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A REPORT TO THE GENERAL ELECTRIC COMPANY CONCERNING A CASE-CONTROL STUDY OF CANCER MORTALITY AT THE GENERAL ELECTRIC PITTSFIELD FACILITY

Executive Summary

(January 2, 1990)

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BACKGROUND

This study of mortality in General Electric workers grew out of a preliminary, unpublished study which was part of a series of worker mortality studies undertaken in the late 1970's. The preliminary study focused on General Electric Company in Pittsfield and found an excess of mortality from leukemia and cancer of the large intestine among those persons where General Electric's name was entered on the death record filed from the town of Pittsfield. The findings from the preliminary study were described in 1978 to the General Electric Company; which cooperated in the further investigation of the problem.

Initially General Electric provided a list of insurance pension records for all employee deaths from 1969 to 1977 which had resulted in death benefit claims. Study of these data, which included last job at General Electric, did not change earlier findings. No specific last job type or exposure was associated with the proportional mortality excesses noted.

In January 1981, it was decided to obtain complete work histories for all pension eligible workers who had died. Subsequently it was decided to undertake a detailed and in depth historical reconstruction of worker exposures to groups of substances considered to be most commonly in use.

This reconstruction of exposures for each former employee in the study was attempted for Pyranol (a mixture of polychlorinated biphenyls and trichlorobenzene), trichloroethylene, benzene, other solvents, asbestos, machining fluids and miscellaneous resin systems. Individual work histories were matched to the exposure data base to generate individual estimates of exposure histories to each group of chemicals.

Since not all subject work history records were still available, the total number of subjects available for study was less than the total number of deaths recorded. In order to maximize the study's statistical power, therefore, the mortality data base was extended twice until finally deaths were included from 1969 through 1984.

The final study population, therefore, includes those pension-eligible workers who died at some time between 1969 and 1984 for whom work history records could be recovered. The protocol for the current study was modified and adopted in its final form in 1985.

The objective of the study was to determine, to the extent possible, if there was evidence for work related cancer risks. A case-control approach was followed: exposure histories of cancer cases were compared with those of a control group consisting of workers who died of causes not thought to be related to the exposure under study.

OVERVIEW OF THE STUDY

Study Subjects

The initial study size was 2,914 white male employees who met "vesting requirements" and whose last place of work was at the GE Pittsfield plant and who died between January 1, 1969 and December 31, 1984. Those included may have died either while actively employed or after retiring. For all individuals included in the study, official death certificates were obtained. Extensive efforts were made to collect complete information on all subjects. After exclusions were made for inadequate or absent work history records and appropriate exclusions made for selection of control subjects, a total of 1,714 subjects were included in the study.

Work History Records

Work history records were sought for all deceased subjects enrolled in the study but turned out to be unavailable for a substantial number largely due to elimination of these records according to standard company policy on record retention. Although there was no evidence that the losses were biased there was no way to evaluate the losses.

Occupational Exposures

The following exposures thought to be of primary importance were rated (primarily by systematic overlapping interviews with long-term employees):

Pyranol: a transformer oil composed of polychlorinated biphenyls (PCBs) (a mixture of isomers but mostly hexachlorobiphenyl), trichlorobenzene (or a mixture of tri- and tetrachloro-benzene), less than 0.25% phenoxypropene oxides and trace amounts of dibenzofurans. The PCB content in Pyranol could vary from 45 to 80%.

Benzene: a solvent used in various departments for general cleaning during machining and assembly operations.

Trichloroethylene (TCE): a solvent used as a degreaser

Other solvents: this group includes Varsol (petroleum spirits), CPE 1000 (petroleum spirits and methylene chloride), methylene chloride, kerosene, paint thinners (primarily xylene or toluene based), solvent based paints, xylene, toluene, and naphtha. Some type of solvent exposure occurred in the majority of plant operations.

Machining fluids: used for machining and fabrication operations. Straight mineral oils were first used, then soluble oils and finally synthetic oils. There was a very minimal usage of straight cutting oils.

Asbestos: Used as wet insulation blankets during brazing and welding. Some insulation pieces were made from asbestos.

Resin systems: primarily phenol formaldehyde and polyvinyl formal resin systems.

Exposures known to be present but not specifically rated were:

Mineral oil: (10C oil) used as transformer oil. Pyranol was used as a transformer fluid only in 15-25% of the transformers built and mineral oil was used in the remainder. A review of the exposure to Pyranol was conducted in March 1988, and the following changes were made to the existing exposure ratings, in order to improve separation between the exposures to Pyranol and to mineral oil: a rating of no exposure was assigned to all jobs in which there was no dielectric fluid used or in which the dielectric fluid used was certainly mineral oil and not Pyranol. As a result, all jobs in buildings 4, 5, 19, 100, 41 and 44 were assigned a rating of 0 for Pyranol.

Metal fumes and dust: exposure occurred during welding, brazing and painting with metal based pigments.

Sawdust: in woodworking shops.

Adhesives: water, solvent based and epoxy (those using petroleum solvents are rated with group 4)

Electromagnetic fields: exposure occurred during testing and development of transformers.

DESIGN AND ANALYSIS

Basic Design

The study was designed as a case control study of cancer mortality risks. Distribution of demographic characteristics was used to obtain a preliminary description of differences between cases and controls. The characteristics of those with and without work histories were compared to examine bias due to excluding those without work histories. The data were then divided into various subcategories (stratified analysis) to examine combinations of exposure and other variables (for example, age, year of death, etc.). This analysis sought to separate exposure effects from effects attributable to other variables.

Initially, the less certain cause of death diagnoses were validated by clinical records. Then case and control status was assigned as follows:

a) Cases are all types of cancer.
b) Controls were the non-cancer deaths excluding diseases of the digestive system, genitourinary diseases, diseases of the blood and the blood forming organs, mental disorders and ill defined conditions.

While the stratified analysis provided an essential description and summary of the data, it was limited when attempting to look at several variables at once. Because of sparse data, special methods were used to examine several variables simultaneously. Careful attention was paid to following a predefined strategy so that the selection of the models would not be inappropriately affected by the results. Finally special attention was directed at the impact of time on risk.

Each exposure was considered first separately and then two or more exposures were placed in the same models in order to obtain estimates of relative risk adjusted for other exposures. Interactions between variables were also considered.

Of greatest concern is the lack of information on the smoking history of study subjects. Smoking is a risk factor for several of the cancer sites under study. Therefore it was necessary to assess its potential confounding effect. This was done by hypothesizing several possible distributions of smoking in the study population.

Statistical Power

Statistical power is a measure of the probability (given a specified magnitude of association) of obtaining a set of data such that level of an effect being sought is likely. A conventional power analysis showed that this study was generally characterized by low power, unless the effects were very strong or the causes of death common (e.g. lung cancer).

RESULTS

The results of the study are summarized in the attached Chapter III that also serves as the summary chapter of the detailed report. The detailed report includes extensive tabular material in support of the epidemiologic conclusions.

In brief, the epidemiologic analysis did not identify any unequivocal or definitive association of the General Electric-Pittsfield work environment with excess cancer risk. With limited power the study failed to find an association between pyranol (containing PCBs) and excess cancer risk among employees. In addition cancer of the large intestine, one of the two cancer sites which was in excess in the exploratory proportional mortality studies, was not found associated with the exposures included in the study.

Several findings, however, suggest further study which may clarify certain of the apparent associations. In particular, the association of lung cancer with operations coded as "resins" needs to be further evaluated. To do so requires new coding of asbestos exposures in these locations to determine whether the associations noted are attributable to unestimated asbestos exposure. Other associations deserving further study include: trichloroethylene and leukemia; benzene and cancer of the esophagus, bladder, kidney, and brain; other solvents and cancers of the kidney and the lymphatic system (especially reticulosarcoma); resin components and cancers of the esophagus, large intestine and lung; and machining fluids and kidney cancer.

COMMENT AND RECOMMENDATIONS

This study was carried out using state of the art epidemiologic and exposure assessment attribution methods. In some instances new methods were developed to address some of the more difficult data problems or analytical dilemmas. Nonetheless, findings from this study must be tempered by the fact that a number of important problems existed which limited the ability of the study to examine fully the question of cancer-

related risks from exposure to toxic agents in this work environment.

The problems of greatest importance include:

1. Records of personnel activity had not been maintained in a manner which serves the needs of an epidemiologic study. There was no effective way to document employment at the Pittsfield plant at a time sufficiently far in the past to undertake a population-based study using an historical cohort approach;

2. Information on previous employees was limited to pension-eligible employees, a designation which changes many times over the study interval. This fact made interpretation of the findings much more difficult. Furthermore, the record of pensioners was reliably available only beginning in 1969; this limited the total number of subjects who could be included in the study;

3. The need to rely on death records limited the efficiency of the study to those cancers which are likely to cause death (a high case-fatality ratio). Hence a cancer with relatively good survival (for example, cancer of the urinary bladder) is not as well studied as for work-related causes since the number of cases will far exceed the number of deaths attributed to this cause;

4. Evidence of cancer had to be based on information listed on the death certificate. Although a major effort was made to verify cases with clinical records, it was only feasible to attempt this for those cancers reported to be less well documented.

5. Very limited data were available on historical work-place exposures to the toxic materials of interest. For most of the exposures of interest there was no information for the vast majority of the study interval. As a result, exposure ratings had to be based predominantly on subjective assessment using only a few categories, which limits the power to distinguish between exposure levels. Furthermore, the exposure ratings do not reflect individual exposure variation. There is a high probability, therefore, that even if elevated cancer risks exist in this environment they might not be found.

6. Work history records, like the general personnel records, were incompletely maintained. Standard policy on record elimination to reduce volume of stored paper resulted in loss of a third of the work history records of potential interest;

7. There had been multiple changes in the work organization, so that operations of interest were carried out in different

plant buildings at different times. The historical record of these changes was very incomplete.

8. Healthy-worker selection effects could not be corrected for. This effect, although less important in studies of cancer mortality, results from the fact that workers at increased risk (e.g. disabled employees) will have a tendency to leave employment early and therefore are more likely not to be included in the study. Methods to correct for this effect require knowledge of the exposure history and date of termination for workers who left employment. This information is not available for this study.

9. Of some concern is the lack of information on the smoking history of study subjects. Therefore, it was necessary to assess its potential confounding effect. It was shown, however, that smoking was unlikely to be a strong confounder in our study.

10. The variety of problems invariably limit the statistical power of the study to find relatively small effects, even if they are present. Conventional statistical power analyses showed that this study is generally characterized by low power, except for very strong effects or for outcomes with a large number of cases (lung cancer).

* * * * *

Based on the associations noted in the epidemiologic study, and on the absence of any definitive findings, the following are recommended:

1. <u>Further study is indicated to attempt to clarify the findings for lung cancer and work in resin systems.</u>

   Because the predominant plastic product manufactured in the resin systems category involved the use of asbestos and phenol-formaldehyde, this finding cannot be clearly interpreted. Asbestos is widely accepted as a human carcinogen and OSHA has recently recognized formaldehyde as a carcinogen. The jobs in this exposure grouping were not characterized for exposure to asbestos nor specifically for formaldehyde and the process has not been operated in the Pittsfield facility for some time. The possibility for further elucidation of work risks for this area should be evaluated to determine whether the source of risk can be better specified. The feasibility of further study will depend upon the estimate of possible statistical power (based on the number of persons who worked in the area and whose work records are available) and the determination that reasonable job specific exposure assignments can be made for asbestos and formaldehyde.

2. The workforce should be notified of the findings of this study.

A summary of the results should be prepared and distributed to all current employees and all retirees. In addition the results should be provided the union for publication in its newspaper, and to the local press for general publication.

3. A meeting should be held with the local physician organization.

This meeting should explain the results and answer questions about the possible follow-up which might be indicated.

4. Follow-up medical examination should be offered in selected circumstances.

There are no accepted screening tests for lung cancer which can be offered to the previous or current employees. It is, however, appropriate to provide for an organized response to requests for health risk appraisal from any who might express a concern regarding lung cancer or other health concerns related to this study. It is recommended that an outside contractor be hired to develop a program along the following lines:

a) All current employees and retirees who can be contacted should be given the opportunity to attend a uniform cancer education and awareness program on company time on the plant's premises. The format should be small group session that address general cancer and cancer of the lung. The content of the program should include an overview and introduction on the study results, the interventions or actions which have taken place or are planned and the medical service program (MSP). The generic discussion of cancer should include what it is, how it develops, how it is treated, the causes of cancer, risk factors, occupation specific risks for the target group, early warning signs and symptoms, early detection and diagnosis, treatment and prognosis and prevention.

b) A panel of physicians (internal medicine, occupational medicine specialties) be created to provide assessment and consultation to any employee who has further concerns about the health problems identified in the educational program, specifically lung cancer. Any participant in the educational program could request this consultation which should be an individual, private consultation with a uniform report submitted to the requestor.

c) A second panel should be created of physicians who are expert in the diagnosis and treatment of lung cancer and asbestos related disease. The first panel would refer any participant who requires additional diagnostic workup for cancer of the lung to this panel. Part of this work-up should be a targeted examination for those judged to have had other than incidental asbestos exposure. (For example, chest X-ray screening for evidence of asbestos-like pleural reaction and/or sputum examination for asbestos fibers could, after further consideration and review, be deemed appropriate to offer workers who were employed in the resin systems areas). Advice on the importance of ceasing cigarette smoking should be provided and an organized program of smoking cessation should be sponsored for any cigarette smoker, but especially for any person with known prior exposure to asbestos.

d) Protocols should be developed to guide decision-making by the two panels to assure uniformity and consistency. these guidelines or protocols should be developed by the physicians and approved by a group which agrees jointly to represents the interests of the community and the company and who serve as an advisory group to any contractor selected to coordinate this overall effort.

CHAPTER I

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A. BACKGROUND
B. LITERATURE REVIEW

A. BACKGROUND

This study of mortality of General Electric - Pittsfield workers grew out of a preliminary, unpublished study as part of a series of proportional mortality studies undertaken in the late 1970's. At that time, as Occupational Hygiene Physician for the Massachusetts Division of Occupational Hygiene, Dr. Wegman conducted studies in selected New England towns, where the worker population was relatively stable. Selection of study sites was based on the further condition that the town was one where one or a few plants or industries had dominated employment. This condition provided the likelihood that a sizable proportion of the deaths of plant employees might be expected to be found in the vital records of that town and neighboring areas.

The preliminary study found an excess of mortality from leukemia and cancer of the large intestine among those persons where General Electric's name was entered on the death record filed from the town of Pittsfield.

The findings from the preliminary study were described in 1978 to the General Electric Company, which cooperated in the further investigation of the problem. The company provided a list of insurance/pension records for all employee deaths from 1969 to 1977 which had resulted in death benefit claims and were among those included in the original proportional mortality study. These records included the department in which the former employee last worked (Transformers, Plastics or Ordnance), the final payroll status (hourly vs. salaried) and the date and reason for leaving work.

Based on these records, proportional mortality studies were conducted again comparing the deaths of these former employees with those of the same race and gender in the US general population who died in the same calendar year interval. The earlier findings remained present, however, no specific job type or exposure was evidently associated with the excess proportional mortality noted.

In January 1981, it was decided to investigate further the relation between work and mortality by obtaining complete work histories for all pension eligible workers who had died. At this time an additional two years of deaths was added to increase the statistical power of the study (therefore, covering the period between 1969 and 1979). The information on work history was collected for use in a case-control mortality study design to seek associations with lifetime job history.

In May 1982, preliminary case-control analysis of the data based on job types resulted in a decision to further extend the protocol to include a detailed and in depth historical

reconstruction of exposure to groups of substances considered to be most commonly in use. This reconstruction was based on information obtained from interview of long-term personnel at General Electric and from past industrial hygiene surveys. This task was carried out by Dr. Thomas Smith and Ms Marilyn Hallock, at that time with the Harvard School of Public Health. Historical reconstructions of exposures in some cases going as far back as the 1930's and assignment of exposure ratings on an ordinal scale were carried out for pyranol (a mixture of polychlorinated biphenyls and trichlorobenzene), trichloroethylene, benzene, other solvents, asbestos, machining fluids and miscellaneous resin systems. Individual work histories are matched to the exposure data base to generate individual estimates of exposure histories to each group of chemicals. (For detail of this activity see Chapter II).

Not all subject work history records were still available, so the total number of subjects available for study was approximately one-third less than the total number of deaths recorded. Therefore, the mortality data base was again extended to include deaths through 1981. In 1984, with Dr. Wegman's relocation, the study was transferred to UCLA. Dr. Sander Greenland from UCLA joined the study team. Further developments and refinements in the protocol were specified and the study was expanded for the last time to include all deaths through the end of 1984. The final study population, therefore, includes those pension-eligible workers who died during the period 1969 and 1984 for whom work history records could be recovered.

The objective of the study is the identification of work related cancer risks. A case-control approach is followed: exposure histories of cancer cases are compared with those of a control group consisting of workers who died of causes not thought to be related to the exposure under study. A priori causes of cancer which were of interest were lung, larynx and digestive cancer (and asbestos exposure), colon and skin cancer (and machining fluids), leukemia (and benzene) and liver cancer (and polychlorinated biphenyls). However, all other cancer sites with observed number of deaths greater than 9 were considered as independent case groups. This latter series of case-control studies were undertaken as hypothesis generating in nature.

B. LITERATURE REVIEW

The substances or substance groups for which exposures were estimated were: asbestos, benzene, trichloroethylene, miscellaneous solvents, mineral oils (machining fluids, cutting oils), dielectric fluids (based on a mixture of polychlorinated biphenyl and trichlorobenzene or on mineral oils), and miscellaneous plastic resin systems. A review of current knowledge regarding these materials as human carcinogens reveals sufficient detail for asbestos, benzene, trichloroethylene, mineral oils and polychlorinated biphenyls so that the International Agency for Research on Cancer has formally considered each. Since the IARC reviews are undertaken in a well accepted manner, the summary statements of those reviews are provided (IARC,1987). The references cited can be found on the appropriate pages of Volume 42 (1987) in the IARC monograph series.

The IARC reviews lead to an overall evaluation of the available data for each agent or process. An agent can be classified as Group 1 (the agent is carcinogenic to humans), Group 2A (the agent is probably carcinogenic to humans), Group 2B (the agent is possibly carcinogenic to humans, Group 3 (the agent is not classifiable at to its carcinogenicity to humans, and Group 4 (the agent is probably not carcinogenic to humans).

For trichloroethylene and polychlorinated biphenyls there are more details on animal studies, mutagenic properties and metabolism and health effects other than cancer in recently published reviews: Kimbrough (1985, 1987), ATSDR (1987) for PCBs and Kimbrough et al. (1985), WHO (1985) and EPA (1985) for TCE (see also Ch. III).

No review was attempted for the literature on petroleum solvents (except for studies including benzene or TCE) or for miscellaneous resin systems, since these groups of chemicals are quite heterogeneous. The Discussion section contains a comparison of our findings with relevant published literature.

Polychlorinated Biphenyls (PCBs)

There is limited human evidence and sufficient animal evidence concerning polychlorinated biphenyls for the International Agency for Research on Cancer to classify them as Group 2A carcinogens (IARC, 1987). There are repeated findings of increased risk from hepatobiliary cancer.

The summary of the IARC updated review of mineral oils follows (references cited are those in IARC, 1987 and are not provided in this document).

A. Evidence for carcinogenicity to humans (limited)

Information on the possible carcinogenic risk of human exposure to polychlorinated biphenyls (PCBs) comes from studies of occupational populations and of populations exposed to the compounds accidentally. PCB mixtures may be contaminated with polychlorinated dibenzofurans dibenzodioxins.

A slight increase in the incidence of cancer, particularly melanoma of the skin, was reported in a small group of men exposed to Aroclor 1254, a mixture of PCBs (1). In a study of over 2500 US workers exposed to a similar mixture of PCBs during the manufacture of electrical capacitors, five deaths due to cancer of the liver and biliary passages were observed, whereas 1.9 would have been expected. This increase was sustained mainly by female workers in one of the two plants in the study (four of five deaths), and all five workers had first been employed before the early 1950s (2,3). Another study of workers in a capacitor plant was conducted in Italy. Exposure in the early years of production (until 1964) was to PCB mixtures containing 54% chlorine (mainly Aroclor 1254 and Pyralene 3010 and 3011). Early results showed a significant excess of all cancers among male workers, which was due mainly to cancers of the digestive system and of the lymphatic and haematopoietic tissues. Among female workers, a slight increase in mortality from cancer of the lymphatic and haematopoietic tissues was reported (4). The study was later enlarged and extended to include 2100 workers and to cover the period 1946-1982. Both male and female workers exhibited significantly increased cancer mortality in comparison with rates for the local population (14 observed, 7.6 expected; and 12 and 5.3, respectively, for men and women). Among male workers, cancers of the gastrointestinal tract (two stomach, two pancreas, one liver and one biliary passages) taken together were significantly increased haematological neoplasms (4 observed, 1.1 expected) (5). In Sweden, among 142 male workers containing up to 42% chlorine had been used, no significant excess of cancer deaths was noted. Cancer incidence was also examined: the number of cases observed corresponded well to that expected. One individual in a subgroup with higher exposure developed two relatively rare tumours, both of which occurred ten years after the start of exposure: a slow-growing mesenchymal tumour (desmoid) and a malignant lymphoma (6).

After contamination of cooking oil with a mixture of PCBs (Kanechlor 400) in Japan in 1968, a large population was intoxicated ("Yusho" disease). An early report on mortality from 1963-1983 showed a significantly increased risk of all cancer. The edible rice oil had also been contaminated by polychlorinated quaterphenyls dibenzofurans. Dose-response relationships were not clarified (7). A further comprehensive study of 887 male "Yusho" patients showed statistically significantly increased mortality from all malignancies (33) observed, 15.5 expected),

from liver cancer (9 observed, 1.6 expected) and from lung cancer (8 observed, 2.5 expected). Use of local rather than national rates in calculating expected number of deaths decreased the observed: expected ratio for liver cancer from 5.6 to 3.9, which was still statistically significant. A closer look at the geographical distribution of liver cancer cases did not allow exclusion of factors other than PCB poisoning as a possible explanation for this finding. For the 874 female patients examined, none of the noted observed: expected ratios was significant (8). In a series of ten autopsies of "Yusho" patients, two adenocarcinomas of the liver were found, with no indication of a direct association with exposure to PCBs (9). Ultrasonic and tumour marker examination of two series of 79 and 125 patients with "Yusho" disease in 1983 and 1984, respectively, did not reveal any case of hepatic-cell carcinoma (10). Two studies of the PCB content of fat tissues and cancer occurrence were available. An association was suggested between PCB concentrations in subcutaneous abdominal adipose tissue and the occurrence of cancers of the stomach, colon, pancreas, ovaries and prostate (11). No indication emerged of a relationship between PCB content in extractable breast fat tissue and the occurrence of breast cancer (12).

