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Carcinogenic Effects of Exposure to Propylene Oxide

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FOREWORD

Current Intelligence Bulletins (CIBs) are issued by the National Institute for Occupational Safety and Health (NIOSH), Centers for Disease Control (CDC), Atlanta, Georgia, to disseminate new scientific information about occupational hazards. A CIB may draw attention to a previously unrecognized hazard, report new data on a known hazard, or disseminate information on hazard control. Our intention is to make this information readily available to anyone who needs it. The documents are distributed to representatives of academia, industry, organized labor, public health agencies, and public interest groups as well as to Federal agencies responsible for ensuring the safety and health of workers.

CIBs are prepared by the staff of the Division of Standards Development and Technology Transfer, NIOSH (Robert A. Taft Laboratories, 4676 Columbia Parkway, Cincinnati, Ohio 45226). We welcome suggestions concerning the content, style, and distribution of these documents.

NIOSH estimates that more than 200,000 workers in the United States are potentially exposed to propylene oxide. Most workers are exposed to propylene oxide during its use as an intermediate in the manufacture of (1) polyols for urethane applications, (2) propylene glycol for polyester resins, and (3) propylene glycol ethers for solvents, coatings, and cleaning compounds. Propylene oxide is also increasingly considered as a substitute for ethylene oxide as a sterilant for medical equipment and a fumigant for foodstuffs.

The potential for propylene oxide to produce cancer in humans has not been determined. However, the results of studies in animals fulfill the criteria in the Occupational Safety and Health Administration (OSHA) Cancer Policy [Title 29 of the *Code of Federal Regulations*, Section 1990.112] for classifying a substance as a potential occupational carcinogen. NIOSH therefore recommends that propylene oxide be regarded as a potential occupational carcinogen and that occupational exposure be reduced to the lowest feasible concentration.

NIOSH recommends that producers and users of propylene oxide disseminate this information to their workers and customers, that professional and trade associations and unions inform their members of the potential hazards of working with propylene oxide, and that appropriate engineering controls and work practices be used to minimize the exposure of workers. Readers seeking more detailed information on the studies cited in this CIB are urged to consult the original publications.

J. Donald Millar, M.D., D.T.P.H. (Lond.)
Assistant Surgeon General
Director, National Institute for
Occupational Safety and Health
Centers for Disease Control

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ABSTRACT

Studies in animals have demonstrated that propylene oxide is a direct-acting carcinogen. $B6C3F_1$ mice exposed by inhalation to propylene oxide developed hemangiomas and hemangiosarcomas of the nasal mucosa. F344/N rats exposed to propylene oxide in air developed papillary adenomas of the nasal epithelium. Degeneration of the olfactory epithelium and hyperplasia of the respiratory epithelium were induced in the nasal cavities of Wistar rats exposed to propylene oxide by inhalation. Squamous cell carcinomas of the forestomach developed in rats administered propylene oxide by gavage. Although epidemiologic data are not available from workers exposed to propylene oxide, the findings of cancer and other tumors in both rats and mice treated with propylene oxide meet the criteria established in the Occupational Safety and Health Administration Cancer Policy [Title 29 of the *Code of Federal Regulations*, Section 1990.112] for regarding propylene oxide as a potential occupational carcinogen. The National Institute for Occupational Safety and Health therefore recommends that occupational exposures to propylene oxide be reduced to the lowest feasible concentration.

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CARCINOGENIC EFFECTS OF EXPOSURE TO PROPYLENE OXIDE

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
CENTERS FOR DISEASE CONTROL
NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH
CINCINNATI, OHIO

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Publications Dissemination, DSDTT
National Institute for Occupational Safety and Health
4676 Columbia Parkway
Cincinnati, Ohio 45226
(513) 533-8287

For further information on other occupational safety and health problems, call
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CURRENT INTELLIGENCE BULLETIN 51

CARCINOGENIC EFFECTS OF EXPOSURE TO PROPYLENE OXIDE

INTRODUCTION

The purpose of this bulletin is to disseminate recent information on the potential carcinogenicity of propylene oxide. Recent studies of the chronic effects of this chemical in animals have produced evidence that cancer is associated with exposure to propylene oxide. This bulletin describes the results of those animal studies, presents the known human health effects of propylene oxide, and suggests guidelines for minimizing occupational exposures.

