NIOSH Comments to DOL

OSHA Proposed Rule on
OCCUPATIONAL EXPOSURE TO ETHYLENE OXIDE
Docket H-200
June 22, 1983

NIOSH has reviewed the proposed standard and offers the following comments in response to specific issues raised by OSHA..

1. Would the proposed provisions provide adequate worker protection from all hazards associated with EtO exposure?

   NIOSH generally supports OSHA's efforts to reduce the PEL for EtO; however, there are provisions for which we believe reconsideration will strengthen the final rule. Specifically, it is our opinion that the medical surveillance provisions will not contribute to a reduction in risk.

2. NIOSH has no comments.

3. NIOSH has no comments.

4. What are the most suitable methods for determining compliance with EtO permissible exposure limits (PEL's) of 0.5 and 1 ppm as 8-hour time-weighted averages and for ceilings ranging from 5 to 50 ppm for 30 minutes or less? What are the problems associated with such monitoring methods? Do they require special training or experience? Are there serious limitations as to the accuracy or precision of the available sampling techniques?

   In our past industrial-hygiene studies, NIOSH has used the procedure of Qazi and Ketchem of the Union Carbide Corporation. Our data suggest the lower limit for measuring ethylene oxide in air using this method is about 3 ppm.

   The OSHA method number 30 is suitable for determining compliance with standards at 0.5 ppm or 1 ppm for 8-hour exposures and 5 ppm as a 15-minute (ceiling) exposure.

   NIOSH staff have evaluated a modification of OSHA method number 30. In this modified method, the charcoal tube specified by OSHA was replaced with a larger one containing 400 mg of activated charcoal in the primary bed and 200 mg in the backup bed. The use of the larger tubes should permit longer sampling periods. This modified method was evaluated at three levels of ethylene oxide (trapped on charcoal), which corresponded to 0.03 ppm to 1.7 ppm in 5-liter (8-hour) air samples. The data revealed that, although the desorption efficiencies of ethylene oxide from the charcoal were nearly quantitative, reaction yields of the ethylene oxide derivative, 2-bromoethanol, were only

about 70%. Our recovery experiments also revealed that migration of ethylene oxide from the primary bed to the backup bed during storage occurred rapidly. Therefore, we recommend that two charcoal tubes b used in series so that the primary and backup sections can be sealed separately prior to shipment to the laboratory. As for the precision of the modified method, the relative standard deviation for replicate samples analyzed on the same day ranged from 3% to 18%, while the relative standard deviation for replicate samples analyzed over a number of days ranged upward to 24%.

NIOSH is currently exploring the availability of other analytical techniques that could be used to make real time determinations of EtO peak concentrations over periods of time of 15 minutes or less. One such method for instanteous readings on EtO exposure that holds promise is the Foxboro/Wilkes Maran 103R Infrared Analyses.

5. Are there other risk assessments besides that developed by OSHA that specifically deal with the risk of cancer or other disease at 50 ppm and the proposed PEL of 1 ppm? Can the risk of adverse reproductive effects resulting from exposure to 1 ppm or less be adequately quantified?

NIOSH is not aware of any other risk assessment describing exposure relationships for EtO and cancer.

6. Is there any group of workers who, because of lifestyle, concurrent exposure to other chemicals, or physiological makeup, are likely to have an increased sensitivity to ethylene oxide? If so, what consideration, if any, should be provided for such workers in the final standard?

NIOSH has no specific data relating to EtO that would assist OSHA with respect to this issue. Even though there are biological differences in human susceptability to certain environmental carcinogens, the lack of specific data pertaining to EtO would dictate that all workers potentially exposed to EtO be treated at equal risk. The study by Yager et al. cited above, however, does indicate that those workers who smoked cigarettes and were exposed to EtO had an increased frequency of sister chromatid exchanges than either EtO exposed workers who did not smoke or control subjects who did smoke. It is significant that among people studied by Yager et al., those who were in the control group smoked an average of 21 cigarettes per day, while those in the exposed group smoked an average of only nine cigarettes per day. Whether the observed effect is synergistic or additive is not at all clear, nor can any relationship between this observation and an increased risk of disease be made. Such a relationship can be made only for sister chromatid exchanges.

