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## I. SUMMARY

We conducted a retrospective cohort mortality analysis of 3588 persons who ever worked at an electric capacitor manufacturer where they were exposed to PCBs. Cox proportional hazards modelling was performed to examine occupational risk factors for specific causes of death within the cohort. All causes mortality (SMR=0.7, 95% CI 0.6, 0.8) and total cancer mortality (SMR=0.8, 95% CI 0.6-1.1) were less than expected. More deaths were observed than expected for skin cancer (8 malignant melanoma deaths, SMR=4.1, 95% CI 1.8-8.0) and cancer of the brain and nervous system (5 deaths, SMR=1.8, 95% CI 0.6-4.2). In the proportional hazards analysis, the average estimated cumulative dose for brain cancer cases (22.9 units) was greater than for other workers in the risk sets (12.9 units), but this difference was not statistically significant. Malignant melanoma was not related to cumulative PCB exposure. These results provide some evidence in support of an association between employment at this plant and malignant melanoma. The brain cancer finding suggests that this outcome be carefully observed in further follow-up of this cohort. The possibility that these observations resulted because of chance, bias, or confounding cannot be excluded as alternative explanations. Additionally, these findings conflict with those from other studies of PCB exposed populations. The continued follow-up of this, and several other large studies of PCB exposed populations, will be essential for the final determination of whether or not PCBs are carcinogenic to man.

NIOSH found that workers at the plant were at excess risk of malignant melanoma. Based on the results of this study, NIOSH recommends that workers included in he study be notified of the study results on an individual basis. NIOSH also recommends that the affected workers be periodically examined according to consensus recommendations for medical screening of malignant melanoma. NIOSH will continue to conduct periodic follow-up of this cohort.

KEYWORDS: SIC 3629 (Electrical industrial apparatus, not elsewhere classified) polychlorinated biphenyl, PCB, Aroclor, malignant melanoma, brain cancer, mortality.

## II. INTRODUCTION AND BACKGROUND

Although banned from production and distribution in the United States, polychlorinated biphenyls (PCBs) remain in the environment. Exposed workers include those involved in the maintenance and replacement of electrical transformers and capacitors and the disposal of materials containing PCBs.[1] In 1985, the Environmental Protection Agency (EPA) estimated that 1.6 million substation capacitors and 21,000 transformers containing PCBs remained in use.[2] Another two million mineral oil transformers were contaminated with more than 50 ppm PCBs. With approximately 2.5% transformers removed from service annually, there will remain 1.4 million contaminated transformers in service in the year 2000.

PCBs are considered potentially carcinogenic to man, based primarily on evidence from animal studies.[3-5] Even so, studies of PCB exposed populations have been inconsistent. The various studies have found excess cancer risks from malignant melanoma, liver and biliary tract cancer, cancer of the rectum, hematopoietic malignancies, and lung cancer.[6-9] Also of note, a meta-analysis[10] of the various PCB cohorts identified an excess from kidney cancer among PCB exposed men.

To further evaluate the carcinogenicity of PCBs, National Institute for Occupational Safety and Health (NIOSH) conducted a retrospective cohort study of workers manufacturing electrical capacitors with known exposure to PCBs.[11,12] The mortality experience of this cohort was previously unknown.

## III. MATERIALS AND METHODS

The study cohort manufactured electric capacitors in the midwest United States beginning in 1957. PCBs were used as a dielectric fluid until late in 1977 when they were replaced with isopropyl biphenyl. Aroclor (Monsanto trade name) 1242 was used through 1970 and Aroclor 1016 was used afterwards. Both mixtures contained 42% polychlorinated biphenyls, the difference being that Aroclor 1016 had fewer biphenyl homologues with 5 or more chlorine atoms per biphenyl nucleus. The facility was contained under a single roof with administrative offices and certain process areas isolated by walls (Figure 1). Manufacture of capacitors involved the production of bails made from foil, paper, and plastic which were placed into metal capacitor boxes. Several capacitors were bound together, placed into a vacuum chamber, and heated to 150**N**C to remove moisture. The vacuum chambers were then flooded with dielectric fluid to fill and impregnate the capacitors. After five days, the remaining fluid was pumped out and filtered for reuse. The doors of the ovens were then opened, releasing PCB containing fumes into the plant. After release from the ovens, these fumes spread throughout the facility, settling onto exposed surfaces. When the capacitors were removed from the ovens, the fill-holes were plugged and soldered shut and the capacitors were degreased and spray-painted. Approximately 10% of the workforce was directly involved in PCB-containing capacitor production. Solvents used at the plant included toluene, xylene, methyl ethyl ketone, trichlorethylene, and l,l,l-trichloroethane. Personal and area environmental sampling of plating, brazing, and soldering operations was conducted for several metals from 1977 through 1984. The results indicated that metal exposures were well below the recommended standards.

Retrospective Cohort Study

Included in the analysis were 3588 male and female workers employed for at least one day between January 1, 1957, when the plant opened, and March 31, 1977, the year when PCB use was discontinued. All personnel records and all death records in possession of the company were microfilmed and abstracted for name, date of birth, sex, race, social security number, and detailed job history. Race was indicated on 12% of the personnel records with the majority of these workers (96%) being white. We considered those workers whose race was unknown to have been white and excluded non-whites from the cohort analysis. (In 1980, 2.6% of the population in the county were black.[13]) Also excluded were persons for whom dates of birth or hire were missing. Detailed job histories were used to identify the dates of first and last employment as well as job location within the facility (department) and dates of employment for each job held. Date first employed at the plant was considered the first day of exposure. The last day of exposure was March 31, 1977 or the actual last day of employment, whichever was earlier.

