

## APPENDIX H

### MEDICAL ASPECTS OF WEARING RESPIRATORS\*

In recommending medical evaluation criteria for respirator use, one should apply rigorous decision-making principles [Halperin et al. 1986];<sup>†</sup> tests used should be chosen for operating characteristics such as sensitivity, specificity, and predictive value. Unfortunately, many knowledge gaps exist in this area. The problem is complicated by the large variety of respirators, their conditions of use, and individual differences in the physiologic and psychologic responses to them. The following guidelines are intended primarily to assist the physician in developing medical evaluation criteria for respirator use.

#### H.1 BACKGROUND INFORMATION

Brief descriptions of the health effects associated with wearing respirators are summarized below. More detailed analyses of the data are available in recent reviews by James [1977] and Raven et al. [1979].

##### H.1.1 Pulmonary Effects

In general, the added inspiratory and expiratory resistances and dead space of most respirators cause an increase in tidal volume and a decrease in respiratory rate and ventilation (including a small decrease in alveolar ventilation). These respirator effects have usually been small both among healthy individuals and, in limited studies, among individuals with impaired lung function [Gee et al. 1968; Altose et al. 1977; Raven et al. 1981; Hodous et al. 1983; Hodous et al. 1986]. This generalization is applicable to most respirators when resistances (particularly expiratory resistance) are low [Bentley et al. 1973; Love et al. 1977]. Although most studies report minimal physiologic effects during submaximal exercise, the resistances commonly lead to reduced endurance and reduced maximal exercise performance [Craig et al. 1970; Raven et al. 1977; Stemler and Craig 1977; Myhre et al. 1979; Deno et al. 1981]. The dead space of a respirator (reflecting the amount of expired air that must be rebreathed before fresh air is obtained) tends to cause increased ventilation. At least one study has shown substantially increased ventilation with a full-face respirator, a type that can have a large effective dead space [James et al. 1984]. However, the net effect of a respirator's added resistances and dead space is usually a small decrease in ventilation [Craig

---

\* Adapted from NIOSH Respiratory Decision Logic [NIOSH 1987b].

<sup>†</sup>References for Appendix H are at the end of this Appendix.

et al. 1970; Hermansen et al. 1972; Raven et al. 1977; Stemler and Craig 1977; Deno et al. 1981; Hodous et al. 1983].

The potential for adverse effects, particularly decreased cardiac output, from the positive pressure feature of some respirators has been reported [Meyer et al. 1975]. However, several recent studies suggest that this is not a practical concern, at least not in healthy individuals [Bjurstedt et al. 1979; Arborelius et al. 1983; Dahlback and Balldin 1984].

Theoretically, the increased fluctuations in thoracic pressure caused by breathing with a respirator might constitute an increased risk to subjects with a history of spontaneous pneumothorax. Few data are available in this area. While an individual is using a negative-pressure respirator with relatively high resistance during very heavy exercise, the usual maximal-peak negative oral pressure during inhalation is about 15 to 17 cm of water [Dahlback and Balldin 1984]. Similarly, the usual maximal-peak positive oral pressure during exhalation is about 15 to 17 cm of water, which might occur with a respirator in a positive-pressure mode, again during very heavy exercise [Dahlback and Balldin 1984]. By comparison, maximal positive pressures such as those during a vigorous cough can generate 200 cm of water pressure [Black and Hyatt 1969]. The normal maximal negative pleural pressure at full inspiration is -40 cm of water [Bates et al. 1971], and normal subjects can generate -80 to -160 cm of negative water pressure [Black and Hyatt 1969]. Thus vigorous exercise with a respirator does alter pleural pressures, but the risk of barotrauma is substantially less with exercise than with coughing.

In some asthmatics, an asthmatic attack may be exacerbated or induced by a variety of factors including exercise, cold air, and stress, all of which may be associated with wearing a respirator. Although most asthmatics who are able to control their condition should not have problems with respirators, a physician's judgment and a field trial may be needed in selected cases.

### **H.1.2 Cardiac Effects**

The added work of breathing from respirators is small and could not be detected in several studies [Gee et al. 1968; Hodous et al. 1983]. A typical respirator might double the work of breathing (from 3% to 6% of the total oxygen consumption), but this is probably not of clinical significance [Gee et al. 1968]. In concordance with this view, several other studies indicated that at the same workloads heart rate does not change with the wearing of a respirator [Raven et al. 1982; Harber et al. 1982; Hodous et al. 1983; Arborelius et al. 1983; Petsonk et al. 1983].

In contrast, the added cardiac stress due to the weight of a heavy respirator may be considerable. A self-contained breathing apparatus (SCBA) may weigh up to 35 lb. Heavier respirators can reduce maximum external workloads by 20% and similarly increase heart rate at a given submaximal workload [Raven et al. 1977]. In addition, it should be noted that many uses of SCBA (e.g., for firefighting and hazardous waste site work) also necessitate the wearing of 10 to 25 lb of protective clothing. Raven et al. [1982] found

statistically significant higher systolic and/or diastolic blood pressures during exercise for persons wearing respirators. Arborelius et al. [1983] did not find significant differences for persons wearing respirators during exercise.

### **H.1.3 Body Temperature Effects**

Proper regulation of body temperature is primarily of concern with the closed circuit SCBA that produces oxygen via an exothermic chemical reaction. Inspired air within these respirators may reach 120°F (49°C), thus depriving the wearer of a minor cooling mechanism and causing discomfort. Obviously this can be more of a problem with heavy exercise and when ambient conditions and/or protective clothing further reduce the body's ability to lose heat. The increase in heart rate because of increasing temperature represents an additional cardiac stress.

Closed-circuit breathing units of any type have the potential for causing heat stress since warm expired gases (after exothermic carbon dioxide removal with or without oxygen addition) are rebreathed. Respirators with large dead spaces also have this potential problem, again because of partial rebreathing of warmed expired air [James et al. 1984].

### **H.1.4 Sensory Effects**

Respirators may reduce visual fields, decrease voice clarity and loudness, and decrease hearing ability. Besides the potential for reduced productivity, these effects may result in reduced industrial safety. These factors may also contribute to a general feeling of stress [Morgan 1983a].

### **H.1.5 Psychologic Effects**

This important topic is discussed in recent reviews by Morgan [Morgan 1983a, 1983b]. There is little doubt that virtually everyone suffers some discomfort when wearing a respirator. The large variability and the subjective nature of the psychophysiologic aspects of wearing a respirator, however, make studies and specific recommendations difficult. Fit testing obviously serves an important additional function by providing a trial to determine if the wearer can psychologically tolerate the respirator. The great majority of workers can tolerate respirators, and experience in wearing them aids in this tolerance [Morgan 1983b]. However, some individuals are likely to remain psychologically unfit for wearing respirators.

### **H.1.6 Local Irritation Effects**

Allergic skin reactions may occur occasionally from wearing a respirator, and skin occlusion may cause irritation or exacerbation of preexisting conditions such as pseudofolliculitis barbae. Facial discomfort from the pressure of the mask may occur, particularly when the fit is unsatisfactory.

### **H.1.7 Miscellaneous Health Effects**

In addition to the health effects (described above) associated with wearing respirators, specific groups of respirator wearers may be affected by the following factors:

a. Perforated tympanic membrane

Although inhalation of toxic materials through a perforated tympanic membrane (ear drum) is possible, recent evidence indicates that the airflow would be minimal and rarely if ever of clinical importance [Cantekin et al. 1979; Ronk and White 1985]. In highly toxic or unknown atmospheres, use of positive pressure respirators should ensure adequate protection [Ronk and White 1985].

b. Contact lenses

Contact lenses are generally not recommended for use with respirators, although little documented evidence exists to support this viewpoint [daRoza and Weaver 1985]. Several possible reasons for this recommendation are noted below:

(1) Corneal irritation or abrasion

Corneal irritation or abrasion might occur with the exposure. This would, of course, be a problem primarily with quarter- and half-face masks, especially with particulate exposures. However, exposures could occur with full-face respirators because of leaks or inadvisable removal of the respirator for any reason. Although corneal irritation or abrasion might also occur without contact lenses, their presence is known to substantially increase this risk.

(2) Loss or misplacement of a contact lens

The loss or misplacement of a contact lens by an individual wearing a respirator might prompt the wearer to remove the respirator, thereby resulting in exposure to the hazard as well as to the potential problems noted above.

(3) Eye irritation from respirator airflow

The constant airflow of some respirators, such as powered air-purifying respirators (PAPR's) or continuous flow air-line respirators, might irritate the eyes of a contact lens wearer.

## **H.2 SUGGESTED MEDICAL EVALUATION AND CRITERIA FOR RESPIRATOR USE**

The following NIOSH recommendations allow latitude for the physician in determining a medical evaluation for a specific situation. More specific guidelines may become available as knowledge increases regarding human stresses from the complex interactions of worker

health status, respirator usage, and job tasks. Although some of the following recommendations should be part of any medical evaluation of workers who wear respirators, others are applicable for specific situations.

