U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES ■ Public Health Service
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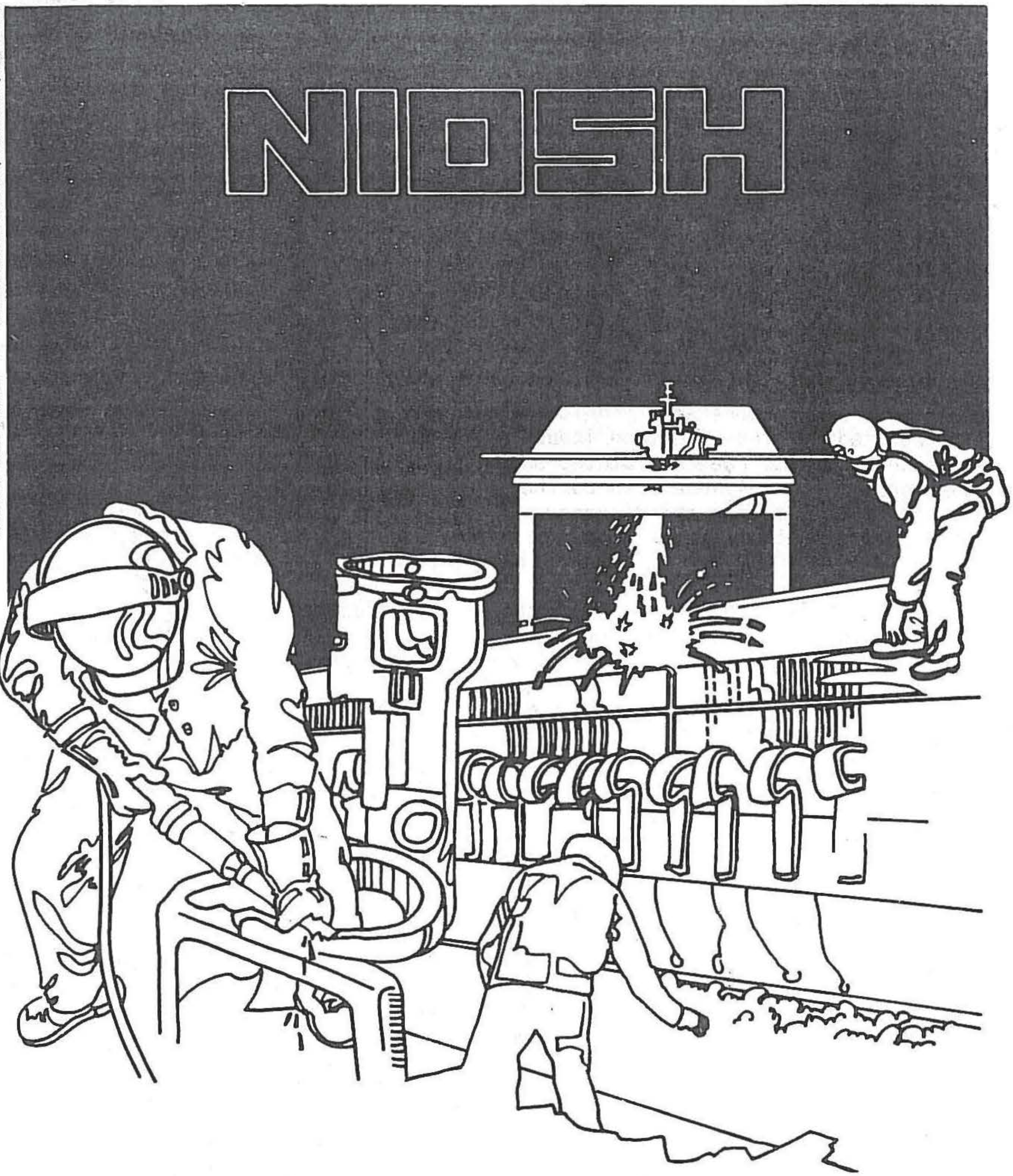

Health Hazard Evaluation Report

HETA 82-146-1388
BOEING VERTOL COMPANY
PHILADELPHIA, PENNSYLVANIA

PREFACE

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

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

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BOEING VERTOL COMPANY
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I. SUMMARY

In March 1982, the National Institute for Occupational Safety and Health (NIOSH) was requested to evaluate occupational exposures to chemicals such as epoxy resins and curing agents (including aromatic amines) in the pattern and blade shops at Boeing Vertol Company, Philadelphia, Pennsylvania. In April and June 1982, NIOSH conducted initial environmental and medical surveys and follow-up surveys were conducted in July and September 1982, and in May 1983.

Environmental air samples were collected to evaluate employee exposures to inert dust, methylenedianiline (MDA), ethylenediamine, methyl isobutyl ketone (MIBK), toluene, cyclohexanone, and butyl glycidyl ether (BGE). NIOSH investigators reviewed medical records and interviewed 20 employees in the pattern shop who work with the epoxy resins and 20 employees in Building 3-25 (packaging and storeroom) who do not. To evaluate the possibility of excess deaths due to cancer-related causes, NIOSH conducted a proportional mortality ratio (PMR) analysis from death notices obtained from the company for all employees known to have died in the years 1968-1980 inclusive.

Airborne concentrations of ethylenediamine and of cyclohexanone were below the limit of detection (0.0005 mg/sample and <0.01 mg/m^3, respectively). Airborne concentrations of dust were 0.2 and 0.41 mg/m^3 in the pattern shop and ranged from 0.17 to 1.30 mg/m^3 (nine samples) in the blade shop. Airborne concentrations of MDA ranged from below the limit of detection to 0.46 mg/m^3; of MIBK, from 2.75 mg/m^3 to 85.0 mg/m^3; of toluene, from 1 to 4 mg/m^3 and of BGE, from <0.01 to 3.0 mg/m^3. All levels were below the applicable environmental criteria and OSHA standards.

