U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
CENTER FOR DISEASE CONTROL
NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH
CINCINNATI, OHIO 45226

HEALTH HAZARD EVALUATION DETERMINATION REPORT
HE 79-113-728

OLIN CHEMICAL COMPANY
BRANDENBURG, KENTUCKY

August 1980

I. SUMMARY

The National Institute for Occupational Safety and Health (NIOSH) conducted a health hazard evaluation into the reproductive problems being experienced by the employees of the toluene diamine (TDA) manufacturing area at Olin Chemical Company (SIC 2810), Brandenburg, Kentucky. The request came from employees alleging increased rates of spontaneous abortions in the wives of TDA workers.

NIOSH responded to the request by conducting an initial walk-through survey September 26-27, 1979. Based on the results of the initial survey which revealed a history of miscarriages, abnormal offspring, and semen abnormalities in TDA unit workers, a followup investigation was scheduled. A detailed medical survey of these workers was conducted and personal and area samples for determination of airborne dinitrotoluene (DNT) and TDA levels were obtained. The follow-up investigation was conducted January 14-18, 1980.

Environmental results from the initial survey showed the two operator DNT exposures to be 0.013 mg/M^3 and 0.023 mg/M^3. Operator TDA exposures were 0.39 mg/M^3 and 0.0233 mg/M^3. An area DNT value of 0.42 mg/M^3 and two TDA area values of 0.023 mg/M^3 and 0.008 mg/M^3 were also found. During the follow-up survey, only the operator doing TDA loading had a measurable exposure of 0.038 mg/M^3 to TDA. Operator DNT exposures during the follow-up were 0.014 mg/M^3 and 0.006 mg/M^3 on the day DNT was unloaded. Area samples for TDA and DNT during the follow-up survey were negligible. All values are calculated as time weighted average (TWA's). Concentrations of DNT and TDA were lower during the follow-up survey than those seen initially in September. All DNT values were below the OSHA standard of 1.5 mg/M^3 TWA. No accepted TDA standard currently exists but it is recommended that levels be kept as low as possible and that the material be handled as a suspected carcinogen. Nine employees currently staff the TDA unit over four rotating shifts.

A total of 44 workers volunteered to participate in the medical survey. Workers were divided into three groups; control, intermediate (past history of low exposures but no exposure for the last two years) and exposed. Medical and occupational histories, physical examinations and blood, urine and semen specimens were obtained. A reproductive history was also elicited. The wives of workers were given a different, more detailed reproductive questionnaire in an attempt to validate the information given by the workers themselves. Medical findings included a significant reduction in sperm count in the exposed group ($p<.05$). An excess of miscarriages in the wives of the exposed workers was found, but this was not statistically significant and may not take into account the influence of other factors on miscarriages.

Based on the results of the studies performed during this evaluation, NIOSH determined that while this study cannot be interpreted as conclusive proof of TDA or DNT toxic effects on the male reproductive system, it is strongly suggestive of a problem in workers exposed to these agents. These effects were observed in the presence of declining DNT and TDA exposures, none of which exceeded current OSHA exposure limits during the survey. Detailed discussion of these findings and recommendations are contained in the text of this report.

II. INTRODUCTION

On June 26, 1979, NIOSH received a request to conduct a health hazard evalution* at the Olin Chemical Group in Brandenburg, Kentucky. The request was submitted by an authorized representative of the TDA unit employees. It alleged overexposure to chemicals used or produced in the unit resulting in reproductive failures among the workers. The purpose of the study was to evaluate DNT and TDA exposures and health effects of workers in the TDA unit.

III. BACKGROUND

A. Basis of Request/Preliminary Action

Olin Chemical Company, Brandenburg, Kentucky, manufactures basic organic chemicals (SIC 2810) for markets throughout the country. The plant area of concern is involved in the manufacture of toluene diamine (TDA). The TDA is shipped to another facility for its ultimate use in the manufacturing of toluene diisocyanate (TDI). The alleged reproductive problem was brought to light by one of the employees working in the TDA area. This particular employee became concerned when his wife had her third consecutive miscarriage occurring over a three year period. All of the miscarriages occurred since the TDA worker had begun employment in that part of the plant. A reproductive evaluation conducted on this individual showed an increased number of abnormally shaped sperm. Based on this finding and on the alleged increased incidence of spontaneous abortions, a health hazard evaluation was submitted to NIOSH by the employees. It requested a more thorough investigation of the reproductive hazards at the plant.

NIOSH followed up the health hazard evaluation request from the employees with an initial survey, conducted September 25-26, 1979. Industrial hygiene measurements and completion of medical questionnaires were included in the initial walk-through survey. Evaluation of the information obtained during the initial survey, especially the medical questionnaires, indicated the need for a more extensive follow-up survey. The follow-up survey, for both medical and industrial hygiene, was conducted January 14-18, 1980.

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*Section 20(a)(6) of the Occupational Safety and Health Act of 1970, 29 U.S.C. 669(a)(6), authorizes the Secretary of Health and Human Services, following a written request by an 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.

B. Environmental

1. Process Description

The toluene diamine unit, built about 1964, is one of many production areas in the plant complex, which was started in about 1951. The TDA unit is a large, open, multiple story unit. The process equipment is located entirely outdoors with the exception of the control room which is housed in a separate building on the edge of the TDA area. Toluene diamine (TDA), specifically 2,4-toluenediamine, is produced through the catalytic hydrogenation of dinitrotoluene. The reaction is carried out by mixing methanol with molten dinitrotoluene and continuously contacting this solution with a stream of hydrogen gas in an agitated reactor in the presence of a nickel catalyst. Water and methanol are removed from the TDA by atmospheric evaporation followed by regular vacuum distillation methods. DNT and TDA are transferred through the unit in a closed system. The methanol is recycled within the unit. The finished TDA is shipped to other Olin facilities to be used as a raw material in the production of toluene diisocyanate.

Fugitive emissions from pumps and clean up operations appear to be the only sources of exposure in the unit besides the DNT unloading and TDA loading procedures. The transfer of raw materials and final product is accomplished through a closed system of mixing, reacting, and storage. Particulate or vaporous DNT and vaporous TDA may enter the ambient atmosphere through leaks around pumps and other equipment during loading and unloading of DNT and TDA, during pressure relief conditions, and during certain maintenance operations such as catalyst changeout. An increased emphasis on spill containment and clean-up was evident as well as reports of efforts to tighten up the system to reduce fugitive emissions. This was being done by tightening pipe connections, resealing values, and repairing and cleaning pumps. The area appeared free of product accumulation. Gravel in spill areas outside the reactor pad had been removed and replaced since the initial survey, especially the unloading and loading areas.

