IV. ENVIRONMENTAL DATA AND ENGINEERING CONTROLS

Environmental Data

Dow Chemical Company [2] reported personnel monitoring data by job classification for its units which produce allyl chloride, epoxy resin, and glycerine. Sampling was conducted with charcoal tubes using a calibrated, battery-operated pump. Quintuplicate samples were taken for each job classification at a rate of 2 liters/minute for 7 hours. Epichlorohydrin and chlorinated hydrocarbons were extracted with 30 ml of carbon disulfide. Epichlorohydrin recovery from the charcoal, after sampling, was found to be 65%. Analysis was performed with a hydrogen flame chromatograph equipped with a 12 feet x 1/8 inch column packed with 15% Oronite NiW on gas chrom CLA (60-80 mesh). In 1973, in the epoxy resin unit, one air sample in the breathing zone of each of four employees (three operators and one helper) showed the average epichlorohydrin concentration to be 0.03 ppm. In the same year, 78 grab samples indicated that epichlorohydrin concentrations ranged from 13 ppm to less than 0.60 ppm, with an average of 3.17 ppm. It should be noted that the "average" was a numerical average between the individual samples, not the TWA concentrations. The results of air monitoring done in 1974 are presented in Table IV-1. In the glycerine distribution unit, five air samples in the breathing zones of an operator, two for the head operator, and two for the technician showed epichlorohydrin concentration to be below 0.01 ppm. These were taken in 1975. Results of air monitoring for epichlorohydrin done in the glycerine plant in 1975 are presented in Table IV-2. Epichlorohydrin concentrations in the allyl chloride unit were below 0.1 ppm.

TABLE IV-1

EPICHLOROHYDRIN CONCENTRATIONS IN THE AIR IN AN EPOXY-PRODUCING UNIT (1974)

Job Classification	No. Samples	Epichlorohydrin (ppm v/v)		
		High	Low	Average
Warehouse operator	4	0.30	0.30	0.30
Machinist	1	0.10	0.10	0.10
Pipefitter	2	0.30	0.30	0.30
Control C operator	3	0.90	0.40	0.66
2d class operator BIS	1	0.10	0.10	0.10
Grab samples	25	15.00	0.60	2.02
Stationary monitoring	23	1.00	0.10	0.26

From reference 2

TABLE IV-2

EPICHLOROHYDRIN CONCENTRATIONS IN THE AIR IN A GLYCERINE-PRODUCING UNIT (1975)

Job Classification	No. Samples	Epichlorohydrin (ppm v/v)		
		High	Low	Average
Control "A"	5	1.37	0.24	0.54
Instrument	2	0.01	0.01	0.01
Lab	6	0.67	0.01	0.11
Shift foreman	3	0.24	0.01	0.08
EPI helper	4	0.18	0.01	0.05
Control "A" finishing	2	0.01	0.01	0.01
Maintenance	13	4.69	0.01	1.50

From reference 2

Pet'ko et al [11] reported the results of environmental monitoring done in epichlorohydrin and dichlorhydrin-glycerine production units in Russia. The sampling technique employed was not specified. Concentrations of epichlorohydrin ranged from 19 to 21 mg/cu m (4.9-5.5 ppm) in the zone of employees who withdrew samples for quality control from the epichlorohydrin-production process. Airborne concentration of epichlorohydrin reached 12-15 mg/cu m (3.1-3.9 ppm) during the filling of tanks with epichlorohydrin. During an emergency caused by mechanical difficulties, a concentration range of 210-211 mg/cu m (54.6-54.9 ppm) was recorded.

Fomin [28] reported that, at about 100-200 meters from a factory discharging epichlorohydrin into the atmosphere, the airborne epichlorohydrin concentration exceeded the maximum permissible concentration of 0.2 mg/cu m by factors of 2.5-6. At a distance of 400 meters, 5 of 29 samples indicated that epichlorohydrin concentrations exceeded the 0.2 mg/cu m limit. No epichlorohydrin was detected at distances of 500-600 meters from the factory.

Sampling and Analysis

There are many general methods of sampling and analysis for organic vapors. A few of these have been adapted or found suitable for epichlorohydrin.

