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DEPARTMENT OF CONSUMER & BUSINESS SERVICES

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SUBJECT: 2-Nitropropane

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DIRECTIVES: OAR 437-02-1910.1000(a)

(1) PURPOSE: To provide information on the hazards of 2-Nitropropane (2-NP), protective measures in its use, and forthcoming code changes.

(2) BACKGROUND: In the last few years, research has been conducted which has shown 2-NP to cause liver cancer in rats. The human epidemiological data is inconclusive in its nature on carcinogen possibilities, but 2-NP has shown definite toxic effects. Continuing exposure to concentration of 20 to 45 ppm of 2-NP caused nausea, vomiting, diarrhea, anorexia, and severe headaches in workers in one plant. 2-NP may be found in vinyl, epoxy paints, nitrocellulose, chlorinated rubber, printing inks, and adhesives. Workers that may be affected include industrial construction and maintenance workers, printers, shipbuilding maintenance using certain marine coatings, highway maintenance people making the traffic markings, in some furniture manufacture, food processing and packaging of plastic products. OSHA and NIOSH recommends that worker exposure be reduced to the lowest feasible levels. 2-NP is a clear colorless liquid with a pleasant odor, but the worker cannot detect the odor until concentrations are reached of about 160 ppm, the present PEL is 25 ppm.

(3) ACTION: To protect workers from exposure to 2-NP, there are several actions that employers should take. These recommendations are outlined in the enclosed OSHA and NIOSH Alert, dated September 26, 1980.

NIOSH Health Hazard Alert

U.S. Department of
Health and Human Services
Pubic Health Service
Center For Disease Control
National Institute for
Occupational Safety and Health

2-Nitropropane

HEALTH HAZARD ALERT - 2-NITROPROPANE (2-NP)

OSHA and NIOSH conclude that 2-nitropropane (2-NP) is a confirmed carcinogen in laboratory rats (1,2,3). In 1977, NIOSH summarized the carcinogenic potential of 2-NF in Current Intelligence Bulletin #17 (4). Since then data have been developed which reinforce and expand the original findings. As a confirmed animal carcinogen, 2-NP has the potential to cause cancer in humans. This document summarizes the cancer studies of 2-NP in laboratory animals and its toxic effects in humans. It recommends that worker exposure to 2-NP be reduced to the lowest feasible levels. The document recommends actions, procedures, and medical programs that should be used to protect workers from exposure to 2-NP.

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Health Hazard Alert- 2-Nitropropane

Production and Exposure

Solvent systems containing 2-NP are used in coatings (e.g., vinyl, epoxy, paints, nitrocellulose, and chlorinated rubber), printing inks, and adhesives. It is also used as a solvent in food processing for fractionation of a partially saturated vegetable oil. Occupational exposure to 2-NP may occur in many industries including industrial construction and maintenance, printing (rotogravure and flexographic inks), highway maintenance (traffic markings), shipbuilding and maintenance (marine coatings), furniture, and plastic products. About 185,000 workers in the U.S. are exposed to 2-NP during its production and use. Commercial Solvents Corporation (CSC) was the only producer of 2-NP until that corporation was purchased about 5 years ago by International Minerals and Chemical Corporation (IMC). International Minerals aud Chemical Corporation is now the sole producer of 2-NP. 2-Nitropropane was -manufactured In a pilot plant in Peoria, Illinois, from 1940 to 1955. Since 1955, it has been manufactured in a plant in Sterlington, Louisiana. Of the estimated 30 million pounds of 2-NP produced annually, 12 million are sold domestically. The remainder is either used internally at IMC or exported. Major distributors of 2-NP, other than Commercial Solvents Corporation, include Amsco Division of Union Oil Company of California, Industrial Chemicals and Solvents Division of Ashland Chemical Company, and Thompson Hayward Chemical Company (4).

Characteristics

2-Nitropropane (CAS No. 000 79-46-9; RTECS No. TZ5250000) is a clear colorless liquid with a pleasant odor. The molecular formula of 2-NP is CH3CH(N02)CH3, the molecular weight is 89.09 and :he specific gravity is 0.992 (5,6). The melting point of 2-NP is -93C, the boiling point is 118-120C, and the solubility in water is 1.7 ml/100 ml at 25C. 2-Nitropropane is soluble in many organic solvents including chloroform. The vapor pressure of 2-NF is 20 = Hg at 250C and the flash point is 1030F (319.40C) (6). The lower flammability limit is 2.6% by volume in air (7). Its vapors may form an explosive mixture with air.

