Nickel Compounds

Hazard Summary

Nickel occurs naturally in the environment at low levels. Nickel is an essential element in some animal species, and it has been suggested it may be essential for human nutrition. Nickel dermatitis, consisting of itching of the fingers, hands, and forearms, is the most common effect in humans from chronic (long-term) skin contact with nickel. Respiratory effects have also been reported in humans from inhalation exposure to nickel. Human and animal studies have reported an increased risk of lung and nasal cancers from exposure to nickel refinery dusts and nickel subsulfide. Animal studies of soluble nickel compounds (i.e., nickel carbonyl) have reported lung tumors. EPA has classified nickel refinery dust and nickel subsulfide as Group A, human carcinogens, and nickel carbonyl as a Group B2, probable human carcinogen.

Please Note: The main sources of information for this fact sheet are EPA's Integrated Risk Information System (IRIS) (2), which contains information on oral chronic toxicity and the RfD, and the carcinogenic effects of nickel including the unit cancer risk for inhalation exposure, EPA's Health Assessment Document for Nickel (1), and the Agency for Toxic Substances and Disease Registry's (ATSDR's) Toxicological Profile for Nickel. (6)

Uses

- Nickel is used for nickel alloys, electroplating, batteries, coins, industrial plumbing, spark plugs, machinery parts, stainless-steel, nickel-chrome resistance wires, and catalysts. (1,6)
- Nickel carbonyl has severely limited use in nickel refining. (1)

Sources and Potential Exposure

- Nickel is a natural element of the earth's crust; therefore, small amounts are found in food, water, soil, and air. (6)
- Food is the major source of nickel exposure, with an average intake for adults estimated to be approximately 100 to 300 micrograms per day (µg/d). (1,6)
- Individuals also may be exposed to nickel in occupations involved in its production, processing, and use, or through contact with everyday items such as nickel-containing jewelry and stainless steel cooking and eating utensils, and by smoking tobacco. (1)
- Nickel is found in ambient air at very low levels as a result of releases from oil and coal combustion, nickel metal refining, sewage sludge incineration, manufacturing facilities, and other sources. (2,6)
- Given its high instability, nickel carbonyl exposure is extremely rare.

Assessing Personal Exposure

- Laboratory tests can detect nickel in blood, urine, feces, and hair samples. (1,6)

Health Hazard Information

Acute Effects:

- One person exposed to an extrememly high level of nickel by inhalation suffered severe damage to the lungs and kidneys. (6)
- Gastrointestinal distress (e.g., nausea, vomiting, diarrhea) and neurological effects were reported in workers who drank water on one shift that was contaminated with nickel as nickel sulfate and nickel chloride. (1,6)
- Pulmonary fibrosis and renal edema were reported in humans and animals following acute (short-term) exposure to nickel carbonyl. (1)
- Acute animal tests in rats have shown nickel compounds to exhibit acute toxicity values ranging from low to high. The soluble compounds, such as nickel acetate, were the most toxic, and the insoluble forms, such as nickel powder, were the least toxic. (6)

Chronic Effects (Noncancer):

- Dermatitis is the most common effect in humans from chronic dermal exposure to nickel. Cases of nickel dermatitis have been reported following occupational and non-occupational exposure, with symptoms of eczema (rash, itching) of the fingers, hands, wrists, and forearms. (1,2,6,7)
- Chronic inhalation exposure to nickel in humans also results in respiratory effects, including a type of asthma specific to nickel, decreased lung function, and bronchitis. (6,7)
- Animal studies have reported effect on the lungs and immune system from inhalation exposure to soluble and insoluble nickel compounds (nickel oxide, subsulfide, sulfate heptahydrate). (1,6)
- Soluble nickel compounds are more toxic to the respiratory tract than less soluble compounds. (6)
- EPA has not established a Reference Concentration (RfC) for nickel. (2,3,4,5)
- The Reference Dose (RfD) for nickel (soluble salts) is 0.02 milligrams per kilogram body weight per day (mg/kg/d) based on decreased body and organ weights in rats. The RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily oral exposure to the human population (including sensitive subgroups) that is likely to be without appreciable risk of deleterious noncancer effects during a lifetime. It is not a direct estimator of risk, but rather a reference point to gauge the potential effects. At exposures increasingly greater than the RfD, the potential for adverse health effects increases. Lifetime exposure above the RfD does not imply that an adverse health effect would necessarily occur. (5)
- EPA has medium confidence in the RfD due to: (1) low confidence in the study on which the RfD for nickel (soluble salts) was based because, although it was properly designed and provided adequate toxicological endpoints, high mortality occurred in the controls; and (2) medium confidence in the database because it provided adequate supporting subchronic studies, one by gavage and the other in drinking water, but inadequacies in the remaining reproductive data. (5)
- Nickel is an essential nutrient for some mammalian species, and has been suggested to be essential for human nutrition. By extrapolation from animal data, it is estimated that a 70-kg person would have a daily requirement of 50 µg per kg diet of nickel. (6)
- The California Environmental Protection Agency (CalEPA) has calculated a chronic inhalation reference exposure level of 0.00005 milligrams per cubic meter (mg/m^3) for nickel based on respiratory and immune system effects reported in rats exposed to a soluble nickel salt. The CalEPA reference exposure level is a concentration at or below which adverse health effects are not likely to occur. (7)
- ATSDR has calculated a chronic-duration inhalation MRL of 0.0002 mg/m^3 for nickel based on respiratory effects reported in rats exposed to a soluble nickel salt. The MRL is an estimate of the daily human exposure to a hazardous substance that is likely to be without appreciable risk of adverse noncancer health effects over a specified duration of exposure. (6)