The available studies suggest an association between cancer and exposure to PCBs. The increased risk from hepatobiliary cancer emerged consistently in different studies. Since, however, the numbers were small, dose-response relationships could not be evaluated, and the role of compounds other than PCBs could not be excluded, the evidence was considered to be limited.

B. Evidence for carcinogenicity to animals (sufficient)

Certain PCBs (particularly with greater than 50% chlorination) produced benign and malignant liver neoplasms in mice and rats after their oral administration (1,13,14). Oral administration of Aroclor 1254 to rats yielded hepatocellular adenomas and carcinomas as well as intestinal metaplasia and a low, statistically nonsignificant incidence of stomach adenocarcinomas (15). PCBs were inadequately tested in mice for induction of skin tumours (16,17). In several studies, oral or intraperitoneal administration of PCBs enhanced the incidences of preneoplastic lesions (18-20) and of neoplasms (21,22) of the liver induced in rats by N-nitrosodiethylamine or 2-acetylaminoflourene. In one study, intragastric administration of PCBs to mice increased the incidence of lung tumours induced by intraperitoneal administration of N-nitrosodimethylamine (23).

B. Other relevant data

No data were available on the genetic and related effects of PCBs in humans.

Dominant lethal effects were not induced in rats administered PCBs orally, but were produced in rats nursed by females that had received PCBs orally. PCBs did not induce chromosomal aberrations in bone-marrow cells or spermatagonia of rats treated *in vitro* ; micronuclei were not induced in bone-marrow cells of mice in one study, while equivocal results were obtained in a second study in which the PCBs were administered in corn oil. They did not transform Syrian hamster embryo cells *in vitro* . PCBs induced DNA strand breaks and unscheduled DNA synthesis in rat hepatocytes *in vitro* . Neither chromosomal breakage nor aneuploidy was induced in Drosophila. PCB mixtures did not induce SOS repair and were not mutagenic to bacteria (24).

2,2',5,5'-Tetrachlorobiphenyl induced DNA strand breaks in mouse cells *in vitro* . 2,4,5,2',4',5'-Hexachlorobiphenyl but not 3,4,5,3',4',5'-hexachlorobiphenyl inhibited intercellular communication in chinese hamster V79 cells. Purified 2,3,2',4'-2,5,2',5'- and 3,4,3',4'-tetrachloro- and 2,4,6,2',4',6'-hexachlorobiphenyl were not mutagenic to bacteria (24).

Trichloroethylene (TCE)

There is inadequate human evidence and limited animal evidence concerning trichloroethylene for the International Agency for Research on Cancer to classify it as a Group 3 carcinogen (IARC, 1987).

The summary of the IARC updated review of trichloroethylene follows (references cited are those in IARC, 1987 and are not provided in this document).

A. Evidence for carcinogenicity to humans (inadequate)

Three cohort studies have been reported, two of which showed no excess of cancer (1,2); the third (3), in an extended and updated version (4), showed slightly increased incidences of cancer of the bladder (3 observed, 0.8 expected) and prostate (4 observed, 2.4 expected) and of lymphoma (2 observed, 0.3 expected). Two case-control studies of lymphoma have been reported: one of Hodgkin's lymphoma, in which three of 25 cases and none of 50 controls had had exposure to trichloroethylene (5), and the other on Hodgkin's and non-Hodgkin's lymphomas combined in which seven of 169 cases and three of 338 controls had been exposed (6). Four studies of liver cancer have indicated no clear association with exposure to trichlroethylene (7-10). A few more cases than controls were exposed in two of the studies, especially when the two studies were analyzed together (7,9). In a proportionate mortality study of polishers and planters with potential exposure to trichloroethylene, but

also to chromates and nickel, there were excesses of esophageal and primary liver cancers. There were also slight excesses of cancers of buccal cavity and pharynx, pancreas and larynx and of lymphoma (Hodgkin's and non-Hodgkin's lymphomas combined, 13 observed, 9.3 expected) (11).

Exposure to trichloroethylene may occur to some extent in laundry and dry-cleaning work, although exposure to tetrachloroethylene probably predominates. Decaffeinated coffee, which is often extracted with trichloroethylene, appeared to be a risk factor for pancreatic cancer in one study, as did dry-cleaning (12).

The inconsistent relationship between liver cancer and dry-cleaning is considered in the summary on tetrachloroethylene. Even if there is some consistency among several studies with regard to an association between lymphatic malignancies and exposure to trichloroethylene, the small numbers involved do not permit any definite conclusion to be drawn about a causal association.

B. Evidence for carcinogenicity to animals (limited)

Trichloroethylene was tested for carcinogenicity by oral administration in mice in one experiment and in rates in two experiments. In mice, it produced hepatocellular carcinomas and lung tumours in both males and females. One study in rats was considered to be inadequate, and the other showed equivocal evidence of carcinogenicity (3). Inhalation studies with trichloroethylene have been conducted in mice, rats and hamsters (13,14). In one study in female mice, it caused lung tumours (13), but it gave negative results in the other study in mice and in rats and hamsters. Administration by skin painting and by subcutaneous injection to mice also gave negative results (15). In inhalation experiments using two strains of mice, trichloroethylene increased the incidences of liver tumours in males of one strain and in females of the other. In rats, a low incidence of adenocarcinomas of the renal tubules was observed following exposure to trichloroethylene by inhalation (16). In mice, oral administration of trichloroethylene containing epichlorohydrin as a stabilizer induced forestomach carcinomas but no liver or lung carcinoma (17). Pure trichloroethylene was tested by oral administration in mice and rats. Hepatocellular carcinomas were induced in male and female mice; none were induced in female rats, and the experiment in male rats was considered inadequate (18). A study by oral administration was conducted in four strains of rats, but it was inadequate because of toxicity and poor survival (19).

C. Other relevant data

Oral administration of trichloroethylene to mice induced hepatic peroxisome proliferation; however, no such effect was observed in rats.

No adequate data were available on the genetic and related effects of trichloroethylene in humans.

Many commercial preparations of trichloroethylene contain stabilizers which are known to be mutagenic. As a rule, the purities of the preparations tested are not given. Trichloroethylene induced micronuclei, somatic mutation (in the spot test), sperm anomalies and DNA strand breaks in the kidney and liver, but not lung, of mice treated in vivo; it did not induce dominant lethal mutations. It induced sister chromatid exchanges and unscheduled DNA synthesis in human lymphocytes *in vitro*. It induced transformation of mouse and rat cells but not of Syrian hamster cells *in vitro* or unscheduled DNA synthesis in rat hepatocyte. It was mutagenic to plant cells and induced mutation, gene conversion and mitotic recombination in Saccharomyces cerevisiae both *in vitro* or in a host-mediated assay. It was mutagenic to bacteria when tested as a gas but not when tested as a liquid, except in one study using a mouse-liver metabolic system (21).

Review of Human Epidemiologic Studies of Asbestos and Cancer

There is sufficient human evidence that asbestos is causally associated with lung cancer and mesothelioma for the International Agency for Research on Cancer to classify it as a Group 1 carcinogen (IARC, 1987). Additional evidence suggests that asbestos may also be causally related to laryngeal cancer and gastrointestinal cancer but the data are less convincing regarding these sites.

The summary of the IARC updated review of asbestos follows (references cited are those in IARC, 1987 and are not provided in this document).

Numerous reports from several countries have described cases or series of pleural and peritoneal mesotheliomas in relation to occupational exposure to various types and mixtures of asbestos (including talc containing asbestos), although occupational exposures have not been identified in all cases (1-21). Mesotheliomas of the tunica vaginalis testis and of the pericardium have been reported in persons occupationally exposed to asbestos (22-24).

Environmental exposure either in the houses of asbestos workers or in the neighbourhood of asbestos mines or factories has been noted in some of the cases (1,2,4-6,9,11,25,26). It has been estimated that a third of the mesotheliomas occurring in the USA may be due to nonoccupational exposure (27). In a study from Israel, the incidence of mesotheliomas was found to be higher among those born in the USA or in Europe relative to those born in Israel (9).

In some of these case reports and in other studies, asbestos fibres were identified in the lungs (5,6,11,28-32). Amphibole fibres usually predominated, but in a few cases mainly or only chrysotile fibres were found (6,28).

The long latency required for mesothelioma to develop after exposure has been documented in a number of publications (11,13,26,28,33-37). An increasing proportion of cases has been seen with increasing duration of exposure (36).

A number of epidemiological studies of respiratory cancer and mesothelioma have been reported in relation to exposure to unspecified or complex mixtures of asbestos in shipyard work (38-45). The risk ratio for lung cancer has usually been moderately increased, both in these studies and in studies on various other occupational groups with similarly job-related but unspecified or complex asbestos exposures (35,46-54). Risk ratios of about 2-5 have been reported in some studies, but the ratio was considerably higher in one rather small study (55) and did not exceed unity in another (42). In one study, individuals suffering from asbestosis had a considerably greater risk for lung cancer, with a risk ratio of 9.056. In some of the studies referred to, a number of mesotheliomas were also observed (41,42,44,47,51,53,55). Abdominal mesotheliomas have sometimes been mistaken for pancreatic cancer (57). Mesothelioma cases have been observed to have relatively lower fibre content in the lungs than lung cancer cases (32).

Laryngeal cancer has been considered in two cases-control studies, resulting in risk ratios of 2.4 and 2.3 that relate to shipyard work and unspecified exposure, respectively (40,58). A cohort study of insulation workers showed a relative risk of 1.9, based on nine cases (57). A case series indicated a high frequency of exposure to asbestos, especially in low-grade smokers (59). A risk ratio of 3.2 for laryngeal cancer was reported among chrysotile miners in an area with generally high incidence (60), but no increased risk was seen in a cohort of workers with exposure to crocidolite (61). Two correlation studies have also indicated a relationship between laryngeal cancer and exposure to asbestos (39,62).

Mesotheliomas related to shipyard work and other exposures, including household contact with asbestos workers, have also been

subject to epidemiological studies (36,63-67), resulting in risk ratios of about 3-15 in comparison with background rates not clearly referable to asbestos exposure.

Some studies have specifically considered environmental exposures with reference to mesotheliomas (66,67). Three correlation studies and one case-control study considering exposure to piped drinking-water (68-71) did not show consistently increased risks for any type of cancer, whereas another study (72) considering chrysotile contamination mainly from natural sources gave some indication of an increase in the incidence of peritoneal and stomach cancers in persons of each sex, although no other cancer site was consistent in this respect.

Exposure to crocidolite has been studied with regard to risk of lung cancer (61,73-76), and risk ratios of about 2-3 have been reported. Three lung cancers and two mesotheliomas occurred in 20 individuals after one year of high exposure to crocidolite; at least 17 of the cases had asbestos-induced lung changes on X-ray films (77).

One study (78) of histological types of lung cancers showed that among persons exposed to crocidolite 45.7% of cases were squamous-cell carcinomas, as compared to 35.2% among unexposed persons. In the context of unspecified and complex exposures, small-cell carcinoma was found to be relatively more prevalent than other forms (50).

Exposure to chrysotile was found in some studies to result in virtually no increase in risk ratio (60,79-81), or a slightly elevated relative risk of lung cancer (82-86). Somewhat higher risk ratios, up to 2.5, 3.5 and 2, respectively, were obtained in one study of chrysotile miners (87) and in two independent studies from one asbestos [chrysotile] textile plant (88,89), the latter being the more comprehensive. With regard to mesotheliomas, one study suggested a particularly high risk of combined exposure to chrysotile and amphiboles (risk ratio, 61), thus almost multiplying the risk ratios (6 and 12, respectively) of exposures to chrysotile and to amphiboles alone (90). Another study showed no mesothelioma among a large worker population with exposure to chrysotile only (91).

A slight excess of lung cancer and some mesotheliomas appeared in some groups with mixed exposures involving amosite, chrysotile and crocidolite (92-94). Exposure predominantly to amosite, but also to chrysotile, was reported to be the probable cause of at least four or five mesotheliomas (one peritoneal) observed in a UK insulation-board factory (95). One cohort with exposure to cummingtonite-gunerite, which is closely related to amosite, had no clear excess of lung cancer, although one case of mesotheliomas was observed (96).

Exposure to tremolite and actinolite has been the subject of a few studies in investigations of vermiculite mining and milling (97,98) and environmental exposure (99). The studies of miners indicated a risk ratio for lung cancer of up to approximately six fold. Deaths from mesothelioma were found in the occupational studies, whereas the study of environmental exposure showed no increase risk, although pleural plaques were reported. Publications of one case report of a mesothelioma after environmental exposure suggests that tremolite was of etiological importance (31).

Cancers other than of the lung or mesothelioma have been considered in many studies (1,17,35,39,41-44,48,51,55,60-62,68-70,72-74,76,87,89,92,93,96,97,99-108). Some indicated an approximately two-fold risk with regard to gastrointestinal cancer in connection with shipyard work (41,43), and some increased risk was also seen in association with exposure to both chrysotile and crocidolite (103), to crocidolite (61,74) or to chrysotile (87). Cancer of the colon and rectum was associated with asbestos exposure during chrysotile production, with an approximately two-fold risk (87); a similar excess was found for unspecified asbestos exposure (104). Some excess of ovarian cancer has been reported in two studies (73,76) but not in another (92); exposure to crocidolite was probably more predominant in the studies that showed excesses. Bile-duct cancer appeared in excess in one study based on record-linking (105), and large-cell lymphomas of the gastrointestinal tract and oral cavity appeared to be strongly related to asbestos exposure in one small study covering 28 cases and 28 controls, giving a risk ratio of 8; however, ten cases and one control also had a history of malaria (106). An excess of lymphopoietic and haematopoietic malignancies has been reported in plumbers, pipe-fitters, sheet-metal workers and others with asbestos exposure (17,54,107,108).

The relationship between asbestos exposure and smoking indicates a synergistic effect of smoking with regard to lung cancer (1). Further evaluations indicate that this synergistic effect is close to a multiplicative model (52,109). As noted previously (1), the risk of mesothelioma appears to be independent of smoking (47,66), and significantly decreasing trend in risk was observed with the amount smoked in one study (65).

The studies of the carcinogenic effect of asbestos exposure, including evidence reviewed earlier (1), show that occupational exposure to chrysotile, amosite and anthophyllite asbestos and to mixtures containing crocidolite results in an increased risk of lung cancer, as does exposure to minerals containing tremolite and actinolite and to tremolitic material mixed with anthophyllite and small amounts of chrysotile. Mesotheliomas

have been observed after occupational exposure to crocidolite, amosite, tremolitic material and chrysotile asbestos. Gastrointestinal cancers occurred at an increased incidence in groups occupationally exposed to crocidolite, amosite, chrysotile or mixed fibres containing crocidolite, although not all studies are consistent in this respect. An excess of laryngeal cancer has been associated with the presence of asbestos fibres in drinking-water. Mesotheliomas have occurred in individuals living in the neighbourhood of asbestos factories and mines and in people living with asbestos workers.

Review of Human Epidemiologic Studies of Benzene and Cancer

There is sufficient human evidence that benzene is causally associated with leukemia for the International Agency for Research on Cancer to classify it as a Group 1 carcinogen. This finding was recently reviewed and confirmed (IARC, 1987) and a similar finding has been reported according to the Environmental Protection Agency Cancer Risk Assessment Guidelines (ATSDR, 1987). The evidence, to date, does not permit an evaluation of whether benzene is associated with other than hematopoietic malignancies in humans.

The summary of the IARC updated review of bemzeme follows (references cited are those in IARC, 1987 and are not provided in this document).

Numerous case reports and series have suggested a relationship between exposure to benzene and the occurrence of various types of leukaemia (1). Several case-control studies have also shown increased odds ratios for exposure to benzene, but mixed exposure patterns and poorly defined exposures render their interpretation difficult.

Three independent cohort studies have demonstrated an increased incidence of acute nonlymphocytic leukaemia in workers exposed to benzene (1,3). An updating of a cohort study published earlier on benzene-exposed workers (1) confirmed the previous findings and added a further case of myelogenous leukaemia, giving a standardized mortality ratio (SMR) of 194 (95% confidence interval, 52-488), based on four cases; a higher excess risk was obtained when only myelogenous leukaemia was considered (4 observed, 0.9 expected; $p = 0.011$) (4). A further cohort study found an excess of acute myeloid leukaemia (SMR, 394; 172-788) among refinery workers, based on eight cases; however, the patients had not worked in jobs identified as having the highest benzene exposure (5). Another study of refinery workers showed no death from leukaemia (0.4 expected); however, the median exposure intensity for benzene was 0.14 ppm (0.45 mg/m3), and only 16% of 1394 personal samples, taken between 1973 and 1982 inclusive, contained more than 1 ppm (3.19 mg/m3). The

median exposure intensity in "benzene-related units" was 0.53 ppm (1.7 mg/m3) (6).

In a Chinese retrospective cohort study, encompassing 28 460 workers exposed to benzene in 233 factories, 30 cases of leukaemia (23 acute, seven chronic) were found, as compared to four cases in a reference cohort of 28,257 workers in 83 machines production, textile and cloth factories. The mortality rate from leukaemia was 14/100,000 person-years among the exposed and 2/100,000 person-years among the unexposed (SMR, 574; $p < 0.01$). Mortality was especially high for workers engaged in organic synthesis, painting and rubber production. The mean concentrations of benzene varied in a wide range, from 10 to 1000 mg/m3, but the range 50-500 mg/m3 covered most of them (7).

Review of human epidemiologic studies on mineral oils and cancer

There is sufficient human evidence that untreated and mildly-treated mineral oils (machining fluids) for the International Agency for Research on Cancer to classify them as Group 1 carcinogens (IARC, 1987). There is agreement that these substances are associated with skin (particularly scrotal) cancer and with gastrointestinal cancer. There is some evidence that they are also associated with lung cancer. Human studies do not permit identification of highly refined oils as carcinogenic and animal studies provide inadequate evidence of their carcinogenicity (IARC classification - Group 3).

The summary of the IARC updated review of mineral oils follows (references cited are those in IARC, 1987 and are not provided in this document).

Exposure to mineral oils that have been used in a variety of occupations, including mulespinning, metal machining and jute processing, has been associated strongly and consistently with the occurrence of squamous-cell cancers of the skin, and especially of the scrotum (1). Production processes for these oils have changed over time, and with more recent manufacturing methods highly-refined products are produced that contain smaller amounts of contaminants, such as polycyclic aromatic hydrocarbons.

Excess mortality or morbidity from gastrointestinal malignancies was seen in two out of three cohort studies of metal workers (stomach cancer in two studies, large-bowel cancer in one); however, the only significant excess was for the sum of stomach cancer plus large-bowel cancer in one study. Four cases of scrotal cancer were detected in one relatively small cohort study of metal industry workers (1). Among 682 turners with five or more years of exposure to mineral oils, five cases of squamous-cell carcinoma of the skin (four of the scrotum)

occurred, with 0.3 expected (2). In a case-control study, a relative risk of 4.9 was reported for the association of scrotal cancer with potential exposure of metal workers to mineral oils. Neither the actual levels of exposure nor the classification of the mineral oil to which the machine workers were potentially exposed was available in the reports of the epidemiological studies (1).

In a case-control study, an excess of sinonasal cancers was seen in toolsetters, set-up men and toolmakers (1). In a series of 344 cases of scrotal cancer from 1936 to 1976, 62% had held occupations in which exposure to mineral oils was likely to have occurred. The median time since first exposure was 34 years (3).

An examination of the incidence of second primary cancers among men with scrotal cancer demonstrated excesses of respiratory, upper alimentary tract and skin cancers; when the occupations were grouped, the excess was largely confined to those with exposure to oil (1).

Excesses of bladder cancer have been reported in case-control studies in several countries among machinists and engineers, who were possibly exposed to cutting oils containing aromatic amines as additives (1).

With regard to printing pressmen, one of two cohort studies addressing lung cancer showed an excess and one of two proportionate mortality studies showed a small excess of lung cancer among newspaper pressmen but no excess among non-newspaper pressmen; the other study did not address lung cancer. One of three proportionate mortality studies on manual workers in the printing industry, not specifically addressing printing pressmen, did not show an increased lung cancer risk, whereas the other two studies found an excess. One of two proportionate mortality studies of printing pressmen indicated an increase of deaths from rectal cancer, and the other showed possibly an increase of deaths from colon cancer; the cohort study considering colorectal cancers did not show an increased occurrence. One proportionate mortality study among newspaper and other commercial printing pressmen showed an excess of mortality from cancers of the buccal cavity and pharynx, whereas no such excess was observed in a cohort study. One case-control study indicated an excess of cancers of the buccal cavity and pharynx. The findings regarding other malignancies were inconsistent; scrotal cancers were not mentioned. The type and amount of exposure were usually not described; exposure to both mineral oils and carbon blacks would probably have been involved (1).

In mortality statistics from the UK and from Washington State, USA, excesses of lung and skin cancer have been registered for jobs entailing exposures to mineral oils (1).

Chapter II

GE Pittsfield Retrospective Exposure Assessment Study

Scope of Exposure Assessment Study

The purpose of the exposure assessment was to reconstruct historical exposures to toxicologically significant chemicals and materials at GE Pittsfield. This was a difficult undertaking because of the large number of materials in use at the plant, the many types of operations performed, and the limited number of past records. A multistep interview process was used to interview long-term employees to obtain and corroborate information on historical exposures.

