

## Nickel refinery dust; no CASRN

Human health assessment information on a chemical substance is included in the IRIS database only after a comprehensive review of toxicity data, as outlined in the [IRIS assessment development process](#). Sections I (Health Hazard Assessments for Noncarcinogenic Effects) and II (Carcinogenicity Assessment for Lifetime Exposure) present the conclusions that were reached during the assessment development process. Supporting information and explanations of the methods used to derive the values given in IRIS are provided in the [guidance documents located on the IRIS website](#).

STATUS OF DATA FOR Nickel refinery dust

**File First On-Line 09/30/1987**

Category (section)	Assessment Available?	Last Revised
Oral RfD (I.A.)	not evaluated	
Inhalation RfC (I.B.)	not evaluated	
Carcinogenicity Assessment (II.)	yes	09/30/1987*

\*A comprehensive review of toxicological studies was completed (June 5, 2006) - please see section II.D.2. for more information.

### I. Chronic Health Hazard Assessments for Noncarcinogenic Effects

#### I.A. Reference Dose for Chronic Oral Exposure (RfD)

Substance Name — Nickel refinery dust  
CASRN —

Not available at this time.

## **I.B. Reference Concentration for Chronic Inhalation Exposure (RfC)**

Substance Name — Nickel refinery dust  
CASRN —

Not available at this time.

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## **II. Carcinogenicity Assessment for Lifetime Exposure**

Substance Name — Nickel refinery dust  
CASRN —  
Last Revised — 09/30/1987

Section II provides information on three aspects of the carcinogenic assessment for the substance in question; the weight-of-evidence judgment of the likelihood that the substance is a human carcinogen, and quantitative estimates of risk from oral exposure and from inhalation exposure. The quantitative risk estimates are presented in three ways. The slope factor is the result of application of a low-dose extrapolation procedure and is presented as the risk per (mg/kg)/day. The unit risk is the quantitative estimate in terms of either risk per ug/L drinking water or risk per ug/cu.m air breathed. The third form in which risk is presented is a drinking water or air concentration providing cancer risks of 1 in 10,000, 1 in 100,000 or 1 in 1,000,000. The rationale and methods used to develop the carcinogenicity information in IRIS are described in The Risk Assessment Guidelines of 1986 (EPA/600/8-87/045) and in the IRIS Background Document. IRIS summaries developed since the publication of EPA's more recent Proposed Guidelines for Carcinogen Risk Assessment also utilize those Guidelines where indicated (Federal Register 61(79):17960-18011, April 23, 1996). Users are referred to Section I of this IRIS file for information on long-term toxic effects other than carcinogenicity.

### **II.A. Evidence for Human Carcinogenicity**

#### **II.A.1. Weight-of-Evidence Characterization**

Classification — A; human carcinogen

Basis — Human data in which exposure to nickel refinery dust caused lung and nasal tumors in sulfide nickel matte refinery workers in several epidemiologic studies in different countries, and on animal data in which carcinomas were produced in rats by inhalation and injection

## II.A.2. Human Carcinogenicity Data

Sufficient. Nickel refinery dust from pyrometallurgical sulfide nickel matte refineries is considered a human carcinogen when inhaled. Evidence of carcinogenicity includes a consistency of findings across different countries (Clydach, Wales; Copper Cliff, Ontario; Port Colborne, Ontario; Kristiansand, Norway; and Huntington, WV) in several epidemiologic studies, specificity of tumor site (lung and nose), high relative risks, particularly for nasal cancer, and a dose-response relationship by length of exposure. Excess risks are greatest in the dustier areas of the respective refineries. At Port Colborne, Roberts et al. (1983) reported high risks of lung (SMR = 298) and nasal (SMR = 9412) cancer among men "ever exposed" to calcining, leaching, and sintering, the dustier areas of the refinery. Similar exposures and high risks of lung and nasal cancer were observed in the calcining sheds at Clydach (lung SMR = 510, nasal SMR = 26,667) (Peto et al., 1984), the sintering furnaces at Copper Cliff (lung SMR = 424, nasal SMR = 1583) (Roberts and Julian, 1982), and the roasting/smelting (lung SMR = 360, nasal SMR = 4000) and electrolysis (lung SMR = 550, nasal SMR = 2700) furnaces at Kristiansand, Norway (Magnus et al., 1982). In the study of refinery and nonrefinery workers at a nickel refinery in West Virginia, nasal cancer was exclusive to the refinery workers, with an SMR of 2443 (Enterline and Marsh, 1982). No large excess of lung cancer was observed in either refinery (SMR = 118) or nonrefinery (SMR = 107.6) employees. The data do show a dose-response relationship between cumulative nickel exposure and lung cancer response (allowing for a 20-year latent period). The dose-response relationship is consistent with findings at nickel refineries in Clydach, Wales (Peto et al., 1984) and Copper Cliff, Ontario (Chovil et al., 1981). While the dust levels and lung cancer relative risks were much higher in the two latter refineries, all dose-response relationships appear linear, and the tumor type and sites are the same, indicating that the functional relationship spans a broad range of nickel exposures.