Vital status was determined through the Social Security Administration (SSA) which reported deaths into 1987 and persons known to be alive as of December 31, 1984. If the SSA could not ascertain vital status, we determined the last known address and verified current mail delivery. Workers whose mailing address was verified were considered alive, otherwise the worker's vital status was unknown. Copies of all death certificates were requested from the respective state vital statistics offices. Underlying cause of death was determined by a qualified nosologist according to the International Classification of Diseases in effect at the time of death. For certain causes of death, medical records and pathology reports were collected for confirmation of diagnosis. We considered only those deaths which occurred before July 1, 1986 in the life-table analysis. Workers known to have been alive as of December 31, 1984 were assumed alive as of June 30, 1986 unless the SSA had reported their subsequent death. Those lost to follow-up and those who died after June 30, 1986 were also considered alive for the purpose of this analysis.

Person-years at-risk (PYAR) of dying were accumulated for each worker starting January 1, 1957 or on their first day of employment at the plant, whichever occurred later and continued until the date of death or the study-end date (June 30, 1986), whichever occurred first. The NIOSH Life Table Analysis System was used to distribute PYAR over sex specific five-year calendar time periods and five-year age groups.[14] Expected numbers of cause-specific deaths were calculated by multiplying the age, sex, and calendar time specific United States mortality rates for all whites by the corresponding number of person-years at-risk. The number of observed cause-specific deaths was divided by the number of expected cause-specific deaths to yield a Standardized Mortality Ratio (SMR). Ninety-five percent confidence intervals (95% CI) around the SMR were calculated using an approximation based on the Poisson distribution.[15]

PYAR were stratified into 5-year duration of employment and latency categories. Latency was calculated from the day of first employment. SMRs were calculated for each duration of employment and latency category.

Cox Proportional Hazards Analysis

The primary purpose of the Cox proportional hazards modelling[16] was to determine if a dose-response relationship existed between cumulative PCB exposure (duration of employment multiplied by an exposure intensity rating) and mortality from either malignant melanoma or brain cancer. Pertinent exposure information included the process description, environmental data collected in 1977,[11] and serum PCB levels collected during a cross-sectional study conducted a few months later.[12] While the environmental and serologic data confirmed that all workers were potentially exposed (Table 1), these data were of limited usefulness for constructing a job-exposure matrix. The environmental sampling was limited by the relatively few samples collected outside of the capacitor processing area. The serologic data were constrained since only the current workforce could contribute sera. Furthermore, the concentration of PCBs in serum were affected by its long half-life[17] and several individual factors; including body weight, age and sex.[12]

Our principal cumulative dose estimate (CUMYR) was based on knowledge of the manufacturing process and available environmental data. We assumed that both airborne and dermal PCB exposures decreased with distance from the ovens and that the lowest exposures were in the office areas which included the engineering and drafting departments. The office area was assigned an exposure weight of 1 and was designated as Zone 1 (Figure 1). The production area was then divided by three equi-distant and concentric semi-circles centered on the baking ovens. The zone surrounding the capacitor ovens was assigned an exposure score of 5 based on the environmental sampling results (Table 1). The process area furthest from the ovens was assigned an exposure score of 2 (Zone 2) and the area adjacent to the ovens a score of 3 (Zone 3). Departments were assigned an exposure weight according to the zone which contained 50% or more of that department. If a department was equally divided by two zones, it was assigned an average weight. Maintenance workers were assigned to Zone 5 if they worked in department F-44, located within Zone 5, or to Zone 4 if their primary work area was in Zone 3 but they were called upon to work in Zone 5 (N=34). The paint area and a clean room within the capacitor winding area (Departments A-35 & F-14) were given scores of 1 because they were isolated from the remainder of the production areas by walls and separate ventilation systems. Hourly workers who could not be located by department (N=125) were assigned to Zone 2.

CUMYR was calculated by multiplying the number of days worked in each department by its exposure weight, summing across departments, and dividing by the number of days in a year. In this manner, five CUMYR units were equivalent to working in Zone 5 for one year or working in Zone 1 for five years. If CUMYR was a predictor variable; 1 year, 5 year, and 10 year lagged doses were calculated in which exposures cumulated just prior to the cases failure were subtracted from CUMYR.

While the environmental data lend support to the weighting scheme for CUMYR, these data include only 14 area samples collected outside Zone 5 (Table 1). At the same time, the serologic data do not support the weights for Zones 2-4. Since the accuracy of CUMYR could not be verified, we estimated cumulative PCB exposure using two additional weighting schemes. One estimate (DURZONE5) was based on the serologic data, assigning a weighting factor of 1 to Zones 1-4 and a weighting factor of 5 to Zone 5. The second estimate (CUM2.5) assumed no exposure difference in Zones 2-4, which were weighted by a factor of 2.5. Zone 1 and Zone 5 retained their original weights.

Environmental sampling data collected in April 1977[11] or obtained through company records and collected from April 1977 to November 1984 were used to identify departments where exposures to 1,1,1 trichloroethane, trichlorethylene, toluene, methyl ethyl ketone, and xylene had been present. Workers were categorized as potentially exposed (or not exposed) to each solvent. Other exposure variables considered were employment in each of the PCB exposure zones (dichotomous) and ever having worked outside of Zone 1. Duration of employment and years since first employment were also analyzed. The analysis did not consider exposure to the various metals as the environmental measurements indicated that these exposures were minimal.

