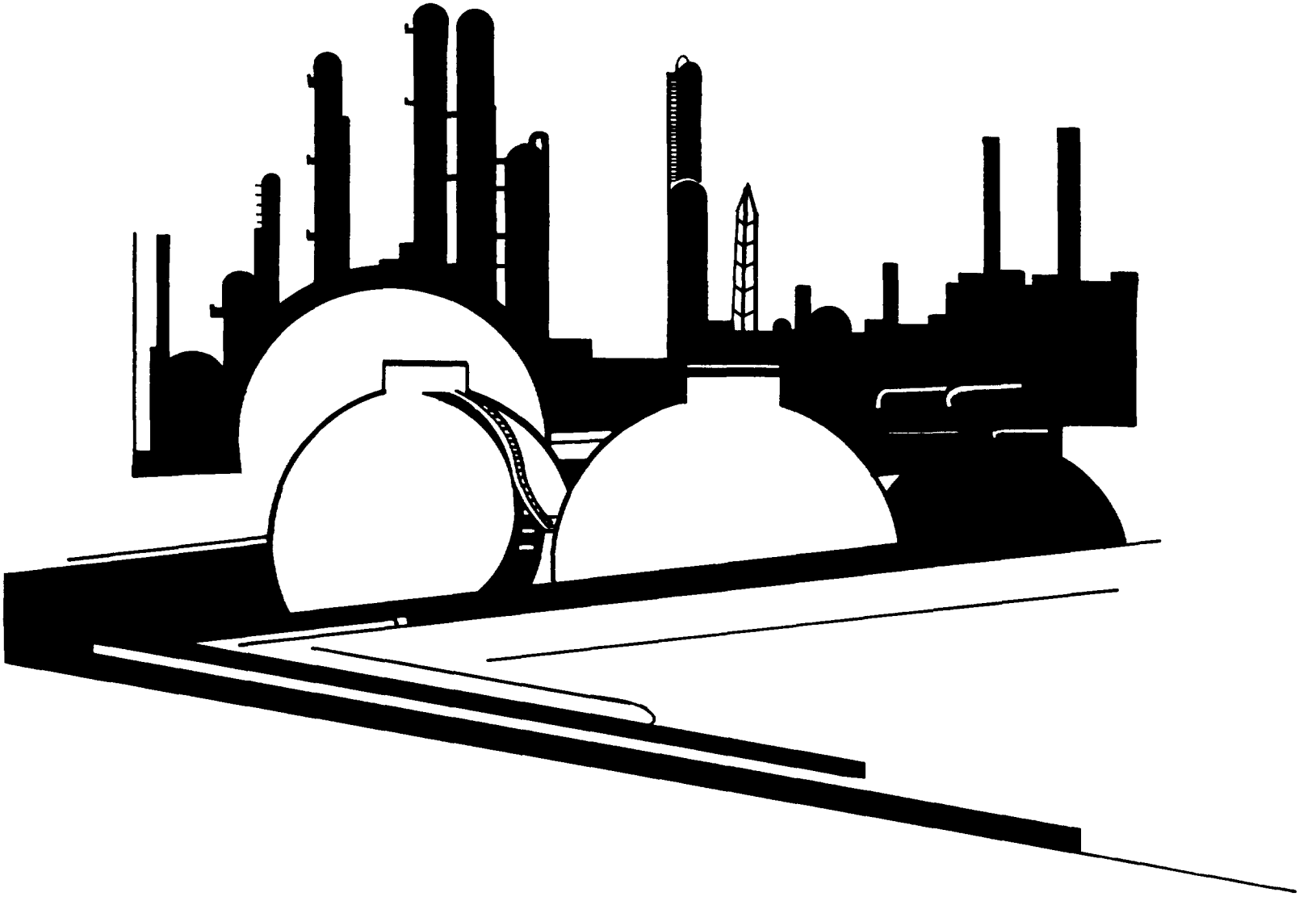
# NIOSH SPECIAL OCCUPATIONAL HAZARD REVIEW AND CONTROL RECOMMENDATIONS FOR NICKEL CARBONYL





U. S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
Public Health Service
Center for Disease Control
National Institute for Occupational Safety and Health

# SPECIAL OCCUPATIONAL HAZARD REVIEW
# AND
# CONTROL RECOMMENDATIONS
# FOR
# NICKEL CARBONYL

prepared by
Jack L. Arthur, M. En.

Department of Health, Education, and Welfare
Public Health Service
Center for Disease Control
National Institute for Occupational Safety and Health
Division of Criteria Documentation and Standards Development

Rockville, Maryland

For sale by the Superintendent of Documents, U.S. Government Printing Office, Washington, D.C. 20402

DHEW (NIOSH) Publication No. 77-184

# PREFACE

The Occupational Safety and Health Act of 1970 emphasizes the need for standards to protect the health and safety of workers exposed to an ever-increasing number of potential hazards in their workplace. Pursuant to the fulfillment of this need, the National Institute for Occupational Safety and Health (NIOSH) has developed a reporting strategy intended to assist employers in providing personal protection for employees from exposure to carcinogenic, mutagenic, and teratogenic substances. This strategy involves the development of Special Occupational Hazard Reviews which serve to support and complement the other major criteria documentation activities of the Institute. It is the intent of a Special Occupational Hazard Review to document, from a health standpoint, the problems associated with a given industrial chemical or process and to recommend the implementation of engineering controls and certain work practices to ameliorate these problems. While Special Occupational Hazard Reviews are not intended to supplant the more comprehensive NIOSH Criteria Documents nor the less comprehensive NIOSH Current Intelligence Bulletins, they are nevertheless prepared in such a way as to be amenable to full regulatory usage if so desired. Dissemination of Special Occupational Hazard Reviews may be accomplished through appropriate trade associations, unions, industries, and members of the scientific community.

John F. Finklea, M.D.

John F. Finklea, M.D.
Director, National Institute for
Occupational Safety and Health

ACKNOWLEDGEMENTS

Norbert P. Page, D.V.M., and Murray L. Cohen, M.P.H. had NIOSH program responsibilities and assisted in the preparation of this document.

The Division review staff for this document consisted of Howard L. McMartin, M.D., (Chairman), J. Henry Wills, Ph.D., Frank L. Mitchell, D.O., Douglas L. Smith, Ph. D., and Jon R. May, Ph.D.

Valuable and constructive comments were also provided by Robert B. O'Connor, M.D., NIOSH consultant in occupational medicine.

## SUMMARY AND CONCLUSIONS

Nickel carbonyl is used in the metallurgy of pure nickel (Mond Process), in nickel-vapor-plating, and in the synthesis of methyl and ethyl acrylate monomers [3]. While NIOSH estimates that no more than 500 US workers are subject to nickel carbonyl exposure from activities directly relating to these industrial operations, this number may increase by an order of magnitude when considering the possible inadvertent formation of nickel carbonyl. Such can occur with the use of nickel catalysts in hydrogenation, in coal gasification, and in petroleum refining.

Nickel carbonyl is an extremely volatile and flammable liquid (igniting spontaneously in air at room temperature) whose toxicity in the vapor form is well documented.

Toxic effects in animals have resulted from inhalation exposures of 17-70 mg nickel carbonyl/cu m (2400-10,000 ppb) for 5-30 minutes and included edema of the lungs and brain and high mortality [5]. Human effects resulting from accidental exposure to nickel carbonyl have included pulmonary edema, interstitial pneumonitis, reduced lung capacity, cardiac irregularities, liver enlargement, and in severe exposure cases, death [26-30].

