane	0.3–4.2 (cases), 0.2–1.0 (controls)	No significant association	Hardell et al. 1996
	<i>trans</i> -Nonachlor	24.9–389 (cases), 16.3–88.2 (controls)	OR=4.1; 95% CI=1.1–15 <sup>c</sup>	
	<i>cis</i> -Nonachlor	4.1–68.3 (cases), 1.7–13.6 (controls)	No significant association	
	Oxychlordane	8.5–144 (cases), 8.9–49 controls)	No significant association	

**Table 2-2. Selected Results from Case-Control Studies in which Possible Associations Between Risk of Selected Cancer Endpoints and Levels of Chlordane or Chlordane-Associated Compounds in Adipose Tissues were Assessed**

Study group	Compound	Adipose tissue levels in ng/g lipid	Result	Reference
<b><u>Pancreatic Cancer</u></b>				
21 Pancreatic cancer cases, 59 controls	<i>trans</i> -chlordane	0.26–5.4 (cases), 0.08–1.2 (controls)	OR=6.49; 95% CI=1.47–28.7 <sup>a</sup>	Hardell et al. 2007
	Oxychlordane	3.8–41 (cases), 3.0–73 (controls)	OR=4.78; 95% CI=1.13–20.3 <sup>a</sup>	
	<i>Trans</i> -Nonachlor	20–407 (cases), 7.3–110 (controls)	OR=18.2; 95% CI=2.67–124 <sup>a</sup>	
	<i>cis</i> -Nonachlor	0.70–27 (cases), 0.21–14 (controls)	OR=8.75; 95% CI=1.81–42.2 <sup>a</sup>	
	Sum of chlordanes	38–443 (cases), 13–192 (controls)	OR=18.4; 95% CI=2.71–124 <sup>a</sup>	

<sup>a</sup>ORs calculated by comparing cases and controls with adipose tissue levels below the control median value to cases

Spinelli et al. (2007) reported significant associations between risk of non-Hodgkin's lymphoma and lipid-adjusted plasma levels of oxychlordane and *trans*-nonachlor in a population-based case-control study involving 422 non-Hodgkin's lymphoma cases and 460 control subjects. In contrast, Cantor et al. (2003) found no significant association between risk of non-Hodgkin's lymphoma and serum levels of *trans*-nonachlor, oxychlordane, or the sum of chlordane-related compounds among 74 non-Hodgkin's lymphoma cases and 174 matched control subjects for which prediagnostic, lipid-adjusted serum chlordane and chlordane residue levels were available.

Table 2-2 summarizes selected results from case-control studies in which possible associations were assessed between risk of selected cancer endpoints and levels of chlordane or chlordane residues in adipose tissues. Quintana et al. (2004) reported a significant association between risk of non-Hodgkin's lymphoma and levels of oxychlordane in adipose tissue samples collected from cadavers and surgical patients within the U.S. EPA National Human Adipose Tissue Survey. Hardell et al. (2006) reported a

significant association between risk of prostate cancer and *trans*-chlordane in adipose tissue. Hardell and colleagues also found a significant association for those prostate cancer cases with prostate-specific antigen (PSA) levels >10 ng/mL. Hardell et al. (2007) reported significant associations between risk of pancreatic cancer and adipose tissue levels of *trans*-chlordane, oxychlordane, *trans*-nonachlor, *cis*-nonachlor, and their sum. Hardell et al. (1996) reported a significant association between risk of non-Hodgkin's lymphoma and *trans*-nonachlor level in adipose tissue. This study also found significantly increased mean concentrations of *trans*-nonachlor, *cis*-nonachlor, and oxychlordane in adipose tissues from non-Hodgkin's lymphoma patients versus controls.