7. Are the proposed medical surveillance provisions, including the suggested examinations found in Appendix D (sic) to the proposal, adequate for the purpose of providing protective medical monitoring of affected employees? Should an examination also be required to be offered at the termination of employment? Should the standard be more specific in the elements required for medical examinations of exposed employees?

The phrase "protective medical monitoring of affected employees" implies that we understand the mechanism of the disease process and that as long as physiological changes are detected at an early stage when they may possibly be reversed. Unfortunately, the mechanism of the disease process is not completely understood, and therefore, NIOSH does not believe that the medical surveillance described by OSHA will provide additional protection to EtO exposed workers.

Specifically, the medical history solicits information concerning symptoms related to the eyes, blood forming organs, lungs, nervous system, reproductive system and skin. Knowledge obtained by the acquisition of this information will not contribute to an understanding of the long-term effects of EtO exposure, nor is such information likely to contribute to the protection of the individual worker.

On the other hand, in the event of an exposure to a high concentration of EtO, the immediate examination might include the elements described by OSHA. These findings could not be used, however, to predict the likelihood of development of cancer or adverse reproductive effects or protect the worker from the development of those effects.

We do recognize that some workers who are potentially exposed to EtO may also be potentially exposed to other substances. In some of those circumstances, the worker may benefit from the examination as described by OSHA but we recommend that such examinations only be performed if the potential health benefit can be demonstrated.

The proposed rule also requires a complete blood count which is to include at least a white cell count, a differential count, hemoglobin and hematocrit. Information such as this has not been demonstrated to be predictive of carcinogenic or adverse reproductive responses. Although hematopoietic abnormalities have been reported by Ehrenberg and Hallstrom in an epidemiological investigation of EtO exposed workers, those investigators were unable to use these findings to predict cancer.

Complete blood counts including white cell counts could incidentally detect leukemia that had not yet become clinically evident, but again these tests would not be predictive and would effectively detect asymptomatic leukemia only if repeated at intervals of several weeks.

The medical surveillance provisions of the proposed rule also call for the routine performance of chromosome studies on individual workers, but the types of tests to be conducted, or the anticipated usefulnes of such testing is not specified. Based on current knowledge, NIOSH does not believe that such tests performed on individual workers will provide any knowledge that will contribute to the protection of individual workers from the long-term effects of exposure to EtO. Chromosomal studies provide a biological end point that is neither predictable or reversible.

The preemployment evaluation of a worker for chromosomal changes will not provide information that can be used to predict that worker's potential risk if exposed to EtO. For a worker already exposed to EtO such studies could not be used to determine whether or not that worker has already sustained a carcinogenic or adverse reproductive effect.

Exposure to EtO can result in chromosomal abnormalities and increased frequencies of sister chromatid exchanges; however, as of yet NIOSH knows of no data that correlates these effects to the manifestation of cancer or adverse reproductive effects in an individual. The chromosome studies of an individual suggested by OSHA are not likely to provide this information. Ability to detect such damage is limited and the disease can be manifested in the absence of detectable chromosomal damage. Conversely, the presence of detectable chromosomal damage does not appear to provide a firm basis for predicting the likelihood of an individual demonstrating a tumorigenic response.

Despite this uncertainty we believe that the identification of such changes in groups of workers is cause for concern about their continued well being, but is not appropriate for inclusion in a standard for EtO.

8. Specific provisions for skin and eye protection against contact with liquid EtO are not included in the proposal. Requirements found in 1910.132 and 1910.133 require the employer to provide protective equipment (gloves, goggles, etc.) where skin and eye exposure to hazardous liquids may occur. Is reliance on these two general provisions sufficient for protecting against potential dermal and eye hazards for liquid EtO? If not, explain and specify what additional provisions are necessary.

NIOSH believes that general requirements for skin and eye protection provided in 1910.132 and 1910.133 will not provide the necessary protection to EtO exposed workers. In addition, the selection of the equipment described in 1910.132 and 1910.133 must be based on thorough knowledge of a variety of factors such as the toxicity and reactivity of the substance.

