

8. REGULATIONS AND ADVISORIES

ATSDR has derived an intermediate-duration inhalation minimal risk level (MRL) of 0.0002 mg Ni/m³ for nickel. This MRL is based on a NOAEL of 0.06 mg Ni/m³ and a LOAEL of 0.11 mg Ni/m³ for chronic active lung inflammation in rats exposed to nickel sulfate 6 hours/day, 5 days/week for 13 weeks (NTP 1996c). The MRL was derived by dividing the NOAEL_{HEC} of 0.0052 mg Ni/m³ by an uncertainty factor of 30 (3 for animal to human extrapolation with dosimetric adjustments and 10 for human variability).

ATSDR has derived a chronic-duration inhalation MRL of 9×10^{-5} mg Ni/m³ for nickel. This MRL is based on a NOAEL of 0.03 mg Ni/m³ and a LOAEL of 0.06 mg Ni/m³ for chronic active lung inflammation and bronchialization in rats exposed to nickel sulfate 6 hours/day, 5 days/week for 2 years (NTP 1996c). The MRL was derived by dividing the NOAEL_{HEC} of 0.0027 mg Ni/m³ by an uncertainty factor of 30 (3 for animal to human extrapolation with dosimetric adjustments and 10 for human variability).

EPA (IRIS 2003) derived an oral reference dose (RfD) of 0.02 mg/kg/day for nickel soluble salts. The RfD was based on a NOAEL of 5 mg/kg/day and a LOAEL of 50 mg/kg/day for decreased body weight and organ weight in rats exposed to dietary nickel for 2 years (Ambrose et al. 1976). The NOAEL was divided by an uncertainty factor of 300 (10 for animal to human extrapolation, 10 to protect sensitive individuals, and 3 for inadequacies in the reproductive toxicity studies).

The Department of Health and Human Services (NTP 2002) has determined that metallic nickel may reasonably be anticipated to be a carcinogen and that nickel compounds are known to be human carcinogens. Similarly, IARC classified metallic nickel in group 2B (possibly carcinogenic to humans) and nickel compounds in group 1 (carcinogenic to humans). EPA has classified nickel refinery dust and nickel subsulfide in Group A (human carcinogen) (IRIS 2003). Other nickel compounds have not been classified by the EPA. Based on the occupational data, inhalation unit risk levels of 2.4×10^{-4} (μg/m³)⁻¹ and 4.8×10^{-4} (μg/m³)⁻¹ were derived for nickel refinery dust and nickel subsulfide, respectively (IRIS 2003).

In an attempt to reduce the prevalence of nickel sensitivity, the European Union has passed a directive to restrict the use of nickel beginning in February 1996 (Delescluse and Dinet 1994). The directive forbids the use of nickel in objects introduced into pierced ears and other parts of the human body during epithelialization of the wound. It forbids the use of nickel in products placed in direct and prolonged

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contact with the skin (e.g., earrings, watches, clothing accessories). The use of nickel is also forbidden in accessories that are plated with another metal, except if the plating is strong enough to restrict liberation of nickel to $<0.5 \mu\text{g}/\text{cm}^2/\text{week}$ during a normal use of 2 years.

National and state guidelines and regulations regarding exposure to nickel and its compounds are summarized in Table 8-1.

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Table 8-1. Regulations and Guidelines Applicable to Nickel

Agency	Description	Information	Reference
<u>INTERNATIONAL</u>			
Guidelines:			
IARC	Carcinogenicity classification Nickel compounds Nickel, metallic	Group 1 ^a Group 2B ^b	IARC 1990
WHO	Air quality guideline Nickel unit risk Drinking water guideline Nickel	$3.8 \times 10^{-5} (\mu\text{g}/\text{m}^3)^{-1}$ 0.02 mg/L	WHO 2000 WHO 1998
<u>NATIONAL</u>			
Regulations and Guidelines:			
a. Air:			
ACGIH	TLV (8-hour TWA) Nickel, elemental (as Ni) Nickel, soluble inorganic compounds Nickel, insoluble inorganic compounds Nickel subsulfide (as Ni) Nickel carbonyl (as Ni)	1.5 mg/m ³ 0.1 mg/m ³ 0.2 mg/m ³ 0.1 mg/m ³ 0.05 ppm	ACGIH 2003
EPA	Chemical accident prevention provisions; toxic end points Nickel carbonyl Hazardous air pollutant pursuant to Section 112 of the Clean Air Act Regulated toxic substance and threshold quantity for accidental release prevention under Section 112(r) of the Clean Air Act Nickel carbonyl	0.00067 mg/L Nickel 1,000 pounds	EPA 2003b 40 CFR 68, Appendix A EPA 2003j 40 CFR 61.01 EPA 2003a 40 CFR 68.130
NIOSH	REL (10-hour TWA) Nickel ^c IDLH Nickel carbonyl ^c IDLH	0.015 mg/m ³ 10 mg/m ³ 0.001 ppm 2 ppm	NIOSH 2003a, 2003b
U.S. NRC	Occupational values Oral ingestion for Class D ^d ⁵⁶ Ni ⁵⁷ Ni ⁵⁹ Ni ⁶³ Ni ⁶⁵ Ni ⁶⁶ Ni (LLI wall) ⁶⁶ Ni	<u>ALI (μCi)</u> 1.0x10 ³ 2.0x10 ³ 2.0x10 ⁴ 9.0x10 ³ 8.0x10 ³ 4.0x10 ² 5.0x10 ²	U.S. NRC 2003 10 CFR 20, Appendix B

