

8. REGULATIONS AND ADVISORIES

The international, national, and state regulations and guidelines regarding α -, β -, δ -, γ -, and ϵ -HCH in air, water, and other media are summarized in Table 8-1.

Five oral MRLs have been derived for the α -, β -, and γ -HCH isomers of HCH, as summarized below and detailed in Section 2.3 and Appendix A.

An MRL of 0.008 mg/kg/day was derived for chronic-duration (365 days and longer) oral exposure to α -HCH. The chronic oral MRL for α -HCH is based on a NOAEL of 0.8 mg/kg/day and LOAEL of 3.5 mg/kg/day for liver effects in rats (Fitzhugh et al. 1950), and an uncertainty factor of 100 (10 for extrapolation from animals to humans and 10 for human variability).

An MRL of 0.05 mg/kg/day was derived for acute-duration (14 days or less) oral exposure to β -HCH. This MRL is based on a NOAEL of 4.5 mg/kg/day and LOAEL of 22.5 mg/kg/day for ataxia, progressive inactivity, and coma in rats exposed to β -HCH for 2 weeks (Van Velsen et al. 1986), and an uncertainty factor of 100 (10 for extrapolation from animals to humans and 10 for human variability).

An MRL of 0.0006 mg/kg/day was derived for intermediate-duration oral exposure to β -HCH (Van Velsen et al. 1986). This MRL is based on a minimal LOAEL of 0.18 mg/kg/day for liver effects in rats (Van Velsen et al. 1986) and an uncertainty factor of 300 (3 for use of a minimal LOAEL, 10 for extrapolation from animals to humans, and 10 for human variability).

An MRL of 0.003 mg/kg/day was derived for acute-duration oral exposure to γ -HCH (lindane). This MRL is based on a minimal LOAEL of 1 mg/kg/day for reproductive effects in male offspring of rats exposed during lactation (Dalsenter et al. 1997b), and an uncertainty factor of 300 (3 for use of a minimal LOAEL, 10 for extrapolation from animals to humans, and 10 for human variability).

An MRL of 1×10^{-5} mg/kg/day was derived for intermediate-duration oral exposure to γ -HCH. This MRL is based on a LOAEL of 0.012 mg/kg/day for immunological/lymphoreticular effects in mice (Meera et al. 1992), and an uncertainty factor of 1,000 (10 for use of a LOAEL, 10 for extrapolation from animals to humans, and 10 for human variability).

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Table 8-1. Regulations and Guidelines Applicable to Hexachlorocyclohexane and Hexachlorocyclohexane Isomers

Agency	Description	Information	Reference
<u>INTERNATIONAL</u>			
Guidelines:			
IARC	Carcinogenicity classification HCH (including isomers)	Group 2B ^a	IARC 2003
WHO	Drinking water guideline γ -HCH	2.0 $\mu\text{g/L}$	WHO 1993
	Temporary ADI γ -HCH	0–0.001 mg/kg bw	WHO 1998
	Proposed drinking water guideline γ -HCH	0.3 $\mu\text{g/L}$	
<u>NATIONAL</u>			
Regulations and Guidelines:			
a. Air:			
ACGIH	TLV (8-hour TWA) γ -HCH ^b	0.5 mg/m ³	ACGIH 2003
NIOSH	REL (10-hour TWA) γ -HCH ^c IDLH	0.5 mg/m ³ 50 mg/m ³	NIOSH 2003
OSHA	PEL (8-hour TWA) for general industry γ -HCH ^d	0.5 mg/m ³	OSHA 2003a 29 CFR 1910.1000, Table Z-1
	PEL (8-hour TWA) for construction industry γ -HCH ^d	0.5 mg/m ³	OSHA 2003c 29 CFR 1926.55, Appendix A
	PEL (8-hour TWA) for shipyard industry γ -HCH ^d	0.5 mg/m ³	OSHA 2003b 29 CFR 1915.1000
USC	Hazardous air pollutant	γ -HCH	USC 2003 42 USC 7412
b. Water			
EPA	Drinking water health advisories for γ -HCH		EPA 2002a
	1-day (10-kg child)	1.0 mg/L	
	10-day (10-kg child)	1.0 mg/L	
	DWEL ^e	0.01 mg/L	
	Lifetime ^f	2.0x10 ⁻⁴ mg/L	
	Hazardous substance designation in accordance with Section 311 (b)(2)(A) of the Clean Water Act	γ -HCH	EPA 2003p 40 CFR 116.4
	Interim primary drinking water standard γ -HCH	0.004 mg/L	EPA 2003f 40 CFR 265, Appendix III

