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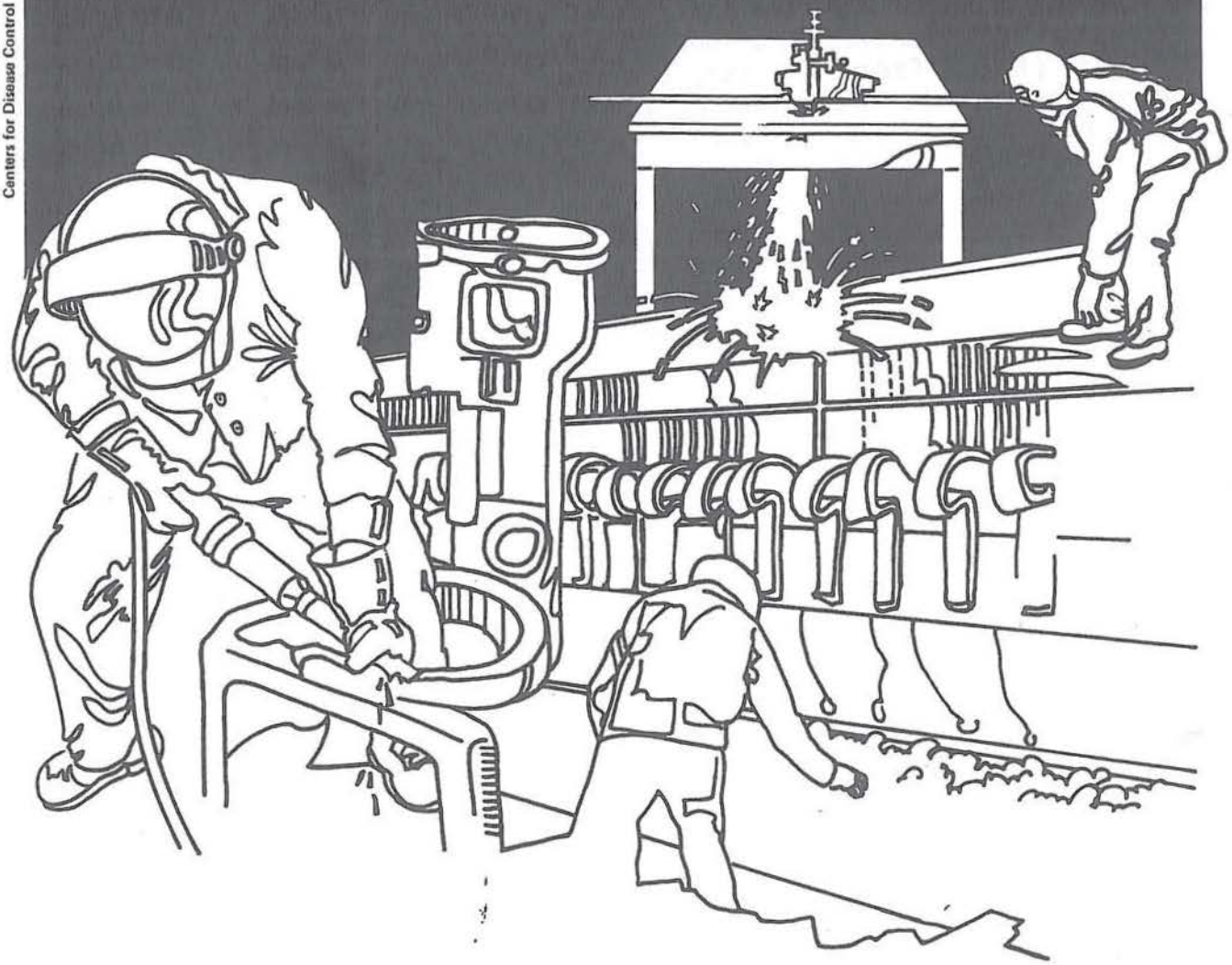
NIOSH



Health Hazard Evaluation Report

HETA 81-226-1048
UNIVERSITY OF GEORGIA
COLLEGE OF VETERINARY MEDICINE
HISTOPATHOLOGY LABORATORY
ATHENS, GEORGIA

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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UNIVERSITY OF GEORGIA
COLLEGE OF VETERINARY MEDICINE
HISTOPATHOLOGY LABORATORY
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I. SUMMARY

On March 16, 1981, the National Institute for Occupational Safety and Health (NIOSH) received a request for a NIOSH health hazard evaluation from the Department Head, Department of Veterinary Pathology, College of Veterinary Medicine, University of Georgia, Athens, Georgia. The request was submitted because laboratory technicians had complained of headaches, nausea, and sinus problems which were suspected to be due to exposures to xylene and formaldehyde vapors. An industrial hygiene survey was conducted by NIOSH on April 27, 1981. Environmental samples were collected and analyzed quantitatively by NIOSH to determine both personal exposures and general area concentrations. Lab technicians were interviewed regarding symptoms possibly related to workplace exposures.