The reported prevalence of skin problems among pattern makers, 14 (70%) of 20, was significantly greater than that among packers and storekeepers, 7 (35%) of 20 ($p<0.05$). PMR analysis of 179 white male deaths among employees who had ever worked in areas with potential exposure to epoxy resins and amine hardeners identified a statistically significant excess for cancer of large intestine (7 observed, 3.10 expected), cancer of bladder (3 observed, 0.80 expected), lymphosarcoma and reticulosarcoma (3 observed, 0.87 expected). In a proportional cancer mortality ratio analysis, only the excess of cancer of the bladder remained significantly elevated. Two cases of bladder cancer among living current or former employees were also noted, both of whom had worked in the pattern or blade shops.

NIOSH has determined that a health hazard exists for employees working with epoxy resins and amine hardeners at Boeing Vertol Company for development of skin problems. Recent toxicological evidence suggests that one amine hardener, MDA, is a suspect carcinogen; it has a structure similar to known human bladder carcinogens. This investigation suggests an association between bladder cancer and work in areas with past or present potential exposure to MDA. Recommendations to reduce employee exposures are contained in Section VIII of this report.

KEYWORDS: SIC 3728 (Aircraft Parts and Auxilliary Equipment, not Elsewhere Classified), epoxy resins, amine hardeners (curing agents), methylenedianiline, dermatitis, cancer, bladder cancer.

II. INTRODUCTION

On March 19, 1982, the National Institute for Occupational Safety and Health (NIOSH) received a request from Local 1069, United Auto Workers, to evaluate employee exposures to epoxy resins, curing agents (including aromatic amines) and chemicals used in the Pattern Shop and the Blade Shop at Boeing Vertol Company, Philadelphia, Pennsylvania. Employee concerns included skin problems and rashes and possible excess deaths due to cancer-related causes.

NIOSH conducted initial environmental and medical surveys at Boeing Vertol in April and June 1982, respectively. NIOSH conducted a follow-up environmental survey in September 1982 and follow-up medical evaluations in July 1982 and May 1983. Interim reports were issued in May 1982 and in August 1983.

III. BACKGROUND

Boeing Vertol Company designs and manufactures helicopters. Twenty employees are engaged in Building 3-56 (pattern shop) making patterns, and 250 employees are engaged in making helicopter blades in Building 3-07. The plant employed about 4600 workers in 1982. During peak production and employment in the late 1960s, the comparable numbers of employees in departments 3-56, 3-07 (or their predecessor departments) and total plant were about 300, 1500 and 14,000, respectively.

In Building 3-56, a wooden mold is made. This mold then is lined with successive layers of fibrous glass and epoxy resin. The epoxy resin can be air dried or baked in an oven. After the pattern is made, the excess material is cut off and the pattern is trimmed. In Building 3-07 the blades are manufactured. Fibrous glass impregnated with epoxy resin is cut to a pattern. This material is then spread on a honeycomb material and baked in ovens. When the resin is cured, the blade is trimmed and balanced. If corrections for balance are necessary, the voids are filled with a two-component epoxy resin. Steel parts necessary for the blades are prepared by an outside contractor. After final machining at Boeing, a protective coating containing methyl isobutyl ketone, toluene and cyclohexanone is applied, either manually or by a dipping operation.

Wet lay-up work using layers of fibrous glass and epoxy systems is still performed much of the time by pattern makers in the pattern shop and was performed in the past in the blade shop. In recent years, in the blade shop, materials pre-impregnated with epoxy resins have been used, and little wet application is involved.

IV. EVALUATION DESIGN AND METHODS

A. Environmental

1. Methylenedianiline - Breathing zone samples were collected during the pattern lay-up, in impingers containing Marcali solution, connected in series. These samples were analyzed by NIOSH method P&CAM #142.[1] The limit of detection was 0.2 micrograms (ug) per sample and the limit of quantitation was 1.0 ug per sample.

2. Ethylenediamine - Three breathing zone samples were collected during the pattern lay-up, on sampling trains consisting of a cassette containing a citric acid coated membrane followed by a citric acid coated silica gel tube. These samples were analyzed by NIOSH method P&CAM #276.[2] Under the condition of this analysis 0.5 ug could have been detected.

3. Nuisance dust - Prior to performing the environmental study, a bulk sample was submitted to the NIOSH laboratory for a preliminary scan for silica and asbestos. These materials were not detected. Personal total dust levels were evaluated during the sawing, trimming and sanding operations. Breathing zone samples were collected on pre-weighed mixed cellulose filters and analyzed gravimetrically. The precision of weighings at one sitting was 0.1 milligram (mg).

4. Methyl Isobutyl Ketone, Toluene, Cyclohexanone - Environmental air samples were collected on charcoal tubes at the parts dipping and manual application of EC 1660 coating. According to Boeing Vertol, the solvents were methyl isobutyl alcohol, toluene, and cyclohexanone. The samples were analyzed by NIOSH method P&CAM #127.[1] The limit of detection for all the above solvents was 0.01 mg/sample.

5. Butyl glycidyl ether - Breathing zone air samples were collected on charcoal tubes during the void filling of the blades, a process in which the epoxy is mixed and injected into fixed marked areas of the blade. These samples were analyzed by NIOSH method P&CAM #S-81.[3] The limit of detection was 0.01 mg/sample.

B. Medical

On June 2-4, 1982, NIOSH investigators conducted private interviews with all 20 employees in the pattern shop who work with epoxy resins and curing agents, and with a sample of 20 employees in building 3-25 (10 from packaging and 10 from the storeroom) who did not work with epoxy resins or other chemicals. The questionnaire included inquiries about demographics, skin problems and other symptoms, exacerbating or relieving factors, possible etiological agents and whether the workers had had cancer. Participants' exposed skin was examined for abnormalities. The records of employees who were alive and known to have cancer were reviewed for histological diagnoses.

