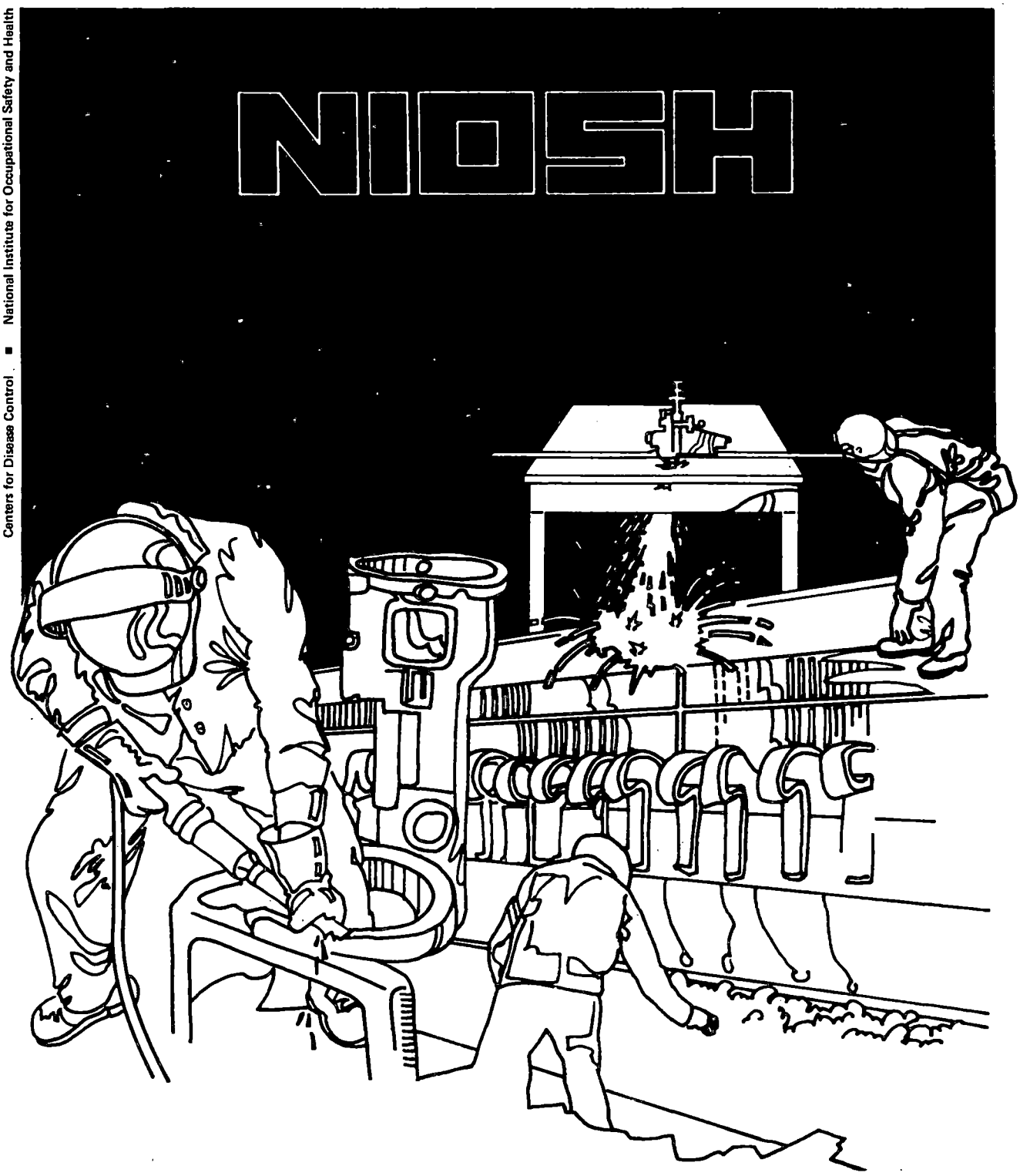
U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES ■ Public Health Service
Centers for Disease Control ■ National Institute for Occupational Safety and Health

NIOSH



Health Hazard Evaluation Report

HETA 80-228-1241
EDWIN COOPER COMPANY
SAUGET, ILLINOIS

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.

HETA 80-228-1241
DECEMBER 1982
EDWIN COOPER COMPANY
SAUGET, ILLINOIS

NIOSH INVESTIGATORS:
Bruce A. Hollett, I.H.
Tar-Ching Aw, M.D.

I. SUMMARY

On August 19, 1980, the National Institute for Occupational Safety and Health (NIOSH) received a request from employee representatives to perform a health hazard evaluation of the oil additive production processes at the Edwin Cooper Company, Sauget, Illinois. The employees' concern was based on findings of a recent animal study which indicated apparent adverse spermatogenic effects from skin absorption tests of a zinc dialkyl dithiophosphate oil additive.

On December 3, 1980, NIOSH investigators conducted an initial survey to obtain process information, toxicology research information, and to conduct employee interviews. A follow-up environmental and medical survey was conducted in October 1981. The environmental component consisted of air sampling for organic vapors and metal particulates. The medical component included administration of a medical questionnaire, limited physical examinations, and analysis of blood, urine, and semen samples for 12 male workers exposed to zinc compounds ("exposed") and 11 workers not exposed ("controls"). Results of the environmental sampling showed levels of isobutanol, isopropanol, and zinc oxide below recommended exposure criteria. The highest time-weighted average (TWA) levels were 2.38 mg/m^3 for isobutanol (recommended criteria 150 mg/m^3), 1.90 mg/m^3 for isopropanol (recommended criteria 980 mg/m^3), and 0.3 mg/m^3 for zinc oxide (recommended criteria 5.0 mg/m^3). The highest TWA levels for 2-ethylhexanol and zinc were 0.95 mg/m^3 and 0.17 mg/m^3, respectively. There is no recommended criteria for either of these chemicals.

Review of medical history showed no significant difference between the "exposed" and "controls" with regards to birth defects in offspring, or infertility, miscarriages and stillbirths experienced by wives or partners. Limited physical examination showed no gross abnormalities in secondary sexual characteristics for exposed and controls. Serum zinc levels were higher for exposed workers than controls though the difference was not statistically significant; all levels were within the laboratory reference range (75-100 ug %). Renal and liver function tests showed no statistically significant differences between exposed and controls. However, there were several readings in both groups above the "normal" values for serum creatinine and some transaminases. The reason for this is not apparent. Semen analysis showed no azoospermia or oligospermia in the exposed group. Other parameters of the semen analysis showed no significant difference between exposed and controls.

