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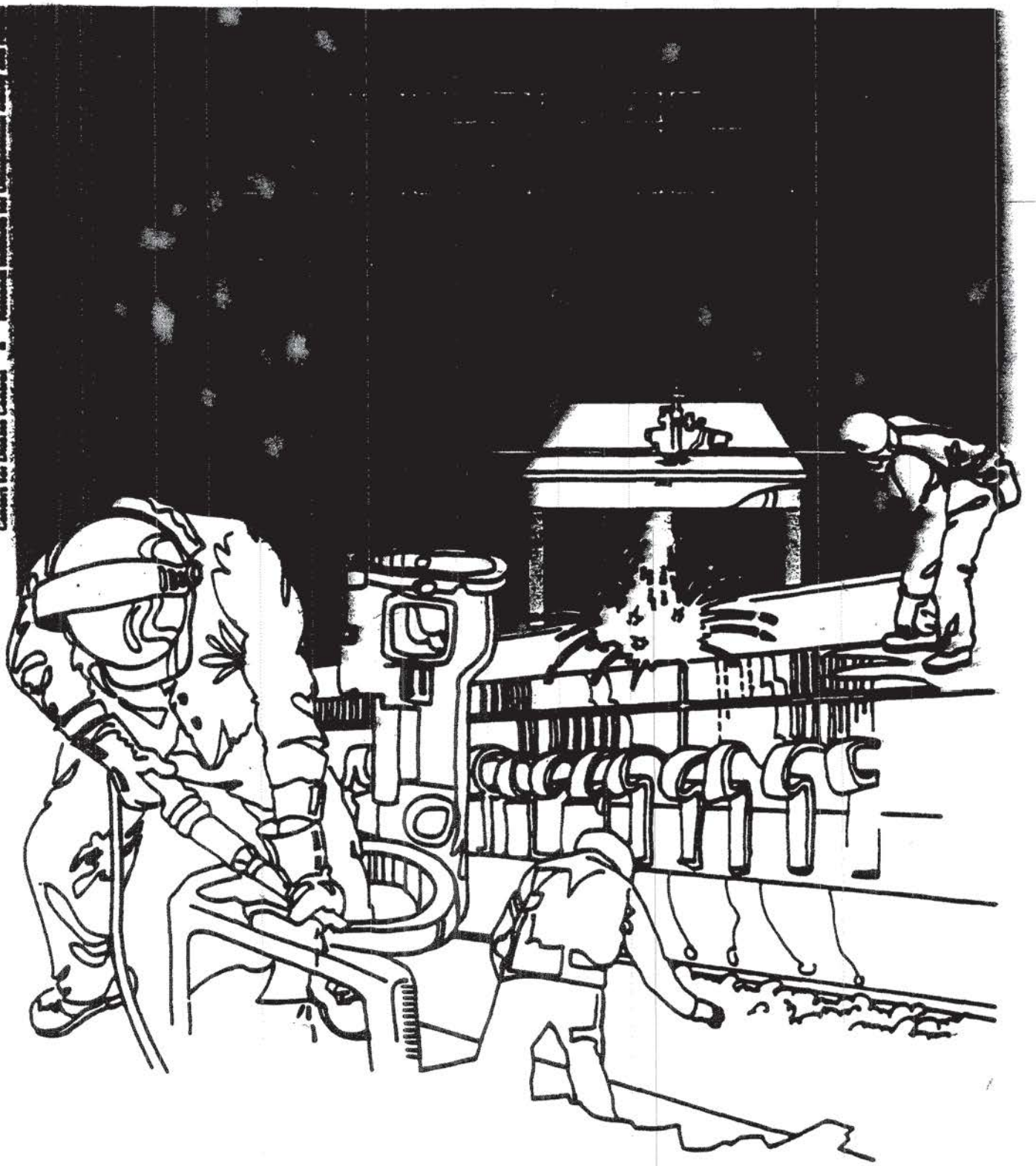

Health Hazard Evaluation Report

HETA 84-535-1690
NATIONAL JEWISH HOSPITAL
DENVER, COLORADO

PREFACE

The Hazard Evaluations and Technical Assistance Branch of NIOSH conducts field investigations of possible health hazards in the workplace. These investigations are conducted under the authority of Section 20(a)(6) of the Occupational Safety and Health Act of 1970, 29 U.S.C. 669(a)(6) which authorizes the Secretary of Health and Human Services, following a written request from any employer or authorized representative of employees, to determine whether any substance normally found in the place of employment has potentially toxic effects in such concentrations as used or found.