Section 6(b)(7) of the Occupational Safety and Health Act specifies what an occupational safety and health standard promulgated under section 6(b) shall include. Protective equipment is specifically included:

". . . Where appropriate, such standard shall also prescribe suitable protective equipment and control or technological procedures to be used in connection with such hazards . . . "

The standard concerning protective equipment (29 CFR sect. 1910.132) and eye and face protection (29 CFR sect. 1910.133) provide only general guidelines and do not address substance specific issues particularly as they relate to the serious hazards presented by liquid ethylene oxide or EtO solutions. Therefore sections 132 and 133 cannot be viewed as prescribing "...suitable protective equipment..." because they do not consider the particular hazards presented by liquid ethylene oxide or EtO solutions spills and splashes. Neither sections 132 nor 133 specify how the equipment is to be used nor how it is to be selected to protect the worker from exposure to ethylene oxide.

NIOSH in the past has provided OSHA with specific protective equipment use recommendations for ethylene oxide. These recommendations were based on the acute effects of ethylene oxide exposure.

The Joint NIOSH/OSHA Standards Completion Program transmitted a Draft Technical Standard for ethylene oxide to OSHA in 1976. This draft standard contained requirements for the use of personal protective equipment and clothing to protect against the acute effects of liquid EtO and EtO solutions exposure. These basic requirements are essentially repeated in Appendix A of the current OSHA proposed rule.

In our 1977, publication Special Occupational Hazard Review with Control Recommendations for the Use of Ethylene Oxide as a Sterilant in Medical Facilities: NIOSH; HEW Publication No. (NIOSH) 77-200, NIOSH made the following recommendations:

> "sustained or intermittent skin contact with liquid EtO may produce dermatitis at the site of contact. However, due to the extreme penetrating ability of EtO, and the consequent ineffectiveness of many types of clothing materials to prevent skin contact, the use of conventional 'impervious' clothing is not suggested. There are, however, certain special types of protective clothing which are effective when working with EtO. For example, one of the large EtO manufacturers provides its workers with knitted gloves which have been coated with certain polymers, including polyvinyl chloride (sic) ..."

(Note: As we will explain below NIOSH has information that indicates that materials made of other substances will afford a greater measure of protection than that afforded by the use of polyvinyl chloride.)

> "...In addition, conscientious adherence to appropriate sanitation practices should eliminate most hazards of skin contact with EtO."

"If EtO splashes into the eye, severe irritation may result. For this reason it is suggested that rubber framed goggles, equipped with approved impact resistant glass or plastic lenses, be worn whenever there is danger of the material coming in contact with t. eyes (I.e., in operations which involve transport bulk containers of EtO from the storage room to the sterilizer unit for installation). Eye wash fountains within easy access from the immediate work area are recommended; they should be so situated that additional contact of the eyes with EtO in vapor form during washing is unlikely."

One study reviewed in this 1977 NIOSH publication reported that extensive skin blistering occured after brief contact with 40 - 80% aqueous solutions of EtO.

NIOSH believes that the recommendations contained in the SCP Draft Technical Standard provide a general basis upon which a standard for personal protective equipment and clothing can be developed. The chronic effects of EtO exposure and the potential for penetration and degradation of chemical protective clothing dictate that such equipment be thoroughly evaluated and tested prior to its routine use.

Permeation studies have shown that garments made of chlorinated polyethylene provide the greatest protection against pure, liquid EtO; breakthrough did not occur for at least one hour. Degradation studies have shown that garments made with nitrile and butyl rubber also have a lifetime of about 1 hour.. (Guidelines for the Selection of Chemical Protective Clothing, Vol. I Field Guide: U.S. EPA Contract No. C-876111, January 19, 1983.) Neoprene is also available in a wide variety of formulations that provide a spectra of different properties. Some guidance in the selection and testing of chemical protective clothing follow.

Exposure can still occur while using Chemical Protective Clothing (CPC) by (1) bulk penetration through pinholes, rips, zippers, seams, etc., (2) material failure due to chemical degradation, or (3) permeation through the material. For many chemicals, test data is available that can help assess the performance of commercially available CPC; however, due to the differences in use and manufacturing conditions, actual field evaluations are recommended under typical use conditions of mixtures, temperatures, and physical abuse.

There are a variety of standard American Society for Testing and Materials (ASTM) and Federal test methods available to determine the flexibility, puncture resistance, and flammability of chemical protective clothing. These methods are being summarized by the ASTM F23.20 Committee.