On the basis of the environmental data obtained during this investigation, NIOSH has determined that exposures to isobutanol, isopropanol, and zinc oxide above recommended criteria levels did not exist. The medical findings did not indicate any abnormal effects on spermatogenesis or fertility. However, in view of the results from current animal and mutagenicity studies of the oil additive suggesting a potential health hazard, care should be exercised in the handling of these compounds.

KEYWORDS: SIC 2899 (Oil Additive Production), zinc dialkyl dithiophosphate, 2-ethylhexyl alcohol, oil additives, reproductive effects, spermatogenesis.

II. INTRODUCTION

On August 19, 1980, the National Institute for Occupational Safety and Health (NIOSH) received a request from Edwin Cooper employees' representatives to perform a health hazard evaluation of the oil additive production processes in Building NB of the Sauget, Illinois, facilities. Their concern was based on findings of a recent animal study sponsored by Ethyl Corporation Toxicology and Industrial Hygiene Department. This study indicated apparent adverse spermatogenic effects from skin absorption tests of product Hitec E-653, a zinc dialkyl dithiophosphate oil additive. Furthermore, Ethyl's review of a previous test of a similar product produced in this facility, E-682, determined that similar effects were present.

The initial survey conducted on December 3, 1980, was reported in the Interim Report No. 1, February 1981. The follow-up survey was conducted on October 25-27, 1981.

III. BACKGROUND

This plant has been operating since the early 1940's. Oil additive production began in 1960 in Department 266. Department 267 was added in 1973 and together with Department 266 constitutes the work force in Building NB. Process additions and modifications have been made in the past 2 years. Department 266 produces four zinc dialkyl dithiophosphate (ZDDP) products and Department 267 produces eight products of various types. The ZDDP products are E-653, E-682, E-685 and E-656. These contain several chemicals including zinc oxide, phosphorus pentasulfide, diatomaceous earth and various alcohols. The production work force, facilities, and activities are described briefly in the paragraphs below.

This plant employs a total of 75 production and 25 maintenance workers. There are six operators in Department 266 and 10 operators in Department 267. The Department 267 Operators are designated A, B, or F Operators. The 16 operators work in three shifts around the clock. Department 266 Reactor operators rotate through the filter operator's position for 1 week in every 5. Production varies according to product demand. Workers noted that, in the 6 months prior to the initial survey, the overtime had been greatly reduced. It had been common to work two or three double shifts per week and to work for 10 days straight if the worker desired. The manhours spent in various areas and on the production of any specific product are variable. Depending on the product and on the difficulties encountered, workers may spend as much as 50% of the shift in the control room.

The facility and work areas are semi-enclosed. Building NB is a shelter with a roof and two sides. Most of the work is conducted on two levels; on the ground below the reactor vessels and on work

platforms near the top of the reactor vessels. The control room and lunch area are fully enclosed.

The Department 266 process has four steps; reaction, degassing, neutralization, and filtration. The various products use different blends of alcohols. The reactor is charged with the appropriate alcohol and phosphorous pentasulfide. The reaction occurs in the presence of a catalyst. The intermediate product is transferred to a degassing vessel, where nitrogen is bubbled through it to remove byproduct gases. This product is next transferred to a neutralizing vessel, which is charged with zinc oxide. After neutralizing, it is sent to a filter feed tank where No. 5 oil and diatomaceous earth are added. The product is then filtered and collected in a holding tank. The progress of each step is monitored from the control room. Activities of the reactor operators on the upper level include taking product samples, gauging the depth of vessels, charging vessels, and operating valves. The filter operator must precoat the filter and, after processing the product, remove the cake from the filter. Operators make brief visits to the ground level to handle bulk containers or adjust catalyst or phosphorous pentasulfide flow rates.

Materials are handled by several means: vessels are charged with bags of zinc oxide (ZnO) and diatomaceous earth by hand through open manways; styrene used in Department 267 reactors is pumped from drums; alcohols and No. 5 oils are charged by closed plumbing; phosphorous pentasulfide is charged by closed conveyor; and products are drummed or piped to tank cars or storage tanks. Wastes are drummed, piped to an incinerator, hauled away in dumpsters, or discharged to open floor gutter drains.

IV. EVALUATION DESIGN AND METHODS

The initial NIOSH survey on December 3, 1980, was directed at obtaining process information, employee medical interviews, and information on the current status of Ethyl's ongoing toxicology research activities. In addition, a few bulk air area and material bulk samples were collected.

Medical interviews during the initial survey were conducted with 14 of the 16 current employees. They expressed a general concern about the possible reproductive effects from their exposures and a willingness to cooperate with NIOSH in medical examinations and tests including a sperm study.

The Ethyl Corporate Toxicology and Industrial Hygiene Department has been working with an industry group to initiate a study of the possible health effects of these zinc dialkyl dithiophosphate products. The group is funding a study of a "representative" product. Skin tests of rabbits and rats are planned. Further studies would depend on the

outcome of these planned tests. A package of information regarding the past toxicology studies was provided for NIOSH information.

Detailed process and employee exposure information was requested following the initial survey. The Ethyl Industrial Hygiene group responded with records of personal breathing zone measurement for zinc oxide exposures and environmental intermediate process phosphorous measurements. Waste stream information requested was not available.

It was decided to conduct a follow-up survey to attempt to determine, by medical and biological evaluation, if any indications of human reproductive hazard or other health effects were present. Also some background environmental measurements were considered appropriate should further studies prove to be necessary.

A. Environmental

The variations in production based on demand made it uncertain which ones of the four zinc dithiophosphate processes would be observed. Due to the large number of products used in the two co-located departments, it was decided to monitor only for the components of the Department 266 products in question at this time. An effort was made to avoid scheduling the survey during or immediately following a periodic week-long shutdown for reactor cleaning. This activity occurs on an irregular basis from a few weeks to several months apart. It was felt such data would be less representative of daily exposure activities.

Personal breathing zone (PBZ) samples for alcohols and metal particulates were collected on all Department 266 workers and two or three of the Department 267 workers on three consecutive shifts the afternoon and midnight shifts of October 26 and the day shift on October 27. This sampling period followed production of Product E-285 through its complete cycle.

Zinc, zinc oxide, and phosphorus (as an indication of phosphorus pentasulfide) samples were collected on DM-5000 PVC filters at 1.5 lpm using DuPont P-4000 sampling pumps. All but two of these samples were full shift. Two respirable samples were taken at 1.7 lpm using 10 mm cyclones for peak exposure observations during two 20-minute zinc oxide bag dumping activities on the midnight shift.