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Table 8-1. Regulations and Guidelines Applicable to Nickel

Agency	Description	Information		Reference	
NATIONAL (cont.)					
U.S. NRC	Occupational values	ALI	DAC	U.S. NRC 2003 10 CFR 20, Appendix B	
	Inhalation ^e for Class D ^d	(μCi)	($\mu\text{Ci/mL}$)		
	⁵⁶ Ni	2.0×10^3	8.0×10^{-7}		
	⁵⁷ Ni	5.0×10^3	2.0×10^{-6}		
	⁵⁹ Ni	4.0×10^3	2.0×10^{-6}		
	⁶³ Ni	2.0×10^3	7.0×10^{-7}		
	⁶⁵ Ni	2.0×10^4	1.0×10^{-5}		
	⁶⁶ Ni (LLI wall)	2.0×10^3	7.0×10^{-7}		
	Occupational values	ALI	DAC		U.S. NRC 2003 10 CFR 20, Appendix B
	Inhalation ^e for Class W ^f	(μCi)	($\mu\text{Ci/mL}$)		
	⁵⁶ Ni	1.0×10^3	5.0×10^{-7}		
	⁵⁷ Ni	3.0×10^3	1.0×10^{-6}		
	⁵⁹ Ni	7.0×10^3	3.0×10^{-6}		
	⁶³ Ni	3.0×10^3	1.0×10^{-6}		
	⁶⁵ Ni	3.0×10^4	1.0×10^{-5}		
	⁶⁶ Ni	6.0×10^2	3.0×10^{-7}		
	Occupational values	ALI	DAC	U.S. NRC 2003 10 CFR 20, Appendix B	
	Inhalation ^e for vapors	(μCi)	($\mu\text{Ci/mL}$)		
	⁵⁶ Ni	1.0×10^3	5.0×10^{-7}		
	⁵⁷ Ni	6.0×10^3	3.0×10^{-6}		
	⁵⁹ Ni	2.0×10^3	8.0×10^{-7}		
⁶³ Ni	8.0×10^2	3.0×10^{-7}			
⁶⁵ Ni	2.0×10^4	7.0×10^{-6}			
⁶⁶ Ni	3.0×10^3	1.0×10^{-6}			
OSHA	PEL (8-hour TWA) for general industry			OSHA 2003a 29 CFR 1910.1000, Table Z-1	
	Nickel, metal and insoluble compounds (as Ni)	1.0 mg/m^3			
	Nickel, soluble compounds (as Ni)	1.0 mg/m^3			
	Nickel carbonyl	0.007 mg/m^3			
	PEL (8-hour TWA) for construction industry			OSHA 2003e 29 CFR 1926.55, Appendix A	
	Nickel, metal and insoluble compounds (as Ni)	1.0 mg/m^3			
	Nickel, soluble compounds (as Ni)	1.0 mg/m^3			
	Nickel carbonyl	0.007 mg/m^3			
	PEL (8-hour TWA) for shipyard industry			OSHA 2003d 29 CFR 1915.1000	
	Nickel, metal and insoluble compounds (as Ni)	1.0 mg/m^3			
Nickel, soluble compounds (as Ni)	1.0 mg/m^3				
Nickel carbonyl	0.007 mg/m^3				
OSHA	Highly hazardous chemicals, toxics, and reactives			OSHA 2003b,f 29 CFR 1926.64, 29 CFR 1910.119, Appendix A	
	Nickel carbonyl Threshold quantity	150 pounds			