Synonyms for 2-NP include dimethylnitromethane, isonitropropane and nitroiso propane. Trade names for 2-NP include N:L-Par S-20TK (a commercial grade 2-NP) and NiPar S-30TH (mixtures of 1-nitropropane and 2-NP) (4).

Carcinogenicity Studies

Data from two carcinogenesis bioassay studies are available. One of these studies is completed (1,2). The other is ongoing (3). Both show that 2-NP is carcinogenic in rats. In the completed study, male Sprague-Dawley rats were exposed to 2-NP for 7 hours/day, 5 days/week for 6 months in whole. body chambers (1,2). Fifty rats were exposed at 207 ppm, 50 at 27 ppm, and 50 were unexposed. Live cancers (hepatocellular carcinoma) were observed in all 10 rats killed after 6 months of exposure at 207 ppm of 2-Np. No tumors were observed in any other animals in. this study, including controls. Rats exposed at 207 ppm developed other adverse liver changes such as hepatocellular hypertrophy. hyperplasia, and necrosis after 3 months. In the second uncompleted study (3), both 3exes of Sprague-Dawley rats were exposed to 2-NP vapors at 200 ppm, 100 ppm. or 25 ppm. . for 7 hours/day, 5 days/week for up to 6 months. Nine of 10 rats exposed for 6 months at 200 ppm. and held unexposed for 6 more months had metastatic liver carcinomas. According to preliminary data male rats exposed at 100 ppm also developed liver tumors. (8). At the end of 22 months no malignancies or any significant pathologic, changes were observed in the livers of any of the male or female rats exposed at 25 ppm. Focal areas of hepatic cellular nodules were noted in 3 of 250 control animals and 13 of 249 exposed animals. Other microscopic observations included focal cytoplasmic vacuolization of hepatocyces and liver congestion (18).

In addition - to carcinogenic changes, 2-NP causes other toxic changes in laboratory animals and in humans (1-3,9-15).

Studies of humans who wexe acc1dentally exposed to 2-NP show that brief exposure to high concentrations may be harmful. One report about two workers attributes the death of one and liver damage in both to high level exposures to 2-NP that occurred while they painted the inside of a tank (9). They had used a zinc-epoxy paint diluted with 2-NF and ethylglycol (2-ethoxyethanol). Another report describes the deaths of four men who were working In confined spaces with paint, surface coating, and polyester based resin products containing 2-HP (15). All four workers had liver damage and destruction of hepatocytes. The authors attributed the deaths to overexposure to 2-NP but admitted that ocher solvents might have played a role since 2-NP was not identified by toxicological analysis (15). Continuing exposure to concentrations of 20 to 45 ppm of 2-NP caused nausea, vomiting, diarrhea, anorexia, and severe headaches in workers in one plant (12). In another instance, toxic hepatitis developed in construction workers applying epoxy resins to the walls of a nuclear power plant (13). Although the hepatitis was attributed to a known hepatoxim, p,p’-methylenedianiline (4,4'-diaminodiphenylmathane), it could have resulted from the 2-NP that the men used to wash the epoxy resins from their skin.

Workers may not be able to detect 2-NP by its, odor, even in the presence of potentially hazardous concentrations. One report starts that humans cannot

detect 2-NP at 83 ppm by its odor (10). Another states that 2-NP cannot be detected by is odor until the concentrations about 160 ppm (15).

In 1979, an epidemiological study of workers exposed to 2-NP was reported by the International Minerals and Chemical Corporation (16). The study included all 1,481 employees who worked at the Sterlington, Louisiana, plant between 1955 when 2-NP production began and the study cutoff date of July, 1977. The company defined the exposure of each employee in the study group as direct, indirect, or not exposed. Since formal industrial hygiene monitoring of work areas was not performed until 1977, individual exposure classifications were based on job titles rather than actual exposure data. Interpretation of the study results is further hampered by several factors, including: (1) the lack of sufficient time since onset of exposure for tumor development, (2) the limited number of workers in the study with long exposures (15 years), and (3) the small number of deaths among the group studied. The authors conclude that "analysis of these data does not suggest any unusual cancer or other disease mortality pattern among this group of workers." They appropriately note, however, that "both because the cohort is small and because the period of latency is, for most, relatively short, one cannot conclude from these data that 2-NP is non-carcinogenic in humans" (16).

There are, in addition, a number of unexplained findings w1th respect to cancer mortality observed among employees whom the company has classified as not exposed to 2-0. When the mortality figures for all males, regardless of exposure category, are combined, there were 4 deaths from lymphatic cancer where only I was expected.