## II.A.3. Animal Carcinogenicity Data

Animal studies indicate that some nickel refinery dusts are potentially carcinogenic. Nickel refinery flue dust (20% nickel sulfate, 59% nickel subsulfide, and 6.3% nickel oxide) from Port Colborne, Canada was tested for carcinogenic potential (Gilman and Ruckerbauer, 1962) by intramuscular injection. It was found to be a strong inducer of injection-site sarcomas in Hooded (52/66) and Wistar (8/20) rats after injection of 20 or 30 mg in one or both thighs and in mice (23/40) after injection of 10 mg/thigh. Fisher et al. (1971), as reviewed by Rigaut (1983), tested nickel refinery dust (20% nickel sulfate, 59% nickel subsulfide, and 6.3% nickel oxide) by inhalation. The refinery dust was one of six types of dust exposures administered to 348 rats at 5 to 15 mg/cu.m. The combined tumor incidence for refinery dust, synthetic dust, nickel subsulfide, and iron sulfide was 11 pulmonary tumors in the 348 rats. When Wistar rats were exposed to a combination of nickel and iron dust at concentrations of 2.1 +/- 0.2 mg Ni/cu.m.

and 1.9 +/- 0.2 mg Fe/cu.m (Kim et al., 1976), one of the 60 surviving rats developed lung cancer.

An intermediate of nickel refinery dust which contains nickel subsulfide, nickel oxide, and metallic nickel (Feinstein dust) was tested in albino (nonpedigree) rats at 70 mg dust/cu.m, 5 hours/day for 6 months (Saknyn and Blohkin, 1978, as reviewed by Sunderman, 1981). Squamous-cell carcinomas were found in two of the five surviving treated rats. Saknyn and Blohkin (1978) also treated the Albino rats by intraperitoneal injection of Feinstein dust at 90 to 150 mg/rat. Six of the 39 survivors developed injection-site sarcomas.

Nickel dust from roasting (31% nickel subsulfide and 33.4% nickel oxide + silicon oxide and oxides of iron and aluminum) was tested for carcinogenicity in rats by inhalation (Belobragina and Saknyn, 1964, as reviewed by Rigaut, 1983). After exposure to 80 to 100 mg/cu.m, 5 hours/day for 12 months, no tumors were found.

Three carcinogenicity studies (Schroeder and Mitchener, 1975; Schroeder et al., 1964, 1974) of nickel acetate and an unspecified nickel salt using doses of 5 ppm of nickel in the drinking water of Long-Evans rats and Swiss mice produced negative results. Ambrose et al. (1976) administered nickel sulfate hexahydrate in the diet of Wistar-derived rats and beagle dogs for 2 years at nickel concentrations of 100 to 2500 ppm. A lack of carcinogenic response was observed in both studies. The dog study may have been inadequate to detect a carcinogenic response, since the duration was relatively short.

#### **II.A.4. Supporting Data for Carcinogenicity**

Nickel refinery dust has not been studied using in vitro short-term test systems or tests for macromolecular interactions.

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### **II.B. Quantitative Estimate of Carcinogenic Risk from Oral Exposure**

Not available.

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### **II.C. Quantitative Estimate of Carcinogenic Risk from Inhalation Exposure**

#### **II.C.1. Summary of Risk Estimates**

Inhalation Unit Risk — 2.4E-4 per (ug/cu.m)

Extrapolation Method — Additive and multiplicative

Air Concentrations at Specified Risk Levels:

<b>Risk Level</b>	<b>Concentration</b>
<b>E-4 (1 in 10,000)</b>	4E-1 ug/cu.m
<b>E-5 (1 in 100,000)</b>	4E-2 ug/cu.m
<b>E-6 (1 in 1,000,000)</b>	4E-3 ug/cu.m

### II.C.2. Dose-Response Data for Carcinogenicity, Inhalation Exposure

Estimates of Incremental Unit Risks for Lung Cancer due to Exposure to 1 ug Ni/cu.m for a Lifetime Based on Extrapolations from Epidemiologic Data Sets

<b>Study</b>	<b>Relative Risk Mode</b>
<b>Huntington, WV (Enterline and Marsh, 1982) (maximum likelihood estimates only):</b>	
<b>Refinery workers</b>	1.5E-5 - 3.1E-5
<b>Nonrefinery workers</b>	9.5E-6 - 2.1E-5
<b>Copper Cliff, Ontario (Chovil et al., 1981)</b>	1.1E-5 - 8.9E-5
<b>Clydach, Wales (Peto et al., 1984)</b>	8.1E-5 - 4.6E-4

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<b>Kristiansand, Norway (Magnus et al., 1982)</b>	1.9E-5 - 1.9E-4
<b>Midpoint of range for refinery workers</b>	2.4E-4

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### II.C.3. Additional Comments (Carcinogenicity, Inhalation Exposure)

Nickel refinery dust is a mixture of many nickel moieties, and it is not certain what the carcinogenic nickel species is in the refinery dust.