The Hazard Evaluations and Technical Assistance Branch also provides, upon request, medical, nursing, and industrial hygiene technical and consultative assistance (TA) to Federal, state, and local agencies; labor; industry and other groups or individuals to control occupational health hazards and to prevent related trauma and disease.

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I. SUMMARY

In October 1984, the National Institute for Occupational Safety and Health (NIOSH) was requested to evaluate glutaraldehyde exposures to research technologists who perform tissue fixing procedures at National Jewish Hospital, Denver, Colorado. It was stated in the request that employees who performed procedures with glutaraldehyde in other departments had experienced symptoms such as eye, skin and respiratory irritations and staining of the skin.

In March 1985, a NIOSH investigator performed an environmental survey in the Electron Microscopy Laboratory and Small Animal Laboratory where the tissue fixing procedures are performed. Two personal breathing zone and four area air samples were collected to measure airborne concentrations of glutaraldehyde. Sampling times were approximately 90 minutes. A ventilation survey was also performed on each of the laboratory hoods used in these departments.

Personal breathing zone samples taken for glutaraldehyde were all non detectable (ND). Area samples ranged from ND to 0.21 mg/M^3 and these were below the American Conference of Governmental Industrial Hygienists (ACGIH) Ceiling-TLV of 0.7 mg/M^3. At present there is no NIOSH Criteria or OSHA Standard. A laboratory hood was used in each of those areas surveyed and these operated with face velocities between 50 and 150 feet per minute which are not effective for all the procedures evaluated.

Finally, it was determined that the employees evaluated had experienced symptoms related to glutaraldehyde exposures in the past, however, due to changes in a portion of the exhaust ventilation, personal protective equipment and work practices these have not occurred since.

On the basis of the environmental sampling results, it was concluded that a health hazard did not exist from glutaraldehyde exposures at National Jewish Hospital for research technologists who perform tissue fixing procedures. Recommendations for reducing potential exposures to glutaraldehyde are included in this report.

KEYWORDS: SIC 8221 (Colleges, Universities, and Professional Schools) and SIC 8062 (General Medical and Surgical Hospitals), glutaraldehyde, tissue fixing and slicing; eye, skin, respiratory irritations, staining of the skin.

II. INTRODUCTION

The National Institute for Occupational Safety and Health (NIOSH) received a request in October 1984 from a representative of National Jewish Hospital, Denver, Colorado. The request was submitted after previous NIOSH studies at this facility (HETA 83-045 and 83-074) determined that both formaldehyde and glutaraldehyde were occupational health hazards under the specific conditions evaluated.

The current request concerned the use of and potential exposures to glutaraldehyde in various stages of tissue processing. Air sampling was performed in both the Small Animal Laboratory (SAL) and Electron Microscopy Laboratory (EML).

The results of the evaluation were presented to the requestor and the employees as they became available. Recommendations to reduce potential exposures were given to the employees during the survey period.

III. BACKGROUND

NIOSH was requested to evaluate potential health problems to technicians who perform tissue fixing operations in both the small animal and electron microscopy laboratories at National Jewish Hospitals. These health problems were thought to be primarily associated with exposures to glutaraldehyde vapors created during various stages of tissue fixing procedures (e.g., tissue slicing and staining). There are normally 2 or 3 employees in the SAL and EML who are involved in the tissue fixing operation.

Glutaraldehyde is purchased in 25 and 50 percent GRADE STOCK and is used in either a 1.5 or 3% solution. The diluted glutaraldehyde solution is actually used for a number of different tissue fixative procedures. For organs, the fixative is perfused through the entire tissue. In the case of lungs, the fixative is poured down the trachea using a perfusion bottle and tubing. For tissue that needs morphometric measurements, the tissue must be perfused in a tank at a constant pressure for 24 hours.