In animal carcinogenicity studies, rats developed lung tumors from both long-term (inhalation of 30 mg/cu m air (4300 ppb), for 30 minutes, 3 times weekly, for 1 year) and acute (single dose of 600 mg/cu m (86,000 ppb) for 30 minutes) exposure to nickel carbonyl vapor [9,10]. Induction of malignant tumors of several organs has also been reported following

intravenous injections of nickel carbonyl. From an occupational health viewpoint, those occurring following inhalation of nickel carbonyl vapor are considered of greater relevance. The nature of its biochemical interactions may support a carcinogenic potential for nickel carbonyl [14-16]. For many years the increased incidence of lung and nasal cancers occurring in nickel refinery workers was attributed to nickel carbonyl. A later analysis of these workers refuted this association. At the present time human epidemiologic data [32-38] are insufficient to either confirm or deny a causal relationship.

In view of its extreme toxicity from either acute or chronic exposure, nickel carbonyl should be designated as a highly hazardous material and regulated as a carcinogen. After a review of the existing data NIOSH supports the current US standard for nickel carbonyl of 1 ppb which approximates the least detectable level for this substance and does not recommend a change in the environmental level. The 1 ppb standard should protect workers from any carcinogenic potential which nickel carbonyl may have, as well as any of the other adverse health effects associated with nickel carbonyl exposure.

Strict control measures should be developed and enforced in all operations involving the manufacture, use, or handling of nickel carbonyl and in operations where the possibility exists for its inadvertent formation. These measures should include; installation of engineering controls (e.g., ventilation and process enclosures), use of personal protective equipment (e.g., positive pressure respirators), posting of signs which warn of the hazard, conducting medical surveillance, instituting spill-disposal procedures, and recordkeeping. In addition, environmental monitoring of nickel carbonyl work areas should be carried

out. Several methods for detecting nickel carbonyl in the sub-ppb to ppm range have been developed, including two instrumental methods (Fourier Transform Infrared Spectroscopy and plasma chromatography) and one wet chemical method (colorimetric).

CONTENTS

PART 1

# HAZARD DOCUMENTATION AND CONTROL RECOMMENDATIONS

The current U.S. standard for nickel carbonyl vapor is 1 part per billion (ppb). Finland, Japan, Poland, and Sweden have also adopted a 1 ppb standard. The USSR and Rumania have lower standards of .07 and .70 ppb, respectively, while the Federal Republic of Germany and Yugoslavia both have a 100 ppb standard.

The 1 ppb U.S. standard was adopted in 1968 from the Threshold Limit Values (TLV) as established by the American Conference of Governmental Industrial Hygienists (ACGIH). It is based on early epidemiologic studies which indicated a high incidence of lung and nasal cancers in Welsh refinery workers using the nickel carbonyl process. In 1975 the ACGIH made a proposal to raise their TLV to 50 ppb after an evaluation of the existing data suggested that substances other than nickel carbonyl may have been the etiologic agents involved in the Welsh refineries. These etiologic agents are discussed in the "NIOSH Criteria for a Recommended Standard ... Occupational Exposure to Inorganic Nickel." Because of the controversy surrounding the issue of nickel carbonyl carcinogenicity and because nickel carbonyl is sufficiently dissimilar from the compounds covered in the Nickel Criteria Document, it was decided to evaluate the two occupational hazards separately. The divergence of established national standards indicates that the carcinogenic potential of nickel carbonyl and the degree to which this substance can be monitored and controlled may be debatable at the international level.

The following is a review of the known hazards of nickel carbonyl. The toxic nature and the possibility of exposure to nickel carbonyl vapor

in certain occupational environments serve as the basis for including control recommendations. The information and recommendations will aid the U.S. Department of Labor, industrial hygienist, physician, and employer, in protecting the worker from the hazards of nickel carbonyl, and will aid the worker in recognizing the hazard so that it can be avoided and/or protected against.

## I. PROPERTIES

### A. Identification

1. synonyms: nickel tetracarbonyl
2. CAS number: 13463-39-3
3. formula: Ni(CO)4
4. molecular weight: 170.75

### B. Physical/Chemical

1. appearance and odor: pale yellow, volatile liquid with weak, soot-like odor detectable between 500-3000 ppb
2. boiling point: 43.2 C (at 760 mm Hg)
3. melting point: -25 C
4. specific gravity: 1.32
5. vapor density: 5.9 (air=1)
6. vapor pressure at 20 C: 315 mm Hg
7. solubility: slightly soluble in water; miscible with ethanol, benzene, chloroform, acetone, and carbon tetrachloride
8. reactivity: reacts slowly with non-oxidizing acids such as hydrochloric acid and sulfuric acid and vigorously with nitric acid and the halogens to form the corresponding bivalent nickel salts; reacts with oxygen forming nickel oxide in dry air and nickel carbonates with prolonged exposure to moist air; in the presence of water, nickel carbonyl reacts with nitric oxide to form nickel nitrosylhydroxide [1]. Decay of nickel carbonyl in air has been studied in the ppb range and has been found to proceed at a simple exponential rate with a half life of about 30 minutes [2].

## II. COMMON OPERATIONS, USES, AND OCCURRENCE

Nickel carbonyl is used in several industrial processes; in the metallurgy of pure nickel (Mond Process), in nickel-vapor-plating, and in the synthesis of methyl and ethyl acrylate monomers [3]. Nickel carbonyl

was at one time used as a catalyst in the petroleum industry. Due to its toxicity, however, its use in this industry has greatly decreased in recent years [4], (See Appendix A for process descriptions). Inadvertent formation of nickel carbonyl is also possible [3]. Conditions favorable for its formation occur if carbon monoxide under high partial pressure contacts an active form of nickel (ie, finely divided nickel) in a temperature range of 50-150 C (written communication, George Buehler, 1976).

NIOSH estimates that no more than 500 workers are subject to nickel carbonyl exposure through current U.S. industrial operations involving the manufacture, use, or handling of this substance. However, this number becomes an order of magnitude larger when considering occupational activities which may lead to the inadvertant formation of nickel carbonyl such as the use of nickel catalysts in hydrogenation, in coal gasification, and in petroleum refining.

## III. BIOLOGICAL EFFECTS OF EXPOSURE

### A. Toxic Effects in Animals

Toxic effects have been observed in animals when exposed to nickel carbonyl by inhalation. Effects noted most often were edema of the lungs and brain.

In 1908, Armit [5] detailed the reaction of and tissue changes in rabbits, cats, and dogs after exposing them to atmospheres containing varying percentages of nickel carbonyl ranging from 0.013-0.075 volume % (130-750 ppb)* for 31-82 minutes.

---

* For comparison with the U.S. standard, all quantities of nickel carbonyl in the text have been converted to ppb and placed in parentheses beside the original value.

Macroscopically observed changes included congestion of all organs, but especially of the lungs, and to a lesser extent of the brain. When death occurred within 24 hours of exposure, the lungs were hyperemic, and contained both punctate and large hemorrhages. When death occurred during the second day, the hyperemia was intense and the lungs contained blood-stained fluid in addition to numerous hemorrhages pervading the entire organ. When death occurred during the third day, extensive sanguinous consolidation and scattered emphysema were noted. Death on the fourth and fifth days showed patchy hemorrhages, and consolidation over the rest of the lungs. Microscopic examination of the lungs revealed that early lesions were in the endothelial lining of the blood vessels and in the interalveolar tissues. The lesions progressed to involve both the alveolar walls and spaces. When the blood vessels lost fluid and the walls ruptured, edema and consolidation followed. Finally, typical broncho-pneumonia developed. The brains of the animals were hemorrhagic and edematous.