2. Job Description

This area employs three chemical operators during the day shift (8-4) and two each during the afternoon and evening shifts (4-12 and 12-8), a total of nine including the fourth shift. Outside of routine rounds and loading, the control room is where most of the operator's time is spent. Grade 8 and Grade 10 operators are the workers who generally work out in the unit, with the Grade 8 operator responsible for the loading of TDA and unloading of DNT from tank cars and tank trucks.

Grade 8 operator (loader) - Unloads DNT from tank cars into storage tanks about once per day. Loads TDA into tank cars from storage tanks every one to two days. Launders work coveralls in control room washer and dryer. The Grade 8 operator was present only on the day shift.

Grade 10 operator - Oversees processes in exterior TDA unit, checking temperature, and pressure conditions about seven times per shift. Spends other time in control room.

Grade 14 operator - Maintains production from within control room, located 20-30 feet from TDA unit.

C. Medical

1. Initial Medical Survey

The medical walk-through included questioning of nine workers, six from the TDA area and three who had been intermittently exposed in this area in the past. Of those workers, only one individual had had a healthly child conceived since beginning work in the TDA area. Two other workers reported having children, both aged five and both males who have abnormalities of growth and mental retardation that have yet to be diagnosed. In addition to this, there was a history of at least 10 miscarriages among the wives of those workers who were questioned during this walk-through evaluation. There were also a number of other medical problems including lipid abnormalities, skin rash, and hypertension in those workers evaluated, the etiology of which was unknown. It was also discovered at the time ot this evaluation that four individuals who were evaluated by the company had semen abnormalities.

Based on the medical interviews conducted during the walk-through survey, it was felt that a reproductive hazard might exist in the TDA operation. As a result a more indepth medical and industrial hygiene evaluation was suggested and performed in January 1980.

IV. METHODS AND MATERIALS

A. Environmental

During both the initial and follow-up surveys personal air samples were taken by mounting sample collection media in the Grade 8 and 10 operators' breathing zones. Area air sampling was generally conducted near transfer pumps. All sampling was done during the first shift when the maximum number of employees and activity occurred on the unit. Unloading of DNT and loading of TDA occurred during the day shift. Initial survey sample locations were repeated during the followup survey along with several additional samples.

1. Dinitrotoluene

Samples for DNT were taken and analyzed according to NIOSH Method No. S215.[1] A mixed cellulose ester membrane filter with stainless steel backup pad and an impinger having a fritted buffler containing ethylene glycol were used to collect the material. Sampling was done at a rate of 1.5 lpm using a calibrated battery powered sampling pump. High pressure liquid chromatography was the analytical method used in Method No. S215. The limit of detection for the analysis of DNT was 2.8 ug per sample, which included the filter and its corresponding impinger solution.

2. Toluenediamine

Samples for TDA were taken and analyzed according to NIOSH Method No. 141.[2] Spillproof midget impingers containing Marcali Solution were used with a calibrated battery operated pump operating at a flow rate of 1 lpm. The method is generally used for toluene diisocycinate (TDI) based on the conversion of TDI to TDA. Standards were made using TDI, and the results were converted to TDA by the appropriate conversion factor. This is a colorimetric analysis, and the limit of detection was 2 ug of TDA per sample.

B. Medical

1. Medical Evaluation Description

The medical evaluation consisted of a detailed questionnaire designed to elicit information from workers concerning their work history, both present and past and to ascertain the range of their potentially toxic exposures. In addition, personal habits such as tobacco and alcohol consumption were obtained. Pertinent medical history including illnesses and treatments which are known to effect the testicles, sexual performance or semen quality were also elicited. A physical examination consisting of evaluation of blood pressure, pulse, respirations, assessment of cardiovascular and pulmonary status and abdominal examination for organ enlargement was performed. A special emphasis was placed on the male reproductive system and secondary sex characteristics including body build, hair distribution, evidence of muscle atrophy, inspection of the external genitalia, palpation of the scrotal contents and testicles, and mesurement of testicular size. A rectal examination for prostatic size and consistency was also performed. Blood specimens were obtained for analyses of blood urea nitrogen (BUN), creatinine, bilirubin, alkaline phosphatase, serum glutamic oxalic transaminase (SGOT) and serum glutamie pyruvic transaminase (SGPT). An additional amount of serum was collected and frozen for later assays of serum testosterone, serum luteinizing hormone and serum follicle stimulating hormone if those assays proved to be warranted. A semen specimen was obtained after 48 hours of abstenence to be analyzed for ejaculate volume, sperm count, and morphologic pattern. Urine was collected for routine dip-stix analysis.

In addition to these evaluations on the workers, a detailed reproductive questionnaire was administered to the workers' wives who chose to participate in this aspect of the study designed primarily to give validity to the reproductive portion of the questionnaire administered to the males.

2. Analytical Methods

Serum specimens were centrifuged and frozen in the field at the time of the study for subsequent transport and storage and were later shipped to Smith-Kline and French Analytical Reference Laboratory in St. Louis, Missouri*, for the performance of a Serum Multiphasic Analysis-21. It was from this analysis that the values for blood urea nitrogen and creatinine, total bilirubin, alkaline phosphatase, SGOT and SGPT were obtained. Urinalysis was performed on site using Ames N-multistix.*

At the time of semen analysis the individual semen specimens (identified only by a study number) were allowed to thaw completely and were mixed well by repetitively drawing the specimen up and discharging from a Pasteur pipet. Two dilutions were made using a 5% bicarbonate-1% formalin solution in a white blood cell diluting pipet. Each of the dilutions were counted twice and the results of the four counts were averaged. In instances where a 20% discrepancy between any of the four counts existed, repeat dilutions were made and a fifth and sixth count made and averaged with the other counts. If in using

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*The use of a laboratory name or product name does not constitute endorsement of the laboratory or the product by the National Institute for Occupational Safety and Health.

this method a large discrepancy still existed, duplicate tubes of .25 mg beta amylase in 0.01 ml 2.3 M $(NH_4)_2SO_4$ and 0.01 ml semen were mixed and allowed to sit for 30-60 minutes at room temperature. This mixture was then further diluted 1:5, 1:10 or 1:25 with distilled H_2O and the sperm counted twice per dilution. Values then for all counts were averaged. All of the diluted sperm specimens were counted using a LEVY Hemocytometer chamber and after charging the chamber, a 5-10 minute interval was used to permit reduction in cell movement for more accurate count. The final average count was logged on the master data sheet for final comparison.

At the same time the frozen specimens were thawed for counting, several slides were made by applying a drop of the well mixed, thawed specimen to a clean glass slide and a smear of the cells made and immediately fixed in a 50% ethyl alcohol 50% ethyl ether fixative bath. After at least 1-2 hours of fixation in this solution specimens were rinsed in distilled H_2O and then manually taken through a multistep process using the Paponuolaou staining technique. On completion of the staining procedure, the slide was then evaluated under oil immersion objective and 300 cells counted. Each sperm cell observed was placed into one of eight morphological categories, i.e., oval, large, small, tapering, amorphous, duplicate heads, duplicate tails or spermatids. The counts were averaged and a percentage figure of each cell type was recorded for final comparison by statistical analysis.