PHYSICAL AND CHEMICAL PROPERTIES

Propylene oxide at room temperature is a volatile, colorless, highly flammable liquid with a sweet, ether-like odor [WHO 1985]. The odor threshold for propylene oxide vapor is reported to be 200 parts of propylene oxide per million parts of air (200 ppm) in humans [Hine et al. 1981]. Chemical and physical properties are summarized in Table 1.

PRODUCTION, USE, AND POTENTIAL FOR OCCUPATIONAL EXPOSURE

Propylene oxide can be produced by the chlorohydrin process (involving the reaction of propylene with chlorine) or by the hydroperoxide process (using an organic hydroperoxide to epoxidize propylene [Kirk and Dempsey 1982]). U.S. production of propylene oxide in 1980 was approximately 1,767 billion pounds [USITC 1981]. Most propylene oxide is used as an intermediate in the production of polyether polyols for polyurethane foams, and in the production of propylene glycol for unsaturated polyester resins. Minor quantities are used for sterilizing medical equipment and for fumigating foodstuffs [IARC 1976].

The National Institute for Occupational Safety and Health (NIOSH) estimates that approximately 209,000 U.S. workers are occupationally exposed to propylene oxide [NIOSH 1983]. An industrial hygiene study conducted at a propylene-oxide-producing plant in the United States found time-weighted average (TWA) exposures to propylene oxide ranging from 0.2 to 2.0 ppm. Peak air concentrations ranged from 10 to 3,800 ppm, with the highest exposures occurring during maintenance operations [Flores 1983].

Other data on occupational exposures to propylene oxide have been reported from a large chemical manufacturing facility that produced more than 200 chemical products, including derivatives of propylene oxide. Propylene oxide was detected in only one of seven personal samples collected at one worksite. That sample contained 1.5 ppm and was obtained for an operator in an area where flexible polyols were produced [Oser et al. 1978].

In a similar study, occupational exposure to propylene oxide was evaluated at three production areas of another large chemical manufacturing facility that produced derivatives of propylene oxide. Worker exposures were reported to range from 0.2 to 2.5 ppm in the polymer polyol and oxide adduct production areas. With an analytical limit of 0.01 mg per sample, propylene oxide was not detected in any samples collected in the flexible polyol production area [Oser et al. 1979].

EXPOSURE LIMITS

The Occupational Safety and Health Administration (OSHA) has recently established an 8-hr TWA of 20 ppm for propylene oxide to protect workers against the risk of primary irritation and central nervous system depression [54 FR* 2,641 (1989)]. However, during the OSHA rulemaking process, NIOSH disagreed with the proposed permissible exposure limit (PEL), recommending that propylene oxide be designated as a potential occupational carcinogen [NIOSH 1988].

The American Conference of Governmental Industrial Hygienists (ACGIH) threshold limit value (TLV®) for propylene oxide is 20 ppm (50 mg/m^3) as an 8-hr TWA [ACGIH 1988]. The ACGIH TLV is based on the acute toxicity of propylene oxide and its "lesser toxicity in relation to ethylene oxide" [ACGIH 1986a].

*Federal Register. See FR in references.