Background

Historically many studies in occupational health have treated what was actually a complex multiple exposure as a study of a single agent. For example, miners in the Erz Mountains are exposed to a variety of metals, radon and radon daughters, and uranium. The first identification of lung cancer occurred in 1879 at which time the etiologic

agents were assumed to be arsenic and cobalt dusts in conjunction with silicosis as a predisposing factor (Harting and Hesse, 1879). Radiation exposure from radon gas was thought to be too low to contribute to disease. In the 1950s, however, theoretical calculations demonstrated that radon daughters produced 20 times the radiation exposure of radon. Subsequent epidemiological studies have only evaluated radon daughter exposure. Any additional contributions of nickel, arsenic, or other metals have not been evaluated (Waxweiler, 1981). Similarly, the strong association of vinyl chloride with liver angiosarcoma in chemical workers has, until recently, prevented the evaluation of other exposures present such as acrylates, caprylyl chloride, methanol, and vinyl acetate (Smith et al., 1981)

Recently an increasing number of studies have attempted to evaluate multiple agents. For example, Axelson et al. (1978) rated jobs at a copper smelter not only for exposure to arsenic, the presumed etiologic agent, but also to copper and other metals. Workers with exposure to either copper or arsenic had elevated relative risks for cerebrovascular disease. However, the arsenic effect disappeared when the copper exposures were controlled for while the copper effect persisted when arsenic exposures were controlled. In a reevaluation of vinyl chloride data, Ott et al. (1974) found what appears to be a synergistic effect of arsenic and vinyl chloride on lung and other types of cancer. Thus multiple

agent studies can evaluate disease etiology, generate new hypotheses, and also test for synergistic effects, something which is rarely done experimentally.

The method of assessment of past exposures to single or multiple agents depends upon the nature of the exposures and the available data. Ideally if substantial industrial hygiene data were available, it could be used to assign quantitative exposures to jobs past and present. In practice extensive industial hygiene data before 1970 is rarely available. Consequently only a few studies have attempted retrospective quantitative exposure assessments (Smith et al., 1984; Ayer et al., 1973; Dement et al., 1982; Stewart et al., 1986).

The majority of studies in occupational epidemiology have not assessed the intensity of exposure but have used only the duration of exposure in a particular job as a surrogate for dose. A study which surveyed and critiqued 48 occupational health epidemiological studies conducted between 1977-1978 found that only 18% of the studies defined exposure both by duration and intensity (Baumbarten and Oseasohn, 1980).

Those studies which evaluated the intensity of exposure in the absence of quantitative data have used a variety of qualitative categorical scales to rate jobs. Typically a knowledgeable plant employee (less frequently, an industrial hygienist) assigns an exposure category to jobs within the plant.

Different categorical scales have been used to rate exposures. Most frequently a low-medium-high scale has been used. Other studies have tailored categorical scales specifically to the exposures under evaluation. Arp et al. (1983) used the scale shown in Table 2-1A to rate exposures to benzene or to other solvents in the rubber industry. Waxweiler et al. (1981) and Kromhout et al. (1987) used scales that included more specific descriptions of work activities (see Table 2-1B and C). Bourquet et al. (1987) used two scales to rate jobs for dermal exposures. Each job was rated for degree of exposure (none, small, large) and frequency of exposure (none, infrequent, frequent). For analysis the scales were combined into the following ordinal scale: none, low (small-infrequent), medium (small-frequent, large-infrequent), and high (large-frequent).

Various sources have been used to assign exposure categories to job titles. Typically a knowledgeable plant employee, such as a production manager or an industrial hygienist, rates work history job titles. Because of the enormous effort required to assign exposures to a large number of job titles, the majority of studies have not attempted to obtain multiple assessments for each job title.

Only recently have studies attempted to check categorical exposure assignments. Tankersley and Checkoway (1983) had two groups of industrial hygienists (plant and corporate) rate a subset of 100 work histories (out of 9000 histories in an epidemiological study) for exposures to 5

chemicals in the nuclear industry. Forty eight per cent of the jobs were rated identically and 49% differed by only one category. Only 3% of the jobs differed by 2 or more categories. No job was assigned to both the highest and lowest category.

Kromhout et al. (1987) compared categorical assignments by industrial hygienists, plant supervisors and workers against quantitative exposure measurements. Industrial hygienists were marginally more accurate than supervisors or workers who in turn gave comparable ratings.

Finally Arp et al. (1983) used extensive purchasing and production records to assign past exposures to solvents in the rubber industry. He checked the quality of the assignments by predicting solvent exposures of current jobs from company records and then determining the actual exposure by walkthrough surveys.

The validation of categorical assignments can be an arduous task depending upon the number of unique jobs and work operations. The type of validation, of necessity, must be tailored to the information available.

Exposure Assessment Study Objectives

Given the issues discussed above, the objectives of the exposure assessment study were the following: 1. To determine what the toxicologically significant exposures were at the GE Pittsfield plant; 2. To choose an

appropriate categorical rating scale; 3. To rate work history jobs for the selected exposures; 4. To check the ratings to the extent possible.

Study Procedures

The general procedure for obtaining information on exposures of job titles derived from work histories is outlined in Table 2-2. While the epidemiology team assembled and reviewed employee work histories, the exposure assessment team constructed a job exposure database for each unique job title appearing in the work history database. Merging the two databases produced a history of job exposures for each worker in the study.

The exposure information was obtained in a series of week long site visits to the GE Pittsfield plant. During the first visit, a plant walkthrough and review of current operations was conducted was well as a review of any plant records on production, chemical usage, purchasing records, industrial hygiene measurements, building maps, etc. Hard copy records on the production of transformers and purchases of dielectric fluids and chemicals were limited and did not extend far back in time. Records of industrial hygiene measurements made since 1978, an inventory of major chemicals by building from 1983, and a record of major

chemicals distributed by Central Stores to different departments were obtained.

To obtain more detailed exposure information, a group of 18 knowledgeable plant employees was selected by GE to represent the range of operations. A large number of interviewees was required to cover the many operations in the plant. Most of the individuals were supervisors or managers. Interviewees were selected on the basis of their knowledge of specific plant operations and their length of service.

A history of positions held was obtained for each interviewee. As of 1983, the average length of employment was 38 years. Twenty two per cent of the interviewees started work in the 1930s, 56% began in the 1940s, and 22% in the 1950s. Eyewitness historical information was therefore available back to the mid 1930s. In addition several of the interviewees' fathers had worked in the plant so that at least the major exposures could be constructed for the period 1900 to 1930. Only two of the seven exposures for which work history jobs were rated were used from the start of the plant (specifically machining fluids and solvents).

Using information on current exposures obtained in the first visit, about 250 component operations or subunits were grouped into about 50 operations based on similarity of exposures or location (see Table 2-6). During the second

site visit, information was obtained from the 18 interviewees on the following:

-All major and many minor chemical and metallurgical exposures within an operation and their use dates.

-History of process and engineering control technology.

-History of location of the operation within the approximately 100 buildings on site (many operations changed location over the years).

Because of the many different types of operations, a standardized questionaire could not be used. Interviews were open-ended though they always included the core group of questions listed above. Interviews were conducted by an industrial hygienist.

Between the second and third visits, the information collected was summarized and a history of each operation listing all exposures was written (see Operation Descriptions Book in Appendix). Material Safety Data Sheets and information on formulations and composition was obtained for those products identified by trade names by the interviewees.

More than 250 chemicals and classes of chemicals were identified as having been used at the plant. A toxicological review was next conducted using sources such as the NIOSH Registry of Toxic Effects of Chemical Substances, IARC Monographs and Bulletins, US PHS Publication No. 149 - Survey of Compounds which have been Tested for Carcinogenecity, and several on line computer data bases.

Of the original 250 chemicals, approximately 30 had possible mutagenic or carcinogenic potential. From these, seven exposures were selected for job exposure ratings based on their carcinogenic potential, the quantity of the material used, and the number of operations where the material was used.

The seven potential exposure hazards were the following: pyranol, benzene, trichloroethylene, solvents, machining fluids, asbestos, and synthetic resin systems. Detailed information on each of the exposures is presented in later sections of this chapter.

During this phase of the study an exposure rating scale was developed (see Table 2-3). A scale using terms describing the nature of contact (direct, indirect) and frequency of contact (infrequent, routine) in addition to intensity was chosen to permit interviewees to more easily distinguish between the different categories.

During the third site visit, interviewees reviewed and critiqued the Operation Descriptions. In addition they began to rate operation job titles for exposures to any of the seven chemicals of interest.

In subsequent site visits, additional job titles were rated as study work histories were entered into a computer database and generated more titles. In the first phase of the study (1982-1984), a total of 4477 unique job-operation titles were rated for exposures. In the second phase of the study (1985-1988), an additional 1800 job titles were

assigned exposures based on the phase I exposure assignments. During the course of the study the Operation Descriptions Book was reviewed for technical accuracy by other plant personnel, including the plant physician, industrial hygienist, and environmental manager. The final review took place after the preliminary findings had been reported to the company. Any changes made in the last phase of the study required hard copy documentation.

Exposure Rating Evaluation

Categorical exposure ratings by long-term employees were evaluated in several ways. The first evaluation method was to compare employee ratings with recent quantitative industrial hygiene measurements. This could be done in a limited fashion for only two exposures (solvents and pyranol) since the numbers of industrial hygiene measurements were small.

Several years after PCB use was terminated, residual airborne PCB levels were determined by the industrial hygiene group. These results are summarized in Table 2-4 which also indicates which operations interviewees identified as pyranol-containing. Employees identified operations with high PCB residual air levels as having contained PCBs. Employees did not identify Tank Fabrication (Building 33) as containing PCBs; this building had the

lowest levels (mean 0.5 ug/m3, range 0.2-0.7 ug/m3). Further investigations revealed that PCBs had never been used in this building; these levels may represent general background levels at the GE Pittsfield plant.

There was also a limited amount of industrial hygiene measurements for various solvents. Between 1975 to 1980, 38 unique job titles were sampled for solvents by the industrial hygiene group. Of these titles, 33 or 87% were identified by interviewees as having solvent exposure.

Where the experience of interviewees overlapped, multiple independent exposure assessments were collected on operations and jobs. Job titles were rated for exposures in two steps: 1. Operations using the selected exposures were identified; 2. Job titles within the identified operations were rated for exposures. Multiple assessments were obtained in both steps and were used to check agreement between the interviewees. Table 2-5 presents the agreement between interviewees on job title ratings. Percent agreement or disagreement was calculated from the number of jobs in a category divided by the number of jobs rated in steps 1 and 2. There was very good agreement among interviewees for the seven exposures. The agreement was excellent for the exposures that were used currently or in the recent past (pyranol, TCE, asbestos, machining fluids, resin systems). The agreement was lower but still very good for benzene, whose use ended in 1950, and for solvents, which represented a very heterogeneous category.

An additional evaluation of agreement among employee job ratings was conducted during Phase II after all 7000 job titles had been rated. Those job titles comprising approximately 85% of total study person-years, about 250 titles, were rated by a separate team of several managers at GE Pittsfield. Again there was very good agreement between the new and old employee group ratings: 78% of the jobs had identical ratings and 89% agreed within one ranking. These findings are consistent with Tankersley and Checkoway (1983).

The next sections of the report present an overview of the different operations at the GE Pittsfield plant and detail relevant information about the coding of the seven rated exposures as well as their use in the different operations. Detailed information on each operation listing all exposures is presented in the Operation Descriptions Book in the Appendix. For sake of completeness the last section describes exposures of toxicological interest that were not rated because they were confined primarily to a single operation or because complete exposure information was lacking.

Overview of GE Pittsfield Operations

There are three basic manufacturing divisions at GE Pittsfield: Power Transformers (PT), Plastics Division (PD), and Ordnance Systems (OS). These occupy approximately 120 buildings at the 500 acre site along the Housatonic River. As of 1982 there were about 3500 workers in PT, 600 in PD and 3500 in OS for a total of 7400 workers. About 3200 were hourly employees and the rest were salaried. Peak employment occurred during World War II when the worker population reached 11,000. During the mid 1980s the transformer division was phased out at Pittsfield.

Transformers have been manufactured at this site since 1890. In 1886 at Great Barrington, VT, William Stanley demonstrated that alternating current could be used to transmit electricity and developed the first ac transformer. A group of Pittsfield, MA investors enabled Stanley to open the Stanley Electric Manufacturing Company in Pittsfield in 1890. GE bought the plant in 1903. At that time the plant already had 1500 employees.

For the last ten years of operation, there was only one transformer department. Up until the mid 1970s, however, there were two major transformer divisions - Power Transformers (north of the railroad tracks or "Northside", see Figure 2-1) and Distribution Transformers (south of the railroad tracks or "Southside"). Power transformers are large transformers used for high voltage transmission of electricity by public utility companies; these transformers

are never connected directly to customer loads. Instead, distribution transformers, as the name indicates, are used to distribute electric power for customer use. Other types of transformers have been manufactured at Pittsfield within these two subdivisions, e.g., dry-type, precipitator, furnace, rectifier, network, and locomotive transformers, concrete reactors, step and ML32 regulators. In addition, other types of electrical equipment, for both in plant use and external sale, have been manufactured including lightning arresters, bushings, capacitors, cutouts, and fuses.

Ordnance Systems was established in 1941 and has primarily developed and manufactured guidance systems for bombers, gun mounts, tanks and ballistic missiles, and the Navy's Trident Missile program. This part of the plant site operations was largely independent of the transformer operations.

The Plastics Division started operations at Pittsfield in 1928 with the manufacture of the first injection moldable phenolic compound, called GENAL resin. This black plastic can withstand high operating temperatures and was sold for the manufacture of automobile ignition and transmission systems, electrical equipment, and household electrical appliances (e.g., bases and handles on toasters). PD also produced phenol-formaldehyde resins used for insulating internal components of Power Transformers.

The vast majority of work history job entries in our case control study were in the Transformer Division (approximately 90%). About 10% were in Ordnance Systems and less than 1% from Plastics Division.

GE divided its manufacturing divisions into approximately 250 "components" for administrative and payroll purposes. For purposes of this study the components have been grouped into 52 "operations" based on similarity of exposure and/or location. Table 2-6 is a list of the 52 operations. For the sake of clarity and to provide a quick overview, the operations have been grouped by function, i.e., manufacturing or plant support, in Table 2-7.

Transformer Manufacture

A transformer is a device that changes electrical power from one current or voltage level to another. Energy is transferred from one alternating current circuit to another, not by direct electrical connection, but by magnetic coupling. This transfer is achieved by the principle of electromagnetic induction, discovered and characterized by physicists in the early 1800s.

Any charged particle in motion, such as an electron, produces a magnetic field. One of the fundamental discoveries in 19th century physics was that magnetism consists, not of distinctive magnetic charges, but of moving electrically charged particles. A current-carrying

electrical wire can deflect or turn the needle of a compass. Alternatively, as Michael Faraday discovered in 1831, a moving magnet (or a magnetic field that is somehow changing with time) can induce an electrical current in a wire loop.

A transformer consists of two solenoids or wire coils that are insulated from one another and connected to separate electrical circuits. Alternating current in the first coil, or primary, induces both a changing magnetic field and hence an electrical current in the second coil, or secondary. Both coils are wound around (and insulated from) a core manufactured from silicon steel which is easily magnetized. The core increases the magnetic coupling between the two coils. The magnetic flux induces the same voltage in each turn of the coil; therefore the total induced voltage is proportional to the number of turns in the winding. A transformer is highly efficient (96%-99%) in the transfer of energy because it has no moving parts and therefore no frictional losses. It can step up or step down the voltage in the secondary depending on the ratio of winding turns between the primary and secondary coils.

Figures 2-2 and 2-3 show the internal structure of core and coil before placement in the transformer tank shown in Figure 2-4. Table 2-8 presents an outline of the major operations of power transformer manufacture. Bear in mind that though the outline of operations looks comparatively straightforward the actual manufacture of a large power transformer, which stands three stories high and weighs 500

tons, requires 4500 different drawings and 100,000 individual parts.

The wire for the coils is prepared in the Wire Mill. Copper wire is drawn, annealed, and insulated with tape or enamel coatings. The major insulation between primary and secondary windings and around which the coils are actually wound are resin bonded cylinders manufactured in Tube Rolling. Layers of paper are wound on a hot steel drum (mandrel) and bonded with a phenol-formaldehyde resin (bakelite) to form the insulating tube. Insulated wire is wound around the tube in Coil Winding to form the primary and secondary coils of the transformer.

The core of the transformer consists of very thin (0.33 mm) layers or laminations of insulated silicon steel. Lamination prevents the development of electrical eddy currents which would interfere with the magnetic flux. Electrical steel is received from the manufacturer and cut to length and width in Core Fabrication. In the past the core "legs" were then insulated (with a clay-containing "slurry coat" or enamels); currently steel is received fully processed from the manufacturer. The core is then built by laying the legs flat on a building jig; beams of nonmagnetic materials such as wood or aluminum are clamped along the top and bottom of the core. Rigid bracing or clamping of all transformer parts is very important as otherwise core laminations and coil will vibrate with current changes to

produce objectionable noise (humming) and ultimately insulation failure and short circuit.

A variety of other internal transformer components are made in departments such as Copper Parts and Cables where parts are machined, brazed or soldered, and insulated. In Insulation, paper and pressboard are treated with phenol-formaldehyde resins (similar to Tube Rolling) and cut to size to form spacers, washers, collars (for the wire leads of the transformer) and other parts. The spacers are inserted between core and coil to create channels or ducts which allow transformer oil to circulate. The quality of the insulating materials of a transformer (which altogether include the resins and enamels of coil and core, the papers and pressboard of insulating cylinders, spacers, and collars, and insulating properties of transformer oils) are important factors in determining the life of the unit.

Load ratio adjusters or load tap changers are insulated switches which "tap" into the secondary coil at various turns to permit a variable voltage output. A transformer is frequently subjected to abnormally high voltage stresses caused by normal operating conditions, such as switching, and abnormal operating conditions, such as lightning, so it therefore contains specialized circuit breakers and fuse links for surge protection. Load ratio and fuse link operations are primarily assembly operations with some machining.

The leads from transformer coils are brought out through glass or porcelain bushings which are designed to protect the windings from ground as they pass through the case of the tank. They look much like insulators on power transmission lines and their size and construction depends on the voltage of the transformer. High voltage bushings have porcelain shells (obtained from outside vendors). The core conducting rod of the bushing is insulated with resin-treated paper; the assembled porcelain shell and rod is filled with oil.

Lightning arresters are similar in appearance to bushings and consist of a porcelain shell (from outside vendors) filled with insulating pellets that have been made of various substances (lead tetraoxide, silicon carbide and zinc oxide) over time. Operations include machining metal parts, pellet manufacture and assembly.

The tanks into which coil and core are ultimately placed as well as other mechanical components such as radiators and coolers are manufactured in the Tank Shop. Operations include numerous machining operations on steel, welding, cleaning and degreasing, leak testing and painting. The structure of the tank and cooling system are chosen to allow adequate heat dissipation. Small tanks have enough surface area for cooling without the addition of radiators. Larger transformers require radiators with the largest power transformers needing separate coolers and forced circulation of oil.

The core and coil and other internal components are assembled together in Internal Assembly. Operations include brazing, soldering, wiring, clamping, drilling, and glueing. In External Assembly the core and coil unit is "tanked", the transformer filled with oil and sealed, and the unit is tested. In the past transformers were filled with either 10c oil, a high-grade mineral oil, or, for applications where fire hazard was a concern, pyranol, which is nonflammable. Since 1976 silicone oil has replaced pyranol. Interviewees at GE estimated that pyranol was used in 10-30% of the transformers manufactured, primarily in small to medium power transformers used in enclosures (underground, in buildings, locomotives, etc.) The GE Marketing Department estimated that 15% of the units in Power Transformer and 5% of the units in Distribution Transformer were pyranol filled.

The oil in a transformer serves both to cool the apparatus as it circulates (as it gains heat it rises up through the coils and core and then sinks as it transfers heat to tank walls) and to insulate the coils. The core and coil assembly and oil must be moisture-free, for as little as 8 ppm of water reduces the insulating quality of oil to substandard. Therefore, the first step in External Assembly is "primary treat" of coil and core in which the unit is heated to 110oC under vacuum to remove moisture. When water ceases to be collected in the exhaust condenser and when insulation resistance of coil and core is adequate, the

drying cycle is terminated. The coil and core are adjusted for shrinkage and then placed in a transformer tank which is filled with oil to impregnate the unit. Oil is then drained from the tank and the assembled transformer undergoes "secondary treat", i.e., a second evacuation to remove water. While still under vacuum, the transformer is refilled with oil and then sent to test. Large transformers are usually drained of oil for shipping.

The manufacture of distribution transformers is similar to that of power transformers, the major difference being the structure and joining of core and coil. The core of a GE distribution transformers is made from silicon steel ribbon which is coiled around preformed coils automatically by a machine which winds the steel spirally through the windings. Thus, core building and core and coil assembly are really one operation called "lacing". Other major operations are similar. It is estimated that 25% of distribution transformers were filled with pyranol. Other types of transformers have been manufactured at Pittsfield including different types of regulators which function to maintain constant voltage under varying load conditions and concrete reactors used in steel mill furnaces. Pyranol was used to fill a small percentage of regulators; concrete reactors are air-cooled.

Details of all GE operations are presented in the Operation Descriptions Book (see Appendix) which contains an operation description, list of all major and most minor

chemical exposures, and building history for each operation. The information is summarized in two tables. Table 2-9 lists the major exposures of each operation grouped by whether or not they were coded or rated for the Exposure History file. For each chemical Table 2-9 also lists information on how the chemical was used and the extent of usage. Table 2-10 summarizes the distribution of coded chemicals by operations for easy visualization of which operations used any of the seven coded chemicals. Table 2-11 presents number and percentage of job-building pairs in the Phase I Exposure History Database that were actually rated for the seven exposures. Forty-two percent of the 4477 jobs were rated for pyranol, 29% for benzene, 9% for trichlorethylene, 64% for solvents, 20% for machining fluids, 15% for asbestos, and 9% for phenol-formaldehyde resins. (These percentages, of course, do not reflect actual exposure-years which will vary with an individual's job history).