3. Statistical Methods

Sperm counts, ejaculate volumes, and morphologic patterns were analyzed using the general linear models procedure in performing an analysis of variance on these data. Results of the findings discovered on physical examination as well as laboratory results (blood urea nitrogen, serum creatinine, total bilirubin, alkaline phosphatase, SGOT, SGPT) were compared using the student t test. Reported spontaneous abortions prior to Olin and after Olin employment were compared using the Chi-square test and the Fisher's exact test. In all of the statistical analyses a P value of 0.05 was considered to be the level of statistical significance.

V. EVALUATION CRITERIA

A. Environmental

The criteria used to evaluate the potential hazards associated with toxic substances found in the employees' work environment are obtained from two major sources: NIOSH Criteria Documents for Recommended Occupational Health Standards and the Occupational Health Standards as promulgated by the U.S. Department of Labor. Other sources are used in addition to the two mentioned, when appropriate. Exposure limits are derived from existing human and animal data and industrial experience.

1. Dinitrotoluene

The current Occupational Safety and Health Administration (OSHA) standard for dinitrotoluene (DNT) is 1.5 mg/M^3 over an entire workshift.[4] A "skin" notation in the standard refers to the potential contribution to the overall exposure by the skin, mucous membranes, and eyes, via airborne and direct contact with the substance.

The standard of 1.5 mg/M^3 for DNT was set by analogy with chemically similar substances, although dinitrotoluene is considered less toxic than other aromatic nitro compounds.[5]

Dinitrotoluene absorption causes anoxia due to the formation of methemoglobin. Signs and symptoms of overexposure are caused by the loss of oxygen - carrying capacity of the blood. Jaundice and anemia from chronic exposure have been reported.[6]

2. Toluenediamine

No occupational standard for TDA appears in the OSHA General Industry Standards, nor was any recommended exposure level listed by NIOSH or the American Conference of Governmental Industrial Hygienists (ACGIH).[7] A maximum permissible concentration of 2 mg/M^3 is mentioned in a Russian article by V.S. Filatova et. al., but no reference or basis for this value is given.[8] The TDA isomer(s) to which this standard refers is also unspecified.

Animal studies have shown effects of TDA exposure to be the production of methemoglobin and liver damage. Studies examining the potential carcinogencity of TDA in animals have shown inconsistent results, one study revealing no problems [9], while three others showed the development of carcinoma of the liver in rats fed a diet containing TDA[10,11,12]. A study by R. H. Cardy[10] on F344 rats and an evaluation conducted on Wistar rats by the International Agency for Research on Cancer[11] show that 2,4-TDA was carcinogenic in these animals under the specified study conditions. No references or studies found address the effects of 2,4-TDA on the male reproductive system.

B. Medical

1. Classification of Study Groups

Employees were divided into three exposure categories. First was the exposed group who had the highest most current and most likely potential exposure to TDA and DNT in the TDA area or those who frequented the TDA area or worked with the chemical to some extent on a daily basis. Second, an intermediate group consisted of those people who had contact with this material for one to several years on an intermittent basis but who had had no exposure for the last two years. Third, there was a control group who had no known exposure toluene diamine during their employment at Olin. The individuals were assigned to these different categories by reviewing job descriptions, discussing exposures with the individuals themselves and discussing particular individuals with the company and local union representatives to get a combined picture of an individual employee's exposure. This was felt to be extremely important as the results from the initial environmental survey showed relatively low airborne levels of toluene diamine, and this made it impossible to categorize employees on that basis alone.

2. Guidelines for Exclusion from the Comparison Study

Prior to the analysis of the final results, historical information, physical examination findings, and other information that might lead an individual to be excluded from the study were compiled. This was to insure as much as possible that those workers included in the final analysis and comparison had no medical reasons for abnormal semen analysis other than those that might be related to occupational and/or environmental causes. Using a control population from the same plant was designed to negate any socioeconomic or local environmental factors.

There are many factors which can cause an abnormality in semen quality other than environmental or occupational exposures. Exposure to radiation, consumption of certain drugs, some illnesses, and other factors must be eliminated as potential causes for abnormalities by history and/or physical examination. For the workers evaluated in this study, an individual would be excluded because of the presence of a vasectomy, a history of prostate surgery, a history of hormonal therapy, a history of fever of greater than 102^{0}F within three months of the study, the presence of a varicocele or a shriveled or missing testicle on physical examination, infertility problems that predated employment at Olin Chemical Co., as well as those workers who elected not to provide a semen specimen but to participate in the remainder of the study. Workers were not excluded based on a history of hernia, previous mumps (unless orchitis was involved), previous prostatitis, previous venereal disease or physical examination findings of hernia or hydrocele.

VI. RESULTS

A. Environmental

Environmental values for DNT, both personal and area samples, were below the OSHA standard of 1.5 mg/M^3. The highest DNT value of 0.42 mg/M^3 was obtained from an area sample located by a piston pump in the TDA unit during the initial survey. DNT concentrations were lower during the followup survey for the same areas where sampling had been conducted during the initial survey.

Environmental values for TDA were very low, with eight of 14 samples below the analytical method limit of detection. The highest value, 0.39 mg/M^3, was obtained from a personal sample for the Grade 8 operator during the initial survey. The personal exposure samples show no detectable TDA exposure for the Grade 8 operator on January 15 and a small but quantifiable exposure (0.038 mg/M^3) to TDA on January 16, 1980. It is important to note that no loading of TDA was done on January 15. During loading of a TDA tank car the worker must walk up to the dome lid of the car to check the fill level as the fill nears completion. The fill level is checked with a "loading tee" which indicates load level and outage. Vapor emissions were observed escaping from the dome hatch. In depth sampling of the load is done by manually dropping a can inside a container connected to a steel rope into the center of the car, through the hatch, and extracting a sample for quality control. The employee wore a half mask equipped with acid gas/organic vapor cartridges, and butyl rubber gloves during the final loading. Other samples taken during the follow-up survey duplicating those taken initially were also lower. Of 10 samples taken during the follow-up survey, both personal and area, only two were above the sampling method limit of detection.

All employees in the unit or those going into the unit, must wear coveralls, rubber boots, safety glasses (goggles or face shield when handling materials) and a hard hat. There is a question concerning the adequacy of using acid gas/organic vapor cartridges alone since TDA has a freezing point of 99^{0}C (210^{0}F) and the TDA vapors could readily form a particulate at ambient temperatures. Also, the presence of a beard significantly reduces any protection provided by the air purifying respirator in use.

The airborne concentrations of DNT and TDA for both personal and area samples obtained during the initial and follow-up survey are presented in Table I.