Table 1.--Chemical and physical properties of propylene oxide*

Item	Description
CAS† registry number	75-56-9
RTECS§ accession number	TZ2975000
Synonyms	Epoxypropane 1,2-epoxypropane Methyl ethylene oxide Methyloxirane Propene oxide Propylene epoxide 1,2-propylene oxide
Molecular formula	C_3H_6O
Structural formula	$CH_2\text{-}CH\text{-}CH_3$ (O)
Molecular weight	58.08
Flash point	-30°C (-22°F)
Color	Colorless
Odor	Ether-like, sweet, alcoholic
Boiling point	34.2°C (93.6°F) at 760 mm Hg
Freezing point	-112°C (-169.6°F)
Vapor pressure	445 mm Hg at 20°C (68°F)
Vapor density	(Air = 1) 2.0
Specific gravity	0.826 at 25°C
Flammability limits	2.1% to 38.5% by volume in air
Odor threshold	200 ppm
Solubility	59% by wt in water at 25°C; miscible with acetone, benzene, carbon tetrachloride, ether, and methanol

*Adapted from Hine et al. [1981].
†Chemical Abstracts Service.
§Registry of Toxic Effects of Chemical Substances.

RESULTS OF ANIMAL STUDIES

Acute Toxicity

Acute toxicity has been reported in several animal species exposed to propylene oxide by various routes of administration. Results of these studies are summarized in Table 2. The gavage-administered dose of propylene oxide that was lethal for 50% of the animals tested (LD_{50}) was 1,140 mg/kg of body weight in rats and 690 mg/kg in guinea pigs. The percutaneous LD_{50} in rabbits was 1.5 ml/kg. The lethal concentrations for 50% of the animals (LC_{50}) for a 4-hr inhalation exposure were 4,126 mg/m^3 in mice and 9,486 mg/m^3 in rats.

Mutagenic Effects

Propylene oxide has been found to be a direct-acting mutagen (i.e., it does not require metabolic activation) in *Salmonella* and *Escherichia coli* assays. A summary of the positive mutagenic responses is presented in Table 3. Reverse mutations (base-pair substitutions) have been demonstrated in *Salmonella* and *E. coli*. Propylene oxide has not caused frameshift mutations in *Salmonella typhimurium* strains TA1537, TA1536, and TA98 [Bootman et al. 1979; McMahon et al. 1979; Pfeiffer and Dunkelberg 1980].

Propylene oxide has been shown to be mutagenic in *Bacillus subtilis*, yeast, and *Drosophila melanogaster*. Exposure to propylene oxide vapor caused increased sex-linked recessive lethal mutations in two germ-cell stages of *D. melanogaster*.

Propylene oxide induced DNA damage (single-strand breaks) in rat hepatocytes and chromosomal aberrations (chromatid gaps, chromosomal gaps, breaks, and fragments) in rat liver cells and human lymphocytes. Dominant lethal mutations were not induced in mice [Bootman et al. 1979] or rats [Hardin et al. 1983]. Mouse sperm-head morphology examinations following propylene oxide exposure did not reveal an increase in abnormal forms [Hardin et al. 1983].

Lynch et al. [1984b] exposed groups of 12 cynomologus monkeys to 0 (filtered air), 100, or 300 ppm of propylene oxide for 7 hr/day, 5 days/week over a 2-year period. Blood was collected during the final month of exposure and used to culture lymphocytes to assay sister chromatid exchanges (SCEs) and chromosomal aberrations. The incidence of SCEs or chromosomal aberrations was not significantly altered compared with the control group.

Table 2.--Acute toxicity of propylene oxide for various animal species and routes of administration

Species	Route	Acute toxicity (LD_{50}/LC_{50})	References
Rat	Oral	1,140 mg/kg	Smyth et al. 1941
Guinea pig	Oral	690 mg/kg	Smyth et al. 1941
Rat	Inhalation	9,486 mg/m^3	Jacobson et al. 1956
Mouse	Inhalation	4,126 mg/m^3	Jacobson et al. 1956
Rabbit	Dermal	1.5 ml/kg	Weil et al. 1963