Table 2-12 lists the exposure rating scales used in the analysis. For analysis, the original rating scale was sometimes collapsed depending either on the detail of exposure information available or the nature of the exposure.

Pyranol

Pyranol was used as a transformer oil from 1936 to 1976 in Power Transformer External Assembly (Operation 17), Distribution Transformer Assembly (Operation 26), and Regulators (Operation 25). It was used to impregnate and fill capacitors (Operation 41) in buildings 42 and 43 from 1936 to 1942 when capacitor manufacture was moved to another plant. Oil quality was monitored in the Laboratory (Operation 49); oil was received, stored, filtered, and pumped to buildings from the "Oil Farm" (Operation 38). These operations were the major operations in which exposure to pyranol occurred. In addition, certain jobs in Construction (Operation 33), Area Maintenance - Crane Repair (Operation 32), and Materials Reclamation (Operation 34) had occasional exposure to pyranol and were rated accordingly.

In the Power Transformer Division, Internal Assembly (Operation 16) and External Assembly (Operation 17) occur or have occurred in the same buildings, specifically buildings 1, 2, 3, 12. (Several interviewees initially reported that pyranol might have been used in assembly building 100 but company records subsequently showed that there was no actual use in the building.) All of transformer assembly buildings are very large (from 400 to 1150 feet in length) in which internal assembly operations start at one end of the building followed by external assembly operations at the other end. Cranes or mechanized assembly lines (for smaller transformers) move the transformers in various stages of completion from one operation to the next. Pyranol is

pumped directly into External Assembly areas where hoses are used to fill and drain transformers. Use of hoses has been described as frequently careless. Pyranol would get on hands, clothing, and in shoes from handling hoses, soaked parts, and from entering drained transformers during adjustments and finishing operations. Pyranol was never used directly in Internal Assembly areas but interviewees judged that workers in these areas would have had some exposure. All workers in Internal Assembly areas have been given a "0.5" pyranol exposure rating.

After Capacitors moved out of buildings 42 and 43 in 1946, Lightning Arresters (Operation 28) was moved into the areas in which pyranol had been used. The pyranol exposure in Capacitors has been described as very high because impregnation required heating of the pyranol soaked capacitors. Residual airborne PCB surveys conducted in 1978-1979 showed air concentrations in building 42 comparable to power transformer and regulator assembly areas (in which pyranol use was terminated in 1976; see Table 2-16). All workers in Lightning Arresters have consequently been assigned a "0.5" pyranol exposure rating for the period 1946-1983.

Unfortunately industrial hygiene surveys that could give actual exposure levels for different job classifications were not available from the period of pyranol use, 1936 to 1976. In 1978 and 1979 residual airborne PCB concentrations were determined in many areas of

PCB use (see Table 2-16). As noted before, interviewees had identified these areas as having contained pyranol.

An unpublished study by KS Rosenman looked at serum PCB levels in GE Pittsfield workers, GE family members, residents in PCB-contaminated areas, and residents in non-contaminated areas. The GE workers with the highest serum PCB levels (greater than 100 ppb) all worked in areas identified by our interviewees as pyranol use areas, specifically buildings 12, 42, and 26. Workers in building 14 and 17 had serum PCB levels higher than non-GE workers but less than 100 ppb. These buildings were not identified as pyranol use areas (except for infrequent repair of returned drained transformers in building 14). Not enough detail is presented in the paper regarding how the subject's job category was selected (i.e., whether most recent job or major job was selected) to interpret the latter results.

Brief Summary of Occupational PCB Literature

Table 2-13 summarizes the major studies on occupational exposure to PCBs. Several early studies from the Japanese literature were not included but are covered by Letz (1981). The major point with respect to our current study is that no one to date has demonstrated a statistically significant increased cancer incidence in a human population. Previous studies, in general, have used less specific exposure assessments resulting in less power to detect relationships

between disease and exposure. Studies by Bahn et al (1976) and Brown and Jones (1980) have been suggestive of increased melanoma and pancreatic cancer and rectal and liver cancer respectively but latency periods in both studies have not been long enough to adequately assess outcome.

For informational purposes data available on GE Pittsfield PCB serum levels are presented in Table 2-14 (KD Rosenman, 1980, unpublished study). Median PCB level in 43 GE workers was 22 ppb with a range of 5-378 ppb, which is somewhat lower than PCB blood levels seen in most of the studies discussed above. In addition, for general comparative purposes, Table 2-15 presents serum PCB levels in the general population (study conducted in South Carolina).

Unfortunately the GE Pittsfield workers selected for serum PCB determinations do not in any way constitute a representative sample. Twenty-five of the 43 workers were members of a retired workers council; information on the date of last exposure or duration of exposure is not presented. Workers with serum levels above 100 ppb did work in areas identified by the UMMC study as pyranol-use areas but quantitative data on this subgroup are not presented. No conclusion can be drawn about actual exposure levels at GE from reported blood levels of this small unrepresentative sample.

Six studies in the literature have measured occupational PCB air concentrations and are listed in Table

2-13. Five measured air concentrations during capacitor manufacture and one during transformer maintenance. Neither type of operation is comparable to transformer manufacture and therefore cannot be used to estimate exposure levels at GE Pittsfield. Table 2-16 summarizes the only available information on PCB air levels at GE Pittsfield. These industrial hygiene surveys were conducted 2 to 3 years after PCB use terminated and so represent residual air levels.

PCBs can be absorbed through the skin (Nishizumi, 1976). The relative importance of skin absorption versus inhalation as routes of exposure to PCBs is unknown though Lees et al. (1987) have suggested that the dermal route is a major contributor. In a capacitor manufacturing plant, Maroni et al. (1981) found that PCB air levels ranged between 48-275 ug/m3, workroom surface and tool contamination ranged between 0.2-159 ug/cm2, and skin contamination (palms of hands) ranged between 2-28 ug/cm2. In this environment, Maroni et al. felt that skin absorption was the more important exposure route.

One major complication in our study lies in the fact that pyranol is a mixed chemical exposure in and of itself. Pyranol is a GE trademark and is composed approximately of 50% PCBs (a mixture of PCB isomers but mostly hexachlorobiphenyl), 50% trichlorobenzene, small amounts of phenoxypropene oxides (<0.25%), and trace amounts of dibenzofurans. According to technical information at Monsanto (the former US producer of PCBs), batches of

pyranol were either formulated by GE using Monsanto PCB mixtures or were formulated by Monsanto per instructions from GE. The PCB content in pyranol actually varied from 45-80% between different batches. Sometimes a mixture of trichlorobenzene and tetrachlorobenzene was used.

The toxicology of the various PCB mixtures has been extensively studied in animals. Excellent reviews are provided by the 1977 NIOSH Criteria Document and Letz (1981).

Benzene

For a period of time, benzene was used as a solvent in various departments throughout the plant for general cleaning during machining and assembly operations (see Table 2-10). It was used to wipe down machined parts in fabrication operation, to clean parts before final assembly, and to clean tools and hands.

The use dates for benzene were estimated to be 1920 to 1950, plant-wide. The year of last usage was averaged from estimates of several interviewees; the estimates ranged from 1945 to 1955. Four of the 18 interviewees started work in 1930s, 10 in the 1940s, and 4 in the 1950s. Most of the interviewees who began work before 1950 remembered using

benzene but felt they could only roughly estimate the year(s) of final usage in the different departments. Therefore, a plant-wide mean estimate was used for all operations.

The start date for benzene usage was based on two sources: one interviewee and general industry use patterns. One interviewee (who started work at GE Pittsfield in 1942) felt reasonably certain that benzene usage went back at least to 1920 based on the recollections of former GE workers (including his father) whom he had known. In his own exposure rating system, he coded benzene exposure back to 1920 since he felt he had no information on exposures before 1920.

The use of benzene as an industrial solvent began in the 1880s. The first cases of chronic benzene poisoning (aplastic anemia) were reported in 1897. After World War I, the use of benzene as a solvent increased in most industrial countries. It is now impossible to determine whether benzene was used at GE Pittsfield before 1920. The more conservative approach was therefore chosen for the exposure assessment: benzene exposures were not coded prior to 1920. Please note that the degree of uncertainly about dates of use was greatest for benzene exposure ratings. The usage dates of the other coded exposures were known with much greater certainty. The start dates of the other exposures frequently corresponded to changes in technology or buildings, for example, about which there was excellent

agreement among the interviewees.

The rating system used for benzene exposure was collapsed to 0, 1, and 2 where 1 equaled indirect exposure and 2 equaled direct exposure. This rating scale was chosen for analysis because interviewees had less certainty regarding benzene exposure ratings. (The pyranol exposure rating scale had an extra category (1,2, or 3) because pyranol exposure continued until 1976 and more reliable discriminations could be made between jobs by the interviewees).

Regarding the identity of the solvent "benzene", there was generally good agreement among interviewees that what was used was benzene. Two interviewees remembered occasionally seeing the term "benzine". The term "benzine" generally refers to a petroleum distillate fraction (also called petroleum spirits or VM and P Naphtha). The term benzene has not generally been used to refer to petroleum spirits. Petroleum spirits are more likely to be marketed under the name of petroleum spirits or VM and P Naphtha. Research in issues of the Thomas Register (a 17 volume compendium of U.S. suppliers of industrial products and services, issued annually) back to 1920 showed that suppliers were much more likely to market products called "benzene" or "naphtha" than benzine. For example, in 1930, about forty suppliers were listed for both benzene and naphtha while about five were listed for benzine. Based on these considerations, it is likely that the solvent called

"benzene" at GE Pittsfield was actually benzene, though other constituents and exact compositions can not be known.

Trichloroethylene

The solvent trichloroethylene (TCE) was used primarily in six operations throughout the plant (see Table 2-10). Its use was almost always in degreasers and, as a result, exposure was comparatively restricted: fewer than 10% of jobs were rated for exposure to TCE (see Table 2-11).

The use dates for TCE varied with department. It has been phased out of most departments over time and replaced with 1, 1, 1 trichloroethane primarily or methylene chloride in a few cases. The last year of use ranges between 1960 and 1977. The start date was somewhat uncertain: interviewees remembered TCE use in the late 1930s and 1940s. Industry wide use increased dramatically in the 1920s and 1930s. Based on these considerations, 1930 was chosen as the plant-wide beginning year of use.

The exposure rating scale for analysis was chosen to be consistent with the solvent rating scale used for benzene and other solvents. The rating system used was therefore 0, 1, and 2 where 1 equaled indirect exposure and 2 equaled direct exposure.

Of all the solvents reportedly used, TCE was chosen to be rated in this study based on the following reasoning. First, it is a known animal carcinogen with the same target organ in animals as PCBs: the liver. In a study of PCB exposed capacitor manufacturing workers by Brown and Jones (1981), those workers exposed to TCE were excluded from the study to eliminate confounding carcinogen exposures. The number of workers actually exposed to TCE in that study was very few and did not permit statistical analysis of TCE contribution to outcome. In our study, the number of exposed jobs appeared large enough to permit analysis.

Other Solvents

The category "other solvents" includes almost all other solvents used at the plant with the exclusion of the following: benzene, trichloroethylene, ethyl alcohol, methyl alcohol, and acetone. It includes: Varsol (petroleum spirits), CPE 1000 (petroleum spirits plus methylene chloride), methylene chloride, kerosene, paint thinners (primarily xylene/toluene based), solvent based paints, xylene, toluene, and naphtha.

Some type of solvent exposure occurred in the majority of operations (see Table 2-10). More jobs were exposed to solvents than any other exposure: 64% of job building pairs were rated as having solvent exposures (see Table 2-11). Solvents were used for general cleaning in machining and

fabrication operations, and for paints and paint thinners in painting operations, as well as various specialized uses around the plant (e.g., kerosene treatment of core and coil during assembly; die cleaning in Wire Mill). Since 1950 Varsol and CPE 1000 have been the primary cleaning solvents at the plant though individual departments frequently use additional solvents. Before 1950, a variety of solvents was used. The specific types of solvents used by departments before 1940 was not obtainable from interviewees or plant records. A variety of solvent based paints and thinners were used in painting operations (performed primarily in operations 13, 15, 23, and 25 with touch-up painting occurring in operations 15, 17, 24, and 26). The paints used were primarily "alkyd resin" paints; many were lead-based. Neither the interviewees nor plant records could provide much detail on exact composition over time.

Given the uncertainties in characterizing the variety of historical solvent and paint exposures, including exact composition and the presence of benzene or suspect carcinogens, a general petroleum solvent exposure category was established. The same rating scale (0, 1, 2) used for benzene and TCE was used to analyze solvents. Plant-wide usage dates were 1901 to 1987. The nature of the light manufacturing operations at GE Pittsfield has been sufficiently stable so that interviewees were certain that solvent use had extended back to 1901 in most departments.

Machining Fluids

Machining fluids are used in various departments for machining and fabrication operations (see Table 2-10). Plant-wide use dates are 1901 to 1987. Various types of machining fluids have been employed over time. The basic use trends were as follows: straight mineral oils were used exclusively until the 1940s; soluble oils were introduced in various departments during the 1940s and 1950s; synthetic machining fluids were introduced in the 1970s. Currently soluble and synthetic oils are primarily used with very minimal usage of straight cutting oils.

Information on exactly when soluble and synthetic coolants were introduced into different departments, the exact composition of these fluids, and the relative quantities of different types used over time was not available from interviewees or plant records. For these reasons, a single exposure category of "machining fluids" was created. For analysis, the rating scale was collapsed to 0 and 1 where 1 was defined as indirect or direct exposure. Given the heterogeneity of the nature of the exposures, an exposure rating scale with more categories did not seem justified.

Asbestos

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Asbestos was used in a number of operations (see Table 2-10) in two ways. The asbestos exposure in the majority of operations came from the use of woven asbestos blankets (used wet) as insulation during brazing or welding. For example, asbestos blankets were used in Coil Winding during the brazing of wire leads to cover the body of the wire coil and prevent damage to wire insulation. This is generally considered a fairly low asbestos exposure. Jobs in operations 1, 9, 16, 17, 18, 25, and 26 had what constituted a low asbestos exposure from the use of woven asbestos blankets. Asbestos blankets were used in these operations from 1940 to 1975.

Asbestos was used to make some pieces of insulation in PT Insulation during the period 1950-1965. It was also used to form one type of cylinder in Tube Rolling between 1950-1960. Some interviewees reported that asbestos tape was used to insulate some types of wire in the Wire Mill between 1957-1970; however, product specification records do not indicate that asbestos was used. Though the asbestos exposure in these operations was higher than what occurred with the use of asbestos blankets, it was far more intermittent and occurred over much shorter time periods. For example, only a small percentage of the total number of insulation pieces was made from asbestos during the period 1950-1965. (Note that the jobs in a given category in insulation would be rated as having potential asbestos

exposure for this period even though only a portion of the workers would be exposed at a given point in time). 62

Since the overwhelming majority of asbestos exposure was a low level exposure from use of asbestos blankets, the rating scale used for asbestos exposure was 0 and 1 where "1" equaled indirect or direct exposure. Despite the uncertainties about the frequency and levels of exposure in PT Insulation, Tube Rolling, and Wire Mill, a "1" rating constitutes, for the most part, a low asbestos exposure in this study. Asbestos was also used in GENAL manufacturing but workers were not coded for asbestos since operations had been shut down 10 years previously and no interviews were feasible.

Synthetic Resin Systems

Exposures from phenol formaldehyde and polyvinyl formal resin systems occurred in seven operations which are listed and described in Table 2-17. A variety of different resin systems were used in these operations - primarily phenol formaldehyde resins (PT Tube Rolling, PT Core Fabrication, PT Insulation, Plastics) and polyvinyl formal resins (Wire Mill). Exposure to decomposition products of Formex polyvinyl formal resins (formaldehyde, phenol, cresol) occurred during brazing in PT and DT Coilwinding.

Several IH surveys have measured exposures to phenol, formaldehyde, cresol, and aniline. In addition, exposures

to other constituents of the resin systems probably occurred. Information on all constituents of all resin systems was not rigorously sought in this study but probably could be obtained.

Formaldehyde is a known mutagen and animal carcinogen. It produced nasal cancer after inhalation exposure in rats and mice in two separate studies. The available toxicological information on the rest of the known exposures is limited. Aniline is a mutagen and produced neoplasms in rats after oral administration for 29 weeks at a dose of 50 mg/kg; its IARC classification is indefinite animal carcinogen. Phenol is a mutagen and has produced skin cancer in mice in two separate studies. Cresol has produced skin cancer in mice in one study. Hexamethyltetramine is a mutagen.

Given the heterogeneous nature of the resin system exposures, a rating scale of 0 and 1 where 1 equaled indirect or direct exposure was used. Use dates depended on department and are listed in Table 2-17.

Other Exposures

This section discusses other exposures at GE Pittsfield which were/are relatively widespread, i.e., used in several

operations, but were not rated by interviewees. These nonetheless could be studied by performing an analysis by operation, job title, or building.

The first exposure class is that of metal fume and dust. Exposure to metals occurred in numerous welding, brazing, soldering, machining, painting, and plating operations throughout the plant site. By and large the overwhelming majority of exposures were to iron and iron oxide in machining and welding operations and copper dust and fume in machining and brazing operations. However, some stainless steel parts are welded in transformer assembly. Several industrial hygiene surveys during 1975-1980 have sampled for nickel and chromium. Nickel levels ranged between non-detectable to 0.015 mg/m3, chromium levels between 0.014 to 0.02 mg/m3. One IH survey in transformers sampled for beryllium during aluminum welding; levels were non-detectable. Beryllium has been most frequently used in Ordnance Systems (levels not available). Cadmium (0.003-0.015 mg/m3) and lead (0.029 mg/m3) exposures have been found during copper brazing in Bushings. Chromium (0.02-0.05 mg/m3) and nickel (0.03-0.07 mg/m3) exposures were found in a metal spraying operation in the Tool Room.

Exact information on all metal alloys, electrodes, solders, and fluxes used at GE Pittsfield was not sought in this study and would be difficult, if not impossible, to obtain. All interviewees and the IH Department agreed that exposures to exotic metals were not significant. However,

if desired, an analysis could be done using job titles - jobs in 5500 series are brazers and those in the 5700 series are welders (see GE Job Code Book).

Metal exposures have also occurred in painting operations: lead, chromate, and zinc based pigments have been used in several operations. The actual extent of usage is unknown but probably considerable. Analysis could be done by operation (all jobs in operations 14 and 23) and by job title (5100 series).

There are several woodworking shops at the plant. An analysis could be conducted either by operation (operation numbers 6 and 20) or by job title (series 5900 and 6100).

During testing of transformers (each manufactured transformer is tested under rated load and surge conditions before shipment) and development of transformers in High Voltage Laboratory, workers and engineers are exposed to electrical and magnetic fields. At least one report (Milham) has observed increased leukemia in workers in various occupations exposed to electrical and magnetic fields. This could be analyzed by job title (series 1700) and operation (39).

Finally, exposure to numerous types of adhesives is widespread at GE Pittsfield, occurring in at least 19 operations. Water, solvent-based, and epoxy adhesives have been used at GE. Exact identification of different types was not possible. The most common type used has been "Glyptal", of which there are two types: polyvinyl butyral

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and phenolic resin in acetone-alcohol and cellulose acetate in acetone. It is likely that the primary exposure from adhesives is the vehicle. Most resin systems have high molecular weights and probably do not constitute a major airborne exposure. In the case of epoxies, some exposure might occur to small molecular weight reactive diluents or unreacted epicholorohydrin but "epoxies" have been the least used class of adhesive at GE Pittsfield. Most of the jobs using adhesives were also exposed to petroleum solvents and have received a solvent exposure rating. Exact information on type of adhesive used by job is not available. An analysis could be done, with considerable uncertainty, by operation.