In 1951, Barnes and Denz [6] exposed rats to nickel carbonyl at concentrations ranging from 17-70 milligrams per cubic meter of air (mg/cu m)(2400-10,000 ppb) for 5-30 minutes and rabbits at concentrations ranging from 10-32 mg/cu m (1400-4600 ppb) for 10-30 minutes. The animals were killed at intervals up to several months after exposure. Mortality and the effects seen upon gross and microscopic examination were very similar to those described by Armit [5]. In addition, they described the presence of an early compensatory fibrogenic lung reaction in those animals which were killed between one and four months after exposure and a complete resolution of that reaction in animals which were killed a year or more after exposure. Also, they found that only 5 to 10% of the calculated amount of

nickel inhaled by the animals was retained in the lungs, suggesting rapid relocation and excretion of that which was absorbed.

Sunderman and Selin [7] investigated the metabolism of nickel carbonyl. Radioactive nickel carbonyl was administered to 78 adult male rats by either intravenous (IV) injection or inhalation. The LD50 value of 5$\mu$L/100g body weight, as determined by Hackett and Sunderman [8], was used. Determination of radioactive nickel in urine, feces, and expired air revealed that 38.4% of the injected dose was exhaled as nickel carbonyl, 31.2% was excreted in the urine, and 2.4% was excreted in the feces. A total of 66.2% of the injected dose was excreted within 24 hours following exposure. Further excretion of nickel carbonyl was extremely slow and reached a maximum of 72.0% of the injected dose at the end of the fourth day. Tissue analyses of rats killed 24 hours after injection revealed 7.3% of the dose in muscle and fat, 5.5% in bone and connective tissue, 4.7% in viscera and blood, and 0.2% in the brain and spinal cord. According to the authors, excretion values obtained after inhalation were not practicable in that there was significant fecal and exhalant contamination as a result of nickel carbonyl adsorbed onto the animals' fur during exposure.

B. Carcinogenicity in Animals

Three animal studies [9-11] have been conducted to assess the carcinogenic potential of nickel carbonyl. Two studies were conducted by inhalation and one by intravenous injection using either multiple or single exposures. Details of the experimental design and pertinent results are presented in Table I.

In the first two studies [9,10] Sunderman and his coworkers observed a single pulmonary carcinoma in each of six groups of exposed rats. A total of six lung cancers occurred in 157 nickel carbonyl-exposed rats that

survived at least 12 months. No lung cancers were observed in 82 controls. This difference is of only marginal statistical significance (P=.073). Spontaneously occurring lung cancer is extremely rare in rats and according to Sunderman and Donnelly [10] none had been observed in their 12-year series of experiments. Comparing the incidence of lung cancer in nickel carbonyl-exposed rats to this much larger, historical control population would increase the level of significance.

These six lung cancers consisted of 2 squamous cell carcinomas, 2 adenocarcinomas, and 2 anaplastic carcinomas, all found between 24-27 months after initial exposure. In addition, lung cancers occurred equally in rats subjected to either a large single exposure or repeated exposures at much lower levels for a long period of time. The major sites of metastases were the kidneys, liver, and heart [10].

A wide variety of tumors other than pulmonary cancers was observed in both nickel carbonyl-exposed and control groups in the second Sunderman study [10]. While the total incidence of tumors in the nickel carbonyl-exposed rats was greater than that in the controls, 50% vs 33%, a causal relationship was considered doubtful [10]. There were no tumors other than the lung cancers reported in the Sunderman et al. [9] study. However, the number of animals that survived to 24 months was very small and the thoroughness of the pathology examination could not be ascertained from the report.

In the studies of Lau et al. [11], nickel carbonyl was injected intravenously into the tail vein of Sprague-Dawley rats, either as a single injection or in six injections administered 2-4 weeks apart. The total dose administered to the multiple - dose group was approximately 2 1/2 times that of the single-injection group.

For the single-injected group, there was little overall difference in the survival or in the incidences of benign tumors of treated and control animals. The incidence of malignant tumors was slightly increased over the controls, 8.3% vs 4.3%. Rats administered multiple injections had a greater increase, 15% vs 4.3%, in the overall incidence of malignant tumors which was of statistical significance ($P<0.05$). Other than two pulmonary lymphomas, no malignant tumors were observed in the controls. Considering only non-lymphomatous malignant tumors, the difference between the exposed and control groups is of greater statistical significance ($P<0.02$). The tumors originated in many organs and most were observed to have metastasized.

In an additional study, not tabulated in Table I, Sanina [12] reported the induction of malignant tumors in various organs including the uterus, ovaries and mammary glands in rats exposed by inhalation for two hours, once every two weeks, at a concentration of 0.0005 - 0.0017 mg/L (70-240 ppb). Tumors were found during examination after having killed the animals at various time intervals up to six months. While the report indicated no tumors in the controls, the total number of exposed animals was small (20) and no data were given on the incidence of each type of tumor or on the time of killing. Due to its lack of details, very little information can be derived from this report.

Thus, the carcinogenicity of nickel carbonyl has been demonstrated in at least three different experiments, by two routes of exposure (inhalation and intravenous injection) and in different organ systems. Perhaps, the most pertinent finding is that of lung cancers in the inhalation studies, closely simulating the most probable route of occupational exposure to this compound. The extent of carcinogen testing has been limited to only

one species, the rat. While it is difficult to determine whether other species, and indeed man, would show a similar response to that of the rat, Laskin and Sellakumar [13] concluded that the common laboratory rat most clearly meets the requirements of the ideal animal model for respiratory carcinogenesis. Their conclusion was based upon the induction of tumors in rats which are similar in morphology and origin to those of man, and the extreme rarity with which these tumors spontaneously occur. In addition, the inhalation and retention kinetics of inhaled particulates and vapors of the rat resembles that of man moreso than do those of the smaller laboratory rodents.

While the empirical results of the animal carcinogenesis tests are considered to be only reasonably conclusive, the interactions of nickel carbonyl with DNA and RNA may support the conclusion that nickel carbonyl has a carcinogenic potential.

The mechanism whereby nickel carbonyl may produce cancer has not been established. Studies have confirmed intracellular biochemical activity possibly related to carcinogenic activity. Beach and Sunderman [14] have conducted several studies demonstrating that nickel carbonyl has an inhibitory effect upon hepatic RNA synthesis. The action appears not to be directly on the DNA-dependent RNA polymerase but to depend, rather, on possible combination with an unidentified intermediate [15]. The inhibition is not related to impaired transport of RNA precursors across the nuclear membrane.

Nickel carbonyl may also function as a co-carcinogen in the carcinogenicity of 3,4- benzpyrene, as it inhibits the induction of benzpyrene hydroxylase. This enzyme transforms 3,4-benzypyrene into its non-carcinogenic hydroxylated derivatives [16].

