Current Intelligence Bulletin 17

April 25, 1977

2-NITROPROPANE

CURRENT INTELLIGENCE BULLETIN:

2-NITROPROPANE

April 25, 1977

A recently completed inhalation study indicates that 2-nitropropane, a widely used solvent in industrial coatings and printing inks, causes liver cancer in rats. In this study sponsored by the National Institute for Occupational Safety and Health (NIOSH), all laboratory rats exposed to 207 ppm 2-nitropropane over a six month period developed hepatocellular carcinoma or hepatic adenoma. Although this study suggests that 2-nitropropane is carcinogenic, its carcinogenic potential in man has not yet been researched.

This Bulletin provides the results of this animal study along with other pertinent data, their implications for occupational health, and precautions for handling 2-nitropropane in the workplace.

Background

Solvent systems containing 2-nitropropane are used in coatings (e.g., vinyl, epoxy, nitrocellulose, and chlorinated rubber), printing inks, and adhesives. Occupational exposure to these products may occur in various industries including industrial construction and maintenance, printing (rotogravure and flexographic inks), highway maintenance (traffic markings), shipbuilding and maintenance (marine coatings), furniture, food packaging, and plastic products. NIOSH estimates that 100,000 workers are potentially exposed to 2-nitropropane in these and other industries.

Synonyms for 2-nitropropane include dimethylnitromethane, isonitropropane, nitroisopropane, and 2-NP. Trade names under which 2-nitropropane is marketed include NiPar S-20™ (commercial grade 2-nitropropane) and NiPar S-30™ (mixtures of 1- and 2-nitropropane). 2-Nitropropane (in concentrations ranging from approximately 5 to 25 percent) is used in a number of solvent systems to contribute desirable properties such as improved drying time, more complete solvent release, better flow and film integrity, retardation of blushing, greater wetting ability, improved electrostatic spraying, and increased pigment dispersion.

The sole known domestic producer of 2-nitropropane has been Commercial Solvents Corporation (recently acquired by International Minerals and Chemical Corporation, IMC). 2-Nitropropane has been manufactured at their Sterlington, Louisiana plant since 1955, and in a pilot plant in Peoria, Illinois from 1940 to 1955. Of the estimated thirty million pounds of 2-nitropropane produced annually, twelve million pounds per year are sold domestically; the remainder is either used internally at IMC or exported.

Toxicology

In an inhalation study conducted by Huntingdon Research Center under a NIOSH contract (HEW/NIOSH Project No. 210-75-0039), Sprague-Dawley male rats and New Zealand White male rabbits were exposed to commercial grade 2-nitropropane for seven hours per day, five days per week. One group of fifty rats and fifteen rabbits was exposed to 207 ppm 2-nitropropane; a second group of the same size was exposed to 27 ppm, while a third group was maintained as a control. Ten rats from each group were killed after exposure periods of two days, ten days, one month, three months, and six months. Liver neoplasms, described as hepatocellular carcinoma or hepatic adenoma, were observed in all ten rats killed after six months of exposure to 207 ppm 2-nitropropane. No tumors were observed in any other animals in this study, including controls. However, hepatocellular hypertrophy, hyperplasia, and necrosis were reported in rats exposed to 207 ppm 2-nitropropane for three months. In addition, elevated liver weights were found in rats exposed to 207 ppm 2-nitropropane for one, three, and six months. Liver histopathology, as well as the liver weights, of rats exposed to 27 ppm 2-nitropropane did not differ from controls.

Although certain shortcomings do exist in the conduct of this study,* the experiment is sufficient to merit the concern of the occupational health community. NIOSH has been advised that further investigation of the toxicity of 2-nitropropane has recently begun (April, 1977) under the sponsorship of the IMC Chemical Group, Inc.

---

* The fifty rats exposed to 207 ppm 2-nitropropane were weanling rats (younger and smaller than the other exposed rats and the control group) which were introduced to replace rats experiencing excess mortality during the first few days of exposure to 400 ppm 2-nitropropane. In addition, throughout the entire study, exposure to 2-nitropropane was conducted while food and water were present, thus introducing the potential for exposure by the oral route.

The effects of 2-nitropropane inhalation in laboratory animals have also been studied by Treon and Dutra (Arch. Ind. Hyg. and Occ. Med., 5:52, 1952). Five species of laboratory animals (2 animals of each species per exposure level) were exposed to various concentrations of 2-nitropropane. Acute exposures ranged up to 9000 ppm for short time periods (as low as one hour), while chronic exposure levels ranged down to 83 ppm 2-nitropropane for as long as 26 weeks. Treon and Dutra reported no histologic changes in the monkeys, rabbits, guinea pigs and rats exposed to 328 ppm or less regardless of exposure time.** However, both cats died within 17 days of exposure to 328 ppm and had severe liver damage and slight to moderate damage to the kidney and heart.

