8. REGULATIONS AND ADVISORIES

ATSDR has derived an intermediate-duration inhalation minimal risk level (MRL) of 0.0002 mg Ni/m^3 for nickel. This MRL is based on a NOAEL of 0.06 mg Ni/m^3 and a LOAEL of 0.11 mg Ni/m^3 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/m^3 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 $9x10^{-5}$ mg Ni/m^3 for nickel. This MRL is based on a NOAEL of 0.03 mg Ni/m^3 and a LOAEL of 0.06 mg Ni/m^3 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/m^3 by an uncertainty factor of 30 (3 for animal to human extrapolation with dosimetric adjustments and 10 for human variability).

EPA (IRIS 2005) 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 2005). Other nickel compounds have not been classified by the EPA. Based on the occupational data, inhalation unit risk levels of $2.4x10^{-4}$ $(\mu g/m^3)^{-1}$ and $4.8x10^{-4}$ $(\mu g/m^3)^{-1}$ were derived for nickel refinery dust and nickel subsulfide, respectively (IRIS 2005).

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 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 μg/cm^2/week during a normal use of 2 years.

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

Table 8-1. Regulations and Guidelines Applicable to Nickel and Nickel Compounds

Agency	Description	Information	Reference
INTERNATIONAL			
Guidelines:			
IARC	Carcinogenicity classification		IARC 1990
	Nickel compounds	Group 1[a]	
	Nickel, metallic	Group 2B[b]	
WHO	Air quality guideline		WHO 2000
	Nickel unit risk	3.8×10^{-5} $(\mu g/m^3)^{-1}$	
	Drinking water guideline		WHO 1998
	Nickel	0.02 mg/L	
NATIONAL			
Regulations and Guidelines:			
a. Air:			
ACGIH	TLV (8-hour TWA)		ACGIH 2003
	Nickel, elemental (as Ni)	1.5 mg/m^3	
	Nickel, soluble inorganic compounds	0.1 mg/m^3	
	Nickel, insoluble inorganic compounds	0.2 mg/m^3	
	Nickel subsulfide (as Ni)	0.1 mg/m^3	
	Nickel carbonyl (as Ni)	0.05 ppm	
NIOSH	REL (10-hour TWA)		NIOSH 2003a, 2003b
	Nickel[c]	0.015 mg/m^3	
	IDLH	10 mg/m^3	
	Nickel carbonyl[c]	0.001 ppm	
	IDLH	2 ppm	
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	
OSHA	PEL (8-hour TWA) for construction industry		OSHA 2003e 29 CFR 1926.55
	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	
	Highly hazardous chemicals, toxics, and reactives		OSHA 2003b, 2003f 29 CFR 1926.64, 29 CFR 1910.119, Appendix A
	Nickel carbonyl		
	Threshold quantity	150 pounds	

Table 8-1. Regulations and Guidelines Applicable to Nickel and Nickel Compounds

Agency	Description	Information	Reference
NATIONAL *(cont.)*			
b. Water			
EPA	Drinking water health advisories		EPA 2002a
	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	
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 paperboard	Nickel	FDA 2003c 21 CFR 176.180(b)(2)
d. Other			
ACGIH	Carcinogenicity classification		ACGIH 2003
	Nickel subsulfide	A1[i]	
EPA	Carcinogenicity classification		IRIS 2005
	Nickel	Not evaluated	
	Nickel refinery dust	A[j]	
	Nickel carbonyl	B2[k]	
	Nickel subsulfide	A[j]	
EPA	RfC		IRIS 2005
	Nickel	No data	
	Nickel refinery dust	No data	
	Nickel carbonyl	No data	
	Nickel subsulfide	No data	
	RfD		IRIS 2005
	Nickel	0.02 mg/kg/day	
	Nickel refinery dust	No data	
	Nickel carbonyl	No data	
	Nickel subsulfide	No data	
NTP	Carcinogenicity Nickel, metallic	Reasonably anticipated to be a human carcinogen	NTP 2002
	Carcinogenicity Nickel compounds	Known human carcinogens	NTP 2002
STATE			
a. Air	No data		
b. Water			
Arizona	Drinking water guideline		HSDB 2003
	Nickel, elemental	150 µg/L	

Table 8-1. Regulations and Guidelines Applicable to Nickel and Nickel Compounds

Agency	Description	Information	Reference
STATE *(cont.)*			
Massachusetts	Drinking water guideline		HSDB 2003
	Nickel and nickel compounds	100 µg/L	
Maine	Drinking water guideline		HSDB 2003
	Nickel and nickel compounds	150 µg/L	
Minnesota	Drinking water guideline		HSDB 2003
	Nickel and nickel compounds	100 µg/L	
c. Food	No data		
d. Other	No data		

[a]Group 1: carcinogenic to humans
[b]Group 2B: possibly carcinogenic to humans
[c]Carcinogen
[d]Class D: refers to the retention (clearance half-times of <10 days) for all compounds except those given for W.
[e]The 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.
[f]Class W: refers to the retention (clearance half-times of 10–100 days) for sulfides, oxides, hydroxides, halides, nitrates, and stannic phosphate.
[g]DWEL: a lifetime exposure concentration protection of adverse, non-cancer health effects, that assumes all of the exposure to a contaminant is from drinking water.
[h]Lifetime: 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.
[i]A1: confirmed human carcinogen
[j]A: human carcinogen
[k]B2: probable human carcinogen
[l]designated as a hazardous substances pursuant to Section 307(a) of the Clean Water Act.
[m]designated as a hazardous substances pursuant to Section 3001 of RCRA.
[n]designated 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; 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; RfC = inhalation reference concentration; RfD = oral reference dose; TCLP = toxicity characteristic leachate procedure; TLV = threshold limit values; TSD = treatment, storage, and disposal; TWA = time-weighted average; USNRC = Nuclear Regulatory Commission; WHO = World Health Organization