All three of the alcohols in use were compatable with standard charcoal tube sampling; isopropyl alcohol, isobutyl alcohol, and 2-ethylhexyl alcohol. Tubes were changed at midshift. These samples were collected at 100 cc/minute with Sipin pumps.

B. Environmental Analytical Methods

Sixteen filter samples and two bulk samples of zinc oxide and diatomaceous earth were submitted for zinc oxide and silica analysis by X-ray powder diffraction (XRD) and zinc plus phosphorous analysis by ICP-AES. In addition, particle size analysis was requested for the diatomaceous earth bulk sample.

Qualitative XRD analysis was performed on the two bulk samples. They were backpacked on XRD holders. Two filters were also analyzed qualitatively and quantitatively by XRD analysis. The two bulk samples were analyzed from 8° to 80° (two theta), and the filters analyzed from 20° to 64° using a computer controlled diffractometer with copper radiation at 40 KV and 35 mA. The resulting diffraction patterns were compared manually to the diffraction patterns of the silica polymorphs - quartz, cristobalite, and tridymite, and to the diffraction pattern of zinc oxide contained in the JCPDS files.

For quantitative XRD analysis, all filters were ashed in a Low Temperature-Radiofrequency Plasma-Asher (LTA). The ash was suspended in isopropanol, agitated in an ultrasonic bath, and deposited by filtration on silver membrane filters. Eighteen zinc oxide standards were prepared on silver membrane filters. The standards and the field samples were analyzed quantitatively by P&CAM No. 222.[1]

Quantitative results indicated that the ZnO recovery after low-temperature ashing was quantitative in all three concentration levels. According to P&CAM 222, the lower limit of quantitation for ZnO is 25 ug/filter and the detection limit has not been established.

The diatomaceous earth sample was wet-sized with isopropanol using a 10 micrometer pore size sieve in an ultrasonic bath and dried. The less than 10 micrometer material was used for quantitative work. Triplicate 2 mg samples were weighed, dispersed ultrasonically in isopropanol, and deposited on silver filters and analyzed for silica according to P&CAM No. 259.[1] The particle size of the calibration standards were also less than 10 micrometers.

Particle-size analysis was performed on a portion of the diatomaceous earth bulk. It was suspended in saline solution. Also a portion of the less than 10 micrometer sieved material was suspended in saline solution. The two suspensions were analyzed with the electrozone computer-controlled particle size analyzer.

ICP-AES analysis was performed after XRD analysis. The filters were removed from the holders and digested with concentrated nitric

acid. The residues were dissolved with dilute nitric acid and the resulting solutions were analyzed for zinc and phosphorous.

The charcoal tube samples were analyzed for solvents according to NIOSH Method No. P&CAM 127[2] (modified) using a gas chromatograph with a flame ionization detector. They were separated into A and B portions and desorbed in carbon disulfide containing a hexane internal standard and sec-butanol as a desorbing acid. The limit of detection was 0.01 mg per sample tube for each analyte.

C. Medical

Twenty-eight male workers were included in the medical study. This included 4 workers from Dept. 266, 8 from Dept. 267, and 16 from other departments including depts. 280, 283, and maintenance. The 12 workers from department 266 and 267 were categorized as "exposed" workers since work in these departments involves some exposure to zinc compounds. Eleven of the remaining 16 workers were categorized as "controls". They consisted of workers in jobs not involving exposure to zinc compounds. Five workers were excluded because they were in jobs with very variable and difficult to quantify exposure to zinc compounds. This included maintenance workers, workers in department 283, and one worker with a previous history of 5 years exposure to zinc compounds. Hence, there were 12 "exposed" and 11 "controls" studied. All "exposed" and "controls" workers were administered a brief questionnaire pertaining to symptoms, chemical exposure, history of reproductive outcome, and an occupational history. Physical examination was limited to the secondary sexual characteristics (distribution of body hair, external genitalia).

Blood samples were collected from all 28 workers for determination of serum zinc levels. Laboratory analysis for zinc was done by atomic absorption spectrometry. Renal and liver function tests were performed on the GEMSAEC centrifugal analyzer. The renal function tests done were serum creatinine and blood urea nitrogen (BUN). The liver function tests were for levels of aspartate aminotransaminase (SGPT), alanine aminotransaminase (SGOT), gamma glutamyl transpeptidase (GGTP), and alkaline phosphatase. Levels of these enzymes may be elevated as a result of alcohol and other organic solvents effect on the liver.

Urine samples were collected and tested by Multistix reagent strips for the presence of protein, glucose, blood, ketones, and bilirubin.

Sixteen valid semen samples were collected and analyzed by NIOSH and the University of Cincinnati Medical Center. These included 8 from the exposed group and 8 from the controls. Semen samples were considered invalid by the laboratory if they showed the presence of many epithelial cells and other debris or if specimens were very

viscous and a suitable slide could not be prepared even after the use of beta-amylase in an attempt to reduce viscosity. Three such invalid samples were identified and excluded. Each worker was provided with a clean polyethylene container with a self-sealing lid. They were requested to produce a semen sample by masturbation after an abstinence period of at least 48 hours. The sample was to be brought for initial analysis within 2 hours of collection. All samples brought to the NIOSH field investigators were immediately checked for motility, progression, pH, and volume. A portion of each sample was frozen and sent to the University of Cincinnati Medical Center for further analysis. Further analysis consisted of counting the number of sperms per unit volume of semen from slides prepared and stained by the Papinacolaou staining technique. The sperms were also checked for abnormal morphology.

V. EVALUATION CRITERIA

Toxicity

Criteria for limiting occupational exposures to toxic chemicals and physical agents considered in the evaluation include: the legal standards of Occupational Safety and Health Administration (OSHA); the National Institute for Occupational Safety and Health (NIOSH) recommended standards; and the American Conference of Governmental Industrial Hygienists Threshold Limit Values®. These criteria are presented for the substances evaluated in this report in Appendix I.