In general, a test appropriate to each situation must be selected. In the case where the protective clothing is reused, the effect of chemical degradation and decontamination (cleaning) must also be evaluated.

More specifically, there are several methods of evaluation available to determine chemical resistance.

1. Degradation can be determined by visual inspection or by determination of changes (weight or size) in material samples after exposure to concentrated chemicals for as brief as minutes or as long as days. Many manufacturers or distributors provide this "chemical resistance guide" for their products. This information may be useful for making relative comparisons; however, since permeation can occur without visual or measurable physical changes being observed, other data must be considered.

2. Penetration can be measured by several tests. Gaseous pressurization of one side of a test cell in which the test material is held can locate quality control defects such as pinholes. A draft ASTM penetration test reportedly applies pressurized chemical onto the outside of the material sample and a colorimetric detector on the inside to determine breakthrough time. This test may also be useful in detecting design defects in zippers and seams.

3. Permeation can be measured using the ASTM F739-81 standard test method which quantifies both breakthrough time and steady-state permeation rate. This method requires a gas chromatograph with an autosampler, as well as knowledge of the rate of vaporization and solubility of EtO. Although other test cells are available which are cheaper and use less chemical, none have been validated as providing results comparable to the ASTM method.

Using degradation, penetration, and permeation test data, candidate garment materials can be knowledgeably selected. Additional evaluation under typical use conditions is also necessary, however, since product formulations and processing conditions can vary from manufacturer to manufacturer or even lot to lot. In addition, in the workplace EtO may actually be present in a mixture, exposures may be intermittent and temperatures may be significantly different than those found in the test laboratory.

In all cases, NIOSH recommends that field tests be conducted by qualified personnel, such as an industrial hygienist, and that such tests address, at a minimum, the following.

1. A determination of the degradation, penetration, and permeation using liquid EtO or solutions containing EtO in the actual formulation encountered, and under those conditions (such as contact sequence, temperature, and reuse) expected to occur in the particular workplace.

2. Simpler field tests, although not currently validated, could provide estimates of breakthrough time. For instance, filling the fingers of a glove or inverting a glove and filling it with the actual chemical formulation may provide an indication of the protection being provided; however, as with the more sophisticated tests, a trained observer must interpret the results of such testing.

3. Additional considerations that should be given to the selection of chemical protective clothing include whether another hazard is being introduced as a result of its use; such as catching on moving equipment or loss of dexterity. Also, a determination must be made of whether more exposure can occur when the clothing is donned, recycled, or stored.

Finally, a determination of whether or not the use of such clothing increases or decreases the incidence of, for instance, a skin disorder may provide information (albiet after the fact) concerning the protection being afforded to the worker.

9. Should genetic screening, chromosome analysis, male fertility testing and pregnancy testing be provided as a part of the routine physical examination? Should these tests be offered to employees exposed to emergency situations, or be provided for those persons wishing to procreate? Should medical removal protection be provided for those wishing to procreate and, if so, under what circumstances?

As we have indicated above, neither genetic screening nor chromosome analysis have been demonstrated to have the ability to predict the likelihood of a carcinogenic response or of an adverse reproductive effect in an individual. Similarly, we do not believe that sperm or pregnancy test results obtained from individual workers will provide meaningful diagnostic information. As with genetic screening, we believe that sperm test results are currently only of value for interpreting effects of EtO exposure on an entire population.

Therefore, NIOSH does not recommend that such tests be performed as part of a routine examination of an individual worker. Given the present state of knowledge NIOSH can only recommend that, because no conditions of exposure to EtO have been demonstrated to be safe, employers should take all reasonable steps to reduce worker exposure to EtO to the lowest feasible limit.

10. In view of the uncertainty as to what constitutes an appropriate physical examination, should a multi-physician review be required if requested by the employee? Should employees who believe that they are suffering from symptoms associated with EtO overexposure be offered an interim medical examination?

NIOSH does not believe that the uncertainty described by OSHA can be resolved by a multi-physician review, since the uncertainty arises from the interpretation and not the performance of such tests.