C. Epidemiologic (Proportional Mortality Ratio Study - PMR)

On June 30-July 2, 1982, discussions were held regarding plans for a mortality study to evaluate whether excess cancer might be occurring or have occurred in the past among employees in the pattern and blade shops. Bladder and colon were sites of subjective concern that had been mentioned *a priori* by the union. To this end, NIOSH obtained copies of *all* "death notices" and available death certificates of deceased active or retired workers for the years 1968-1980 inclusive. These death certificates had been collected by the company as part of a death benefits program. An employee must have been employed 10 years to be eligible for these benefits. Causes of death were determined by a nosologist from death certificates and coded according to the Eighth Revision of the International Classification of Diseases, Adapted (ICDA). The social security number, name, sex, race, birthdate, date of death, underlying and contributing causes of death were keypunched and a computer file created. In all, there were 552 death notices collected by the company. For six of these known dead, death certificates were not available; they were coded as "cause unknown". Of the deaths, 502 (91%) were white males. All analyses were confined to this group. A NIOSH computer program was used to calculate cause-specific expected deaths for each five-year age group and five-year calendar time periods. This was done by multiplying the cause- and age-specific proportionate mortality of the United States white males for 5-year age and calendar time periods, by the total number of deceased employees within each group. These cause-specific expected deaths were then summed over all five-year age groups. Proportionate mortality ratios (PMRs) for each cause were then defined by dividing the observed number of deaths by the expected number of deaths. This analysis was done for all 502 white male deaths.

A PMR study can only evaluate the proportion of one cause of death relative to another. Thus, a deficit in one cause of death will necessarily result in all other causes of death appearing proportionately greater. Specifically, deficits of non-cancer deaths could make the proportion of cancer deaths appear artificially high. To address this problem, proportional cancer mortality ratios (PCMRs) were calculated. The procedure is the same as the PMR except that the expected numbers of specific cancer deaths were calculated from the total number of cancer deaths, rather than all deaths.

NIOSH obtained from the company the work histories of those employees for whom death certificates had been collected. The last of these arrived in April 1983. Those employees considered to have worked for more than one month in an area potentially exposed to epoxy resins and curing agents were selected according to the following rules for "exposed areas":

(1) Prior to 1965: Building 102 (Center 1) and organizations 3930 or 3960 (prior location of pattern shop)
(2) Prior to 1960: Building 700 (prior location of blade shop)
(3) Building 3-07 (current location of blade shop)
(4) Building 3-56 (current location of pattern shop)
(5) certain 8000 organizations (rotating jobs such as inspectors)

On May 13, 1983, at the request of the company, a follow-up visit was conducted. During this visit, the type of study and possible follow-up of any positive results were explained. In addition, the 8000 organizations involving rotating jobs, such as inspectors, were discussed. Since it had been noticed that the building indicated on the work history may not accurately reflect location of work for this subgroup, the possibility of misclassification due to inconsistencies in the work histories of such employees was explained jointly to union and management representatives. To address this possibility, individuals who knew the approximately 50 deceased employees who had ever held an 8000 job, examined their detailed histories. This assessment was obtained in July 1983. A total of 200 individuals were identified who met the above criterion for ever working in an exposed area, of whom 179 were white males. PMR and PCMR studies were then performed on this subgroup.

V. EVALUATION CRITERIA

A. Environmental Criteria

As a guide to the evaluation of the hazards posed by workplace exposures, NIOSH field staff employ environmental evaluation criteria for assessment of a number of chemical and physical agents. These criteria are intended to suggest levels of exposure to which most workers may be exposed up to 10 hours per day, 40 hours per week for a working lifetime without experiencing adverse health effects. It is, however, important to note that not all workers will be protected from adverse health effects if their exposures are maintained below these levels. A small percentage may experience adverse health effects because of individual susceptibility, a pre-existing medical condition, and/or a hypersensitivity (allergy).

In addition, some hazardous substances may act in combination with other workplace exposures, the general environment, or with medications or personal habits of the worker to produce health effects even if the occupational exposures are controlled at the level set by the evaluation criterion. These combined effects are often not considered in the evaluation criteria. Also, some substances are absorbed by direct contact with the skin and mucous membranes, and thus potentially increase the overall exposure. Finally, evaluation criteria may change over the years as new information on the toxic effects of an agent become available.

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

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

Following are the evaluation criteria for sampled substances:

	Evaluation Criteria (mg/m^3)		
Substance	NIOSH	OSHA	ACGIH
Butyl glycidyl ether	30	270	135
Dust (nuisance particulate)	none	15	10
MDA	none	none	0.8 (TLV) 4.0 (STEL)
MIBK	200	410	205
Toluene	375	750	375

B. Physiological Effects

1. Solvents

Solvents used in the protective coating include methyl isobutyl ketone, toluene and cyclohexanone. Exposure to organic solvents can cause varying degrees of anaesthesia, headaches, lightheadedness, "drunkenness", and even unconsciousness. They may have a disagreeable odor and can be irritating to the eyes and upper respiratory tract (nose and throat). Skin contact with solvents can, if prolonged, remove the natural oil from the skin causing dryness and cracking.