B. Medical

Forty-four males volunteered to participate in the medical portion of the study, six of these workers were excluded from the final comparisons because they failed to provide a semen specimen, two workers were excluded from the analysis for medical problems and six individuals' semen specimens could not be examined because of clumping in the liquified specimen. This clumping persisted even after treating the specimens with digestive enzymes. The total study group numbered 30 workers.

The exposed group consisted of nine men, 15 workers were available in this group, only 12 elected to participate, of these 12, one did not supply a semen specimen and two had to be excluded from the analysis, one for medical reasons, the other because of the semen clumping problem. The intermediate group consisted of 12 workers who volunteered from a large group of people with past TDA exposures. The original intermediate group had 18 workers, three workers failed to submit a semen specimen, one had a medical problem and two could not be analyzed because of clumping. The control group consisted of nine workers who volunteered from a large number of non TDA exposed men. The original group consisted of 14 workers, two men failed to submit semen specimens and three were excluded because of semen clumping.

The mean age in the exposed group was 40.3 years with a range of 28-49 years. The mean years employed at Olin was 14.5 years. The mean age in the intermediate group was 38.6 years with a range of 24-60 years and a mean work duration at Olin of 13.3 years. The control group had a mean age of 31.4 years with a range of 24-43 years and the mean work duration at Olin was 8.4 years.

After elimination of those who could not be used for comparison the groups showed no significant differences in any of the information collected by medical history or by physical examination.

Table II shows comparisons of the means and standard deviations regarding the renal profile (BUN, creatinine) and hepatic profile (T. bilirubin, SGOT, SGPT, Alkaline phosphatase) among the control, intermediate and exposed groups. There were no statistically significant differences ($p=.05$) between any of the groups tested.

Table III shows the reported number of spontaneous abortions, congenital defects and total pregnancies in the groups involved. The incidences of these occurrences were compared before and after employment at Olin. There were no statistically significant differences ($p=.05$) between any of the groups. The exposed and control groups did have a $p=.08$ value for spontaneous abortions with the exposed group reporting a higher percentage.

Table IV shows the sperm volumes, sperm counts and morphologic picture of the groups. Mean, standard deviations and medians are included. All of the comparisons between groups show the sperm counts to be significantly lower ($p=.03$) in the exposed when compared to the control group and the exposed group to have a significant reduction in large forms on morphological evaluation when compared to the control group.

VII. DISCUSSION

Little is known regarding the potential gonadal toxicity of TDA and DNT, the two major chemicals to which the employees are exposed in the TDA area. The reported problems encountered with exposure to DNT are those related to anoxia secondary to the formation of methemoglobin. Cyanosis with headache, irritability, dizziness, weakness, nausea and vomiting and other symptoms may occur. Ethyl alcohol ingestion appears to increase susceptibility and repeated or prolonged exposure may cause anemia.[13] TDA, theoretically can cause methemoglobinemia and the same signs and symptoms as DNT but has not been reported to do so.[14] TDA can produce liver damage with jaundice that may be related to damage of the epithelium of the large biliary duct with passage of bile into the lymph ducts, the thoracic ducts and ultimately the blood, it may be of hemolytic nature or it may cause biliary thrombi forcing the blockage of the central biliary ducts causing a static icterus.[15] TDA has been shown to be inhaled or absorbed through the skin of animals[16] and absorbed through human skin[17].

While the analine-like effects of these compounds are well documented, the major organ susceptibility appears to be in the liver. Chronic studies indicate the possibility of carcinogenesis,[9,12] however, little if any substantive evidence exists with respect to the effects of TDA and DNT on the male reproductive system or on pregnancy outcome.

The important findings in this study can be considered neither completely conclusive nor can they be dismissed as insignificant. The population size n=30 is small and a large number of individuals must be investigated to corroborate the findings at this plant.

Three major findings discovered by this study are deserving of further comment. First is the borderline significant ($p=.08$) increase in the spontaneous abortions in the exposed group when compared to the control group using pregnancies before and after employment at Olin. This borderline significant increase in the number of spontaneous abortions before and after Olin employment in the exposed group is of interest, but because of the many other variables involved, this should be examined carefully.

The wives and husbands histories agreed quite well with one another when historically relating number and dates of miscarriages in all the groups questioned. However, the group sizes were small, the women had advancing age as a significant factor, previous pregancy histories were not similar from group to group and recall for events occurring in the past is always questionable. Many spontaneous abortions cannot be documented and so this area is open to much bias and error in reporting. Despite these problems the spontaneous abortions issue will be addressed in future studies in the hopes of gathering more information to futher investigate this problem.

The second finding is the significant reduction (p=.015) in the numbers of large morphologic forms in the exposed group when compared to the other groups. The meaning of this is unknown at the present time and needs further investigation in future studies.

The third and potentially the most significant finding is the reduction in sperm counts in the exposed versus the control group. The small sample size and the wide range of normal values for sperm counts necessitated using a square root transformation of the data for comparison purposes.[18] Using this method the exposed workers had a statistically significant reduction in counts (p=.03) when compared to the control workers. The difference persisted when these data were corrected for age. There appeared to be no direct dose response relationship to time in the TDA area although all workers had been employed for at least one year in that area.

These results are strongly suggestive of a reproductive problem but more workers must be studied to reenforce and corroborate the data already collected.

Environmental values, both personal and area, for TDA and DNT were low with about half the total samples falling below the analytical limits of detection. Reported environmental values undoubtedly reflect the results of improved spill containment and cleanup and increased maintenance of the system. Exposure by inhalation appeared limited due to the construction of the unit, methods of handling the materials, and necessity to keep the compounds in a heated, steam jacketed, air excluded system to prevent solidification and degradation of the product. Employees were conscientious about work practice but the layout of facilities in the control room building did not lend itself to separation of contaminated (e.g., work clothes, protective equipment) and uncontaminated areas (e.g., lunch area, street clothes locker, offices of TDA unit supervisory staff).

Due to the absence of any recognized TDA standard it is not clear what significance should be attached to the levels found during this survey. The documentation of carcinogenic activity in rats suggests that TDA exposures be kept as low as possible and that the material be handled as a suspected carcinogen.

VIII. CONCLUSIONS

The results of medical testing strongly suggest a problem of toxicity to the male reproductive system affecting workers exposed to TDA and DNT.

Environmental values declined over the course of the investigation to where DNT and TDA levels were negligible. The environmental and medical results together suggest that past exposures were higher before the study was initiated.

IX. RECOMMENDATIONS

1. Increased maintenance efforts, including cleaning, replacement and/or repacking of valve seats, pumps, and pump connections should be continued. Insure that all access points to the system seal properly. Completion of spill containment and cleanup facilities at loading and unloading areas is recommended.

2. A method of loading TDA tank cars which does not require the operator to get up by the open hatch cover should be instituted. It was reported that this plant was the only one still using a top loading procedure.