- A physician should determine fitness to wear a respirator by considering the worker's health, the type of respirator, and the conditions of respirator use.

The recommendation above leaves the final decision of an individual's fitness to wear a respirator to the person who is best qualified to evaluate the multiple clinical and other variables. Much of the clinical and other data could be gathered by other personnel. It should be emphasized that the clinical examination alone is only one part of the fitness determination. Collaboration with foremen, industrial hygienists, and others may often be needed to better assess the work conditions and other factors that affect an individual's fitness to wear a respirator.

- A medical history and at least a limited physical examination are recommended.

The medical history and physical examination should emphasize the evaluation of the cardiopulmonary system and should elicit any history of respirator use. The history is an important tool in medical diagnosis and can be used to detect most problems that might require further evaluation. Objectives of the physical examination should be to confirm the clinical impression based on the history and to detect important medical conditions (such as hypertension) that may be essentially asymptomatic.

- Although chest X-ray and/or spirometry may be medically indicated in some fitness determinations, these should not be routinely performed.

In most cases, the hazardous situations requiring the wearing of respirators will also mandate periodic chest X-rays and/or spirometry for exposed workers. When such information is available, it should be used in the determination of fitness to wear respirators.

Data from routine chest X-rays and spirometry are not recommended solely for determining if a respirator should be worn. In most cases, with an essentially normal clinical examination (history and physical), these data are unlikely to influence the respirator fitness determination; additionally, the X-ray would be an unnecessary source of radiation exposure to the worker. Chest X-rays in general do not accurately reflect a person's cardiopulmonary physiologic status, and limited studies suggest that mild to moderate impairment detected by spirometry would not preclude the wearing of respirators in most cases. Thus it is recommended that chest X-rays and/or spirometry be done only when clinically indicated.

- The recommended periodicity of medical fitness determinations varies according to several factors but could be as infrequent as every 5 years.

Federal or other applicable regulations shall be followed regarding the frequency of respirator fitness determinations. The guidelines for most work conditions for which respirators are required are shown in Table H-1.

**Table H-1.—Suggested frequency of medical fitness determinations\***

Type of working conditions	Worker age (yr)		
	<35	35 to 45	>45
Most work conditions requiring respirators	Every 5 yr	Every 2 yr	1-2 yr
Strenuous working conditions with a SCBA <sup>†</sup>	Every 3 yr	Every 18 mo	Annually

\*Interim testing would be needed if changes in health status occur.

<sup>†</sup>SCBA = self-contained breathing apparatus.

These guidelines are similar to those recommended by ANSI, which recommends annual determinations after age 45 [ANSI 1984]. The more frequent examinations with advancing age relate to the increased prevalence of most diseases in older people. More frequent examinations are recommended for individuals performing strenuous work involving the use of a SCBA. These guidelines are based on clinical judgment and, like the other recommendations in this section, should be adjusted as clinically indicated.

- The respirator wearer should be observed during a trial period to evaluate potential physiological problems.

In addition to considering the physical effects of wearing respirators, the physician should determine if wearing a given respirator would cause extreme anxiety or claustrophobic reaction in the individual. This could be done during training while the worker is wearing the respirator and is engaged in some exercise that approximates the actual work situation.

Present OSHA regulations state that a worker should be provided the opportunity to wear the respirator “in normal air for a long familiarity period . . .” [29 CFR\* 1910.134(e)(5)]. This trial period should also be used to evaluate the ability and tolerance of the worker to wear the respirator [Harber 1984]. This trial period need not be associated with respirator fit testing and should not compromise the effectiveness of the vital fit testing procedure.

- Examining physicians should realize that the main stress of heavy exercise while using a respirator is usually on the cardiovascular system and that heavy respirators (e.g., SCBA) can substantially increase this stress. Accordingly, physicians may want to consider exercise stress tests with electrocardiographic monitoring when heavy respirators are used, when cardiovascular risk factors are present, or when extremely stressful conditions are expected.

\*Code of Federal Regulations. See CFR in references.

Some respirators may weigh up to 35 lb and may increase workloads by 20%. Although a lower activity level could compensate for this added stress [Manning and Griggs 1983], a lower activity level might not always be possible. Physicians should also be aware of other added stresses, such as heavy protective clothing and intense ambient heat, that would increase the worker's cardiac demand. As an extreme example, fire fighters who use a SCBA inside burning buildings may work at maximal exercise levels under life-threatening conditions. In such cases, the detection of occult cardiac disease, which might manifest itself during heavy stress, may be important. Some authors have either recommended stress testing [Kilbom 1980] or at least its consideration in the fitness determination [ANSI 1984]. Kilbom [1980] has recommended stress testing at 5-yr intervals for fire fighters below age 40 who use SCBA and at 2-yr intervals for those aged 40 to 50. He further suggested that firemen over age 50 not be allowed to wear SCBA.

Exercise stress testing has not been recommended for medical screening for coronary artery disease in the general population [Weiner et al. 1979; Epstein 1979]. It has an estimated sensitivity and specificity of 78% and 69%, respectively, when the disease is defined by coronary angiography [Weiner et al. 1979; Nicklin and Balaban 1984]. In a recent 6-yr prospective study, stress testing to determine the potential for heart attacks indicated a positive predictive value of 27% when the prevalence of disease was 3.5% [Giagnoni et al. 1983; Folli 1984]. Although stress testing has limited effectiveness in medical screening, it could detect individuals who may not be able to complete the heavy exercise required in some jobs.

A definitive recommendation regarding exercise stress testing cannot be made at this time. Further research may determine whether this is a useful tool in selected circumstances.

- An important concept is that "general work limitations and restrictions identified for other work activities also shall apply for respirator use" [ANSI 1984].

In many cases, if a worker is physically able to do an assigned job while not wearing a respirator, the worker will in most situations not be at increased risk when performing the same job while wearing a respirator.

- Because of the variability in the types of respirators, work conditions, and workers' health status, many employers may wish to designate categories of fitness to wear respirators, thereby excluding some workers from strenuous work situations involving the wearing of respirators.

Depending on the various circumstances, several permissible categories of respirator usage are possible. One conceivable scheme would consist of three overall categories: full respirator use, no respirator use, and limited respirator use including "escape only" respirators. The latter category excludes heavy respirators and strenuous work conditions. Before identifying the conditions that would be used to classify workers into various categories, it is critical that the physician be aware that these conditions have not been validated and are presented only for consideration. The physician should modify the use of these conditions based on actual experience, further research, and individual worker sensitivities. He may

also wish to consider the following conditions in selecting or permitting the use of respirators:

- History of spontaneous pneumothorax
- Claustrophobia/anxiety reaction
- Use of contact lenses (for some respirators)
- Moderate or severe pulmonary disease
- Angina pectoris, significant arrhythmias, recent myocardial infarction
- Symptomatic or uncontrolled hypertension, and
- Advanced age

Wearing a respirator would probably not play a significant role in causing lung damage such as pneumothorax. However, without good evidence that wearing a respirator would not cause such lung damage, the physician would be prudent to prohibit the individual with a history of spontaneous pneumothorax from wearing a respirator.

Moderate lung disease is defined by the Intermountain Thoracic Society [Kanner and Morris 1975] as being present when the following conditions exist—a forced expiratory volume in 1 sec ( $FEV_1$ ) divided by the forced vital capacity (FVC) (i.e.,  $FEV_1/FVC$ ) of 0.45 to 0.60, or an FVC of 51% to 65% of the predicted FVC value. Similar arbitrary limits could be set for age and hypertension. It would seem more reasonable, however, to combine several risk factors into an overall estimate of fitness to wear respirators under certain conditions. Here the judgment and clinical experience of the physician are needed. Many impaired workers would even be able to work safely while wearing respirators if they could control their own work pace, including having sufficient time to rest.

### **H.3 CONCLUSION**

Individual judgment is needed to determine the factors affecting an individual's fitness to wear a respirator. Although many of the preceding guidelines are based on limited evidence, they should provide a useful starting point for a respirator fitness screening program. Further research is needed to validate these and other recommendations currently in use. Of particular interest would be laboratory studies involving physiologically impaired individuals and field studies conducted under actual day-to-day work conditions.

### **H.4 REFERENCES**

Altose MD, McCauley WC, Kelsen SG, Cherniack NS [1977]. Effects of hypercapnia and inspiratory flow-resistive loading on respiratory activity in chronic airways obstruction. *J Clin Invest* 59:500-507.



ANSI [1984]. American national standard for respirator protection-respirator use-physical qualifications for personnel, ANSI Z88.6-1984. New York, NY: American National Standards Institute, Inc., pp. 7-15.

Arborelius M, Dahlback GO, Data P-G [1983]. Cardiac output and gas exchange during heavy exercise with a positive pressure respiratory protective apparatus. *Scand J Work Environ Health* 9:471-477.

Bates DV, Macklem PT, Christie RV [1971]. Respiratory function in disease: an introduction to the integrated study of the lung. 2nd ed. Philadelphia, PA: W.B. Saunders Co., p. 43.