There are a number of published reports concerning acute health effects of occupational exposure to 2-nitropropane. One report of two workers attributes the death of one and liver damage in both workers to high level exposure to 2-nitropropane while painting the inside of a tank (Gaultier, M., et. al., Arch. d. Mal. Prof. 25:425, 1964). Another paper relates that continual exposure to concentrations of 20 to 45 ppm 2-nitropropane caused workers in one plant to experience nausea, vomiting, diarrhea, anorexia, and severe headaches (Skinner, J.B., Ind. Med. 16:441, 1947). A third report indicates that workers exposed to from 165 to 445 ppm mixed 1-and 2-nitropropane also experienced nausea, dizziness, headaches, and diarrhea (Documentation of Threshold Limit Values, American Conference of Governmental Industrial Hygienists, 1971). In addition, Williams, et. al., (New Eng. J. of Med., 291:1256, 1974) reported an excess of toxic hepatitis among construction workers applying epoxy resins to the walls of a nuclear power plant. Although the hepatitis in this case was attributed to exposure to a known hepatotoxin, p,p'-methylenedianiline (4,4'-diaminodiphenylmethane), these men were also observed to have used 2-nitropropane to remove the hardened resin from their skin.

**On subsequent examination by a NIOSH pathologist in March 1977, liver sections from two rats in this study which were exposed to about 300 ppm 2-nitropropane for seventeen exposures (7 hours each) showed clear cell foci. These and similar lesions are frequently seen prior to the development of hepatocellular carcinoma in rats exposed to known hepatic carcinogens. The lesions observed in the Treon and Dutra study are similar to those found in the liver sections of the rats in the Huntingdon study which were sacrificed after three months exposure to 207 ppm 2-nitropropane.

NIOSH Action and Recommendation

In order to characterize the potential for exposure to 2-nitropropane in the work environment, the National Institute for Occupational Safety and Health plans to conduct industrial hygiene surveys at facilities where 2-nitropropane is manufactured or consumed. In addition, an attempt will be made to identify a suitable worker population for epidemiologic studies.

The current Occupational Safety and Health Administration (OSHA) standard for occupational exposure to 2-nitropropane is 25 ppm. However, in light of the new information generated by the Huntingdon study, and while the carcinogenic potential of 2-nitropropane is being further evaluated, NIOSH believes that it would be prudent to handle 2-nitropropane in the workplace as if it were a human carcinogen. The attached interim recommended industrial hygiene practices were developed by NIOSH to help reduce occupational exposure to 2-nitropropane.

John F. Finklea, M.D.

John F. Finklea, M.D.
Director

Attachment

INDUSTRIAL HYGIENE PRACTICES TO REDUCE EXPOSURE TO 2-NITROPROPANE

The following are suggested good industrial hygiene practices that can help to reduce exposure to 2-nitropropane. The recent finding of liver cancer in laboratory rats exposed by inhalation to 207 ppm 2-nitropropane for six months has indicated a need to reduce worker exposure.

A. Regulated Area. Regulated areas should be established during manufacture, filling operations, use, release, handling or storage.

1. Access. Access should be restricted to employees who have been properly informed of the potential hazard of 2-nitropropane exposure and proper control measures.

2. Engineering Controls. The most effective control of any contaminant is control at the source of generation wherever possible. Effective engineering measures may include the use of walk-in hoods, or specific local exhaust ventilation. Suitable collectors should be used to prevent community air pollution.

   a. Due to the explosive potential of 2-nitropropane spark proof ventilation systems should be selected.

   b. Wherever possible the operations utilizing 2-nitropropane should be enclosed (with appropriate ventilation) to reduce exposures to the operators and others in the area.

3. Respirators. Personal respiratory protective devices should only be used as an interim measure while engineering controls are being installed, for non-routine use and during emergencies. Considering the carcinogenic potential of 2-nitropropane and the current Occupational Safety and Health Administration (OSHA) standard based on other toxicity, the appropriate personal respiratory protective measure is the use of a positive pressure supplied air respirator, or a positive pressure self-contained breathing apparatus.

4. Protective Clothing. Protective full body clothing should be provided and its use required for employees entering the regulated area. Upon exiting from the regulated area, the protective clothing should be left at the point of exit. With the last exit of the day, the protective clothing should be placed in a suitably marked and closed container for disposal or laundering. (Laundry personnel should be made aware of the potential hazard from handling contaminated clothing.)

5. Cleanliness. Employees should be required to wash all exposed areas of the body upon exiting from the regulated area.

6. Isolation. Any operations involving 2-nitropropane should be placed in an isolated area, in combination with other engineering controls, to reduce exposure to employees not directly concerned with the operations.

B. Medical Monitoring. All employees with a potential exposure to 2-nitropropane should be placed under a medical monitoring program including history and medical examinations with specific emphasis on liver function tests.

C. Substitution. The substitution of a solvent that does not contain 2-nitropropane is another possible control measure. Caution should be exercised in selecting a substitute for 2-nitropropane, giving full consideration to the possible toxic effects of the substitute.

NIOSH

Current Intelligence Bulletin

Reprints-Bulletins 1thru18 (1975-1977)

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