Reproductive/Developmental Effects:

- No information is available regarding the reproductive or developmental effects of nickel in humans. (6)

- Animal studies have reported reproductive and developmental effects, such as a decreased number of live pups per litter, increased pup mortality, and reduction in fetal body weight, and effects to the dam from oral exposure to soluble salts of nickel. (5,6)
- Sperm abnormalities and decreased sperm count have been reported in animals exposed to nickel nitrate orally and nickel oxide by inhalation, respectively. (6)

Cancer Risk:
Nickel Salts

- Nickel sulfate via inhalation and nickel acetate in drinking water were not carcinogenic in either rats or mice. (6)
- EPA has not evaluated soluble salts of nickel as a class of compounds for potential human carcinogenicity. (5)

Nickel Refinery Dust and Nickel Subsulfide

- Human studies have reported an increased risk of lung and nasal cancers among nickel refinery workers exposed to nickel refinery dust. Nickel refinery dust is a mixture of many nickel compounds, with nickel subsulfide being the major constituent. (3,4,6)
- Animal studies have also reported lung tumors from inhalation exposure to nickel refinery dusts and to nickel subsulfide. (3,4)
- EPA has classified nickel refinery dust and nickel subsulfide as Group A, human carcinogens. (3,4)
- EPA uses mathematical models, based on animal studies, to estimate the probability of a person developing cancer from breathing air containing a specified concentration of a chemical. EPA calculated an inhalation unit risk estimate of 2.4×10^{-4} $(\mu g/m^3)^{-1}$ for nickel refinery dusts. EPA estimates that, if an individual were to continuously breathe air containing nickel refinery dusts at an average of 0.004 $\mu g/m^3$ (4×10^{-6} mg/m^3) over his or her entire lifetime, that person would theoretically have no more than a one-in-a-million increased chance of developing cancer as a direct result of breathing air containing this chemical. Similarly, EPA estimates that continuously breathing air containing 0.04 $\mu g/m^3$ would result in not greater than a one-in-a-hundred thousand increased chance of developing cancer, and air containing 0.4 $\mu g/m^3$ would result in not greater than a one-in-ten thousand increased chance of developing cancer. For a detailed discussion of confidence in the potency estimates, please see IRIS. (3)
- For nickel subsulfide, EPA calculated an inhalation unit risk estimate of 4.8×10^{-4} $(\mu g/m^3)^{-1}$. EPA estimates that, if an individual were to continuously breathe air containing this nickel compound at an average of 0.002 $\mu g/m^3$ (2×10^{-6} mg/m^3) over his or her entire lifetime, that person would theoretically have no more than a one-in-a-million increased chance of developing cancer as a direct result of breathing air containing this chemical. Similarly, EPA estimates that continuously breathing air containing 0.02 $\mu g/m^3$ would result in not greater than a one-in-a-hundred thousand increased chance of developing cancer, and air containing 0.2 $\mu g/m^3$ would result in not greater than a one-in-ten thousand increased chance of developing cancer. (4)

Nickel Carbonyl

- Nickel carbonyl has been reported to produce lung tumors in rats exposed via inhalation. (2)
- EPA has classified nickel carbonyl as a Group B2, probable human carcinogen. (2)

