BACKGROUND INFORMATION ON CHLOROPRENE

Office of Occupational Health Surveillance and Biometrics

National Institute for Occupational Safety and Health

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CHLOROPRENE

Introduction

In a letter to Mr. Edward J. Baier, Acting Director, NIOSH, dated December 16, 1974, Dr. John A. Zapp, Director, Haskell Laboratory, E.I. du Pont de Nemours and Company (Du Pont), Louisville, Kentucky, expressed concern over the potential carcinogenicity of chloroprene (2-chlorobutadiene). Du Pont had begun looking closely at this substance recently because of the similarity in chemical structure with vinyl chloride. Du Pont has utilized chloroprene in the production of neoprene (polychloroprene) since 1931.

In the course of a literature search on chloroprene toxicity, Du Pont uncovered two recent Russian articles that suggest an increased incidence of skin and lung cancer in workers exposed to chloroprene. Also, two other articles in the Russian literature were located that described animal experiments in which chloroprene adversely affected embryo development in rats and mice.

Du Pont has informed its employees of the Russian reports and has alerted its customers to the possibility of "escaping chloroprene" during the processing of neoprene. The Company is conducting epidemiological studies in humans and animals to ascertain the carcinogenic potential of chloroprene.

Background Information

Chloroprene is a colorless liquid that is slightly soluble in water. It is soluble in alcohol and diethyl ether, and has a vapor density of 3.0, three times that of air, with a boiling point of 59.4°C. Chloroprene is used as a chemical intermediate largely as a monomer for the manufacture of a synthetic rubber.[1] It is a chlorine-substituted derivative of 1,3-butadiene. Chloroprene can polymerize spontaneously at room temperature, the process being catalyzed by

light, peroxides, and other free radical initiators. It can also react with oxygen to form polymeric peroxides. Because of its instability, flammability, and toxicity, chloroprene has no end product uses. It is produced in large quantities mainly for polymerization and marketing under the trade name of Neoprene.[2]

Neoprene was developed in the U.S. by Carothers[3] and was originally introduced by Du Pont in 1931 under the brand name Duprene.[4] Although during recent years other suppliers have come on the market with their own brand name, neoprene is generally used as a generic name for polychloroprene rubbers.

Neoprene is obtained by emulsion polymerization of chloroprene (2-chlorobutadiene) and consists mainly of 1,4-transpolychloroprene. There are two main classes, the sulfur modified type and the non-sulfur modified type, indicating the differences in polymerization techniques. Several subtypes of both are available, differing in viscosity and crystalization rate.[4]

Neoprene's most valuable properties are its resistance to weathering and oil. It is also resistant to abrasion, heat, flame, oxygen, ozone, and solvents. The main applications of neoprene are in high performance articles such as cable sheaths, hoses, fabrics, adhesives, and a large number of technical rubber articles. The automotive industry is the largest consumer of neoprene.[5]

Toxicity

Human: The primary responses to chloroprene appear to be central nervous system depression and significant injury to lungs, liver, and kidneys.[1] Humans exposed to chloroprene have been reported to develop dermatitis, conjunctivitis, corneal necrosis, anemia, temporary loss of hair, nervousness, and irritability.[6]

Two Russian reports suggest that chloroprene exposure is associated with an increased incidence of skin and lung cancer.[7,8]

These studies concern a large-scale epidemiological investigation of industrial workers in the Yerevan region of Russia. During the period 1956-1970, 137 cases of skin cancer were discovered through examination of 24,989 persons over age 25. The population was subdivided into five subgroups according to the character of their employment:

Group I: Persons who never worked in industrial plants

Group II: Persons working in non-chemical industries

Group III: Persons with extended work experience in chloroprene production

Group IV: Persons working in industries using chloroprene derivatives

Group V: Persons working with chemicals unrelated to chloroprene

The following table depicts the results of the study:

	Exposure Group				
	I	II	III	IV	V
Number examined	8520	8755	684	2250	4780
Number of cases	11	35	21	38	32
Percent	0.12	0.40	3.00	1.60	0.66
Average age of cases	72.1	68.9	59.6	59.1	64.4
Average duration of employment for cases (in years)	16.3	15.4	9.5	8.7	13.8