Impingers or bubblers containing distilled water have been used for epichlorohydrin vapor collection. [38,79] A 2-liter air sample is drawn

through two bubblers in series, containing 8 ml of water each, at a sampling rate of 0.5 liter/minute. [79] When a test atmosphere was used, the percentage of epichlorohydrin trapped in the first bubbler decreased as the atmospheric concentration decreased. At a concentration of 20 mg/cu m (approximately 5.2 ppm), the efficiency of one bubbler was 80%. For greater accuracy, two bubblers were recommended. The main disadvantage of such a sampling system is the difficulty in obtaining a personal sample. Since the collection medium is liquid, some sample loss can occur from spillage and evaporation. Epichlorohydrin vapor has also been collected in bubblers containing sulfuric acid. [80]

Plastic bags [81-84] and glass bottles [85] have been used for sampling industrial air. Usually, this has involved obtaining a volume of air over a very short time, from a few seconds to 2 minutes. Such sampling techniques are best suited for obtaining information on ceiling concentrations. However, sampling with plastic bags has been modified to determine TWA concentrations. [84] Aluminum foil-polyester laminate bags or Teflon bags were used. The advantage of this technique is that both TWA and excursion values can be estimated. However, 24-hour sample losses were 20-26% and 19-40% for epichlorohydrin stored in Teflon and aluminum foil-polyester laminate bags, respectively. These losses occurred when the epichlorohydrin concentration in the air sampled ranged from 5 to 27 ppm. [84] Bulkiness of the containers has created transportation problems.

Adsorption on silica gel [80,86,87] or activated charcoal [88-90] is commonly used to collect organic vapors. Reid and Halpin [91] found charcoal tubes both efficient and practical for sampling a number of chlorinated hydrocarbons. At present, a major manufacturing company uses

charcoal tubes for sampling epichlorohydrin. [2] Epichlorohydrin in air has been sampled at 20-30 liters/hour through a glass tube (45-mm long and 3 mm in diameter) containing 0.1 g silica gel. [80] Data on collection efficiency were not given. However, sampling with silica gel in high humidity may result in considerable sample loss from the displacement of the organic vapors by water vapor. Whitman and Johnston [92] reported that this problem could be overcome with a molecular sieve prefilter. They used a 5-Angstrom molecular sieve to remove water vapor from gas streams without interfering with the passage of aromatic hydrocarbons. White et al [89] have described the design of activated charcoal tubes suitable for sampling, and such tubes are commercially available. Adsorption on activated charcoal is the preferred sampling method for epichlorohydrin alone for several reasons: epichlorohydrin is not displaced by water vapor as it is from silica gel; it is a simpler, more convenient procedure than the use of plastic bags or of a bubbler; it uses a small, portable sampling device, and the difficulties associated with handling liquids are eliminated. Disadvantages are that the amount of sample that can be collected is limited by the number of milligrams that the charcoal tube will hold before overloading, and that the more volatile compounds can migrate to the backup section during storage before analysis.

Various methods used for analyzing the collected samples have included colorimetry, [79,80] infrared analysis, [93,94] and gas chromatography. [90,95] Colorimetric analysis suitable for analyzing epichlorohydrin in an aqueous solution has been used. [79] The colorimetric method [79] is based on the oxidation of epichlorohydrin in aqueous solution by periodic acid. Epichlorohydrin in water is hydrolyzed

to a glycol which is then oxidized to formaldehyde. Epichlorohydrin solutions of known concentrations are prepared to obtain the standard curve. The formaldehyde further reacts with sodium arsenite and acetylacetone reagent to form a yellow complex. The acetylacetone reagent solution is prepared by mixing ammonium acetate, acetylacetone, and glacial acetic acid in water. Maximum optical density of the yellow complex occurs at about 412 nm. This method was capable of determining as little as 20μg of epichlorohydrin. Data on the efficiency of the analytical technique were not given. [79] Formaldehyde, or any substance that may yield formaldehyde under the test conditions, will interfere. Compounds that contain or would form vicinal terminal hydroxy groups, such as ethylene glycol and ethylene oxide, will also interfere.