In general, it was determined that glutaraldehyde exposures were potentially present during placement/removal of lungs in the perfusion tank, during tissue staining/slicing procedures, and during maintenance operations on equipment used in these procedures (i.e., tank cleaning, equipment repair and/or draining and replacement of the fixing solution).

The perfusion tank is located in the SAL and has been used in a lab hood since NIOSH made its original recommendations in previous studies performed at the hospital (refer to HETA 83-045 and 83-074). A lab hood is also used in the EML for the preparation of new glutaraldehyde solution and during the actual tissue slicing procedure.

1. Exhaust Ventilation

Each of the laboratory hoods are laminar-flow type hoods. The window sash in both hoods is normally positioned with approximately a four to six inch gap during the majority of the tissue fixing operations. The face velocity obtained during these conditions was considered effective for exhausting the contaminant from the operators breathing zone. During maintenance procedures, however, the sash is opened approximately 24 to 30 inches which drops the velocity to less than half, which is not considered effective in removing the contaminant.

2. Maintenance

Maintenance is performed approximately once per month on the fixing tank by one to two employees. This requires the tank to be drained, (residual materials manually removed) and the tank flushed with tap water repeatedly. The tank is then refilled from a container of fresh glutaraldehyde solution which has been prepared in the EML. Normally, all maintenance tasks involving the glutaraldehyde tank are accomplished as rapidly as possible in order to minimize vapors released when the lab hood is raised and the tank is opened.

3. Personal Protective Clothing

During each of the operations employees wear a variety of personal protective clothing. This includes a lab coat, apron, gloves, goggles, and/or respirators as deemed necessary for the particular procedure. Three different types of protective gloves are available including latex, rubber, and polyvinyl. Two different types of respirators are available to the employees and these include surgical or disposal organic vapor type respirators.

IV. SAMPLING DESIGN AND METHODS

Six air samples, two (2) personal and four (4) general area samples were collected by drawing air through sorbent tubes to trap the glutaraldehyde vapors. The sampling pumps drew air through the tubes at 0.2 liters per minute for approximately 90 minutes. The samples were analyzed using reverse phase High Pressure Liquid Chromotography (HPLC).

An exhaust ventilation survey was performed in each of the hoods used during the various tissue fixing procedures (e.g., tissue fixing, slicing and maintenance operations). Each of the employees was also questioned regarding any adverse health effects experienced while working with glutaraldehyde.

V. EVALUATION CRITERIA

A. Environmental

As a guide to the evaluation of the hazards posed by workplace exposures, NIOSH field staff employ environmental evaluation criteria for assessment of a number of chemical and physical agents. These criteria are intended to suggest levels of exposure to which most workers may be exposed up to 10 hours per day, 40 hours per week for a working lifetime without experiencing adverse health effects. It is, however, important to note that not all workers will be protected from adverse health effects if their exposures are maintained below these levels. A small percentage may experience adverse health effects because of individual susceptibility, a pre-existing medical condition, and/or a hypersensitivity (allergy). In addition, some hazardous substances may act in combination with other workplace exposures, the general environment, or with medications or personal habits of the worker to produce health effects even if the occupational exposures are controlled at the level set by the evaluation criterion. These combined effects are often not considered in the evaluation criteria. Also, some substances are absorbed by direct contact with the skin and mucous membranes, and thus potentially increase the overall exposure. Finally, evaluation criteria may change over the years as new information on the toxic effects of an agent become available.

The primary sources of environmental evaluation criteria for the workplace are: 1) NIOSH Criteria Documents and recommendations, 2) the American Conference of Governmental Industrial Hygienists' (ACGIH) Threshold Limit Values (TLV's), and 3) the U.S. Department of Labor (OSHA) occupational health standards. Often, the NIOSH recommendations and ACGIH TLV's are lower than the corresponding OSHA standards. Both NIOSH recommendations and ACGIH TLV's usually are based on more recent information than are the OSHA standards. The OSHA standards also may be required to take into account the feasibility of controlling exposures in various industries where the agents are used; the NIOSH-recommended standards, by contrast, are based primarily on concerns relating to the prevention of occupational disease. In evaluating the exposure levels and the recommendations for reducing these levels found in this report, it should be noted that industry is legally required to meet those levels specified by an OSHA standard.