Among the total of 147 female employees there were 8 deaths from all causes compared to 2.9 expected deaths, and 4 deaths from cancer compared to 0.8 expected. Finally, the authors report that 7 deaths in the small study cohort were observed from sarcomatous cancer, which is a relatively rare form of malignancy. This number seems unusually high. However, it was not possible to generate an expected number of deaths for comparison to determine statistically if the sarcomatous cancers were in excess because they cannot be broken out in the standard method of reporting and classifying deaths. The International Classification of Diseases (ICD), used in the study, does not have a unique code for those cancers. The authors recommend that follow-up of the cohort be continued and that. the data be re-analyzed periodically. The company has committed itself to a program that includes these suggestions. OSHA and NIOSH agree that the present study is inconclusive, and that it is appropriate to continue follow-up and re-analysis to confirm or to modify the observations made thus far.

Recommendations

2-Nitropropane should be handled in the workplace as a potential human carcinogen. OSHA's current Permissible Exposure Limit for 2-NP is 25 ppm or 90 mg/m3 (8-hour, time-weighted averages). Evidence of carcinogenicity was not considered in setting the limit. Because 2-NP has now been shown to be carcinogenic in rats, occupational exposure to it should be reduced to the lowest feasible levels. Methods of sampling for 2-HP in air include use of a sorbent tube containing Chromosorb 105 to trap organic vapors (17). Gas chromatographic and other methods for analyzing concentrations of 2-NP at levels of 300 ppb are also available (17).

To protect workers from exposure to 2-HP, there are several actions that employers, employees. and their physicians should take.

Table I contains acceptable respirators that may be used to reduce exposure to 2-NP by inhalation.

I. Employers Should:

1. Inform all employees working with 2-NP, or mixtures containing 2-NP, of the possible adverse symptoms or health effects that could result from exposure to it. Provide all employees with a copy of this hazard report.

2. When possible, substitute a solvent that does not contain 2-NP. Caution should be exercised in selecting a substitute for 2-NP, giving full consideration to the possible toxic effects of the replacement.

3. Provide a11 employees with potential exposure to 2-NF with a medical monitoring program that includes work history and medical examinations with specific emphasis on liver function tests. Physicians in this program should be provided with a copy of this Health Hazard Alert.

4. Provide wash or shower areas as appropriate for employees to decontaminate themselves after leaving the work area where exposure to 2-NP occurs.

5. Establish where possible restricted area for the manufacture, filling operations, use, handling or storage of 2-NP to reduce exposure of employees not directly involved with these operations. Access to these restricted areas should be limited to employees who have been properly informed of the potential hazards of 2-HP exposure and instructed in the proper control measures.

6. Establish appropriate engineering controls. The most effective way to control any contaminant is the use of a closed system. Engineering controls may include the use of walk-in hoods or specific local exhaust ventilation. Due to the explosive potential of 2-NP vapor, ignition-proof ventilation system should be selected. Suitable collectors should be used to prevent pollution of adjacent work areas.

7. Provide MSHA/NIOSH-approved personal respiratory protective devices to be used as an interim ineasure. to control the inhalation of 2-NP while engineering controls are being installed. Respiratory protective d-evices, may be used in areas where exposure to 2-NP oscurs infrequently or during emergencies. Table I contains respirators that may be used to reduce exposure to 2-NP by inhalation.

8. Provide full-body clothing for protection against splashes of 2-NP. Care should be used to select appropriate protective clothes since 2-NP may dissolve or penetrate many materials (19). The protective clothing should be left at the point of exit when an employee leaves the restricted area. At the end of the vork day, employees should place the protective clothing in a suitably marked and closed container for disposal or laundering. Laundry personnel should be made aware of the potential hazards from handling contaminated clothing.

II. Employees Should:

1. Use the correct safety equipment and protective devices provided by the employer. Contaminated clothing should be left at the worksite and laundered by the employee as noted in I (8).

2. Wash all exposed areas of the body upon leaving the restricted area.

3. Report signs or symptoms of health problems to your physician. If a private physician is used, he/she should be given a copy of this Health Hazard Alert.

III. As part of the medical surveillance program presented under recommendation I-3, physicians should:

1. Obtain a careful occupational and exposure history.

2. Inquire about constitutional complaints including nausea, vomiting, diarrhea, dizziness, anorexia, and headache.

3. Perform a physical examination with emphasis on the cardiovascular, renal, and hepatic systems.

4. Order laboratory studies of blood, particularly for liver and kidney function, and a urinalysis with microscopic examination.