A. Alcohols

Alcohols in general are lipid soluble, mucous membrane irritants. In high concentrations, they can cause dizziness, drowsiness, headache, and nausea. Their toxicity varies with the type of alcohol. Most are absorbed through the skin and some can cause impairment of renal and liver function.[3] Isopropyl alcohol in particular is potentially narcotic at high concentrations. Its vapors are mildly irritant to the conjunctiva and mucous membranes of the respiratory tract. No cases of poisoning from industrial exposure have been recorded for either isopropyl or normal alcohol.[4] The odor threshold of isopropyl alcohol is reported to be 40 to 200 ppm.[5] The NIOSH recommended exposure limit of 400 ppm for this alcohol was established to prevent narcosis, although slight upper respiratory irritation may still be experienced.[5] The current OSHA permissible exposure limit is 400 ppm.[6]

B. Silica

The crystalline forms of silica can cause severe tissue damage when inhaled. Silicosis is a form of pulmonary fibrosis caused by the deposition of fine particles of crystalline silica in the lungs. Symptoms usually develop insidiously, with cough, shortness of

breath, chest pain, weakness, wheezing, and nonspecific chest illnesses. Silicosis usually occurs after years of exposure, but may appear in a shorter time if exposure concentrations are very high. This latter form is referred to as rapidly-developing silicosis, and its etiology and pathology are not as well understood. Silicosis is usually diagnosed through chest X-rays, occupational exposure histories, and pulmonary function tests. The manner in which silica affects pulmonary tissue is not fully understood, and theories have been proposed based on the physical shape of the crystals, their solubility, toxicity to macrophages in the lungs, or their crystalline structure. There is evidence that cristobalite and tridymite, which have a different crystalline form from that of quartz, have a greater capacity to produce silicosis.[3,7]

C. Zinc Compounds

Zinc is an essential trace element. Of all its compounds, the oxide is best known as an occupational hazard in its ability to produce metal-fume fever. The syndrome of metal-fume fever occurs with exposure to freshly formed zinc oxide fumes or dust of respirable particle size.[3] Zinc oxide powder may cause dermatitis though other systemic effects are doubtful. Zinc chloride is corrosive to the skin and mucus membranes.

Zinc may be necessary for gonadal growth and spermatogenesis.[8,9] Experimentally, injections of zinc chloride and zinc sulphate solution have produced tumors of the testes in fowls,[10,11] hamsters,[12] and rats.[13] Intramuscular injections of zinc ammonium sulphate in cockerels have been shown to cause decreased testicular weight, inhibited spermatogenesis, and disturbed testicular hormone production.[14] Studies have also shown that zinc accumulates in the testes and may protect the testes from cadmium injury.[15] Hence, evidence exists for differing effects of zinc compounds on the testes in different animal species. These effects range from protective to destructive, varying with dose, animal species, route of administration, nature of the specific zinc compounds used, and other factors. The OSHA standard for zinc oxide fumes is 5 mg/m^3 TWA. NIOSH has recommended that, in addition, a ceiling level of 15 mg/m^3 sampled over a 15-minute period also be imposed.[16]

D. Phosphorus pentasulfide

Phosphorus pentasulfide (P_2S_5) is used for the introduction of sulfur into organic carbon. On contact with moisture, it hydrolyses rapidly to hydrogen sulfide and phosphoric acid, and this can cause irritation of the eyes and respiratory tract. In large quantities, the hydrogen sulfide formed may cause olfactory paralysis, pulmonary oedema and polyneuritis. The threshold limit

value[4] for phosphorus pentasulfide is 1 mg/cu.m (TWA) and 3 mg/cu.m (STEL).

VI. RESULTS

A. Environmental

Qualitative XRD results indicate that the zinc oxide bulk sample did not contain any silica polymorphs. The diatomaceous earth bulk contained mainly cristobalite. Quantitative results of the less than 10 micrometer fraction indicated a 40.0(±)5.6% cristobalite concentration in the diatomaceous earth bulk sample. Quartz could not be fully confirmed as present in the bulk sample because of lack of secondary diffraction peaks.

The results of the personal breathing zone filter samples for ZnO and Zn are listed in Tables 1, 2, and 3. The limit of detection for zinc was 0.0014 mg/filter.

All of the zinc oxide levels are very low compared to the NIOSH recommended TWA zinc oxide fumes or dust criteria of 5.0 mg/m^3, and recommended ceiling criteria of 15.0 mg/m^3 for a 15-minute sampling period. The highest TWA ZnO exposure observed in Department 266 was 0.3 mg/m^3, and in Department 267 all were below the lower limit of detection.

The toxic effect of metal fume fever is caused by very fine particulates that can penetrate into the respiratory tract. Therefore, the hazard is usually defined as related to freshly formed fumes which have not yet increased in size by floculation. Therefore, the respirable fraction of zinc oxide dust may be a better indicator of the actual risk of metal fume fever. The two short-term peak respirable exposure measurements were 2.1 and 1.7 mg/m^3, which were taken in the breathing zone of the same worker who had the highest TWA total ZnO exposure, the 266 reactor operator on midnight shift. The reactor operators wear a disposable mask when charging the reactors with zinc oxide, thereby reducing the inhaled dose.

The limits of detection of ZnO are twenty times higher than for Zn. Since the zinc oxide levels observed were below the detection limit in all but two TWA samples, it is not possible to make an overall comparison of the amount of Zn present in forms other than zinc oxide. Excluding the peak respirable fraction samples, the maximum Zn level measured in Department 266 was 0.167 mg/m^3 and in Department 267 was 0.008 mg/m^3.

The sample results for phosphorus (as an indicator of phosphorus pentasulfide) were all below the limit of detection of 0.011 mg/filter.

Isobutyl-, isopropyl-, and ethylhexyl alcohol were found in varying amounts in breathing zones samples taken on workers in both departments. The results are shown in Tables 1, 2, and 3. The isobutyl and isopropyl results were below the respective criteria by two and three orders of magnitude. The highest levels in Department 266 were 2.38, 1.90, and 0.93 mg/m^3, respectively. There was no positive isobutyl alcohol finding in Department 267. The only isopropyl alcohol in Department 267 was 1.89 mg/m^3 for the "A" Operator on evening shift. Ethylhexyl alcohol was found in two "A" Operator samples and a "B" and an "F" Operators sample the highest level being 0.93 mg/m^3 in the same "A" Operators sample with the only Department 267 isopropyl alcohol exposure.

The Department 267 "A", "B", and "F" Operators handled a number of chemicals associated with their production items, which were not evaluated during this survey. The Department 266 workers would likewise have been exposed to these chemicals to the extent that they are handled in their working environment.

The results of the diatomaceous earth particle size analysis are incomplete since many large size particles did not stay suspended in the beaker. The suspended particles that were analyzed plugged up the orifice of the analyzer many times indicating that there were particles of at least 38 u in diameter. Of the particles that went through the orifice and were counted for size, 60% of volume is at 10.06 u and larger.