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Table 8-1. Regulations and Guidelines Applicable to Nickel

Agency	Description	Information	Reference
NATIONAL (cont.)			
b. Water			
EPA	Drinking water health advisories		EPA 2002
	1-day (10-kg child)	1.0 mg/L	
	10-day (10-kg child)	1.0 mg/L	
	DWEL ^g	0.7 mg/L	
	Lifetime ^h	0.1 mg/L	
	Effluent guidelines and standards; toxic pollutants pursuant to Section 307(a)(1) of the Clean Water Act	Nickel and compounds	EPA 2003f 40 CFR 401.15
	National primary drinking water regulations; best technology and treatment techniques for nickel	Ion exchange, lime softening, and reverse osmosis	EPA 2003l 40 CFR 141.62
	Pollutant of initial focus in the Great Lakes Water Quality Initiative	Nickel	EPA 2003s 40 CFR 132, Table 6
c. Food			
FDA	Bottled drinking water		FDA 2003a
	Nickel	0.1 mg/L	21 CFR 165.110
	Generally recognized as safe as a direct human food ingredient with no limitation other than current good manufacturing practices	Nickel	FDA 2003b 21 CFR 184.1537
	Indirect food additives; components of paper and paper-board	Nickel	FDA 2003c 21 CFR 176.180
d. Other			
ACGIH	Carcinogenicity classification		ACGIH 2003
	Nickel subsulfide	A1 ⁱ	
EPA	Carcinogenicity classification		IRIS 2003
	Nickel	Not evaluated	
	Nickel refinery dust	A ^j	
	Nickel carbonyl	B2 ^k	
	Nickel subsulfide	A ^j	
	RfD		IRIS 2003
	Nickel	0.02 mg/kg/day	
	Nickel refinery dust	No data	
	Nickel carbonyl	No data	
	Nickel subsulfide	No data	
EPA	Community right-to-know; release reporting; effective date of reporting for nickel	01/01/87	EPA 2003r 40 CFR 372.65
	Criteria for municipal solid waste landfills; hazardous constituent	Nickel	EPA 2003c 40 CFR 258, Appendix II

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Table 8-1. Regulations and Guidelines Applicable to Nickel

Agency	Description	Information	Reference
NATIONAL (cont.)			
EPA	Emergency planning and notification		EPA 2003g 40 CFR 355, Appendix A
	Nickel carbonyl		
	Reportable quantity	10 pounds	
	Threshold planning quantity	1 pound	
	Land disposal restrictions; universal treatment standards		EPA 2003i 40 CFR 268.48
	Nickel		
	Waste water	3.98 mg/L	
	Non-waste water	11 mg/L TCLP	
	Reportable quantity; designated as a hazardous substance		EPA 2003d 40 CFR 302.4
	Nickel ^l	Not assigned	
	Nickel compounds ^m	Not assigned	
	Nickel carbonyl ^{l,n}	10 pounds	
	Standards for owners and operators of hazardous waste treatment, storage, and disposal facilities; health-based limits for exclusion of waste-derived residues; residue concentration limit		EPA 2003o 40 CFR 266, Appendix VII
	Nickel	7x10 ¹ mg/kg	
	Standards for the management of specific hazardous waste and hazardous waste management facilities; risk specific dose		EPA 2003n 40 CFR 266, Appendix V
Nickel	2.4x10 ⁻¹ µg/m ³		
Nickel refinery dust	2.4x10 ⁻¹ µg/m ³		
Nickel subsulfide	4.8x10 ⁻¹ µg/m ³		
Standards for the use or disposal of sewage sludge; pollutant limits (risk specific concentration)		EPA 2003q 40 CFR 503.43	
Nickel	2.0 µg/m ³		
U.S. NRC	Effluent concentrations for Class D ^d	Air	Water
		(µCi/mL)	(µCi/mL)
	⁵⁶ Ni	3.0x10 ⁻⁹	2.0x10 ⁻⁵
	⁵⁷ Ni	7.0x10 ⁻⁹	2.0x10 ⁻⁵
	⁵⁹ Ni	5.0x10 ⁻⁹	3.0x10 ⁻⁴
	⁶³ Ni	2.0x10 ⁻⁹	1.0x10 ⁻⁴
	⁶⁵ Ni	3.0x10 ⁻⁸	1.0x10 ⁻⁴
	⁶⁶ Ni (LLI wall)	2.0x10 ⁻⁹	6.0x10 ⁻⁶