As can be seen from the table, the incidence of skin cancer was greatest in the chloroprene exposed group, and was substantially greater than that for the three unexposed groups. Persons exposed only to chloroprene derivatives also showed an increased incidence of skin cancer. A gradient in the skin cancer incidence is seen among the five groups reflecting the potential for exposure to toxic chemicals in the work environment. The average age of the cases in both the chloroprene and chloroprene derivative groups was signifi-

cantly less than that for the other groups. The average duration of employment was much shorter for the chloroprene and chloroprene derivative groups than for the other non-exposed groups. The investigators concluded that development of chloroprene-induced skin cancer is preceded by chronic dystrophic and inflammatory skin ailments which are caused by the binding of chloroprene to the free SH groups in the cells, with the formation of RS-CH compound types.

The incidence of lung cancer among 19,979 workers in the same region was also studied. During the period 1956-1970, 87 cases of lung cancer were identified from the records of the local oncology department. The population was subdivided into four subgroups according to type of employment:

Group I: Workers who had extended contact with chloroprene and/or its derivatives

Group II: The first "control group" consisting of truck drivers, polishers, cabinet makers, stokers, gasoline station attendants, typesetters, painters, and others

Group III: The second "control group" consisting mainly of electricians, carpenters, joiners, arc welders, tinsmiths, furnace workers, etc.

Group IV: The third "control group" consisting of persons who worked in professional occupations

The following table summarizes the results of the analysis:

	Exposure Group			
	I	II	III	IV
Number at risk	2934	4780	6045	6220
Number of cases	34	22	11	4
Percent	1.16	0.46	0.18	.064
Average age of cases	44.5	54.9	59.3	60.2
Average duration of employment for cases (in years)	8.7	10.3	19.9	18.5

As can be seen from the table, the group with exposure to chloroprene or its derivatives experienced the highest incidence of lung cancer. A gradient in the lung cancer incidence is seen according to exposure group which reflects (roughly) the potential for exposure to toxic chemicals in the work environment. As with the results for skin cancer, the average age and duration of employment for the cases in the chloroprene exposure group is substantially less than for the non-chloroprene control groups. It is interesting to note that the average age of the lung cancer cases in the chloroprene group (44.5) is significantly less than the average age of the skin cancer cases in the same group (about 59).

The authors note that the magnitude of the lung cancer risk in chloroprene-exposed workers is about the same as for chromate workers in the same district.

Of the 34 cases of lung cancer in workers exposed to chloroprene or its derivatives, 18 were among persons having direct and prolonged exposure to chloroprene monomer. The remaining 16 cases were persons whose exposure was to chloroprene latexes. If this breakdown is applied

to the two chloroprene subgroups shown in the skin cancer table (Groups III & IV), the lung cancer rates would be 2.6 (18÷684) for the group with exposure to chloroprene monomer and 0.7 (16 ÷ 2,250) for the group exposed to chloroprene latexes. This difference presumably reflects the gradient in total amount of exposure to chloroprene.

Animal: Animal experiments have shown that a concentration of 250ppm in air is toxic and a concentration of 75ppm may be toxic with continued exposure. Exposure to vapor first causes irritation of the respiratory tract, followed by depression of respiration and, if exposure is continued, asphyxia. The vapor is a central nervous system depressant. It causes severe degenerative changes in the vital organs, particularly the liver and kidneys. In addition, blood pressure is lowered and lung changes accompany exposure, especially at the higher concentrations.[6]

Chloroprene has caused hyperplasia of lymph nodes and a decrease in the number of lymphocytes in rats.[9] During acute and chronic chloroprene exposure, changes in adrenal gland function have also been noted.[10]

Even in low concentrations, chloroprene affects male reproductive organs causing degenerative changes resulting in reproduction interferences. Male reproductive organs appear to be more susceptible to the effect of chloroprene than female.[11]

Chloroprene has an effect on embryogenesis. In rats and mice, it causes an increase in the total embryonal mortality and reduction in the fetal weight of offspring of females exposed during pregnancy.[12,13]

Permissible Occupational Exposures:

The American Conference of Governmental Industrial Hygienists established the threshold limit of chloroprene at 25ppm (90mg/m^3).[14] This level was based

on the work of Cook[15] and Von Oettingen,[11] and is the current Occupational Safety and Health Administration, Department of Labor standard.

