NIOSH

REVISED
RECOMMENDED STANDARD. . .

OCCUPATIONAL
EXPOSURE TO

ETHYLENE DICHLORIDE
(1,2 DICHLOROETHANE)

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

REVISED
RECOMMENDED STANDARD. . .

OCCUPATIONAL EXPOSURE TO

ETHYLENE DICHLORIDE
(1,2 DICHLOROETHANE)

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

SEPTEMBER 1978

DISCLAIMER

Mention of company name or product does not constitute endorsement by the National Institute for Occupational Safety and Health.

DHEW (NIOSH) Publication No. 78-211

NIOSH REVISED RECOMMENDATIONS FOR AN OCCUPATIONAL EXPOSURE STANDARD FOR ETHYLENE DICHLORIDE (1,2-dichloroethane)

INTRODUCTION

In 1975, a criteria document containing a recommended standard for occupational exposure to ethylene dichloride (1,2-dichloroethane) was prepared by the National Institute for Occupational Safety and Health (NIOSH) and transmitted to the Department of Labor for consideration in promulgation of Federal regulations (1). In that document, NIOSH recommended that the present Federal occupational health standard of 50 parts per million (ppm), determined as an 8-hour time-weighted average (TWA), be reduced to a TWA of 5 ppm for a 10-hour workshift, 40-hour workweek. NIOSH based its recommendations on a wide range of potentially serious health effects involving the nervous, respiratory, hepatic, and cardiovascular systems. NIOSH also expressed concern regarding the potential carcinogenicity of one possible metabolite of ethylene dichloride and noted the carcinogenic study being conducted by the National Cancer Institute. This recently completed study has demonstrated that ethylene dichloride is carcinogenic in rats and mice (2).

NIOSH recommends, on the basis of this study and on the basis of studies demonstrating mutagenicity (3-5), that ethylene dichloride be controlled as an occupational carcinogen and that the previous recommended standard be revised downward from 5 ppm (20 mg/cu m), to 1

ppm (4 mg/cu m) determined as a TWA exposure for up to a 10-hour workshift. NIOSH further recommends a ceiling concentration of 2 ppm (8 mg/cu m) as determined over a 15-minute sampling period. The present Federal standard (PEL) of 50 ppm (200 mg/cu m) measured as a TWA, includes a ceiling of 100 ppm, and a maximal allowable peak above the ceiling of 200 ppm allowed for not more than 5 minutes during any 3-hour period (6).

Because it is not possible at present to establish a safe exposure level for a carcinogen, NIOSH recommends restricting exposure to very low levels that can be reliably measured in the workplace. Procedures for sampling and analysis of workroom air are provided in Appendices I and II of the NIOSH criteria document on ethylene dichloride (1). Based on the sampling and analytical method recommended in the criteria document, the lowest detectable level of ethylene dichloride in air that can be measured is 1 ppm. The recommended standard is readily measurable by techniques that are valid, reproducible, and available to industry and government agencies (7-9).

In addition to the potential for causing cancer in humans, exposure to ethylene dichloride may result in disorders of the skin, eye, lung, liver, kidney, and heart (1). Compliance with all sections of this NIOSH recommended standard should substantially reduce the risk of ethylene dichloride-induced cancer as well as prevent non-carcinogenic adverse effects of occupational exposure to ethylene dichloride.

NIOSH estimates on the basis of a national survey (10) that approximately 2 million workers in 148,165 workplaces are potentially

exposed to ethylene dichloride; some 200,000 of these workers are estimated to receive exposure continuously in the workplace. The compound is used in such diverse operations as: A raw material for producing vinyl chloride and numerous other structurally related chlorinated chemicals, a constituent of antiknock compounds for gasoline, a basic component of thiokol A (a polysulfide rubber), a grain and seed fumigant, and a commonly-used extractant/solvent for research and development laboratories. A more complete listing of industries utilizing ethylene dichloride is given in Supplement I.

Although the major use of EDC is in the manufacture of vinyl chloride, an outstanding potential for exposure occurs during the pouring of containers of ethylene dichloride into open vats where it is subsequently used for fumigation of grains. Emphasis, therefore should be placed on prohibiting the occupational use of ethylene dichloride as a solvent or diluent in all open-type operations. Furthermore, product substitution should be a paramount consideration wherever ethylene dichloride is identified or its presence suspected, and it should be replaced wherever feasible with less harmful substitutes. The recommended standard would apply to the processing, manufacture, and use of ethylene dichloride and products containing ethylene dichloride.

I. BASIS FOR A REVISED ETHYLENE DICHLORIDE STANDARD

No epidemiologic studies that were designed to investigate the carcinogenicity of ethylene dichloride in humans have been found in the literature. The seven epidemiologic studies referenced in the criteria document refer to physiological alterations and morbidity (1).

Studies at the National Cancer Institute have been completed on an animal bioassay of ethylene dichloride (EDC) given by gastric intubation. The results are summarized in Table I.

There is a statistically significant positive association between the dosage of ethylene dichloride and the incidence of squamous-cell carcinomas of the forestomach and hemangiosarcomas of the circulatory system in male rats. In female rats, there was a statistically significant increased incidence of adenocarcinomas of the mammary gland. Ethylene dichloride was carcinogenic in mice also, causing mammary adenocarcinomas and endometrial tumors in female mice, as well as producing lung adenomas in mice of both sexes. There was a dose-response relationship for total tumors in both mice and rats, as well as a dose-response relationship for most specific types of tumors. Table I depicts the relative incidences of tumors seen in controls and at the two dose levels administered (1).