Table 3.--Summary of positive mutagenic responses to propylene oxide

Mutation	Organism	References
Reverse mutation (base-pair substitutions)	*Escherichia coli*	McMahon et al. 1979 Bootman et al. 1979 Hemminki et al. 1980 Dean et al. 1985
	Salmonella typhimurium TA1535, TA100	Wade et al. 1978 Bootman et al. 1979 McMahon et al. 1979
	Bacillus subtilis	Phillips et al. 1980 Bootman et al. 1979
Forward mutation	*Schizosaccharomyces pombe*	Migliore et al. 1982
	Bacillus subtilis phage ϕ 105	Garro and Phillips 1980
Sex-linked recessive lethal mutation	*Drosophila melanogaster*	Hardin et al. 1983
DNA damage (single-strand breaks)	Rat hepatocytes	Sina et al. 1983
Chromosome damage	Human lymphocytes Epithelial rat liver	Bootman et al. 1979 Dean and Hodson-Walker 1979

Carcinogenic and Other Chronic Effects

Inhalation

The National Toxicology Program (NTP) has completed a bioassay to determine the carcinogenicity of propylene oxide in F344/N rats and B6C3F$_1$ mice [NTP 1985]. Groups of 50 animals of each sex and species were exposed to propylene oxide (greater than 99.9% pure) by inhalation at concentrations of 0 (chamber control), 200, or 400 ppm for 6 hr/day, 5 days/week for a period of 103 weeks. The survival rate of the exposed rats was comparable with that of the controls; however, the survival rate for the mice was lower than that of the controls. Rats and mice exposed at 400 ppm had lower terminal body weights than controls [NTP 1985].

In both rats and mice, the primary tissue affected by inhalation of propylene oxide was the respiratory epithelium of the nasal turbinates. Suppurative inflammation, epithelial hyperplasia, and squamous metaplasia occurred in male and female rats in a concentration-related manner. Papillary adenomas of the nasal turbinate epithelium and underlying submucosal glands were observed in 3/50 female rats and 2/50 male rats exposed at 400 ppm. These tumors were not observed in the control group or in animals exposed at 200 ppm. The NTP Peer Review Panel concluded that under the conditions of these studies there was "some evidence of carcinogenicity" for F344/N rats, as indicated by the increased incidence of papillary adenomas of the nasal turbinates in the male and female rats exposed at the higher concentration (400 ppm) [NTP 1985].

Inflammation of the respiratory epithelium was observed in a concentration-related pattern among male and female mice exposed to propylene oxide. One squamous-cell carcinoma and one papilloma were found in the nasal cavities of male mice exposed at 400 ppm, and two adenocarcinomas were seen in the nasal cavities of female mice exposed at 400 ppm. In addition, nasal cavity hemangiomas were observed in 5/50 male and 3/50 female mice exposed at 400 ppm, and hemangiosarcomas were observed in 5/50 males and 2/50 females. The increased incidences of hemangiomas and hemangiosarcomas in males were statistically significant ($p=0.028$, Fisher exact tests). Because of the rarity of these vascular tumors in the B6C3F$_1$ strain, the NTP Peer Review Panel concluded that under the conditions of these studies, there was "clear evidence of carcinogenicity" for male and female B6C3F$_1$ mice [NTP 1985].

In a study by Lynch et al. [1984a], groups of 80 male Fischer 344 rats were exposed to propylene oxide (98% pure) at concentrations of 0 (filtered air), 100, and 300 ppm (0, 237, and 711 mg/m^3) for 7 hr/day, 5 days/week over a period of 104 weeks. The survival rates for the two exposed groups were lower than those for the controls. Rats exposed to propylene oxide at 100 and 300 ppm had an increased incidence of inflammatory lesions of the respiratory system and a dose-dependent increase of complex epithelial hyperplasia in the nasal cavity. Two rats exposed at 300 ppm developed nasal cavity adenomas. Statistically significant ($p<0.05$) increases occurred in the incidences of adrenal phaeochromocytomas in the propylene-oxide-exposed rats (25/78 at 100 ppm and 22/80 at 300 ppm compared with 8/78 at 0 ppm). Increases also occurred in the incidences of peritoneal mesotheliomas (8/78 at 100 ppm and 9/80 at 300 ppm compared with 3/78 for the controls). All rat groups were affected by an outbreak of *Mycoplasma pulmonis* infection, which occurred about 16 months into the study. Both the infection and the propylene oxide exposure affected the survival of rats in this study. Although the proliferative lesions of the nasal mucosa appeared to be treatment-related, the authors could not ascertain how their development was influenced by the intercurrent inflammatory disease [Lynch et al. 1984a].