Barrass et al. (1993) reported approximately 50% incidence of hepatocellular tumors among male C57B1/10J mice that had received chlordane in the diet at a concentration of 50 ppm for 2 years (estimated intake of 8.6 mg chlordane/kg/day); hepatic tumor incidence among 400 control mice at the same research facility was approximately 2%. Malarkey et al. (1995) reported 100% incidences of hepatocellular adenomas in groups of male B6C3F1 mice (10 or 20 per group) administered technical chlordane at 55 ppm in the diet for periods of 513–568 days (estimated intake of 9.4 mg chlordane/kg/day). Hepatocellular carcinomas during the same time period were noted in 80–100% of the chlordane-treated mice. Incidences of hepatocellular adenomas and carcinomas in a group of untreated controls at 759 days were 7/43 (16%) and 3/43 (7%), respectively. Results of similar exposure of male B6D2F1 mice indicated that male B6C3F1 mice are more sensitive than are male B6D2F1 mice.

Barrass et al. (1993) found no macroscopic evidence of chlordane-induced thyroid tumor development in groups of male C57B1/10J mice that had received chlordane in the diet at a concentration of 50 ppm for 2 years (estimated intake of 8.6 mg chlordane/kg/day).

## 2.3 TOXICOKINETICS

### 2.3.2 Distribution

Human data include reports of chlordane residues in blood, adipose tissue, and cord blood (Brock et al. 1998; Glynn et al. 2000; Kang et al. 2008; Rhainds et al. 1999; Tanabe et al. 1993), and adipose tissue and brain and liver autopsy samples (Dewailly et al. 1999).

#### 2.3.2.1 Inhalation Exposure

Asakawa et al. (1996) exposed groups of female ddY mice to airborne technical chlordane continuously for at least 1 month and up to approximately 6 months. Asakawa and colleagues then assessed levels of chlordane residues in adipose tissue samples at various intervals. Two groups of control mice without chlordane exposure were included in the study. Mean measured concentrations of five major components of technical chlordane ranged from 4.22 to 11.36  $\mu\text{g}/\text{m}^3$  and included *trans*- and *cis*-chlordane (38 and 31%, respectively, of the total chlordanes), *trans*- and *cis*-nonachlor (14 and 2%, respectively), and heptachlor (15%). During the exposure period total chlordane concentrations in adipose tissues ranged from 4.19 to 10.63 ppm. At all time-points, heptachlor and *trans*-chlordane levels were below the detection limit. *Trans*-nonachlor (concentrations ranging from 2.09 to 4.79 ppm) accounted for approximately 50% of the chlordane residues in the adipose tissue samples. Oxychlordane and heptachlorepoide were the other major chlordane residues detected, accounting for approximately 25 and 22 %, respectively, of the total chlordane residues. The proportion of *trans*-nonachlor tended to decrease with increasing exposure time, whereas that of oxychlordane tended to increase.

### 2.3.2.2 Oral Exposure

(Bondy et al. 2000) observed dose-related increasing concentrations of oxychlordane, *cis*-nonachlor, *trans*-nonachlor, heptachlor, and *trans*-chlordane in adipose tissue of male and female rats administered technical chlordane by gavage at doses ranging from 0.25 to 25 mg/kg/day for 28 days. Oxychlordane and *trans*-nonachlor represented the majority of chlordane residues in adipose tissues and levels of these residues were >2-fold higher in dosed female rats compared with similarly dosed male rats.

### 2.3.4 Excretion

Numerous studies include reports of chlordane residues such as oxychlordane, *trans*-nonachlor, *cis*-nonachlor, *trans*-chlordane, and *cis*-chlordane in the breast milk of nursing mothers in North America, Europe, Asia, and Australia (Erdoğrul et al. 2004; Gladen et al. 1999; Johansen et al. 1994; Konishi et al. 2001; Kunisue et al. 2004a, 2004b; Mes 1994; Mes et al. 1993; Minh et al. 2004; Nakagawa et al. 1999; Newsome et al. 1995; Shen et al. 2008; Stevens et al. 1993; Sudaryanto et al. 2006). Concentrations of individual chlordane-related compounds and total chlordanes were within a range of nondetectable to as high as 26 ng/g lipid.