2. Epoxy resins and glycidyl ethers[6,7]

Glycidyl ethers are often used as diluents in epoxy resin systems and are formed by the reaction of various alcohols with epichlorohydrin. As with epoxy resins in general, they can be both irritants and sensitizers of the skin. Some of these compounds have been associated in laboratory animals with adverse effects on the hematopoietic (blood cell-forming) system and on the testes, including testicular atrophy with decreased spermatogenic activity. Positive tests for mutagenicity for some glycidyl ethers have been reported but only one, butyl glycidyl ether (BGE), was mutagenic in mammals in the dominant lethal test.[6] Tumorigenic activity in laboratory animals has also been reported.[6]

3. 4,4' Methylenedianiline (MDA)

Although MDA is used at this facility as an aromatic amine type epoxy hardener, about 98% of MDA is used to produce methylene bisphenyl isocyanate (MDI). The 1981 consumption of MDA (pure and polymeric) in the U.S. was 230 million pounds.[8] Of that total, only 4-5 million pounds was used for non-MDI uses.[8] The non-MDI uses have been classified into four categories: intermediates in pigments, antioxidants and curatives in the rubber industry, epoxy hardening agents, and raw materials in the preparation of resins.[8] In epoxy applications, MDA is employed as a cross-linking agent to produce a harder, higher molecular weight material that provides improved chemical resistance and good high temperature properties for applications such as coatings, laminates, casting and molding, flooring and adhesives.

MDA was reported to cause acute toxic hepatitis, in a community setting in the 1960s[9] ("Epping Jaundice") and in the workplace in the 1970s,[10] and has also been associated with contact dermatitis. Soon thereafter, the long-term effects were tested in an 8-month feeding study in which liver and kidney tumors in rats were induced as well as chronic liver changes.[11] It was noted that MDA acted like aminofluorene to which it is structurally related. Also of note, is the similarity of its structure to known human bladder carcinogens such as benzidine (Figure 1). The recently completed bioassay by the National Toxicology Program[12] found that under the conditions of the bioassay, 4,4' methylenedianiline diydrochloride was considered carcinogenic for F344/N rats and $B6C3F_1$/N mice of each sex, causing a significantly increased incidence of thyroid, liver and adrenal tumors. In addition, several rare tumors observed in the study (bile duct adenomas in male rats and ovarian granulosa-cell tumors and urinary bladder transitional-cell papillomas in female rats) may also have been related to administration of the compound.

VI. RESULTS

A. Environmental

1. Total Particulate - Two breathing zone samples were collected in Building 3-56 during the mold trimming and grinding operation, which is performed in an exhaust ventilated hood. The time-weighted averages (TWA) were 0.41 and 0.21 milligram per cubic meter of air sampled (mg/m^3) (Table I). Nine breathing zone samples were collected in Building 3-07 during the blade trimming and sanding operations. The airborne dust concentrations ranged from 0.17-1.30 mg/m^3 (Table III). The airborne dust concentrations were below the Occupational Safety and Health Administration (OSHA) standard 15 mg/m^3 for nuisance or inert particulates and the ACGIH TLV of 10 mg/m^3. No asbestos or silica was detected in the bulk samples.

2. Methylenedianiline - Three breathing zone samples were collected during the application of the epoxy in Building 3-56. (Table II). The highest airborne concentration found was 0.47 mg/m^3. This was below the ACGIH TLV of 0.8 mg/m^3 (TWA) or 4.0 mg/m^3 (STEL).

3. Methyl Isobutyl Ketone (MIBK), Toluene, Cyclohexanone - Four air samples on operators (one of whom wore a respirator) were collected in Building 3-07 during the parts dipping and coating operations. These samples were analyzed for MIBK, toluene and cyclohexanone. The MIBK levels ranged from 3 to 85 mg/m^3, all below the OSHA standard of 410 mg/m^3. Toluene ranged from 1 to 4 mg/m^3, all below both the OSHA standard of 750 mg/m^3 and NIOSH recommended standard of 375 mg/m^3. Although the Material Safety Data Sheet (MSDS) stated that this material contained cyclohexanone, none was detected in the air samples. The calculated exposure to the mixtures of these solvents ranged from 0.01 to 0.42. The permissible upper limit is one[1] (Table IV).

4. Ethylenediamine - Two breathing zone samples were collected during the void filing of the blades. No ethylenediamine was detected (the lower limit of detection for ethylenediamine was 0.0005 milligram per sample).

5. Butyl Glycidyl Ether - Two employee breathing zone air samples were collected during the void filling of blades operation in Building 3-07. One concentration was less than the limit of detection (0.01 mg/sample); the other was 3.0 mg/m^3.

B. Medical

1. Demographic data

The sex and race distribution and the average age and duration of employment in current job were similar in the pattern makers and the comparison group (Table V).

2. Questionnaire data

Skin problems were reported by 14 (70%) of 20 pattern makers vs 7 (35%) of 20 packers and storekeepers (Table VI). This difference was statistically significant ($p<0.05$). Areas that were reported affected were usually the hands, palms and wrists, with the neck, face and arms less frequently affected. The lesions included redness, itching and cracking of the skin. There were no significant differences in the prevalence of reporting of the following symptoms during the month prior to the survey: eye irritation, nose irritation, throat irritation, cough, nausea, tiredness or fatigue. Among the 14 pattern makers with positive responses, the skin problems were attributed to the resins and epoxy materials alone by 10, to resins and "fumes" by 2, and to fibrousglass and dust by one. One worker was not sure of the etiology. The resin system # 2353 A and B (epoxy and methylenedianiline, an amine hardener), was mentioned by eight of these as being a major offender. Among those in the comparison group reporting skin problems, the sulfur boxes in the storeroom (also being investigated at that time), were mentioned by three of seven, while three did not know the cause and one attributed the problem to sweating.

The pattern makers reported that the skin problems were generally made worse by hot weather and by continued use of the epoxy materials, and were made better by washing, vacations, discontinuing use of the epoxy materials, or the use of "cortisone" creams. The season for exacerbations of the problem was reported to be summer by seven, winter by two.

A history of cancer was reported by none of the comparison group and by one of the current pattern makers. Bladder cancer and kidney cancer had been diagnosed in this worker who had had 14 years duration of current employment and about 30 years experience as a pattern maker. A retired (living) employee, who had worked for the company for over 25 years, including a period in woodworking and as an inspector in the blade shop, had also been diagnosed to have bladder cancer about seven years previously. These cases are not included among the death statistics.