Bentley RA, Griffin OG, Love RG, Muir DCF, Sweetland KF [1973]. Acceptable levels for breathing resistance of respiratory apparatus. *Arch Environ Health* 27:273-280.

Bjurstedt H, Rosenhamer G, Lindborg B, Hesser CM [1979]. Respiratory and circulatory responses to sustained positive-pressure breathing and exercise in man. *Acta Physiol Scand* 105:204-214.

Black LF, Hyatt RE [1969]. Maximal respiratory pressures: normal values and relationship to age and sex. *Am Rev Respir Dis* 99:696-702.

Cantekin EI, Bluestone CD, Saez CA, Bern SA [1979]. Airflow through the eustachian tube. *Ann Otol* 88:603-612.

CFR. Code of Federal Regulations. Washington, DC: U.S. Government Printing Office, Office of the Federal Register.

Craig FN, Blevins WV, Cummings G [1970]. Exhausting work limited by external resistance and inhalation of carbon dioxide. *J Appl Physiol* 29(6):847-851.

Dahlback GO, Balldin UI [1984]. Physiological effects of pressure demand masks during heavy exercise. *Am Ind Hyg Assoc J* 45(3):177-181.

daRoza RA, Weaver C [1985]. Is it safe to wear contact lenses with a full-facepiece respirator? Lawrence Livermore National Laboratory manuscript UCRL-53653, pp. 1-3.

Deno NS, Kamon E, Kiser DM [1981]. Physiological responses to resistance breathing during short and prolonged exercise. *Am Ind Hyg Assoc J* 42(8):616-623.

Epstein SE [1979]. Limitations of electrocardiographic exercise testing [editorial]. *N Engl J Med* 301(5):264-265.

Folli G [1984]. Exercise EKG in asymptomatic normotensive subjects [reply to letter to the editor]. *N Engl J Med* 310(13):852-853.

Gee JBL, Burton G, Vassallo C, Gregg J [1968]. Effects of external airway obstruction on work capacity and pulmonary gas exchange. *Am Rev Respir Dis* 98:1003-1012.

Giagnoni E, Secchi MB, Wu SC, Morabito A, Oltrona L, et al. [1983]. Prognostic value of exercise EKG testing in asymptomatic normotensive subjects. *N Engl J Med* 309(18):1085-1089.

Halperin WE, Ratcliffe JM, Frazier TM, Becker SP, Schulte PA [1986]. Medical screening in the workplace: proposed principles. *J Occup Med* 28(8):547-552.

Harber P, Tamimie RJ, Bhattacharya A, Barber M [1982]. Physiologic effects of respirator dead space and resistance loading. *J Occup Med* 24(9):681-684.

Harber P [1984]. Medical evaluation for respirator use. *J Occup Med* 26(7):496-502.

Hermansen L, Vokac Z, Lereim P [1972]. Respiratory and circulatory response to added air flow resistance during exercise. *Ergonomics* 15(1):15-24.

Hodous TK, Petsonk L, Boyles C, Hankinson J, Amandus H [1983]. Effects of added resistance to breathing during exercise in obstructive lung disease. *Am Rev Respir Dis* 128:943-948.

Hodous TK, Boyles C, Hankinson J [1986]. Effects of industrial respirator wear during exercise in subjects with restrictive lung disease. *Am Ind Hyg Assoc J* 47:176-180.

James RH [1977]. Breathing resistance and dead space in respiratory protective devices. Cincinnati, OH: U.S. Department of Health, Education, and Welfare, Public Health Service, Center for Disease Control, National Institute for Occupational Safety and Health, DHEW (NIOSH) Publication No. 77-161.

James R, Dukes-Dobos F, Smith R [1984]. Effects of respirators under heat/work conditions. *Am Ind Hyg Assoc J* 45(6):399-404.

Kanner RE, Morris AH, ed. [1975]. *Clinical pulmonary function testing: a manual of uniform laboratory procedures for the intermountain area*. 1st ed. Salt Lake City, UT: Intermountain Thoracic Society.

Kilbom A [1980]. Physical work capacity of firemen. *Scand J Work Environ Health* 6:48-57.

Love RG, Muir DCF, Sweetland KF, Bentley RA, Griffin OG [1977]. Acceptable levels for the breathing resistance of respiratory apparatus: results for men over the age of 45. *Br J Ind Med* 34:126-129.

Manning JE, Griggs TR [1983]. Heart rates in firefighters using light and heavy breathing equipment: similar near-maximal exertion in response to multiple work load conditions. *J Occup Med* 25(3):215-218.

Meyer E, Gurtner HP, Scherrer M [1975]. Physiological appraisal of a new respirator with positive pressure. *Pneumology* 153:61-72.

Morgan WP [1983a]. Psychological problems associated with the wearing of industrial respirators: a review. *Am Ind Hyg Assoc J* 44(9):671-676.

Morgan WP [1983b]. Psychological problems associated with the wearing of industrial respirators. *J Int Soc Respir Prot* 1:67-108.

Myhre LG, Holden RD, Baumgardner FW, Tucker D [1979]. Physiological limits of firefighters. Brooks AFB, TX: Air Force School of Aerospace Medicine, ESL-TR-79-06.

Nicklin D, Balaban DJ [1984]. Exercise EKG in asymptomatic normotensive subjects [letter to the editor]. *N Engl J Med* 310(13):852.

NIOSH [1987]. NIOSH respirator decision logic. Cincinnati, OH: U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 87-108.

Petsonk EL, Hancock J, Boyles C [1983]. Physiologic effects of a self-contained self-rescuer. *Am Ind Hyg Assoc J* 44(5):368-373.

Raven PB, Davis TO, Shafer CL, Linnebur AC [1977]. Maximal stress test performance while wearing a self-contained breathing apparatus. *J Occup Med* 19(12):802-806.

Raven PB, Dodson AT, Davis TO [1979]. The physiological consequences of wearing industrial respirators: a review. *Am Ind Hyg Assoc J* 40(6):517-534.

Raven PB, Jackson AW, Page K, et al. [1981]. The physiological responses of mild pulmonary impaired subjects while using a "demand" respirator during rest and work. *Am Ind Hyg Assoc J* 42(4):247-257.

Raven PB, Bradley O, Rohm-Young D, McClure FL, Skaggs B [1982]. Physiological response to "pressure-demand" respirator wear. *Am Ind Hyg Assoc J* 43(10):773-781.

Ronk R, White MK [1985]. Hydrogen sulfide and the probabilities of "inhalation" through a tympanic membrane defect. *J Occup Med* 27(5):337-340.

Stemler FW, Craig FN [1977]. Effects of respiratory equipment on endurance in hard work. *J Appl Physiol* 42:28-32.

Weiner DA, Ryan TJ, McCabe CH, et al. [1979]. Exercise stress testing: correlations among history of angina, ST-segment response and prevalence of coronary-artery disease in the coronary artery surgery study (CASS). *N Engl J Med* 301(5):230-235.

## REFERENCES

- Abbondandolo A, Bonatti S, Corsi C, Corti G, Fiorio R, Leporini C, et al. [1980]. The use of organic solvents in mutagenicity testing. *Mut Res* 79:141-150.
- ACGIH [1962]. Documentation of threshold limit values. Cincinnati, OH: American Conference of Governmental Industrial Hygienists, pp. 18, 23, 67-68.
- ACGIH [1980]. Documentation of the threshold limit values. 4th ed. Cincinnati, OH: American Conference of Governmental Industrial Hygienists, pp. 171-172, 253.
- ACGIH [1984]. Threshold limit values—discussion and thirty-five year index with recommendations. Vol. 9. Cincinnati, OH: American Conference of Governmental Industrial Hygienists, pp. 343-346, 360-361.
- ACGIH [1988]. Industrial ventilation—a manual of recommended practice. 20th ed. Cincinnati, OH: American Conference of Governmental Industrial Hygienists, Committee on Industrial Ventilation.
- ACGIH [1991]. 1991-1992 Threshold limit values for chemical substances and physical agents and biological exposure indices. Cincinnati, OH: American Conference of Governmental Industrial Hygienists.
- Adolph EF [1949]. Quantitative relations in the physiological constitutions of mammals. *Science* 109:579-585.
- Amoore JE, Hautala E [1983]. Odor as an aid to chemical safety: odor thresholds compared with threshold limit values and volatilities for 214 industrial chemicals in air and water dilution. *J Appl Toxicol* 3(6):272-290.
- Anderson D, Brinkworth MH, Jenkinson PC, Clode SA, Creasy DM, Gangolli SD [1987]. Effect of ethylene glycol monomethyl ether on spermatogenesis, dominant lethality, and F<sub>1</sub> abnormalities in the rat and the mouse after treatment of F<sub>0</sub> males. *Teratogenesis, Carcinog, Mutagen* 7:141-158.
- Andrew FD, Buschbom RL, Cannon WC, Miller RA, Montgomery LF, Phelps DW, et al. [1981]. Teratologic assessment of ethylbenzene and 2-ethoxyethanol. Final report. NIOSH contract no. 210-79-0037. Richland, WA: Battelle Pacific Northwest Laboratories, p. 99.
- ANSI [1979]. American national standard—fundamentals governing the design and operation of the local exhaust systems. New York, NY: American National Standards Institute, Inc., ANSI Z9.2-1979.

