

## VI. DEVELOPMENT OF STANDARD

### Basis for Previous Standards

In 1961, the American Conference of Governmental Industrial Hygienists (ACGIH) published tentative threshold limit values (TLV's) for a number of glycidyl ethers. The tentative TLV's were: AGE, 45 mg/cu m; BGE, 270 mg/cu m; DGE, 55 mg/cu m; IGE, 240 mg/cu m; and PGE, 310 mg/cu m [86]. The ACGIH adopted these TLV's in 1962 [87].

In 1963, the ACGIH [88] recognized that TLV's expressed as 8-hour time-weighted average (TWA) concentrations did not provide a safety margin for certain fast-acting substances comparable with that provided by a TWA limit for slow-acting substances. A "C" or "ceiling" designation was therefore affixed to AGE and DGE, indicating that the limit should not be exceeded under any circumstances. The TLV for DGE was lowered to 2.8 mg/cu m at the same time. According to the 1966 Documentation of Threshold Limit Values [89], the earlier limits had been based on a single study by Hine et al [23] and a determination of the LD50 for PGE by Smyth et al [34]; no other data were available. The former report [23] described extensive animal studies but contained limited human data. The change in the limit for DGE was based on a 1962 written communication to the ACGIH from NG White, who had concluded on the basis of industrial experience that the TLV was too high. The documentation indicated that animal studies suggested that 2.8 mg/cu m would be a no-effect level.

In 1968, the TLV for PGE was lowered from 310 mg/cu m to 60 mg/cu m [90]. In 1970, an intent to change the limit for AGE from 45 to 22 mg/cu m

and to drop the ceiling designation was published [91].

The TLV's and accompanying notations for BGE, DGE, and IGE remained unchanged through 1971, and the 1971 Documentation of Threshold Limit Values for Substances in Workroom Air [92] used the previously cited study by Smyth et al [34] as the basis for the change in the limit for PGE and the study by Hine et al [23] as the basis for the proposed change for AGE. The earlier limits were not considered sufficiently low to protect against irritation or against systemic effects such as sensitization [92].

In 1972, the limit for AGE remained a ceiling concentration of 45 mg/cu m [93]. In 1973, the ACGIH adopted the proposed TLV for AGE of 22 mg/cu m without a ceiling designation [94], and in 1974 AGE was given a "skin" designation to indicate that skin contact should be prevented if possible and that contact with the skin should be considered in the evaluation of exposure [95]. ACGIH TLV's for BGE, DGE, IGE, and PGE have remained unchanged since 1968. However, tentative short-term exposure limits (STEL's) of 360 mg/cu m for IGE and 90 mg/cu m for PGE were proposed by ACGIH in 1976 [96]; these limits were for periods of up to 15 minutes, separated by at least 1 hour and not to exceed four such exposures in an 8-hour day. Changes in ACGIH TLV's for the glycidyl ethers are summarized in Table VI-1 [86,88,90,94,95].

According to the 1976 joint report of the International Labour Office (ILO) and the World Health Organization (WHO) [97], nine other countries have set limits to regulate exposure to the glycidyl ethers. These maximum allowable concentrations (MAC's) are presented in Table VI-1.

TABLE VI-1

## PERMISSIBLE ENVIRONMENTAL LIMITS FOR GLYCIDYL ETHERS (MG/CU M)

Standard	AGE	BGE	DGE	IGE	PGE
<u>ACGIH TLV's</u>					
1962	45	270	55	240	310
1963	45 C*	"	2.8	"	"
1968	"	"	"	"	60
1973	22	"	"	"	"
1974	22 S*	"	"	"	"
<u>Current US Federal Standard</u>					
	45 C*	270	2.8	240	60
<u>Foreign MAC's**</u>					
Australia	22 C*	270	2.8	240	60
Belgium	22 H*	"	"	"	"
Federal Republic of Germany	45 SP*	-	2.8	"	310 SP*
Finland	22 H*	270	2.8 C*	"	60
Netherlands	"	"	"	"	"
Rumania	Average: 100 Maximum: 200	100 200	- 2.0	50 100	75 100
Sweden	-	-	2.8 C*	-	-
Switzerland	22 H*	270	"	240	60 SP*
Yugoslavia	45	"	2.8	"	60