3. Examination of the skin

Examination of the skin was normal in 14 (70%) of the pattern makers and in 18 (90%) of the comparison group. Among the other six pattern makers, the abnormalities observed included an apparent lipoma (a non-cancerous fat tumor); thickened, cracked skin with scarring (from old blisters) on the hands and palms; vesicular lesions on the hands, and a few small vesicles on the wrists; an area of dry, scaling skin on the wrist and hands and itching brown macules, apparently representing a resolving eruption on the forearms. Lesions observed during examination of the comparison group included an apparent case of atopic dermatitis and a 2-centimeter-diameter area of papules on the left forearm. The lipoma and the atopic dermatitis are unlikely to be associated with work. The other abnormalities are compatible with epoxy resin contact.

C. Epidemiologic

1. All deaths

PMR: There were 502 deaths among white males available for analysis. The average age of death was 55 years. Table VII lists the observed, expected, PMR and 95% confidence limits (CL) for various causes of death. Of these deaths, 139 were due to malignant neoplasms, while 107.8 were expected, yielding a PMR (observed deaths divided by expected deaths) of 1.29 (95% CL 1.11 - 1.49). This is equivalent to stating that a 29% increased proportion of mortality due to cancer appeared to be present. Among the various subcategories of malignant neoplasms, elevated PMRs were observed for cancer of large intestine, rectum, respiratory system (larynx, lung), bladder, skin, brain, and bone, lymphosarcoma and reticulosarcoma, Hodgkin's disease, leukemia and all lymphopoietic cancer. The excess PMRs were statistically signficant for cancer of large intestine, cancer of respiratory system (lung), and all lymphopoietic cancer. Most non-malignant causes of death had PMRs lower than expected (PMR less than 1), including a 4% deficit in deaths due to disease of the circulatory system, a 38% deficit for all respiratory diseases and a 40% deficit of external causes of death. The latter deficit was statistically significant.

PCMR: Because of the number of cause-specific cancer categories that were found to be in excess, PCMRs were calculated to control for the bias that might have been introduced by any differences in ascertainment of death differences between chronic and acute illness. There were 139 cancer deaths considered in the PCMR analysis (Table VIII). The average age of deaths was 54 years. None of the cancer death subcategories associated with statistically significant elevated PMRs remained significantly elevated in the PCMR analysis.

2. Deaths among employees who ever worked in "exposed" areas

PMR: There were 179 deaths available for analysis among white males who ever worked at least one month in the areas defined above to be "exposed". The average age of death was 55 years. Table IX lists the observed and expected number of deaths, the PMRs and 95% CL for the causes of death. Of these deaths, 46 were due to malignant neoplasms, while only 38.82 were expected, yielding a PMR of 1.18 (95% CL 0.92 - 1.53). Among the various subcategories of malignant neoplasms, elevated PMRs were observed for cancer of digestive organs (large intestine), respiratory system (lung), bladder, skin, lymphosarcoma and reticulosarcoma, and all lymphopoietic cancer. The elevated PMRs for cancer of large intestine (7 observed, 3.10 expected, PMR 2.26, 95% CL 1.11 - 4.61), cancer of bladder (observed 3, expected 0.80, PMR 3.74, 95% CL 1.31 - 10.71) and lymphosarcoma and reticulosarcoma (observed 3, expected 0.87, PMR 3.45, 95% CL 1.20 - 9.95) were statistically significant. Although there were deficits in most non-malignant diseases, none were statistically significant.

PCMR: There were 46 cancer deaths considered in the PCMR analysis (Table X). The average age of death was 55 years. Only cancer of the bladder (observed/expected = 3.41, 95% CL 1.19 - 9.76) remained statistically significant in this analysis, although the excesses for cancer of large intestine and for lymphosarcoma and reticulosarcoma (lower CL of 0.97 and 0.95, respectively), remained suggestive of an association with work in the "exposure" areas.

The age at death, duration of work in "exposure areas", and interval from onset of exposure to time of death (or to diagnosis) for the three bladder cancer deaths and two living employees are shown below.

Age at death	Duration of employment in "exposure areas"	Latency
62	2	8
63	1	5
63	3	23
--*	9	22
--*	> 20	26

* These individuals are not deceased but are confirmed bladder cancer cases. They are not considered in any of the mortality analyses.

VII. DISCUSSION

The prevalence of reported skin problems among pattern makers was significantly greater than that among the other hourly group that was similar in sex, race, age and duration of employment but that was not working with epoxy compounds. The skin problems were generally attributed to work with the epoxy resins and hardeners. The skin abnormalities noted were not severe, but were compatible with those expected from contact with these materials. One should interpret these minimal findings with caution because the examinations were conducted in late June, prior to the very hot and humid weather, which may exacerbate these conditions.

Past exposures to methylenedianiline in Building 3-56 may have exceeded those determined in this survey. The operation involving MDA was performed in all areas of the building during the initial visit with only general dilution ventilation. However, at the time of air sampling, during this evaluation, the operation was carried out near windows which had two 40-inch fans. The two employees wore protective clothing, gloves, goggles and NIOSH approved organic vapor respirators.

The proportional mortality ratio study, based on 502 deaths in white males known to the company death benefit fund, found a statistically significant elevated proportion of deaths due to all malignant neoplasms and several subcategories of cancer. These, however, did not remain significantly elevated in the PCMR analysis, suggesting that these excesses may have been related to deficits or decreases in proportions due to other causes of death.

When the analysis was limited to those who ever worked in areas at risk for exposure to epoxy resins and hardeners, the excess proportion of deaths due to all malignant neoplasms persisted (although no longer statistically significant), and statistically significant excesses appeared for three specific sites. The PMRs for these sites were higher than in the analysis for all 502 deaths. Cancer of the bladder remained statistically significantly elevated in the PCMR analysis. The elevated PMR in the overall group can be attributed almost entirely to the excess deaths in the exposed group.