### 2.3.5 Mechanisms of Action

Gauthier and Girard (2001) found that chlordane-induced neutrophil superoxide production in human neutrophils in a concentration-related manner occurred similarly to that induced by the known neutrophil-agonist, phorbol 12-myristate 13-acetate. Chlordane was further shown to enhance significantly neutrophil phagocytosis of sheep red blood cells without altering chemotaxis and apoptosis. Evidence that chlordane-induced superoxide production might involve protein kinase C-dependent mechanisms included findings that staurosporine and calphostin C (transduction signal inhibitors) inhibited the effect of chlordane on superoxide production.

Bagchi and coworkers (Bagchi et al. 1995; Stohs et al. 1997) examined the effects of chlordane on the production of hepatic and brain lipid peroxidation and DNA single-strand breaks (indices of oxidative stress and oxidative tissue damage) in female rats administered two 0.25 LD<sub>50</sub> gavage doses of chlordane 21 hours apart and sacrificed 3 hours later. Chlordane treatment resulted in approximately 3- and 2-fold increases in lipid peroxidation in liver and brain, respectively, and approximately 4- and 1.8-fold increases in single-strand breaks in liver and brain, respectively. The investigators also assessed chlordane-induced changes in the release of lactate dehydrogenase (a measure of cellular damage and cytotoxicity) and DNA single-strand breaks from cultured neuroactive PC-12 cultures. Increases in both releases of lactate dehydrogenase and DNA single strand breaks were observed. The *in vivo* and *in vitro* results support the notion of chlordane-induced generation of reactive oxygen species.

Miyagi et al. (1998) examined the effect of chlordane on chemotaxis of monkey neutrophils and monocytes *in vitro*. Chlordane was found to inhibit chemotaxis of neutrophils and monocytes toward interleukin-8 and RANTES (chemokines), respectively, suggesting that chlordane might alter leukocyte-related immune functions. Rought et al. (1999) demonstrated the ability of chlordane to reduce retinoblastoma tumor-suppressor gene expression in CEM x 174 cells (a hybrid of human T and B lymphocytes). These results suggest that chlordane is capable of down-regulating retinoblastoma expression at the post-transcriptional level. The authors indicated that such a mechanism could be involved in chlordane's immune-modulatory and tumor-promoting effects.

Lack of DNA adduct formation in male and female mice administered chlordane by single gavage dose at 50 mg/kg or in the diet at 200 ppm for 2 weeks (Whysner et al. 1998) and generally negative results from previous standard genotoxicity assays suggest an epigenetic mechanism of action for chlordane hepatocarcinogenicity.

## **2.6 INTERACTIONS WITH OTHER CHEMICALS**

Al-Omar et al. (2000) assessed possible interactions between commercial chlordane (75% active ingredient) and lead oxide on testicular tissues in male BALB-C mice. As discussed in Section 2.2.2.5 (Reproductive Effects), gavage administration of commercial chlordane at 75 or 275 mg/kg/day resulted in significant effects, including decreased testicular weight, reduced diameter of seminiferous tubules, decreased numbers of spermatogonia, primary and secondary spermatocytes, and spermatids. These effects were markedly increased in mice that were co-administered lead oxide at 50 mg/kg/day; whether the combined effect was additive or represented a synergistic effect was not determined.

## **3. CHEMICAL AND PHYSICAL INFORMATION**

No updated data.

## **4. PRODUCTION, IMPORT/EXPORT, USE, AND DISPOSAL**

No updated data.

## 5. POTENTIAL FOR HUMAN EXPOSURE

### 5.3 ENVIRONMENTAL FATE

#### 5.3.2 Transformation and Degradation

##### 5.3.2.3 Sediment and Soil

Hirano et al. (2007) assessed the anaerobic biodegradation potential of *trans*- and *cis*-chlordane in samples of river sediments from the Kamogawa River in Japan during 20 weeks of anaerobic incubation in the dark at 30 °C. An initial lag period lasted approximately 4 weeks, residual ratios for *trans*- and *cis*-chlordane after 20 weeks were 67 and 88%, respectively.