\*C = ceiling limit never to be exceeded; S = skin contact should be prevented if possible and should be considered in evaluating exposure; H = skin irritant; SP = sensitization potential

\*\*Maximum Allowable Concentrations

Adapted from references 86,88,90,94,95,97

Present Federal standards (29 CFR 1910.1000(a)), expressed as 8-hour TWA concentrations for the workplace environment, are BGE, 270 mg/cu m; IGE, 240 mg/cu m; and PGE, 60 mg/cu m. The present Federal standards for AGE and DGE, designated as ceilings, are 45 mg/cu m and 2.8 mg/cu m, respectively. These limits are based on the TLV's for workplace exposure adopted by the ACGIH in 1968.

#### Basis for the Recommended Standard

Adverse effects reported in humans occupationally exposed to glycidyl ethers have been limited to irritation of the skin and mucous membranes and sensitization, and systemic effects in animals have generally been reported only at relatively high concentrations or doses. However, the glycidyl ethers are biologically reactive compounds because of the presence of the epoxide group. They have been shown to have cytotoxic effects and to be mutagenic in bacteria and other test systems. At least one, DGE, should be regarded as a potential occupational carcinogen on the basis of animal tests. Because there is evidence that some glycidyl ethers have the potential to produce tumorigenic, mutagenic, or reproductive effects, and because few have been adequately tested for such effects, occupational exposure to glycidyl ethers is defined in this document as work in any area where these substances are manufactured, stored, used, or handled. All employees working in such areas should receive adequate medical surveillance and their environmental exposures should be evaluated. Appropriate engineering controls, monitoring and recordkeeping, sanitation procedures, work practices, protective clothing and equipment, and training

programs should be used to keep worker exposure to the glycidyl ethers as low as is technically feasible.

(a) Permissible Exposure Limits

Data currently available make it possible to set environmental limits for only five of the glycidyl ethers. The primary effect of these compounds at relatively low concentrations is irritation of the skin, eyes, and respiratory system. To minimize irritative effects by preventing exposures at high concentrations of airborne glycidyl ethers, NIOSH recommends environmental limits as ceiling concentrations based on a 15-minute sampling period.

Although no data have been found on possible additive effects, employers should consider the possibility of such effects when employees are simultaneously exposed to more than one glycidyl ether. The following formula can be used to calculate the appropriate environmental limit when such additive effects may occur:

$$CPEL_n \cong \left\{ 1 - \left( \frac{C_1}{PEL_1} + \dots + \frac{C_{n-1}}{PEL_{n-1}} \right) \right\} PEL_n$$

$CPEL_n$  = conditional permissible exposure limit  
for the nth compound

$C_1$  to  $C_{n-1}$  = measured concentrations of compounds 1 to n-1

$PEL_1$  to  $PEL_n$  = permissible exposure limits for compounds 1 to n

(1) Allyl Glycidyl Ether (AGE)

Eye irritation has been noted by one worker and by experimenters exposed at unknown concentrations to AGE vapor [23]. Corneal opacity has been observed in rats exposed to AGE at vapor concentrations as low as 400 ppm (1,870 mg/cu m) for 7 hours/day, 5 days/week, for 10 weeks. This exposure also produced emphysema, bronchiectasis, and

bronchopneumonia. Inflammation and congestion have been observed in various organ systems of rats after inhalation of AGE [23,48]. Inhalation exposure of rats at concentrations of 260 ppm (1,210 mg/cu m) for 7 hours/day, 5 days/week, for 10 weeks caused decreased weight gain, slight irritation of the eyes, and mild respiratory distress for the duration of exposure [23]. AGE has shown mutagenic activity in bacteria [57], but mutagenicity has not been confirmed in other tests.