3. Exploration of an alternative method of doing depth sampling should be explored, one in which the operator would not need to stand directly adjacent to the open hatch. A suggested example was the use of a pulley system on a moveable arm from which the sample container could be dropped into the tank car.

4. Continued use of protective clothing will prevent skin exposure. The use of air purifying respirators by bearded employees should not be permitted. Proper use of protective clothing and respiratory protection by maintenance crews is also necessary.

5. Clean and contaminated areas of the control room building should be more completely separated.

6. A medical follow-up program for exposed employees should be instituted.

X. NIOSH Future Actions

1. Further analysis of the serum specimens collected at the time of the study will be completed for serum testosterone, follicle stimulating hormone and leutinizing hormone because of the results of the semen analyses.

2. Other plants using TDA should be identified and similar studies conducted to determine if the problems identified in this evaluation exist among other TDA workers.

3. NIOSH will recommend that the National Toxicology Program conduct animal studies to assess whether similar reproductive effects can be demonstrated in animals.

XI. AUTHORSHIP AND ACKNOWLEDGEMENTS

Evaluation Conducted and Report Prepared by:

Steven H. Ahrenholz, M.S.
Principal Environmental Investigator
Industrial Hygiene Section
Hazard Evaluations and Technical Assistance Branch
Cincinnati, Ohio

Channing R. Meyer, M.D.
Assistant Professor of Environmental Health
Department of Environmental Health
University of Cincinnati Medical Center
Cincinnati, Ohio

Originating Office:

Hazard Evaluations and Technical Assistance Branch
Division of Surveillance, Hazard Evaluations and Field Studies
NIOSH
Cincinnati, Ohio

Report Typed by:

Jackie Woodruff
Clerk/Typist
Industrial Hygiene Section

XII. DISTRIBUTION AND AVAILABILITY OF DETERMINATION REPORT

Copies of this report are currently available upon request from NIOSH, Division of Technical Services, 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 22161.

Copies of this report have been sent to:

a. Authorized employee representative
b. Authorized representative of Local 320, International Brotherhood of Firemen and Oilers
c. Olin Chemicals Group
d. Kentucky State Health Commissioner
e. Kentucky State Epidemiologist
f. Kentucky State OSH Agency
g. U.S. Department of Labor, Region IV
h. NIOSH, Region IV

For the purpose of informing the nine "affected employees", the employer shall promptly "post" the determination report for a period of 30 days in a prominent place near where exposed employees work.

XIII. REFERENCES

1. NIOSH Manual of Analytical Methods. 2nd Edition, Vol. 1, DHEW (NIOSH) Pub. No. 77-157-A, 1977.

2. NIOSH Manual of Analytical Methods, 2nd Edition, Vol. 4, DHEW (NIOSH) Pub. No. 78-175, 1978.

3. Clinical Diagnosis by Laboratory Methods. Ed. Todd and Sanford. Publisher W. B. Saunders, Philadelphia, Pennsylvania, 1978.

4. General Industry. OSHA Safety and Health Standards (29 CFR 1910), U.S. Department of Labor, OSHA 2206, Revised November 1978.

5. Documentation of the Threshold Limit Values. American Conference of Governmental Industrial Hygienists, 3rd Edition, 1971, 4th Printing 1977, page 93.

6. Proctor, N.H. and V.P. Hughes: Chemical Hazards of the Workplace. J.B. Lippincott Company, pages 233-235, 1978.

7. Threshold Limit Values for Chemical Substances and Physical Agents in the Workroom Environment with Intended Changes for 1979. American Conference of Governmental Industrial Hygienists, Cincinnati, Ohio 45201.

8. Filatova V.S., et. al.: Hygienic Aspects of Work and Health of Workers in the Production of Toluylenediamine. Hygiene and Sanitation, Vol. 35 Nos. 1-3, pages 189-193, 1970.

9. Kinkel, H.J. and Holzman, S.: Study of Long-term Percutaneous Toxicity and Carcinogenicity of Hair Dyes in Rats. Fd. Cosmet. Toxicol. Vol. II. pages 641-648, Pergamon Press. 1973.

10. Cardy, R.H.: Carcinogenicity and Chronic Toxicity of 2,4-Toluenediamine in F344 Rats. J Nat Cancer Institute. Vol. 62, No. 4, pages 1107-1116, 1979.

11. 2,4-Diaminotoluene IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Man, International Agency for Research on Cancer, Vol. 16, pages 83-95, 1978.

12. ITO, N, et. al.: The development of Carcinoma in the Liver of Rats Treated with m toluylene diamine and the Synergistic and Antagonistic Effects With Other Chemicals. CA. Research 29:1137-1145. May 1969.

13. Occupational Diseases: A Guide to Their Recognition. DHEW Publication No. 77-181, pages 278-279, 1977.

14. Patty, F.A.: Industrial Hygiene and Toxicology. 2nd Editon, Vol. 2, pages 2101-2121, 1963.

15. Green, H. H. and W. Schall: Beitr, Pathol Anat. U. Allegen.Pathol. 89 61 1932.

16. Kiese, M., et. al.: Absorption of Some Phenylene Diamines Through the Skin of Dogs. Tox. and Applied Pharm. 12:495-507, 1968.

17. Kiese, M. and Rauscher, E.: The Absorption of p-Toluenediamine Through Human Skin in Hair Dyeing. Tox. and Applied Pharm. 13:325-331.

18. Snedecor, G.W., Cochran, W.G.: Statistical Methods. 6th Edition, pages 325-326. Ames Press.

Table I

Sampling Results for Dinitrotoluene (DNT) and Toluene Diamine (TDA)
for September 26, 1979 and January 15 & 16, 1980

Olin Chemical Group
Brandenburg, Kentucky

Sample Description Job Title or Location	Sample Type[a]	DNT Concentration (mg/M^3) (duration minutes)[b] 9/26/79	1/15/80	1/16/80	TDA Concentration (mg/M^3) (duration minutes)[b] 9/26/79	1/15/80	1/16/80
Grade 8 operator	BZ	0.013 (370)	N.D.[c] (313)	0.014 (399)	0.39 (370)	N.D. (310)	0.038 (398)
Grade 10 operator	BZ	0.023 (420)	N.D. (326)	0.006 (422)	0.023 (420)	N.D. (265)	N.D. (422)
Grade 14 operator	BZ	--	--	0.008 (414)	--	N.D. (337)	N.D. (414)
DNT piston pumps	A	0.42 (390)	--	0.10 (436)	--	--	--
Base of methanol topping Column (pump P56-18B)	A	--	--	--	0.023 (376)	N.D. (477)	N.D. (435)
Column (pump P56-18B) Base of falling film evaporator (pump P51-19B)	A	--	--	--	0.008 (420)	0.006 (474)	--
TDA pump P51-19A	A	--	--	--	--	--	N.D. (435)
TDA unit control room deck	A	--	N.D. (496)	--	--	--	--

Evaluation Criteria: (reference 4) Dinitrotoluene: 1.5 mg/M^3

a. BZ denotes breathing zone sample
A denotes area sample
b. Generally full shift sampling was conducted.
c. N.D. denotes none detected.