Reuzel and Kuper [1983] exposed groups of 100 Wistar rats of each sex to propylene oxide at concentrations of 0 (filtered air), 30, 100, or 300 ppm (71, 238, or 713 mg/m^3) for 6 hr/day, 5 days/week over a period of 28 months. Ten rats of each sex from each exposure group were killed for examination after 12, 18, or 24 months of exposure. Body weight reduction, increased mortality, hyperplasia of the mucosa, and degeneration of the olfactory epithelium were found in the male and female animals exposed at 300 ppm. Female rats exposed at 300 ppm had a higher incidence ($p<0.05$, chi-square test) of myocardial degeneration than did the controls (10/69 at 300 ppm compared with 3/69 for the controls). Females exposed at 30 or 100 ppm showed an increased number of fibroadenomas of the mammary glands, but the number of fibroadenoma-bearing animals did not increase compared with controls. However, for females exposed at 300 ppm, a statistically significant increase was reported in the number of rats with two or more fibroadenomas and in the number of fibroadenoma-bearing animals (Table 4). Compared with the controls, female rats exposed to propylene oxide had a statistically significant increase in the incidence of malignant mammary tumors. However, this incidence did not exceed the historical control incidences (0% to 15%) derived from six different long-term studies by the same laboratory on the same strain of rats. The number of females with benign mammary tumors and the mean number of fibroadenomas per fibroadenoma-bearing animal were both higher than the historical control data. No significant increase occurred in the incidence of any specific type of tumor other than mammary tumors in exposed Wistar rats compared with controls. However, the total

Table 4.-- Incidence of mammary tumors in female Wistar rats exposed to propylene oxide by inhalation for 28 months*

Item	Propylene oxide concentration (ppm)			
	0	30	100	300
Number of rats with benign mammary tumors	32/69	30/71	39/69	47/70†
Mean number of fibroadenomas per fibroadenoma-bearing animal	1.3	2.1	2.2	2.4§
Number of rats with malignant mammary tumors	3/69	6/71	5/69	8/70**

*Reuzel and Kuper [1983].
†$p<0.01$, Cox's test, adjusted for time to tumor appearance.
§$p<0.001$, chi square testing for trends (number expressed as average).
**$p=0.04$, Cox's test, adjusted for time to tumor appearance.

incidence of all tumors other than mammary tumors was significantly increased ($p<0.01$) in the females exposed at 300 ppm compared with controls. In the male and female rats exposed at 300 ppm, the total number of animals bearing malignant tumors other than mammary tumors was significantly higher than in controls ($p<0.05$ in males and $p<0.01$ in females, chi-square test) [Reuzel and Kuper 1983]. The authors questioned whether the observed effects on the mammary glands and the increase in total tumor incidence were due to the direct action of propylene oxide or to some indirect mechanism. They concluded that propylene oxide enhances the development of malignant neoplasms through an indirect, non-specific mechanism.

Oral Administration

Dunkelberg [1982] administered 15 or 60 mg of propylene oxide (99% pure) per kg of body weight in salad oil by gavage to groups of 50 female Sprague-Dawley rats 2 times/week for 150 weeks. Control groups consisted of 50 untreated female rats and 50 female rats dosed with salad oil. Survival rates for rats treated with propylene oxide were not statistically different from those of the controls. Treated animals developed hyperplasia, hyperkeratosis, or papillomas of the forestomach (incidence rates were 7/50 at the 15-mg/kg dose and 17/50 at the 60-mg/kg dose) [Dunkelberg 1982]. Squamous-cell carcinomas of the forestomach developed in a dose-dependent manner in rats treated with propylene oxide (incidence rates were 0/50 for controls, 2/50 at the 15-mg/kg dose, and 19/50 at the 60-mg/kg dose). The first of these tumors was observed during the 79th week in the high-dose group. One additional animal in the 60-mg/kg group had an adenocarcinoma.