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Agency	Description	Information			Reference
NATIONAL (cont.)					
EPA	Lifetime cancer risks (oral) in water ($\mu\text{g/L}$)	10^{-4}	10^{-5}	10^{-6}	IRIS 2005
	HCH (technical)	2.0	0.2	0.02	
	α -HCH	0.6	0.06	0.006	
	β -HCH	2.0	0.2	0.02	
	MCL for criteria for classification of solid waste disposal facilities and practices				EPA 2003a 40 CFR 257, Appendix I
	γ -HCH	0.004 mg/L			
	Pollutants of initial focus of the Great Lakes Water Quality Initiative; pollutants that are bioaccumulative chemicals of concern	HCH (technical) α -HCH β -HCH δ -HCH γ -HCH			EPA 2003q 40 CFR 132, Table 6
	Primary drinking water standards (MCL)				EPA 2003i 40 CFR 141.61
	γ -HCH	2.0×10^{-3} mg/L			
	Primary drinking water standards (MCLG)				EPA 2003h 40 CFR 141.50
γ -HCH	2.0×10^{-3} mg/L				
Reportable quantity of hazardous substances designated pursuant to Section 311 of the Clean Water Act				EPA 2003j 40 CFR 117.3	
γ -HCH	1 pound				
c. Food					
EPA	Residue Tolerances for γ -HCH				EPA 2003n 40 CFR 180.133
	Cattle, goat, horse, and sheep (fat of meat)	7 ppm			
	Hog (fat of meat)	4 ppm			
	Cucumber, lettuce, melon, mushroom, pumpkin, squash, summer, and tomato	3 ppm			
	Apple, apricot, asparagus, avocado, broccoli, Brussels sprouts, cabbage, cauliflower, celery, cherry, collards, eggplant, grape, guava, kale, kohlrabi, mango, mustard greens, nectarine, okra, onion (dry bulb only), peach, pear, pepper, pineapple, plum, prune, quince, spinach, strawberry, and Swiss chard	1 ppm			

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Agency	Description	Information	Reference
NATIONAL (cont.)			
EPA	Residue Tolerances for γ -HCH Pecans	0.01 ppm	EPA 2003n 40 CFR 180.133
FDA	Bottled drinking water allowable level γ -HCH	2.0×10^{-3} mg/L	FDA 2003 21 CFR 165.110
d. Other			
ACGIH	Carcinogenicity classification γ -HCH	A3 ^g	ACGIH 2003
EPA	Carcinogenicity classification HCH-technical α -HCH β -HCH δ -HCH ϵ -HCH γ -HCH γ -HCH	B2 ^h B2 ^h C ⁱ D ^j D ^j Not available Suggestive evidence ^k	IRIS 2005 EPA 2002b IRIS 2005
	RfD HCH-technical α -HCH β -HCH δ -HCH ϵ -HCH γ -HCH	Not available Not available Not available Not available Not available 3.0×10^{-4} mg/kg/day	
	Community right-to-know; release report; effective date of reporting α -HCH γ -HCH	01/01/95 01/01/87	EPA 2003o 40 CFR 372.65
	Extremely hazardous substance for (γ -HCH) Reportable quantity Threshold planning quantity	1 pound 1,000/10,000 pounds	EPA 2003d 40 CFR 355, Appendix A
	Identification and listing of hazardous waste; maximum concentration for the toxicity characteristic γ -HCH	0.4 mg/L	EPA 2003e 40 CFR 261.24
	Land disposal restrictions; universal treatment standards α -HCH β -HCH δ -HCH γ -HCH	<u>Waste water</u> 14×10^{-3} mg/L 14×10^{-3} mg/L 0.023 mg/L 0.0017 mg/L	<u>Non-waste water</u> 0.066 mg/kg 0.066 mg/kg 0.066 mg/kg 0.066 mg/kg
			EPA 2003g 40 CFR 268.48