Table I. Summary of Experiments to Assess Carcinogenicity of Ni(CO)4

| | Exposure Regimen | Number Initially on Test |
|---|---|---|
| I. RATS<br>Male Wistar (Sunderman, et al, 1959) [9] | Route: Inhalation<br>Observation Period: 2 1/2 years<br>Exposure Period: 30 minutes | |
| | A. 0.03 mg/L (4300 ppb) 3x weekly - 1 year | 64 |
| | B. 0.06 mg/L (8600 ppb) 3x weekly - 1 year | 32 |
| | C. 0.25 mg/L (3600 ppb) single exposure | 80 |
| | D. Controls (vehicle) for A&B | 41 |
| II. RATS<br>Male Wistar (Sunderman and Donnelly, 1965), [10] | Route: Inhalation<br>Observation Period: 3 years<br>Exposure Period: 30 minutes | |
| | A. 0.6 mg/L (86,000 ppb) single exposure | 285[b] |
| | B. 0.6 mg/L (86,000 ppb) single exposure & Dithiocarb, 50 mg/kg, subcutaneous, 15 minutes after Ni(CO)4 exposure | 60 |
| | C. 0.03 mg/L (4300 ppb) 3x weekly - life | 64 |
| | D. Controls (vehicle) for A | 19 |
| | E. Controls (vehicle + Dithiocarb for B) | 19 |
| | F. Controls (vehicle) for C | 32 |

| Survival Data | | Malignant Lung Tumors | Other Malignant Tumors[a] |
|---|---|---|---|
| >12mos | >24mos | | |
| 16 | 5 | 1-squamous cell carcinoma | none observed |
| 4 | 1 | 1-squamous cell carcinoma | none observed |
| 8 | 3 | 1-anaplastic carcinoma | none observed |
| 14 | 3 | none observed | none observed |
| 63[c] | 35[c] | 1-adenocarcinoma | 14 total. lymphomas(9);myel. leukemia(1);fibrosarcoma(1), subcut; osteosarcoma(1); Leydig cell carcinoma(1); sq-carcinoma(1) of skin |
| 58 | 27 | 1-anaplastic | 16 total. lymphomas(8); fibrosarcomas(4); subcut. carcinomas(2) of skin; sarcomas(2), origin unknown |
| 48 | 8 | 1-adenocarcinoma | 6 total. lymphomas(5); sq-carcinoma(1) in salivary gland and adrenal gland |
| 19 | 22 | none observed | 5 total. lymphomas(3); angiosarcomas(1);sq-carcinoma(1) of skin |
| 19 | | none observed | 6 total. lymphomas(4); fibrosarcoma(1)intra-abdominal;adenocarcinoma(1) of thyroid |
| 30 | 22 | none observed | 4 total. lymphoma(1);myel. leukemia(1);fibrosarcoma(1) intra-abdominal; adenocarcinoma(1) of pancreas |

Table I. Summary of Experiments to Assess Carcinogenicity of Ni(CO)4 (cont'd)

| | Exposure Regimen | Number Initially on Test | Survival Data | Malignant Lung Tumors | Other Malignant Tumors |
|---|---|---|---|---|---|
| III. RATS | Route: Intravenous Injection<br>Observation Period: Until death | | Median Age at Death (Months)[d] | | |
| Male & Female Sprague-Dawley (Lau, et al.,1972) [11] | A. 2.2 mg/100 gm b.wt. - single exposure | 26 M<br>46 F | 22<br>23 | 2-lymphomas<br>2-lymphomas | 7 total. fibrosarcomas(3) of orbit, pinna and neck; undif. sarcoma(1) of lung; hemangioendothelioma(1) of s.c. tissue; undif. leukemia(1);carcinoma(1) of kidney |
| | B. 0.9 mg/100 gm body wt. - 6 exposures at 2-4 week intervals | 61 M<br>60 F | 21<br>24 | 3-lymphomas<br>2-lymphomas | 7 total. undif. sarcomas(5) of pleura, liver, pancreas, uterus and abdominal wall; carcinomas(2) of liver and breast |
| | C. Controls (vehicle) | 15 M<br>32 F | 24<br>24 | none observed<br>2-lymphomas | none observed<br>none observed |

a. Benign tumors occurred in both Ni(CO)4-exposed and control groups at approximately the same ratio and type

b. Only 71 survived first 3 weeks

c. Number calculated from survival graphs and percentages provided in referenced reports

d. No other data on survival provided

C. Toxic Effects in Humans

In view of its volatility and its general use in the vapor state, the major occupational exposure to nickel carbonyl is by inhalation. Skin absorption [17] and ingestion [18] also may be routes of entry into the body.

The initial signs and symptoms resulting from exposure to toxic amounts of nickel carbonyl have been most often described as dyspnea, fatigue, nausea, and headache [19-21]. These signs and symptoms, except in the most severe exposures, usually ceased in the first 24 hours following exposure and the exposed persons appeared to have recovered [21,22]. Delayed signs and symptoms usually develop gradually during the 2-10 day period following nickel carbonyl exposure and may include dyspnea, coughing, muscular weakness, excessive sweating, substernal pain, elevated temperature, and death [19-24]. Kincaid et al. [25] have suggested 3 ppm (3000 ppb) for 30 minutes (approximately one tenth of the LD50 value for rats) as the exposure limit of nickel carbonyl below which no serious acute symptoms in man will occur.

Scientific reports on the human pathologic changes induced by nickel carbonyl have come from acute, work-exposure cases. Since these exposures were accidental in nature, no exposure-level measurements were obtained. Upon medical examination of 125 victims in various exposure cases and performance of autopsies on two of these victims, respiratory damage (ie, lung edema, bronchial pneumonia, interstitial pneumonitis, bronchitis, and reduced pulmonary capacity) was found to be the most frequent significant manifestation [19, 20, 22, 26-30]. In the two fatal-exposure cases, the investigators, Brandes [27] in 1934 and Jones [30] in 1973 reported finding

edema of the brain in addition to damage of the lungs in the decedents. A report was published in Lancet [23] in 1903 concerning two other deaths associated with exposure to nickel carbonyl but the description of pathologic changes found in the bodies of the victims is of questionable accuracy.

Cardiac irregularities [28], liver enlargement [28], and spleen enlargement [31] are some of the other significant human health effects of nickel carbonyl exposure reported in the literature. A case of an allergic reaction known as Loffler's Syndrome was attributed to nickel carbonyl exposure by Sunderman and Sunderman [26].

D. Epidemiology Studies of Cancer in Humans

In 1939, Hill [32] observed an apparent increase in lung and nasal cavity cancers occurring in Mond nickel refinery workers in South Wales. Morgan [33] and Doll et al. [34] conducted followup studies on these same workers and confirmed Hill's earlier findings.

Of 482 workers, 113 died of lung cancer and 39 of nasal cancer. Of these, all nasal cancers and all but 8 lung cancers occurred in workers employed prior to 1925. The risk of developing lung cancer for those employed prior to 1925 was 5-10 times that expected and that for nasal cancer, 100-900 times that expected [32-34]. For those employed after 1925, the observed incidences approximated the national averages, perhaps indicating the reduction or elimination of a causal factor.

Based upon the observations of Hill [32] the British government attributed nickel carbonyl as the causative agent for development of these cancers [34].

Morgan [33] and Doll et al. [34] refuted an association with exposure to nickel carbonyl and believed that metal dust, copper sulfate, and/or arsenic were the more likely causative agents. This conclusion was based upon the following considerations; (1) although no changes had been made in the nickel carbonyl process for 50 years prior to 1958, the occurrence of lung and nasal cancers was confined exclusively to those workers employed prior to 1925, (2) very few cases of acute toxicity attributable to nickel carbonyl inhalation were recorded, indicating that substantial exposure to the vapor of nickel carbonyl was unlikely, (3) between 1920 and 1925, major changes were made in the refinery that resulted in less dust, use of masks to reduce dust inhalation, and use of arsenic-free sulfuric acid, and (4) studies of the personnel in nickel refineries not using the nickel carbonyl process also indicated an increased risk to develop cancers of the lungs and nasal sinuses [35-38].

Additionally, Doll et al. [34] have speculated that differences in cigarette smoking might help to account for the difference between the incidences of cancer of the lungs in the Welsh workers hired before and after 1925.

From a review of the epidemiologic data it is not possible to confirm or deny an association of lung cancer with nickel carbonyl exposure .

E. Summary of Carcinogenicity Data

While the animal data are suggestive of the carcinogenic potential of nickel carbonyl, the human epidemiologic data are insufficient to support or deny a causal relationship. Animal studies suggest that cancer may not be confined solely to the respiratory tract, but involve other organ systems as well. They also indicate that the route of exposure may modify the carcinogenic response. Cancers of the respiratory system were observed following inhalation exposure whereas, tumors of other organ systems were reported subsequent to IV injection. Further, animal studies have elucidated cellular biochemical activity which may be compatible with generally accepted mechanisms for carcinogenicity.