Cases were selected from the entire original population at risk. Those who had died with a primary cancer of the brain or a malignant melanoma listed as an underlying or contributory cause of death were included. If a case had been diagnosed prior to their first day of employment, they were excluded. All workers born within 5 years of a case, and the same sex as the case, were eligible for inclusion in a risk set for that case. Risk sets were further limited to workers who survived to the age at which the case died and were employed at the facility prior to that age. The work history of each member of the risk set was truncated at the age at which the index case had died.

An exposure-response relationship was determined if the regression coefficient for cumulative dose was statistically significant for a two-tailed test. Ninety-five percent confidence intervals were calculated for the estimated rate ratios using a test based method proposed by Miettinen.[18]

## IV. RESULTS

The entire cohort included 3,643 workers; 2,785 of whom were men and 858 were women (Table 2). Excluded were 15 known non-whites and 40 workers whose work histories were incomplete or otherwise failed to meet study inclusion criteria. This left 3,588 persons in the final cohort to be analyzed. Of these, 192 were dead and 3,396 were considered alive at the study end date. For the final cohort; the median latency was 18.6 years (mean=19.2 yrs; range: 0.04 to 32.5 yrs), the median duration of employment was 1.3 years (mean=4.1 yrs; range: 1 day to 20.2 yrs), and the median age at hire was 24.2 years (mean=27.0; range: 16.8 to 62.6 yrs). The distribution of PYAR by duration of employment and latency is provided in Table 3.

Overall mortality was significantly less than expected (observed=192: SMR=0.7; 95% CI 0.6-0.8), as were mortality from diseases of the heart (observed=60: SMR=0.7; 95% CI 0.5-0.9) and accidental deaths (observed=28: SMR=0.7; 95% CI 0.5-1.0) (Table 4). The SMR for all cancers was also below expected (observed=54: SMR=0.8; 95% CI 0.6-1.1). There were no excess deaths from cancers of the rectum, the lung, or hematopoietic malignancies. A single death from cancer of the biliary passages, liver, and gall bladder was observed as were two deaths from kidney cancer. The SMR for deaths due to cancer of the skin was significantly elevated (8 observed: SMR=4.1; 95% CI 1.8-8.0). All eight skin cancer deaths were due to malignant melanoma. A nonsignificant increase was also noted for cancer of the brain and nervous system (5 observed: SMR=1.8, 95% CI 0.6-4.2).

Both men and women experienced excess mortality from melanoma and brain cancer. The risk of mortality from skin cancer in men (6 observed: SMR=3.6; 95% CI 1.3 - 7.9) was

lower than that in women (2 observed: SMR=6.3; 95% CI 0.8 - 22.7). For brain and central nervous system cancers, men (4 observed: SMR=1.8; 95% CI 0.5 - 4.5) and women (1 observed: SMR=2.0; 95% CI 0.1 - 11.1) had similar SMRs, though the SMR for women was based on a single case.

For malignant melanoma there was no clear relationship between latency or duration of employment and risk (Table 5). All 8 melanoma deaths occurred five or more years after initial employment and three cases worked at the plant for more than ten years. A ninth worker (Case G) died in 1987 with a malignant melanoma listed as a contributory cause of death (Table 6). He was not included in the life-table analysis. Case G had worked for 1 month at the plant and had accumulated 20 years of latency before his death.

Pathology reports were obtained for eight of the nine cases and all confirmed malignant melanoma. The primary site for Case C was reported to be the gallbladder. Although rare, primary and metastatic melanomas have been reported at this site.[19,20] A pathology report was not obtained for Case E, but the medical record confirmed the diagnosis. Case H had been diagnosed with a malignant melanoma approximately two months prior to working at the facility. He was then employed for ten years and died of metastatic disease 14 years after the original diagnosis. The excess mortality remained after this case was removed from the life-table analysis (SMR=3.5, 95% CI 1.4 - 7.3). Two malignant melanoma deaths occurred during 1965-69, four more during 1975-79, one during 80-84, and two during 1985-87. At diagnosis, three cases (Cases A, B, I) had extensive metastatic disease and died within 6 months.

All five brain cancer deaths occurred five or more years after the date of hire (Table 5). There was an indication that the brain cancer deaths were more common among those with a longer duration of employment. Three deaths occurred among those with 10 or more years duration of employment (3 obs., SMR=4.8, 95% CI 1.0 - 14.0). Two additional brain cancer cases were not included in the life-table analysis (Table 6). A white male worker (Case DD) died of a glioblastoma 7 months after the study-end date, having accumulated 24 years latency and approximately 6 months duration of employment. A black female (Case GG) died 13 years after beginning work at the plant where she was employed for 11 years.

One pathology record for a brain cancer case was obtained and identified the tumor as a glioblastoma. Medical records or death certificates indicated that two additional cases were glioblastomas while two others were astrocytomas. The death certificates for the remaining two cases indicated carcinomas of the brain, but did not specify the cell type. The underlying cause of death for all 7 cases was coded as a primary cancer of the brain by an independent, certified nosologist.

Cox proportional hazards models

Malignant melanoma

The proportional hazards analysis for malignant melanoma included 8 cases and 3455 workers in all risk sets combined. The eight risk sets varied in size from 111 to 1112 workers. Excluded from this analysis was Case H, who had been diagnosed with a primary malignant melanoma two months prior to his employment at the plant. Four cases and 33 percent of the comparison group worked in Zone 1 (Table 7). Two cases and 33 percent of the comparison

group worked in Zone 5, closest to the baking ovens. Only one case worked in a department that had been monitored for solvents. There were no statistically significant differences between cases and the comparison group for years since first employment, duration of employment, or cumulative PCB exposures (Table 8).

Cancer of the brain.