### 5.4 LEVELS MONITORED OR ESTIMATED IN THE ENVIRONMENT

#### 5.4.1 Air

A number of reports are available regarding levels of chlordane compounds in the outdoor air of various regions within North America (Aulagnier and Poissant 2005; Bidleman et al. 1998; Cortes et al. 1998; Hung et al. 2002; Jantunen et al. 2000; Leone et al. 2001; Moreau-Guigon et al. 2007; Offenberg et al. 2004; Shen et al. 2005; Sun et al. 2006). Chlordane levels in sampled outdoor air were consistently <1 ng/m<sup>3</sup>. One study reported higher average air concentrations indoors than outdoors at test locations in Los Angeles County, California; Elizabeth, New Jersey; and Houston, Texas (average indoor levels of

1.98, 1.3, and 4.18 ng/m<sup>3</sup>, respectively, versus average outdoor levels of 0.58, 0.17, and 0.28 ng/m<sup>3</sup>, respectively) (Offenberg et al. 2004).

### 5.4.3 Soil

Martinez et al. (2013) conducted an urban soil study analyzing chlordane in 66 soil samples taken on August 25th, 2008 in Cedar Rapids, Iowa. Cedar rapids, Iowa experienced major flooding 70 days prior to the samples being taken; the samples were primarily taken from residential land use areas in the flooding zone downstream and west of the main urban river that flooded, Cedar River. Chlordane levels in Cedar River had not been previously identified, though chlordane was detected at high levels in an urban lake that also flooded. Chlordane samples were analyzed using a Gas Chromatography/Mass Selective Detector Mode (GC/MSD) in selected ion monitoring mode. Chlordane concentrations in soil ranged from 0-7500 ng/g dry weight (d.w), though the distribution was highly skewed (median= 4 ng/g d.w.; mean=130 ng/g d.w.) Generally, *trans*-nonachlor (median= 1.8 ng/g d.w; mean= 24.0 ng/g d.w.) was found at higher concentrations than *cis*-chlordane (median=1.0 ng/g d.w.; mean= 64.0 ng/g d.w.) and *trans*-chlordane (median=0.86 ng/g d.w.; mean=40 ng/g d.w.). No spatial correlation between the samples was found. Additionally, no significant difference was found between samples collected inside or outside the flooding area. The mean ratios for the soil samples in this study are: *cis*-chlordane:*trans*-chlordane=1.40 ± 0.48; *trans*-chlordane:*trans*-nonachlor= 2.40 ± 1.50; *cis*-chlordane:*trans*-nonachlor=0.96 ± 1.50. Given these ratios, it is likely that significant weathering of technical chlordane occurred if direct soil application is the source of the observed concentrations.

## 5.5 GENERAL POPULATION AND OCCUPATIONAL EXPOSURE

In the Fourth National Report on Human Exposures to Environmental Chemicals (CDC 2009), *trans*-nonachlor and oxychlordane levels in serum (lipid adjusted) were reported according to various age groups, sex, and race/ethnicity. Results are depicted in Tables 5-1 and 5-2.

**Table 5- 1 Geometric Means of Serum Concentrations (Lipid Adjusted) of *trans*-Nonachlor for the U.S. Population Aged 12 Years and Older<sup>a</sup>**

Geometric mean and selected percentiles of serum concentrations (in ng/g of lipid or parts per billion on a lipid-weight basis) for the U.S. population from the National Health and Nutrition Examination Survey.