The limited data available suggest that the current Federal standard provides an adequate safety margin to prevent systemic effects from inhalation of AGE. NIOSH therefore recommends that worker exposure to airborne AGE be limited to 45 mg/cu m (9.6 ppm), measured as a 15-minute ceiling concentration.

(2) Isopropyl Glycidyl Ether (IGE)

No effects have been demonstrated in workers exposed to IGE [23]. Inhalation exposure to IGE at a concentration of 400 ppm (1,900 mg/cu m), 7 hours/day, 5 days/week, for 10 weeks caused only slight eye irritation, respiratory distress, and decreased weight gain in rats [23].

Because only slight irritation was produced in these animals and because there are no reports of human effects, NIOSH recommends that the present Federal standard for IGE of 240 mg/cu m (50 ppm) be retained, but that it be changed from a TWA value to a ceiling concentration for a 15-minute sampling period to provide adequate protection against irritative effects.

(3) Phenyl Glycidyl Ether (PGE)

No reports were found of adverse effects in humans from exposure to airborne PGE. Respiratory tract irritation [23] and skin

irritation [39] have been reported in rats exposed repeatedly to airborne PGE at concentrations of 5-12 ppm (30-72 mg/cu m). Exposure to PGE at 12 and 5 ppm caused skin damage and loss of hair in rats, but no effects were observed at 1 ppm (6 mg/cu m) [39]. The only effects reported in rats exposed to PGE at about 10 ppm (60 mg/cu m) 5 days/week for 10 weeks were respiratory tract inflammation and early stages of necrosis in the liver [23]. The weight gain and tissues of these animals did not differ from those of controls. PGE has shown mutagenic activity in bacteria, but it produced no dominant lethal or teratogenic effects in mice exposed at 11.5 ppm (71 mg/cu m) for 12-19 days [49]. Inconclusive evidence of testicular degeneration was reported in some rats exposed to PGE at 1.75-11.20 ppm (11-71 mg/cu m) [49].

Because irritation has been observed in animals after exposure at concentrations as low as 5 ppm (30 mg/cu m), and in order to provide an adequate safety margin, NIOSH recommends that the environmental limit for PGE be set at 5 mg/cu m (1 ppm), designated as a ceiling concentration for a 15-minute sampling period.

#### (4) n-Butyl Glycidyl Ether (BGE)

No reports were found of adverse effects in humans from exposure to airborne BGE. In LC50 studies with BGE, some exposed rats developed focal inflammatory cells with moderate congestion in the liver and hyperemia of the adrenal glands at unspecified vapor concentrations [23]. The only other study found that investigated systemic effects of BGE reported minimal toxic effects and a slight increase in leukocyte counts in rats given three im injections of 400 mg/kg [48].

BGE was mutagenic in microbial and mammalian test systems [57,58]. It produced a significant increase in the number of fetal deaths in the dominant lethal test when applied to the skin of male mice in doses of 1.5 g/kg during an 8-week period [58].

No studies have investigated the effects of long-term inhalation of BGE at low concentrations in humans or animals; thus, calculation of a safe exposure concentration is not possible. However, BGE has been implicated as a mammalian mutagen, and it has caused skin and eye irritation and sensitization. NIOSH therefore recommends that the limit for worker exposure to BGE be set at the lower limit of detectability permitted by the NIOSH-recommended sampling and analytical method, 30 mg/cu m (4.4 ppm), as a ceiling concentration for a 15-minute sampling period.

(5) Di(2,3-epoxypropyl) Ether (DGE)

DGE is not widely used in industry, and no reports of effects on humans have been found. When tested in animals, it was the most irritating and the most toxic of the glycidyl ethers [23]. DGE has produced a 40% incidence of skin papillomas in those mice that survived a dose of 0.75 millimole [51]. It has also shown mutagenic activity in bacteria [57]. Corneal opacity has been reported in rabbits exposed to airborne DGE at concentrations of 20-27 ppm (106-144 mg/cu m) [47]. In single 24-hour exposures, DGE at 24 ppm (128 mg/cu m) killed three rabbits and produced changes in the lungs, liver, kidneys, and testes [41]. A similar exposure at 6 ppm (32 mg/cu m) produced basophilia in rabbits, but no effects were observed in those exposed at 3 ppm (16 mg/cu m).