## IV. HAZARDS: PRECAUTIONS, PREVENTION, AND EMERGENCY PROCEDURES

A. Fire, Explosion, and Reactivity Data

Nickel carbonyl vapor (2% in air by volume or 20,000 ppm) can ignite spontaneously at room temperature [18]. Nickel carbonyl liquid can explode if heated rapidly to around 60 degrees C or above in the presence of air [39]. Because of its extreme flammability, the following safeguards should be taken in nickel carbonyl work areas:

1. Nickel carbonyl should be stored in tightly closed containers in a cool, well ventilated area, away from heat and such oxidizers as nitric acid and chlorine

2. Nickel carbonyl should be transported in steel bottles under a protective (carbon dioxide) atmosphere [40]

3. Such sources of ignition as lighted devices for smoking tobacco and open flames should be prohibited wherever nickel carbonyl is handled, used, or stored

4. Where a fan is located in ductwork in which nickel carbonyl is present in a concentration greater than 5,000 ppm, the fan blades and the throat should be made of a nonsparking material

5. Foam, carbon dioxide, or dry-chemical fire extinguishers should be readily accessible (A solid stream of water will scatter and spread the fire)

B. Spill, Leak, and Disposal Procedures

If nickel carbonyl is spilled or leaks, the following steps should be immediately taken:

1. Evacuate all but those persons necessary to clean-up activities

2. Remove all ignition sources

3. Ventilate area of spill or leak

4. For small quantities, absorb on paper towels, evaporate in a safe place (such as a fume hood), allow sufficient time for vapor to completely clear hood ductwork, and then burn the paper [39,41]

5. Large quantities should be collected and atomized in a suitable combustion chamber equipped with an appropriate effluent gas-cleaning device

Nickel carbonyl should not be allowed to enter a confined space, such as a sewer, because of its toxicity and the possibility of an explosion. Further, in the clean-up of leaks or spills and maintenance or repair operations on contaminated systems or equipment, authorized personnel should be required to wear air-supplied respirators (see Section V.C.).

C. Medical Surveillance

Medical surveillance should be made available to all persons subject to occupational exposure to nickel carbonyl as described below.

1. Preplacement medical examinations should include at least:

   a. Comprehensive medical and work histories with special emphasis directed to symptoms related to the lungs and upper respiratory tract

b. A physical examination

c. Pulmonary function tests

d. Analysis for urinary nickel content

e. 14" x 17" posterior-anterior chest X-ray

f. A judgment of workers' ability to use positive pressure respirators

2. Periodic examinations should be made available at least on an annual basis. These examinations should include at least:

a. Interim medical and work histories

b. A physical examination as described above for the preplacement examination

3. In addition, samples of urine should be analyzed for nickel content on a monthly basis.

D. Sanitation Practices

Employers should institute appropriate sanitation practices which include the following:

1. Clothing which becomes wet with liquid nickel carbonyl should be removed as soon as possible and placed in vapor-tight, sealed containers for storage until it can be discarded (into decontamination furnace or decontaminated for reuse by laundering, steaming, or comparably effective treatment)

2. Persons involved with the handling and/or treatment of contaminated clothing should be informed of the hazard and should take appropriate precautions (e.g., wear respirators)

3. Personal items (e.g., watches, wallets, etc.) should not be permitted in nickel carbonyl work areas for their usefulness following any needed decontamination treatment may be diminished

4. Employees whose skin becomes wet with nickel carbonyl should immediately wash or shower to remove any nickel carbonyl from the skin (if possible, auxiliary, self-contained breathing apparatus should be left on while washing, to protect against vapor)

5. Employees who handle nickel carbonyl should wash their hands thoroughly before eating, smoking, or using toilet facilities

6. Employees should not eat or smoke in nickel carbonyl work areas

E. Informing Employees of Hazards

Each employee, prior to being permitted to work in a nickel carbonyl area, should receive instruction and training on:

1. The nature of the potential carcinogenic hazard and the toxicity of nickel carbonyl, including recognition of the signs and symptoms of acute exposure and the urgency of reporting these immediately to designated health personnel

2. The specific nature of the operation involving nickel carbonyl which could result in exposure

3. The purpose for and operation of respirator equipment

4. The purpose for and application of decontamination practices

5. The purpose for and significance of emergency practices and procedures, and the employees' specific role in such activities

6. The recognition and evaluation of conditions and situations which may result in the release of nickel carbonyl

7. The purpose for and nature of medical examinations

## V. CONTROL INFORMATION

A. Posting of Signs

Entrances to areas where nickel carbonyl is manufactured, used, or stored should be posted with signs indicating:

DANGER!
NICKEL CARBONYL AREA
AUTHORIZED PERSONNEL ONLY
CANCER SUSPECT AGENT

Emphasis in any sign should be placed on the possible danger and the restricted nature of the area. In addition, containers of nickel carbonyl should be labelled: Nickel Carbonyl, Flammable Liquid, Poison.

B. Protective Clothing

Absorption of nickel carbonyl through the skin has not been demonstrated but has been suggested [12]. Therefore, the necessity for the use of protective gloves and impervious [e.g., rubber] clothing is

uncertain. However, in view of nickel carbonyl's volatility and the major threat of exposure to its vapor, the use of protective clothing is not suggested. Appropriate sanitation practices should eliminate any possible hazard from skin contact.

C. Respiratory Protection

In addition to engineering control recommendations outlined in Section D. below, all personnel upon entering and during the entire time period spent in nickel carbonyl areas should wear a supplied-air respirator with a full facepiece operated in pressure-demand or other positive pressure or continuous flow mode. An auxiliary self-contained breathing apparatus operated in pressure-demand or other positive pressure mode should be readily accessible in the event that emergency conditions warrant extended mobility. Respirators should comply with the standards jointly approved by the National Institute for Occupational Safety and Health and the Mining Enforcement and Safety Administration (formerly Bureau of Mines) as specificed under the provisions of 30 CFR II.

D. Engineering and Other Control Technology

Areas where nickel carbonyl is manufactured, used, or stored, should be isolated from all other process areas. In any event, regulated areas, except for outdoor systems, should be maintained under pressure, negative with respect to non-regulated areas. In order to accomplish this, each nickel carbonyl operation should be provided with continuous local exhaust ventilation so that air movement is always from nonregulated to regulated areas. Where a fan is used to affect such air movement, the fan blades and

throat should be made of a nonsparking material. Exhaust air should not be discharged to regulated areas, nonregulated areas or the external environment unless decontaminated. This may be accomplished by discharging exhaust air directly to the fire box of a decontamination furnace, with subsequent discharge of this air to the environment. A portable suction-vent system is recommended so that in the event of a localized leakage of process gas into the regulated area, a hood and suction hose could be placed near the leak for direct removal of the process gas.

Laboratory work involving the use of nickel carbonyl should adhere to the same ventilation and decontamination strategies as stated above. All work should be done under laboratory hoods and only the amount of nickel carbonyl needed for that day's work should be at hand. There should be no connection between the regulated laboratory areas and nonregulated areas through the ventilation system.

E. Confined Spaces

Entry into such confined spaces as tanks, pits, process vessels, and trenches should be restricted to authorized personnel only and the following precautionary measures should be instituted:

1. Confined spaces which have contained nickel carbonyl should be inspected and tested for oxygen deficiency, nickel carbonyl, and other contaminants and should be thoroughly ventilated, cleaned, neutralized or washed, and then retested for nickel carbonyl and oxygen prior to and during entry and occupation.
2. Possible entrance of nickel carbonyl into the confined space while work is in progress should be prevented by positive means (e.g., forced-air ventilation of closed spaces during repair of leaks or

equipment maintenance; securing intake valves or disconnecting intake lines).