	Survey years	Geometric		Selected percentiles						Sample size		
		Mean (95% conf. interval)	(95% confidence interval)									
			50th	75th	90th	95th						
<b>Total</b>	99-00	<b>18.3</b>	(16.7-20.0)	<b>17.9</b>	(16.1-20.1)	<b>31.9</b>	(28.9-36.0)	<b>55.1</b>	(48.4-62.6)	<b>79.4</b>	(67.6-88.1)	1933
	01-02	<b>17.0</b>	(15.2-18.9)	<b>17.9</b>	(15.5-20.5)	<b>33.7</b>	(30.2-37.2)	<b>56.3</b>	(49.6-66.0)	<b>78.2</b>	(64.0-113)	2286
	03-04	<b>14.7</b>	(13.1-16.5)	<b>14.8</b>	(13.5-17.0)	<b>30.2</b>	(26.7-32.5)	<b>49.0</b>	(42.6-54.7)	<b>68.3</b>	(58.6-82.3)	1955
<b>Age group</b>												
12-19 years	99-00	*		< LOD		< LOD		<b>18.8</b>	(<LOD-20.6)	<b>25.2</b>	(19.1-28.4)	664
	01-02	*		< LOD		< LOD		<b>13.4</b>	(11.8-16.4)	<b>19.2</b>	(15.2-23.5)	758
	03-04	*		< LOD		<b>8.70</b>	(<LOD-12.5)	<b>16.1</b>	(10.7-23.7)	<b>22.6</b>	(16.1-34.6)	589
20 years and older	99-00	<b>20.8</b>	(19.0-22.8)	<b>20.7</b>	(18.0-23.5)	<b>35.4</b>	(30.9-40.3)	<b>59.9</b>	(51.8-67.6)	<b>82.7</b>	(74.9-89.6)	1269
	01-02	<b>19.8</b>	(17.6-22.3)	<b>20.9</b>	(19.0-23.1)	<b>36.6</b>	(32.8-41.1)	<b>60.6</b>	(52.5-69.9)	<b>84.9</b>	(66.0-123)	1528
	03-04	<b>16.9</b>	(15.1-18.9)	<b>17.3</b>	(14.6-20.0)	<b>31.8</b>	(28.9-35.3)	<b>51.4</b>	(45.9-58.6)	<b>74.7</b>	(59.8-90.0)	1366
<b>Gender</b>												
Males	99-00	<b>17.7</b>	(16.5-19.1)	<b>17.2</b>	(14.9-20.1)	<b>30.2</b>	(27.7-34.2)	<b>51.1</b>	(47.3-58.6)	<b>78.2</b>	(60.2-88.1)	922
	01-02	<b>17.0</b>	(14.8-19.5)	<b>18.3</b>	(14.8-21.1)	<b>34.4</b>	(28.3-39.3)	<b>54.8</b>	(45.0-68.9)	<b>78.2</b>	(59.7-113)	1062
	03-04	<b>14.8</b>	(12.7-17.3)	<b>14.6</b>	(12.2-18.0)	<b>30.8</b>	(26.7-35.3)	<b>51.0</b>	(42.0-59.4)	<b>68.6</b>	(56.0-93.8)	955
Females	99-00	<b>18.8</b>	(16.7-21.1)	<b>18.4</b>	(16.1-22.2)	<b>32.9</b>	(29.0-38.3)	<b>59.0</b>	(48.4-67.6)	<b>80.8</b>	(71.5-95.5)	1011
	01-02	<b>17.0</b>	(15.4-18.7)	<b>17.6</b>	(15.0-20.3)	<b>32.8</b>	(30.4-36.7)	<b>56.9</b>	(51.9-65.5)	<b>78.1</b>	(65.5-111)	1224
	03-04	<b>14.5</b>	(13.1-16.1)	<b>15.0</b>	(13.8-16.3)	<b>28.2</b>	(25.3-32.8)	<b>48.1</b>	(41.4-52.7)	<b>68.3</b>	(56.8-79.9)	1000
<b>Race/ethnicity</b>												
Mexican Americans	99-00	*		< LOD		<b>25.1</b>	(22.7-29.5)	<b>40.7</b>	(35.1-51.8)	<b>56.3</b>	(45.8-77.2)	650
	01-02	<b>11.9</b>	(<LOD-14.6)	<b>10.6</b>	(<LOD-14.5)	<b>26.0</b>	(19.3-30.4)	<b>47.9</b>	(36.3-57.2)	<b>59.8</b>	(49.3-74.1)	558
	03-04	<b>10.2</b>	(7.86-13.2)	<b>9.10</b>	(<LOD-11.1)	<b>20.7</b>	(11.1-34.7)	<b>39.5</b>	(25.9-65.5)	<b>62.2</b>	(36.0-93.4)	457
Non-Hispanic blacks	99-00	<b>20.3</b>	(17.0-24.1)	<b>17.5</b>	(15.4-23.5)	<b>35.7</b>	(28.9-45.5)	<b>77.0</b>	(60.8-90.7)	<b>107</b>	(84.0-143)	404
	01-02	<b>18.8</b>	(15.4-22.9)	<b>19.2</b>	(14.7-22.0)	<b>36.8</b>	(28.3-50.5)	<b>73.6</b>	(50.8-110)	<b>112</b>	(68.7-160)	514
	03-04	<b>14.4</b>	(12.2-17.0)	<b>13.8</b>	(11.2-16.3)	<b>30.8</b>	(26.5-36.1)	<b>59.9</b>	(47.7-77.7)	<b>86.6</b>	(56.8-129)	486
Non-Hispanic whites	99-00	<b>19.1</b>	(17.2-21.1)	<b>19.0</b>	(16.9-22.2)	<b>32.8</b>	(28.0-37.6)	<b>52.5</b>	(44.9-64.4)	<b>74.0</b>	(62.3-86.7)	722
	01-02	<b>17.5</b>	(15.6-19.7)	<b>19.0</b>	(16.3-21.1)	<b>34.0</b>	(29.7-38.1)	<b>55.5</b>	(45.9-69.4)	<b>78.7</b>	(59.1-126)	1052
	03-04	<b>15.8</b>	(13.7-18.2)	<b>16.0</b>	(13.8-19.3)	<b>30.8</b>	(26.4-35.0)	<b>48.8</b>	(42.1-55.7)	<b>67.6</b>	(57.5-87.3)	889