Exposure to DGE at 3 ppm (16 mg/cu m) for 4 hours/day, 5 days/week, for 19 exposures during 29 days killed 5 of 30 rats and caused



bronchopneumonia, inflammation of the larynx, peribronchiolitis, and necrosis of pancreas, spleen, and testicular tubules [41]. Rats exposed at this concentration also showed significant decreases, compared with controls, in weight gain, organ weight/body weight ratio of thymus and spleen, leukocyte count, percentage of polymorphonuclear cells, and bone marrow nucleated cells, and a significant increase in the ratio of myeloid to erythroid cells. Rats exposed to DGE at 0.3 ppm (1.6 mg/cu m) had no significant changes in weight gain, bone marrow, or blood; however, "poorly defined" degeneration of the testes was reported in 5 of 10 rats killed after 60 exposures [41].

Because DGE has shown tumorigenic activity in mice and produced mutations in bacteria, it should be regarded as a potential occupational carcinogen. Exposure to DGE at 3 ppm (16 mg/cu m) has produced irritative and systemic effects in rats, including evidence of cytotoxicity, and testicular changes have been reported in rats exposed at concentrations as low as 0.3 ppm (1.6 mg/cu m). NIOSH therefore believes that the current Federal standard of 2.8 mg/cu m does not provide adequate protection and recommends that exposure to airborne DGE not exceed 1.0 mg/cu m (0.2 ppm) as a ceiling concentration determined in a 15-minute sampling period.

#### (6) Other Glycidyl Ethers

Limited data are available on several other glycidyl ethers. All glycidyl ethers that have been tested have been mutagenic in bacteria [49,57,58], and CGE and neopentyl glycol diglycidyl ether have also induced unscheduled DNA synthesis in human white blood cells [58]. Triethylene glycol diglycidyl ether, which is not currently used or manufactured in the United States, has produced lung tumors in mice receiving ip doses in

excess of 3.6 g/kg [52]. Resorcinol diglycidyl ether [51] and diphenylol propane diglycidyl ether [37] each produced a single skin papilloma in tests on mice. Only hydroquinone diglycidyl ether has given clearly negative results in a test of its tumorigenicity [51]. In addition, all glycidyl ethers that have been tested, including alkyl glycidyl ethers, diphenylol propane diglycidyl ether, neopentyl glycol diglycidyl ether, and butanediol diglycidyl ether, have produced sensitization [28,32,44].

The complete absence of inhalation toxicity data on these compounds makes it impossible to set limits for environmental concentrations. The vapor pressures of some of the compounds, such as diphenylol propane diglycidyl ether and resorcinol diglycidyl ether, are extremely low at ambient temperatures, so that the risk to workers from inhalation of these compounds is probably negligible. Other glycidyl ethers in this document may have appreciable vapor pressures at ambient or higher temperatures, but no data are currently available on which limits can be based.

Because the epoxide moiety is highly strained, all the glycidyl ethers are chemically reactive. In biologic reactions, the epoxide ring may cleave to form a carbonium ion, which can react with nucleophilic centers such as protein, RNA, and DNA [6]. For the diglycidyl ethers, this reaction may result in crosslinking of nucleophilic centers, which may be responsible for the high biologic activity of DGE. These considerations and the similar effects of the glycidyl ethers in producing sensitization and bacterial mutations suggest that the glycidyl ethers have the potential to produce harmful effects under occupational exposure conditions. Therefore, glycidyl ethers for which limits have not been recommended should be treated with the same caution required for the manufacture,

handling, and storage of those for which there are environmental limits.

(b) Sampling and Analysis

Little information on methods other than those recommended by NIOSH for the sampling and analysis of glycidyl ethers has been found in the literature.