07

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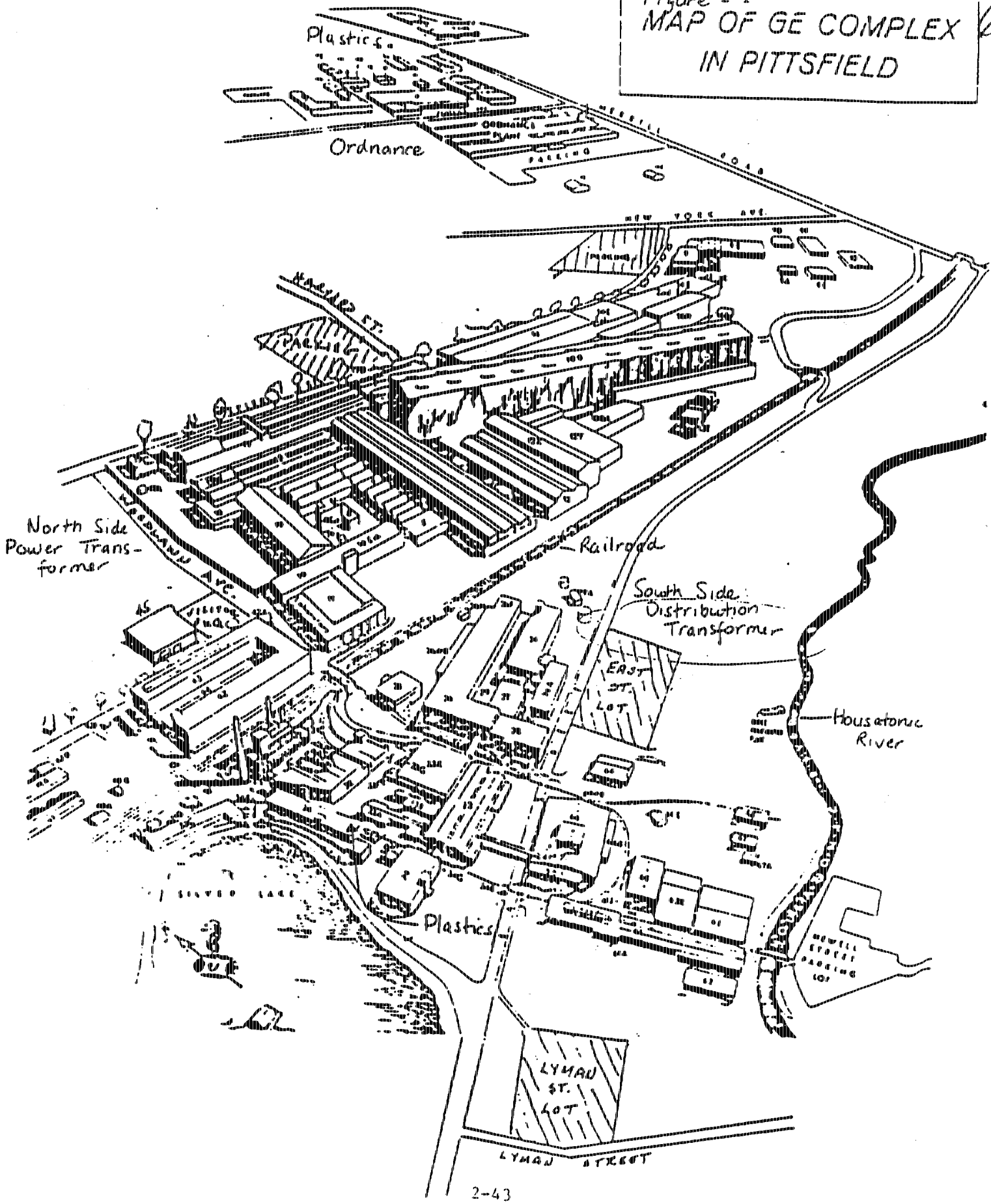
Figure 2-1
MAP OF GE COMPLEX IN PITTSFIELD



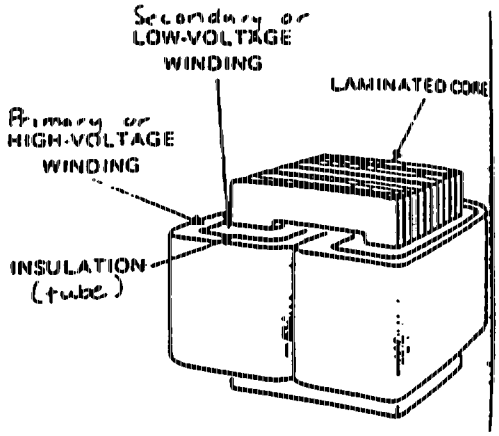


Fig 2-2 Coil arrangement for core-type transformer

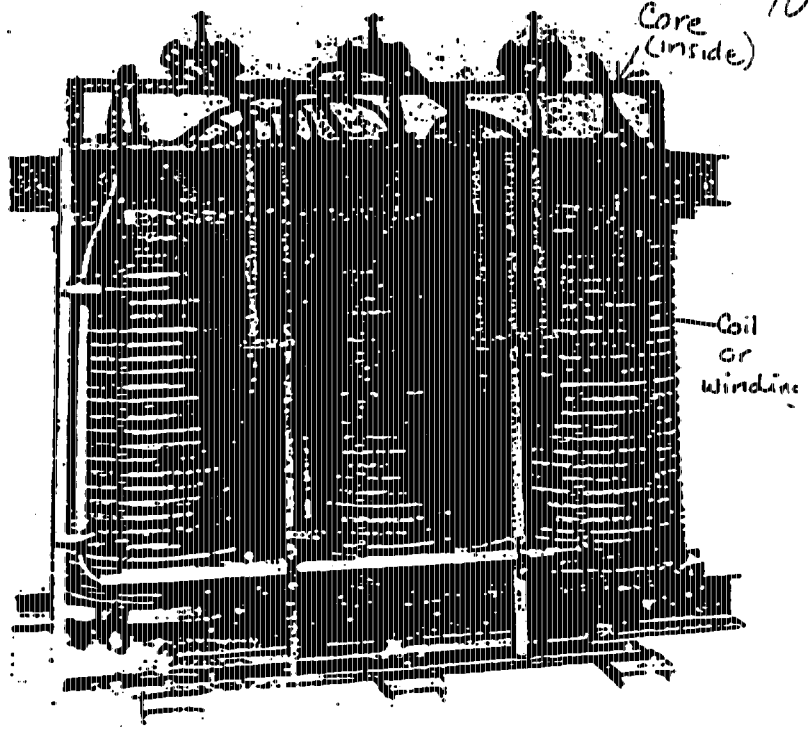


Fig 2-3 Coil and core of power transformer before tanking

Fig 2-4 Finished power transformer (3000 kva at 161,000 Volts)

Table 2-1

Examples of Categorical Exposure Rating Scales

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Exposure Classification	Assignment Criteria
A. Arp et al. (1983)	
Primary benzene	Direct routine use or handling
Secondary benzene	No direct handling but benzene used in work area
Primary solvent	Dirent routine use or handling
Secondary solvent	No direct handling but solvents used in work area
B. Waxweiler (1981)	
0	No exposure
1	Minimal exposure to low levels (Chemical in building—not handled, low vapor pressure and dust level, probably works on different floor)
2	Moderate exposure (Works around the chemical, but exposure is minimal)
3	Works in areas where subject to occasional high excursions (Normally exposure is minimal but occasional spills, leaks, or dust exposure may occur
4	Works in areas where level is high (Exposure levels in the area are frequently high. Might consider that some risk is involved if chemical is very toxic)
5	Intimate contact—skin or high inhalation (such as poly cleaners, handling slurry)
C. Kromhout et al. (1987)	
1 = No exposure	No contact; chemical is present, but this task is not involved
2 = Minor exposure	Minor contact; chemical is handled in a closed system; there are no special activities in this task, which enhance exposure; exposure takes place because of presence in this department
3 = Medium exposure	Varying and mainly passive contact; chemical is in a closed system, but now and then handwork is needed through which exposure is enhanced
4 = High exposure	Regular contact; because of the character of the production process and necessary handwork, regular contact is required

Table 2-2

CONSTRUCTION OF JOB-EXPOSURE HISTORY DATA BASE

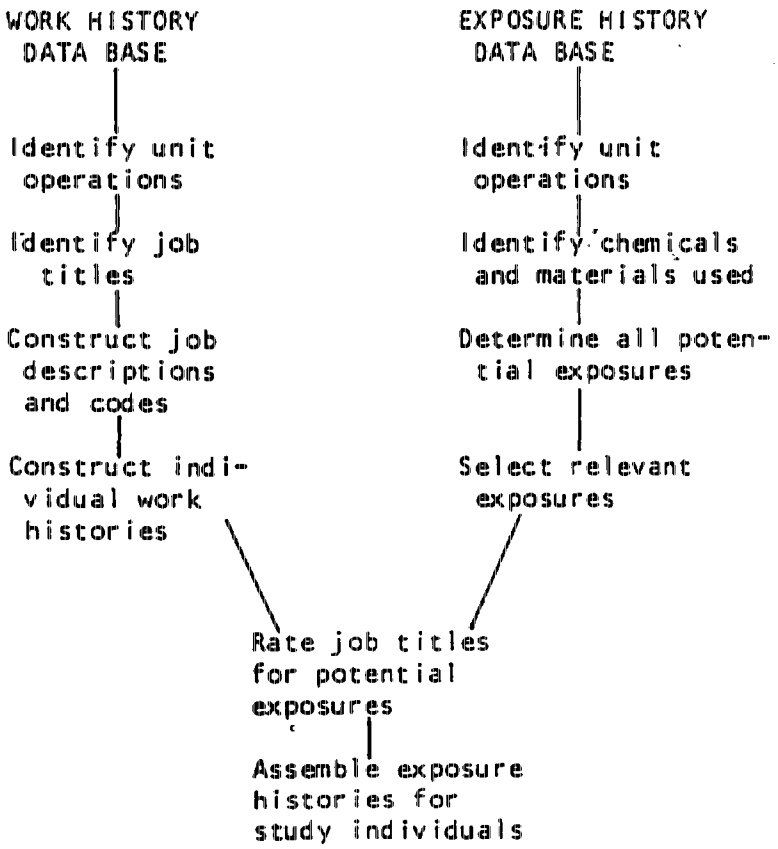

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Table 2-3

UMMC Exposure Rating Scale

Exposure Rating	Assignment Criteria
0, No exposure	No exposure to chemical
1, Indirect exposure	Chemical in work area but does not work directly with chemical
2, Direct low or infrequent exposure	Works directly with chemical but exposure is low or infrequent
3, Direct medium to high exposure	Works directly with chemical at medium to high levels on a routine basis

Table 2-4

EXTERNAL VALIDATION: INDUSTRIAL HYGIENE SURVEYS OF RESIDUAL AIRBORNE PCBS

Building Surveyed	Air PCB level, $\mu g/m^3$	Building identified by interviewees as PCB use area
Laboratory	6.3	+
Power Transformer Assembly	4.6	+
Distribution Transformer Assembly	14.4	+
Regulator Assembly	6.3	+
Tank Fabrication (Bldg 33)	0.5	-
Capacitor Fabrication	1.4	+
Scrap and Salvage	6.2	+

Table 2-5

Agreement Between Interviewees On
Job Title Ratings

Exposure	Percent Identical Rating	Percent One Rank Difference	Percent Two Rank Difference
Pyranol	90	7	3
Benzene	84	13	3
Trichloroethylene	94	5	1
Solvents	70	23	7
Asbestos	95	4	1
Resin Systems	98.5	1	0.5
Machining Fluids	92	5	3

TABLE 2-6 OPERATIONS OF HSPH CASE/CONTROL STUDY.

HSPH ASSIGNED OPERATION NUMBER	OPERATION (GE COMPONENT NUMBER)
	POWER TRANSFORMERS
1	Coil-Winding (5310-5318)
2	Tube Rolling (5330-5332)
3	Wire Mill (5350-5359)
	PT-INTERNAL COMPONENTS
4	Annealing
5	Core Fabrication and Core Building (5450, 5451, 5454, 5456)
6	Woodworking (5455)
7	Insulation (5461, 5462)
8	Cables (5463)
9	Copper Fabrication (5464)
10	Load Ratio (5481, 5482)
	PT-MECHANICAL COMPONENTS - SMALL PARTS AND LARGE COMPONENTS
11	Fabrication: Structural Steel, Sheet Metal Operations, and Machining (5521-5526, 5551)
12	Welding (5521, 5524, 5551-5553)
13	Radiators (5520)
14	Painting (5521, 5524, 5552, 5555)
15	Tank Test, finish, assembly (5554, 5555)
	PT-TRANSFORMER ASSEMBLY
16	Internal Assembly (5620-5624)
17	External Assembly and Test (5630-5636, 5638, 5639, 5680, 5681)
	DISTRIBUTION TRANSFORMERS
18	Coil Winding (5721)
19	Insulation (5722)
20	Woodworking (5722)
21	Fabrication: Core-cutting, tank fabrication, machining (5723-5725)
22	Welding (5724, 5725)
23	Painting (5724, 5725)
24	Tank test and finish (5724)
25	ML-32 and Inductrol Regulators (5741-5743, 5752, 5753)
26	Lacing (core-building), Assembly Inspection (5751, 5754, 5780)
27	Concrete Reactors (5726)

OPERATION NUMBER	OPERATION (GE COMPONENT NUMBER)
	PROTECTIVE EQUIPMENT
28	Lightning Arresters (5841-5855, 5870, 5880, 5890, 5891)
29	Bushings (5900-5990)
30	Cutouts (5856)
	OTHER OPEATIONS
31	Area Maintenance - Tool Room and Machine Shop (5298, 5299)
32	Area Maintenance - Instrument and Equipment Repair; Crane, Elevator, and Motor Repair (5291-5295)
33	Construction (5037-5039)
34	Transportation and Materials Reclamation (5020-5025)
35	Cleaning (5026)
36	Power Station and Gas Plant (5029-5033)
37	Specialty Process Control: Chemical Storage and Mixing
38	Oil Farms
39	High Voltage Lab
40	MgO Manufacture
41	Capacitors
42	Photo Dept/Multilith Operation
44	Medical
45	Ordnance
46	Phenol Plant
47	Plastics
48	PT Plating/Galvanizing (Bldg 41)
49	Laboratory
50	Engineering and Drafting
51	Shipping/Receiving
52	Plant Protection

TABLE 2-7 PLANT OPERATIONS GROUPED BY FUNCTION (MANUFACTURING vs. PLANT SUPPORT)

MANUFACTURING OPERATIONS

Power Transformer Division (multiple operations)
Distribution Transformer Division (multiple operations)
Capacitors
Protective Equipment Division (multiple operations)
Ordnance
Plastics (multiple operations)

PLANT SUPPORT OPERATIONS

Area Maintenance - Tool Room, Machine Shop, Instrument & Equipment Repair, Crane, Elevator and Motor Repair
Construction
Cleaning
Transportation
Materials Reclamation
Power Station and Gas Plant
Oil Farms
Laboratories
Medical
Engineering/Drafting
Shipping/Receiving
Plant Protection
Specialty Process Control - Chemical Storage and Mixing

TABLE 2-8 POWER TRANSFORMER MANUFACTURE

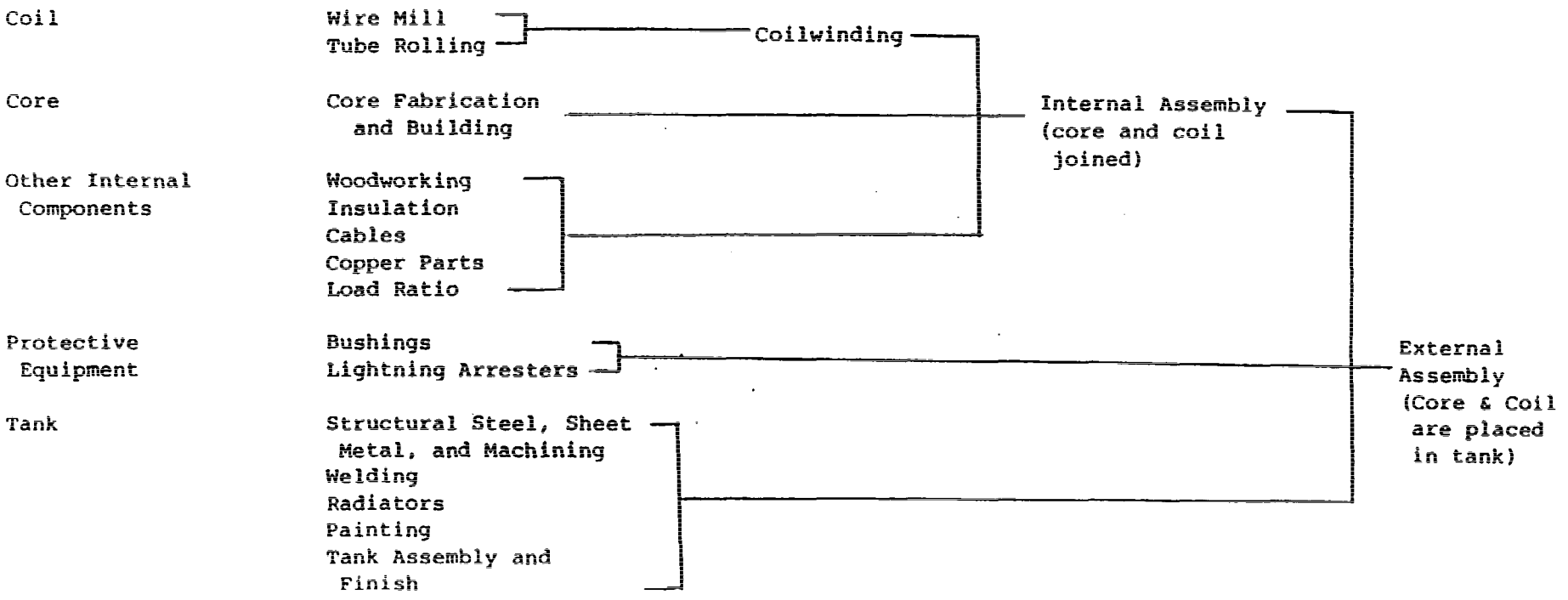

Table 2-9 Compunds of Toxicological Interest at GE Pittsfield: Explanation

Exposure Estimate Key

1. "Level" - refers to average exposure rating assigned to job titles in operation.
   Definitions: L=indirect low or direct low or infrequent exposure
   M-H = direct, medium to high level exposure

2. "Extent of Usage" - refers to number of jobs exposed within an operation.
   Definitions: 1 = minimal usage, less than 10% of job titles exposed
   2 = moderate usage, 10-50% of job titles exposed
   3 = widespread usage, greater than 50% of job titles exposed

Glossary

CPE 1000 - benzine plus methylene chloride
Glyptal - either polyvinyl butyral and phenolic resins in acetone/alcohol or cellulose acetate in alcohol
Gly ptal 1500 Thinner - xylene plus VM and P Naphtha
Varsol - benzine or petroleum spirits

Note: benzine, petroleum spirits, and mineral spirits are usually synonomous, constituting a petroleum distillate fraction of boiling point range 150-200°C, primarily C_6 aliphatics. VM and P Naphtha is a petroleum distillate fraction of boiling point range 95-160°C - primarily C_5 - C_{11} aliphatics. See Patty's, 3rd Edition, Volume 2B, ρ.3370 for more information.

Table 2-9 Compounds of Toxicological Interest at GE Pittsfield

Operation	Exposure (* = coded)	Use	Dates of Use	Levels	Extent of Usage
Coil Winding	*Formex enamel decomposition products	phenol, cresol, formaldehyde generated during brazing to join leads	1936-p	L	3
	*Asbestos cloth	wet woven cloth used as insulation around wire during brazing	1940-75	L	3
	*Varsol	general cleaning other unknown solvents used prior to this; coded as Solvents 1901-1983	1950-p	L-M	3
	Metal solders including Cu, Zn, Ag			L-M	3
	Adhesives - Glyptal, 50P77 (phenolic resin in ether-xylene), 2150 (cellulose acetate in acetone/isopropanol)			L	3
	Formic gel (formic acid plus ethylene dichloride)	lead stripping for brazing, ethylene dichloride exposures can be high (25-194 ppm) but usage is recent	1972-p	M-H	2
Tube Rolling	*phenol formaldehyde resin powder (various types)	heated to form insulating tubes high levels (0.5-8 mg/m³ phenol; 0.36 mg/m³ aniline)	1936-p	H	3
	*asbestos	used to make one type of cyclinder	1950-60	M	1
	*Varsol	general cleaning other unknown solvents used prior to this; coded as solvents 1901-1983	1950-p	M	3

Table 2-9 con't p2

tion	Exposure (* = coded)	Use	Dates of Use	Levels	Extent of Usage
) Wire Mill	*Formex (phenolic resin in aromatic hydrocarbons and phenol containing cresylic acid)	wire insulation (high levels 0.8–6 mg/m³ phenol, 0-9 mg/m³ cresol)	1951-p	H	3
	*asbestas tape	some wire insulation	1957-1970	M	2
	*Varsol, xylene	general cleaning; cleaning dies through which wire is drawn (levels: 35-185 ppm xylene) unknown solvents used in past; coded as solvents 1901-1983	uncertain for these particular solvents	M	3
	Epoxy resins	some wire insulation	recent		
) Annealing	*Solvents - various petroleum solvent; identity uncertain)	general cleaning	1901-1983	M	3
	acrolein & oil thermal degradation products from oil quench bath			M-H	3
) Core Fabrication and Building	*Core plate/phenol formaldehyde resins	steel insulation	1936-82	M	3
	*Benzene	general cleaning	1920-1950	L	3
	*Varsol, Glyptal 1500 Thinner, naphtha and kerosine as resin vehicle	general cleaning and vehicle for insulating resin	1901-1983	L-M	3
Woodworking	*Varsol, CPE 1000	general cleaning other unknown solvents used prior to this coded as solvents 1901-1983	1950-p	L	3

ion	Exposure (* = coded)	Use	Dates of Use	Levels	Extent of Usage
Insulation	*phenol-formaldehyde resin varnish	paper insulation	1936-p	M	3
	*asbestos	used for some pieces of insulation	1950-65	M	3
	*Varsol	general cleaning unknown solvents used prior to this, coded as Solvents 1901-1983	1950-p	L	3
	adhesives - Glyptal, KC804 Cement (resin in methanol and MEK)			L	2
) Cables	*Varsol	general cleaning unknown solvents used prior to this, coded as solvents 1901-1983	1950-p	L	3
	Glyptal	adhesive		L	3
	Metal dust + fume - Cu dust from machining; Ag solder in brazing			M	3
;er Shop	*Varsol	general cleaning unknown solvents used prior to this; coded as solvents 1901-1983	1950-p	M	3
	*asbestos	wet insulation during brazing	1940-1975	L	3
	Metal dust + fume - Cu. machining, soldering, brazing			M	3

Table 2-9 cont'd p4

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...tion	Exposure (* = coded)	Use	Dates of Use	Levels	Extent of Usage
) Load Ratio	*machining fluids		1901-83	L-M	3
	* benzene	general cleaning	1920-50	M	3
	* Varsol	general cleaning additional unknown solvents used prior to this; coded as solvents 1901-1983	1950-p	M	3
	*trichloroethylene	degreasing	1930-60	L	3
	Glyptal	adhesive		L	3
	1,1,1 trichloroethane	degreasing	1955-p	L	3
Tank ation	*machining fluids		1901-83	L-M	3
	*benzene	general cleaning	1920-50	L-M	3
	* trichloroethylene	degreasing	1930-66	L	1
	*Varsol, CIPE 1000, carbon tetrachloride, xylene	general cleaning coded as solvents	1901-1983	L-M	3
) welding	no coded exposures other exposures: welding fumes primarily from carbon steel; also some welding on tin-plated aluminum, aluminum, stainless steel; primary exposure is to iron oxide; limited exposure to aluminum oxide, nickel, chrome, beryllium, tin, and zinc oxide				

Table 2-9 cont p5

ion	Exposure (* = coded)	Use	Dates of Use	Levels	Extent of Usage
) Radiator oating and inting	*Solvent based paints, paint thinners (xylene, toluene). Coded as Solvents 1901-1983	Radiator painting	1901-1983	M-H	3
	Metal based alkyd resin (dicarboxylic acid plus polyols) paints - lead * chromate pigments used.				
	Epoxy paints.		1975-p		
) Tank Painting	*Solvent based paints * thinners (xylene, toluene); Varsol * CPE 1000 * other Solvents used as cleaners Coded as solvents 1901-1983	Tank painting	1901-1983	M-H	3
	Metal based alkyd resin (dicarboxylic acid plus polyols) paints - lead and chromate pigments used	Tank painting		M-H	3
	Epoxy paints	used on some parts * one type of transformer		M-H	1
) Tank test and finish	*Benzene	general cleaning	1920-1950	L	3
	*Varsol, CPE 1000 and other unspecified solvents Coded as solvents 1901-1983	general cleaning	1901-1983	L	3
	welding fumes from spot or tack welding				