3. Individuals entering confined spaces where they may possibly be exposed to nickel carbonyl should be equipped with the respiratory protective equipment outlined in Section V.C. of this document. Each individual should also wear a suitable harness with a lifeline tended by another employee outside the space who should also be equipped with the necessary protective equipment, including the aforementioned respiratory apparatus. Communications (visual, voice, signal line, telephone, radio, or other suitable means) should be maintained by the standby person with the employee inside the enclosed space.

## VI. RECORDKEEPING AND AVAILABILITY OF RECORDS

The employer should keep accurate records on the following:

A. All measurements taken to determine employee exposure to nickel carbonyl, including:

1. Date of measurement
2. Operations being monitored
3. Sampling and analytical method used
4. Number, duration, and results of samples taken
5. Name and airborne exposure concentrations of employees in monitored areas

(records to be replaced on a yearly basis)

B. Measurements demonstrating the effectiveness of mechanical ventilation (e.g., air velocity, static pressure, or air volume), including:

1. Date of measurement
2. Type of measurement taken

3. Result of measurement

(records to be replaced on yearly basis)

C. Employee medical surveillance, including:

1. Name of employee

2. All information obtained from medical examinations which is pertinent to nickel carbonyl exposure

3. Any employee medical complaints relative to exposure to nickel carbonyl

4. Any treatment for exposure to nickel carbonyl and the results of that treatment

All of the aforementioned records should be made available upon request to authorized representatives of the Assistant Secretary of Labor for Occupational Safety and Health and the Director of the National Institute for Occupational Safety and Health. All employees or former employees should have access to the exposure measurement records which indicate their own exposure to nickel carbonyl. Employee medical records should be available upon written request to a physician designated by the employee or former employee. Records should be maintained for the duration of the workers' employment and for 40 years following the termination of their employment.

## VII. SAMPLING AND ANALYTICAL METHODS

No report describing the equipment and methods for continuous personal monitoring of nickel carbonyl was found in the literature. Air sampling for nickel carbonyl is therefore accomplished by an area-monitoring method and, as such, careful attention to the collection points is necessary to ensure a representative sample.

Non-sophisticated instruments and methods have been developed for detecting nickel carbonyl leaks. The color change of a butane flame in the presence of nickel carbonyl has been used for leak testing with a

reported sensitivity of 1-2 ppm (1000-2000 ppb) [42]. A Draeger tube [43] with a sensitivity of 50 ppb and a "Sniffer" [42], with a detection range of 4-70 ppm (4000-70,000 ppb), have also been used.

Three methods have received general acceptance for analyzing ambient levels of nickel carbonyl in the sub-ppb to ppm range, supporting the U.S. standard of 1 ppb as approximately the least detectable level. Two of these methods are instrumental and one is chemical.

The first of the two instrumental methods, Fourier Transform Infrared Absorption Spectroscopy (FTIR), has been used to continuously monitor low levels of nickel carbonyl in the ambient air [42]. A Fourier Transform Michelson Interferometer provided resolution and a 42 mm path-length cell was adequate to obtain a limit of detection of 0.2 ppb, with a precision of $\pm$ 0.2 ppb and an accuracy of $\pm$ 0.5 ppb at the 1.0 ppb level. A thousand-fold excess of carbon monoxide did not interfere in the measurement of 75.0 ppb of nickel carbonyl.

The second generally accepted instrumental method for continuous monitoring of nickel carbonyl is plasma chromatography. The plasma chromatograph has a detection range of 0.2-2.0 ppb [42]. Both the FTIR and the plasma chromatograph are commercially available.

A third instrumental method which is not commercially available has been developed by Stedman and Tammara [2]. They have demonstrated the chemilumunescent detection of nickel carbonyl in air using a reaction with oxygen/ozone and purified CO. Th detection limit of their prototype detector is 0.01 ppb. Since their original system was conceived, a portable detector has been built which has a response time of 3-5 seconds, with about a 1.0 ppb detection limit (written communication, David A. Tammaro, 1976).

In analyses performed in the field, plasma chromatography and FTIR have been superior to chemical methods for area monitoring of nickel carbonyl at the 1 ppb level [42]. While the major users of nickel carbonyl have been innovative in the development of these superior instrumental methods of analysis, their cost may be prohibitive to the short-term or intermittent user of nickel carbonyl. Only for this reason should the following chemical method be used as an alternative.

The chemical method [42] suggested is a modification of the colorimetric one developed by Brief et al. [44].

In general, an air sample containing nickel carbonyl is bubbled through an alcoholic-iodine solution. The entire bubbler solution is dried and dissolved in dilute acid, this solution is neutralized and alpha-furildioxime is added to form a chloroform-extractable complex with nickel. The absorbance at 425 nanometers (nm) is determined and compared to the absorbance of standards.

The detection limit of nickel carbonyl is in the sub-ppb to ppm range. The specific materials and methods used to carry-out this analysis are as follows:

Apparatus

Colorimeter and 1-cm cuvettes
Air sampler
Gas washing bottle, 125 ml, with extra coarse fritted bubbler tube
Hot plate
500 ml Erlenmeyer flasks

Volumetric flasks, pipets, separatory funnels

Reagents

Doubly distilled or deionized water
Alcoholic iodine, 1% (10 g iodine in 990 g isopropyl alcohol)
3% HCL (83 ml of stock acid diluted to 1 liter with deionized water)
Alpha-furildioxime, 1% (1 g alpha-furildioxime

in 99 g of 50:50 w/w ethanol/water)
NaOH, 20% aqueous
Ammonium hydroxide, concentrated
Phenolphthalein, 1% in alcohol
Chloroform
Standard nickel solution (50 @g Ni/ml -
powdered nickel, 50 mg, is dissolved in 10 ml
of 1:1 nitric acid and brought up to volume
in a 1 liter volumetric flask)

Procedure

1. Cleaning of equipment

New glassware should be cleaned by soaking it for 24 hours in 5% nitric acid. Rinse thoroughly with warm tap water and then with doubly distilled water. After glassware is used, wash it first in detergent and rinse with tap water. Then soak it in 5% nitric acid for 1 hour, rinse it thoroughly with doubly distilled water, and allow it to dry. Use plastic containers for washing and do not handle the glassware without gloves which are impervious to sweat.

2. Collection of samples

The air sample is bubbled through 80-100 ml of alcoholic-iodine solution. A 0.8 micron millipore filter is placed in front of the scrubber to exclude nickel particulates. For long collection times, the scrubbing liquid volume may be replenished with isopropyl alcohol. The sampling rate is measured at the start and end of the sample period, and the average of the two rates is used to calculate the volume of air sampled. Sampling times usually range from 6-24 hours.