- Apol AG [1976]. Health hazard evaluation determination: Custom Furniture and Cabinets, Inc., Post Falls, ID. Cincinnati, OH: U.S. Department of Health, Education, and Welfare, Public Health Service, Center for Disease Control, National Institute for Occupational Safety and Health, NIOSH Report No. 75-146-254.
- Apol AG, Cone J [1983]. Health hazard evaluation report: Bay Area Hospital, Coos Bay, OR. Cincinnati, OH: U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health, NIOSH Report No. HETA 82-053-1263.
- Ballew M, Hattis D [1989]. Reproductive effects of glycol ethers in females—a quantitative analysis. Cambridge, MA: Center for Technology, Policy and Industrial Development, Massachusetts Institute of Technology, Report No. CTPID 89-7.
- Barbee SJ, Terrill JB, DeSousa DJ, Conaway CC [1984]. Subchronic inhalation toxicology of ethylene glycol monoethyl ether in the rat and rabbit. *Environ Health Perspect* 57:157-164.
- Beattie PJ, Welsh MJ, Brabec MJ [1984]. The effect of 2-methoxyethanol and methoxyacetic acid on Sertoli cell lactate production and protein synthesis *in vitro*. *Toxicol Appl Pharmacol* 76:56-61.
- Blair AH, Vallee BL [1966]. Some catalytic properties of human liver alcohol dehydrogenase. *Biochemistry* 5(6):2026-2034.
- Boiano JM [1983]. Health hazard evaluation determination report: Downing Displays, Incorporated, Cincinnati, OH. Cincinnati, OH: U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health, NIOSH Report No. HETA 82-330-1252.
- Bolt HM, Golka K [1990]. Maternal exposure to ethylene glycol monomethyl ether acetate and hypospadias in offspring: a case report. *Br J Ind Med* 47:352-353.
- Brown NA, Holt D, Webb M [1984]. The teratogenicity of methoxyacetic acid in the rat. *Toxicol Lett* 22:93-100.
- Bryant CJ [1978]. Health hazard evaluation determination report: Pre Finish Metals, Inc., Elk Grove Village, IL. Cincinnati, OH: U.S. Department of Health, Education, and Welfare, Public Health Service, Center for Disease Control, National Institute for Occupational Safety and Health, NIOSH Report No. HHE 77-78-466.
- Burroughs GE [1979]. Health hazard evaluation determination report: J and M Printing Co., Gwinner, ND. Cincinnati, OH: U.S. Department of Health, Education, and Welfare, Public Health Service, Center for Disease Control, National Institute for Occupational Safety and Health, NIOSH Report No. HHE 78-100-590.
- CAL/OSHA [1984]. Occupational exposures to glycol ethers and their acetate derivatives. Berkeley, CA: CAL/OSHA Special Studies Unit, Division of Occupational Safety and Health, Department of Industrial Relations, State of California.

Carpenter CP, Pozzani UC, Weil CS, Nair III JH, Keck GA, Smyth HF Jr. [1956]. The toxicity of butyl Cellosolve solvent. *AMA Arch Ind Health* 14:114-131.

CFR. Code of Federal Regulations. Washington, DC: U.S. Government Printing Office, Office of the Federal Register.

Chapin RE, Lamb IV JC [1984]. Effects of ethylene glycol monomethyl ether on various parameters of testicular function in the F344 rat. *Environ Health Perspect* 57:219-224.

Chapin RE, Dutton SL, Ross MD, Lamb IV JC [1985a]. Effects of ethylene glycol monomethyl ether (EGME) on mating performance and epididymal sperm parameters in F344 rats. *Fund Appl Toxicol* 5:182-189.

Chapin RE, Dutton SL, Ross MD, Swaisgood RR, Lamb IV JC [1985b]. The recovery of the testis over 8 weeks after short-term dosing with ethylene glycol monomethyl ether: histology, cell-specific enzymes, and rete testis fluid protein. *Fund Appl Toxicol* 5:515-525.

Cheever KL, Plotnick HB, Richards DE, Weigel WW [1984]. Metabolism and excretion of 2-ethoxyethanol in the adult male rat. *Environ Health Perspect* 57:241-248.

Chrostek WJ, Levine MS [1981]. Health hazard evaluation report: Palmer Industrial Coatings, Inc., Williamsport, PA. Cincinnati, OH: U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health, NIOSH Report No. HHE 80-153-881.

Clapp DE, Smallwood AW, Moseley C, DeBord KE [1987]. Workplace assessment of exposure to 2-ethoxyethanol. *Appl Ind Hyg* 2(5):183-187.

Clapp DE, Zaebst DD, Herrick RF [1984]. Measuring exposures to glycol ethers. *Environ Health Perspect* 57:91-95.

CMA [1987]. Air monitoring for glycol ethers, Appendix F. Washington, DC: Chemical Manufacturers Association. Chemical Manufacturers Association Glycol Ethers Program Panel research summary report and comments in response to OSHA's ANPR, July 31, 1987.

Cohen R [1984]. Reversible subacute ethylene glycol monomethyl ether toxicity associated with microfilm production: a case report. *Am J Ind Med* 6:441-446.

Cohen SR, Maier AA [1973]. Health hazard evaluation determination report: Westinghouse Electric Corp.-Lamp Division, Bloomfield, NJ. Cincinnati, OH: U.S. Department of Health, Education, and Welfare, Public Health Service, Center for Disease Control, National Institute for Occupational Safety and Health, NIOSH Report No. 72-67-87.

Cohen SR, Vandervort R [1972]. Health hazard evaluation report: North American Rockwell Reinforced Plastic Operation, Ashtabula, OH. Cincinnati, OH: U.S. Department of Health, Education, and Welfare, Public Health Service, Center for Disease Control, National Institute for Occupational Safety and Health, NIOSH Report No. 72-68-25, NTIS No. PB-229122.

Cook RR, Bodner KM, Kolesar RC, Van Peenen PFD, Dickson GS, Flanagan KD [1982]. A cross-sectional study of ethylene glycol monomethyl ether process employees. *Arch Env Health* 37(6):346-351.

Crandall MS, Hartle RW [1984]. Health hazard evaluation report: Henry R. Hinckley and Co., Southwest Harbor, ME. Cincinnati, OH: U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health, NIOSH Report No. HETA 83-128-1485.

Creasy DM, Foster PMD [1984]. The morphological development of glycol ether-induced testicular atrophy in the rat. *Exp Mol Pathol* 40:169-176.

DOT [1990]. Department of Transportation. Emergency response guidebook. Chicago, IL: Labelmaster Division, American Labelmaker Company, 1990 DOT P5800.5, Guide No. 26.

Doe JE, Samuels DM, Tinston DJ, Wickramaratne GAD [1983]. Comparative aspects of the reproductive toxicology by inhalation in rats of ethylene glycol monomethyl ether and propylene glycol monomethyl ether. *Toxicol Appl Pharmacol* 69:43-47.

Doe JE [1984a]. Ethylene glycol monoethyl ether and ethylene glycol monoethyl ether acetate teratology studies. *Environ Health Perspect* 57:33-41.

Doe JE [1984b]. Further studies on the toxicology of the glycol ethers with emphasis on rapid screening and hazard assessment. *Environ Health Perspect* 57:199-206.

Donley DE [1936]. Toxic encephalopathy and volatile solvents in industry. Report of a case. *J Ind Hyg Toxicol* 18(8):571-577.

Dugard PH, Walker M, Mawdsley SJ, Scott RC [1984]. Absorption of some glycol ethers through human skin *in vitro*. *Environ Health Perspect* 57:193-197.

ECETOC [1985]. Technical report no. 17. The toxicology of glycol ethers and its relevance to man: an up-dating of ECETOC technical report no. 4. Brussels, Belgium: European Chemical Industry, Ecology and Toxicology Centre.

EPA [1987]. Recommendations for and documentation of biological values for use in risk assessment. Cincinnati, OH: U.S. Environmental Protection Agency, Environmental Criteria and Assessment Office, Office of Health and Environmental Assessment, Office of Research and Development.

Exon JH, Mather GG, Bussiere JL, Olson DP, Talcott PA [1991]. Effects of subchronic exposure of rats to 2-methoxyethanol or 2-butoxyethanol: thymic atrophy and immunotoxicity. *Fund Appl Toxicol* 16:830-840.

45 Fed. Reg. 79318-79373 [1980]. Part V. Environmental Protection Agency. Water quality criteria documents; availability.

54 Fed. Reg. 9386 [1989]. Environmental Protection Agency proposed amendments to the guidelines for the health assessment of suspect developmental toxicants; request for comments, notices.

Feuston MH, Kerstetter SL, Wilson PD [1990]. Teratogenicity of 2-methoxyethanol applied as a single dermal dose to rats. *Fund Appl Toxicol* 15:448-456.