In interpreting the importance of these findings, one must bear in mind the limitations of a PMR study. There is a potential for bias if certain causes of death are over- or underrepresented in the data set. The causes that are overrepresented will appear to be in excess. Another source of bias seen with PMR studies is the "seesaw effect",[13] associated with the requirement, by definition, that the cause-specific PMRs balance out to an overall PMR of 1.00. Thus, if one cause of death is in excess (i.e. greater than one), whether due to unequal representation or due to a real excess, then other causes will have PMRs generally in the opposite direction. For example, a deficit of circulatory deaths might result in cancer deaths appearing to be in excess. One way to control this source of bias is to exclude causes of death not of interest, by calculating the PCMR as was done in this study.

The duration of exposure and latency for the bladder cancer cases are shorter than that usually associated with occupationally- or chemically-induced solid tumors. In addition, one cannot discount the possibility of this being a chance cluster of cases to which attention has been focused through the hazard evaluation. However, the following factors lend more weight to the importance of the findings: 1) the detectable airborne MDA and suggestion of greater exposures in the past (contact could also be a route of exposure); 2) the known toxicological evidence; 3) the similarity of MDA with known bladder carcinogens (structure-activity relationship); 4) the bladder site was of concern a priori; 5) the fact that there were cases of bladder cancer among living employees with longer exposure and compatible latency.

VIII. RECOMMENDATIONS

1. All lay-up of patterns should be done in a booth with local exhaust ventilation. The mold should be placed on a roundtable, and the employee should station himself so that the organic vapors are drawn away from his face.

2. Pattern makers should use effective personal protective equipment, including gloves, during wet lay-ups.

3. The ideal method for further confirmation of the possible association of MDA exposure and cancer would be a cohort or standardized mortality ratio (SMR) study. However, it is best to look at the problem in another group of workers with similar exposures rather than in this already identified group. This is currently being pursued by NIOSH in conjunction with Environmental Protection Agency (EPA).

4. Because MDA is a suspect carcinogen and exposure was observed, efforts should be made to reduce exposures to the lowest possible level.

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1. Boeing Vertol Company
2. Local 1069, United Auto Workers
3. NIOSH, Region III
4. OSHA, Region III

For the purpose of informing affected employees, 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 I

Results of Sampling for Total Dust * (containing fibrous glass)
Operator's Breathing Zone
Building 3-56 (Pattern Shop)

Boeing Vertol Company
Philadelphia, Pennsylvania
HETA 82-146

April 19, 1982

Location	Sample #	Time Period	Dust Concentration	TWA
3-56	7794	9:57-14:01	1.08	0.41
3-56	7777	9:53-13:59	0.50	0.21

* Denotes milligram of contaminant per cubic meter of air sampled (mg/M^3)

Evaluation Criteria

	OSHA	ACGIH
Inert Dust	15 mg/M^3	10 mg/M^3

Table II

Results of Sampling for Methylenedianiline*
Building 3-56

Boeing Vertol Company
Philadelphia, Pennsylvania
HETA 82-146

April 15, 1982

Operation	Sample	Time	Concentration	Remarks
Molding	1	9:37- 9:57	0.23	OBZ***
	2	14:21-14:41	LLD**	OBZ
	3	16:21-16:41	0.46	OBZ

*Denotes milligram of contaminant per cubic meter of air samples.
**Denotes less than the lower limit of detection, .022 milligram per sample.
***Denotes operator's breathing zone.

Evaluation Criteria

OSHA	NIOSH	ACGIH
-	LFL****	0.8 (TLV) 4.0 (STEL)

****Denotes lowest feasible limit.

Table III

Airborne Concentrations Epoxy Containing Dust*
Building 3-07 (Blade Shop)

Boeing Vertol Company
Philadelphia, Pennsylvania
HETA 82-146

September 21, 1982

Sample#	Location/Operation	Time	Concentration	Remarks
M-9154	3670 Trim & Sand	08:16-14:55	1.07	OBZ**
M-9153	3670 Trim & Sand	08:20-14:54	0.27	OBZ
M-9161	3670 Trim & Sand	08:32-14:50	0.53	OBZ
M-9160	3634 Finishing	08:50-14:45	0.49	OBZ
M-9155	3634 Finishing	08:32-14:45	0.58	OBZ
M-9159	3671 Trimmer	07:55-14:44	0.17	OBZ
M-9166	3671 Trimmer	07:57-14:44	1.30	OBZ
M-9165	3634 Foreman	08:03-14:40	0.31	OBZ
M-9172	3634 Trimmer	09:10-14:37	12.54	Invalid, sample tampered-with

*Denotes - Milligram of contaminant per cubic meter of air sampled mg/M^3

**Denotes - operators' breathing zone.

Criteria

Inert Dust

OSHA 15 mg/M^3

ACGIH 10

Table IV

Airborne Concentrations of Solvents
Building 3-07

Boeing Vertol Company
Philadelphia, Pennsylvania
HETA 82-146

Sample #	Operation	Time	MIBK*	Toluene*	Cyclo-hexanone*	Level for** Mixture ACGIH	OSHA	Remarks
September 21, 1982								
1	Dipping	07:45-14:55	14.42	0.93	<0.01	0.08	0.04	OBZ[a]
2	Coater	07:55-14:55	33.33	1.67	<0.01	0.16	0.08	OE[b]
3	Bonder	07:57-14:40	2.75	0.50	<0.01	0.01	0.01	OE
September 23, 1982								
3	Coater	09:10-10:30	85.0	3.75	0.01	0.42	0.22	OE

*Denotes milligrams of contaminant per cubic meter of air samples (mg/M^3).
**Denotes that if the sum of the following fractions: $\frac{C^1}{L^1} + \frac{C^2}{L^2} + \cdots + \frac{C_n}{L_n}$

exceeds unity, then the acceptable level of the mixture should be considered as being exceeded.