Table 2-9 con't p6

on	Exposure (* = coded)	Use	Dates of Use	Levels	Extent of Usage
6) Internal Transformer Assembly	*pyranol	indirect exposure from external assembly operations at other end of buildings. Coded as level "0.5"	1936-1976	very low	3
	*asbestos cloth	wet woven cloth used as insulation during brazing	1940-75	L	2
	*machining fluids		1901-1983	L	2
	*benzene	general cleaning	1920-1950	L-M	3
	*Varsol, CPE 1000, Glyptal 1500 thinner (xylene plus VM+P Naphtha) Coded as solvents 1901-83	general cleaning	1901-1983	L-M	3
	adhesives - Glyptal			L	3
	formic gel (formic acid plus ethylene dichloride)	lead stripping for brazing ethylene dichloride exposures can be high (25-194 ppm) but usage is recent	1972-p	M-H	2
	metal fumes from brazing			L	2
7) External Transformer Assembly	*pyronol	transformer oil	1936-1976	M-H	3
	*asbestos cloth	wet woven cloth used as insulation during brazing	1940-1975	L	1
	*benzene	general cleaning	1920-1950	L	3
	*Varsol, CPE 1000, Glyptal 1500 thinner (xylene plus VM+P Naphtha), solvent based paints, paint thinners (xylene, toluene), kerosine Coded as solvents 1901-83	general cleaning, touch-up painting, coil + core "treat"	1901-1983	L-M	3
	welding fumes	spot welding + welding of covers to tanks		L	1
	adhesives - Glyptal			L	3

Table 2-9 cont'd p7

ion	Exposure (* = coded)	Use	Dates of Use	Levels	Extent of Usage
7) External Assembly cont'd	10c Oil - highly refined mineral oil with <0.3% stabilizers (such as di-tertiary-butyl-para-cresol)	transformer oil	1901-p	M-H	3
	metal based alkyd resin paints - lead & chromate pigments used	touch up painting		M	1
8) DT Coil Winding	*Formex enamel decomposition products	phenol, cresol, formaldehyde generated during brazing to join leads	1936-p	L	3
	*Asbestos cloth	wet woven cloth used as insulation around wire during brazing	1940-75	L	3
	*Varsol; other unknown solvents used prior to this. Coded as solvents 1901-1983	general cleaning	1950-p	M	3
	acrylic emulsions & varnishes; acrylonitrile as contaminant (0.4-1.8 ppm)	coil insulation		M	2
	adhesives - Glyptal			L	3
	metal fumes & dust (Cu, Ag)	brazing & mechanical lead cleaning		L-M	3
19) DT Insulation	*Varsol; other unknown solvents used prior to this. Coded as solvents 1901-1983	general cleaning	1950-p	L	2
	adhesives - Glyptal			L	3
20) DT Inserting	*Varsol, CPE 1000; other unknown solvents used prior to this. Coded as solvents 1901-1983	general cleaning	1950-p	L	3
	adhesives - Glyptal			L	3

Table 2-9 cont-t p8

tion	Exposure (* = coded)	Use	Dates of Use	Levels	Extent of Usage
) DT one and ank Fabri- ation	*machining fluids		1901-1983	L-M	3
	*benzene	general cleaning	1920-1950	L	3
	*Varsol, CPE 1000, other unknown solvents used prior to this. Coded as solvents 1901-1983	general cleaning	1950-p	L-M	3
	*trichloroethylene	degreasing	1930-1973	L-M	1
	adhesives - Glyptal, A50P134 (rubber adhesive in MEK)			L	3
DT) Welding	no coded exposures welding fumes primarily from carbon steel; also some welding on tin-plated aluminum, aluminum, stainless steel; primarily exposure to iron oxide; some exposure to aluminum oxide, nickel, chrome, beryllium, tin, and zinc oxide				
) DT ainting	*solvent-based paints, paint thinners (xylene, toluene, etc). Coded as solvents 1901-1983	painting transformer tanks	1901-p	M-H	3
	metal based alkyd (dicarboxylic acid plus polyols) resin paints - lead pigments used			M-H	3
	epoxy paints		1975-p		

Table 2-9 cont'd p9

ion	Exposure (* = coded)	Use	Dates of Use	Levels	Extent of Usage
) OT Tank est and inish	*benzene	general cleaning	1920-50	L	3
	*Varsol, CPE 1000; other unknown solvents used prior to this. Coded as solvents 1901-1983	general cleaning	1950-p	L-M	3
	welding fumes	tack or spot welding		L	1
ML32 and inductrol egulators	*pyranol	transformer oil	1936-76	L-M	3
	*asbestos cloth	wet woven cloth used as insulation during welding or brazing	1940-75	L	3
	*machining fluids		1901-83	L-M	3
	*benzene	general cleaning	1920-50	L	2
	*trichloroethylene	degreasing	1930-70	L-M	2
	*Varsol, Glyptal 1500 thinner (xylene plus VM and P Naphtha), kerosine, solvent based paints. Coded as solvents 1901-83	general cleaning, painting, thinning	1901-83	L	3
	Adhesives - Glyptal			L	2
	10c Oil (highly refined mineral oil)	transformer oil	1901-p	L-M	3
	welding, soldering fumes			L-M	2
	metal based alkyd (dicarboxylic acid plus polyols) resin paints - lead pigments sometimes used	transformer tank painting		M	2

Table 2-9 con't (D10

ion	Exposure (* = coded)	Use	Dates of Use	Levels	Extent of Usage
) DT Lacing nd Trans- ormer ssembly	* pyranol	transformer oil	1936-76	M-H	3
	* asbestos cloth	wet woven cloth used as insulation during brazing and welding	1940-78	L	1
	*benzene	general cleaning	1920-50	L	3
	*trichloroethylene	degreasing	1930-73	L	2
	*Varsol, CPE 1000, Kerosine, solvent based paints + thinners. Coded as solvents 1901-1983	general cleaning, touch up painting, coil + core "treat"	1901-1983	L-M	3
	welding fumes	spot welding; welding of covers to tanks		L	1
	adhesives - Glyptal			L	3
	10C Oil - highly refined mineral oil with <0.3% stabilizers (such as di-tertiary-butyl-para-cresol)	transformer oil	1901-p	M-H	3
	metal based alkyd (dicarboxylic acid plus polyols) resin paints - lead + chromate pigments used	touch up painting		M	1
) Concrete Reactors	*coal tar varnish and petroleum solvent thinners. Coded as Solvents 1901-1983	reactor coil insulation		L	2
	welding fumes			L	1
	epoxy	reactor supports	1978-p		

Table 2-9 Cont'd

ion	Exposure (* = coded)	Use	Dates of Use	Levels	Extent of Usage
) Lightning Arresters	*pyranol	not actually used in operation; operation moved into Capacitor buildings (42, 43, 44) where high levels of pyranol were used prior to 1946. 1978 IH surveys showed significant levels still present. Coded as level "0.5" pyranol exposure 1946-83			
	*machining fluids		1901-83	L	2
	*Kerosine & other solvents. Coded as solvents 1901-1983	general cleaning	1901-83	L-M	3
	Coal tar pitch fumes, 236 Compound (silica plus pitch	used for filling some types of arresters		L-M	2
	adhesives			L	2
	metals - lead, zinc, chrome, nickel, antimony, cobalt, arsenic, aluminum oxide	exposure from manufacture of pellets used to fill arresters		L-M	2
) Bushings	*machining fluids		1901-83	L	3
	*benzene	general cleaning	1920-50	L-M	3
	*trichloroethylene	degreasing	1930-77	L	2
	*Varsol, Kerosine, Glyptal 1500 thinner (xylene and VM & P Naphtha), CPE 1000, solvent based paints and thinners Coded as solvents 1901-1983	general cleaning, painting, thinning	1901-83	L-M	3

Table 2-9 con't p 12

12

ion	Exposure (* = coded)	Use	Dates of Use	Levels	Extent of Usage
(29) Bushings con't	metal fumes (Cu, Ag, Pb, Cd, fluoride)	exposure from brazing and silver plating		L	2
	metal pigment solvent based paints - lead pigments used			M	1
	adhesives - 3M adhesivie 826 (ethyl acetate vehicle), Glyptal			L	3
	10c Oil - highly refined mineral oil plus <0.3 % stabilizers	used to fill high voltage bushings	1901-83	L-M	2
(31) Area Maintenance - Tool Room and Machine Shop	*machining fluids		1901-83	L-M	3
	*Varsol, Kerosine, & other unknown solvents. Coded as solvents 1901-1983	general cleaning	1901-83	L-M	3
(32) Area Maintenance - Instrument Service, Crane & Elevator Repair	*Varsol & other unknown solvents. Coded as solvents 1901-1983	general cleaning	1901-83	L	2
	*pyranol	exposure during crane repair	1936-76	L	1

Table 2-9 cont p 13

ion	Exposure (* = coded)	Use	Dates of Use	Levels	Extent of Usage
Construction	* pyranol	Workers would have occasional exposure depending on work location and task	1936-76	L-M	1
	* benzene		1920-50	L-M	1
	* trichloroethylene		1930-73	L-M	1
	* solvents		1901-83	L-M	1
Transportation and terials clamation	* pyranol	exposure from pyranol soaked flooring & pipes	1976-p	L-M	1
	* solvents	general cleaning	1901-83	L-M	1
) caning	* trichloroethylene	cleaning degreasers	1930-73	M	1
	* solvents	cleaning spray paint booths	1901-83	M	1
...ler ...tion	no exposures coded				
	mercury exposures from mercury boiler				
)Specialty rocess ntrol emical torage and ixing)	* benzene	mixing chemicals; cleaning	1920-50	M-H	3
	* Varsol, CPE 1000, Glyptal 1500 thinner (xylene plus VM&P Naphtha), kerosine, solvent based paints & thinners. Coded as solvents 1901-83	mixing chemicals; cleaning	1901-83	M-H	3
	* phenol-formaldehyde resin in petroleum solvent (core-coating enamel, Formex)	mixing chemicals	1936-83	M	2
	formic gel (formic acid plus ethylene dichloride)	mixing chemicals	1972-p	M	2

Table 2-9 con't p14

ion	Exposure (* = coded)	Use	Dates of Use	Levels	Extent of Usage
7) Specialty Process Control con't	epoxy resin in petroleum solvent (containing cellosolve acetate); epoxy paints			M	2
	adhesives - cellulose in acetone and alcohol; phenolic resin in MEK and MEOH; rubber adhesive in MEK			M	2
	coal tar pitch plus silica filler			L	2
	10c Oil plus stabilizers			M	2
8) Oil farms	*pyranol	pumping + filtering transformer oil	1936-76	H	3
	Kerosine Coded as Solvents 1901-1983	used for coil + core "treat"	1901-83	H	3
11) Capacitors	*pyranol	filling + impregnating capacitors	1936-46	M-H	3
	* solvents, solvent-based paints	cleaning, painting	1901-83	M	3

TABLE 2/0 RATED EXPOSURES BY OPERATION

PERATION	BUILDINGS	PYRANOL	ASBESTOS	MACHINE FLUIDS	BENZENE	TCE	SOLVENT	RESIN
) Coilwinding	1, 2, 17, 51		x				x	x
) Tube Rolling	61, 63, 65		x				x	x
) Wire Mill	43, 66		x				x	x
) Annealing	11, 15					x		
) Core Fab/Bldg	3, 15				x		x	x
) Woodworking	7						x	
) Insulation	4, 6		x				x	x
) Cables	1, 4, 5, 7, 17, 19						x	
) Cu Fab	4, 5, 10, 14		x				x	
) Load Ratio	9, 19, 42			x	x	x	x	
) Tank Fab	9, 14, 42			x	x	x	x	
) Welding	14							
) Radiators	14						x	
) Painting	14						x	
) Tank test, finish	14				x		x	
) Int. Assembly	1, 2, 3, 12, 100	x	x	x	x		x	
) Ext. Assembly	1, 2, 3, 12, 100	x	x		x		x	
) Coilwinding	24. 33		x				x	x
) Insulation	24, 33						x	
) Woodworking	24, 33						x	
) Fab (Core & Tank)	24, 33			x	x	x	x	
2) Welding	24, 33							
3) Painting	24, 33						x	
4) Tank test, finish	24, 33				x		x	
5) ML32, Induc Regulators	4, 5, 19	x	x	x	x	x	x	
6) Lacing Assembly	26, 29	x	x		x	x	x	

?ERATION	BUILDINGS	PYRANOL	ASBESTOS	MACHINE FLUIDS	BENZENE	TCE	SOLVE...	RESIN
7) Concrete Reactors	7, 12, 24						x	
3) Lightning Arrestor	12, 41, 42, 43, 44, 61	x		x			x	
9) Bushings	12, 17, 41, 51, 59			x	x	x	x	
0) Cutouts	42			x			x	
1) Area Main - TR & MS	32, 42, 43, 63			x			x	
2) Area Main - I & E Serv, Crane Repair	7, 8, 32, 43, 63	x					x	
3) Construction	32, 42, 43, 63	x	x		x	x	x	
4) Trans, Mat Reclam	9, 11, 33, 64	x					x	
5) Cleaning	25					x	x	
6) Power Station	31, 62, 78							
7) Spec. Process	12, 34				x		x	x
8) Oil Farm	3, 12, 29, 68	x					x	
9) High Voltage Laboratory	9							
0) MgO Manufacture	95, 96							
1) Capacitors	42, 43	x					x	
2) Photo/Multilith Dept	11							
4) Medical	11							
5) Ordnance	90, 91, 95			x			x	
6) Phenol Plant	34						x	
7) Plastics	36, 101				x		x	x
8) PT Galvanizing/Plating	41							
9) Laboratory	11	x					x	
0) Engineering and Drafting	16							
1) Receiving	17							
2) Plant Protection	17							

TABLE 2-11 PERCENTAGE OF JOB-BUILDING PAIRS IN EXPOSURE HISTORY FILE RATED FOR EXPOSURES.

CHEMICAL EXPOSURE	RATING CATEGORY	NUMBER OF JOB-BUILDING PAIRS	PERCENTAGE JOB-BUILDING PAIRS
Pyranol	0	2600	58
	0.5	860	19
	1.0	756	17
	2.0	174	4
	3.0	87	2
Benzene	0	3171	70
	1	950	21
	2	356	8
Trichloroethylene	0	4088	91
	1	333	7
	2	56	2
Other Petroleum Solvents	0	1586	35
	1	1855	41
	2	1034	23
Machining Fluids	0	3566	80
	1	911	20
Asbestos	0	3811	85
	1	666	15
Resin Systems	0	4069	91
	1	408	9

TABLE 2-12 CODED EXPOSURES AND EXPOSURE RATING DEFINITIONS

SURE	EXPOSURE RATING DEFINITIONS
Pyranol	0 No Exposure 0.5 Potential exposure from adjacent or prior high exposure areas 1 Indirect Exposure (chemical in workplace; does not work directly with chemical) 2 Direct Low or Infrequent Exposure (works directly with chemical but exposure is low or infrequent) 3 Direct Medium to High Exposure (works directly with chemical at medium to high levels on a routine basis)
Benzene	0 No Exposure 1 Indirect Exposure (chemical in workplace; does not work directly with chemical) 2 Direct Exposure (works directly with chemical irrespective of level or frequency)
Trichloroethylene	See Benzene Exposure Rating
Petroleum Solvents	See Benzene Exposure Rating
-bestos	0 No Exposure 1 Indirect or Direct Exposure
achining Fluids	See Asbestos Exposure Rating
Resin Systems	See Asbestos Exposure Rating

Table 2-13
RESIDUAL AIRBORNE PCB
CONCENTRATIONS IN PITTSFIELD

	BUILDING LOCATION	DATE SAMPLED	CONCENTRATION, LEVEL IN $\mu G/M^3$
Laboratory	11-2	2/7/78	7.9
	"		6.5
	11-3		6.4
	"		9.1
	"		6.6
	Outside 11		1.2
Power Transformer External Assembly	12-1		4.7
			3.2
			2.9
			4.8
			4.6
			9.6
	Outside 12		2.1
Distribution Transformer Assembly	26-2		22.3
	"		19.8
	26-3		23.2
	"		5.2
	Outside 26		1.6
DT and Regulator Assembly	29-1		4.7
			6.8
			3.5
			2.3
			16.8
			3.8
			6.3
DT Tank Shop	33-2	9/23/79	.7
			.3
			.2
			.6
Capacitors	42-1	5/15/79	.1
	42-2		.9
	42-3		3.0
	"		1.0
	42-4		3.0
	"		2.0
	42-5		N.D.
Scrap and Salvage	60	2/7/78	7.9
	Outside 60A (> Oil-Water Separator)		17.4
	64X		5.3
	64S		3.0
	64W		1.4
	Between 64X & 64W		2.1
	3/4 Mi. W of plant	9/26/78	.06
	2 Mi. SE of plant		.15
	3-1/2 Mi. N of plant		.06

TABLE OCCUPATIONAL EXPOSURE TO PCBs

STUDY	EXPOSURE	POPULATION	BODY LEVELS	CANCER/MORTALITY	OTHER HEALTH EFFECTS
Ouw et. al, 1976: Study of capacitor manufacturing workers.	Arochlor 1242 capacitor impregnation at 70°C 1.1-2.2 mg/m^3 Assembly: 0.32 mg/m^3 (1-23 yrs)	34 exposed 30 unexposed	Whole blood mean 400 ppb (N.D. in unexposed)		Mild burning, irritation of face & eyes; 10 with skin problems. BSP elevated in 4 of 7 with blood levels 500 ppb No adverse reactions with blood levels 200 ppb
Bahn et. al, 1976: Study of workers in petrochemical refinery	Arochlor 1254 No levels (a year)	72 exposed		2 malignant melanomas observed (0.4 expected, based on TNCS data) Also pancreas	Preliminary results report in letter to editor; workers exposed to other chemicals; study in progre
Fishbein, et. al, 1979: Cross-sectional field survey of capacitor manufacturing workers.	Several Arochlor types, Exposure rated as: none - 0-0.07 mg/m^3 low - 0.07-0.41 medium - 0.41-0.6 high - 0.6-11.0 (90% 5 years exposure)	353 exposed	Plasma mean 172 ppb, range 0-2530 ppb. Broken down as 124 ppb lower PCB isomers and 48 higher PCB isomers.		50% reported dermatologica 18% GI, and 50% neurologic complaints. Association of S60T with serum PCB but low incidence of abnormal values. Association of exposure ratings and serum PCB. Reduced FVC in 34 of 243 (14%) workers.
Brown & Jones, 1980: Cohort mortality study of capacitor manufacturers.	Several Arochlor types: Plant 1 0.024-0.393 mg/m^3 Plant 2 0.06-1.26 mg/m^3 (office level 0.05 mg/m^3) (90% exposed 10 years)	2567		All cause mortality & all cancer mortality lower than expected. Rectal & liver cancer slightly but not signigicantly elevated. Short latency period; followup is continuing.	

TABLE CONTINUED

TABLE ONTINUED

STUDY	EXPOSURE	POPULATION	BODY LEVELS	CANCER/MORTALITY	OTHER HEALTH EFFECTS
Vannucchi, et.al 1980. Study of air levels in capacitor manufacturing facility (Italy)	Apirolio 1431 (42% chlorine). Capacitor impregnation 0.8 mg/m^3. Assembly and finishing 0.6-1.4 mg/m^3				
Maroni, et.al 1981: Study of capacitor manufacturing workers (Italy)	Apirolio 1431 & Pyralene 3010 (42% chlorine). Air levels 48-275 ug/m^3 Workroom surface and tools 0.2-159 ug/cm^2	80	Whole blood Means (plants A & B) 200, 377 ppb Range 41-1319 ppb Skin (palms of hands) (also broken down by lower and higher PCB homologues)		Mean blood PCBs correlated with employment duration: low chlorinated PCBs associated with recent exposure and high chlorinated PCBs with past exposure. Authors felt skin exposure more important than inhalation. 15 had skin diseases; 16 had pronounced hepatic involvement; 2 had bleeding haemangiomas, 1 with chroni myelocytic leukemia.
Chase, et. al 1982: Study of locomotive transformer maintenance workers	Many types of transformer oils No air levels; employees rated as exposed, nominally exposed, and not exposed (65% of exposed 5 years exposure)	120	Plasma exposed-mean 33 ppb, range 10-312 ppb, nominally exposed Mean 14 ppb, range 10-27 ppb, Fat, exposed mean 5.6 ppm, range 1-22 ppm, Nominally exposed, mean 1.4 ppm, range 1-1.8 ppm, nonexposed mean 1.3 ppm, range 1-2 ppm.		Some skin problems in exposed; weak correlations between plasma and fat PCB levels and serum triglyceride and SGOT with low incidence of abnormal values.