The Cox proportional hazards models of brain cancer included 7 cases and 1670 workers in all of the risk sets combined. The risk sets varied in size from 42 workers to 489 workers. Two brain cancer cases worked in Zone 1 compared to 37% of the workers in the comparison group (Table 7). In contrast, five cases (72%) and 47% of the comparison group worked in Zone 3 (rate ratio = 3.4, 95% CI 0.7 - 16.8). Only one case worked in a department where environmental samples for solvents had been collected.

The number of years since first employment was similar between both the cases and their comparison group. Brain cancer cases had a longer average duration of employment than the comparison group, but this difference was not statistically significant.(Table 8) Of the three measures of cumulative exposure, the two estimates that weighted departments by proximity to the capacitor ovens (CUMYR and CUM2.5) were stronger predictors of brain cancer. On average, brain cancer cases had more than twice the estimated cumulative PCB dose (CUMYR) than the comparison group, but again, this difference was not statistically significant. The rate ratio associated with a ten unit increase in CUMYR was 1.27 (95% C.I 0.88 - 1.86).

## V. DISCUSSION

This group of workers had an overall survival that was better than expected when compared to standardized mortality rates for white men and women in the United States. At the same time, we observed a four-fold excess mortality from cancer of the skin, which was entirely due to malignant melanoma. Malignant melanoma risk did not vary by duration of employment, latency, or estimated cumulative PCB exposure. There was also a nonsignificant excess of brain cancer mortality which increased with duration of employment. The average estimated cumulative PCB exposure for the brain cancer cases was twice that of a comparison group comprised of other workers at the plant, but this difference was not statistically significant.

Predisposing risk factors or environmental exposures probably do not account for the excess deaths reported in this study. Since, in contrast to brain cancer, several strong predisposing risk factors have been reported for malignant melanoma,[21] the next-of-kin of eight of the workers who died of malignant melanoma were interviewed (Table 9). The spouse of one case reported that the cases's mother also died of malignant melanoma, but the medical record for the case indicated that another type of cancer had been responsible. None of the cases were related and five had no known risk factor for malignant melanoma other than race. An environmental cause, peculiar to the geographic area where the plant was located, was also unlikely since the county mortality rates for malignant melanoma and brain cancer were similar to the state and national rates.[22]

The skin is a recognized target organ for several nonmalignant effects caused by PCBs and, in the workplace, is a primary route of exposure. Chloracne[23-25] and hyperpigmentation[26] have been reported among PCB exposed workers. While PCBs appear to affect melanocytes,

their ability to promote or initiate melanoma in these cells is unknown and the mechanisms of hyperpigmentation and carcinogenesis probably differ.

Our results, and those of similar studies,[6-9] have been inconsistent. Excess malignant melanoma has been reported once, in a retrospective cohort morbidity study of 72 workers thought to be exposed to Aroclor 1254.[6] That study was considered inconclusive[27] since PCB exposures could not be quantified, the presence of other known carcinogens was considered possible but had not been evaluated, and the excess was based on only three cases. PCB exposed workers with a history of skin cancer, type unknown, have been reported in two cross-sectional surveys.[28-29] Since none of the previously published studies reported an excess mortality from brain cancer, we did not consider it an a priori hypothesis. However, an unpublished cohort mortality analysis[30] of transformer manufacturing workers exposed to Aroclor 1254 did find such an excess (4 observed, 0.8 expected). In addition, an Italian cohort[8] experienced a similar excess (2 observed, 0.3 expected) that was not reported until a later meta-analysis.[10]

Other retrospective cohort studies reported excesses in hepatobiliary cancers,[7,9] carcinoma of the rectum,[7] hematopoietic tumors,[8] and lung cancer.[8] Two small cohorts[31-32] reported no cancer excesses. Three investigators[7,10,33] followed workers from the same plants and their results should not be considered independently. Unrecognized differences between the study populations, exposures from subtle manufacturing differences, exposures to other carcinogens in the workplace, or chance may explain the discrepancies between the various studies. At the same time, statistical power[34] for even the largest cohort studies has been limited by the relatively small numbers of deaths observed (Table 10).

One of the strengths of this study was the substantial evidence that most of the cohort had been exposed to PCBs. Exposures occurred throughout the study facility, and there exists limited documentation that workers developed nonmalignant skin problems related to their exposure. In 1977, biological serum PCB data for workers in the plant, compared to persons in the community, were 7-fold greater for salaried workers and 50-fold greater for capacitor processing workers, the most heavily exposed workers in Zone 5. Zone 5 workers were also more likely to report unusually darkened areas of the skin than workers in other areas of the plant, and this difference was statistically significant.[35] Also of interest, the personnel record of Case G, documented that he had developed a severe dermatitis while working in Zone 5 as a result of contact with the dielectric fluid containing Aroclor 1242.

Our study had several limitations. Mortality may not be the best index of risk for malignant melanoma as differences in health care quality and access may affect survival. Besides PCBs, solvents, and metals, other workplace exposures were not evaluated since the necessary data were unavailable. Fewer than 10% of the PYAR were accumulated with 20 or more years of latency. In addition, there have been relatively few deaths in this cohort. Thus, it has not been possible to assess the risk of cancers with long latency periods and the small number of observed deaths resulted in risk estimates with relatively broad confidence intervals. The sparsity of the environmental data resulted in weighting scales that should be considered approximations and a detailed job-exposure matrix that incorporated changes over time could not be created.

Various forms of bias or confounding should also be considered. A selection bias known as the healthy worker effect[36] could explain, in part, the low overall SMR. This effect may be

enhanced in a relatively young cohort, such as this, where the median age at the study-end date was 44.5 years. Since the pathology records could not be obtained for several brain cancer cases, the possibility of misclassification cannot be excluded. The limitations of the weighting scales may have lead to substantial exposure misclassification and obscured a dose-response relationship.[37] Finally, any association of excess mortality with PCBs may have been confounded by simultaneous exposures to PCB contaminants, such as polychlorinated dibenzofurans,[10] or other unidentified substances in the workplace.