<sup>a</sup>(CDC,2009)

Limit of detection (LOD, see Data Analysis section) for Survey years 99-00, 01-02, and 03-04 are 14.5, 10.5, and 7.8, respectively. < LOD means below the limit of detection, which might vary for some chemicals by year and by individual sample.

\* Not calculated: proportion of results below the limit of detection was too high to provide a valid result.

**Table 5- 2 Geometric Means of Serum Concentrations (Lipid Adjusted) of Oxychlordane for the U.S. Population Aged 12 Years and Older<sup>a</sup>**

Geometric mean and selected percentiles of serum concentrations (in ng/g of lipid or parts per billion on a lipid-weight basis) for the U.S. population from the National Health and Nutrition Examination Survey.

	Survey years	Geometric mean		Selected percentiles						Sample size		
		(95% conf. interval)		(95% confidence interval)								
		50th	75th	90th	95th							
<b>Total</b>	99-00	*	< LOD	<b>20.8</b>	(17.8-23.0)	<b>34.4</b>	(30.5-38.6)	<b>44.8</b>	(40.2-49.6)	1661		
	01-02	<b>11.4</b>	(<LOD-	<b>11.1</b>	(<LOD-	<b>21.7</b>	(19.3-24.4)	<b>36.4</b>	(31.5-41.4)	<b>49.7</b>	(42.0-61.2)	2249
	03-04	<b>9.37</b>	(8.69-10.1)	<b>10.3</b>	(9.20-11.0)	<b>18.0</b>	(16.8-20.1)	<b>29.0</b>	(26.8-32.1)	<b>37.7</b>	(34.8-43.8)	1978
<b>Age group</b>												
12-19 years	99-00	*	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	663		
	01-02	*	< LOD	< LOD	< LOD	< LOD	< LOD	<b>11.5</b>	(<LOD-12.6)	752		
	03-04	*	< LOD	< LOD	< LOD	<b>9.20</b>	(<LOD-11.5)	<b>11.5</b>	(8.10-18.9)	595		
20 years and older	99-00	*	< LOD	<b>23.3</b>	(21.0-25.9)	<b>37.7</b>	(32.3-43.5)	<b>47.7</b>	(43.1-50.8)	998		
	01-02	<b>12.9</b>	(11.7-14.3)	<b>13.3</b>	(11.4-14.9)	<b>23.9</b>	(21.2-26.7)	<b>38.5</b>	(33.4-45.9)	<b>53.1</b>	(44.1-65.9)	1497
	03-04	<b>10.6</b>	(9.82-11.5)	<b>11.4</b>	(10.6-12.4)	<b>19.9</b>	(17.9-21.5)	<b>31.3</b>	(28.8-33.2)	<b>39.2</b>	(36.5-44.8)	1383
<b>Gender</b>												
Males	99-00	*	< LOD	<b>18.1</b>	(16.1-19.6)	<b>31.3</b>	(25.9-38.2)	<b>42.4</b>	(35.3-49.6)	793		