To monitor the concentration of glycidyl ethers in the employee's breathing zone, one must periodically take air samples. NIOSH recommends sampling by drawing a known volume of air, which will vary according to the ether being sampled, through a tube containing charcoal or, for AGE, resin, to adsorb any organic vapors that are present. The organic material should then be desorbed with carbon disulfide (for BGE, IGE, or PGE), diethyl ether (for AGE), or methylene chloride (for DGE), and an aliquot of this extract should be analyzed by gas chromatography. Because the other glycidyl ethers are structurally similar to AGE, BGE, and IGE, the method should be adequate for them as well if certain factors, such as solvents, adsorbents, and gas chromatographic conditions, are appropriately adjusted. The NIOSH-recommended method for these three compounds is presented in Appendix I, and the proposed NIOSH method for the sampling and analysis of AGE is presented in Appendix II. A similar method for DGE is described in Appendix III. These methods have not been validated for detecting these glycidyl ethers at the recommended ceiling concentrations. However, it is probable that their sensitivities can be increased by increasing the sampling rate, as is proposed in Appendix I. The method recommended for DGE was not validated by NIOSH because the recovery of DGE was unacceptably low [79]. Preliminary data indicated that desorption efficiency may be a function of the temperature and length of storage. It is reasonable to

assume that, when the roles of these variables have been determined so that a standard procedure of maximal efficiency and reliability can be established, this method will be useful for determinations of DGE at the recommended ceiling concentration.

(c) Medical Surveillance and Recordkeeping

Glycidyl ethers are primary skin and eye irritants and may sensitize the skin [23-26,30]; NIOSH recommends, therefore, that preplacement and periodic medical examinations, with special attention to the skin and eyes, be made available to all employees occupationally exposed to glycidyl ethers. Although some glycidyl ethers had effects on the hemopoietic system [23,41,48], these have been observed only at high exposure concentrations or doses. Blood changes in workers would therefore be expected to appear only at exposure concentrations much higher than those that would produce irritation or sensitization of the skin. Because important toxic effects of the glycidyl ethers on the lungs, CNS, and kidneys have been found in animals, examination of the functions of these systems is suggested as a part of the general medical examination.

During the medical examination, workers in places of employment where DGE or BGE is used should be warned that DGE was tumorigenic in mice and that BGE was mutagenic in tests on mice [49,50,52,57,58].

Pertinent medical and other records should be maintained for all employees occupationally exposed to glycidyl ethers. These records should be kept for at least 30 years after termination of employment.

(d) Personal Protective Equipment and Clothing

Because of the irritating and sensitizing potentials of glycidyl ethers, personal protective equipment and impervious clothing should be

worn to prevent skin and eye contact with the compounds or their vapors or mists. Gloves, boots, aprons, faceshields (8-inch minimum), and goggles or safety glasses with side shields are recommended. Tests performed at the Argonne National Laboratories in 1964 showed that protective gloves made from natural rubber (latex), neoprene natural rubber (latex), milled neoprene, neoprene with nylon, milled Buna-1, vinyl and polyethylene (disposable), and polyvinyl chloride would not protect the skin dependably from contact by AGE and PGE [84]. Only milled butyl rubber and polyvinyl alcohol proved to be adequate. Gloves made of polyvinyl chloride or polyethylene-coated fabric may be used for a single workshift exposure. The employer should ensure that the gloves and protective clothing worn by the employees are impervious to glycidyl ethers and that they are maintained in good condition and replaced as necessary. An alternative and less desirable tactic is to issue new gloves each day.

The use of protective hand creams is suggested as a supplement to gloves where manual dexterity requirements limit the types of gloves that can be worn. Because absorption of and sensitization by glycidyl ethers occurs more readily through irritated and cracked skin, lipid solvents should not be used for cleaning the skin [28,45,71]. When leather clothing or equipment, such as belts or shoes, becomes obviously contaminated with a glycidyl ether, it should be made unfit for use and discarded [17(p 5)].