Workers who believe that they are suffering from the acute or chronic effects of EtO exposure should be offered appropriate medical evaluation and treatment. The affected workers should also be informed that such an examination cannot with any certainty predict the likelihood of a carcinogenic or adverse reproductive response. In addition, workers should also be informed that results from such an examination will not provide a basis for medical intervention that will protect that worker's health.

With respect to Appendix C--Medical Surveillance Guidelines for Ethylene Oxide we offer the following comments.

Because physical examinations and biological measurements will not provide information about an individual worker from which to predict subsequent manifestation of carcinogenic or adverse reproductive effects due to EtO in that individual, no routine physical examination or biological testing procedures can be recommended that will protect the individual worker from the effects of exposure to EtO. Complete blood count data, including white cell count, could indicate an already manifest malignancy of the hematopoietic system, but would not protect an individual worker against development of the disease.

Cross sectional chromosomal studies could detect evidence of ongoing genetic damage to a group of workers, but routine chromosome studies for an individual worker are not recommended because the data would not have specific diagnostic meaning for that worker. If such testing is indeed conducted, the uncertainties of interpreting both positive and negative findings should be explained clearly to the worker.

11. What is the incidence of persistence of quadriradial or other chromosomal aberrations and sister chromatid exchanges in peripheral lymphocytes over time after exposure to EtO ceases? Is this persistence or lack of persistence a function of dose and/or duration of exposure?

The persistance of the damage detected within an individual is determined by at least four factors. First, the amount or extent of the induced damage. Second, the efficiency of the repair mechanism. Third, elapsed time between the exposure and the observation of damage, and fourth the turnover rate of the damaged cells.

In addition, the determination of the persistence of such damage in humans is complicated by genetic variability unlike similar determinations made in an essentially genetically homogeneous population such as laboratory rodents.

As we described in response to issue three, there is some evidence that suggests that the acute genotoxic responses observed in animals and humans are related to the manifestation of chronic illnesses.

12.-14. NIOSH has no comments.

15. Are there conditions under which respirator use should be permitted in addition to those proposed? What respirator fit testing requirements should be included in the final standard and when should such testing be performed?

NIOSH has reviewed the proposed provisions for respirator use and has determined that the provisions set forth by the proposed standard would not provide adequate protection. Since EtO has an odor threshold of between 430 and 700 ppm, it does not have adequate warning properties at and below 50 ppm. Therefore, NIOSH recommends that unless air purifying respirators are equipped with an effective end of service indicator they should not be permitted for use in EtO containing atmospheres.

The proposed standard also allows the use of supplied air respirators in atmospheres having EtO concentrations as great as 2,000 ppm. However, the NIOSH/OSHA Guide to Chemical Hazards states that EtO at 800 ppm is Immediately Dangerous to Life or Health (IDLH). NIOSH/MSHA approvals for supplied air respirators are given only for use in non-IDLH atmospheres. Therefore, we recommend that the maximum concentration at which supplied air respirators are permitted for use against EtO be reduced to 800 ppm

NIOSH further recommends that OSHA require use of quantitative respirator fit testing for air purifying respirators and that they review the NIOSH publication "Alternatives to Di-2-Ethylhexyl Phthalate ("DOP") Respirator Quantitative Fit Testing," DHHS (NIOSH) Publication No. 83-109.

16.-17. NIOSH has no comments.

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15. Supplementary Notes

16. Abstract (Limit: 200 words) This testimony concerns the opinions of NIOSH concerning the proposed standard from OSHA. NIOSH generally supports the efforts to reduce the PEL for ethylene-oxide (75218) (EtO), but feels that the medical surveillance provisions of the proposed rule would not contribute to a reduction in risk. Concerning suitable methods for determining compliance with EtO permissible exposure limits, NIOSH suggests the procedure of Qazi and Ketchem of the Union Carbide Corporation, which has as its lower limit 3 parts per million. The possibility of lifestyle factors entering into the increased risk for cancer from exposure to EtO was discussed as well as proposed medical surveillance provisions, the use of personal protective equipment, the usefulness of field tests, the extent of the routine physical examination, the incidence of quadriradial or other chromosome aberrations and sister chromatid exchanges in peripheral lymphocytes over time after exposure to EtO, and circumstances for the wearing of respirators.

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