C_1 = observed atmospheric concentration
L^1 = threshold limit

a OBZ = operator's breathing zone (respirator worn)
b OE = operator's exposure zone

Table V

Demographic Data

Boeing Vertol Company
Philadelphia, Pennsylvania
HETA 82-146

	Pattern Makers (n = 20)	Packers and Storekeepers (n = 20)
Sex (M/F)	19/1	18/2
Race (white/black)	17/3	17/3
Age (Yr): mean (S.D.)	45 (8.6)	44 (12.3)
range	32-67	25-60
Years at current job: mean (S.D.)	12.2 (7.8)	10.7 (7.5)
range	1.5 - 27	0.25 - 23

Table VI

Reported Symptoms, Pattern Makers vs Packers and Storekeepers

Boeing Vertol Company
Philadelphia, Pennsylvania
HETA 82-146

	20 Pattern Makers	20 Packers and Storekeepers	
	# (%)	# (%)	P value[a]
Reported skin problems	14 (70)	7 (35)	< 0.05
Symptoms in past month:			
Eye irritation	12 (60)	12 (60)	N.S.
Nose irritation	5 (25)	6 (30)	N.S.
Throat irritation	4 (20)	5 (25)	N.S.
Cough	1 (5)	3 (15)	N.S.
Nausea	2 (10)	1 (5)	N.S.
Tiredness and fatigue	4 (20)	3 (15)	N.S.

a = Chi-square or Fisher's Exact Test

Table VII

Cancer Specific Proportional Mortality
for all 502 Deaths

Boeing Vertol Company
Philadelphia, Pennsylvania
HETA 82-146

CAUSE OF DEATH	OBSERVED DEATHS	EXPECTED DEATHS	OBSERVED/ EXPECTED	95% CONFIDENCE LIMITS
All infective & parasitic disease	3	3.71	0.81	0.26 - 2.49
All malignant neoplasms	139	107.8	1.29	1.11 - 1.49
Buccal cavity	2	3.90	0.51	0.13 - 1.99
Digestive organs	26	26.5	0.98	0.68 - 1.43
Stomach	3	4.31	0.70	0.23 - 2.13
Large Intestine	15	8.62	1.74	1.06 - 2.86
Rectum	3	2.81	1.07	0.35 - 3.30
Pancreas	4	5.81	0.69	0.26 - 1.81
Respiratory System	58	42.21	1.37	1.08 - 1.75
Larynx	2	1.77	1.13	0.28 - 4.51
All lung	56	40.08	1.40	1.09 - 1.79
Kidney	3	3.04	0.99	0.32 - 3.05
Bladder	4	2.24	1.79	0.68 - 4.68
Skin	4	2.43	1.65	0.63 - 4.33
Brain	7	4.18	1.67	0.81 - 3.47
Lymphosarcoma & Reticulosarcoma	5	2.47	2.02	0.86 - 4.76
Leukemia	7	3.97	1.76	0.85 - 3.65
Other lymphatic	5	2.83	1.77	0.75 - 4.19
All lymphopoietic	18	10.85	1.66	1.06 - 2.61
Other	4	7.82		
Endocrine & Metabolic	8	8.87	0.90	0.45 - 1.79
Diabetes Mellitus	7	6.76	1.03	0.50 - 2.16
Nervous System	20	26.96	0.74	0.49 - 1.13
Vascular of CNS	15	22.42	0.67	0.41 - 1.09
All circulatory	205	214.02	0.96	0.87 - 1.06
Rheumatic Heart	5	4.73	1.06	0.44 - 2.53
Arteriosclerotic Heart	176	182.51	0.96	0.86 - 1.08
All respiratory	15	24.17	0.62	0.38 - 1.01

Table VII (continued)

Cancer Specific Proportional Mortality
for all 502 Deaths

Boeing Vertol Company
Philadelphia, Pennsylvania
HETA 82-146

CAUSE OF DEATH	OBSERVED DEATHS	EXPECTED DEATHS	OBSERVED/ EXPECTED	95% CONFIDENCE LIMITS
All pneumonia	4	8.30	0.48	0.19 - 1.25
Emphysema	4	6.69	0.60	0.23 - 1.56
Digestive System	31	31.33	0.99	0.70 - 1.39
Ulcer	4	2.64	1.51	0.57 - 3.99
Cirrhosis of Liver	20	20.62	0.97	0.63 - 1.49
Genitourniary System	6	4.21	1.43	0.65 - 3.15
Senility	7	7.33	0.96	0.46 - 1.99
External Causes	39	64.58	0.60	0.46 - 0.79
All accidents	21	40.29	0.52	0.36 - 0.76
Motor Vehicle Accidents	11	18.98	0.58	0.33 - 1.00
Suicide	9	16.10	0.56	0.30 - 1.05
Deaths not classified above	32	14.13	2.26	
Cancer deaths not classified above	15	7.77	1.93	

Table VIII

Cause Specific Proportional Cancer Mortality
for all 502 Deaths

Boeing Vertol Company
Philadelphia, Pennsylvania
HETA 82-146

CAUSE OF DEATH	OBSERVED DEATHS	EXPECTED DEATHS	OBSERVED/ EXPECTED	95% CONFIDENCE LIMITS
All malignant neoplasms	139			
Buccal cavity	2	5.00	0.40	0.11 - 1.49
Digestive System	26	33.23	0.78	0.56 - 1.09
Esophagus	1	3.37	0.30	0.05 - 1.83
Stomach	3	5.45	0.55	0.18 - 1.64
Large Intestine	15	10.81	1.39	0.86 - 2.25
Rectum	3	3.51	0.85	0.28 - 2.61
Pancreas	4	7.30	0.55	0.21 - 1.40
Respiratory System	58	53.35	1.09	0.89 - 1.33
Larynx	2	2.21	0.90	0.23 - 3.57
Lung	56	50.63	1.11	0.90 - 1.36
Prostate	1	3.56	0.28	0.05 - 1.70
Kidney	3	3.92	0.77	0.25 - 2.33
Bladder	4	2.69	1.49	0.57 - 3.90
Skin	4	3.45	1.16	0.44 - 3.03
Brain	7	5.86	1.19	0.58 - 2.46
Bone	1	0.73	1.38	0.20 - 9.63
Lymphosarcoma & Reticulosarcoma	5	3.38	1.48	0.63 - 3.49
Hodkin's Disease	1	2.40	0.42	0.07 - 2.62
Leukemia	7	5.59	1.25	0.61 - 2.57
Other lymphatic	5	3.66	1.37	0.58 - 3.23
All lymphopoietic	18	15.23	1.18	0.77 - 1.81