TABLE II

MEAN AND STANDARD DEVIATION VALUES OF THE RENAL AND HEPATIC PROFILES OF THE CONTROL, INTERMEDIATE AND EXPOSED GROUPS STUDIED AT OLIN CHEMICAL CO.

CONTROL n=9

	BUN	Creatinine	T.Bili.	SGOT	SGPT	Alk. Phos.
Mean	14.9	1.18	0.42	22.1	22	81
Std.Dev.	±2.7	±0.10	±0.08	±6.3	±15.2	±17.6

INTERMEDIATE n=12

	BUN	Creatinine	T.Bili.	SGOT	SGPT	Alk.Phos.
Mean	15.9mg/dl	1.18mg/dl	0.48mg/dl	22.3u/l	21u/l	82.2u/l
Std.Dev.	±4.4	±0.15	±0.27	±7.1	±11.3	±15.5

EXPOSED n=9

	BUN	Creatinine	T.Bili.	SGOT	SGPT	Alk.Phos.
Mean	16.3mg/dl	1.24mg/dl	0.43mg/dl	27.7u/l	32.8u/l	76.3u/l
Std.Dev.	±6.9	±0.14	±0.19	±10.8	17.3	±30.8

TABLE III

TOTAL PREGNANCIES, LIVE BIRTHS, CONGENITAL DEFECTS AND SPONTANEOUS ABORTIONS WITHIN GROUPS AT OLIN CHEMICAL

CONTROL

	Totals	Before Olin Employment	After Olin Employment
Total Pregnancies	23	9	14
Live Births	19	8	11
Congenital Defects	1	1	0
Spontaneous Abortions	4	1	3

INTERMEDIATE

	Totals	Before Olin Employment	After Olin Employment
Total Pregnancies	49	27	22
Live Births	40	24	16
Congenital Defects	4	2	2
Spontaneous Abortions	9	3	6

EXPOSED

	Totals	Before Olin Employment	After Olin Employment
Total Pregnancies	44	26	18
Live Births	36	24	12
Congenital Defects	0	0	0
Spontaneous Abortions	8	2	6

TABLE IV

MEDIAN, MEAN AND STANDARD DEVIATION VALUES
OF SPERM COUNT, VOLUME AND MORPHOLOGIC
PARAMETERS IN THE CONTROL, INTERMEDIATE
AND EXPOSED GROUPS AT OLIN CHEMICAL CO.

CONTROL n=9

	Volume	Count	Oval	Large	Small	Taper	Amorph	Dup Heads	Dup Tails	Sperma-tids
Mean	2.5cc	156.8×10^6	52	7.3	14.6	0.4	24.6	.2	0.0	.4
Std.Dev.	±1.4cc	±111.8	±8.6	±4	±7.2	±0.4	±6.5	±.6	±0.0	±.9
Median	-	121×10^6	-	-	-	-	-	-	-	-

INTERMEDIATE n-12

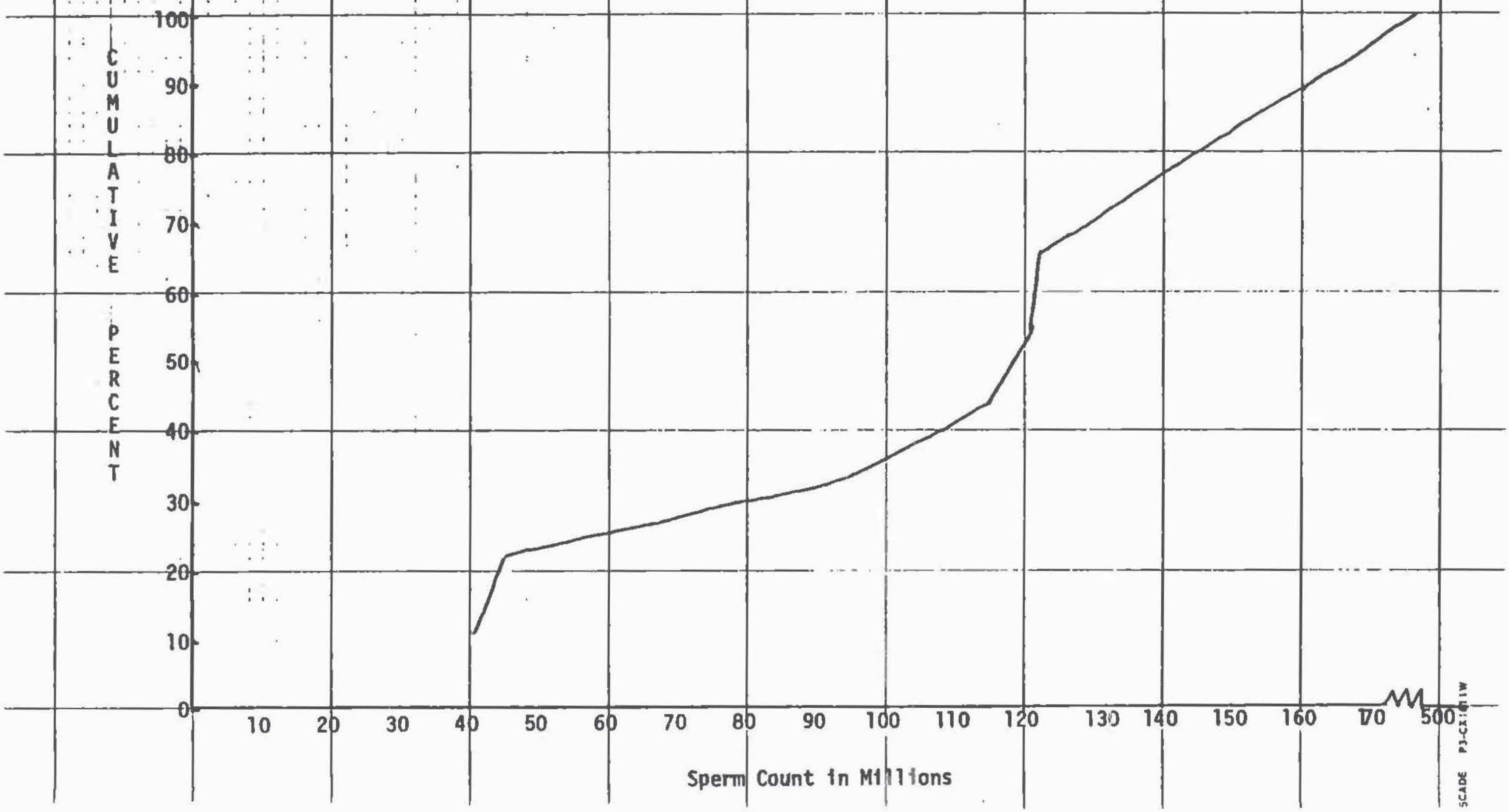
	Volume	Count	Oval	Large	Small	Taper	Amorp	Dup Heads	Dup Tails	Sperma-tids
Mean	3.0cc	121.3×10^6	55.5	3.2	11.8	1.2	27.9	0.0	.08	0.2
Std.Dev.	±1.8cc	±95.1	±18	±3.0	±6.1	±1.1	±13.9	±0.0	±.3	±0.6
Median	-	95×10^6	-	-	-	-	-	-	-	-