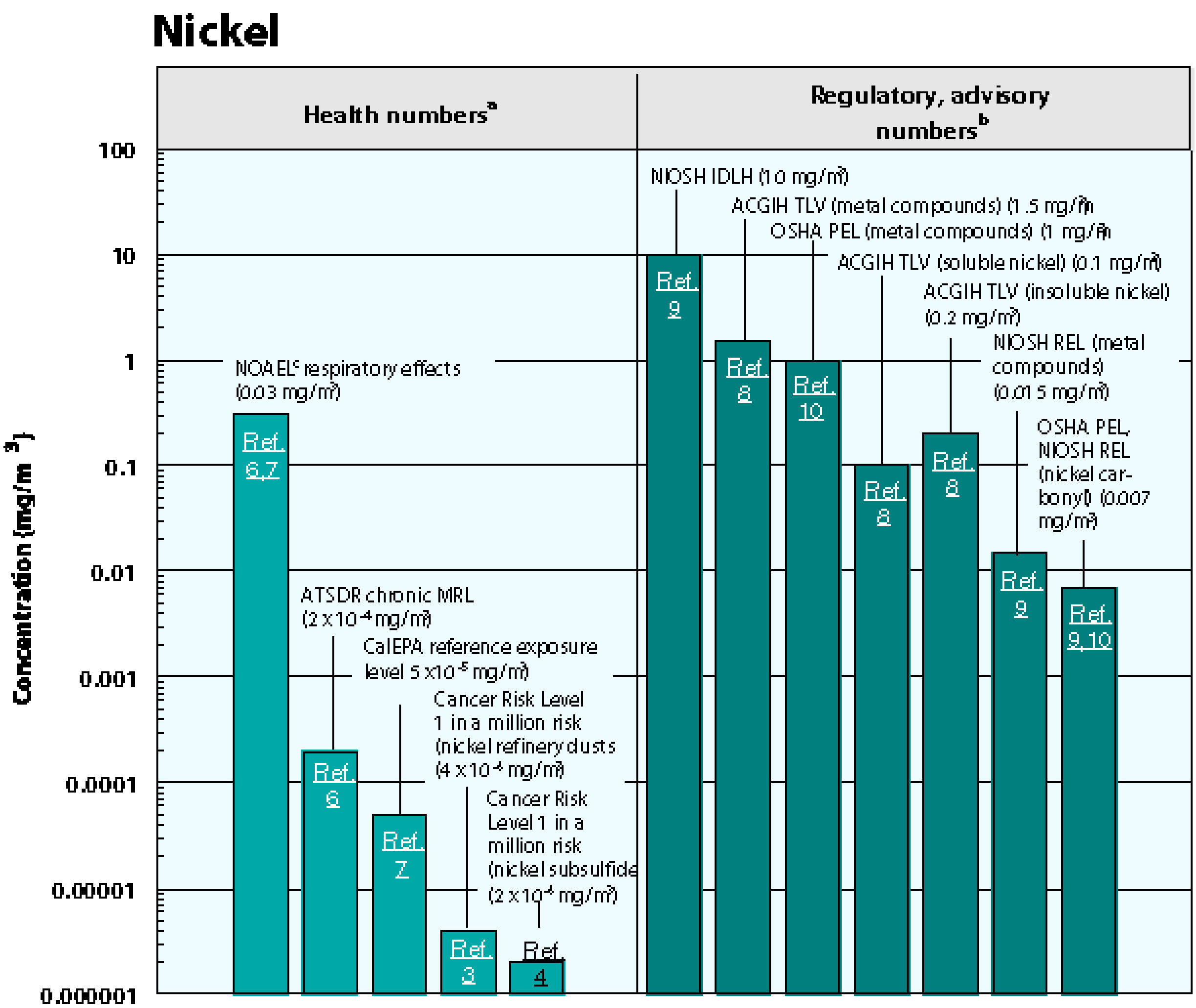
Physical Properties

- Nickel is a silvery-white metal that is found in nature as a component of silicate, sulfide, or arsenide ores. (1)

- In the environment, nickel is found primarily combined with oxygen or sulfur as oxides or sulfides. (1)
- Each form of nickel exhibits different physical properties. (1,6)
- Soluble nickel salts include nickel chloride, nickel sulfate, and nickel nitrate. (6)
- Nickel carbonyl, a highly unstable form, is not found naturally and decomposes rapidly. (1)
- The chemical symbol for nickel is Ni, and it has an atomic weight of 58.71 g/mol. (1)

Conversion Factors (only for the gaseous form):
To convert concentrations in air (at 25°C) from ppm to mg/m^3: mg/m^3 = (ppm) × (molecular weight of the compound)/(24.45). For nickel: 1 ppm = 2.4 mg/m^3. To convert concentrations in air from $\mu g/m^3$ to mg/m^3: mg/m^3 = ($\mu g/m^3$) × (1 mg/1,000 μg).

Health Data from Inhalation Exposure



ACGIH TLV --American Conference of Governmental and Industrial Hygienists' threshold limit value expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effects.
NIOSH REL --National Institute of Occupational Safety and Health's recommended exposure limit; NIOSH-recommended exposure limit for an 8- or 10-h time-weighted-average exposure and/or ceiling.

NIOSH IDLH -- NIOSH's immediately dangerous to life or health concentration; NIOSH recommended exposure limit to ensure that a worker can escape from an exposure condition that is likely to cause death or immediate or delayed permanent adverse health effects or prevent escape from the environment.
OSHA PEL--Occupational Safety and Health Administration's permissible exposure limit expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effect averaged over a normal 8-h workday or a 40-h workweek.

The health and regulatory values cited in this factsheet were obtained in December 1999.
[a] Health numbers are toxicological numbers from animal testing or risk assessment values developed by EPA.
[b] Regulatory numbers are values that have been incorporated in Government regulations, while advisory numbers are nonregulatory values provided by the Government or other groups as advice. OSHA numbers are regulatory, whereas NIOSH and ACGIH numbers are advisory.
[c] The NOAEL is from the critical study used as the basis for both the ATSDR chronic MRL and CalEPA chronic reference exposure level.

Summary created in April 1992, updated January 2000

References

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