Data sets from nickel refineries in Huntington, WV (Enterline and Marsh, 1982), Copper Cliff, Ontario (Chovil et al., 1981), Clydach, Wales (Peto et al., 1984), and Kristiansand, Norway (Magnus et al., 1982) provide information available for choice of model or for separation of risk by the type of nickel exposure. The dose-response curves for nasal cancer were not used for risk estimation because nasal cancer risk from nickel is thought to be an occupational hazard associated only with the pyrometallurgical process, and these tumors are not found in the general public to the same extent as lung tumors. The same lung tumor type was found in all epidemiologic studies of occupational exposure to nickel refinery dust. The average relative risk model was applied to the Huntington, WV and Copper Cliff, Ontario data sets.

For the four data sets analyzed, both the additive and multiplicative excess risk models were fitted whenever possible. The relative risk or multiplicative model follows the assumption that the background cause-age-specific rate at any time is increased by an amount proportional to the cumulative dose up to that time. The model assumes the standardized mortality ratio (SMR) is linearly related to dose and is constant for a set cumulative exposure. Excess mortality for a set cumulative exposure is constant over time, and excess risk remains constant once exposure ceases. The relative risk model differs from the additive risk model in that the latter model assumes that the excess cause-age-specific rate is increased by an amount proportional to the cumulative exposure up to that time.

The unit risk estimates ranged from 1.1E-5 to 4.6E-4 per (ug/cu.m). The estimates from the Huntington refinery were somewhat lower, but this may be a result of only the small sample size. If the nasal cancer deaths are added to the eight lung cancer deaths, the unit risk estimate becomes 1.3E-4 per (ug/cu.m), well within the range of the other estimates. As the best estimate, the midpoint of the range, 2.4E-4 per (ug/cu.m), is taken as the incremental unit risk due to a lifetime exposure to nickel matte refinery dust. When the additive risk model is applied to the data for Huntington, WV, the estimates (2.8E-4 and 1.8E-4 for refinery and nonrefinery workers, respectively) are close to those derived by the relative risk model.

The above unit risk should not be used if the air concentration exceeds 40 ug/cu.m, since above this concentration the unit risk may not be appropriate.

#### **II.C.4. Discussion of Confidence (Carcinogenicity, Inhalation Exposure)**

Four data sets, all from humans, offer a range of incremental unit risk estimates which are consistent with each other.

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#### **II.D. EPA Documentation, Review, and Contacts (Carcinogenicity Assessment)**

##### **II.D.1. EPA Documentation**

Source Document — U.S. EPA, 1986

The 1986 Health Assessment Document has received both Agency and external review.

##### **II.D.2. EPA Review (Carcinogenicity Assessment)**

Agency Work Group Review — 04/01/1987

Verification Date — 04/01/1987

A comprehensive review of toxicological studies published through June 2006 was conducted. No new health effects data were identified that would be directly useful in the revision of the existing carcinogenicity assessment for Nickel refinery dust and a change in the assessment is not warranted at this time. For more information, IRIS users may contact the IRIS Hotline at [hotline.iris@epa.gov](mailto:hotline.iris@epa.gov) or (202)566-1676.

##### **II.D.3. EPA Contacts (Carcinogenicity Assessment)**

Please contact the IRIS Hotline for all questions concerning this assessment or IRIS, in general, at (202)566-1676 (phone), (202)566-1749 (FAX) or [hotline.iris@epa.gov](mailto:hotline.iris@epa.gov) (internet address).

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**III. [reserved]**

**IV. [reserved]**

**V. [reserved]**

## **VI. Bibliography**

Substance Name — Nickel refinery dust  
CASRN —

### **VI.A. Oral RfD References**

None

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### **VI.B. Inhalation RfC References**

None

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### **VI.C. Carcinogenicity Assessment References**

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U.S. EPA. 1986. Health Assessment Document for Nickel and Nickel Compounds. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Research Triangle Park, NC. EPA/600/8- 83/012FF.

## VII. Revision History

Substance Name — Nickel refinery dust

CASRN —

<b>Date</b>	<b>Section</b>	<b>Description</b>
<b>10/28/2003</b>	<b>II.D.2.</b>	Screening-Level Literature Review Findings message has been added.
<b>07/05/2006</b>	<b>II.D.2.</b>	Screening-Level Literature Review Findings message has been removed and replaced by comprehensive literature review conclusions.

## VIII. Synonyms

Substance Name — Nickel refinery dust

CASRN —

Last Revised — 09/30/1987

- 7440-02-0
- NICKEL DUST
- NICKEL PARTICLES
- Nickel Refinery Dust