EXPOSED n=9

	Volume	Count	Oval	Large	Small	Taper	Amorp	Dup Heads	Dup Tails	Sperma-tids
Mean	2.8cc	55.9×10^6	48.1	3.5	14.2	2.8	29.7	0.3	0.2	1.0
Std.Dev.	±2.1cc	±47.3	±8.5	±1.9	±9.7	±3.5	±76	±0.5	±0.4	±1.4
Median	-	49×10^6	-	-	-	-	-	-	-	-

Figure 1

Cumulative Percent Distribution Sperm Count Control Group at Olin Chemical Co.



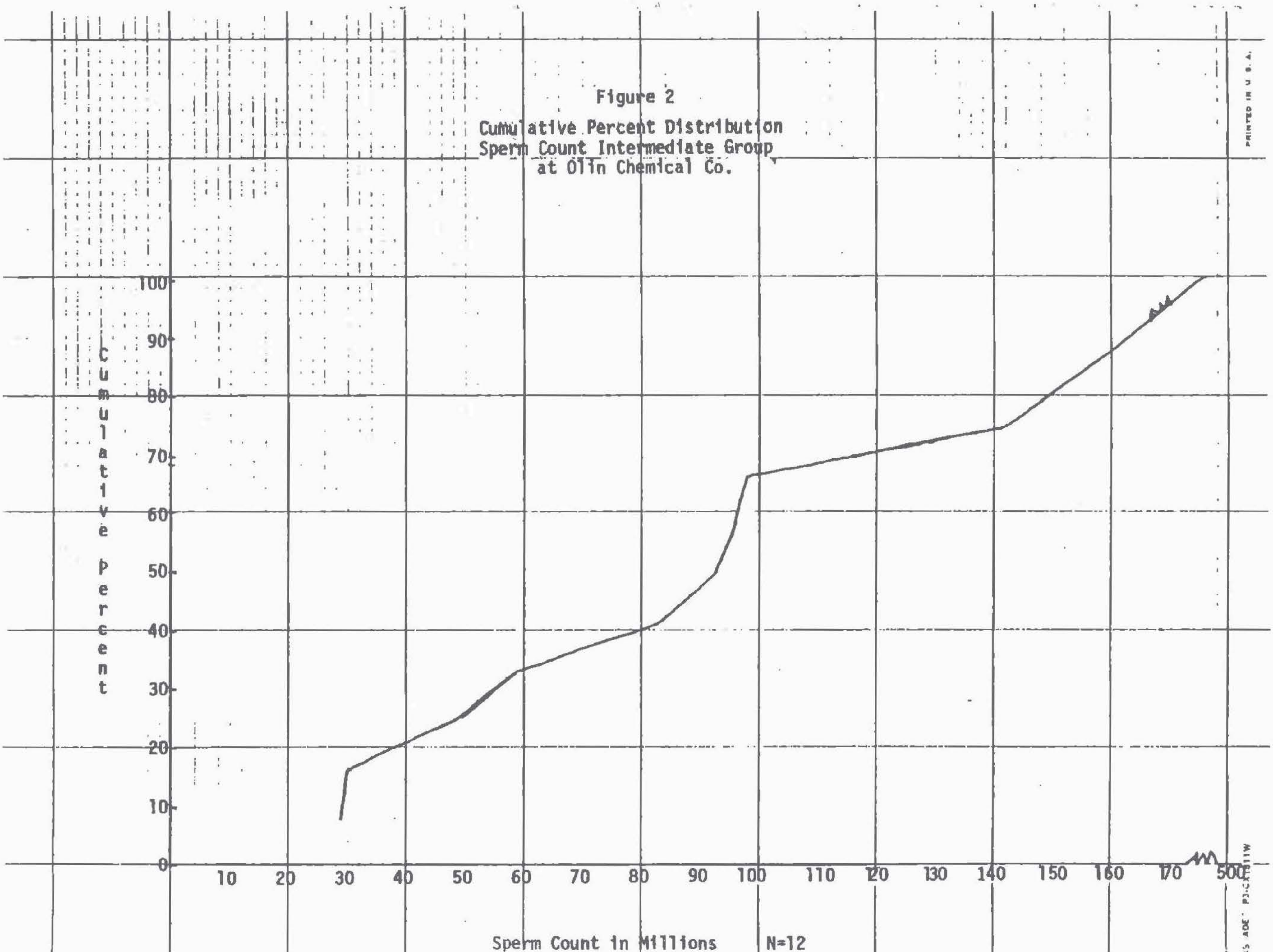


Figure 2
Cumulative Percent Distribution
Sperm Count Intermediate Group
at Olin Chemical Co.
Cumulative Percent
100
90
80
70
60
50
40
30
20
10
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
500
Sperm Count in Millions
N=12