Three of four lab technicians interviewed complained of eye, nose, and throat irritation with occasional headache and fatigue. Results of air sampling indicate exposures to xylene vapors are not significant under normal procedures used by the lab technicians at the time of the NIOSH evaluation. The "coverslipping" of microscopic slides, which requires the use of xylene as a clearing agent, was being performed under an exhaust ventilated hood. Xylene was not measureable in 5 of 6 samples collected. A concentration of 66 parts per million was detected (ppm) during coverslipping but this value is questionable because of possible contamination of the sample after sample collection.

Lab technicians are exposed to high concentrations of formaldehyde vapors when changing formalin solution in tissue processors. This task, performed once a week and requiring approximately 30 minutes, resulted in a personal exposure of 12.8 ppm. Although an exhaust fan is located behind the processors, it is not able to capture vapors released when transferring formalin solution from one container to another prior to pouring formalin into processors.

Based on the air sampling results, it is apparent that lab technicians are exposed to high concentrations of formaldehyde vapors when changing formalin solution in tissue processors. Some exposure to formaldehyde is also possible when "cutting in" formalin saturated tissue samples unless the task is performed under a properly designed laboratory hood. Considering that NIOSH has now classified formaldehyde as a suspect carcinogen, exposures should be reduced to the lowest level feasible. All tissue processors should be located in well ventilated areas, and changing of formalin solutions should be performed using transfer methods which will minimize exposure.

KEYWORDS: SIC 8071 (pathological laboratories), formaldehyde, tissue processing, xylene, coverslipping, headache, irritation

II. INTRODUCTION

On March 16, 1981, the National Institute for Occupational Safety and Health (NIOSH) received a request for a NIOSH health hazard evaluation from the Department Head, Department of Veterinary Pathology, College of Veterinary Medicine, University of Georgia, Athens, Georgia. The requester had asked NIOSH to evaluate workplace exposures to xylene and formaldehyde vapors during processing and mounting ("coverslipping") of tissue specimens in the Histopathology Laboratory. Some laboratory technicians had complained of headaches, inability to concentrate, nausea, and sinus problems. In response to this request, an industrial hygiene survey was conducted on April 27, 1981. The purpose of the survey was to conduct atmospheric sampling for formaldehyde and xylene and to evaluate the effectiveness of laboratory ventilation hoods. Laboratory technicians were interviewed and laboratory procedures observed. An interim report, with preliminary findings and recommendations, was provided by NIOSH on July 17, 1981.

III. BACKGROUND

The Histopathology Laboratory employs four technicians, the Chief Technician and three assistants. The lab is divided into two rooms. One room is used for processing tissue samples and the other area is used for mounting, staining, and coverslipping microscopic slides.

In the tissue processing area, tissues (stored in 10% buffered formalin solution) are sliced in sections and placed into small (1" x 1-1/4" x 1/4") plastic cassettes. The cassettes are then loaded in a basket and placed in a tissue processor machine. Four machines are available but only two are used on a regular basis. The processor machine automatically processes tissues from the 10% formalin solution through a graded series of alcohol solutions, from 70% - 100%, and then into xylene which serves as a clearing agent to remove all water and alcohol from the tissues. After clearing, the tissues are immersed in hot paraffin. Tissues are run through the processor overnight and removed the next morning. The changing of the tissue processor solvents was the task which was believed to present the most significant exposure. The technician performing this job was provided a NIOSH approved organic vapor respirator, rubber gloves, and apron. The solvents in the tissue processors are partially changed every day but a full change of all solutions is performed only once a week and requires about 30 minutes to complete.

In the coverslipping area, the wax impregnated tissues from the processor machines are wax incapsulated using the "tissue imbedding center" machine. The incapsulated tissues are then sliced to 4 micron thickness on a microtome, placed on glass slides, stained, and heated in an oven. Slides are then submerged in xylene prior to coverslipping. Coverslipping involves removing the tissue mounted glass slides from a xylene tray, wiping off excess xylene, adding one or two drops of mounting solution, and placing a glass coverslip over mounted tissue.