A colorimetric method [80] suitable for analyzing epichlorohydrin collected in sulfuric acid also has been used. Air containing epichlorohydrin was drawn through two bubblers containing 3 ml of 20% sulfuric acid and 4 ml of 10% sulfuric acid, respectively. The content of the first bubbler was diluted 1:1 with water. A 3-ml sample was then oxidized with 0.5 ml of 3% potassium iodate solution and allowed to stand for 30 minutes, during which time a yellow color developed. A 10% sodium sulfite solution was added and the mixture was shaken until the color disappeared. One milliliter of Schiff's reagent was then added and the intensity of the resulting color (magenta) was measured 1 hour later. The initial reactions occurring were similar to those in the previously discussed colorimetric method. [79] Epichlorohydrin is hydrolyzed by sulfuric acid and the resulting glycol is oxidized to formaldehyde by the iodate. The formaldehyde then reacts with Schiff's reagent to form a

magenta complex. Sodium sulfite is added to reduce the unreacted iodate. It was found that this method was capable of analyzing 0.01-0.1 mg epichlorohydrin in a 6-ml solution. Data on sensitivity, specificity, and interferences were not reported. However, the same compounds that would interfere with the previously discussed colorimetric technique, [79] such as ethylene oxide and ethylene glycol, would also interfere with this method. In addition, many aldehydes would interfere.

The formaldehyde can also react with phenylhydrazine hydrochloride to form phenylhydrazone. [38] The phenylhydrazone of formaldehyde reacts with potassium ferricyanide to form a colored complex. The maximum optical density of this complex occurs at about 500 nm. Epichlorohydrin concentrations ranging from 0.45 to 14 mg/cu m in air were determined by this method. Precision tests indicated the maximum error between the two determinations to be only 0.3%.

The infrared absorption spectrum of epichlorohydrin showed the typical terminal epoxide absorption bands. [93] The minimum amount of epichlorohydrin that was detected by infrared absorption was 0.3% (v/v in aqueous solution). [94] However, a practical and detailed technique using infrared analysis for a quantitative determination of epichlorohydrin has not been developed.

In recent years, gas chromatography has become the method of choice of most investigators for separation and the analysis of organic materials. [89,90] It offers excellent specificity and sensitivity and is suitable for analyzing samples of airborne contaminants collected on charcoal. Interferences are few, and most of those which do occur can be eliminated by altering the instrumental conditions. Muganlinsky et al [95] developed

a linear temperature program to analyze epichlorohydrin in the presence of chlorinated hydrocarbons which may be present as impurities.

The recommended methods for sampling and analyzing epichlorohydrin are collection by charcoal tube and analysis by gas chromatography. Sampling involves the collection of personal samples on charcoal tubes, and analysis involves desorption with carbon disulfide and measurement with a gas chromatograph equipped with a suitable detector. [90] Details of the recommended methods are given in Appendices I and II. The recommended methods are not validated for monitoring or for an environment that may contain other substances that may interfere. Other sampling and analytical methods equivalent in accuracy, precision, and sensitivity may be used.

Engineering Controls

Engineering design for safety in working with epichlorohydrin should be such as to reduce the concentration of airborne epichlorohydrin. Closed systems, properly operated and maintained, should be used in all cases where practicable. Frequent tests must be conducted for leaks in closed systems. Where closed systems are not feasible, well-designed local exhaust ventilation systems must be provided. Guidance for design can be found in Industrial Ventilation--A Manual of Recommended Practice, [96] or more recent revisions, and in Fundamentals Governing the Design and Operation of Local Exhaust Systems, ANSI Z9.2-1971. [97] In operations where epichlorohydrin is transferred, changed, or discharged into otherwise normally closed systems, continuous local exhaust should be provided at the transfer point. Sufficient ventilation with clean air should be maintained

in the area to permit the correct operation of the local exhaust system.

Respiratory protective equipment is not an acceptable substitute for proper engineering controls but should be available in emergencies and for nonroutine maintenance and repair work situations.