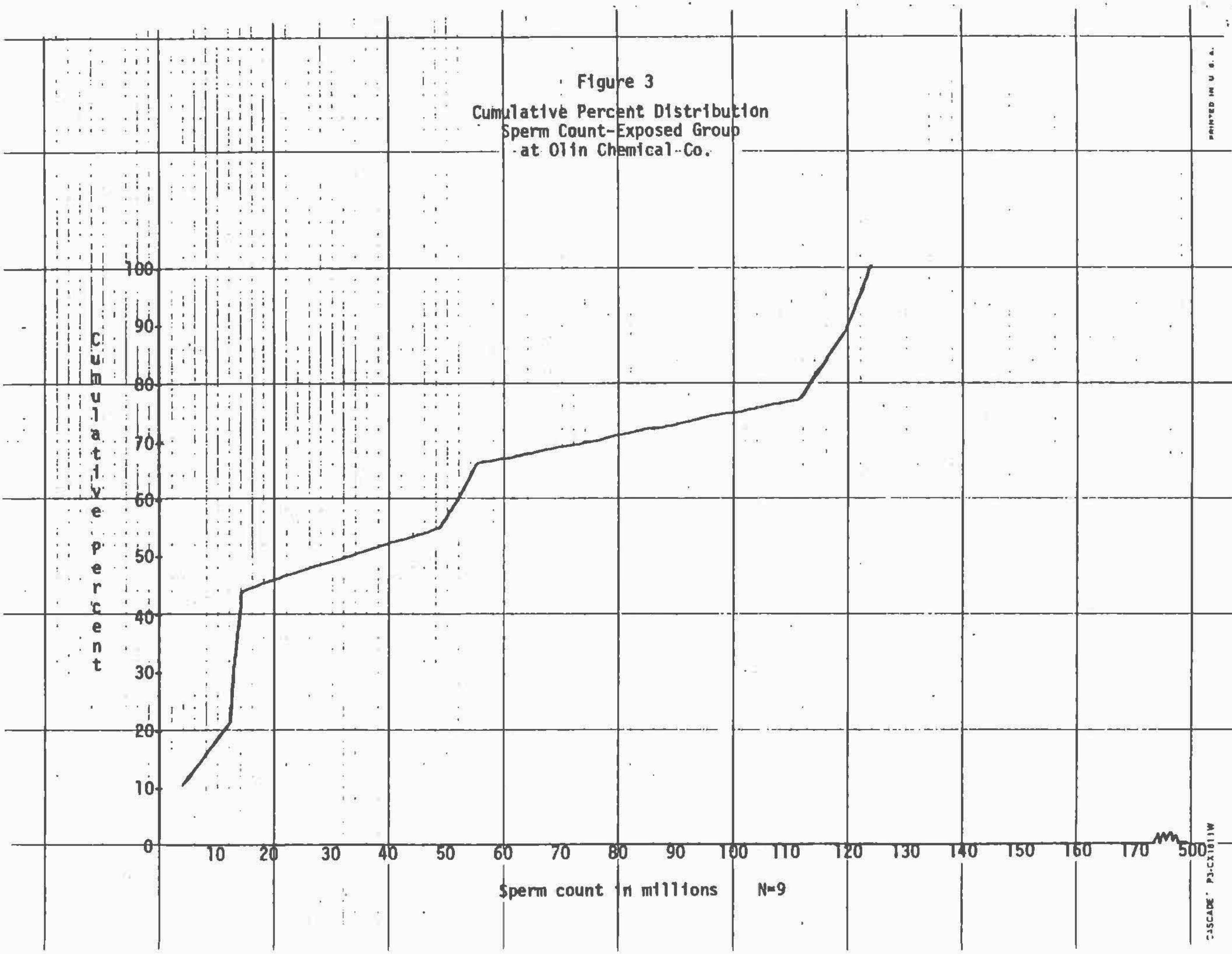


Figure 3
Cumulative Percent Distribution
Sperm Count-Exposed Group
at Olin Chemical Co.
Cumulative percent
100
90
80
70
60
50
40
30
20
10
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
500
Sperm count in millions N=9
PRINTED IN U.S.A.
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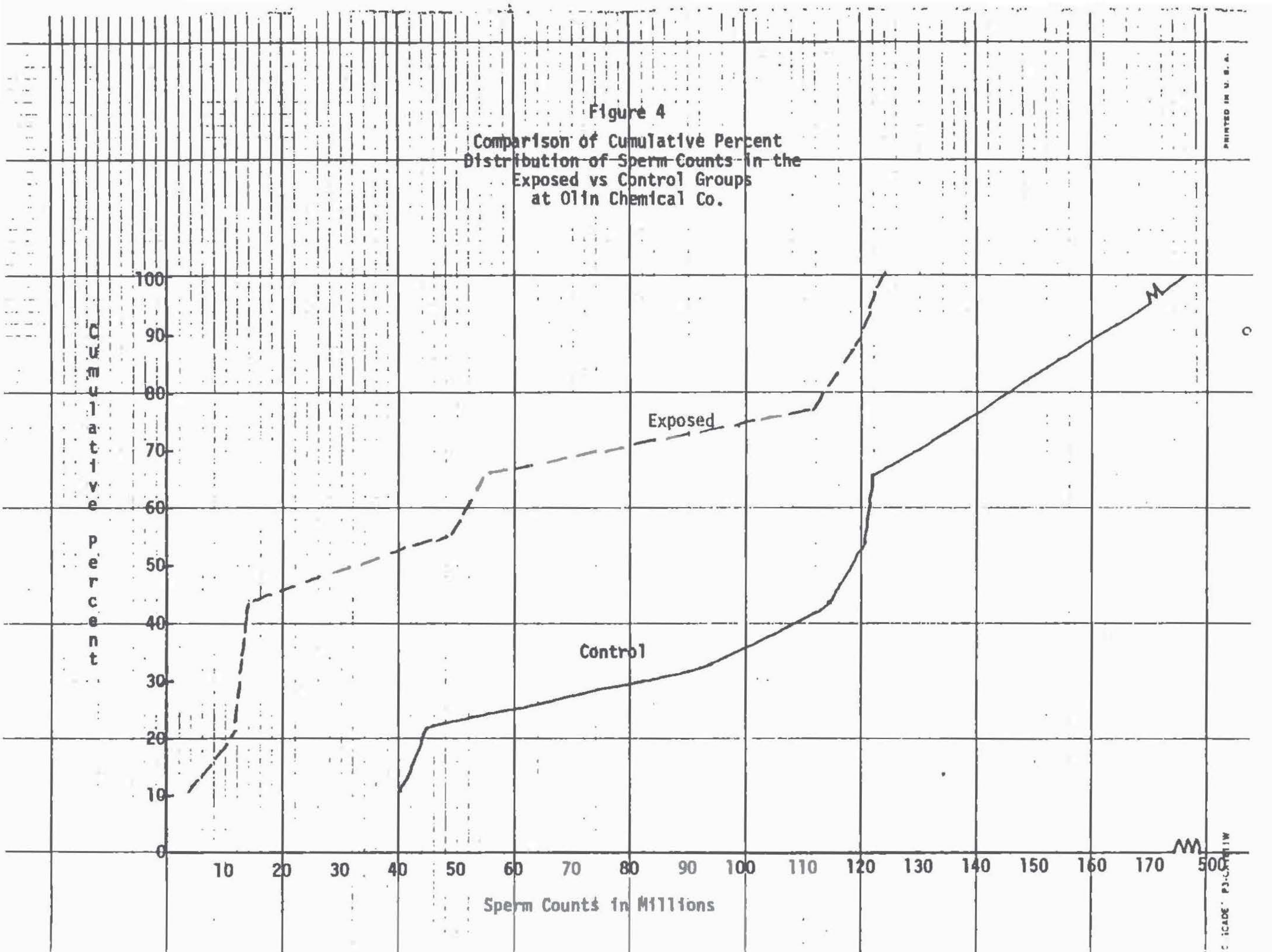
Figure 4
Comparison of Cumulative Percent
Distribution of Sperm Counts in the
Exposed vs Control Groups
at Olin Chemical Co.
Exposed
Control
Cumulative Percent
0
10
20
30
40
50
60
70
80
90
100
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
500
Sperm Counts in Millions