Subcutaneous Administration

Dunkelberg [1981] injected groups of 100 female NMRI mice subcutaneously with 0.1, 0.3, 1.0, or 2.5 mg of 99% pure propylene oxide (in 0.1 ml tricaprylin) once/week for 95 weeks. Control groups consisted of 200 untreated female mice and 200 female mice injected with 0.1 ml tricaprylin (i.e., the vehicle control group). A dose-related increase in cancers (mostly fibrosarcomas) occurred at the injection site. The incidences of sarcomas (fibrosarcomas and pleomorphic sarcomas) at propylene oxide injection sites were 3/100 at 0.1 mg, 2/100 at 0.3 mg, 12/100 at 1.0 mg, and 15/100 at 2.5 mg. Four fibrosarcomas were observed in the vehicle control group, and no sarcomas were observed in the untreated control group [Dunkelberg 1981].

HUMAN HEALTH EFFECTS

The human health effects of propylene oxide exposure include corneal burns, contact dermatitis, and a reduced capacity to repair DNA lesions. McLaughlin [1946] reported that humans exposed to propylene oxide vapor received

corneal burns. Contact dermatitis was involved in two case reports--one concerning an electron microscopy technician and the other concerning two laboratory assistants. All three individuals had positive responses to propylene oxide in standard allergy patch tests [Jensen 1981; van Ketel 1979].

Twenty-three workers aged 25 to 59 were exposed to propylene oxide in a factory producing alkylated starch. Lymphocytes from these workers were examined for a reduced capacity for unscheduled DNA synthesis following the *in vitro* induction of DNA damage to their lymphocytes [Pero et al. 1982]. Unscheduled DNA synthesis is a step in the enzymatic repair of DNA damage. Estimates of airborne exposure were obtained using both personal and area sampling. Eight-hour TWA exposure concentrations of propylene oxide were calculated for five of the most highly exposed workers over 5 workdays (8-hr shifts). These concentrations ranged from 0.6 to 12 ppm. The control group consisted of 12 workers aged 21 to 46 who were not exposed to propylene oxide. Under the conditions of this experiment, unscheduled DNA synthesis was significantly inhibited ($p<0.001$, t-test) in the group exposed to propylene oxide.

CONCLUSIONS

The research data presented in this Current Intelligence Bulletin (CIB) have focused primarily on the carcinogenic effects of propylene oxide in exposed animals. The animal studies described provide sufficient evidence to conclude that propylene oxide is carcinogenic in laboratory animals.

RECOMMENDATIONS

Several systems exist for classifying a substance as a carcinogen. Such classification systems have been developed by NTP [NTP 1985], the International Agency for Research on Cancer (IARC) [IARC 1985], and OSHA, in its "Identification, Classification, and Regulation of Potential Occupational Carcinogens" [29 CFR* 1990.112], also known as "The OSHA Cancer Policy." NIOSH considers the OSHA classification system the most appropriate for use in identifying occupational carcinogens.†

Exposure to propylene oxide has been shown to produce cancer and benign tumors in both rats and mice. NIOSH therefore recommends that propylene oxide be considered a potential occupational carcinogen in conformance with the OSHA Cancer Policy. The excess cancer risk for workers exposed to propylene oxide has not yet been established, but the probability of developing cancer should be decreased by minimizing exposure. As a matter of prudent public health policy, employers should assess the conditions under which workers may be exposed to propylene oxide and take reasonable precautions (such as appropriate engineering and work practice controls) to reduce exposures to the lowest feasible concentrations.

GUIDELINES FOR MINIMIZING WORKER EXPOSURE

The following guidelines for reducing worker exposure to propylene oxide are general and should be adapted to specific work situations as required.