## VI. CONCLUSIONS

Despite the conflicting results from the epidemiologic studies, PCBs are considered potentially carcinogenic to man by NIOSH[3] and EPA[5]. The International Agency for Research on Cancer (IARC) classifies PCBs as animal carcinogens with limited evidence to suggest that they are also carcinogenic to man.[4] This study provides some evidence for an association between PCB exposure in an occupational environment and mortality from malignant melanoma. The brain cancer finding suggests that this outcome be carefully observed in further follow-up of this cohort. The possibility that these observations resulted because of chance, bias, or confounding cannot be excluded as alternative explanations. The continued follow-up of this, and several other large studies of PCB exposed populations, will be essential for the final determination of whether or not PCBs are carcinogenic to man.

## VII. RECOMMENDATIONS

NIOSH found that workers at the plant were at excess risk of malignant melanoma. Based on the results of this study, NIOSH recommends that workers included in the study be notified of the study results on an individual basis. NIOSH also recommends that the affected workers be periodically examined according to consensus recommendations for medical screening of malignant melanoma. NIOSH will continue to conduct periodic follow-up of this cohort.

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## X. DISTRIBUTION AND AVAILABILITY OF REPORT

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1. Westinghouse Electric Corporation
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5. Indiana State Board of Health
6. Environmental Protection Agency
7. Agency for Toxic Substances and Disease Registries
8. International Agency for Research on Cancer
9. Occupational Safety and Health Administration

For the purpose of informing affected employees who are still employed at the facility, copies of this report shall be posted by the employer in a prominent place accessible to the employees for a period of 30 calender days.

Table 1: Environmental and biologic measurements for polychlorinated biphenyls in March 1977.

**Environmental Measurements ug/m$^3$**

| | Zone 1<br>N mean<br>(sd) | Zone 2<br>N mean<br>(sd) | Zone 3<br>N mean<br>(sd) | Zone 5<br>N mean<br>(sd) |
|---|---|---|---|---|
| *Area air sampling* | | | | |
| | 2 16<br>(15) | 4 48<br>(13) | 8 59<br>(19) | 4 76<br>(52) |
| *Personal Sampling* | | | | |
| | ns | ns | ns | 38 94 (68) |

**Serum Measurements (ng/ml)**

| | All Salaried Workers | | Hourly Workers Only | |
|---|---|---|---|---|
| | Zone 1 | Zone 2 | Zone 3 | Zone 5 |
| Current job | 66 126<br>(101) | 51 199<br>(377) | 23 98<br>(45) | 71 305<br>(479) |
| Only worked in | 36 119<br>(26) | 7 121<br>(61) | 5 100<br>(27) | 8 763<br>(1117) |

ns = not sampled.
Serum PCB values are lower chlorinated biphenyl molecules with no more than 4 chlorine atoms per molecule.[6]
Salaried workers could not be separated into exposure zones according to serum PCB values.
No environmental or serum data were collected for Zone 4.

Table 2: Cohort description and vital status.

**A. Cohort Status Breakdown**

| Sex | Total Cohort | Rejected | Final Cohort |
|---|---|---|---|
| Males* | 2785 | 43 | 2742 |
| Females* | 858 | 12 | 846 |
| Total | 3643 | 55** | 3588 |

**B. Vital Status**

| Vital Status | Total Cohort | Rejected | Final Cohort |
|---|---|---|---|
| Alive | 3288 | 47 | 3396 |
| Dead | 216 | 7 | 192*** |
| Unknown | 139**** | 1 | |
| Total | 3643 | 55 | 3588 |

* Persons of unknown race were included as white.

** Rejected from analysis because of an unknown date of first employment, not employed between January 1, 1957 and March 31, 1977, and 15 non-whites (10 men and 5 women).

*** 17 workers died after June 30, 1986 and were considered to be alive at the study end date.

**** 139 workers with a vital status unknown (3.8%) were included in the analysis and considered alive as of June 30, 1986.

Table 3: Person-years at-risk by latency and duration of employment.

| | **Duration of Employment** | | | | | |
|---|---|---|---|---|---|---|
| Latency | <6 mos | 6 mos | 5-9 | 10-14 | ≥15 | Total |
| < 5 yrs | 6999 | 10863 | | | | 17862 |
| 5-9 yrs | 5768 | 7005 | 4977 | | | 17750 |
| 10-14 yrs | 5407 | 6458 | 2041 | 2873 | | 16778 |
| 15-19 yrs | 3873 | 4495 | 1536 | 1528 | 1248 | 12681 |
| ≥ 20 yrs | 1176 | 2463 | 1012 | 653 | 1795 | 7109 |
| Total | 23223 | 31284 | 9566 | 5055 | 3043 | 72180 |

Table 4: Observed and expected deaths, standardized mortality ratios (SMR), and 95% Confidence Intervals.