3. Analysis of samples

a. Prepare at least 3 standard nickel solutions in 3% HCL to cover the range of the analysis (generally 1 to 3 $\mu$g Ni)

b. Quantitatively transfer the nickel carbonyl sample from the collector to a 500 ml Erlenmeyer flask

c. Prepare a reagent "blank" of alcoholic-iodine in isopropyl alcohol

d. Place the sample and the blank on a hot plate in a fume hood and heat to dryness and expulsion of all iodine vapor

e. Cool and dissolve the sample in 10 ml of 3% HCL. Handle the blank similarly

f. Quantitatively transfer the HCL solutions to small separatory funnels. Also place 10 ml of each Ni standard in individual separatory funnels

g. To each sample, including the standards and the "blank", add 2 drops of phenolphthalein and 6 drops of ammonium hydroxide.

h. Titrate the contents of each funnel to the phenolphthalein end-point with 20% NaOH and add three drops in excess

i. Add 3 ml of alpha-furildioxime and 10 ml of chloroform to each separatory funnel

j. Shake each funnel and its contents for 1 minute and allow chloroform layer to separate

k. Draw off the chloroform layer, place in a cuvette, and immediately cover the container

l. Measure the absorbance at 425 nanometers for each sample and subtract the reagent blank

4. Calculations

A calibration curve is drawn by plotting, on linear graph paper, the absorbance versus the concentration of nickel in $\mu$g for each standard. The concentration of Ni in the sample is read from the calibration curve as $\mu$g of nickel. The concentration of nickel carbonyl in the air is calculated as:

$$\text{ppm } Ni(CO)4 = \frac{\mu g \text{ Ni} \times \frac{MW\ Ni(CO)4}{MW\ Ni} \times R \times T(\text{deg K}) \times 760 \text{ mm Hg}}{\text{liters sample} \times MW\ Ni(CO)4 \times 298 \text{ deg K} \times P \text{ (mm Hg)}}$$

$$R = \frac{24.45 \text{ L Atm}}{\text{deg K mole}}$$

$$\text{ppb } Ni(CO)4 = 1000 \times \text{ppm } Ni(CO)4$$

## REFERENCES


1. Antonsen DH, Springer DB: Nickel compounds, in Kirk-Othmer Encyclopedia of Chemical Technology, ed rev 2. New York, Interscience Publishers, 1967, vol 13, pp 753-65

2. Stedman DH, Tammaro DA: Chemiluminescent measurement of parts-per-billion levels of nickel carbonyl in air. Anal Lett 9:81-89, 1976

3. International Agency for Research on Cancer: Nickel and nickel compounds. IARC MONOGRAPHS 11:75-112, 1976

4. Medical and Biological Effects of Environmental Pollutants: Nickel, Washington, DC, National Academy of Sciences, 1975, 277 pp

5. Armit HW: The toxicology of nickel carbonyl. J Hyg 8:565-600, 1908

6. Barnes JM, Denz FA: The effect of 2-3 dimercapto-propanol (BAL) on experimental nickel carbonyl poisoning. Br J Ind Med 8:117-26, 1951

7. Sunderman FW Jr, Selin CE: The metabolism of nickel-63 carbonyl. Toxicol Appl Pharmacol 12:207-18, 1968

8. Hackett RL, Sunderman FW Jr: Nickel carbonyl effects upon the ultrastructure of hepatic parenchymal cells. Arch Environ Health 19:337-43, 1969

9. Sunderman, FW, Donnelly AJ, West B, Kincaid JF: Nickel poisoning -- IX. Carcinogenesis in rats exposed to nickel carbonyl. AMA Arch Ind Health 20:44-49, 1959

10. Sunderman FW, Donnelly AJ: Studies of nickel carcinogenesis metastasizing pulmonary tumors in rats induced by the inhalation of nickel carbonyl. Am J Pathol 46:1027-41, 1965

11. Lau TJ, Hackett RL, Sunderman FW Jr: The carcinogenicity of intravenous nickel carbonyl in rats. Cancer Res 32:2253-58, 1972

12. Sanina YP: The toxicology of nickel carbonyl. Toksikol Nov Prom Khim Veshchestv 10:144-49, 1963 (RUS)

13. Laskin S, Sellakumar A: Models in chemical respiratory carcinogenesis. Experimental Lung Cancer: Carcinogenesis and Bioassays. New York, Springer-Verlag, 1974, pp. 7-19

14. Beach DJ, Sunderman FW Jr: Nickel carbonyl inhibition of RNA synthesis by a chromatin-RNA polymerase complex from hepatic nuclei. Cancer Res 30:48-50, 1970

15. Beach DJ: Aspects of the molecular biology of nickel carbonyl, thesis. University of Florida, Gainesville, Florida, 1968, 84 pp. (unpublished)

16. Sunderman FW Jr, Roszel NO: Effect of nickel carbonyl upon the detoxification and mobilization of 3,4, Benzpyrene, Am J Clin Pathol 49:240, 1968

17. Braker W, Mossman A: Nickel carbonyl--Matheson Gas Data Book, ed 5. East Rutherford, NJ, Matheson Gas Products, 1971, pp 401-03

18. Nickel Carbonyl, AIHA Hygienic Guide Series. Am Ind Hyg Assoc J 29:304-07, 1968

19. Vuopola U, Huhti E, Fakkunen J, Huikko M: Nickel carbonyl poisoning. Am Clin Res 2:214-22, 1970

20. Ludewigs HF, Thiess AM: Medical knowledge of nickel carbonyl poisoning Experience of forty-six cases of nickel carbonyl intoxication. Zentralbl Arbeitsmed Arbeitsschutz 20:329-39, 1970

21. Sunderman FW, Kincaid JF: Nickel poisoning -- II. Studies on patients suffering from acute exposure to vapors of nickel carbonyl. JAMA 155:889-94, 1954

22. Carmichael JL: Nickel carbonyl poisoning. Arch Ind Hyg Occup Med 8:143-48, 1953

23. Nickel carbonyl poisoning. Lancet 1:268-69, 1903

24. Armit HW: The toxicology of nickel carbonyl. J Hyg 7:525-51, 1907

25. Kincaid JF, Stanley EL, Bechworth CH, Sunderman FW: Nickel poisoning. Am J Clin Pathol 26:107-19, 1956

26. Sunderman FW, Sunderman FW Jr: Loffler's syndrome associated with nickel sensitivity. Arch Intern Med 107:405-08, 1961

27. Brandes WW: Nickel carbonyl poisoning. JAMA 102:1204-06, 1934

28. Tsereteli MN, Mandzhavidze RP: Clinical aspects of acute nickel carbonyl poisoning. Gig Tr Prof Zabol 13:46-47, 1969 (Rus)

29. Zhdaneveva GS: X-ray changes in the lungs with nickel carbonyl poisoning in the acute phase and later. Kazan Med Zh 1:47-50, 1970 (Rus)

30. Jones CC: Nickel carbonyl poisoning -- Report of a fatal case. Arch Environ Health 26:245-48, 1973

31. Kotzing K: Nickel carbonyl poisoning. Arch Gewerbepathol Gewerbehyg 4:500-07, 1933 (Ger)

32. Report by Bradford Hill (1939). Unpublished summary submitted to NIOSH by International Nickel Company, Ontario, Canada, 1976

33. Morgan JG: Some observations on the incidence of respiratory cancer in nickel workers. Br J Ind Med 15:224-34, 1958

34. Doll R, Morgan LG, Speizer FE: Cancers of the lung and nasal sinuses in nickel workers. Br J Cancer 24:623-32, 1970

35. Loken AC: Lung cancer in nickel workers. Tidsskr Nor Laegeforen 70:376, 1950 (NOR)

36. Tartarskaya AA: Cancer of the respiratory tract in people engaged in nickel industry. Vopr Onkol 13:58-60, 1967 (Rus)

37. Mastromatteo E: Nickel -- A review of its occupational health aspects. J Occup Med 9:127-36, 1967

38. Sutherland RB: Respiratory cancer mortality in workers employed in an Ontario nickel refinery covering the period 1930 to 1957. Ontario, Division of Industrial Hygiene, Ontario Department of Health, 1959 (unpublished)

39. Toxic and Hazardous Industrial Chemicals Safety Manual for Handling and Disposal with Toxicity and Hazard Data -- Nickel. International Technical Information Institute, 1975, pp 358-60

40. Hackert W, Clauss H, Meyer A, Sprunk A, Fritze H: Nickel carbonyl. Sozialversicherung Arbeitschutz 15:24-25, 1969 (Ger)