Forsberg K, Mansdorf SZ [1989]. *Quick selection guide to chemical protective clothing*. New York, NY: Van Nostrand Reinhold.

Foster PMD, Creasy DM, Foster JR, Thomas LV, Cook MW, Gangolli SD [1983]. Testicular toxicity of ethylene glycol monomethyl and monoethyl ether in the rat. *Toxicol Appl Pharmacol* 69:385-399.

Foster PMD, Creasy DM, Foster JR, Gray TJB [1984]. Testicular toxicity produced by ethylene glycol monomethyl and monoethyl ethers in the rat. *Environ Health Perspect* 57:207-217.

Foster PMD, Lloyd SC, Blackburn DM [1987]. Comparison of the in vivo and in vitro testicular effects produced by methoxy-, ethoxy- and n-butoxy acetic acids in the rat. *Toxicology* 43:17-30.

Fucik J [1969]. Ethylene glycol monoethyl ether intoxication. *Pracovni Lekarstvi* 21(3):116-118.

Gibaldi M, Perrier D [1982]. *Pharmacokinetics*. 2nd ed. New York, NY: Marcel Dekker, Inc., pp. 451-457.

Gill J [1977]. Health hazard evaluation determination report: L.L. Bean, Inc., Freeport ME. Cincinnati, OH: U.S. Department of Health, Education, and Welfare, Public Health Service, Center for Disease Control, National Institute for Occupational Safety and Health, NIOSH Report No. 76-46-375, NTIS No. PB-270927.

Gilles D [1977]. Health hazard evaluation determination report: Dap Derusto, Inc., Tipp City, OH. Cincinnati, OH: U.S. Department of Health, Education, and Welfare, Public Health Service, Center for Disease Control, National Institute for Occupational Safety and Health, NIOSH Report No. 77-101-441, NTIS No. PB-278046.

Goldberg ME, Haun C, Smyth HF Jr. [1962]. Toxicologic implication of altered behavior induced by an industrial vapor. *Toxicol Appl Pharmacol* 4:148-164.

Grant D, Sulsh S, Jones HB, Gangolli SD, Butler WH [1985]. Acute toxicity and recovery in the hemopoietic system of rats after treatment with ethylene glycol monomethyl and monobutyl ethers. *Toxicol Appl Pharmacol* 77:187-200.

Gray TJB, Moss EJ, Creasy DM, Gangolli SD [1985]. Studies on the toxicity of some glycol ethers and alkoxyacetic acids in primary testicular cell cultures. *Toxicol Appl Pharmacol* 79:490-501.



- Greenburg L, Mayers MR, Goldwater LJ, Burke WJ, Moskowitz S [1938]. Health hazards in the manufacture of "fused collars." I. Exposure to ethylene glycol monomethyl ether. *J Ind Hyg Toxicol* 20(2):134-147.
- Greene JA, Sleet RB, Morgan KT, Welsch F [1987]. Cytotoxic effects of ethylene glycol monomethyl ether in the forelimb bud of the mouse embryo. *Teratology* 36:23-34.
- Groeseneken D, Van Vlem E, Veulemans H, Masschelein R [1986a]. Gas chromatographic determination of methoxyacetic and ethoxyacetic acid in urine. *Br J Ind Med* 43:62-65.
- Groeseneken D, Veulemans H, Masschelein R [1986b]. Respiratory uptake and elimination of ethylene glycol monoethyl ether after experimental human exposure. *Br J Ind Med* 43:544-549.
- Groeseneken D, Veulemans H, Masschelein R [1986c]. Urinary excretion of ethoxyacetic acid after experimental human exposure to ethylene glycol monoethyl ether. *Br J Ind Med* 43:615-619.
- Groeseneken D, Veulemans H, Masschelein R, Van Vlem E [1987a]. Pulmonary absorption and elimination of ethylene glycol monoethyl ether acetate in man. *Br J Ind Med* 44:309-316.
- Groeseneken D, Veulemans H, Masschelein R, Van Vlem E [1987b]. Ethoxyacetic acid: a metabolite of ethylene glycol monoethyl ether acetate in man. *Br J Ind Med* 44:488-493.
- Groeseneken D, Veulemans H, Masschelein R, Van Vlem E [1988]. Comparative urinary excretion of ethoxyacetic acid in man and rat after single low doses of ethylene glycol monoethyl ether. *Toxicol Lett* 41:57-68.
- Groeseneken D, Veulemans H, Masschelein R, Van Vlem E [1989a]. Experimental human exposure to ethylene glycol monomethyl ether. *Int Arch Occup Environ Health* 61:243-247.
- Groeseneken D, Veulemans H, Masschelein R, Van Vlem E [1989b]. An improved method for the determination in urine of alkoxyacetic acids. *Int Arch Occup Environ Health* 61:249-254.
- Groetschel H, Schuermann D [1959]. Mass toxic effects in printing works where ethylene glycol monomethyl ether was used as a solvent. *Arch Toxicol* 17:243-251.
- Gross E [1943]. The individual solvents. In: Lehmann KB, Flury F, eds. *Toxicology and hygiene of industrial solvents*. Translated by King E, Smyth HF Jr. Baltimore, MD: The Williams and Wilkins Co.
- Guest D, Hamilton ML, Deisinger PJ, DiVincenzo GD [1984]. Pulmonary and percutaneous absorption of 2-propoxyethyl acetate and 2-ethoxyethyl acetate in beagle dogs. *Environ Health Perspect* 57:177-184.
- Guidotti TL, Cortez JH, Abraham HL [1983]. Taking the occupational history. *Ann Intern Med* 99(15):641-651.

Gunter BJ, Lucas JB [1974]. Health hazard evaluation determination report: Head Ski Company, Boulder, CO. Cincinnati, OH: U.S. Department of Health, Education, and Welfare, Public Health Service, Center for Disease Control, National Institute for Occupational Safety and Health, NIOSH Report No. HHE 73-84-119.

Gunter BJ, Barkman HW, Wood SD [1980]. Health hazard evaluation determination report: Hewlett Packard Co., Loveland, CO. Cincinnati, OH: U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health, NIOSH Report No. HETA 79-59-696, NTIS No. PB 81-112138.

Gunter BJ [1985]. Health hazard evaluation determination report: TRW Electronics, Inc., Colorado Springs, CO. Cincinnati, OH: U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health, NIOSH Report No. HETA 85-25-1620.

Guyton AC [1947]. Measurement of the respiratory volumes of laboratory animals. *Am J Physiol* 150:70-77.

Hagopian JH, Bastress EK [1976]. Recommended industrial ventilation guidelines. Cincinnati, OH: U.S. Department of Health, Education, and Welfare, Public Health Service, Center for Disease Control, National Institute for Occupational Safety and Health, DHEW (NIOSH) Publication No. 76-162, p. 330.

Hanley TR Jr., Yano BL, Nitschke KD, John JA [1984]. Comparison of the teratogenic potential of inhaled ethylene glycol monomethyl ether in rats, mice, and rabbits. *Toxicol Appl Pharmacol* 75:409-422.

Hardin BD, Bond GP, Sikov MR, Andrew FD, Beliles RP, Niemeier RW [1981]. Testing of selected workplace chemicals for teratogenic potential. *Scand J Work Environ Health* 7(Suppl 4):66-75.

Hardin BD, Niemeier RW, Smith RJ, Kuczuk MH, Mathinos PR, Weaver TF [1982]. Teratogenicity of 2-ethoxyethanol by dermal application. *Drug Chem Toxicol* 5(3):277-294.

Hardin BD, Goad PT, Burg JR [1984]. Developmental toxicity of four glycol ethers applied cutaneously to rats. *Environ Health Perspect* 57:69-74.

Hardin BD, Eisenmann CJ [1987]. Relative potency of four ethylene glycol ethers for induction of paw malformations in the CD-1 mouse. *Teratology* 35:321-328.

Hartle R [1980]. Health hazard evaluation report: Long Island Railroad, Richmond Hill, NY. Cincinnati, OH: U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health, NIOSH Report No. HETA 80-057-781.

Hervin RL, Cromer JW, Butler GJ [1974]. Health hazard evaluation determination report: The Vendo Company, Kansas City, MO. Cincinnati, OH: U.S. Department of Health, Education, and Welfare, Public Health Service, Center for Disease Control, National Institute for Occupational Safety and Health, NIOSH Report No. 74-218-164.

Hervin RL, Thoburn TW [1975]. Health hazard evaluation determination report: Trans World Airlines Main Overhaul Facility, Kansas City International Airport, Kansas City, MO. Cincinnati, OH: U.S. Department of Health, Education, and Welfare, Public Health Service, Center for Disease Control, National Institute for Occupational Safety and Health, NIOSH Report No. 72-96-237.

Hobson DW, D'Addario AP, Bruner RH, Uddin DE [1986]. A subchronic dermal exposure study of diethylene glycol monomethyl ether and ethylene glycol monomethyl ether in the male guinea pig. *Fund Appl Toxicol* 6:339-348.