Exposure Monitoring

NIOSH recommends that each employer who manufactures, transports, packages, stores, or uses propylene oxide in any capacity determine whether a potential exists for any worker to be exposed to the chemical. In work areas where exposures may occur, an initial survey should be done to determine the extent of worker exposure. TWA exposures should be determined by collecting samples over a full shift. When the potential for exposure is periodic, short-term sampling may be needed to replace or supplement full-shift sampling. Personal sampling (i.e., sampling conducted in the worker's breathing zone) is preferred over area sampling. If personal sampling is not feasible, area sampling can be substituted only if the results can be used to approximate the workers' exposure. Sampling should be used to (1) identify the sources of emissions so that effective engineering or work practice controls can be instituted, and (2) ensure that controls already in place are operational and effective. Method 1612 of the *NIOSH Manual of Analytical Methods* [NIOSH 1985] provides detailed descriptions of sampling and analytical techniques for propylene oxide. The limit of quantitation is 0.1 mg propylene oxide per sample, which corresponds to 13 ppm (31 mg/m^3) for a 15-min sampling period, or 8 ppm (19 mg/m^3) for the maximum recommended sample volume (5 liters).

The NIOSH *Occupational Exposure Sampling Strategy Manual* [Leidel et al. 1977] provides guidance for developing effective strategies to monitor worker exposures to toxic

*Code of Federal Regulations. See CFR in references.

†"'Potential occupational carcinogen' means any substance, or combination or mixture of substances, which causes an increased incidence of benign and/or malignant neoplasms, or a substantial decrease in the latency period between exposure and onset of neoplasms in humans or in one or more experimental mammalian species as the result of any oral, respiratory, or dermal exposure, or any other exposure which results in the induction of tumors at a site other than the site of administration. This definition also includes any substance which is metabolized into one or more potential occupational carcinogens by mammals." [29 CFR 1990.103]

chemicals. The manual contains information on determining the need for exposure monitoring, the number of samples to be collected, and the appropriate sampling times.

Controlling Worker Exposure

Maintaining equipment and educating workers are both vital components of a good program for controlling occupational exposures. Workers should be informed of any materials that may contain or be contaminated with propylene oxide, the nature of the potential hazard, and methods for reducing exposure. Every attempt should be made to minimize exposure to propylene oxide by using the following work practices and controls: product substitution, closed systems and ventilation, worker isolation, personal protective equipment (such as chemical protective clothing and equipment, and respiratory protective devices), and decontamination and waste disposal. These measures as well as medical monitoring procedures are discussed here briefly.

Product Substitution

When feasible, employers should substitute a less hazardous material for propylene oxide. However, extreme care must be used when selecting substitutes. Possible adverse health effects from exposure to the substitute should be evaluated before selection.

Closed Systems and Ventilation

Engineering controls should be the principal method for reducing propylene oxide exposure in the workplace. Achieving and maintaining reduced concentrations of airborne propylene oxide depend on adequate engineering controls such as closed-system operations and ventilation systems that are properly constructed and maintained.

Closed-system operations provide the most effective means for minimizing worker exposures to propylene oxide. Closed systems should be used for producing, storing, transferring, packaging, and processing propylene oxide. For quality control laboratories or laboratories where production samples are prepared for analyses, exhaust ventilation systems should be designed to capture and contain vapors.

One company has developed techniques that allow for the maintenance of a closed system while process and tank car samples of propylene oxide are obtained and analyzed for quality control. These automated techniques have virtually eliminated the need for manual sampling and have reportedly been successful in reducing exposures [Flores 1983].

Guidance for designing local exhaust ventilation systems can be found in *Recommended Industrial Ventilation Guidelines* [Hagopian and Bastress 1976], *Industrial Ventilation--A Manual of Recommended Practice* [ACGIH 1986b], and *Fundamentals Governing the Design and Operation of Local Exhaust Systems* [ANSI 1979].

