

Nickel carbonyl; CASRN 13463-39-3

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 carbonyl

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

I. Chronic Health Hazard Assessments for Noncarcinogenic Effects

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

Substance Name — Nickel carbonyl

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Not available at this time.

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

Substance Name — Nickel carbonyl
CASRN — 13463-39-3

Not available at this time.

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — Nickel carbonyl
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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 — B2; probable human carcinogen

Basis — Based upon the observation of pulmonary carcinomas and malignant tumors at various sites in rats administered nickel carbonyl by inhalation and intravenous injection, respectively. Nickel administered as nickel carbonyl binds to DNA.

II.A.2. Human Carcinogenicity Data

Inadequate. Nickel carbonyl was the first nickel compound suspected of causing cancer in humans in a detailed analysis of epidemiologic data from a study of workers at a sulfide nickel matte refinery at Clydach, Wales. No excess risk of cancer, however, was reported in the workers in the reduction area where nickel carbonyl exposure was present (Peto et al., 1984).

II.A.3. Animal Carcinogenicity Data

Sufficient. Nickel carbonyl administered by inhalation has been found to be carcinogenic in animals in the lung (Sunderman et al., 1959, Sunderman and Donnelly, 1965). Sunderman et al. (1959) exposed male Wistar rats to nickel carbonyl; 64 rats were exposed to 0.03 mg/L three times weekly for 1 year, 32 rats were exposed to 0.06 mg/L three times weekly for 1 year, and 80 rats were exposed once to 0.25 mg/L. In each case, exposure was for 30-minute periods. Of the nine animals exposed to nickel carbonyl and surviving 2 or more years, four were reported to have tumors. One animal with repeated exposure to 0.03 mg/L had a squamous-cell carcinoma; one animal with repeated exposure to 0.06 mg/L showed masses of clear-cell carcinoma having an adenocarcinomatous pattern; and of two animals from a single heavy exposure, one exhibited masses of clear-cell carcinoma having the adenocarcinomatous pattern, and the other had two small papillary bronchial adenomas. No pulmonary tumors were seen in the three surviving controls.

Sunderman and Donnelly (1965) treated male Wistar rats in six groups (three were controls). The exposure groups consisted of the following: (a) 285 animals exposed to 0.6 mg/L of carbonyl for 30 minutes and followed for their lifetimes; (b) 60 animals exposed as in (a), but receiving an injection of "dithiocarb" nickel chelate 15 minutes after exposure; and (c) 64 animals exposed for 30 minutes three times weekly to 0.03 mg/L carbonyl for the remainder of their lifetimes. In the chronic and acute nickel carbonyl exposure groups, three animals of the 80 surviving the 2-year exposure and/or observation period showed pulmonary carcinomas and metastases: one with pulmonary adenocarcinoma, one with anaplastic carcinoma, and one with adenocarcinoma. No pulmonary neoplasms were observed in any of the 44 surviving controls.

Intravenous injection of Sprague-Dawley rats produced malignant tumors at various sites (Lau et al., 1972).

II.A.4. Supporting Data for Carcinogenicity

Hui and Sunderman (1980) found that after exposure of rats to radioactive nickel carbonyl, nickel was bound to the liver and kidney DNA.

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

The low survival rate for both control and treated animals in the studies of Sunderman and coworkers and the intravenous route of exposure in the study by Lau et al. (1972) preclude a quantitative risk estimate.

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

None.

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

Screening-Level Literature Review Findings — A screening-level review conducted by an EPA contractor of the more recent toxicology literature pertinent to the cancer assessment for Nickel carbonyl conducted in November 2001 did not identify any critical new studies. IRIS users who know of important new studies may provide that information to the IRIS Hotline at 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 (internet address).

III. [reserved]

IV. [reserved]

V. [reserved]

VI. Bibliography

Substance Name — Nickel carbonyl

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VI.A. Oral RfD References

None

VI.B. Inhalation RfC References

None

VI.C. Carcinogenicity Assessment References

Hui, G. and F.W. Sunderman. 1980. Effects of nickel compounds on incorporation of thymidine - 3H into DNA in rat liver and kidney. *Carcinogenesis*. 1: 297-304.

Lau, T.J., R.L. Hackett and F.W. Sunderman. 1972. The carcinogenicity of intravenous nickel carbonyl in rats. *Cancer Res*. 32: 2253.

Peto, J., H. Cuckle, R. Doll, C. Hermon and L.G. Morgan. 1984. Respiratory cancer mortality of Welsh nickel refinery workers. *Nickel in the Human Environment: Proceedings of a Joint Symposium, March 1983*. International Agency for Research of Cancer, Lyon, France. IARC Scientific Pub. No. 53. p. 36-46.

Sunderman, F.W. and A.J. Donnelly. 1965. Studies of nickel carcinogenesis metastasizing pulmonary tumors in rats induced by the inhalation of nickel carbonyl. *Am. J. Pathol*. 46: 1027.

Sunderman, F.W., A.J. Donnelly, B. West and J.F. Kincaid. 1959. Nickel poisoning. IX. Carcinogenesis in rats exposed to nickel carbonyl. *Arch. Ind. Health*. 20: 36.

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

VII. Revision History

Substance Name — Nickel carbonyl
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Date	Section	Description
12/03/2002	II.D.2.	Screening-Level Literature Review Findings message has been added.

VIII. Synonyms

Substance Name — Nickel carbonyl
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Last Revised — 09/30/1987

- 13463-39-3
- NICHEL TETRACARBONILE
- Nickel carbonyl
- NICKEL CARBONYLE
- NICKEL TETRACARBONYL
- NICKEL TETRACARBONYLE
- NIKKELTETRACARBONYL
- RCRA WASTE NUMBER P073
- UN 1259