IV. EVALUATION METHODS

A. Formaldehyde Sampling

Formaldehyde air samples were collected to determine both personal breathing zone and general area concentrations. Formaldehyde exposures were evaluated during two frequently performed procedures: (1) the "cutting in" procedure, where the Pathologist (frequently assisted by a technician) removes tissues stored in formalin and cuts them into small sections and (2) the changing of solvent solutions in the tissue processor machines, a job performed by one of the technicians. Cutting in was performed under a laboratory hood. A small exhaust hood located in the tissue process area (Room 115) had been previously used but the exhaust air velocity was not considered adequate. A larger laboratory hood, located in room 177, was being used at the time of the survey. In order to evaluate the effectiveness of both hoods for controling formaldehyde exposure, the cutting in procedure was sampled in both locations.

B. Xylene Sampling

Personal and general air samples for xylene were collected during coverslipping and near the tissue imbedding center where "process covers" were being cleaned in a xylene bath. Xylene was also sampled during the changing of solvents in the tissue processors.

C. Sampling Methods

Formaldehyde was sampled using NIOSH method No. P & CAM 318. A calibrated, battery powered air sampling pump, set for a flow rate of approximately 0.2 liters of air per minute (LPM), was used to draw a known volume of air through a glass tube containing activated charcoal that had been treated with an oxidizer chemical. The oxidizer reacts with formaldehyde changing it to formate which is adsorbed by the charcoal. The tubes were sent to the NIOSH contract laboratory where the amounts of formate collected in the charcoal tubes were determined by ion chromatography analysis. Personal samples were collected by attaching the charcoal tube holder to the individual's shirt collar. Xylene samples were collected in the same manner using standard organic vapor adsorbing charcoal tubes. The tubes were sent to the NIOSH laboratory and analyzed for xylene by gas chromatography in accordance with NIOSH method No. S318 (modified)

D. Ventilation

The effectiveness of laboratory exhaust hoods was determined by measuring the face velocities with a Kurz Model 441 air velocity meter. The average of 10-12 flow rate measurements, taken along the face of the hood openings (fully opened sash), was compared to NIOSH recommended guidelines.

E. Employee Interviews

Lab technicians were given confidential interviews and asked to describe the symptoms they had experienced. The interviews included questions regarding work history, smoking history, current health condition, and recent illnesses. Technicians were also asked if they believed certain laboratory activities had caused their reported symptoms or if they associated any of their reported symptoms with the work environment.

V. EVALUATION CRITERIA

A. Environmental Criteria

The environmental criteria described below are intended to represent airborne concentrations of substances to which workers may be exposed for eight hours a day, 40 hours per week for a working lifetime without adverse health effects. Because of wide variation in individual susceptibility, a small percentage of workers may experience discomfort from some substances at concentrations at or below the recommended criteria.[1] A smaller percentage may be more seriously affected by aggravation of a pre-existing condition or by a hypersensitivity reaction. The time-weighted average (TWA) exposure refers to the average concentration during a normal 8-hour workday. The Short-Term Exposure Limit is the maximum allowable concentration, or ceiling, to which workers can be exposed during a period of up to 15 minutes, provided that no more than four excursions per day are permitted, with at least 60 minutes between exposure periods.

The primary sources of environmental evaluation criteria considered for this study were: 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) federal occupational health standards. The criteria judged most appropriate for this study are as follows:

Substance	Short Term Exposure Limits	8-Hour Time Weighted Average	Source
Formaldehyde	5 ppm (30 min.)	3 ppm	OSHA
"	LFL	LFL	NIOSH
"			ACGIH
(current)	2 ppm (max. ceiling)		"
(proposed)	A_2	A_2	"
Xylene	--	100 ppm	OSHA
"	150 (15 min.)	100 ppm	ACGIH
"	200 (10 min.)	100 ppm	NIOSH

NOTE: ppm = parts per million parts of air, by volume
LFL = lowest feasible level (suspected carcinogen)

A_2 - Industrial substances suspect of carcinogenic potential for man (exposures by all routes should be carefully controlled - no TLV recommended at this time).[1]

B. Toxicity and Adverse Health Effects from Exposure

The adverse health effects from excess exposure (exposures to airborne concentrations above the evaluation criteria) are summarized below:

1. Formaldehyde

Irritation of the eyes, nose, mouth, and throat are the most common worker health effects from inhalation of formaldehyde gas. Formaldehyde has a very pungent, offensive odor that is noticeable even in very small concentrations, producing burning and tearing of the eyes. Higher concentrations usually bring difficulty in breathing, intense burning of the eyes, nose and throat, profuse tearing, and severe coughing. Prolonged exposure to high concentrations may cause headache, heart palpitations, and serious inflammation of the bronchial tubes and lungs. In extreme cases, death may result due to swelling or spasm of the vocal cords. Asthmatic symptoms, such as wheezing, may occur, even at very low concentrations, in persons with an allergic sensitivity to formaldehyde.