| | Observed Deaths | Expected Deaths | SMR | 95% C.I. Lower | - | Upper |
|---|---|---|---|---|---|---|
| | | Underlying Cause of Death | | | | |
| All Causes | 192 | 283.3 | 0.7** | 0.6 | - | 0.8 |
| All Cancers | 54 | 63.7 | 0.8 | 0.6 | - | 1.1 |
| **Site Specific Cancers** | | | | | | |
| Buccal & Pharynx | 0 | 1.7 | ---- | | | |
| Digestive Organs | 8 | 13.9 | 0.6 | 0.2 | - | 1.1 |
| Biliary Passages, Liver and Gall Bladder | 1 | 0.8 | 1.1 | 0.0 | - | 6.4 |
| Pancreas | 2 | 2.8 | 0.7 | 0.1 | - | 2.5 |
| Rectum | 1 | 1.2 | 0.8 | 0.0 | - | 4.5 |
| Respiratory System | 15 | 20.2 | 0.7 | 0.4 | - | 1.2 |
| Kidney | 2 | 1.5 | 1.3 | 0.2 | - | 4.8 |
| Lymph & Hematopoietic | 7 | 7.2 | 1.0 | 0.4 | - | 2.0 |
| Skin*** | 8 | 2.0 | 4.1** | 1.8 | - | 8.0 |
| Brain & Nervous Sys**** | 5 | 2.8 | 1.8 | 0.6 | - | 4.2 |
| All other sites combined | 5 | 8.5 | 0.6 | 0.2 | - | 1.4 |
| Diseases of the Heart | 60 | 85.4 | 0.7** | 0.5 | - | 0.9 |
| Diseases of the Respiratory System | 10 | 12.3 | 0.8 | 0.4 | - | 1.5 |
| Accidents | 28 | 41.1 | 0.7* | 0.5 | - | 1.0 |
| Violence | 14 | 21.5 | 0.6 | 0.5 | - | 1.1 |

* - $p < 0.05$; ** - $p < 0.01$

*** - Expected number of deaths were calculated using mortality rates for basal cell carcinoma, squamous cell carcinoma, and malignant melanoma combined. All observed skin cancer deaths were malignant melanomas.

**** - Cancer of the brain and central nervous system included the following ICD codes: ICD 193 (6th & 7th revision); ICD 191, 192 (8th & 9th revision).

Table 5: Deaths (observed/expected) from selected causes; by duration of employment and latency.

| | Latency | | Duration of Employment | | | |
|---|---|---|---|---|---|---|
| | <6 mos | 6mos -4yrs | 5-9 yrs | 10-14 yrs | ≥15 yrs | Total |
| <5 all neoplasms | 0/1.8 | 2/3.7 | | | | 2/5.4 |
| skin | 0/0.1 | 0/0.1 | | | | 0/0.2 |
| brain&CNS | 0/0.1 | 0/0.2 | | | | 0/0.4 |
| 5-9 all neoplasms | 4/2.2 | 1/2.8 | 4/3.6 | | | 9/8.6 |
| skin | 1/0.1 | 0/0.1 | 1/0.1 | | | 2/0.3 |
| brain&CNS | 1/0.1 | 0/0.2 | 1/0.2 | | | 2/0.5 |
| 10-14 all neoplasms | 5/3.3 | 3/4.1 | 3/1.7 | 5/4.1 | | 16/13.2 |
| skin | 1/0.1 | 0/0.2 | 0/0.1 | 2/0.1 | | 3/0.5 |
| brain&CNS | 0/0.2 | 0/0.2 | 0/0.1 | 1/0.2 | | 1/0.6 |
| 15-20 all neoplasms | 4/4.1 | 4/4.9 | 1/2.0 | 4/3.5 | 2/2.5 | 15/17.0 |
| skin | 0/0.1 | 1/0.2 | 0/0.1 | 1/0.1 | 0/0.1 | 2/0.5 |
| brain&CNS | 0/0.2 | 0/0.2 | 0/0.1 | 1/0.1 | 1/0.1 | 2/0.7 |
| ≥ 20 all neoplasms | 1/2.8 | 4/5.2 | 0/2.4 | 2/3.4 | 5/6.2 | 12/19.4 |
| skin | 0/0.1 | 1/0.1 | 0/0.1 | 0/0.1 | 0/0.1 | 1/0.1 |
| brain&CNS | 0/0.1 | 0/0.2 | 0/0.1 | 0/0.1 | 0/0.2 | 0/0.6 |
| Total all neoplasms | 14/14 | 14/21 | 8/10 | 11/10 | 7/9 | 54/64 |
| skin | 2/0.5 | 2/0.7 | 1/0.3 | 3/0.2 | 0/0.2 | 8/2.0 |
| brain&CNS | 1/0.7 | 0/1.0 | 1/0.4 | 2/0.3 | 1/0.3 | 5/2.8 |

Expected numbers of skin cancer deaths calculated for basal cell carcinoma, squamous cell carcinoma, and malignant melanoma combined. All observed skin cancer deaths were malignant melanoma.

Expected numbers of cancer of the brain and central nervous system included the following ICD codes: ICD 193 (6th & 7th revision); ICD 191, 192 (8th & 9th revision).

Table 6: Descriptive Statistics of Malignant Melanoma and Brain Cancer Deaths.

Malignant Melanoma

| | Sex | Age at death | Hire Date | Diagnosis Date | Date of Death | Microscopic Confirmation | Location of primary |
|---|---|---|---|---|---|---|---|
| A | F | 37 | 02/58 | 09/67 | 11/67 | Yes | anterior chest |
| B | M | 44 | 06/58 | 10/74 | 01/75 | Yes | scalp |
| C | M | 43 | 03/59 | 01/67 | 03/69 | Yes | gallbladder |
| D | M | 52 | 04/66 | 08/78 | 10/81 | Yes | neck |
| E | M | 32 | 08/64 | 11/72 | 02/75 | Yes* | shoulder |
| F | M | 47 | 05/59 | 10/80 | 06/85 | Yes | back |
| G | M | 63 | 10/66 | 06/87 | 06/87 | Yes | anterior chest |
| H | M | 68 | 01/61 | 11/60 | 10/75 | Yes | back |
| I | F | 40 | 06/70 | 05/76 | 01/77 | Yes | unknown |

G - malignant melanoma considered a contributory cause of death.
H - began employment two months after diagnosis.