The Cancer Clearing House noted in their meeting of March 6 & 7, 1978, after accepting the results, "The potential carcinogenic risk that this compound poses to humans was emphasized "(11).

Other investigations, as yet unpublished, may provide negative results on the carcinogenic potential of ethylene dichloride. The

Manufacturing Chemists Association (MCA) in a communication to NIOSH has reported on a study on ethylene dichloride in Italy by Maltoni (12). Rats and mice were exposed to 150 ppm ethylene dichloride in air. Referring to tumor incidence in rats, Maltoni stated "No relevant changes in the incidence of the tumours normally occurring in the bred (sic) of rats used have been observed, following the treatment, apart from a moderate overall increase in benign mammary tumours (fibroma and fibroadenomas) in treated rats when compared to controls, however, without a dose-response relationship, within exposed groups." This moderate overall increase was 46/90 at 150 ppm, 41/90 at 50 ppm, 29/90 at 10 ppm, 40/90 at 5 ppm, and 30/90 in the matched controls. The control animals (not kept in chambers) corresponding to the experimentals had an incidence of 39/90. The status report concluded that "the presented data may be considered almost conclusive." In this study the highest concentration to which rats were exposed was 150 ppm. While increases in tumor incidences were not significantly different from controls at this level, increased incidences did occur, and higher levels of exposure may result in still greater incidences of tumors. At the present time, NIOSH considers the evidence for a carcinogenic potential of ethylene dichloride via inhalation to be inconclusive.

In addition, Dr. B.M. Goldschmitt in a personal communication to NIOSH reported that a study at the Institute of Environmental Medicine at New York University showed no increased incidence of tumors following application of ethylene dichloride to the skin of mice (13). When tested as an initiating agent for the tumor promoter phorbol myristate acetate "for more than one year, (the combined treatment) yielded one

animal (in 30) with one papilloma." This study was not originally intended to test the carcinogenicity of ethylene dichloride per se when applied to the skin. Greater numbers of experimental animals and greater quantities of ethylene dichloride applied to the skin would be necessary before any definitive conclusions could be made. NIOSH therefore considers the carcinogenic potential of ethylene dichloride via the dermal route to be undetermined at this time.

Consistant observations of the mutagenicity of ethylene dichloride continue to be reported (3-5). It is reported as both a "moderate mutagen" alone and a "potent mutagen" when applied together with liver enzymes (4). While the relation of mutagenesis to carcinogenicity is not firmly established, the consistant positive mutagenicity findings support a conclusion that ethylene dichloride be considered a carcinogen.

Vozovanya (14,15) reported that in pregnant rats exposed to 15 mg/cu m ethylene dichloride in air, preimplantation embryonic deaths were 5 times higher than controls. There were hematomas in the region of the head, neck and upper extremities of the fetuses, and total embryonic mortality was increased. Deformities were neither reported, nor discussed.

TABLE I

A COMPARISON OF THE INCIDENCE OF VARIOUS TUMORS IN ANIMALS GIVEN ETHYLENE DICHLORIDE

(Low Dose: 50 mg per Kg PO; High Dose 100 mg per Kg PO)

(PO = per os, delivered to the animal by intragastric intubation)

Rats - male	Pooled Vehicle Control	Matched Vehicle Control	Dose in mg/kg 50	100
Hemangiosarcomas	1/60	0/20	9/50	7/50
Fibroma of Subcutaneous tissue	0/60	0/20	5/50	6/50
Squamous cell carcinoma	0/60	0/10	3/50	9/50

Rats - female	Pooled Vehicle Control	Matched Vehicle Control	Dose in mg/kg 50	100
Mammary carcinoma	1/59	0/20	1/50	18/50
Hemangiosarcoma	0/59	0/20	4/50	4/50
Mammary carcinoma or adenoma	6/59	0/20	15/50	24/50

Mice - males	Pooled Vehicle Control	Matched Vehicle Control	Dose in mg/kg 50	100
Lung adenomas	0/59	0/19	1/47	15/48
Hepatocellular Carcinomas	4/59	1/19	6/47	12/48

Mice - females	Pooled Vehicle Control	Matched Vehicle Control	Dose in mg/kg 50	100
Lung adenomas	2/60	1/20	7/50	15/48
Mammary carcinoma	0/60	0/20	9/50	7/48
Stromal polyp or sarcoma	0/60	0/20	5/49	5/47

Summary and Conclusion:

NIOSH considers the evidence of carcinogenicity of ethylene dichloride reported by the National Cancer Institute to be conclusive in two mammalian species (the rat and the mouse). Since ethylene dichloride causes progressive, malignant disease of various organs in two species of animals, NIOSH recommends that ethylene dichloride be considered carcinogenic in man. Therefore, because it is not presently possible to establish an exposure level at which ethylene dichloride may be regarded to be without risk, NIOSH recommends that exposure to ethylene dichloride be kept as low as feasible. The use of ethylene dichloride as a solvent, diluent, or fumigant in open operations should be prohibited. Product substitution should be a paramount consideration, and wherever ethylene dichloride is identified or its presence suspected, it should be replaced by a less harmful substitute.

NIOSH recommends a sampling and analytical method for ethylene dichloride in air (1, 7-9) that employs adsorption of ethylene dichloride on charcoal followed by carbon disulfide desorption, and gas chromatographic measurement. One part per million represents the lowest level at which a reliable estimate of ethylene dichloride concentration can be determined at this time.