Workers repeatedly exposed to low concentrations of formaldehyde during normal work periods seem to develop a physical tolerance to formaldehyde and can work in concentrations that are intolerable to many outsiders. Chronic symptoms that are associated with repeated exposure are itching eyes, dry and sore throat, disturbed sleep, and unusual thirst upon awakening.

Dermatitis may result from formaldehyde contact with the skin. Formaldehyde acts on the skin cells both as an irritant and as a tanning agent. The dermatitis usually appears first as a reddening of the skin and then small blisters may form similar to those caused by poison ivy. Formaldehyde may also make the fingernails soft and brownish. Skin irritation seldom results from exposure to formaldehyde gas in the air, but individuals who have developed an allergic sensitivity show dermatitis symptoms from exposure to concentrations easily tolerated by nonallergic persons.[2]

Recently, formaldehyde vapor has been found to cause a rare form of nasal cancer in rats by two different research institutions. These results have prompted NIOSH to recommend that formaldehyde be handled as a potential occupational carcinogen.[3]

The U.S. Department of Labor, Occupational Safety and Health Administration (OSHA) standard for formaldehyde requires an 8-hour time-weighted average (TWA) concentration limit of 3 ppm, with a ceiling concentration of 5 ppm permitted for no more than 30 minutes during an 8-hour shift. At no time shall the concentration be allowed to exceed 10 ppm. OSHA adopted this standard from an old American National Standards Institute (ANSI) standard Z 37.16 - 1967.[4]

In 1976, NIOSH issued a publication "Criteria for a Recommended Standard for Occupational Exposure to Formaldehyde", NIOSH Publication No. DHEW (NIOSH) 77-126. In this document, NIOSH recommended, based upon the irritant effects of formaldehyde, that employee exposure to formaldehyde in the occupational environment be controlled to a concentration no greater than 1 ppm for any 30-minute sampling period. The carcinogenic potential of formaldehyde was not known at that time, and therefore was not considered in developing the recommendations. Evidence for the carcinogenicity of formaldehyde was first reported in October 8, 1979. Preliminary data from an ongoing inhalation study of rats and mice, sponsored by the Chemical Industry Institute of Toxicology (CIIT), indicated that for exposures of 15 ppm for 6 hours/day, 5 days/week for 16 months formaldehyde is carcinogenic in rats.[3]

In April 1981, NIOSH issued Current Intelligence Bulletin 34, "Formaldehyde: - Evidence of Carcinogenicity", DHHS (NIOSH) Publication No. 81-111. According to this bulletin, "Formaldehyde has induced a rare form of nasal cancer in both Fischer 344 rats and B6C3F1 mice as reported in an ongoing study by the CIIT. In a second study by NYU, formaldehyde appears to have induced the same type of cancer in Sprague-Dawley rats. Although humans and animals may differ in their susceptibility to specific chemical compounds, any substance that produces cancer in experimental animals should be considered a cancer risk to humans..... Based on these results, NIOSH recommends that formaldehyde be handled in the workplace as a potential occupational carcinogen. Safe levels of exposure to carcinogens have not been demonstrated, but the probability of developing cancer should be reduced by decreasing exposure."[3]

2. Xylene

Xylene vapor may cause irritation of the eyes, nose, and throat. Repeated or prolonged skin contact with xylene may cause drying and defatting of the skin which may lead to dermatitis. Liquid xylene is irritating to the eyes and mucous membranes, and aspiration of few milliliters may cause chemical pneumonitis, pulmonary edema, and hemorrhage. Repeated exposure to the eyes to high concentrations of xylene vapor may cause reversible eye damage. Acute exposure to xylene vapor may cause central nervous system depression and minor reversible effects upon liver and kidneys. At high concentrations xylene vapor may cause dizziness, staggering, drowsiness, and unconsciousness.[5] Workers exposed to concentrations above 200 ppm complain of loss of appetite, nausea, vomiting, and abdominal pain. Brief exposure of humans to 200 ppm has caused irritation of the eyes, nose, and throat.[6]