V. DEVELOPMENT OF STANDARD

Basis for Previous Standards

In 1965, the American Conference of Governmental Industrial Hygienists (ACGIH) adopted a threshold limit value (TLV) of 5 ppm (approximately 19 mg/cu m) for epichlorohydrin. [98]

In a personal communication cited in the Documentation of Threshold Limit Values for Substances in Workroom Air, [99] Smyth and Pozzani stated that cases of skin burns and sensitization, with resulting intolerance to trivial exposures, occurred in workers during the handling and production of epichlorohydrin. Systemic poisoning caused by epichlorohydrin penetration of the skin also was reported. Therefore, the ACGIH epichlorohydrin TLV listing was accompanied by a "skin" notation. [99] Such a notation refers to the potential contribution to overall exposure by the cutaneous route, including mucous membranes and eyes, either by airborne or, more particularly, by direct skin contact with liquid epichlorohydrin. This designation is intended to indicate the need for appropriate measures for the prevention of cutaneous absorption so that the TLV is not invalidated.

The present federal standard (29 CFR 1910.1000) for occupational exposure to epichlorohydrin is 5 ppm as an 8-hour TWA limit. This standard was based on the ACGIH TLV.

In Russia and in France, the maximum allowable concentration (MAC) in the industrial environment is 1 mg/cu m (0.26 ppm). [100] In the Rumanian Socialist Republic, 10 mg/cu m (approximately 2.6 ppm) of epichlorohydrin is the maximum concentration allowed in the occupational environment. [38]

In the Federal Republic of Germany, the permissible environmental exposure limit is 18 mg/cu m (approximately 3.6 ppm), and 5 mg/cu m (approximately 1 ppm) in the German Democratic Republic. [100] The bases for these standards are not given. Air and water quality standards have not been found, although one recommendation of such a value (0.2 mg/cu m) has been presented. [28]

Basis for the Recommended Standard

The induction of severe necrotic lesions occurring after dermal contact with epichlorohydrin has been reported. [35] A latency period lasting from several minutes to several hours between contact with liquid epichlorohydrin and the appearance of skin damage was observed. Epichlorohydrin penetrates the skin and can induce adverse systemic effects following dermal contact. [25,27,35] These necrotic lesions have been compared with those induced by X-rays or by other alkylating agents such as ethylene oxide or propanesultone. [35] These observations require, therefore, that complete skin protection be provided to employees handling epichlorohydrin. Care must be taken to ensure that shoes, gloves, and other protective clothing are made of material impervious to epichlorohydrin.

Reports on humans occupationally exposed to epichlorohydrin have identified the effects resulting from acute exposure. [28,37,38] Transient burning of the eyes and nasal passages in persons after exposure to epichlorohydrin at a concentration of 20 ppm was reported, [37,38] while exposure at 40 ppm caused eye and nasal irritation lasting 48 hours. [37,38] Lung edema and kidney lesions were reported in humans exposed to

epichlorohydrin at concentrations greater than 100 ppm for very short periods. [37,38] Changes in the voltage of the peaks of the alpha rhythm of the EEG measurements of volunteers exposed to epichlorohydrin at 0.08 ppm for a few minutes were reported by Fomin. [28] Since the significance of the changes observed in this component of the EEG measurements is not known, further research needs to be conducted in this area before any interpretations can be made. Acute exposure to epichlorohydrin at a high, but unknown, concentration [33] caused irritation of the eyes and throat, nausea, and dyspnea; bronchitis with bronchiolar constrictions and enlarged liver were suspected to have resulted from this single overexposure. These findings [28,37,38] suggest that a ceiling is required. Since acute effects have been observed on humans at 20 ppm, and the lowest concentration which induces effects during a short interval has not been identified, a ceiling concentration of 19 mg/cu m (5 ppm), based on professional judgment, is recommended to protect even the more sensitive fraction of the working population from these adverse effects.

The existing federal standard of 5 ppm is based on the 1968 TLV. Further information on cumulative aspects of toxicity such as sterility, carcinogenesis, and mutagenesis have been reported in subsequent studies. [28,31,32,39,64-66,74]

The report by Shumskaya et al [32] indicated that disrupted liver function and kidney damage developed in rats after single 4-hour exposures to epichlorohydrin at concentrations of 91, 5.2, or 1.8 ppm, the effects being least severe at 1.8 ppm. The authors did not indicate whether the chamber was static or dynamic. Thus, data from this study suggest that minor adverse effects are observed on animals inhaling a total amount of

1.0 mg/kg within 4 hours. The data demonstrate the induction of measurable biochemical perturbations, but cannot be used to predict the cumulative effects to be expected from long-term exposures to epichlorohydrin.