Table IX

Cause Specific Proportional Mortality
for 179 Deaths among "Ever Exposed"

Boeing Vertol Company
Philadelphia, Pennsylvania
HETA 82-146

CAUSE OF DEATH	OBSERVED DEATHS	EXPECTED DEATHS	OBSERVED/ EXPECTED	95% CONFIDENCE LIMITS
All infective & parasitic disease	2	1.31	1.53	0.39 - 6.03
All malignant neoplasms	46	38.82	1.18	0.92 - 1.53
Digestive organs	10	9.48	1.05	0.58 - 1.93
Stomach	1	1.53	0.65	0.09 - 4.52
Large Intestine	7	3.10	2.26	1.11 - 4.61
Pancreas	2	2.09	0.96	0.24 - 3.79
Respiratory System	19	15.30	1.24	0.81 - 1.90
All lung	19	14.54	1.31	0.85 - 2.01
Bladder	3	0.80	3.74	1.31 - 10.71
Skin	3	0.88	3.43	1.19 - 9.89
Brain	1	1.50	0.67	0.10 - 4.62
Lymphosarcoma & Reticulosarcoma	3	0.87	3.45	1.20 - 9.95
Other lymphatic	2	1.04	1.93	0.50 - 7.50
All lymphopoietic	5	3.88	1.29	0.54 - 3.06
Other	4	7.82		
Endocrine & Metabolic	3	3.17	0.95	0.31 - 2.91
Diabetes Mellitus	3	2.42	1.24	0.40 - 3.81
Nervous System	9	9.53	0.94	0.50 - 1.78
Vascular of CNS	5	7.91	0.63	0.27 - 1.48
All circulatory	67	76.13	0.88	0.74 - 1.05
Rheumatic Heart	2	1.67	1.20	0.30 - 4.75
Arteriosclerotic Heart	56	64.99	0.86	0.70 - 1.06
All respiratory	6	8.65	0.69	0.32 - 1.50
All pneumonia	1	2.94	0.34	0.05 - 2.17
Emphysema	2	2.36	0.85	0.21 - 3.34
Digestive System	13	11.21	1.16	0.69 - 1.96
Ulcer	2	0.92	2.18	0.57 - 8.38
Cirrhosis of Liver	9	7.41	1.21	0.64 - 2.30
Genitourniary System	2	1.46	1.37	0.35 - 5.42
Senility	2	2.64	0.76	0.19 - 2.99
External Causes	15	22.86	0.66	0.43 - 1.01
All accidents	9	14.12	0.64	0.35 - 1.15
Motor Vehicle Accidents	2	6.56	0.30	0.09 - 1.05
Suicide	5	5.74	0.87	0.37 - 2.04
Deaths not classified above	15	3.56	4.23	
Cancer deaths not classified above	5	2.80	1.78	

Table X

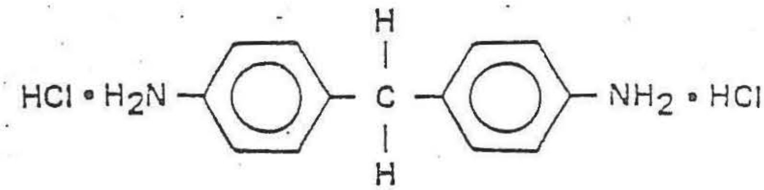
Cause Specific Proportional Cancer Mortality
for 179 Deaths among "Ever Exposed"

Boeing Vertol Company
Philadelphia, Pennsylvania
HETA 82-146

CAUSE OF DEATH	OBSERVED DEATHS	EXPECTED DEATHS	OBSERVED/ EXPECTED	95% CONFIDENCE LIMITS
All malignant neoplasms	46			
Digestive System	10	10.90	0.92	0.53 - 1.57
Stomach	1	1.78	0.56	0.08 - 3.73
Large Intestine	7	3.58	1.95	0.97 - 3.93
Pancreas	2	2.40	0.83	0.22 - 3.20
Respiratory System	19	17.66	1.08	0.76 - 1.53
Lung	19	16.79	1.13	0.79 - 1.61
Bladder	3	0.88	3.41	1.19 - 9.76
Skin	3	1.20	2.50	0.86 - 7.30
Brain	1	1.98	0.50	0.08 - 3.27
Lymphosarcoma & Reticulosarcoma	3	1.08	2.77	0.95 - 8.06
Other lymphatic	2	1.26	1.59	0.41 - 6.17
All lymphopoietic	5	5.07	0.99	0.44 - 2.23

Figure I

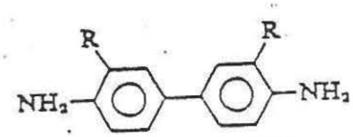
Chemical Structures of Methylenedianiline and some carcinogenic Aromatic Amines



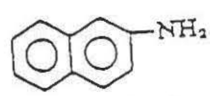
4,4'-METHYLENEDIANILINE DIHYDROCHLORIDE

CAS NO. 13552-44-8

$C_{13}H_{14}N_2$ Mol. Wt. 198.27



Benzidine (R = H)



2-Naphthylamine

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