B. Medical

The characteristics of the "exposed" and "control" group are summarized below:

Category	No. of workers	Race	Age	Smoking Status	Alcohol Consumption*
Exposed	12	10 white 2 non-white	25 - 52 yrs Mean = 34 yrs	4 non-smokers 8 current and ex-smokers	yes = 12 no = 0
Controls	11	8 white 3 non-white	28 - 48 yrs Mean = 38 yrs	3 non-smokers 8 current and ex-smokers	yes = 6 no = 5

* 1 drink/week or more

1. History and Physical Examination

One person in the exposed group gave a history of birth defects or abnormalities in his 2 children. These abnormalities were described as "mental retardation" in one child and "undescended testis" in the other. However, these children were born before he started working in dept. 266/267. Two men in the control group also gave a history of birth abnormalities in their offsprings. In one of these cases the birth occurred before the person concerned started working in this factory.

A total of 7 miscarriages in the wives or partners were reported by 4 workers in the exposed group. All of these occurred before they began working in dept. 266/267. Five such miscarriages were reported by 4 workers in the control group. No stillbirths were reported by either "exposed" or "controls".

Three "exposed" workers and one "control" reported ever experiencing a period of infertility (defined in this study as an absence of pregnancy after a year of unprotected regular intercourse). The period of infertility in the case of the exposed workers was before any of them started working in dept. 266/267. All of the exposed workers have since been successful in fathering children.

Physical examination showed no gross abnormalities in the secondary sexual characteristics in both "exposed" and "control" group.

2. Zinc Absorption

The serum zinc levels for "exposed" and "controls" are as shown in the table below:

	Serum Zinc in Micrograms Percent	
Category	Range	Mean
Exposed	95 - 157	126
Controls	82 - 131	110

The mean serum zinc levels are higher for the exposed group than the controls, though the difference is not statistically significant ($p>0.05$; student's "t" test). All the values are within the laboratory reference range of 75 - 160 ug %.

3. Renal and Liver Function Tests

The renal and liver function test results for "exposed" and "controls" are summarized below:

Parameter	Exposed		Controls		Normal Values
	Mean	S.D.*	Mean	S.D.*	
Blood urea nitrogen in mg/dl	16.3	3.4	17.9	5.1	6 - 22
Serum creatinine in mg/dl	1.3	0.17	1.1	0.30	0.4 - 1.3
SGPT in IU	24.9	6.7	23.6	6.2	7 - 24
SGOT in IU	29.7	14.1	26.2	9.3	4 - 50
Alkaline phosphatase in U/L	48.8	9.3	51.5	12.5	15 - 65
GGTP in IU	26.4	16.0	29.2	26.3	5 - 37

* Standard deviation

The difference between the exposed and controls for all the renal and liver function test results was not statistically significant ($p>0.05$; student's "t" test).

Six of the 12 exposed workers had serum creatinine levels above the laboratory reference range of 0.4 - 1.3 mg/dl. Five of these workers had readings of 1.4 mg/ml which is marginally above the upper limit of the reference range. Only one of the 11 controls had a serum creatinine level (1.4 mg/ml) above the reference range. Blood urea nitrogen levels were normal for all six exposed workers. The difference between serum creatinine levels in exposed and controls was not statistically significant ($p>0.05$; student's "t" test). The reason for the marginally high serum creatinine levels with normal blood urea nitrogen levels is uncertain. It is however unlikely to be due to zinc exposure since environmental and serum zinc levels were not elevated and the difference in serum zinc between exposed and controls was not statistically significant.

Seven of the 12 exposed workers had serum aspartate aminotransaminase (SGPT) levels above the laboratory reference range of 7 - 24 IU. Two of these workers also had two other additional liver function test results each being abnormal. In one case this was an elevated serum alanine aminotransaminase

(SGOT) and an elevated gamma glutamyl transpeptidase (GGTP) level, and in the other the alkaline phosphatase and GGTP levels were raised. Three controls had elevated SGOT levels and two of them had in addition raised GGTP readings. The exposed group had 100% workers (12 out of 12) with a history of regular alcohol consumption (more than 1 alcoholic drink a week), while the controls had 55% (6 out of 11 workers). The exposed group are also exposed to some industrial alcohols at work while the controls are not. Both these factors may have contributed to the raised SGOT levels seen. However GGPT is usually more sensitive than SGOT to alcohol effect, and GGPT levels were elevated only in two exposed and also two controls who had raised SGOT readings. Environmental measurements of isopropyl, isobutyl, and 2-ethylhexyl alcohol showed no elevated levels of these alcohols. The difference between mean SGOT levels in exposed and controls was also not statistically significant ($p>0.05$; student's "t" test). None of the exposed nor controls had a past history of diagnosed hepatitis nor jaundice. The reason for these liver function abnormalities is not apparent. It may be some factor common to both "exposed" and "controls", but no such factor was identified.

4. Semen Analysis

a) Sperm Counts

Sperm counts expressed in millions per ml

	Mean	Standard Deviation	Median	Range
Exposed	61.3	34.4	50.6	23.9 - 125.1
Controls	106.2	108.4	76.8	7.1 - 316.7

The mean sperm counts for the 8 controls was higher than that for the exposed, though the difference was not statistically significant ($p>0.05$; student's "t" test). Log transformation of the sperm counts and analysis of these by the student's "t" test also showed no significant difference. Two workers in the control group had oligospermia (sperm counts below 20 million per ml.) compared to none in the exposed group. There were two workers in both exposed and controls with sperm counts between 20 million and 40 million per ml. All others had counts above 40 million per ml.

b. Motility

	% Motile sperms		
Exposed	Mean = 61%	Median = 62.5%	Range = 40 - 80%
Controls	Mean = 61 %	Median = 65.0 %	Range = 40 - 85%

There is no difference in sperm motility between the two groups. The semen samples in the exposed group were examined after a mean interval of 1 hour from production (Range: 45 mins. - 1 hour 30 mins). Those in the control group were examined after a mean interval of 1 hour from production (Range: 30 mins. - 1 hour 30 mins).

c. Progression

The progression of sperm movement was graded on a scale of 1 to 4. In the exposed group progression ranged from 2+ to 4, and in the controls progression was from 2 to 3+. This difference was not statistically significant (Fisher's exact test, $p>0.05$)

d. Sperm Morphology

The mean percentages for the different morphological types of spermatozoa are as follows:

Morphological Types	Mean Percentages	
	Exposed	Controls
Oval	42%	40%
Large	3%	2%
Small	19%	29%
Tapered	0%	1%
Amorphous	34%	28%
Dup. heads	1%	1%
Dup. tails	1%	0%
Spermatids	0%	0%

There is no striking difference between exposed and controls in the proportions of the different morphological forms seen.

VII. DISCUSSION

A. Environmental

The environmental measurements did not identify any significant exposures. The presence of low level exposures to ZnO dust should be adequately protected against by continued use of the disposable respirators during charging of the ZnO. Alcohol exposures were not remarkable, although there is no recommended criteria to evaluate the ethyl hexyl alcohol exposures. This was the most common alcohol exposure observed.