Kremneva and Tolgskaya [27] have reported neither mortality nor signs of intoxication in rats exposed for 3 hours at about 5.2-15.6 ppm daily for up to 6.5 months. Lags in body weight gains, initial increases in the excitability thresholds, elevations in blood pressures, and fluctuations in oxygen consumptions were observed in the animals when compared with the controls. They concluded that 5.2-15.6 ppm of epichlorohydrin approximated the threshold in rats, which is interpreted to mean that no measurable adverse effects occurred below these concentrations.

The minimal concentration which has been observed to induce effects on rats (about 5 ppm) is used to approximate the permissible exposure in the occupational environment by weighing additional risk factors. The chronic effects for which risk must be considered are carcinogenesis, mutagenesis, and antifertility, as well as liver, kidney, and lung damage.

Van Duuren et al [64] found that a single application of 2.0 mg of epichlorohydrin on mouse skin initiated the tumorigenic process in at least 9 of the 30 experimental mice when it was followed by triweekly applications of a promoter (phorbol myristate acetate) for the remainder of the 385-day experiment. The promoter alone induced papillomas in 3 of 30 mice. No initiation was observed in the control animals. Weil et al [63] and Van Duuren et al [64] found that repeated applications of epichlorohydrin on mouse skin did not induce a significant number of skin lesions. Van Duuren et al [64] found that sarcoma and adenocarcinoma were induced in 6 of 50 mice given weekly subcutaneous injections of 1.0 mg of

epichlorohydrin in 0.05 ml of tricaprylin (P values less than 0.05). Only 1 of the 50 control animals injected with tricaprylin alone developed sarcoma. No sarcomas developed in untreated control animals. The results were considered significant only when the P value was less than or equal to 0.05.

Antifertility effects, including persistent sterility, have been induced in animals exposed to epichlorohydrin. [39-41] Twelve repeated oral doses of 15 mg/kg of epichlorohydrin sterilized male rats. [41] Even though sterility occurred in animals following oral administration of epichlorohydrin, it is probable that similar effects would be produced by inhalation, since severe systemic effects have been observed after both dermal and inhalation exposures. [25,27] Epstein et al [61] did not observe any increase in the frequency of dead implantations in the uteri of mice following ip injections of 150 mg/kg of epichlorohydrin into the male rats mated to the females, nor did they provide any evidence of reduced fertility at this dosage.

Mutagenic effects of epichlorohydrin have been observed in microbial organisms and in the eukaryotic fruit fly, Drosophila melanogaster, following exposure to epichlorohydrin. [70] The number of point mutations observed in several microbial species increased as a function of epichlorohydrin concentration and duration of exposure. At present, an experimental relationship between the frequency of dead implantations and that of point mutations has not been observed. The positive results from the point mutation test systems in lower organisms, such as bacteria, [73-76] fungi, [71] and Drosophila melanogaster, [70] indicate that an increased risk of occurrence of point mutations may exist in human

populations exposed to epichlorohydrin. The fact that preparations derived from the urine of workers exposed to 25 ppm of epichlorohydrin influenced the genetic mechanisms in Salmonella typhimurium (DJ Kilian, written communication, April 1976) is consistent with the existence of a genetic risk to human populations exposed to epichlorohydrin.

The total risk to the health of employees occupationally exposed to epichlorohydrin is the result of the independent risks due to carcinogenesis, mutagenesis, sterility, and damage to kidneys, liver, respiratory tract, and to the skin. At present, evidence for the existence of the risks, other than to skin depends primarily on data from experimental animal models. Concern for employee health requires that the probability of the occurrence of chronic effects be minimized. NIOSH recommends, therefore, that worker exposure to epichlorohydrin be limited to a concentration of 2 mg/cu m (0.5 ppm) as a TWA concentration. This value has been chosen on the basis of professional judgment, rather than on quantitative data which clearly distinguish no-effect concentrations from those at which adverse effects have been shown to occur in human populations. A TWA concentration of 2 mg/cu m of epichlorohydrin should protect the employee against injury to organs during the individual's working lifetime, according to existing information. However, additional research is needed to provide support for the recommended environmental limit or to indicate the need for a different limit. The environmental limit implicitly assumes that the absorbed epichlorohydrin molecules will be detoxified by biochemical mechanisms, thereby reducing the risk of induction of human disease resulting from the cumulative toxicity of epichlorohydrin.