TABLE 2-[illegible] CONTINUED

STUDY	EXPOSURE	POPULATION	BODY LEVELS	CANCER/MORTALITY	OTHER HEALTH EFFECTS
Mosely et. al 1982: Study of air levels during building transformer maintenance.	Several Arochlor types, Inside transformer vault background 0.2-0.9 ug/m^3, during maintenance - 2.6-60 ug/m^3. Outside vault - background - 0.2-0.9 ug/m^3, during maintenance - 0-1.4 ug/m^3				

Table 2-15 Pittsfield, MA residents:
Serum PCB Level of Participants Divided into Four Groups on the Basis of Information Obtained on the Occupational and Residency History Questionnaires

		n	Median PCB (ppb)	Range (ppb)	> 20 ppb n	> 20 ppb %
A.	History of having worked at General Electric	43	21.7	4.8-378	23	53.5
B.	History of having lived with someone who worked at General Electric but no history of the individual ever working there	12	15.6	1.7-31.8	5	41.7
C.	Residents of the contaminated neighborhood and no association with General Electric	7	8.3	5.9-14.1	0	0
D.	Residents of non-contaminated neighborhood and no association with General Electric	9	6.9	3.2-17.1	0	0

Table 2-16 Blood serum concentrations in general population in South Carolina

Race and Residence	No. in Sample	PCBs Measureable In		PCB Concentrations	
		No.	%	Ave* ppb	Max ppb
Rural black	107	5	4.67	9.45	20.6
Urban black	151	57	37.75	5.22	29.0
Rural white	192	119	61.98	5.12	16.6
Urban white	166	89	53.61	4.38	22.0

*Average of measureable concentrations

Reference: Finklea et al. (1972)

TABLE 2-17 PHENOL FORMALDEHYDE AND POLYVINYL FORMAL RESIN EXPOSURES

OPERATION (Number)	CHEMICAL	USE DATES	OPERATION DESCRIPTION
Wire Mill (3)	Formex enamel - polyvinyl formal resin GE 73039 Wire Enamel polyvinyl formal resin (formvar) and phendic resin in cresylic acid and aromatic hydrocarbon (xylene, naphtha) mixed solvent. EOE-ZC 11560 Ecn-1299 Epoxy 184 lbs. 55L32 Eponol 400 lbs. Xylol 2 Gals. 6005 Epon Resin 46 lbs. $B.F._3$400 7 lbs. Isomid B polyester-imide resin based wire enamel in cresylic acid and petroleum spirits	1951 - present	Various types of enamels (primarily polyvinyl formal and phenol formaldehyde resins) have been used to insulate wire of transformer coils since 1951. Wire is run through liquid enamel and dried in ovens. Despite partial enclosure, fumes are detectable within building from a considerable distance. IH surveys in building 66 in 1978 showed phenol levels between 0.8-6mg/m^3 and cresol levels between 0-9 mg/m^3 during use of Isomid B resin.
Tube Rolling (2)	Resin 1237 phenol formaldehyde powder resin Resin 1830 phenol formaldehyde resin in ethanol	1936-present	Rolls of paper are put on a hot mandrel (steel drum) and are sprinkled with resin powder. Resin melts and bonds paper together forming a strong insulating tube. Resins most extensively used have been phenol-formaldehyde resins produced by plastics. The phenol formaldehyde powder resins had mineral (sometimes asbestos) or cellulose fillers and contain 5-10% by weight of a cross linking

TABLE 2-17 CONTINUED

OPERATION	CHEMICAL	USE DATES	OPERATION DESCRIPTION
			agent (hexamethylene tetramine). Dust and fume have been described as considerable, especially prior to 1951 when canopy hoods were installed. IH surveys in 1978 in building 65 showed phenol levels between 0.4-0.7 mg/m^3 during tube rollin operation. Surveys in building 61 showed phenol levels between 0.5-8 mg/m^3 and anilene levels of 0.36 mg/m^3 during resin grinding.
PT Core Fabrication (5)	KC 1461 or A15B138 Varcum Resin 370 lbs. Brown Linseed Oil 365 lbs. Naptha 270 lbs. Kerosene 270 lbs. Lead Napthanate 43 lbs. Manganese Napthanate 3 lbs. (Note: varcum resin is a phenol formaldehyde resin)	1936-1982	Thin sheets of steel are cut to size and then coated with an insulating material and baked. Up until 1960, the steel "legs" were first coated with "slurry coat" (insulating material containing clay) followed by enamel. From 1960-1982, only an insulating enamel was applie Since 1982, fully processed steel has been used. Different types of enamel have been used predominantly phenol-formaldehyde resins. Enamel fumes from oven were described as very irritating.
PT and DT Coil Winding (1, 18)	Formex degradation products during brazing (phenol, formaldehyde, cresol, CO_1 CO_2) Study done by Ed Bates (Manufacturing Engineering)	1951-present	As wire leads are joined during coil winding by brazing, Formex enamel on wire decomposes.
PT Insulatin (7)	Phenol-formaldehyde resins similar to Tube Rolling	1936-present	Some paper insulation is treated with resins and heated in pressing machines. Exposures described as considerably less than Tube Rollin

TABLE 2-17 CONTINUED

OPERATION	CHEMICAL	USE DATES	OPERATION DESCRIPTIONS
Plastics (47)	Phenol-formaldehyde resin Manufacture GENAL* resins	1936-present	Plastics manufactured phenol-formaldehyde resins used in Tube Rolling and Insulation in addition to other resins. Primarily an enclose operation. Some exposure to phenol, formaldehyde, asbestos and other fillers, cross-linking agents (hexamethyl tetramine) solvent vehicles, etc.

CHAPTER III

SUMMARY

OF EPIDEMIOLOGIC ANALYSIS

A. Introduction

B. Materials

C. Methods

D. Summary results

E. Interpretation of results: general considerations

F. Interpretation of specific findings

G. Connections to previous literature

H. Summary and recommendations for further research

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A. INTRODUCTION

In this chapter we present a summary report of our analysis of the 1969-1984 mortality data from the General Electric (G.E.) Pittsfield facility, using exposure ratings supplied by Marilyn Hallock and Thomas Smith (University of Massachusetts), as described in Chapter II. Our objective was to detect possible excess cancer risks associated with any of the exposure ratings. This chapter summarizes our methods and results, presents our epidemiologic interpretation of these results, and offers some recommendations for further research. Technical details of our statistical methods are given in Appendices III and V-VII. Annotated computer tabulations of our data and our statistical analyses are given in Appendices IV-VII. An analysis of potential confounding by smoking is given in Appendix VIII.

B. MATERIALS

Subjects for the analysis were deceased G.E. employees who met all the following criteria:

1) Had been employed at G.E. before Dec. 31, 1984.

2) Date of death was in the interval 1969-1984 (no pension records were available for employees who died before 1969);

3) Death was reported to and recorded by the G.E. pension office (benefits were available to next-of-kin of employees vested in the pension fund, and next-of-kin of employees who died on the job);

4) Had a job-history record available for exposure rating.

Subjects were restricted to white males, because there were too few nonwhites or females to allow analytic control for race or sex. Vesting requirements for G.E. workers varied over time, but for most of the

exposure period under study required 10-15 years employment at G.E. Further data restrictions were imposed in the course of the analysis; these will be described below.

Figure III-1 provides a flow chart of entry into the initial data set. Note that the size of the employee cohort and the number of persons passing through each step is unknown, except for the final node. Work history records turned out not to be available for a large fraction of the candidate subjects, especially in the earlier years of death (Table III-1). We note that lack of job-history availability arose from routine disposal of records by G.E. over time and from misfiling. Possible biases arising from the selection process illustrated in fig. III-1 will be discussed in the Interpretation section.

After initial data description, the following further restrictions (summarized in Figure III-2) were imposed on the 1,911 subjects:

1) To eliminate concerns with confounding or diagnostic error at extremes of age, only deaths age 21-90 were analyzed

2) All subjects but one stopped work at Pittsfield in 1946 or later. The single exception, who retired in 1932, was excluded from the analysis.

3) The subjects for whom more than 50% of their work history was unrated for Pyranol exposure were excluded from the analysis.

Of the 1,821 subjects remaining after the last exclusions, those with incomplete ratings had their exposures in unrated periods imputed from the time-weighted average of exposures in rated periods. For example, suppose a subject had 20 rated years, 12 of them at Pyranol level 2, 4

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of them at Pyranol level 1, and 5 unrated years: then the subject was imputed to have had 5 additional years of Pyranol level

$[12(2) + 4(1) + 4(0)]/(12 + 4 + 4) = 1.4$ (rounded to 1).

Less than 2% of the 51,063 person-years of employment had their exposure level assigned by imputation. Subjects had also accumulated 16,432 person-years of retirement.

Table III-2 displays the distribution of deaths according to job-history availability, and the distribution of deaths meeting the final restrictions among those with an available job history. The latter deaths, listed in the first column of Table III-2, comprise the subjects for our analysis. A more complete tabular description of these data is given in Appendix IV. (Ten included subjects were listed as having two primary cancers at death and were thus counted in two site-specific groups; thus the total of the site-specific numbers exceeds the total number of cases, which is 512.)

One hundred and seven noncancer deaths were excluded because of conditions listed on the death certificate which we felt might be related to exposure, and so would render them unsuitable as controls in a cancer case-control analysis (see Fig. III-2).

C. METHODS

The exposures and the method of rating individual subjects were described in Chapter II (by Marilyn Hallock and Thomas Smith, University of Massachusetts). Briefly, for the most common job sites at G.E. Pittsfield, an industrial hygienist rated the site on qualitative scales for the following exposures which occurred from 1901 to the end of the

study, in 1984:

1) Pyranol: A transformer oil composed of 50% polychlorinated biphenyls (PCBs) (a mixture of isomers but mostly hexachlorobiphenyl), 50% trichlorobenzene (or a mixture of tri- and tetrachlorobenzene), less than 0.25% phenoxypropene oxides and trace amounts of dibenzofurans. The PCB content in Pyranol could vary from 45 to 80%.

2) Benzene: Used in various departments for general cleaning during machining and assembly operations.

3) Trichloroethylene (TCE): Used as a degreaser.

4) Other solvents: this group includes Varsol (petroleum spirits), CPE 1000 (petroleum spirits and methylene chloride), methylene chloride, kerosene, paint thinners (primarily xylene or toluene based), solvent based paints, xylene, toluene and naphtha. Some type of solvent exposure occurred in the majority of plant operations.

5) Machining fluids: Used for machining and fabrication operations. Straight mineral oils were first used, then soluble oils and finally synthetic oils. There was usage of straight cutting oils.

6) Asbestos: Used as wet insulation blankets during brazing and welding. Some insulation pieces were made from asbestos. Also used as powdered additive in some resins operations (this component of asbestos exposure was not rated).

7) Resins systems: primarily phenol formaldehyde and polyvinyl formal resin systems. Asbestos was used in some resins operations as a powdered additive.

The unrated exposures were:

a) Mineral oil (10c oil), used as transformer oil.

a) Metal fumes and dust: exposure occurred during welding, brazing and painting with metal based pigments.

b) Sawdust in woodworking shops.

c) Adhesives: water-based, solvent-based and epoxy (those using petroleum solvents are rated with group 4)

d) Electromagnetic fields: exposure occurred during testing and development of transformers.

The effect of some of the non-rated exposures could be evaluated with a job-site analysis, which we did not carry out.

The levels for asbestos, resins, and machine fluid ratings were 0 = no exposure, 1 = some exposure; levels for TCE, benzene, and solvent ratings were 0 = no exposure, 1 = indirect exposure, 2 = direct exposure; the levels for Pyranol ratings were 0 = no exposure, 1 = indirect exposure, 2 = direct low or infrequent exposure, 3 = direct medium to high exposure. A rating of 0.5 for Pyranol had been used initially to identify potential exposure from adjacent or prior high-exposure areas, but this rating was later collapsed with the 0 level, as suggested by the industrial hygienist who conducted the exposure assessment. Individual exposure scores were computed from these ratings entered in a job-exposure matrix and from the individual job histories.

Initially, we examined exposure scores of the form

score = Σ_j w_j × years spent at level j,

where the weight w_j could equal j for all j ("linear score"), or could equal j^2 for all j ("quadratic score"), or could equal 1 for all j at or above a certain level and zero for all lower levels, in which case the score is simply the time spent at or above a certain level. We also examined various categorizations of these scores. Each score was lagged

by two years, so that exposures accumulated in the last two years before death could not contribute to the score. This was done to minimize counting exposures after onset of the disease that led to death.

We also examined binary indicators of exposure. For all but solvents level 1, these were coded 1 = ever exposed, 0 = never exposed. Because most subjects had at least several years of solvents level 1 exposure, the solvent level 1 indicator was coded 1 = over 20 years, 0 = 20 or fewer years of exposure.

For each exposure score and cancer site involving more than 8 cases, we examined the crude and age-stratified contingency table of the two variables. We also examined a modification of the Mantel trend test (see Appendix V) both crude and stratified (up to two at a time) on each of the covariates. Exposure score-cancer pairs meeting a special screening criterion (described in Appendix I and, in more detail, in Appendix V) were subjected to further contingency-table analyses, including stratification on other exposure scores. Cancer sites involving 4-8 cases were screened using crude tables; sites involving fewer than 4 cases were not examined. For most analyses, certain sites with few cases were combined based on the assumption that any carcinogenic effect of the exposures should be similar at these sites because of anatomic proximity, tissue similarity, similarity of exposure routes, or similarity of diagnostic categories: Liver, gall bladder, and biliary cancers (ICD8 155-156) were combined into a single category, "livbil"; buccal, pharyngeal, and laryngeal cancers were combined into a single category, "orolx" (ICD8 140-149, 161); malignant and unspecified brain tumors were combined into a single category, "brainp" (ICD8 191-192, 238) ; all lymphosarcomas and reticulosarcomas were combined into a single category, "lymphomas" (ICD8 200-202) and all leukemias were

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combined (ICD8 204-207). Nevertheless, we also performed tabular analyses on the separate component sites as well.

Contingency tables were analyzed using the EGRET™ (SERC, 1989) software package, which supplies both asymptotic and (where computable) exact P values and confidence intervals for category-specific odds ratios, as well as tests for trend and homogeneity (see Breslow and Day, 1980, for a description of these statistics).

Logistic regressions were also carried out using EGRET™. Exposures were screened for entry into continuous-variable regressions using liberal inclusion criteria (for exposures, $p < 0,15$ and relative-risk estimate above 1.5 in screening analyses; see Appendix V for details). Age and death year were entered in all regressions displayed below, and other covariates were entered when their inclusion altered an estimate by more than 20%.

Some covariate combinations were exactly or nearly collinear. For example, age at death always equals death year minus birth year; duration of employment usually equalled year stopped work minus hire year, and was also highly correlated with death year minus hire year. Therefore, we eliminated birth year from further consideration, considered hire year only in combination with death year, and considered duration of employment only in combination with year stopped work. The death year-hire year combination always gave results close to the duration of employment-year stopped work combination, and so we preferentially employed the former combination when hire year or duration appeared important.

Final regressions with continuous exposures were run twice, once for each of two forms of exposures: Winsorized (pulled back to a maximum

permissible value) exposures and original exposures. In our Winsorized analyses, the 97th or the 98th percentile of the control exposure distribution was used as the maximum permissible value. A large difference between results from the two regressions indicates the presence of subjects with influential (leveraging) values for exposure.

Selected associations in the modelling analyses were further subjected to a formal induction-latency analysis. Exposure scores were recomputed, using weights according to time before death. Appendix III (section G) and Appendix II give details of the weight function. In brief, the function used is unimodal and gives maximum weight to exposures at time θ before death minus 2 years; θ_0 is the modal induction-latency period. Different values of θ were employed in formulating exposure scores, and the different scores so obtained were entered in logistic models. The resulting model log likelihoods could then be compared to obtain likelihood-based estimates for θ.

Several multiple-comparisons techniques were applied to our results in order to obtain an overall summary of the degree to which our findings fall within chance expectations. P-value plots (Schweder and Spjotvoll, 1982) were made of the basic trend-test results and the basic binary-exposure modelling results (see Appendices V and VI). Empirical Bayes estimates of the binary-exposure modelling results were also computed using a modification of the technique presented by Thomas et al. (1985); Appendix VII gives a summary of this method and presents the results. Here, we present the P-value plots from the modelling results.

For further discussion of the study methods, see Appendix III.

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D. SUMMARY RESULTS

Contingency-Table and Screening Analyses

Since we examined thousands of contingency tables and most of these tables involved multiple strata and exposure categories, no tabular summary of the purely categorical analyses seems practical. Key tables are reported in Appendix V. Here, we limit ourselves to descriptive tables III-3 to 5, which summarize the covariate and exposure score distributions, and table III-6 to 12, which summarize exposure distributions, separately for controls and for cancer sites with more than 8 cases. We report results for selected dichotomous-exposure indicators based on the following considerations:

1) There were too few cases with Pyranol time at level 3 or TCE time at level 2 to allow meaningful analyses of these levels as separate entities. Therefore, Pyranol levels 2 and 3 were combined into Pyranol level greater than 1 (gt1), and TCE levels 1 and 2 were combined into TCE level greater than 0 (gt0).

2) Pyranol level 1, benzene level 1, and solvents level 1 did not show notable associations with any cancer site (except Pyranol with pancreatic cancer); we note that level 1 for these variables represented extremely low exposure. Also, nearly everyone was exposed to some degree of solvents level 1, which also represented a very low exposure. Therefore, for these three variables, levels 0 and 1 were combined into a single reference level in tables III-6 to 12. Analyses were also performed using only level 0 as the reference level (not shown).

Most of the stratified data analyses involved finer categorizations of covariates and multiple-level exposure categorizations. Since the purely categorical analyses led to the same results as the regression analyses, tables III-6 to III-12 summarize the exposure-cancer associations using the odds ratio estimated from the logistic regressions including age, death year, and dichotomous (exposed/not exposed) exposures. For comparison to the logistic P values, we also give the P values from the age + death-year stratified Mantel trend test using the continuous exposures, with 5 age strata (21-40, 41-60, 61-70, 71-80, 81-90) and 2 death-year strata (1969-1976, 1977-1984). These results were used to select variables for analysis by continuous logistic regression (see next section and table III-13 for selections).

Note that the dichotomous-regression results and the trend-test results sometimes conflict. The most common cause of such conflict is more controls than cases exposed but exposed cases more highly exposed than controls (in which case the regression results appear negative but the trend test can be positive), or more cases than controls exposed but exposed controls more highly exposed than cases (in which case the regression results appear positive but the trend test can be negative).

Figure III-3 provides a plot of the 98 exposure-cancer P values from the multiple-exposure regressions. The plot closely follows a diagonal line, which is the result expected if all the underlying associations are null. This result indicates that few, if any, of the observed associations correspond to non-null underlying associations.

Continuous Logistic Regressions

Modelling was limited to the 14 sites with more than 8 cases. For each site, we began modelling by entering the dichotomized form of each exposure in a logistic regression model which also contained age and death year. Exposures identified as important in these regressions or in the contingency-table screening, according to the criteria given in Appendix V, were further modelled in a continuous form.

Table III-13 summarizes the odds ratios (estimated relative risks) for the 97th control percentile versus no exposure, based on logistic regressions using continuous exposures, along with age, death year, and hire year. The 97th percentile was chosen because it was usually close to the maximum case value at each site, and so estimates based on it would be rough estimates of the maximum possible effect among these subjects. Only the estimates, and not the P values, would change if a different percentile was used. Note that the logistic regression coefficient per unit variation of exposure can be obtained by taking the log of the odds ratio in table III-13 and dividing by the 97th exposure percentile in table III-5.

More extensive tabulations of the models we fit are given in Appendix VI. Tabulated estimates include the 23 exposure-cancer associations which yielded odds ratios greater than 1.0 upon modelling, out of the 28 selected from stratified or the dichotomous-regression analyses for modelling. Also included are associations of asbestos with lung cancer and benzene with leukemia (selected on a priori grounds).

We caution that the 23 results in table III-13 are themselves the end product of a 3-stage selection process: Out of the 98 associations in tables III-6 to 12, 28 were selected for continuous modelling

according to the inclusion criterion given in Appendix I; 23 of the 28 showed positive continuous associations; and the models presented in table III-13 give the best fit among several dose-response combinations. As a result of this selection process, the reported significance levels must be downwardly biased (i.e., the P values tend to be too small) and the estimates must be upwardly biased. Furthermore, several of the results (especially for benzene) are sensitive to influential data points, as indicated by the Winsorized P values given parenthetically in the last column (see Appendix VI for coefficients using Winsorized exposure scores). Therefore, the "significant" results shoud not be regarded as positive by the usual (e.g. 0.05) criteria; they only represent the most significant associations after selection.

In comparing the continuous-exposure results in table III-13 to the dichotomous-exposure results in tables III-6 to 12, we note that the Pyranol-lymphomas, TCE-pancreas, solvents-orolx, and solvents-lung associations are greatly reduced in apparent importance in the continuous regressions (in fact, the solvents-lung association becomes slightly negative). For each of these associations, this discrepancy may be attributed to the fact that a much higher proportion of cases than controls are exposed, but the difference between cases and controls in average time exposed is not as large.

In regressions with multiple exposures, we attempted to enter product terms to check for departures from the linear-logistic model. Where such terms could be fitted, none approached conventional (0.05) significance levels and all had extremely large variance, no doubt reflecting the small number of cases available for all sites (except the lung). Similar results occurred when we attempted to fit quadratic

terms for single exposures. We also modelled the resin-lung cancer association using cubic-spline logistic regression but again found no significant departure from the linear-logistic model.

Subtypes analyses

As numbers permitted, we also examined subtypes within the compound sites of orolx, livbil, lymphomas, and leukemias. Most subtypes had too few cases to produce any meaningful (i.e., significant and/or unusually large) associations. Nevertheless, the solvents association with lymphomas (lymphosarcomas + reticulosarcomas) was entirely concentrated in the reticulosarcomas. In fact, 5 of the 6 reticulosarcomas were exposed to solvents level 2, compared to 654 of 1202 controls (54%), yielding a crude odds ratio of 4.2 and a (two-sided) P value of 0.01 in an age-death-year stratified trend test. Furthermore, all the exposed cases had at least 8 years of exposure. Pyranol level gt 1 and benzene level 2 also showed associations with reticulosarcoma (P = 0.02 and 0.04 in age-death-year stratified trend tests), but both results were entirely attributable to two cases who had long-term exposures to Pyranol, benzene, solvents, and asbestos.

Induction-latency analyses

We used the induction-latency analysis method described in Appendix II and Appendix III, to further analyze the associations of resins with rectal and lung cancer, asbestos with lung and kidney cancer, benzene, solvents, and machine-fluids with kidney cancer, solvents with reticulosarcoma, and TCE with leukemias. Figures III-4 to III-8 summarize the main results.