The employer should institute a respiratory protection program in accordance with 29 CFR 1910.134, and respirator types approved under provisions of 30 CFR 11 for the concentrations specified should be provided. Approved respiratory protective equipment, as shown in Tables I-1, I-2, I-3, and I-4, should be used during nonroutine maintenance,

emergencies, or installation of equipment, and at any other time when employees are potentially exposed to glycidyl ethers at concentrations above the recommended ceiling concentrations. Because of the potential of these compounds for irritating and sensitizing the skin and eyes, full-body protective clothing should be worn in any situation in which a respirator is required. Workers should be properly trained in the use and care of all respirators assigned to them.

(e) Informing Employees of Hazards

The employer should initiate a continuing education program to ensure that employees have current knowledge of job hazards and of proper work practices and emergency procedures. Employees should also be informed before job placement that irritation and sensitization may result from exposure to glycidyl ethers and that DGE has caused skin tumors in mice and BGE has been found to be a mammalian mutagen.

(f) Work Practices

Glycidyl ethers are primary irritants and sensitizers, and several of them have been mutagenic or tumorigenic. Safe handling of these compounds depends, therefore, upon work practices and engineering controls that are designed to prevent or minimize inhalation of and skin and eye contact with them.

Many glycidyl ethers are combustible or flammable liquids, which can present a fire hazard. Many of them may polymerize violently after slight heating, so that precautions should also be taken to prevent fires and explosions. In the event of a fire, media such as water, carbon dioxide, or dry chemicals should be used to extinguish it [3]. Workers must also be protected from the possible hazards of inhaling or ingesting or becoming

contaminated with glycidyl ethers during fires or other emergencies.

To reduce the fire and explosion hazards, smoking and the carrying of open flames or ignition sources should be prohibited in the work area. Electrical wiring should comply with appropriate sections of the National Electrical Code as adopted by OSHA in 29 CFR 1910.309. The tools used to open containers should be of nonsparking materials, and the containers should be bonded and electrically grounded before glycidyl ethers are transferred.

To minimize inhalation of the chemicals, processes should be enclosed whenever possible. When this is not feasible, ventilation systems, such as specifically placed hoods, can be used. Epoxy-based adhesives containing glycidyl ethers should be used only with adequate ventilation.

To prevent the ingestion of glycidyl ethers, food and beverages should not be prepared, dispensed, consumed, or stored in work areas. Employees should be advised to wash their hands before eating or using toilet facilities. Employees should also be cautioned not to touch or rub their eyes with hands that may be contaminated with glycidyl ethers. These general practices, which are discussed in more detail in Chapter V, apply uniformly to the handling, storage, manufacture, and use of all glycidyl ethers.

(g) Monitoring and Recordkeeping Requirements

Workers are not considered to be overexposed to glycidyl ethers if industrial hygiene surveys show that the concentration of airborne glycidyl ethers in the employees' breathing zones are below the recommended ceiling concentrations. However, employee exposures to those glycidyl ethers for which no environmental limits have been recommended should also be

evaluated, and appropriate records of these exposures should be maintained.

Surveys to determine employee exposure should be repeated at least semiannually and within 30 days of any process change likely to result in increases in concentrations of airborne glycidyl ethers. For each ceiling determination, a sufficient number of samples should be taken and analyzed to characterize each employee's exposure during each workshift. Variations in work or production schedules and in employment location and job function should be considered in choosing sampling times, locations, and frequency.

If it is determined that an employee's exposure to a glycidyl ether exceeds the recommended ceiling concentration, control measures should be initiated, the employee should be notified of the exposure and of the control measures being implemented to correct the situation, and the exposure of that employee should be monitored at least once every 30 days. Such monitoring should continue until two consecutive determinations, at least 1 week apart, indicate that exposure no longer exceeds the recommended ceiling concentration. When no ceiling concentration has been recommended, the discovery of any free glycidyl ethers in the workplace should lead to an analysis of engineering controls, work practices, and sanitation procedures to determine that they are operating as effectively as possible, or that those practices and procedures in use are the most efficient ones for preventing access of the glycidyl ethers to the employee.