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Agency	Description	Information	Reference
<u>NATIONAL</u> (cont.)			
	Effluent concentrations for Class W ^f	<u>Air (μCi/mL)</u>	U.S. NRC 2003 10 CFR 20, Appendix B
	⁵⁶ Ni	2.0×10^{-9}	
	⁵⁷ Ni	4.0×10^{-9}	
	⁵⁹ Ni	1.0×10^{-8}	
	⁶³ Ni	4.0×10^{-9}	
	⁶⁵ Ni	4.0×10^{-8}	
	⁶⁶ Ni	4.0×10^{-10}	
U.S. NRC	Effluent concentrations for Vapors	<u>Air (μCi/mL)</u>	U.S. NRC 2003 10 CFR 20, Appendix B
	⁵⁶ Ni	2.0×10^{-9}	
	⁵⁷ Ni	9.0×10^{-9}	
	⁵⁹ Ni	3.0×10^{-9}	
	⁶³ Ni	1.0×10^{-9}	
	⁶⁵ Ni	2.0×10^{-8}	
	⁶⁶ Ni	4.0×10^{-9}	
	Release to sewers for Class D ^d	<u>Monthly average concentration (μCi/mL)</u>	U.S. NRC 2003 10 CFR 20, Appendix B
	⁵⁶ Ni	2.0×10^{-4}	
	⁵⁷ Ni	2.0×10^{-4}	
	⁵⁹ Ni	3.0×10^{-3}	
	⁶³ Ni	1.0×10^{-3}	
	⁶⁵ Ni	1.0×10^{-3}	
	⁶⁶ Ni	6.0×10^{-5}	
NTP	Carcinogenicity Nickel, metallic	Reasonably anticipated to be human carcinogens	NTP 2002
	Nickel compounds	Known human carcinogens	
<u>STATE</u>			
a. Air	No data		
b. Water			
Arizona	Drinking water guideline Nickel, elemental	150 μg/L	HSDB 2003
Massachusetts	Drinking water guideline Nickel and nickel compounds	100 μg/L	HSDB 2003
Maine	Drinking water guideline Nickel and nickel compounds	150 μg/L	HSDB 2003
Minnesota	Drinking water guideline Nickel and nickel compounds	100 μg/L	HSDB 2003

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Agency	Description	Information	Reference
<i>STATE (cont.)</i>			
c. Food	No data		
d. Other	No data		

^aGroup 1: carcinogenic to humans

^bGroup 2B: possibly carcinogenic to humans

^cCarcinogen

^dClass D: refers to the retention (clearance half-times of <10 days) for all compounds except those given for W.

^eThe ALIs and DACs for inhalation are given for an aerosol with an activity median aerodynamic diameter (AMAD) of 1 µm and for class D and W of radioactive material, which refers to their retention (clearance half-times of <10 days and 10–100 days, respectively) in the pulmonary region of the lung.

^fClass W: refers to the retention (clearance half-times of 10–100 days) for sulfides, oxides, hydroxides, halides, nitrates, and stannic phosphate.

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

^hLifetime: 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 health advisory is based on exposure of a 70-kg adult consuming 2 L water/day.

ⁱA1: confirmed human carcinogen

^jA: human carcinogen

^kB2: probable human carcinogen

^ldesignated as a hazardous substances pursuant to Section 307(a) of the Clean Water Act,

^mdesignated as a hazardous substances pursuant to Section 3001 of RCRA

ⁿdesignated as a hazardous substances pursuant to Section 112 of the Clean Air Act

ACGIH = American Conference of Governmental Industrial Hygienists; ALI = annual limits on intake; CFR = Code of Federal Regulations; DAC = derived air concentration; DWEL = drinking water equivalent level; EPA = Environmental Protection Agency; FDA = Food and Drug Administration; HAP = hazardous air pollutant; HSDB = Hazardous Substances Data Bank; IARC = International Agency for Research on Cancer; IDLH = immediately dangerous to life or health; IRIS = Integrated Risk Information System; LLI = lower large intestine; NIOSH = National Institute for Occupational Safety and Health; NTP = National Toxicology Program; OSHA = Occupational Safety and Health Administration; PEL = permissible exposure limit; RCRA = Resource Conservation and Recovery Act; REL = recommended exposure limit; RfD = reference dose; TCLP = toxicity characteristic leachate procedure; TLV = threshold limit values; TSD = treatment, storage, and disposal; TWA = time-weighted average; USC = United States Code; U.S. NRC = Nuclear Regulatory Commission; WHO = World Health Organization