The current OSHA standard for xylene is 100 ppm averaged over an 8-hour work shift. NIOSH has recommended that the permissible exposure limit be changed to 100 ppm, averaged over a work shift of up to 10 hours per day, 40 hours per week, with an acceptable

ceiling level of 200 ppm averaged over a 10-minute exposure.[6] The ACGIH TLV first adopted in 1967, is retained with a short term exposure limit (STEL) of 150 ppm for a 15 minute exposure and a 100 ppm time weighted average for an 8-hour exposure.[7]

C. Ventilation

According to NIOSH's Recommended Industrial Ventilation Guidelines Manual[8], the hood applications and minimum exhaust velocity requirements for laboratory hoods based on contaminant class are as follows:

Contaminant Class	Face Velocity	
	Minimum	Average
I - Substances with exposure limits of 100 ppm and above. (e.g.xylene)	50 fpm	100 fpm
II - Substances with exposure limits of 1 ppm and above (up to 100 ppm)	75 fpm	100 fpm
III - Substances with exposure limits below 1 ppm; also radio-isotopes, carcinogens, and cancer suspect agents. (e.g. formaldehyde)	125 fpm	150 fpm

Note: fpm = feet per minute

VI. RESULTS

A. Employee Interview Results

Three of the four lab technicians interviewed complained of job related health effects which they associated with coverslipping, "cutting in", and changing of solution in tissue processors. Most frequent symptoms experienced were eye, nose, and throat irritation and occasional headache and fatigue. One technician who believed she was the most severely affected admitted to having allergy problems for the past 5 years and stated she could no longer tolerate exposures when changing solutions in processors. She believed she had become "hypersensitive to solvents" since working in the lab.

B. Environmental Sample Results

Results from analysis of personal and area samples indicate exposures to xylene were below the evaluation criteria of 100 ppm. Corrected for blank sample contamination, the non-measureable results from 5 out of 6 air samples collected, indicate that xylene concentrations were less than 28 ppm under most conditions of use. One sample, collected during

coverslipping, detected a concentration of 66 ppm. However, this value is suspect because the blank charcoal tubes used to sample xylene may have been contaminated. One of the caps on a charcoal tube sample had come off during shipment of the samples to the NIOSH laboratory. Another sample taken from a different technician performing coverslipping at the same work station did not detect xylene above blank sample values. At the time of this survey, coverslipping was performed under the laboratory hood. The hood face velocity was 170 feet per minute (fpm) which exceeds NIOSH recommendations (100 fpm).

Results from the formaldehyde samples indicate that lab technicians are exposed to high concentrations (12.8 ppm) of formaldehyde vapors when changing formalin solution in tissue processors. Although an exhaust fan is located behind the processors, it is not able to capture vapors released when transferring formalin from one container to another prior to pouring formalin into processors. Although the small vent hood in Room 115 does provide some control of exposure to formaldehyde during cutting in, the measured flow rate for this hood (85 fpm) is below the NIOSH guidelines and does not reduce exposure to the lowest feasible level. The vent hood in Room 177 which has a face velocity of 190 fpm, was effective in controlling exposure, as no formaldehyde was detected in this area.

The results of all air samples collected during the survey are presented in the Table 1.

VII. DISCUSSION AND CONCLUSIONS

Based on results from atmospheric samples, it is apparent that lab technicians are exposed to high concentrations of formaldehyde vapors when changing formalin solution in tissue processors. Some exposure to formaldehyde is also possible when cutting in formalin saturated tissue samples unless the task is performed under a properly designed laboratory hood.

Airborne exposure levels to xylene vapors during coverslipping were within recommended limits. Therefore, it is believed that no long-term or serious short-term health effects will result. As long as coverslipping is performed under the laboratory hood, significant airborne exposure should not occur.

VIII. RECOMMENDATIONS

1. Appropriate solvent dispenser pumps, tubing, etc. should be used to permit changing of solvents in tissue processors without pouring of solvents from one container to another.

2. Tissue processors containing formalin should provide for proper vapor control. Processors currently in use have non-sealing lids on solution containers.

3. Although the vent hood in Room 115 does provide some capture of formaldehyde, the hood in Room 177 is far superior and should be used for cutting in tissues whenever possible.