	01-02	<b>11.1</b>	(<LOD-	<b>11.1</b>	(<LOD-	<b>20.6</b>	(16.6-24.9)	<b>33.1</b>	(27.5-43.8)	<b>48.1</b>	(40.2-56.9)	1049
	03-04	<b>9.10</b>	(8.20-10.1)	<b>9.90</b>	(8.30-11.2)	<b>17.1</b>	(15.6-18.4)	<b>27.6</b>	(25.3-32.2)	<b>36.0</b>	(32.7-39.2)	963
Females	99-00	*	< LOD	<b>22.3</b>	(20.1-25.9)	<b>36.9</b>	(31.5-40.3)	<b>46.2</b>	(39.1-51.8)	868		
	01-02	<b>11.7</b>	(10.7-12.7)	<b>11.0</b>	(<LOD-	<b>23.1</b>	(20.7-25.0)	<b>37.5</b>	(34.5-42.1)	<b>52.8</b>	(42.7-70.0)	1200
	03-04	<b>9.63</b>	(8.89-10.4)	<b>10.6</b>	(9.10-11.3)	<b>20.1</b>	(17.4-21.7)	<b>30.3</b>	(27.5-32.7)	<b>41.9</b>	(36.3-45.5)	1015
<b>Race/ethnicity</b>												
Mexican Americans	99-00	*	< LOD	<b>16.3</b>	(<LOD-19.9)	<b>28.9</b>	(18.8-42.0)	<b>39.9</b>	(26.8-61.0)	628		
	01-02	*	< LOD	<b>13.9</b>	(11.0-18.4)	<b>27.2</b>	(21.0-33.1)	<b>37.9</b>	(29.9-42.0)	557		
	03-04	*	< LOD	<b>12.8</b>	(10.1-15.8)	<b>22.9</b>	(15.8-31.4)	<b>31.4</b>	(22.4-51.6)	462		
Non-Hispanic blacks	99-00	*	< LOD	<b>18.7</b>	(<LOD-32.2)	<b>39.9</b>	(26.5-47.3)	<b>48.6</b>	(43.5-65.5)	350		
	01-02	<b>11.7</b>	(<LOD-	< LOD	<b>22.8</b>	(17.2-28.3)	<b>41.4</b>	(30.6-53.7)	<b>56.5</b>	(41.8-73.5)	501	
	03-04	<b>8.74</b>	(<LOD-	<b>8.70</b>	(<LOD-	<b>18.9</b>	(15.9-21.5)	<b>35.1</b>	(25.4-40.2)	<b>44.2</b>	(37.7-56.8)	493
Non-Hispanic whites	99-00	*	< LOD	<b>21.8</b>	(18.6-24.6)	<b>34.2</b>	(28.9-40.9)	<b>44.0</b>	(37.2-49.8)	559		
	01-02	<b>12.1</b>	(11.0-13.3)	<b>11.8</b>	(10.5-13.9)	<b>23.0</b>	(20.1-25.7)	<b>37.5</b>	(31.6-45.1)	<b>52.2</b>	(41.0-67.4)	1031
	03-04	<b>10.2</b>	(9.36-11.1)	<b>11.2</b>	(10.0-12.1)	<b>19.7</b>	(17.2-21.7)	<b>30.3</b>	(26.8-33.6)	<b>37.7</b>	(34.3-45.5)	898

<sup>a</sup>(CDC,2009)

Limit of detection (LOD, see Data Analysis section) for Survey years 99-00, 01-02, and 03-04 are 14.5, 10.5, and 7.8, respectively.

< LOD means below the limit of detection, which might vary for some chemicals by year and by individual sample.

\* Not calculated: proportion of results below the limit of detection was too high to provide a valid result.

## 6. ANALYTICAL METHODS

No updated data.