Hooper ML, Subak-Sharpe JH [1983]. Metabolic cooperation between cells. *Int Rev Cytol* 69:45-104.

Horton VL, Sleet RB, John-Greene JA, Welsch F [1985]. Developmental phase-specific and dose-related teratogenic effects of ethylene glycol monomethyl ether in CD-1 mice. *Toxicol Appl Pharmacol* 80:108-118.

Houchens DP, Overja AA, Niemeier RW [1984]. Effects of ethylene glycol monomethyl (EGME) and monoethyl (EGEE) ethers on the immunocompetence of allogeneic and syngeneic mice bearing L1210 mouse leukemia. *Environ Health Perspect* 57:113-118.

House RV, Lauer LD, Murray MJ, Ward EC, Dean JH [1985]. Immunological studies in B6C3F<sub>1</sub> mice following exposure to ethylene glycol monomethyl ether and its principal metabolite methoxyacetic acid. *Toxicol Appl Pharmacol* 77:358-362.

Jäckh R, Gelbke H-P, Helmstädter G [1985]. In vitro cytotoxicity of glycol ethers and oxidation products in CHO cells. *Toxicol Lett* 26:73-77.

Johanson G [1988]. Aspects of biological monitoring of exposure to glycol ethers. *Toxicol Lett* 43:5-21.

Johnson PL, Boxer P [1983]. Health hazard evaluation report: Goodyear Aerospace Corp., Akron, OH. Cincinnati, OH: U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health, NIOSH Report No. HETA 82-123-1258.

Jönsson A-K, Pedersen J, Steen G [1982]. Ethoxyacetic acid and N-ethoxyacetyl glycine: metabolites of ethoxyethanol (ethylcellosolve) in rats. *Acta Pharmacol Toxicol* 50:358-362.

Karel L, Landing BH, Harvey TS [1947]. The intraperitoneal toxicity of some glycols, glycol ethers, glycol esters and phthalates in mice. *J Pharmacol Exp Ther* 90:338-347.

Kawalek JC, Andrews AW [1980]. The effect of solvents on drug metabolism *in vitro*. *Drug Metab Dispos* 8(6):380-384.

Laug EP, Calvery HO, Morris HJ, Woodard G [1939]. The toxicology of some glycols and derivatives. *J Ind Hyg Tox* 21(5):173-200.

Leaf DA [1985]. Glycol ethers: an overview. Washington, DC: U.S. Environmental Protection Agency, Office of Pesticides and Toxic Substances.

Lee S [1982]. Health hazard evaluation report: Perry Nuclear Power Plant, Perry, OH. Cincinnati, OH: U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health, NIOSH Report No. HETA 82-186-1203.

Leidel NA, Busch KA, Lynch JR [1977]. Occupational exposure sampling strategy manual. Cincinnati, OH: U.S. Department of Health, Education, and Welfare, Public Health Service, Center for Disease Control, National Institute for Occupational Safety and Health, DHEW (NIOSH) Publication No. 77-173, NTIS No. PB-274-792/A07.

Levy BS [1976]. Health hazard evaluation determination report: Cooper Union School of Art, New York, NY. Cincinnati, OH: U.S. Department of Health, Education, and Welfare, Public Health Service, Center for Disease Control, National Institute for Occupational Safety and Health, NIOSH Report No. 75-12-321.

Loch-Carusio R, Trosko JE, Corcos IA [1984]. Interruption of cell-cell communication in Chinese hamster V79 cells by various alkyl glycol ethers: implications for teratogenicity. *Environ Health Perspect* 57:119-123.

Love RJ, Donohue MT [1983]. Health hazard evaluation determination report: International Brotherhood of Painters and Allied Trades, Electric Boat Division of General Dynamics Corp., Groton, CT. Cincinnati, OH: U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health, NIOSH Report No. HETA 78-135-1333.

Lowry LK [1987]. The biological exposure index: its use in assessing chemical exposures in the workplace. *Toxicology* 47:55-69.

Markel HL, Moody PL [1982]. Health hazard evaluation determination report: Dallas Times Herald, Dallas, TX. Cincinnati, OH: U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health, NIOSH Report No. HETA 80-91-1185.

McArdle WD, Katch FI, Katch VI [1981]. Exercise physiology: energy, nutrition, and human performance. Philadelphia, PA: Lea and Febiger, pp. 111-113.

McGregor DB, Willins MJ, McDonald P, Holmstrom M, McDonald D, Niemeier RW [1983]. Genetic effects of 2-methoxyethanol and bis(2-methoxyethyl)ether. *Toxicol Appl Pharmacol* 70:303-316.

- McGregor DB [1984]. Genotoxicity of glycol ethers. *Environ Health Perspect* 57:97-103.
- McLouth LD, Gorman R [1980]. Health hazard evaluation report: Video Merchandisers, Inc., New York, NY. Cincinnati, OH: U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health, NIOSH Report No. HHE 80-783-779, NTIS No. PB 82-149758.
- McManus KP, Moseley C, Lowry LK, Morris JA, Hattis D, Berg R [1989]. Health hazard evaluation report: Electric Boat Division, General Dynamics Corporation, Groton, CT. Cincinnati, OH: U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health, NIOSH Report No. HETA 84-474-1946.
- McQuilken SD [1980]. Health hazard evaluation determination report: Continental Columbus Corporation, Columbus, WI. Cincinnati, OH: U.S. Department of Health, Education, and Welfare, Public Health Service, Center for Disease Control, National Institute for Occupational Safety and Health, NIOSH Report No. 78-102-677.
- Melnick R [1982]. Letter of January 7, 1982, to NIOSH from R. Melnick of the National Toxicology Program regarding mutagenicity of glycol ethers. Cincinnati, OH: U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health.
- Melnick RL [1984]. Toxicities of ethylene glycol and ethylene glycol monoethyl ether in Fischer 344/N rats and B6C3F<sub>1</sub> mice. *Environ Health Perspect* 57:147-155.
- Meridian Research, Inc. [1987]. Industry profile and analyses of processes, occupational exposures, and substitutes for glycol ethers. Interim report prepared for Occupational Safety and Health Administration. Silver Spring, MD: Meridian Research, Inc.
- Mickelsen RL, Roder MM, Berardinelli SP [1986]. Permeation of chemical protective clothing by three binary solvent mixtures. *Am Ind Hyg Assoc J* 47(4):236-240.
- Mickelsen RL, Hall RC [1987]. A breakthrough time comparison of nitrile and neoprene glove materials produced by different manufacturers. *Am Ind Hyg Assoc J* 48(11):941-947.
- Mihlan GJ, Mitchell RI, Willson RD [1983]. Preliminary control technology survey on Fairchild Semiconductor, South Portland, ME. Columbus, OH: Battelle Columbus Laboratories. Contract report for interagency agreement between U.S. Environmental Protection Agency, Cincinnati, OH, and National Institute for Occupational Safety and Health, Division of Physical Sciences and Engineering, Cincinnati, OH, July 28, 1983.
- Miller RR, Ayres JA, Calhoun LL, Young JT, McKenna MJ [1981]. Comparative short-term inhalation toxicity of ethylene glycol monomethyl ether and propylene glycol monomethyl ether in rats and mice. *Toxicol Appl Pharmacol* 61:368-377.
- Miller RR, Carreon RE, Young JT, McKenna MJ [1982]. Toxicity of methoxyacetic acid in rats. *Fund Appl Toxicol* 2:158-160.

Miller RR, Ayres JA, Young JT, McKenna MJ [1983a]. Ethylene glycol monomethyl ether. I. Subchronic vapor inhalation study with rats and rabbits. *Fund Appl Toxicol* 3:49-54.

Miller RR, Hermann EA, Langvardt PW, McKenna MJ, Schwetz BA [1983b]. Comparative metabolism and disposition of ethylene glycol monomethyl ether and propylene glycol monomethyl ether in male rats. *Toxicol Appl Pharmacol* 67:229-237.

Morris HJ, Nelson AA, Calvery HO [1942]. Observations on the chronic toxicities of propylene glycol, ethylene glycol, diethylene glycol, ethylene glycol mono-ethyl-ether, and diethylene glycol mono-ethyl-ether. *J Pharmacol* 74:266-273.

Moss EJ, Thomas LV, Cook MW, Walters DG, Foster PMD, Creasy DM, et al. [1985]. The role of metabolism in 2-methoxyethanol-induced testicular toxicity. *Toxicol Appl Pharmacol* 79:480-489.

Nagano K, Nakayama E, Koyano M, Oobayashi H, Adachi H, Yamada T [1979]. Mouse testicular atrophy induced by ethylene glycol monoalkyl ethers. *Jap J Ind Health* 21:29-35.

Nagano K, Nakayama E, Oobayashi H, Yamada T, Adachi H, Nishizawa T, et al. [1981]. Embryotoxic effects of ethylene glycol monomethyl ether in mice. *Toxicology* 20:335-343.