Records of environmental monitoring, including the basis for the determination that an employee's exposure is below the recommended ceiling concentration, and medical records should be kept for 30 years after termination of employment. The Toxic Substances Control Act of 1976



requires that "Records of...adverse reactions to the health of employees shall be retained for thirty years from the date such reactions were first reported to or known by the person maintaining such records." Because medical examinations will often provide the first recognized evidence of an adverse reaction, whether at the time of the examination or retrospectively, requiring medical records on glycidyl ether workers to be maintained for 30 years seems to be consonant with the Toxic Substances Control Act. Records of environmental exposures should be kept for the same period, to allow correlation of glycidyl ether workers' exposures with changes in their health status.

## VII. RESEARCH NEEDS

By current standards for appraising toxicologic and health hazards, the relevant information available on glycidyl ethers is limited. Dose-response information is especially scarce. No information on the possible carcinogenic and mutagenic hazards of these compounds in humans was found. This scarcity of reported effects is remarkable in light of the widespread use of glycidyl ethers. The number of persons exposed has gone from very few in the 1930's to more than 1,000,000 each year in the 1970's. Many glycidyl ethers are primary irritants, cause allergic reactions, and have the potential to cause cross-sensitization; however, the lack of reports of serious adverse effects in workers exposed to these compounds is encouraging.

The existing data, which come primarily from animal experiments, indicate that some glycidyl ethers are relatively toxic [23,25,27,41,48] and are potentially cytotoxic or mutagenic [6,56,58]. Only a few of the ethers have been assessed for toxicity, even though others, such as CGE, are used in industry. BGE has been shown to be mutagenic [58], and DGE and triethylene glycol diglycidyl ether, at high doses, were tumorigenic and carcinogenic, respectively [51,52]. Further studies of the toxicity of glycidyl ethers should therefore include examination of the carcinogenic, mutagenic, and teratogenic potential of each glycidyl ether that is widely used in industry. Information is especially needed on the effects of these compounds at low doses or concentrations. The similarity in structure of these compounds and the fact that they are potential alkylating agents give

reason for concern about their potential mutagenic and carcinogenic properties.

No epidemiologic studies of workers exposed to glycidyl ethers have been found. There are no existing data on human inhalation exposure to glycidyl ethers. Studies of effects on humans from inhalation exposure that include data on exposure durations and concentrations are needed. Epidemiologic studies that address the problems of sensitization and cross-sensitization, the effects of long-term exposure to the glycidyl ethers, and the influence of age, sex, and other factors on the toxicologic effects of these compounds are also needed. These studies should be designed to investigate eye, respiratory, and skin irritation, in addition to other toxic effects. Although the sensitization potential of some of the glycidyl ethers has been examined in humans [25,27], more research is needed that examines allergic reactions and possible cross-sensitization in glycidyl ether workers with occupational dermatitis.

Sampling and analytical methods have been validated for only four of the glycidyl ethers--BGE [75], IGE [77], AGE [78], and PGE [76]. These methods have not been validated at concentrations as low as the recommended environmental limits, so further refinement of the methods is necessary. No sampling and analytical method has been validated for measuring DGE at the low concentrations at which toxic effects have been reported. Study of the influences of temperature and duration of storage of DGE samples on desorption efficiency may permit the establishment of an improved analytic method for this compound. Other glycidyl ethers, such as resorcinol diglycidyl ether and CGE, are used in industry, and methods of sampling and analysis need to be developed for them. Research to develop continuous

monitoring techniques for the glycidyl ethers would be very desirable. Methods for biologic monitoring should also be developed to permit characterization of accumulated body burden.

Although it appears that there exist in humans two enzymes capable of metabolizing the glycidyl ethers [60,64], little is known about the fate of the ethers in the human body. More information about the metabolism of these compounds and on the toxicology of their metabolites is needed. Pharmacokinetic studies to characterize metabolic pathways would be valuable, especially in the interpretation of experimental data on cytotoxic and mutagenic effects and other aspects of systemic toxicity.

Research related to work practices is also needed. For example, materials impervious to glycidyl ethers and suitable for use in protective clothing, aprons, and gloves need to be identified. Further data on the toxic effects and physical and chemical properties of some of the ethers used in industry are needed, so that appropriate respirator selection guidelines can be developed for them.

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