

## 8. REGULATIONS AND ADVISORIES

ATSDR has derived an intermediate-duration inhalation minimal risk level (MRL) of  $0.0002 \text{ mg Ni/m}^3$  for nickel. This MRL is based on a NOAEL of  $0.06 \text{ mg Ni/m}^3$  and a LOAEL of  $0.11 \text{ mg Ni/m}^3$  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  $\text{NOAEL}_{\text{HEC}}$  of  $0.0052 \text{ mg Ni/m}^3$  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  $9 \times 10^{-5} \text{ mg Ni/m}^3$  for nickel. This MRL is based on a NOAEL of  $0.03 \text{ mg Ni/m}^3$  and a LOAEL of  $0.06 \text{ mg Ni/m}^3$  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  $\text{NOAEL}_{\text{HEC}}$  of  $0.0027 \text{ mg Ni/m}^3$  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  $0.02 \text{ mg/kg/day}$  for nickel soluble salts. The RfD was based on a NOAEL of  $5 \text{ mg/kg/day}$  and a LOAEL of  $50 \text{ mg/kg/day}$  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  $2.4 \times 10^{-4} (\mu\text{g/m}^3)^{-1}$  and  $4.8 \times 10^{-4} (\mu\text{g/m}^3)^{-1}$  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 Dinot 1994). The directive forbids the use of nickel in objects introduced into pierced ears and other parts of the human body during

## 8. REGULATIONS AND ADVISORIES

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  $<0.5 \mu\text{g}/\text{cm}^2/\text{week}$  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.

## 8. REGULATIONS AND ADVISORIES

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

Agency	Description	Information	Reference
<u>INTERNATIONAL</u>			
Guidelines:			
IARC	Carcinogenicity classification Nickel compounds Nickel, metallic	Group 1 <sup>a</sup> Group 2B <sup>b</sup>	IARC 1990
WHO	Air quality guideline Nickel unit risk	$3.8 \times 10^{-5} (\mu\text{g}/\text{m}^3)^{-1}$	WHO 2000
	Drinking water guideline Nickel	0.02 mg/L	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 <sup>3</sup> 0.1 mg/m <sup>3</sup> 0.2 mg/m <sup>3</sup> 0.1 mg/m <sup>3</sup> 0.05 ppm	ACGIH 2003
NIOSH	REL (10-hour TWA) Nickel <sup>c</sup> IDLH Nickel carbonyl <sup>c</sup> IDLH	0.015 mg/m <sup>3</sup> 10 mg/m <sup>3</sup> 0.001 ppm 2 ppm	NIOSH 2003a, 2003b
OSHA	PEL (8-hour TWA) for general industry Nickel, metal and insoluble compounds (as Ni) Nickel, soluble compounds (as Ni) Nickel carbonyl	1.0 mg/m <sup>3</sup> 1.0 mg/m <sup>3</sup> 0.007 mg/m <sup>3</sup>	OSHA 2003a 29 CFR 1910.1000, Table Z-1
OSHA	PEL (8-hour TWA) for construction industry Nickel, metal and insoluble compounds (as Ni) Nickel, soluble compounds (as Ni) Nickel carbonyl	1.0 mg/m <sup>3</sup> 1.0 mg/m <sup>3</sup> 0.007 mg/m <sup>3</sup>	OSHA 2003e 29 CFR 1926.55
	PEL (8-hour TWA) for shipyard industry Nickel, metal and insoluble compounds (as Ni) Nickel, soluble compounds (as Ni) Nickel carbonyl	1.0 mg/m <sup>3</sup> 1.0 mg/m <sup>3</sup> 0.007 mg/m <sup>3</sup>	OSHA 2003d 29 CFR 1915.1000
	Highly hazardous chemicals, toxics, and reactives Nickel carbonyl Threshold quantity	150 pounds	OSHA 2003b, 2003f 29 CFR 1926.64, 29 CFR 1910.119, Appendix A

## 8. REGULATIONS AND ADVISORIES

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

Agency	Description	Information	Reference
<u>NATIONAL</u> (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 <sup>g</sup>	0.7 mg/L	
	Lifetime <sup>h</sup>	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 <sup>i</sup>	
EPA	Carcinogenicity classification		IRIS 2005
	Nickel	Not evaluated	
	Nickel refinery dust	A <sup>j</sup>	
	Nickel carbonyl	B2 <sup>k</sup>	
	Nickel subsulfide	A <sup>j</sup>	
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		NTP 2002
	Nickel, metallic	Reasonably anticipated to be a human carcinogen	
	Carcinogenicity		NTP 2002
	Nickel compounds	Known human carcinogens	
<u>STATE</u>			
a. Air			
	No data		
b. Water			
Arizona	Drinking water guideline		HSDB 2003
	Nickel, elemental	150 µg/L	

## 8. REGULATIONS AND ADVISORIES

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

<sup>a</sup>Group 1: carcinogenic to humans

<sup>b</sup>Group 2B: possibly carcinogenic to humans

<sup>c</sup>Carcinogen

<sup>d</sup>Class D: refers to the retention (clearance half-times of <10 days) for all compounds except those given for W.

<sup>e</sup>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.

<sup>f</sup>Class W: refers to the retention (clearance half-times of 10–100 days) for sulfides, oxides, hydroxides, halides, nitrates, and stannic phosphate.

<sup>g</sup>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.

<sup>h</sup>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.

<sup>i</sup>A1: confirmed human carcinogen

<sup>j</sup>A: human carcinogen

<sup>k</sup>B2: probable human carcinogen

<sup>l</sup>designated as a hazardous substances pursuant to Section 307(a) of the Clean Water Act.

<sup>m</sup>designated as a hazardous substances pursuant to Section 3001 of RCRA.

<sup>n</sup>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