The analysis of the diatomaceous earth sample did indicate that the respirable fraction, with a diameter of <10 u, was 40% cristobalite. This is considered to be a more toxic form of crystalline silica. Although it was not found on the 266 reactors breathing zone sample, it is more likely to be present in the filter operators breathing zone. Unfortunately, this analysis was not performed. While this activity would be comparable to the charging of the ZnO, it should be recognized that it is a more toxic material and the use of respirators should be emphasized. There was a local exhaust canopy over the manway to the filter feed tank which was not operating properly due to lack of filter maintenance. This filter should be cleaned regularly and the control efficiency will be improved.

B. Medical

The results from the medical assessments indicate no major difference between the exposed and control group. However the numbers of workers involved in this study were small primarily due to the small total number of exposed workers in this firm. The small numbers involved meant that a dramatic effect would be needed to show significant differences between the exposed and controls. No oligospermia nor azoospermia was detected in the exposed workers. The results of animal toxicological tests showed supression of spermatogenesis in rabbits though not in rats. Repeat 21-day dermal toxicity studies (done by Bio-dynamics for the Chemical Manufacturers Association - Projects no. 81-2558 and 81-2559) showed testicular changes and aspermatogenesis in New Zealand white rabbits but not in Sprague-Dawley rats following treatment with zinc dialkyl dithiophosphates. Thus, there appears to be a difference in species response to the spermatogenic effect of such compounds.

Mutagenicity studies have also been done on Hitec E-682. The salmonella/microsomal assay for bacterial mutagenicity and the micronucleus test[17] were negative. (Microbiological Associates and Pharmakon Laboratories. reports to Ethyl Corporation) In vitro mouse-embryo cell point mutation assays both in the presence

and absence of exogenous metabolic activation showed E-682 to have positive mutagenic activity in these cells. In vitro mammalian cell transformation assays in the absence of exogenous metabolic activation also shows that E-682 exhibits positive cell transforming activity. This was however not observed in similar assays in the presence of exogenous metabolic activation. (Microbiological Associates reports to Ethyl Corporation) NIOSH was informed that a report has been filed with the Environmental Protection Agency (EPA) regarding these results.

VIII. CONCLUSION

This study showed no effect on spermatogenesis in workers exposed to zinc dialkyl dithiophosphates when compared to workers not exposed to such compounds. Limitations of this study include the small number of workers involved, and the fact that exposed workers were not exposed to these zinc compounds alone, but also to a variety of alcohols, phosphorus salts, and silica.

IX. RECOMMENDATIONS

1. Until further information becomes availble which better delineates the occupational risks of these compounds, care should be exercised in the handling of similiar dialkyl zinc phosphate-based oil additives, and to minimize worker contact with such chemicals by good housekeeping, good personal hygiene, and personal protection. In this regard there is a need to improve maintenance of the local exhaust ventilation systems, several of which were inoperative.

IX. REFERENCES

1. National Institute for Occupational Safety and Health. NIOSH manual of analytical methods. Vol 1, 2nd ed. Cincinnati, OH: National Institute for Occupational Safety and Health, 1977. (DHEW (NIOSH) publication no. 77-157-A).

2. National Institute for Occupational Safety and Health. NIOSH manual of analytical methods. Vol 2, 2nd ed. Cincinnati, OH: National Institute for Occupational Safety and Health, 1977. (DHEW (NIOSH) publication no. 77-157-B).

3. National Institute for Occupational Safety and Health. Occupational diseases: a guide to their recognition. Revised ed. Cincinnati, OH: National Institute for Occupational Safety and Health, 1977. (DHEW (NIOSH) publication no. 77-181).

4. American Conference of Governmental Industrial Hygienists. Documentation of the threshold limit values. 4th ed. Cincinnati, Ohio: ACGIH, 1980.

5. National Institute for Occupational Safety and Health. Criteria for a recommended standard: occupational exposure to isopropyl alcohol. Cincinnati, Ohio: National Institute for Occupational Safety and Health, 1976. (DHEW (NIOSH) publication no. 76-142).

6. Occupational Safety and Health Administration. OSHA safety and health standards. 29 CFR 1910.1000. Occupational Safety and Health Administration, revised 1980.

7. National Institute for Occupational Safety and Health. Criteria for a recommended standard: occupational exposure to crystalline silica. Cincinnati, Ohio: National Institute for Occupational Safety and Health, 1975. (DHEW (NIOSH) publication no. 75-120).

8. Gunn SA, Gould TC, Anderson WAD. Zinc in rat testis. Archives of Pathology 1963;75:21-7/33-9.

9. Prasad AS. Metabolism of zinc and its deficiency in human subjects. in Prasad AS ed. Zinc metabolism. Springfield, IL: Charles C. Thomas, 1966.

10. Guthrie J. Observations on the zinc induced testicular teratomas of fowl. Br. J. Cancer 1964;18:130-42.

11. Falin LI, Gromzewa KE. Experimental teratoma testis in fowl produced by injections of zinc sulphate solution. Am. J. of Cancer 1939;36:233-6.

12. Guthrie J, Guthrie OA. Embryonal carcinomas in Syrian Hamsters after intratesticular innoculation of zinc chloride during seasonal testicular growth. Cancer Research 1974;34:2612-4.

13. Riviere MR, Chouroulinkor I, Guerin M. The production of tumors by means of intra-testicular injections of zinc chloride in the rat. Bulletin del'Association Francaise pour l'Etude du Cancer 1960;47(1):55-87.

14. Eltohamy MM, Takahara H, Okamoto M. Effects of zinc on intact and castrated cockerels. Br. Poultry Science 1980;21(5):363-9.

15. Webb M. Protection by Zinc against Cadmium toxicity. Biochem. Pharmacology 1972;21:2766-71.

16. National Institute for Occupational Safety and Health. Criteria for a recommended standard: occupational exposure to zinc oxide. Cincinnati, Ohio: National Institute for Occupational Safety and Health, 1976. (DHEW (NIOSH) publication no. 76-104).