5. Advise the employee of the results of the medical examination and laboratory analyses.

TABLE 1. RESPIRATOR SELECTION FOR 2-NITROPROPANE*

Maximum Exposure Concentration	Recommended Respirator* (or Conditions of Use)
Not in excess of 1,000 ppm	Half-mask positive-pressure supplied air respirator. full facepiece is required if eye irritation is experienced
Between 1,000 and 2,000 ppm	Positive-pressure supplied air respirator with full facepiece, helmet or hood.
Over 2,000 ppm or unknown concentration	1. Full facepiece positive unknown concentration pressure self-contained breathing apparatus. 2.Full facepiece positive with an auxiliary positive-pressure self-contained air supply.
Firefighting Situations	Full facepiece positive-pressure self-contained breathing apparatus.
Escape Situations	Any full facepiece, self-contained breathing apparatus.

Note: Respirators using canisters that contain oxidation promoting catalysis should never be used with 2-NP (19)

References

1. Ulrich, C., Dorato, M., Ledbetter, A., Harold, B. and Ward, C. (1977). Chronic Inhalation Exposure of Rats and Rabbits to Nitromethane and 2-Nitropropane. Huntingdon Research Center, New City. N.Y., HEW/NIOSH Project No. 210-75-0039.

2. Lewis, T., Ulrich, C. and Busey, W. (1979). Subchronic Inhalation Toxicity of Nitromethane and 2-Nitropropane. J. Environ. Pathol. and Toxicol., 2: .233-249.

3. Coulston, F. and Benitz, X. (1978). Chronic Inhalation of 200 ppm of2-Nitropropane in Rats. Six Month Report. Institute of Comparative and Human Toxicology, Albany Medical College, Albany, N.Y..

4. Fihklea, J.(1977).Current Intelligence Bulletin 17. 2-Nitropropane. National Institute for Occupational Safety and Health.

5. The Merck Index 9th Ed. (1968). P. Stecher (Ed.), Merck and Co.. Inc., Rahway, N.J., 741.

6. Browning, E. (1965).Toxicity and Metabolism of Industrial, Solvents, Elsevier Publishing Co., New York, 285-288.

7. Monto, N. (1977). 2-Nitropropaue Early Warning Report (Draft). Environmental Protection Agency.

8. Benitzi X. (1979). Microscopic Changes in Liver. Lungs, Lung Rilus, Mesenteric Lymph Nodes, Spleen, Thyroid Glands and Kidneys from Male Rats Exposed to 100 ppm. of 2-Nitropropane/m3 Air for 9 months. Interim Report. Institute of Comparative and Human Toxicology, Albany Medical College, Albany, N.Y.

9. Gaultier, M., Fournier, P., Gervais, P. and Sicot, C. (1964) Intoxication par le Nitropropane. Arch. Hal. Prof. Med., 25:425-428.

10. Machle, W., Scott, E. and Treon, J. (1940). The Physiological Response of Animals to Some Simple Moaouitroparaffins and to Certain Derivatives of These Compounds. J. Ind. Eyg. and Toxicol., 22:315-332.

11. Treon, J. and Dutra, F. (1952). Physiological Response of Experimental Animals to the Vapor of 2-Nitropropane. Arch. Ind. Hyg. Occup. Med., 5: 52-61.

12. Skinnex, J. (1947). The Toxicity of 2-Nitropropane. Ind. Med., 16: 441-443.

13. Williams, S., Bryan, J.. Burk, J. and Wolf, F. (1974). Toxic Hepatitis and Methylenedianiline. N. Engl. J. Med., 291: 1256.

14. Sutton, W. (1963). Aliphatic 'Nitro Compound, Nitrates, Nitrites. In: Industrial Hygiene and Toxicology 2nd Ed., F. Patty (Ed.) Vol. 2, John Wiley & Son&, Inc., New York, N.Y., 2069-2079.

15. Hine, C., Pasi, A. and Stephens, B. (1978). Fatalities Following Exposure to 2-Nitropropane. J. Occup. Med., 10., 333-337.

16. Miller, M. and Temple, G. (1979). 2-NP Mortality Epidemiology Study of the Sterlington, La. Employees. International Minerals and Chemical Corporation, Mundelein, Ill.

17. Glaser, R. (1978). 2-Nitropropane In:. NIOSH Manual of Analytical Methods, 2nd Ed. . D. Taylor (Coordinator), Vol. 4, 272-1 - 272-9.

18. Griffin, T., Coulston, P.. and Stein, A. (1980). Chronic Inhalation - Exposure of Rats to Vapors of 2-Nitropropane at 25 ppm. Ecotoxicol. Environ. Saf., 4 (In press).

19. The Storage and Handling of Nitropropane Solvents (1976). NP Series TDS No. 20. I.M.C. Chemical Group Inc., Technical Data Sheet, Des Plains,Il., 1-7.