Worker Isolation

The area in which propylene oxide is produced or used should be restricted to workers who are essential to the process or operation. If feasible, these workers should be isolated from direct contact with propylene oxide by use of automated equipment operated from a closed control booth or room. This room should be maintained at greater air pressure than that surrounding the process equipment so that air flows out rather than in. When workers must enter the general work area to perform process checks, adjustments, maintenance, assembly line tasks, and related operations, they should take special precautions such as the use of personal protective equipment.

Personal Protective Equipment

Chemical Protective Clothing and Equipment.--To minimize skin contact and absorption, workers using propylene oxide should wear appropriate chemical protective clothing (CPC) such as gloves and aprons. CPC made from butyl rubber and Teflon® should provide adequate protection for at least 1 hr [Schwope et al. 1985]. Note, however, that the quality of gloves may vary significantly among glove producers [Mickelsen and Hall 1987]. Product-specific chemical permeation data should therefore be obtained from the glove manufacturer. Splashproof goggles or face shields should be worn if there is any possibility that liquid propylene oxide will contact the eyes. Safety showers and eye wash stations should be located close to operations that involve propylene oxide.

Respiratory Protective Devices.--The use of respirators is the least desirable method of controlling worker exposures and should not be used as the primary control method during routine operations. However, NIOSH recognizes that respirators may be required to provide protection in certain situations such as implementation of engineering controls, certain short-duration maintenance procedures, and emergencies. NIOSH maintains that only the most protective respirators should be used for situations involving carcinogens. These respirators include

--any self-contained breathing apparatus with a full facepiece operated in a pressure-demand or other positive-pressure mode, and

--any supplied-air respirator with a full facepiece operated in a pressure-demand or other positive-pressure mode in combination with an auxiliary self-contained breathing apparatus operated in a pressure-demand or other positive-pressure mode.

Any respiratory protection program must, at a minimum, meet the requirements of 29 CFR 1910.134. Respirators should be approved by NIOSH and the Mine Safety and Health Administration [NIOSH 1987b]. A complete respiratory protection program should include regular training and medical evaluation of personnel, fit testing, periodic environmental monitoring, and maintenance, inspection, and cleaning of equipment. The program should be evaluated regularly. The following publications contain additional information about medical evaluations of respirator users and the selection, fit testing, use, storage, and cleaning of respiratory equipment: *Guide to Industrial Respiratory Protection* [NIOSH 1987a] and *NIOSH Respirator Decision Logic* [NIOSH 1987c].

Decontamination and Waste Disposal

If propylene oxide contacts the skin, promptly wash the contaminated area with soap or a mild detergent and water.

The following steps should be taken in the event of a propylene oxide spill [Mackison et al. 1981]:

1. Remove all ignition sources.

2. Ventilate the area of a spill or leak.

3. Absorb small quantities on paper towels and permit the vapor to evaporate completely in a safe place (such as under a fume hood). Allow sufficient time for the vapor to clear completely from the hood ductwork; then burn the paper towels in a suitable location away from combustible materials.

4. Collect large quantities and dissolve in alcohol of greater molecular weight than butyl alcohol. Atomize the solution and burn it in a suitable combustion chamber.

5. Do not allow propylene oxide to enter a confined space such as a sewer because it may explode.

Medical Monitoring

A medical monitoring program should be established for prevention or early detection of the acute, chronic, or carcinogenic effects of propylene oxide. Medical and work histories (including previous exposure to propylene oxide or other toxic agents) should be taken for each worker before job placement and updated periodically. The worker's physician should be given information on the adverse health effects of propylene oxide exposure and an estimate of the worker's potential for exposure. This information should include results of workplace sampling and a description of any protective devices or equipment the worker is required to use. The examining physician should direct particular attention to the skin and to the nasal and respiratory tracts, as these sites are the most likely to be affected by propylene oxide. The occurrence of disease or other work-related health effects requires immediate evaluation of primary preventive measures (e.g., industrial hygiene monitoring, engineering controls, and personal protective equipment). Medical personnel should ensure that workers are informed of the health effects associated with propylene oxide exposure.

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