It is recognized that many employees handle small amounts of epichlorohydrin or work in situations where, regardless of the amount used, there is only negligible contact with epichlorohydrin. Under these conditions, it should not be necessary to comply with all of the provisions of the recommended standard, which has been prepared primarily to protect employee health under all circumstances. For these reasons, "occupational exposure to epichlorohydrin" is defined as exposure above one-half the TWA environmental limit, thereby delineating those work situations which do not require the expenditure of resources for environmental monitoring and associated recordkeeping. Because of nonrespiratory hazards such as the production of burns on the skin in the use of epichlorohydrin, NIOSH recommends that appropriate work practices and protective measures to limit such contact be required regardless of the concentration of airborne epichlorohydrin. Further, the observation of changes in the concentration of biochemical constituents [48] following human and animal exposure to epichlorohydrin suggest that the health of the exposed workers be monitored frequently. Thus, it is recommended that comprehensive medical examinations be offered to all employees subject to occupational exposure to epichlorohydrin and that the responsible physician consider the advisability of also administering any liver and kidney function tests.

VI. WORK PRACTICES

Work practices must be designed to minimize or to prevent inhalation of epichlorohydrin and skin and eyes from coming into contact with epichlorohydrin. Good work practices are a primary means of controlling certain exposures and will often supplement other control measures.

Enclosure of materials, processes, and operations is completely effective as a control only when the integrity of the system is maintained. Such systems should be inspected frequently for leaks and any leaks found should be promptly repaired. Special attention should be given to the condition of seals and joints, access ports, and other such places. [101] Similarly, points of wear should be inspected regularly for damage.

Ventilation systems require regular inspection and maintenance to ensure their effective operation. The effects of any changes or additions to the ventilating system or to the operations being ventilated should be assessed promptly, including measurements of airflow and of environmental levels of epichlorohydrin under the new conditions. Work practices should not introduce obstructions or interferences which would reduce the effectiveness of the ventilating system.

A major hazard of handling epichlorohydrin that can be minimized by good work practice is that from skin contact. Observation of animals indicates that severe systemic poisoning and death may result from skin contact with epichlorohydrin. [25,27] Ippen and Mathies [35] reported several cases of severe chemical burns caused by dermal contact with epichlorohydrin. Brief skin contact causes chemical burns, while extended skin contact may cause extensive skin burns and severe systemic effects.

The authors [35] also reported the occurrence of severe burns in an individual who spilled epichlorohydrin on his shoes which were not immediately removed. The severe effects are intensified by the penetration of epichlorohydrin into the clothing and shoes which act as reservoirs and continue the contact. For this reason, clothing contaminated with epichlorohydrin must be removed immediately and thoroughly laundered before reuse. Shoes on which epichlorohydrin is spilled are to be rendered unusable and discarded. The protective clothing must be made of material not permeable to epichlorohydrin. Penetration through three types of rubber has been measured [3] and found to be 9-11 minutes for nitrile rubber, 20-22 minutes for neoprene rubber, and 38-43 minutes for natural rubber. Since the penetration time is dependent on both the type of the rubber and the thickness, it is noteworthy that in this test [3] the thickness for each type of rubber was: 0.015 inches for nitrile rubber, 0.02 inches for neoprene rubber, and 0.030 inches for natural rubber. Since uniform thickness was not used, the data provide only a rough estimate of relative rate of epichlorohydrin penetration through different types of rubber. Nevertheless, it is evident that epichlorohydrin does penetrate rubber. When it is necessary to work with liquid epichlorohydrin, special handling techniques should be employed routinely. All body surfaces should be protected against contact with the liquid by the use of gloves, aprons, face shields, goggles, and other protective equipment or clothing. Ippen and Mathies [35] have pointed out that enclosed processes minimize any exposures; therefore, engineering controls are the most suitable control measures. Closed systems operating under negative pressure are particularly effective.

The flash point of epichlorohydrin is 93 F (70 C). [2] It is classified, therefore, as a flammable liquid of Class IC in 29 CFR 1910.106(a)(19)(iii). The lower and upper explosive limits in air at 20 C are 3.8 and 21.0%, respectively. [2] Hence, fire is a potential hazard because of the presence of epichlorohydrin. Recommended work practices should ensure that no flames or other sources of ignition, such as smoking, be permitted in the area where epichlorohydrin is stored or handled.