Cancer of the Brain and Nervous System

| | Sex | Age at death | Hire Date | Diagnosis Date | Date of Death | Microscopic Confirmation | Histology |
|---|---|---|---|---|---|---|---|
| AA | M | 66 | 08/74 | 01/81 | 10/82 | NA | glioblastoma |
| BB | M | 51 | 03/62 | NA | 04/75 | NA | unknown |
| CC | F | 52 | 01/59 | NA | 12/74 | NA | unknown |
| DD | M | 45 | 08/62 | 03/86 | 02/87 | Yes | glioblastoma |
| EE | M | 67 | 11/59 | 11/75 | 04/76 | NA | astrocytoma |
| FF | M | 34 | 07/58 | NA | 10/64 | NA | astrocytoma |
| GG | F | 44 | 05/66 | NA | 01/79 | NA | glioblastoma |

DD - died of brain cancer after June 30, 1986.
GG - non-white female.

* Pathology report not available. Tumor was microscopically confirmed as a malignant melanoma according to the hospital tumor registry.

NA = medical record or pathology reports could not be obtained. If medical record and pathology report were not obtained, histology refers to statement on death certificate.

Table 7: Work in PCB exposure zones and potential exposure to solvents.

| | Malignant Melanoma | | Brain Cancer | |
|---|---|---|---|---|
| | Cases | All Workers in Risk Sets | Cases | All Workers in Risk Sets |
| N | 8 | 3455 | 7 | 1670 |
| Ever working in: | | | | |
| Zone 1 | 4 | 1144 | 2 | 618 |
| Zone 2 | 4 | 1176 | 1 | 554 |
| Zone 3 | 0 | 1680 | 5 | 790 |
| Zone 4 | 0 | 37 | 1 | 26 |
| Zone 5 | 2 | 1136 | 2 | 544 |
| Any job with exposure to: | | | | |
| Trichlorethylene | 0 | 269 | 1 | 111 |
| 1,1,1 trichloroethane | 1 | 411 | 0 | 179 |
| methyl ethyl ketone | 1 | 133 | 0 | 49 |
| toluene & xylene | 0 | 480 | 0 | 208 |

Cases include deaths listing malignant melanoma or brain cancer as an underlying or contributary cause of death with the date of diagnosis following the date of first employment.

Jobs with potential for exposure to various solvents were those in departments where environmental sampling conducted by NIOSH in April 1977 or by the company from 1977 to 1984 found the presence of these solvents.

Table 8: Cox proportional hazards modelling; years since first employment (YSFE), duration (DURATION), and estimates of cumulative PCB exposure.

| | N | YSFE mean (s.d.) | DURATION mean (s.d.) | CUMYR mean (s.d.) | DURZONE5 mean (s.d.) | CUM2.5 mean (s.d.) |
|---|---|---|---|---|---|---|
| | | | Malignant Melanoma | | | |
| Cases | 8 | 14.5 (6.5) | 4.5 (4.5) | 8.2 (11.9) | 7.3 (10.6) | 8.6 (12.5) |
| All workers in risk sets: | 3455 | 13.5 (6.8) | 4.6 (5.5) | 10.8 (14.9) | 7.2 (11.3) | 10.9 (15.1) |
| Rate Ratio* | | 1.16 | 0.82 | 0.83 | 0.97 | 0.85 |
| Lower bound | | 0.21 | 0.22 | 0.47 | 0.50 | 0.50 |
| Upper bound | | 6.48 | 3.03 | 1.44 | 1.88 | 1.46 |
| Brain Cancer | | | | | | |
| Cases | 7 | 14.1 (6.1) | 8.8 (6.5) | 22.9 (22.0) | 14.2 (16.4) | 21.8 (20.4) |
| All workers in risk sets: | 1670 | 14.9 (7.5) | 5.2 (5.7) | 12.0 (15.8) | 8.3 (12.7) | 12.1 (16.1) |
| Rate Ratio | | 0.54 | 2.18 | 1.27 | 1.18 | 1.23 |
| Lower bound | | 0.10 | 0.61 | 0.88 | 0.75 | 0.84 |
| Upper bound | | 2.82 | 7.80 | 1.86 | 1.84 | 1.75 |

*The rate ratios 95% confidence intervals presented estimate the risk associated with a 10 unit increase in these continuous variables.

CUMYR= estimate of cumulative PCB dose based on duration weighted by distance from capacitor ovens.

DURZONE5= estimate of cumulative PCB dose based on duration with a weight of 5 for days worked in Zone 5.

CUM2.5= estimate of cumulative PCB dose based on duration with a weight of 1 for days worked in Zone 1, a weight of 2.5 for days worked in Zones 2-4, and a weight of 5 for days worked in Zone 5.

Table 9: Malignant melanoma risk factors in case series; results of interviews with next-of-kin.

| CASE | A | B | C | D | E | F | G | H | I |
|---|---|---|---|---|---|---|---|---|---|
| Family history | +* | - | - | - | - | - | | - | - |
| Dysplastic mole | + | - | - | - | - | - | | - | - |
| Congenital mole | DK | - | - | - | - | - | | - | - |
| Previous melanoma | - | - | - | - | - | - | | - | - |
| Sun sensitivity | DK | + | - | - | + | - | | DK | DK |
| Celtic origin | DK | - | - | - | + | - | | DK | DK |

+ = next-of-kin reported the presence of the risk factor.
- = next-of-kin reported the absence of the risk factor.
DK = next-of-kin did not know.
The next-of-kin for Case G could not be located.