41. Laboratory Waste Disposal Manual. Washington, DC, Manufacturing Chemists Association, 1974, pp 1-6, 23, 81, 139, 148-49, 152, 160, 173-76

42. Renshaw FM: Nickel carbonyl health hazard information. Unpublished report submitted to NIOSH by Rohm and Haas Co., Philadelphia, PA, March 1976

43. Nickel and its inorganic compounds -- Including nickel carbonyl. Unpublished report submitted to NIOSH by International Nickel (US) Inc., New York, March 1976

44. Brief RS, Venable FS, Ajemian RS: Nickel carbonyl -- Its detection and potential for formation. Am Ind Hyg Assoc J 26:72-76, 1965

## APPENDIX A

## PROCESS DESCRIPTIONS FOR MAJOR USES OF NICKEL CARBONYL

Nickel carbonyl is used world-wide as an intermediate in the Mond process for extracting pure nickel from its ores [3]. In this process, crude nickel is exposed to carbon monoxide gas at controlled temperature and pressure [4]. This results in the formation of nickel carbonyl vapor which is diverted to a decomposition chamber. In this chamber, the combination of higher temperature and the existence of a "seeded" nickel compound promotes the formation of tiny nickel particles and the release of carbon monoxide. The nickel particles are allowed to "grow" until they reach the size of small pellets, termed "nickel shot" at which time they are removed from the process.

Similarly, nickel is recovered from nickel sulfide by the carbonyl process [4]. The nickel sulfide, NiS and/or Ni3S2, is "roasted" (oxidized) to produce the oxide, NiO, which is then reduced with "water gas" to form crude "sponge nickel". The "sponge nickel" is then treated with carbon monoxide to form nickel carbonyl which is decomposed with heat (as described earlier) to make nickel pellets or nickel powder.

In a process to produce methyl and ethyl acrylate monomers, nickel carbonyl, acetylene, carbon monoxide, an alcohol, and hydrogen chloride react continuously in carefully controlled ratios [42]. Although carbon monoxide gas will not enter into this reaction initially, once the reaction has started CO will react with acetylene and alcohol to produce acrylate. The carbonyl group in the acrylate ester is derived from both carbon

monoxide and nickel carbonyl, with the latter contributing about 20% of the carbonyl needed.

Nickel carbonyl has found some application in the nickel plating industry [1]. By using nickel carbonyl, nickel can be deposited on metal or other surfaces without the use of electric current. The process simply involves decomposition of nickel carbonyl vapor by heat in the presence of the target surface.

PART 2
SUBSTANCE SAFETY DATA SHEET FOR EMPLOYEES

The following guidelines are designed to help the employee understand the possible hazards and ways in which the hazard may be avoided for Nickel Carbonyl.

I. SUBSTANCE IDENTIFICIATION

A. Trade names: Nickel carbonyl, nickel tetracarbonyl
B. Scientific Names: Same as above

II. APPEARANCE AND ODOR

Pale yellow, volatile liquid with weak soot-like odor which is nearly undetectable

III. ROUTES OF EXPOSURE

Nickel carbonyl is extremely volatile and its toxicity in vapor form has been well-documented. Inhalation is the most likely route of exposure and presents the greatest hazard to the worker.

IV. HEALTH HAZARD DATA

A. Reported Carcinogenic Effects Due to Exposure

In animal studies, rats developed tumors from both long-term exposure (inhalation of 30 mg nickel carbonyl/cu m of air (4300 ppb), for 30 minutes, 3 times weekly, for 1 year) and acute exposure (single dose of 600 mg/cu m or 86,000 ppb) to nickel carbonyl vapor.

From a review of the human epidemiologic data it is not possible to confirm or deny an association of lung cancer to nickel carbonyl.

B. Other Reported Health Effects Due to Exposure

1. Acute Short-term Effects

Short-term effects can include; pulmonary edema and inflammation (interstitial pneumonitis), reduced lung capacity, heart

irregularity, liver enlargement, elevated blood and urinary glucose levels, and in severe cases, death.

2. Chronic Long-term Effects

If treatment is prompt and effective or if exposure is only slight the adverse health effects should disappear in 2-3 weeks. However, in one reported case, four patients who had appeared to have recovered were found to have radiographic evidence of fibrosis, a year after exposure.

C. Reporting Signs and Symptoms

Signs and symptoms of acute exposure to nickel carbonyl can include, shortness of breath, fatigue, nausea, and headache. These initial signs and symptoms may pass away except in the case of massive exposures. However, delayed signs and symptoms usually occur 2-10 days later and can include shortness of breath, coughing, muscular weakness, excessive sweating and substernal pain. Any worker engaged in activities which may entail the use (e.g., Mond process for nickel refining or nickel-vapor-plating) or formation (e.g., use of nickel catalysts or finely divided nickel in the presence of excess carbon monoxide) of nickel carbonyl and who experiences the aforementioned signs and symptoms should report immediately to his or her clinic or chief medical personnel. If no such facilities or personnel exist, the worker should report to the emergency room of the nearest hospital.

## V. EMERGENCY FIRST AID, PRECAUTIONS FOR SAFE USE, HANDLING AND STORAGE PROCEDURES

A. Emergency First Aid

In most exposure cases, the effects are not immediately disabling and the exposed persons are able to report to the appropriate health personnel under their own power. In extreme cases where the degree of asphyxia is severe, the immediate treatment should be that for carbon monoxide

poisoning. A mixture of 95% oxygen and 5% carbon dioxide should be administered. It is of great importance to keep the patient warm but if no oxygen supply equipment is available, he should be removed into fresh air regardless of the surrounding temperature. In addition it may be necessary to apply artificial respiration. If so, the arm-lift-back pressure (Nielsen) method should be employed and not mouth-to-mouth resuscitation.

B. Precautions for Safe Use

Precautions taken in any area where nickel carbonyl is manufactured and/or used should include proper ventilation. Continuous local exhaust ventilation should provide air movement which is always from non-nickel carbonyl areas to areas containing nickel carbonyl. Where a fan is used to affect such air movement, the fan blades and throat should be made of a nonsparking material. Further, the exhaust from such exposure-risk areas should pass through a decontamination furnace before emission into the environment. These practices should be followed in the laboratory as well as in the commercial processing plant.

C. Handling and Storage Precautions

Because nickel carbonyl is extremely volatile and flammable, it should be handled only when it is contained in steel bottles. Carbon dioxide fire extinguishers should be readily accessible in all nickel carbonyl storage and handling areas.

## IV. RESPIRATORS AND PROTECTIVE CLOTHING

A. Respirators

In all areas where nickel carbonyl is manufactured, stored, or used, workers should wear full facepiece supplied-air respirators. The extreme toxicity and volatility of nickel carbonyl coupled with its nearly undetectable odor emphasize the need for careful observance of this recommendation.

B. Protective Clothing

Absorption of nickel carbonyl through the skin has not been demonstrated but has been suggested. Therefore, the necessity for the use of protective gloves and impervious (e.g., rubber) clothing is uncertain. However, in view of nickel carbonyl's volatility and the major threat of exposure to its vapor, the use of protective clothing is not suggested.



☆ U.S. GOVERNMENT PRINTING OFFICE: 1977— 757-057/6704

DEPARTMENT OF
HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
CENTER FOR DISEASE CONTROL
NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH
ROBERT A. TAFT LABORATORIES
4676 COLUMBIA PARKWAY, CINCINNATI, OHIO 45226

OFFICIAL BUSINESS
PENALTY FOR PRIVATE USE $300


POSTAGE AND FEES PAID
U.S. DEPARTMENT OF H.E.W.
HEW 399

DHEW (NIOSH) Publication No. 77-184