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Agency	Description	Information		Reference			
NATIONAL (cont.)							
EPA	Municipal solid waste landfills; hazardous constituents	<u>Suggested method</u>	<u>PQL (µg/L)</u>	EPA 2003b 40 CFR 258, Appendix II			
					α-HCH	8080	0.05
			8270		10		
		β-HCH	8080		0.05		
			8270		20		
		δ-HCH	8080		0.1		
			8270		20		
		γ-HCH	8080		0.05		
			8270		20		
		Reportable quantity of hazardous substance in accordance with Section 307(a) of the Clean Water Act for all isomers of HCH	Not assigned to the generic or broad class		EPA 2003c 40 CFR 302.4		
		Reportable quantity of hazardous substance in accordance with Section 311 (b)(2) and 307(a) of the Clean Water Act, Section 112 of RCRA, and Section 112 of the Clean Air Act for γ-HCH	1 pound		EPA 2003c 40 CFR 302.4		
		Standards for owners or operators of hazardous waste TSD facilities; maximum concentration for groundwater protection	<u>Suggested method</u>		<u>PQL (µg/L)</u>	EPA 2003I 40 CFR 264, Appendix IX	
							α-HCH
					8250		10
			β-HCH		8080		0.05
	8250		40				
δ-HCH	8080		0.1				
	8250		30				
γ-HCH	8080		0.05				
	8250	10					
Standards for owners or operators of hazardous waste TSD facilities; maximum concentration for groundwater protection			EPA 2003k 40 CFR 264.94				
	γ-HCH	0.004 mg/L					

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Agency	Description	Information	Reference
<u>NATIONAL</u> (cont.)			
EPA	Standards for the management of specific hazardous waste and types of hazardous waste management facilities	<u>Risk specific doses ($\mu\text{g}/\text{m}^3$)</u>	EPA 2003m 40 CFR 266, Appendix V
	HCH (technical)	2.0×10^{-2}	
	α -HCH	5.6×10^{-3}	
	β -HCH	1.9×10^{-2}	
	γ -HCH	2.6×10^{-2}	
NTP	Carcinogenicity classification for γ -HCH and other HCH isomers	Reasonably anticipated to be a human carcinogen	NTP 2002
<u>STATE</u>			
a. Air	No data		
b. Water			
Arizona	Drinking water guideline γ -HCH	0.2 $\mu\text{g}/\text{L}$	HSDB 2003
California	Drinking water guideline α -HCH β -HCH	0.7 $\mu\text{g}/\text{L}$ 0.3 $\mu\text{g}/\text{L}$	HSDB 2003
Florida	Drinking water guideline α -HCH β -HCH δ -HCH	0.05 $\mu\text{g}/\text{L}$ 0.1 $\mu\text{g}/\text{L}$ 0.05 $\mu\text{g}/\text{L}$	HSDB 2003
Maine	Drinking water guideline γ -HCH	0.2 $\mu\text{g}/\text{L}$	HSDB 2003
New Hampshire	Drinking water guideline HCH α -HCH β -HCH	0.02 $\mu\text{g}/\text{L}$ 0.006 $\mu\text{g}/\text{L}$ 0.02 $\mu\text{g}/\text{L}$	HSDB 2003
c. Food	No data		

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<u>STATE</u> (cont.)			
d. Other	No data		

^aGroup 2B: possibly carcinogenic to humans

^bSkin notation: refers to the potential significant contribution to the overall exposure by the cutaneous route, including mucous membranes and the eyes, either by contact with vapors or, of probable greater significance, by direct skin contact with the substance.

^cSkin designation: indicates the potential for dermal absorption; skin exposure should be prevented as necessary through the use of good work practices and gloves, coveralls, goggles, and other appropriate equipment.

^dSkin designation

^eDWEL: a lifetime exposure concentration protective of adverse, non-cancer health effects, that assumes all of the exposure to a contaminant is from drinking water.

^fLifetime: the concentration of a chemical in drinking water that is not expected to cause any adverse noncarcinogenic effects for a lifetime of exposure. The Lifetime HA is based on exposure of a 70-kg adult consuming 2 L water/day.