A time-weighted average (TWA) exposure refers to the average airborne concentration of a substance during a normal 8 to 10-hour workday. Some substances have recommended short-term exposure limits or ceiling values which are intended to supplement the TWA where there are recognized toxic effects from high short-term exposures.

At present there is no OSHA Standard or NIOSH criteria for glutaraldehyde. The American Conference of Governmental Industrial Hygienists (ACGIH) TLV for glutaraldehyde is 0.2 (C) parts per million (ppm) which is equal to 0.7 mg/M^3. The designation (C) refers to a ceiling concentration that should not be exceeded even instantaneously.

B. Toxicology

The use of glutaraldehyde has expanded over the last 20 years and it is now used in a variety of different medical fields. It was originally developed as a quick-acting sporicidal agent without the undesirable health effects associated with formaldehyde. Today, glutaraldehyde is used primarily for disinfection and/or sterilization of a variety of medical, dental, and hospital equipment.

Glutaraldehyde has a pungent odor, an odor recognition threshold of 0.04 parts per million (ppm) by volume in air, and an irritation response level of 0.3 ppm (0.7 mg/M^3). In contrast to formaldehyde, which is a simple aldehyde, glutaraldehyde has two active carbonyl groups.

Glutaraldehyde is a relatively strong irritant to the nose and a severe irritant to the eye. It can produce staining and may be slightly irritating to the skin, however, it can cause skin sensitization (allergic contact dermatitis) from occasional or incidental occupational exposures. Activated glutaraldehyde appears to retain the same skin sensitizing properties as those described for pure glutaraldehyde. Furthermore, it appears that the relatively strong irritant effect of pure glutaraldehyde on the eyes, nasal passages, upper respiratory tract and skin are slightly enhanced when the dialdehyde is activated. Recent information suggests that glutaraldehyde should not be considered mutagenic or teratogenic, but that it can produce central nervous system, musculoskeletal, craniofacial and fetotoxic effects in animals. The reader is referred to Health Hazard Evaluation Reports 83-045 and 83-074 for further information on the chemical and toxicological properties of glutaraldehyde.

VI. RESULTS AND DISCUSSION

NIOSH's evaluation included environmental air monitoring, surveying of the ventilation systems, and a review of the personal protective clothing used by the employees. The following are the results of NIOSH's study:

A. Environmental

Six samples were taken at National Jewish Hospital, two personal and four area samples, and the sampling times were approximately 90 minutes. The results for the personal samples were all non-detectable (ND). The area air samples ranged from ND to 0.21 mg/M^3. All sample results were below the ACGIH Ceiling-TLV of 0.7 mg/M^3 (refer to Table 1).

B. Ventilation

The exhaust hoods used in both labs had an exhaust flow velocity rate of 125 to 150 fpm when the window sash was in its proper position. During lung placement and removal, as well as during general maintenance operations, the velocity dropped below 50 fpm. This was primarily because it was necessary for the operator to open the window sash two to three feet in order to perform these activities. This situation would then potentially expose the operator to higher levels of glutaraldehyde. Refer to HETA 83-074 for further information on exposures during maintenance procedures.

C. Personal Protective Clothing

A variety of personal protective clothing was available to the employees while working with glutaraldehyde. This included lab coats, protective goggles, aprons, respirators (surgical and organic vapor disposable types), and gloves (either latex, rubber or polyvinyl). In conjunction with proper exhaust ventilation, these personal protective garments should be more than sufficient to protect against occasional exposures. During placement/removal of tissue, as well as during the maintenance operations, the employees should wear all the personal protective clothing and equipment available.

D. Medical Concerns

The employees were questioned regarding any health problems which were thought to be attributable to their work with glutaraldehyde. Symptoms, such as, eye, noise, throat irritation and chest tightness were described by the employees during past exposures. These symptoms have, however, been resolved for the most part with improved ventilation, personal protective clothing and work practices.