Nakaaki K, Fukabori S, Tada O [1980]. An experimental study on percutaneous absorption of some organic solvents. *J Sci Labour* 56(12, Part II):1-9.

NBOSH (National Board of Occupational Safety and Health) [1989]. Occupational exposure limit values. *Newsletter* 3/89:8-9.

Nelson BK, Brightwell WS, Setzer JV, Taylor BJ, Hornung RW, O'Donohue TL [1981]. Ethoxyethanol behavioral teratology in rats. *Neurotoxicology* 2:231-249.

Nelson BK, Brightwell WS, Setzer JV [1982a]. Prenatal interactions between ethanol and the industrial solvent 2-ethoxyethanol in rats: maternal and behavioral teratogenic effects. *Neurobehav Toxicol Teratol* 4:387-394.

Nelson BK, Brightwell WS, Setzer JV, O'Donohue TL [1982b]. Prenatal interactions between ethanol and the industrial solvent 2-ethoxyethanol in rats: neurochemical effects in the offspring. *Neurobehav Toxicol Teratol* 4:395-401.

Nelson BK, Brightwell WS, Burg JR, Massari VJ [1984a]. Behavioral and neurochemical alterations in the offspring of rats after maternal or paternal inhalation exposure to the industrial solvent 2-methoxyethanol. *Pharmacol Biochem Behav* 20:269-279.

Nelson BK, Setzer JV, Brightwell WS, Mathinos PR, Kuczuk MH, Weaver TE, et al. [1984b]. Comparative inhalation teratogenicity of four glycol ether solvents and an amino derivative in rats. *Environ Health Perspect* 57:261-271.

New DAT [1978]. Whole embryo culture and the study of mammalian embryos during organogenesis. *Biol Rev* 53:81-122.

NFPA [1987]. Fire protection guide on hazardous materials. 9th ed. Quincy, MA: National Fire Protection Association, p. 325M-51.

NIOSH [1974]. A recommended standard—an identification system for occupationally hazardous materials. Cincinnati, OH: U.S. Department of Health, Education, and Welfare, Public Health Service, Center for Disease Control, National Institute for Occupational Safety and Health, DHEW (NIOSH) Publication No. 75-126, p. 63.

NIOSH [1978]. The recirculation of industrial exhaust air: symposium proceedings. Cincinnati, OH: U.S. Department of Health, Education, and Welfare, Public Health Service, Center for Disease Control, National Institute for Occupational Safety and Health, DHEW (NIOSH) Publication No. 78-141.

NIOSH [1983a]. Current Intelligence Bulletin 39: glycol ethers—2-methoxyethanol and 2-ethoxyethanol. Cincinnati, OH: U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 83-112.

NIOSH [1983b]. National occupational exposure survey (NOES), 1981-83: estimated total and female employees, actual observation and trade-named exposure to EGEE, EGME, EGBE, and their acetates. Cincinnati, OH: U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health, Division of Surveillance, Hazard Evaluations, and Field Studies, Surveillance Branch, Hazard Section. Unpublished data base.

NIOSH [1984]. Manual of analytical methods. 3rd ed. Cincinnati, OH: U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 84-100.

NIOSH [1987a]. Guide to industrial respiratory protection. Morgantown, WV: U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 87-116.

NIOSH [1987b]. NIOSH respirator decision logic. Cincinnati, OH: U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 87-108.

NIOSH [1987c]. Registry of toxic effects of chemical substances: 1985-86 edition. Cincinnati, OH: U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 87-116.

Nitter-Hauge S [1970]. Poisoning with ethylene glycol monomethyl ether: report of two cases. *Acta Med Scand* 188:277-280.

NSC [1980]. Accident prevention manual for industrial operations—engineering and technology. 8th ed. Chicago, IL: National Safety Council, pp. 94, 530, 586, 641.

NTP [1988]. Chemicals considered or being evaluated for short term toxicity and for long term toxicology and carcinogenesis effects (data received up to July 8, 1988). Research Triangle Park, NC: National Toxicology Program. Chemical status report produced from NTP Chemtrack System.

O'Brien DM, Hurley DE [1981]. An evaluation of engineering control technology for spray painting. Cincinnati, OH: U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health, Division of Physical Sciences and Engineering, DHHS (NIOSH) Publication No. 81-121.

Ohi G, Wegman DH [1978]. Transcutaneous ethylene glycol monomethyl ether poisoning in the work setting. *J Occup Med* 20(10):675-676.

Ong T [1980]. Memorandum of September 29, 1980, to Director, DCDS, NIOSH, regarding mutagenicity testing of 2-ethoxy/methoxy ethanol. Cincinnati, OH: U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health.

OSHA [1990]. Method No. 79. 2-Methoxyethanol (methyl Cellosolve<sup>®</sup>, 2ME), 2-methoxyethyl acetate (methyl Cellosolve<sup>®</sup> acetate, 2MEA), 2-ethoxyethanol (Cellosolve<sup>®</sup>, 2EE), 2-ethoxyethyl acetate (Cellosolve<sup>®</sup> acetate, 2EEA). Salt Lake City, UT: U.S. Department of Labor, Occupational Safety and Health Administration, Organic Methods Evaluation Branch, OSHA Analytical Laboratory.

Oudiz DJ, Zenick H, Niewenhuis RJ, McGinnis PM [1984]. Male reproductive toxicity and recovery associated with acute ethoxyethanol exposure in rats. *J Toxicol Environ Health* 13:763-775.

Oudiz DJ, Zenick H [1986]. *In vivo* and *in vitro* evaluations of spermatotoxicity induced by 2-ethoxyethanol treatment. *Toxicol Appl Pharmacol* 84:576-583.

Parsons CE, Parsons ME [1938]. Toxic encephalopathy and "granulopenic anemia" due to volatile solvents in industry: report of two cases. *J Ind Hyg Toxicol* 20(2):124-133.

Piacitelli G, Votaw DM, Krishnan ER [1988]. Industrial hygiene survey report of Martin Marietta Missile and Electronics Group, Orlando, FL. Cincinnati, OH: U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health, Division of Surveillance, Hazard Evaluations, and Field Studies, Industrywide Studies Branch, Industrial Hygiene Section, Report No. 134.20.10.

Ramos H, Lucas JB [1973]. Health hazard evaluation determination report: Universal Oil Products, Norplex Division, Franklin, IN. Cincinnati, OH: U.S. Department of Health, Education, and Welfare, Public Health Service, Center for Disease Control, National Institute for Occupational Safety and Health, NIOSH Report No. 72-82-86, NTIS PB-232562.

Rao KS, Cobel-Geard SR, Young JT, Hanley TR Jr., Hayes WC, John JA, et al. [1983]. Ethylene glycol monomethyl ether II. Reproductive and dominant lethal studies in rats. *Fund Appl Toxicol* 3:80-85.



Ratcliffe J, Clapp D, Schrader SM, Turner TW, Oser J, Tanaka S, et al. [1986]. Health hazard evaluation determination report: Precision Castparts Corporation, Portland, OR. Cincinnati, OH: U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health, NIOSH Report No. 84-415-1688.

Rawlings SJ, Shuker DEG, Webb M, Brown NA [1985]. The teratogenic potential of alkoxy acids in post-implantation rat embryo culture: structure-activity relationships. *Toxicol Lett* 28:49-58.

Ritter EJ, Scott WJ Jr., Randall JL, Ritter JM [1985]. Teratogenicity of dimethoxyethyl phthalate and its metabolites methoxyethanol and methoxyacetic acid in the rat. *Teratology* 32:25-31.

Roder MM [1990]. A guide for evaluating the performance of chemical protective clothing. Morgantown, WV: U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 90-109.

Romer KG, Balge F, Freundt KJ [1985]. Ethanol-induced accumulation of ethylene glycol monoalkyl ethers in rats. *Drug Chem Toxicol* 8(4):255-264.

Rowe VK, Wolf MA [1982]. Derivatives of glycols. In: Clayton GD, Clayton FE, eds. *Patty's industrial hygiene and toxicology*. 3rd rev. ed. Vol. 2. New York, NY: John Wiley and Sons, pp. 3909-4052.

Samuels DM, Doe JE, Tinston DJ [1984]. The effects on the rat testis of single inhalation exposures to ethylene glycol monoalkyl ethers, in particular ethylene glycol monomethyl ether. *Arch Toxicol (Suppl 7)*:167-170.

SANSS/CIS [1988]. Structure and Nomenclature Search Systems/Chemical Information System, Inc. Washington, DC: U.S. Environmental Protection Agency. Unpublished data base.

Sax NI, Lewis RJ Sr. [1987]. *Hawley's condensed chemical dictionary*. 11th ed. New York, NY: Van Nostrand Reinhold Company, pp. 488-489.

Schuler RL, Hardin BD, Niemeier RW, Booth G, Hazelden K, Piccirillo V, et al. [1984]. Results of testing fifteen glycol ethers in a short-term *in vivo* reproductive toxicity assay. *Environ Health Perspect* 57:141-146.