^gA3: confirmed animal carcinogen with unknown relevance to humans

^hB2: probable human carcinogen; sufficient evidence of carcinogenicity from animal studies and inadequate evidence from epidemiological studies.

ⁱC: possible human carcinogen

^jD: not classifiable as to human carcinogenicity

^kSuggestive evidence of carcinogenicity, but not sufficient to assess human carcinogenic potential.

ACGIH = American Conference of Governmental Industrial Hygienists; ADI = allowable daily intake; CFR = Code of Federal Regulations; DWEL = drinking water equivalent level; EPA = Environmental Protection Agency; FDA = Food and Drug Administration; HCH = hexachlorocyclohexane; HSDB = Hazardous Substances Data Bank; IARC = International Agency for Research on Cancer; IDLH = immediately dangerous to life or health; IRIS = Integrated Risk Information System; MCL = maximum contaminant level; MCLG = maximum contaminant level goal; NIOSH = National Institute for Occupational Safety and Health; NTP = National Toxicology Program; OSHA = Occupational Safety and Health Administration; PEL = permissible exposure limit; PQL = practical quantitation level; RCRA = Resource Conservation and Recovery Act; REL = recommended exposure limit; RfD = reference dose; TLV = threshold limit values; TSD = treatment, storage, and disposal; TWA = time-weighted average; USC = United States Code; WHO = World Health Organization

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EPA derived an oral reference dose (RfD) of 0.0003 mg/kg/day for γ -HCH (IRIS 2005). The RfD is based on a NOAEL of 0.33 mg/kg/day for liver and kidney toxicity in female rats (Zoecon Corporation 1983), and uses an uncertainty factor of 1,000 (10 for use of a subchronic versus a lifetime assay, 10 to account for interspecies variation, and 10 to protect sensitive human subpopulations).

EPA has classified HCH in the following cancer weight-of-evidence classifications: technical HCH and α -HCH, Group B2 (probable human carcinogen); β -HCH, Group C (possible human carcinogen); and δ -HCH and ϵ -HCH, Group D (not classifiable as to human carcinogenicity) (IRIS 2005). γ -HCH is classified as having "suggestive evidence of carcinogenicity, but not sufficient to assess human carcinogenic potential" (EPA 2002b).

EPA estimates that concentrations of HCH (technical) in water of 2.0, 0.2, and 0.02 $\mu\text{g/L}$ are associated in humans with excess lifetime cancer risks of 10^{-4} , 10^{-5} , and 10^{-6} , respectively. α -HCH in water at concentrations of 0.6, 0.06, and 0.006 $\mu\text{g/L}$ are associated in humans with excess lifetime cancer risks of 10^{-4} , 10^{-5} , and 10^{-6} , respectively, and concentrations of β -HCH in water of 2.0, 0.2, and 0.02 $\mu\text{g/L}$ are associated in humans with excess lifetime cancer risks of 10^{-4} , 10^{-5} , and 10^{-6} , respectively (IRIS 2005).

δ -HCH and γ -HCH are on the list of chemicals appearing in "Toxic Chemicals Subject to Section 313 of the Emergency Planning and Right-to-Know Act of 1986" (EPA 2003o).

Tolerances are established for γ -HCH in or on raw agricultural commodities as follows: 7 ppm in or on the fat of meat from cattle, goats, horses, and sheep; 4 ppm in or on the fat of meat from hogs; 3 ppm in or on cucumbers, lettuce, melons, mushrooms, pumpkin, squash, summer, and tomatoes; 1 ppm in or on apples, apricots, asparagus, avocado, broccoli, Brussels sprouts, cabbage, cauliflower, celery, cherry, collards, eggplant, grape, guava, kale, kohlrabi, mango, mustard greens, nectarine, okra, onion (dry bulb only), peach, pear, pepper, pineapple, plum, prune, quince, spinach, strawberry, and Swiss chard; and 0.01 ppm in or on pecans (EPA 2003n).

The use of γ -HCH has been restricted by EPA since 1977 and is to be applied only by a certified applicator following label directions (EPA 1985b).