VII. Summary and Conclusions

We were unable to confirm an overexposure to the research technologists from glutaraldehyde used in any of the tissue fixing operations evaluated. It was determined, however, that the use of glutaraldehyde had created health problems in the past. Therefore, based on these findings and glutaraldehyde's Ceiling-TLV, it is recommended that it not come in contact with the skin or the mucous membranes of the eyes and not be inhaled for even a short period.

VIII. Recommendations

Based on NIOSH's evaluation, as well as personal communications with individuals who have performed activities with glutaraldehyde in the past and currently, the following recommendations are made to reduce and/or eliminate potential health hazards to the employees covered by this investigation.

A. Environmental

1. If possible, substitution of materials which are less hazardous is an excellent way to avoid exposures to the employees and should be investigated.

2. The use of personal protective clothing should be mandatory when using glutaraldehyde. A written program on correct clothing is recommended (refer to HETA 83-074-1525 for specific information). This recommendation should be directed to those employees involved in placement/removal of tissue and maintenance operations. It is further recommended that two gloves be worn on each hand during these procedures to further reduce the potential for skin absorption. The ACGIH recommends that a variety of different materials be used when working with aldehydes. This includes butyl rubber (described as excellent); polyurethane, polyethylene, PVC and styrene butadiene rubber (described as good to fair) and polyvinyl alcohol and Viton (described as only acceptable).

3. An organic vapor/formaldehyde cartridge respirator is recommended for protection against glutaraldehyde. This type of respirator is specifically designed for organic vapors and formaldehyde, however, they are also suitable for other aldehydes, such as, glutaraldehyde.

4. Work practices in all areas where glutaraldehyde is used should be reviewed periodically in order to prevent overexposures. Emphasis on the avoidance of exposures in confined spaces, as described in HETA 83-074 should be a primary concern.

5. The training and education of current employees regarding safe work practices is essential in reducing and/or eliminating chemical exposures. All employees should be instructed on the potential hazards associated with glutaraldehyde, proper use of personal protective clothing, safe work practices, avoidance of confined space exposures and on personal hygiene concerns. This would include signs and symptoms associated with overexposures to glutaraldehyde, as well as the avoidance of eating, drinking or smoking in the work area while using this chemical.

6. A program to instruct new employees on the hazards of glutaraldehyde should be implemented. An annual review of the various hazards and safety procedures associated with glutaraldehyde should also be implemented for all concerned employees as described above.

7. Air monitoring should be performed periodically and records kept of the results. This is especially important if there is any modification in the operation; that is, if location or process changes are made and/or there is an increase in the use of glutaraldehyde.

8. Anon: Regulations for the Enforcement of the Federal Insecticide, Fungicide, and Rodenticide Act, part 162, Federal Register 40: 28279 (July 3) 1975

9. "Human Sensory Irritation Threshold of Glutaraldehyde Vapor - Report to Dr. N.A. Miner," Arbrook, Inc., Arlington, TX (February 19, 1976)

10. Jordan, W.P., et al.: "Contact Dermatitis from Glutaraldehyde," Arch. Derm. 105: 94 (1972)

11. NIOSH: Registry of Toxic Substances V.2, p. 376 (1981-82)

12. Frederick Van Lente, et al., "Identification of Specific Cross-linked Histones After Treatment of Chromatin with Formaldehyde," with discussion on glutaraldehyde, Cell. Vol. 5, 45-50, May 1975

13. Thomas, A.M., et al., "Influence of Formaldehyde and Sonacide (Potentiated Acid Glutaraldehyde) on Embryo and Fetal Development in Mice," Teratology 22: 51-58 (1980)

14. Fisher, A.A., "Reaction to Glutaraldehyde," with particular reference to radiologists and x-ray technicians, CUTIB Vol. 28, 2, pp. 113-114 and 119-122, 1981

15. ACGIH, Threshold Limit Values (TLV) for Chemical Substances in the Work Environment, 1984-85

16. Personal Communication Concerning Respiratory Protection - Nancy Bollinger, Division of Safety Research, NIOSH, Morgantown, WV.