Priority List Status

Chloroprene is listed as number 412 on the NIOSH Priority List for Criteria Development for Toxic Substances and Physical Agents. An estimated 2,500 workers are exposed to chloroprene in the United States. The severity rating for chloroprene is 325 on a scale of 0 to 6,000.

Producers and Suppliers

The following is a list of the major producers and suppliers of chloroprene and neoprene in the U.S.:

Chloroprene

	Location
Dupont	Victoria, Texas Laplace, Louisiana
Petro-tex Chemical Corp. Petro-tex Chemical Subsid.	Houston, Texas

Neoprene

	Location
Dupont	Laplace, Louisiana Louisville, Kentucky Montague, Michigan*
Petro-tex Chemical Corp. Petro-tex Chemical Subsid.	Houston, Texas

*Shut Down in 1972

Source: Adapted from 1974 Directory of Chemical Producers, USA, Stanford Research Institute, Menlo Park, California, 1974.

Annual production figures for chloroprene are not available. Following are the annual figures for neoprene:

Year	Neoprene Production (millions of pounds)
1968	340
1969	350
1970	325
1971	340
1972	370
1973	385

Source: Chemical Economics Handbook, Stanford Research Institute, Menlo Park, California, 1974.

BIBLIOGRAPHY

1. Patty, F.R.: Industrial Hygiene and Toxicology. Interscience Publishers, New York, Vol. II, pp. 1319-1321, 1963

2. Van Oss, J.F.: Chemical Technology: An Encyclopedic Treatment, Barnes and Noble Books, New York, Vol. IV, pp. 211-212, 1972

3. Carothers, W.H., Williams, I., Collins, A.M., Kirby, J.E.: Acetylene Polymers and Their Derivatives. II. A new synthetic rubber: Chloroprene and its polymers. J. Amer. Chem. Soc., Vol. 53:4203-4225, 1931

4. Van Oss, J.F.: Chemical Technology: An Encyclopedic Treatment, Barnes and Noble Books, New York, Vol. V, pp. 482-483, 1972

5. Chemical Economics Handbook. Stanford Research Institute, Menlo Park, California, Vol. A-B, p. 620 5022R-S, 1974

6. Sax, N.I.: Dangerous Properties of Industrial Materials. Van Nostrand Reinhold Company, 3rd Edition, p. 567, New York, 1968

7. Khachatryan, E.A.: The role of chloroprene in the process of skin neoplasm formation, Gig. Tr. Prof. Zabol., Vol. 18, pp. 54-55, 1972

8. Khachatryan, E.A.: The occurrence of lung cancer among people working with chloroprene. Problems in Oncology, Vol. 18, p. 85, 1972

9. Agakhanyan, A.G., Fridenshtein, A.Y., Allverdyan, A.G.: Immunomorphology of chloroprene toxicosis. Zh. Eksp. Klin. Med., Vol. 13, pp. 3-7, 1973

10. Allaverdyan, A.G.: Changes in adrenal glands during acute and chronic chloroprene poisoning. Tr. Klin. Otd. NAUCH., Vol. I, pp. 150-157, 1970

11. Von Oettingen, W.F., Hueper, W.C., Deichmann-Grubler, W., and Wiley, F.H.: 2-Chloro-Butadiene (Chloroprene): Its toxicity and pathology and the mechanism of its action. J. Ind. Hyg. and Toxicology, Vol. 18:240-270, 1936

12. Salnikova, L.S.: Embryotropic effects of volatile substances given off by polychloroprene latices. Toksikologiya Novykh Promyshlennykh Khimicheskikh Veschestv, No. 11, pp. 106-111, 1968

13. Salnikova, L.S., Fomenko, V.N.: Experimental investigation of the influence of chloroprene on embryogenesis. Gig. Tr. Prof. Zabol., Vol. 8, pp. 23-26, 1973

14. American Conference of Governmental Industrial Hygienists, Documentation of the Threshold Limit Values for Substances in Workroom Air, 3rd Edition, pp. 54-55, 1971

15. Cook, W.A.: Maximum allowable concentrations of industrial atmospheric contaminants. Ind. Med., Vol. 14, p. 936, 1945