Safety showers, eyewash fountains, and fire extinguishers shall be located in or near areas where epichlorohydrin splashes are likely to occur and shall be properly maintained. Handwashing facilities, soap, and water must be available to the employees. As good hygiene practices, eating in epichlorohydrin work areas shall be prohibited and handwashing before eating recommended.

In summary, precautions must be exercised against overexposure to epichlorohydrin. It is important that employees be informed before job placement of hazards associated with the use of epichlorohydrin and when any process changes are made that may alter their epichlorohydrin exposure. Appropriate emergency procedures should be stressed. Recommended labels and posters must be displayed. The US Department of Labor "Material Safety Data Sheet," or a similar OSHA-approved form, must be filled out. In addition, all employees in the epichlorohydrin area should know where the safety sheet is posted. If all these work practices are observed and good engineering controls are installed, employees working with epichlorohydrin should be adequately protected from hazards associated with epichlorohydrin.

VII. RESEARCH NEEDS

Epidemiologic Study

One epidemiologic study involving workers exposed to epichlorohydrin has been found (DJ Kilian, written communication, April 1976). However, deficiencies such as the lack of a control group, the absence of measurements of exposure concentrations, and failure to indicate people lost to observation have limited the usefulness of the study. A retrospective controlled cohort study of a working population exposed chiefly to epichlorohydrin for a longer duration should provide valuable information.

Mutagenic Effect

This effect must be systematically investigated in greater depth with respect to dose, time, and route in both lower organisms and mammals. Animal tests using various doses, schedules, and routes of administration should be performed to see whether epichlorohydrin is a mutagen in mammals. Specific locus tests or heritable translocations should be considered. Animals should also be tested to see whether epichlorohydrin has any cytogenic effects.

Kidney Function in Workers Exposed to Epichlorohydrin

The impairment of kidney function as a result of epichlorohydrin exposure has been found in animals. As yet, there is no evidence that such injury also occurs in workers exposed to epichlorohydrin. Since a segment

of a working population which is exposed primarily to epichlorohydrin can be identified, kidney function tests should be given periodically to determine whether any changes in kidney function are occurring as a result of occupational exposure to epichlorohydrin.

Skin Sensitization

Although epichlorohydrin is commonly stated to be a sensitizer of the skin, the data that have been found in this regard are far from complete or persuasive. [11,36] Additional information on the degree and character of sensitization of the skin of humans is highly desirable. Some measure of variability in the skin response would be most useful.

Electroencephalographic (EEG) Studies

The index of effect by epichlorohydrin on humans that seems to be the most sensitive on the basis of the available information is a change in the voltage of the alpha rhythm of the EEG. [28] More information on the dose-response relationship for this effect and on its correlation with more usual alterations of function would be of great value.

Chronic Animal Exposure Studies

Inhalation exposure of various species of animals at several concentrations of epichlorohydrin up to the maximum tolerated concentration, 8 hours/day, 5 days/week, for at least 2 years, is recommended. These experiments should include measurement of food intake, monitoring of several biochemical parameters, gross and histopathologic

examinations of important organs and tissues including at least the liver, kidneys, respiratory tract, and CNS.

Metabolism and Distribution

The pathways of distribution and of elimination of epichlorohydrin as a function of dose route and dose rate in mammals have not been investigated. It is critical to determine which fraction of the dose reacts with the functionally essential biomolecules and which fraction is inactivated by detoxifying reactions. Both in vivo and in vitro studies should be conducted to determine the pathways. It is critical to determine the concentration at which reaction with functional biomolecules is a linear function of dose in intact animals.

Chemical Reactivity Toward all Classes of Biologic Nucleophiles

To acquire a better understanding of the reaction of epichlorohydrin with cells and organelles, experiments to determine its reaction with various classes of nucleophiles found in biologic systems should be carried out.

Hypertension

Kidney damage is often accompanied by hypertension. Since epichlorohydrin causes kidney damage in animals, studies should be conducted to see whether hypertension is also induced by epichlorohydrin exposure.