B. Medical

1. Eye contact with glutaraldehyde should, after prompt irrigation with water, be reported to a physician. Skin contact should be avoided and the skin should be promptly washed if contact is made.

2. Preplacement or initial medical questionnaires and examinations for employees who will be expected to work with glutaraldehyde should include questions on skin sensitization, eye, and respiratory irritations.

3. Medical evaluations should be provided when adverse effects to workers from past or current exposures exist. If overexposures are suspected of causing skin sensitization or asthma like symptoms the employee should not be required to work with the solution. It should be understood that engineering controls should be the first consideration if an overexposure does exist in the work area.

IX. REFERENCES

1. Pryor, P.D., "National Jewish Hospital-Glutaraldehyde Evaluation," Health Hazard Evaluation No. 83-074. NIOSH, March, November 1984

2. Pryor, P.D., "National Jewish Hospital-Formaldehyde Evaluation," Health Hazard Evaluation No. 83-045-1347. NIOSH, August 1983

3. Stonehill, A.A., et al., "Buffered Glutaraldehyde - A New Chemical Sterilizing Solution," A.J.H.P. 20: 458-465 (September) 1963

4. Miner, N.A., et al., "Automicrobial and Other Properties of a New Stabilized Alkaline Glutaraldehyde Disinfectant/Sterilizer," A.J.H.P. 34: 376-382 (April) 1977

5. Borick, P.M.: Chemical Sterilizers (Chemosterilizers), In Advances in Applied Microbiology, Academic Press, New York, NY, 1968, pp. 291-312

6. Glutaraldehyde - Documentation of the Threshold Limit Values - Fourth Edition, ACGIH, 1983, pp. 204-205

7. Anon: Regulations for the enforcement of the Federal Insecticide, Fungicide, and Rodenticide Act, section 362.116, 7 CFR part 362, Federal Register 34: 6106-6112 (April 4) 1969

X. AUTHORSHIP AND ACKNOWLEDGMENTS

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NIOSH wishes to thank the employees at National Jewish Hospital for their cooperation and assistance with this Health Hazard Evaluation. The information gathered from this study will not only assist in maintaining the health and safety of those persons working here, but also other facilities that perform similar operations.

XI. DISTRIBUTION AND AVAILABILITY

Copies of this report are currently available upon request from NIOSH, Division of Standards Development and Technology Transfer, Information Resources and Dissemination Section, 4676 Columbia Parkway, Cincinnati, Ohio 45226. After 90 days the report will be available through the National Technical Information Service (NTIS), Springfield, Virginia. Information regarding its availability through NTIS can be obtained from NIOSH, Publication Office, at the Cincinnati address.

Copies of this report have been sent to:

1. National Jewish Hospital
2. U.S. Department of Labor/OSHA Region VIII
3. NIOSH - Region VIII
4. Colorado Department of Health
5. State Designated Agency

For the purpose of informing affected employees, a copy of this report shall be posted in a prominent place accessible to the employees for a period of 30 calendar days.

TABLE 1

BREATHING ZONE AND AREA AIR CONCENTRATIONS
FOR GLUTARALDEHYDE

National Jewish Hospital
Denver, Colorado
March 1985

JOB/AREA DESCRIPTION	SAMPLING TIME (MINUTES)	mg/m^3 GLUTARALDEHYDE
Tissue Fixing and "Maintenance"*		
Operator	90	ND
Operator	90	ND
Lab Hood - Front Left	90	ND
Lab Hood - Front Right	90	0.04
Lab Hood - Back Left	90	0.21
Lab Hood - Right side	90	ND

EVALUATION CRITERIA: (ACGIH) 0.7 mg/m^3

LABORATORY LIMIT OF DETECTION: 3.0 ug/sample

ND = Non Detectable (no glutaraldehyde was detected on these samples).

mg/m^3 = milligrams of substance per cubic meter of air.

ug/sample = micrograms per sample.

* = sampled with lab hood opened during tissue fixing procedures.