## 7. REGULATIONS AND ADVISORIES

**Table 7-1 Regulations and Guidelines Applicable to Chlordane**

Agency	Description	Information	Reference
<u>INTERNATIONAL</u>			
Guidelines:			
IARC	Carcinogenicity classification	Group 2B <sup>a</sup>	IARC 2009
WHO	Air quality guidelines	No	WHO 2000
	Drinking water quality guidelines	0.0002 mg/L	WHO 2006
<u>NATIONAL</u>			
Regulations and Guidelines:			
a. Air			
ACGIH	TLV (8-hour TWA)	0.5 mg/m <sup>3 b</sup>	ACGIH 2009
	TLV-basis (critical effect)	Liver damage	
NIOSH	REL (10-hour TWA)	0.5 mg/m <sup>3 c</sup>	NIOSH 2005
	IDLH	100 mg/m <sup>3</sup>	
	Potential Occupational Carcinogen	Yes	
	Target organs	Central nervous system, eyes, lungs, liver, kidneys	
OSHA	PEL (8-hour TWA) for general industry	0.5 mg/m <sup>3 c</sup>	OSHA 2009 29 CFR 1910.1000, Table Z-1

b. Water

**Table 7-1 Regulations and Guidelines Applicable to Chlordane**

Agency	Description	Information	Reference
EPA	Drinking water standards and health advisories		EPA 2009 <sup>a</sup>
	1-day health advisory for a 10-kg child	0.06 mg/L	
	10-day health advisory for a 10-kg child	0.06 mg/L	
	DWEL	0.02 mg/L	
	Lifetime	No	
	10 <sup>-4</sup> Cancer risk	0.01 mg/L	
	National primary drinking water standards		EPA 2009 <sup>b</sup>
	MCL	0.002 mg/L	
	Potential health effects from exposure above the MCL	Liver or nervous system problems; increased risk of cancer	
	Common sources of chlordane in drinking water	Residue of banned termiticide	
<u>NATIONAL</u> (cont.)			
	Public health goal	zero	
c. Other			
ACGIH	Carcinogenicity classification	A3 <sup>d</sup>	ACGIH 2009
	Biological exposure indices	No	
U.S. EPA	Carcinogenicity classification	B2 <sup>e</sup>	IRIS 2009
	RfC	7.0x10 <sup>-4</sup> mg/m <sup>3</sup>	
	Air unit risk	1.0x10 <sup>-4</sup> (µg/m <sup>3</sup> ) <sup>-1</sup>	
	RfD	5.0x10 <sup>-4</sup> mg/kg-day	
	Oral slope factor	3.5x10 <sup>-1</sup> (mg/kg-day) <sup>-1</sup>	
	Drinking water unit risk	1.0x10 <sup>-5</sup> (µg/L) <sup>-1</sup>	
NTP	Carcinogenicity classification	None	NTP 2011

**Table 7-1 Regulations and Guidelines Applicable to Chlordane**

Agency	Description	Information	Reference
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<sup>a</sup> Group 2B: possibly carcinogenic to humans.

<sup>b</sup> Skin notation: refers to the potential significant contribution to the overall exposure by the cutaneous route, including mucous membranes and the eyes, by contact with vapors, liquids, and solids.

<sup>c</sup> Skin designation: indicates the potential for dermal absorption.

<sup>d</sup> A3: confirmed animal carcinogen with unknown relevance to humans.

<sup>e</sup> B2: probable human carcinogen.

ACGIH = American Conference of Governmental Industrial Hygienists; CFR = Code of Federal Regulations; DWEL = drinking water equivalent level;; IARC = International Agency for Research on Cancer; IDLH = immediately dangerous to life or health; IRIS = Integrated Risk Information System; MCL = maximum contaminant level; NIOSH = National Institute for Occupational Safety and Health; NTP = National Toxicology Program; OSHA = Occupational Safety and Health Administration; PEL = permissible exposure limit; REL = recommended exposure limit; RfC = inhalation reference concentration; RfD = oral reference dose; TLV = threshold limit values; TWA = time-weighted average; U.S.EPA = Environmental Protection Agency; WHO = World Health Organization

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