4. Although a NIOSH approved organic vapor chemical cartridge respirator was available, for formaldehyde exposure, NIOSH recommends a full face piece mask to prevent eye irritation. The half-mask face piece worn by the technician interfered with the wearing of safety glasses. A full face piece type respirator should be used.

5. Tissue storage bags containing formalin should be stored in a well ventilated area and bags should be periodically inspected for leakage.

IX. AUTHORSHIP AND ACKNOWLEDGEMENTS

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X. DISTRIBUTION AND AVAILABILITY

Copies of this report are currently available upon request from NIOSH, Division of Standards Development and Technology Transfer, Publications Dissemination Section, 4676 Columbia Parkway, Cincinnati, Ohio 45226. After ninety (90) days the report will be available through the National Technical Information Service (NTIS), Springfield, Virginia 22161. Information regarding its availability through NTIS can be obtained from the NIOSH Publications Office at the Cincinnati, Ohio address.

Copies of this report have been sent to:

1. Univ. of Ga., College of Vet. Med., Dept. of Pathology
2. U.S. Dept. of Labor, OSHA, Region IV
3 NIOSH, Region IV
4. Georgia Department of Human Resources
5. OSH Consultaion Program-EES, Georgia Inst. of Tech,

For the purpose of informing the approximately 4 "affected employees", the employer will promptly "post" this report for a period of thirty (30) calendar days in a prominent place(s) near where the affected employees work.

XI. REFERENCES

1. "Threshold Limit Values for Chemical Substances and Physical Agents in the Workroom Environment with Intended Changes for 1981", American Conference of Governmental Industrial Hygienists (ACGIH), Cincinnati, Ohio.

2. Working With Formaldehyde, DHEW Publication No. (NIOSH 74-119), 1975.

3. Formaldehyde, Evidence of Carcinogenicity, NIOSH Current Intelligence Bulletin (CIB) No. 34, DHHS (NIOSH) Publication No. 81-111, April 1981.

4. Occupational Safety and Health (OSHA) General Industry Standards, Title 29 CFR Part 1910.1000, Subpart Z.

5. Occupational Diseases, A Guide to Their Recognition, Revised Edition, DHEW (NIOSH) Publication No. 77-181, June 1977.

6. NIOSH/OSHA Occupational Health Guidelines for Chemical Hazards, DHHS (NIOSH) Publication No. 81-123: U.S. Gov. Printing Office, Washington, D.C.; January 1981.

7. Documentation of the Threshold Limit Values, Supplements for Those Substances Added or Changed Since 1971, American Conference of Industrial Hygienists (ACGIH) 3rd. Edition, Cincinnati, Ohio: ACGIH; 1971.

8. Recommended Industrial Ventilation Guidelines, DHEW Publication No. (NIOSH) 76-162, January, 1976.

TABLE 1

UNIVERSITY OF GEORGIA
COLLEGE OF VETERINARY MEDICINE
HISTOPATHOLOGY LABORATORY
ATHENS, GEORGIA

April 27, 1981

FORMALDEHYDE SAMPLING RESULTS

Job Description/Location	Type Sample	Duration (min.)	Formaldehyde Conct. (ppm)
Pathologist "cutting in" Rm 177	Personal	29	None-Detected
Pathologist "cutting in" Rm 115	Personal	34	None-Detected
Exhaust hood opening-Room 115	Area	35	0.8
Top of curtain near tissue proc.	Area	22	1.0
Changing solvents in tissue proc.	Personal	24	12.8

Evaluation Criteria:	(in ppm)
NIOSH Recommended Exposure Limit	Lowest feasible limit
Current OSHA Standard	3.0 8-hr. TWA
Current OSHA Standard	5.0 30 min ceiling
CURRENT OSHA Standard	10.0 max. peak

XYLENE SAMPLING RESULTS

Job Description/Location	Type Sample	Duration (min.)	Xylene Conct. (ppm)
Changing solvents in tissue proc.	Personal	23	not measurable
Top of curtain near tissue proc.	Area	23	"
Coverslipping	Personal	40	"
"	Personal	42	66*
Tissue imbedding center	Area	31	not measurable

Minimum level of quantitation, corrected for contamination = 28 ppm

*Charcoal tube likely contaminated during shipment to NIOSH lab.

Evaluation Criteria:		
NIOSH Recommended Exposure Limit	(10 hour average)	100 ppm
	(10 minute ceiling)	200 ppm
ACGIH TLV (8-hour TWA)		100 ppm
(15 minute STEL)		150 ppm