17. Schmid W. The Micronucleus test. Mutation Research 1975; 31:9-15.

X. AUTHORSHIP AND ACKNOWLEDGEMENTS

Report Prepared by:	Bruce A. Hollett, C.I.H., P.E. Industrial Hygienist Industrial Hygiene Section
	Tar-Ching Aw, M.D. Medical Officer Medical Section
Field Support:	Gary Liss, M.D. Medical Officer Medical Section
	James Collins Health Technician Medical Support Section
Laboratory Analyses:	Channing Meyer, M.D. Assistant Professor Environmental Health University of Cincinnati Medical Center
	Frederick Phipps Chemist Clinical & Biochemical Support Division
Originating Office:	Hazard Evaluations and Technical Assistance Branch Division of Surveillance, Hazard Evaluations, and Field Studies
Report Typed By:	Debra A. Lipps Clerk-Typist Industrial Hygiene Section

XI. DISTRIBUTION AND AVAILABILITY OF REPORT

Copies of this report are currently available upon request from NIOSH, Division of Standards Development and Technology Transfer, 4676 Columbia Parkway, Cincinnati, Ohio 45226. After 90 days, the report will be available through the National Technical Information Service (NTIS), 5285 Port Royal, Springfield, Virginia 22161. Information regarding its availability through NTIS can be obtained from NIOSH Publications Office at the Cincinnati address. Copies of this report have been sent to:

1. Edwin Cooper Company, Sauget, Illinois
2. I.C.W.U. Local No. 871
3. NIOSH, Region V
4. OSHA, Region V

For the purpose of informing all employees involved, copies of this report shall be posted by the employer in a prominent place accessible to the employees for a period of 30 calendar days.

TABLE 1

RESULTS OF AIR SAMPLES FOR
ISOBUTYL, ISOPROPYL, AND 2-ETHYL HEXYL ALCOHOLS;
ZINC AND ZINC OXIDE

EDWIN COOPER
SAUGET, ILLINOIS
HETA 80-228

OCTOBER 26 EVENING SHIFT

DEPT NO.	JOB CLASSIFICATION	SAMPLE PERIOD DATE	START	STOP	TIME (min)	RATE (lpm)	VOL. (l)	ZINC mg/m³	ZINC OXIDE mg/m³	ISOBUTYL mg/m³	ISOPROPYL mg/m³	ETHYL HEXYL mg/m³
266	FILTER OPERATOR	10/26	2:35p.m.	6:30p.m.	235	0.10	23.50			1.28	1.70	0.85
266	FILTER OPERATOR	10/26	2:35p.m.	10:18p.m.	463	0.05	23.15			<0.43	<0.43	0.43
266	FILTER OPERATOR	10/26	6:30p.m.	10:18p.m.	228	1.5	342.00	0.009	0.269			
266	REACTOR OPERATOR	10/26	2:45p.m.	10:17p.m.	452	1.5	678.00	0.004	<0.037			
266	REACTOR OPERATOR	10/26	2:45p.m.	6:30p.m.	225	0.10	22.50			<0.44	1.78	0.89
266	REACTOR OPERATOR	10/26	6:30p.m.	10:17p.m.	227	0.10	22.70			<0.44	0.44	0.88
267	"A" OPERATOR	10/26	2:55p.m.	10:16p.m.	441	1.5	661.50	0.005	<0.038			
267	"A" OPERATOR	10/26	2:55p.m.	6:30p.m.	215	0.10	21.50			<0.47	1.86	0.93
267	"A" OPERATOR	10/26	6:30p.m.	10:16p.m.	226	0.10	22.60			<0.44	<0.44	0.44
267	"F" POERATOR	10/26	3:23p.m.	10:14p.m.	411	1.5	616.50	0.003	<0.041			
267	"F" OPERATOR	10/26	3:23p.m.	6:35p.m.	192	0.09	17.28			<0.58	<0.58	<0.58
267	"F" OPERATOR	10/26	6:35p.m.	10:14p.m.	219	0.09	19.71			<0.51	<0.51	<0.51
LIMITS OF DETECTION: (units per sample)								0.0014 mg/spl	0.025 mg/spl	0.01 mg/spl	0.01 mg/spl	0.01 mg/spl
EVALUATION CRITERIA:												
NIOSH	-TWA							N/A	5.0	N/A	980	N/A
	-Ceiling							N/A	15.0	N/A	1960	N/A
	(sample period)							N/A	15(min)	N/A	15(min)	N/A
ACGIH	-TLV							N/A	5.0	150	980	N/A
	-STEL-TLV							N/A	10.0	225	1,225	N/A
OSHA-PEL	-TWA							N/A	5.0	300	980	N/A

NOTES:
< LESS THAN-These samples were below the detection limit and therefore airborne levels, if present at all, were less than the level shown.

ISOBUTYL	ISPBUTYL ALCOHOL
ISOPROPYL	ISOPROPYL ALCOHOL
ETHYL HEXYL	ETHYL HEXYL ALCOHOL

TABLE 2

RESULTS OF AIR SAMPLES FOR
ISOBUTYL, ISOPROPYL, AND 2-ETHYL HEXYL ALCOHOLS;
ZINC AND ZINC OXIDE

EDWIN COOPER
SAUGET, ILLINOIS
HETA 80-228

OCTOBER 26 MIDNIGHT SHIFT

DEPT NO.	JOB CLASSIFICATION	SAMPLE PERIOD DATE	START	STOP	TIME (min)	R/TE (lpm)	VOL. (l)	ZINC mg/m³	ZINC OXIDE mg/m³	ISOBUTYL mg/m³	ISOPROPYL mg/m³	ETHYL HEXYL mg/m³
266	FILTER OPERATOR	10/26	NONE ON DUTY THE MIDNIGHT SHIFT ON THIS DATE									
266	REACTOR OPERATOR	10/26	11:03p.m.	6:10a.m.	427	1.5	640.50	0.167	0.301			
266	REACTOR OPERATOR	10/26	11:31p.m.	11:49p.m.	18	1.7	30.60	0.654	2.124	(Peak Respirable Fraction Sample)		
266	REACTOR OPERATOR	10/27	2:38a.m.	2:57a.m.	19	1.7	32.30	0.495	1.703	(Peak Respirable Fraction Sample)		
266	REACTOR OPERATOR	10/26	11:03p.m.	3:05a.m.	242	0.09	21.78			<0.46	0.92	0.46
266	REACTOR OPERATOR	10/27	3:05a.m.	6:10a.m.	185	0.09	16.65			1.80	1.80	0.60
267	"A" OPERATOR	10/27	0:19a.m.	6:00a.m.	341	1.5	511.50	0.006	<0.049			
267	"A" OPERATOR	10/26	10:33p.m.	3:10a.m.	277	0.09	24.93			<0.40	<0.40	<0.40
267	"A" OPERATOR	10/27	3:10a.m.	6:00a.m.	170	0.09	15.30			<0.65	<0.65	<0.65
267	"B" OPERATOR	10/26	10:59p.m.	6:10a.m.	431	1.5	646.50	0.008	<0.039			
267	"B" OPERATOR	10/26	10:59p.m.	3:15a.m.	256	0.08	20.48			<0.49	<0.49	0.49
267	"B" OPERATOR	10/27	3:15a.m.	6:10a.m.	175	0.09	15.75			<0.63	<0.63	<0.63
267	"F" OPERATOR	10/26	10:30p.m.	5:30a.m.	420	1.5	630.00	0.006	<0.040			
267	"F" OPERATOR	10/26	10:30p.m.	3:05a.m.	275	0.09	24.75			<0.40	<0.40	0.40
267	"F" OPERATOR	10/27	3:05a.m.	5:30a.m.	145	0.09	13.05			<0.77	<0.77	<0.77
LIMITS OF DETECTION: (units per sample)								0.0014 mg/spl	0.0025 mg/spl	0.01 mg/spl	0.01 mg/spl	0.01 mg/spl
EVALUATION CRITERIA:												
NIOSH	-TWA							N/A	5.0	N/A	980	N/A
	-Ceiling							N/A	15.0	N/A	1960	N/A
	(sample period)							N/A	15(min)	N/A	15(min)	N/A
ACGIH	-TLV							N/A	5.0	150	980	N/A
	-STEL-TLV							N/A	10.0	225	1,225	N/A
OSHA-PEL	-TWA							N/A	5.0	300	980	N/A