Spouse's report that case's mother died from malignant melanoma conflicts with patient's medical record which indicated that the mother died of cancer of the female organs.

Table 10: Power considerations for the three mortality studies of electrical capacitor workers exposed to polychlorinated biphenyls.

| | Study by Author | | |
|---|---|---|---|
| | Sinks et al | Brown et al[5] | Bertazzi et al[6] |
| N | 3583 | 2588 | 2150 |
| PYAR | 71985 | 55545 | 41007 |
| Cancer Outcome Observed/Expected (Study Power*) | | | |
| M. Melanoma | 8/2.0** | 1/1.5 (80%) | 0/0.1 (14%) |
| Brain & CNS | 5/2.8** | 0/2.7 (30%) | 2/0.3 ( 9%) |
| Liver & Biliary | 1/0.9 (31%) | 5/1.9** | 2/0.4 (13%) |
| Rectum | 1/1.2 (26%) | 4/1.9** | 0/0.4 (11%) |
| Hematopoietic | 7/7.2 (99%) | 5/7.4 (99%) | 7/2.6** |
| Lung & Bronchus | 15/19.2 (99%) | 10/16.9 (99%) | 4/2.1** |

* The power to detect a statistically significant excess of the magnitude reported by one of three studies using a one-sided hypothesis with p less than 0.05.[15]*

** This ratio of observed/expected was used to calculate the power of the other two studies.

Observed and expected numbers for Bertazzi et al come from Nicholson[10].

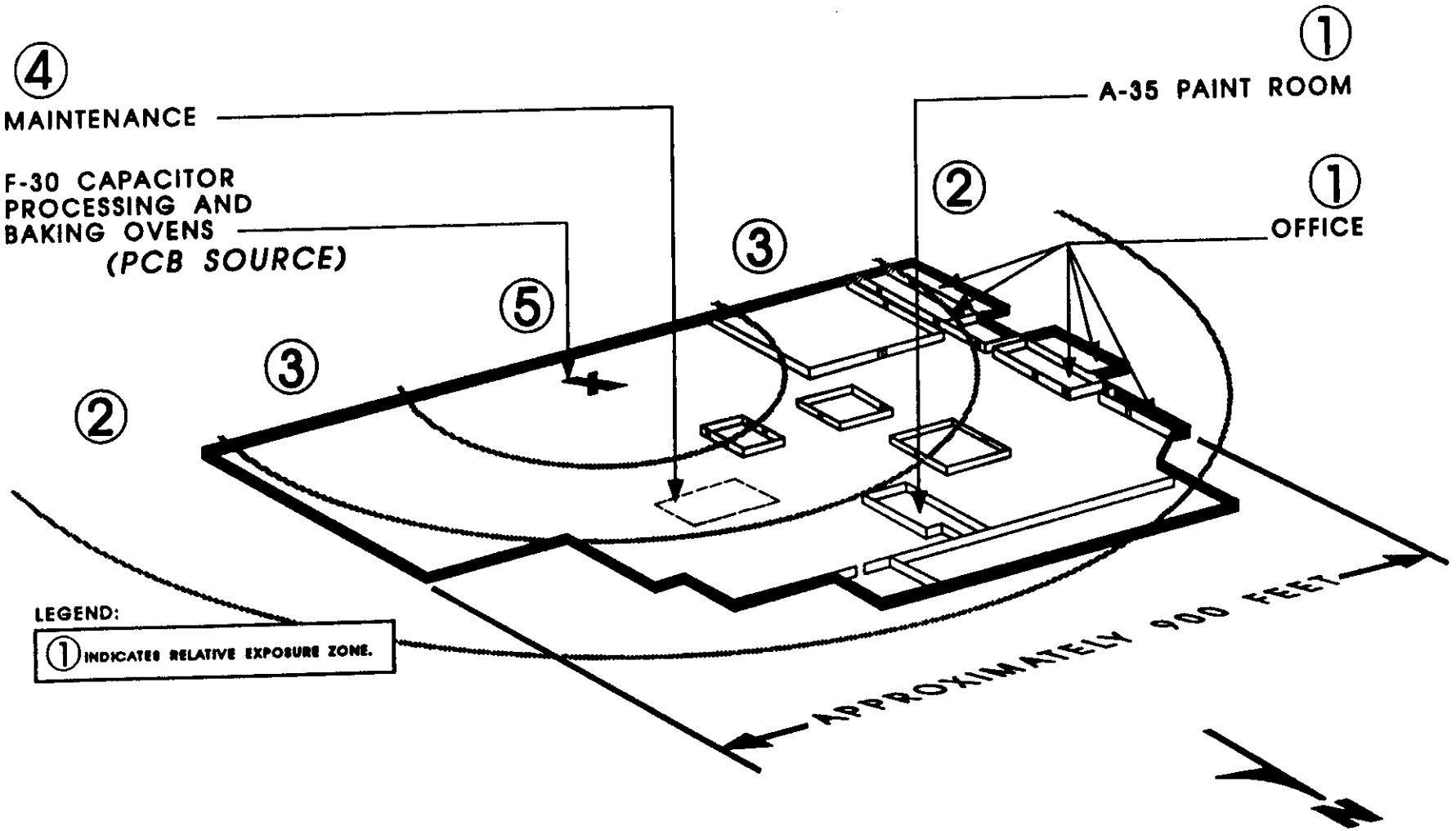


Figure 1: Floor plan for a capacitor manufacturing plant showing capacitor baking ovens and PCB-exposure zones based on a point source exposure.