Scott WJ, Fradkin R, Wittfoht W, Nau H [1989]. Teratologic potential of 2-methoxyethanol and transplacental distribution of its metabolite, 2-methoxyacetic acid, in non-human primates. *Teratology* 39:363-373.

Sleet RB, Greene JA, Welsch F [1987]. Teratogenicity and disposition of the glycol ether 2-methoxyethanol and their relationship in CD-1 mice. In: Welsch F, ed. *Approaches to*

elucidate mechanisms in teratogenesis. Washington, DC: Hemisphere Publishing Corporation, pp. 33-57.

Sleet RB, Greene JA, Welsch F [1988]. The relationship of embryotoxicity to disposition of 2-methoxyethanol in mice. *Toxicol Appl Pharmacol* 93:195-207.

Smallwood AW, DeBord KE, Lowry LK [1984]. Analyses of ethylene glycol monoalkyl ethers and their proposed metabolites in blood and urine. *Environ Health Perspect* 57:249-253.

Smallwood AW, DeBord K, Burg J, Moseley C, Lowry L [1988]. Determination of urinary 2-ethoxyacetic acid as an indicator of occupational exposure to 2-ethoxyethanol. *Appl Ind Hyg* 3(2):47-50.

Smialowicz RJ, Riddle MM, Luebke RW, Copeland CB, Andrews D, Rogers RR, et al. [1991]. Immunotoxicity of 2-methoxyethanol following oral administration in Fischer 344 rats. *Toxicol Appl Pharm* 109:494-506.

Smyth HF Jr., Seaton J, Fischer L [1941]. The single dose toxicity of some glycols and derivatives. *J Ind Hyg Toxicol* 23(6):259-268.

Smyth HF Jr., Carpenter CP [1948]. Further experience with the range finding test in the industrial toxicology laboratory. *J Ind Hyg Toxicol* 30(1):63-68.

Sparer J, Welch LS, McManus K, Cullen MR [1988]. Effects of exposure to ethylene glycol ethers on shipyard painters: I. Evaluation of exposure. *Am J Ind Med* 14:497-507.

Stenger E-G, Aeppli L, Muller D, Peheim E, Thomann P [1971]. The toxicology of ethyleneglycol monoethylether. *Arzneim Forsch* 21(6):880-885.

Szybalski W [1958]. Special microbiological systems. II. Observations on chemical mutagenesis in microorganisms. *Ann NY Acad Sci* 76(3):475-489.

Terrill JB, Daly IW [1983a]. A 13-week inhalation toxicity study of ethylene glycol monoethyl ether in the rabbit. Report #82-7589 to the Chemical Manufacturers Association. Washington, DC: Chemical Manufacturers Association.

Terrill JB, Daly IW [1983b]. A 13-week inhalation toxicity study of ethylene glycol monoethyl ether in the rat. Report #82-7588 to the Chemical Manufacturers Association. Washington, DC: Chemical Manufacturers Association.

Tinston DJ [1983]. Ethylene glycol monoethyl ether (EE): probe teratogenicity study in rabbits. Alderley Park, Macclesfield, Cheshire, UK: Imperial Chemical Industries PLC, Central Toxicology Laboratory, Report No. CTL/T/1909.

Toraason M, Stringer B, Stober P, Hardin BD [1985]. Electrocardiographic study of rat fetuses exposed to ethylene glycol monomethyl ether (EGME). *Teratology* 32:33-39.

- Trosko JE, Chang CC, Netzloff M [1982]. The role of inhibited cell-cell communication in teratogenesis. *Teratogenesis Carcinog Mutagen* 2:31-45.
- Truhaut R, Dutertre-Catella H, Phu-Lich N, Huyen VN [1979]. Comparative toxicological study of ethylglycol acetate and butylglycol acetate. *Toxicol Appl Pharmacol* 51:117-127.
- Tsai CS [1968]. Relative reactivities of primary alcohols as substrates of liver alcohol dehydrogenase. *Can J Biochem* 46:381-385.
- TSCA [1977]. Toxic substances control act inventory. Washington, DC: U.S. Environmental Protection Agency. Unpublished data base.
- Tyl RW, Pritts IM, France KA, Fisher LC, Tyler TR [1988]. Developmental toxicity evaluation of inhaled 2-ethoxyethanol acetate in Fischer 344 rats and New Zealand white rabbits. *Fund Appl Toxicol* 10:20-39.
- UCC [1984]. Protective clothing (gloves) for glycol ethers. Danbury, CT: Union Carbide Corporation, Solvents and Coating Materials, Publication No. F-485111, 3/84-15M.
- UCC [1985]. Material safety data sheets for Cellosolve<sup>®</sup>, Cellosolve<sup>®</sup> acetate, methyl Cellosolve<sup>®</sup>, methyl Cellosolve<sup>®</sup> acetate. Danbury, CT: Union Carbide Corporation.
- Ungers LJ, Mihlan GJ, Jones JH [1984a]. In-depth survey report: control technology for microelectronics industry at Xerox Corporation Microelectronic Center, El Segundo, CA. Cincinnati, OH: U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health, Division of Physical Sciences and Engineering, NIOSH Report No. 115-12B.
- Ungers LJ, Mitchell RI, Jones JH [1984b]. In-depth survey report: control technology for the microelectronics industry at NEC Electronics USA, Mountain View, CA. Cincinnati, OH: U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health, Division of Physical Sciences and Engineering, NIOSH Report No. 115-24b.
- USITC [1986]. Synthetic organic chemicals, United States production and sales, 1986 (Investigation No. 332-135). Washington, DC: U.S. International Trade Commission, Publication No. 2009, pp. 211-212.
- Veulemans H, Groeseneken D, Masschelein R, Van Vlem E [1987a]. Field study of the urinary excretion of ethoxyacetic acid during repeated daily exposure to the ethyl ether of ethylene glycol and the ethyl ether of ethylene glycol acetate. *Scand J Work Environ Health* 13:239-242.
- Veulemans H, Groeseneken D, Masschelein R, Van Vlem E [1987b]. Survey of ethylene glycol ether exposures in Belgian industries and workshops. *Am Ind Hyg Assoc J* 48(8):671-676.
- Veulemans H [1989]. Telephone conversation in September 1989, between H. Veulemans, Laboratorium voor arbeidshygiene en-toxicologie (Leuven, Belgium) and J.A. Wess, Division

of Standards Development and Technology Transfer (Cincinnati, OH), National Institute for Occupational Safety and Health, Centers for Disease Control, Public Health Service, U.S. Department of Health and Human Services.

von Oettingen WF, Jirouch EA [1931]. The pharmacology of ethylene glycol and some of its derivatives in relation to their chemical constitution and physical chemical properties. *J Pharmacol Exp Ther* 42(3):355-372.

Waite CP, Patty FA, Yant WP [1930]. Acute response of guinea pigs to vapors of some new commercial organic compounds. III. "Cellosolve" (mono-ethyl ether of ethylene glycol). *Public Health Rep* 45:1459-1466.

Welch LS, Cullen MR [1988]. Effect of exposure to ethylene glycol ethers on shipyard painters: III. Hematological effects. *Am J Ind Med* 14:527-536.

Welch LS, Schrader SM, Turner TW, Cullen MR [1988]. Effects of exposure to ethylene glycol ethers on shipyard painters: II. Male reproduction. *Am J Ind Med* 14:509-526.

Welsch F, Stedman DB [1984]. Inhibition of metabolic cooperation between Chinese hamster V79 cells by structurally diverse teratogens. *Teratogenesis Carcinog Mutagen* 4:285-301.

Werner HW, Nawrocki CZ, Mitchell JL, Miller JW, von Oettingen WF [1943a]. Effects of repeated exposures of rats to vapors of monoalkyl ethylene glycol ethers. *J Ind Hyg Toxicol* 25(8):374-379.

Werner HW, Mitchell JL, Miller JW, von Oettingen WF [1943b]. Effects of repeated exposure of dogs to monoalkyl ethylene glycol ether vapors. *J Ind Hyg Toxicol* 25(9):409-414.

Werner HW, Mitchell JL, Miller JW, von Oettingen WF [1943c]. The acute toxicity of vapors of several monoalkyl ethers of ethylene glycol. *J Ind Hyg Toxicol* 25(4):157-163.

Wickramaratne GA [1986]. The teratogenic potential and dose-response of dermally administered ethylene glycol monomethyl ether (EGME) estimated in rats with the Chernoff-Kavlock assay. *J Appl Toxicol* 6(3):165-166.

Wiley FH, Hueper WC, Bergen DS, Blood FR [1938]. The formation of oxalic acid from ethylene glycol and related solvents. *J Ind Hyg Toxicol* 20(4):269-277.

Yonemoto J, Brown NA, Webb M [1984]. Effects of dimethoxyethyl phthalate, monomethoxyethyl phthalate, 2-methoxyethanol and methoxyacetic acid on post-implantation rat embryos in culture. *Toxicol Lett* 21:97-102.

Zavon MR [1963]. Methyl cellosolve intoxication. *Am Ind Hyg Assoc J* 24:36-41.