NOTES:
< LESS THAN-These samples were below the detection limit and therefore airborne levels, if present at all, were less than the level shown.

ISOBUTYL	ISPBUTYL ALCOHOL
ISOPROPYL	ISOPROPYL ALCOHOL
ETHYL HEXYL	ETHYL HEXYL ALCOHOL

TABLE 3

RESULTS OF AIR SAMPLES FOR
ISOBUTYL, ISOPROPYL, AND 2-ETHYL HEXYL ALCOHOLS;
ZINC AND ZINC OXIDE

EDWIN COOPER
SAUGET, ILLINOIS
HETA 80-228

OCTOBER 27 DAY SHIFT

DEPT NO.	JOB CLASSIFICATION	SAMPLE PERIOD DATE	START	STOP	TIME (min)	RATE (lpm)	VOL. (l)	ZINC mg/m³	ZINC OXIDE mg/m³	ISOBUTYL mg/m³	ISOPROPYL mg/m³	ETHYL HEXYL mg/m³
266	FILTER OPERATOR	10/27	6:30a.m.	2:10p.m.	460	1.5	690.00	0.006	<0.036			
266	FILTER OPERATOR	10/27	6:30a.m.	10:05a.m.	215	0.09	19.35			<0.52	<0.52	<0.52
266	FILTER OPERATOR	10/27	10:05a.m.	2:10p.m.	245	0.09	22.05			<0.45	<0.45	0.45
266	REACTOR OPERATOR	10/27	6:30a.m.	2:15p.m.	465	1.5	697.50	0.006	<0.036			
266	REACTOR OPERATOR	10/27	6:30a.m.	10:00a.m.	210	0.10	21.00			2.38	1.90	0.95
266	REACTOR OPERATOR	10/27	10:00a.m.	2:15p.m.	255	0.09	22.95			<0.44	<0.44	0.44
267	"A" OPERATOR	10/27	6:40a.m.	1:58p.m.	438	1.5	657.00	0.005	<0.038			
267	"A" OPERATOR	10/27	6:40a.m.	10:10a.m.	210	0.09	18.90			<0.53	<0.53	0.53
267	"A" OPERATOR	10/27	10:10a.m.	1:58p.m.	228	0.09	20.52			<0.49	<0.49	<0.49
267	"F" OPERATOR	10/27	6:20a.m.	1:58p.m.	458	1.5	687.00	0.006	<0.036			
267	"F" OPERATOR	10/27	6:20a.m.	10:00a.m.	220	0.09	19.80			<0.51	<0.51	<0.51
267	"F" OPERATOR	10/27	10:00a.m.	1:58p.m.	238	0.09	21.42			<0.47	<0.47	<0.47
LIMITS OF DETECTION: (units per sample)								0.0014 mg/spl	0.025 mg/spl	0.01 mg/spl	0.01 mg/spl	0.01 mg/spl
EVALUATION CRITERIA:												
NIOSH	-TWA							N/A	5.0	N/A	980	N/A
	-Ceiling							N/A	15.0	N/A	1960	N/A
	(sample period)							N/A	15(min)	N/A	15(min)	N/A
ACGIH	-TLV							N/A	5.0	150	980	N/A
	-STEL-TLV							N/A	10.0	225	1,225	N/A
OSHA-PEL	-TWA							N/A	5.0	300	980	N/A

NOTES:
< LESS THAN-These samples were below the detection limit and therefore airborne levels, if present at all, were less than the level shown.

ISOBUTYL	ISPBUTYL ALCOHOL
ISOPROPYL	ISOPROPYL ALCOHOL
ETHYL HEXYL	ETHYL HEXYL ALCOHOL

APPENDIX I

Evaluation Criteria and Primary Health Effects

Edwin Cooper Company
Sauget, Illinois
HETA 80-228

May 1982

Substance	Evaluation Criteria* (mg/m^3) NIOSH	OSHA	ACGIH	Primary Health Effects
Crystalline Silica	0.05	$\frac{10\ mg/m^3}{\%\ SiO_2 + 2}$	$\frac{10\ mg/m^3}{\%\ SiO_2 + 2}$	Effects the respiratory system and lungs. Cause of silicosis-progressive impairment of breathing.
Isobutyl Alcohol	-	-	150	Irritation of the eyes and respiratory tract, also cracking of skin and headache, dizzy, drowsy.
Isopropyl	984	984	980	Irritation of the eyes and respiratory tract, also cracking of skin and headache, dizzy, drowsy.
Zinc Oxide Fume Zinc Oxide Dust	5 -	- -	5 5	Metal fume fever, chills, fatigue, headache, nausea, respiratory system effects.

* NIOSH criteria represent Time-Weighted Averages (TWA) for up to a 10-hour workday; OSHA Permissible Exposure Limits and ACGIH Threshold Limit Values are TWA's based on an 8-hour workday. (See References 4-7 and 16).

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
CENTERS FOR DISEASE CONTROL
NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH
ROBERT A. TAFT LABORATORIES
4676 COLUMBIA PARKWAY, CINCINNATI, OHIO 45226

OFFICIAL BUSINESS
PENALTY FOR PRIVATE USE, $300

Third Class Mail

POSTAGE AND FEES PAID
U.S. DEPARTMENT OF HHS
HHS 396