The resins-lung cancer and TCE-leukemias analyses yielded fairly flat likelihoods for the induction-latency periods, and none of the latency-weighted scores showed associations different from those in table III-13. The benzene-kidney and solvents-reticulosarcoma associations appeared strongest for longer induction-latency periods, although the long apparent latency for benzene effects probably reflects the fact that benzene use was discontinued in the 1950's and deaths were not entered in this study before 1969. The machine-fluids-kidney-cancer association appeared strongest for shorter induction-latency periods, with a P value of 0.001 for the association when the mode of the period was fixed at 8 years before death, but the estimated strength of the association was numerically unstable.

Using latency-weighted scores, the asbestos-lung, asbestos-kidney, and solvents-kidney associations remained very nonsignificant after other exposures were controlled and so are omitted here. Because of the doubtful validity of our method when fewer than five exposed cases are available, we did not pursue a resins-esophagus analysis. We also did not pursue the Pyranol-pancreas association because this association was entirely concentrated in Pyranol level 1 exposure, rather than higher levels.

More complete tabulations of the induction-latency results are given in Appendix VII.

Epoch analyses

For the associations subjected to induction-latency analysis (except those involving benzene), we also performed a parallel analyses in which the unweighted exposure scores were divided into two

components. One component measured exposure up to Dec. 31, 1950; we labelled these components "epoch 1," which on average contributed to about half the recorded employment time. The other component measured exposure after that date, and we labelled this component "epoch 2." Both components were entered in logistic regressions in place of the original variable. The procedure was not carried out for benzene because very little benzene exposure was recorded in our data beyond 1950.

Table III-14 summarizes the logistic-regression results. The associations of resins with rectal and lung cancer, machine fluids with kidney cancer, and TCE with leukemias appeared to be largely or entirely concentrated in the post-1950 exposures. Crosstabulations showed that the association of solvents level 2 with reticulosarcoma was also concentrated in the post-1950 exposures, with crude odds ratios of 1.4 for pre-1950 exposure and 8.3 for post-1950 exposure. More complete tabulations of the epoch analysis results are given in Appendix VII. There, we show that the resins-lung cancer association is largely concentrated among post-1950 exposures to resins in operations with uncoded asbestos.

Resins by Operation

It has been suggested that the observed resins-cancer associations may be due to uncoded exposure to hazardous levels of asbestos dusts in the operations in which asbestos-filled phenol-formaldehyde resin was produced. To test this hypothesis, we examined the associations of resins with esophageal, rectal, and lung cancer, separating resins within operations involving uncoded asbestos exposure from resins within

operations not involving uncoded asbestos exposure. If a resins-cancer association was due to asbestos confounding, we should expect the association to be concentrated in operations involving uncoded asbestos exposure.

This appeared to be the case for lung cancer. For example, the logistic-regression odds ratio for resins exposure without uncoded asbestos was 1.8 (95% CL = 0.68, 4.7; P = 0.24), while the odds ratio for resin exposure potentially with uncoded asbestos was 2.4 (95% CL = 1.4, 4.1; P = 0.002). (Both odds ratios are computed at the 97th percentile of total resins exposure.) Furthermore, these results are sensitive to outliers. Considering these results, we cannot reject the hypothesis that the resins-lung cancer association is due to confounding. As would be expected from the epoch analysis, the associations were concentrated in post-1950 exposure.

On the other hand, the resins-esophageal and resins-rectal cancer associations were <u>not</u> concentrated in the operations with uncoded asbestos (in fact, they appeared more significant in operations without uncoded asbestos, contrary to the confounding hypothesis).

<u>Deletion of Respiratory Controls</u>

All lung-cancer analyses were repeated after deleting all deaths with ICD codes for nonmalignant respiratory diseases from the control group. This deletion had only trivial impact on the results.

E. INTERPRETATION OF RESULTS:

GENERAL CONSIDERATIONS

As the most general caution, we wish to emphasize that this is a mortality case-control study (i.e., a relative mortality study), with no enumerated population base. This means that our study data cannot provide an estimate of the absolute risks of any outcome among former G.E. Pittsfield workers, even in the absence of bias. This section discusses some of the biases that may have affected the relative-risk estimates (odds ratios) presented in this report.

Possible explanations for positive associations .

One can hypothesize numerous explanations for each association that appears to be positive in table III-13. These explanations may be classified into seven broad categories:

1) Direct causation: Exposure X caused (some cases of) cancer Y.
2) Inverse causation: Exposure X prevented (some cases of) one or more of the control diseases, or is associated with some factor that is preventive of the control diseases.
3) Confounding: Exposure X was more frequent among workers who, for other reasons (e.g., smoking), were already at elevated risk for cancer Y.
4) Differential errors in exposure assessment, such as elevated detection of exposure among cases compared to controls.
5) Differential errors in death certificates, such as cancer Y more frequently detected and recorded among workers who were exposed to X.

6) Differential selection of deaths: The proportion of deaths with cancer Y recorded by the G.E. pension office was different from the proportion of control deaths recorded, and the ratio of these selection proportions was higher among the exposed (or highly exposed) workers.

7) Differential availability of job histories: The proportion of deaths with cancer Y among deaths with a job history was different from the proportion of control deaths with a job history, and the ratio these availability proportions was higher among the exposed (or highly exposed) workers.

These explanations are not mutually exclusive. Nor are they exhaustive, although we hope they subsume all the plausible possibilities. The remaining possibilities include an eighth "explanation":

8) "Random error", which may be thought of as an aggregate of various isolated, nonsystematic errors. For associations examined on a priori grounds (such as asbestos and lung cancer), it is accounted for in the confidence limits if the distributional assumptions used to obtain the limits are correct. Unfortunately, the confidence limits do not fully account for random error in associations selected by data screening.

We will discuss each of the above explanations in turn:

1) We cannot rule out direct causation as an explanation for any of the positive associations in our study.

2) Inverse causation does not seem plausible as an explanation, for if an exposure prevented an important amount of control deaths it should appear to be significantly associated with most (if not

all) of the cancer sites. This was not the case for any of the exposures.

3) Confounding: None of the covariates recorded in our data could be invoked as explanatory of any of the associations. In a few instances, covariate adjustments produced moderate changes (20%-30%) in quantitative but not qualitative results.

On the other hand, exposure levels were inaccurately estimated and some (especially benzene and solvents) were strongly correlated. This means that the exposures would confound one another, and their individual effects (if real) could not always be clearly separated. This was a particular problem for esophageal, kidney, and brain tumors.

We have no evidence regarding the status of possible unmeasured confounders, except smoking and uncoded asbestos. As noted in Appendix VIII, external and internal evidence argues against the hypothesis that confounding by smoking could largely explain the results. Confounding by uncoded asbestos was addressable only through operation-stratified analyses. For the most part, confounding by unmeasured factors remains an important possibility in our study.

4-5) Differential errors in exposure or disease assessment seem implausible to us, since exposure assessment was blinded with respect to status at death, and death certification was performed before the study (and exposure ratings) were carried out. If, however, the interviewees for the assessment gave biased answers, differential errors could result. Nondifferential errors were certainly common, but these would produce bias towards the null.

6) Evaluation of differential selection requires fairly specific elaboration of mechanisms. We have no external or internal information for testing any hypothesized mechanism of differential selection, and so we cannot address this possibility.

7) We may evaluate differential availability of job histories by comparing availability among recorded cancer and control deaths. This is done in table III-2, which reveals only small differences in job-history availability relative to sampling error (chi-squared p = 0.13 after adjustment for overlap of outcomes). Although this does not rule out the possibility of differential availability by joint-exposure-outcome-status, we have no further information bearing on this possibility.

8) Random error seems most implausible as an explanation for the resin-lung cancer association. It also seems difficult to invoke as an explanation for the solvent-reticulosarcoma association, and for the excess of kidney cancers among subjects with exposure to benzene, asbestos, or machine fluids (although we cannot reliably evaluate which of these exposures is responsible for the excess). Except for resins-lung cancer, random error ("chance") should be considered as an important alternative explanation, especially since the total number of significant associations in the screening analyses (tables III-6 to 12) does not deviate from the number expected if all the underlying associations are null.

In summary, we regard differential selection as the one alternative explanation reasonable for all the detected associations, although (with the exception of inverse causation) we would not rule out the other alternatives.

Possible explanations for negative or null associations

We wish to emphasize that any exposure and cancer that did not appear to have a positive association in our analysis should not be regarded as having no causal effect. In particular, "false negative" associations may have arisen through confounding, differential or nondifferential errors in exposure assessment or death certificates, differential selection, differential job-history availability, or random error. One may also invoke direct causation of control deaths (in place of inverse causation) as an explanation for failure to detect an effect:

> Direct causation: Exposure X caused (some cases of) one or more of the control deaths, or is associated with some cause of the control deaths.

If an exposure caused an important amount of control deaths, it would introduce a downward bias in all the cancer effect estimates for that exposure. We cannot rule out this possibility, for general risk factors (such as cigarette smoking) could produce such an effect.

For benzene, there is the additional consideration that its use at the plant was phased out in the 1950's, and yet deaths before 1969 were not included in our study. Thus, effects of benzene with induction-latency periods under 20 years could not be detected by our study.

We are certain there is nondifferential misclassification of exposures and cause of death in our data, with a resulting downward bias in our estimates of effect. Taking into account this bias would strengthen positive and negative associations, and could also change certain null findings to positive or negative ones.

Finally, with the exception of lung cancer, there were few cases available at each cancer site. The resulting low power of our study should further militate against overinterpreting our failure to identify certain associations as positive.

Interpretation of Epoch-Analysis Results

We offer three possible explanations for those instances in which associations appear to be concentrated in exposure after 1950 (epoch 2):

1) The induction-latency periods for these associations are under 20 years, so that effects of exposures before 1950 cannot be detected in our study (which used only deaths 18-33 years after 1950).

2) The exposures before 1950 were much more poorly evaluated than those after 1950; this would lead to much greater attenuation of the estimates of associations for pre-1950 exposures.

3) The ingredients of composite exposures were more hazardous after 1950 than those before 1950, due to changes in solvent, resin, or machine-fluid composition, or in some operation associated with these compounds.

Of these, we have no data bearing on explanations 1 and 3. Given the uniform method of exposure rating we do not see how a difference in evaluation (measurement) error between epochs could be large enough to create such dramatic differences in association. Explanation 1 is most compatible with the results of our induction-latency analyses. Explanation 3 might be further studied by examining the composition of solvents, resins, and machine fluids over time. We note that the three explanations are not mutually exclusive. We also note that a majority of the exposures occurred after 1950, so that effects of pre-1950

exposures are less precisely estimated. This would not, however, explain the uniformity with which effects are concentrated in the post-1950 epoch.

F. INTERPRETATION OF SPECIFIC FINDINGS

In this section we comment further on those sites for which specific bias or collinearity considerations arose. As a general caution in interpreting the site-specific findings (tables III-6 to III-14), we note again that all the exposure measurements should be regarded as heavily nondifferentially misclassified relative to the true exposure doses. This has several important implications:

1) Exposure associations with outcomes will be underestimated.

2) Correlations among the exposures will be underestimated.

3) As a consequence of 1 and 2, the confounding of one exposure by another will be underestimated.

4) As a consequence of 1-3, the fact that one exposure appears more important than another in (say) a regression may reflect better measurement of the apparently more important exposure, rather than a stronger true association.

Esophageal Cancer

Although benzene, solvents, and resins each appeared associated with esophageal cancer, the overall test for the association of these three exposures with esophageal cancer yielded $P \doteq 0.12$. These three exposures are also too collinear to allow any reliable separation of their associations with esophageal cancer. Resins appears to have the strongest association of the three. From the operations-stratified analysis, it appears unlikely that the resins association might be due in part to an effect of uncoded asbestos.

Rectal Cancers

From our data, resins appears a more likely candidate as a risk factor than its collinear exposures (benzene, solvents). From the operations-stratified analysis, it appears unlikely that the resins association arose from confounding by uncoded asbestos. Nevertheless, we caution that our estimate of this association is highly unstable.

Lung Cancer

Based on contingency-table and modelling analyses, by far the most consistent positive finding in our study is the highly significant association of resins with lung cancer. This finding contrasts to the virtual absence of association of asbestos with lung cancer. This absence is disconcerting, since the asbestos-lung cancer association is probably the one most supported by earlier studies among all the associations we examined. Several people familiar with the G.E. Pittsfield operations suggest that the absence of the expected asbestos-lung cancer association only reflects the fact that jobs coded as involving asbestos exposure in fact involved extremely low levels of exposure.

Our analyses of resins within operations leave open the possibility that resins are a proxy for uncoded asbestos. Nevertheless, it remains plausible that the resins themselves contain a lung carcinogen (see section G) and the result only reflects a less intense resin exposure in asbestos-free operations than in other operations (recall that our resin measurement recorded only duration of exposure, not intensity). And of course we cannot rule out any of the general biases discussed above.

Kidney Cancer

The collinearity of benzene, solvents, asbestos, and machine fluids in our data, along with the small number of kidney-cancer cases, make it impossible to disentangle the associations of these exposures with kidney cancer with any certitude. Nevertheless, the total association of these exposures with kidney cancer has a very low nominal P value ($P < 0.005$).

In our data, benzene and machine fluids emerge as more precisely and consistently associated with kidney cancer than solvents or (especially) asbestos. Yet some authors are now convinced that current evidence firmly incriminates asbestos as a kidney carcinogen (Smith et al., 1989). As with lung cancer, our failure to replicate the latter findings may reflect the very low level of asbestos exposure recorded by the exposure-assessment process. But with only 12 cases to assess 4 exposures (with 3 covariates), we would strongly caution against overinterpreting our findings.

Lymphomas

The strength and specificity of the solvents-reticulosarcoma association must be weighed against the fact that we observed only six cases total. Thus, unlike the resins-lung cancer association, the statistical error in the reported estimate is very large. Furthermore, our data leave open the possibility that the association may reflect an effect of Pyranol.

Leukemias

Benzene is generally regarded as a leukemogen, but failed to show any association with leukemias in our data. One highly plausible explanation for this failure is that the induction-latency period for benzene-induced leukemia is much shorter (under 20 years) than the time from the last heavy benzene exposure at G.E. Pittsfield (about 1950) and the first deaths among our subjects (1969). Under this hypothesis, most or all benzene-related leukemias would have occurred before our case-occurrence period, leaving nothing for us to detect.

Brain Tumors

As with esophageal and kidney cancers, the collinearity of the exposures, coupled with the small number of cases, prohibit any reliable disentanglement of the associations. Nevertheless, the overall test of the three associations (benzene, solvents and asbestos) yielded a small nominal P value (0.02). The benzene association emerges as the most significant of the brain-tumor exposures, and this result is essentially unchanged if unspecified brain tumors (ICD8 238) are deleted from the case series. We caution, however, that our estimate of this association is highly unstable, because it pivots on the benzene exposure of a few cases.

G. CONNECTIONS TO PREVIOUS LITERATURE

In this section we comment further on those associations for which there is previous evidence in the literature. As a general caution, we reiterate that all the biases discussed above cannot be ruled out as an explanations of our findings. Some of the associations reported below were observed with a very large statistical error in our study and are mentioned here only because of previous evidence.

Pyranol

Both animal studies (IARC, 1978, 1982) and, much less clearly so, previous human cohort studies (Nicholson, 1987) suggest an association of polychlorinated biphenyls with cancer of the liver/biliary tract. We found a moderate but inconsistent association of Pyranol above level 1 with cancer at this site. A subtype analysis showed no association with liver/intrahepatic bile duct cancer (5 cases of which 1 was exposed). The association of Pyranol is entirely with gallbladder cancer (4 cases, 2 exposed) and has an extremely large statistical error.

Our data showed a small to moderate association of Pyranol with lymphomas with an extremely large statistical error. The review by Nicholson (1987) presented some weak evidence for an association of leukemias and lymphomas with PCB exposure.

It is possible that the associations we observed could be due to trichlorobenzene (TCB), the other major component of Pyranol. There is however no previous information on the carcinogenicity of TCB.

Benzene

Benzene is a risk factor for acute leukemia, mainly of the myelogenous type, and, with less clear evidence, for malignant lymphomas and myeloma (Rinsky et al., 1987, Brandt, 1987). Earlier, we gave a possible explanation for our failure to detect a benzene-leukemia association in our study. The association of benzene and multiple myeloma had an extremely large statistical error, since we only observed four cases.

Trichloroethylene

Consistency across previous studies seems to suggest possible associations of TCE exposure with hemo-lymphatic malignancies (Blair et al., 1979; Hardell et al., 1981; Katz and Jowett, 1981; Axelson et al., 1984). We detected an association of TCE and leukemias in some but not all the analyses, and this association had a large statistical error.

Asbestos

Exposure to asbestos is associated with cancer of the lung and with mesothelioma of the pleura and peritoneum. Asbestos may also be associated with laryngeal and digestive cancers (see, e.g., Rom, 1983), and with kidney cancer (Smith et al., 1989). One study (Seidman et al., 1982) found a small association of asbestos with brain tumors among insulation workers. Earlier, we gave a possible explanation for failing to detect an association of asbestos with lung cancer in our study. We

did see suggestions of an asbestos association with brain and kidney tumors.

Other solvents.

In our study, solvents constitute a very heterogeneous group of chemicals, excluding only benzene and TCE.

Previous studies are difficult to interprete because of multiple exposures to several types of solvents. Exposure to solvents has been associated with respiratory, bladder, and kidney cancer, although not consistently. Observed associations with hemolymphatic malignancies may be due, at least in part, to benzene contamination (Rothman and Emmett, 1988), although a role of non-benzene solvents cannot be excluded (Brandt, 1987).

We observed a strong association of solvents with reticulosarcoma, although with a large statistical error, and a suggestion of a solvent association with kidney cancer.

Machining fluids

Exposure to unrefined mineral oils has been associated with skin and gastrointestinal cancers. Association with other sites (lung, pancreas, bladder, oral cavity, pharynx and sinonasal cavity) were reported with little consistency in the literature (IARC, 1987, Bingham, 1988, Silverstein et al., 1988). In our study, machining fluids were associated only with kidney cancer.

In our study, machining fluids were only associated with kidney cancer, but collinearity with other exposures prevented a separation of this association.

Resin systems

In this heterogeneous group of chemicals, exposure to the formaldehyde component of phenol-formaldehyde resins is the main source of concern. Previous evidence on the carcinogenicity of formaldehyde is controversial. Blair et al. (1986) found little evidence of excess cancer mortality associated with exposure to formaldehyde; nevertheless, a re-analysis of their data seemed to indicate a dose-related excess of lung cancer (Sterling and Weinkam, 1988).

Since we observed a strong and consistent association of duration of exposure to resins with lung cancer, the question arises of a possible role of formaldehyde in determining this finding. Because of the limited nature of our exposure data, we cannot shed any light on the formaldehyde-lung cancer controversy. It may be noted that whereas some consistency in the literature suggests an association of formaldehyde with sinonasal or nasopharyngeal cancer (Hayes et al., 1986; Olsen et al., 1986; Blair et al., 1987, Roush et al., 1987), only one case of cancer of the nasopharynx was recorded in our study.

A highly unstable association of resins with rectal cancer was observed in our study. There is some weak previous evidence suggesting an association of formaldehyde with colorectal cancers (Liebling et al., 1984; Bertazzi et al., 1986).

H. SUMMARY AND RECOMMENDATIONS FOR FURTHER RESEARCH

Summary Interpretation

In a one-sided hypothesis-screening analysis designed to detect positive associations between exposures and cancer sites, we employed a liberal statistical screening criterion. We chose a liberal criterion in a partial attempt to compensate for low study power (due to nondifferential misclassification and small numbers of cases).

Because of the null biases and low power of our study, it is reasonably likely that an association representing a real exposure effect would be missed in our screening. Thus we do not regard the nonpositive results of our analysis as providing useful information for guiding further research.

Because we choose a liberal criterion to screen multiple associations, it is probable that most (and possibly all) of the positive associations reported here do not represent any real exposure effects. Hence further screening of our positive results is needed in order to determine whether any of these results represent real effects. We next give our recommendations for such screenings.

Recommendations

Because of the clear association of resins with lung cancer, and the concentration of this association in specific operations, we strongly recommend that the following further research be conducted:

1. In order to determine whether the resins associations are attributable to uncoded asbestos exposure,

a) A more complete rating of asbestos exposure for pertinent job-building pairs recorded in our data should be undertaken.

b) The new asbestos information should be used to recompute asbestos exposure scores for our study subjects.

c) A reanalysis of the joint asbestos-resin association with esophageal, rectal, and (especially) lung cancer should be conducted, in order to determine whether the resins associations in our study are attributable to unmeasured asbestos exposure.

d) The new asbestos score should also be examined for its association with other sites, especially kidney cancer.

2. An analysis of cancers by job site should be conducted. As demonstrated in the analysis of the resins-lung cancer association within operations, such an analysis may identify concentrations of risk in certain job sites, and so suggest or eliminate possible explanations of our study findings.

Suggestions for future research

Because of the highly inconclusive nature of our other results, we would like to see future studies of occupational hazards include, where practical, analyses of the follow associations:

1. Tricholorethylene (TCE) and leukemias.
2. Benzene and cancers of the esophagus, bladder, kidney, and brain.
3. Other solvents and cancers of the kidney and the lymphatic system. In the latter case, we recommend special attention to subtype (in particular, to reticulosarcomas).

4. Resin components and cancers of the esophagus, large intestine, and lung.

5. Machine fluids and kidney cancers.

Benzene and asbestos effects may not be of current interest, since both these exposures are now generally recognized as hazardous and have been subject to increasingly strict controls. On the other hand, we would be especially interested in learning of studies that provide information relevant to the resin-lung, machine fluid-kidney, and solvents-reticulosarcoma associations observed in our study, especially if specific components of these exposures can be examined.

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TABLE III-1 AVAILABILITY OF WORK HISTORIES BY YEAR OF DEATH

YEAR OF DEATH	WORK HISTORY NO	WORK HISTORY YES	TOTAL SOUGHT
69	117	49	166
	70.48	29.52	100.00
70	130	57	187
	69.52	30.48	100.00
71	116	39	155
	74.84	25.16	100.00
72	85	104	189
	44.97	55.03	100.00
73	60	103	163
	36.81	63.19	100.00
74	97	93	190
	51.05	48.95	100.00
75	64	124	188
	34.04	65.96	100.00
76	32	143	175
	18.29	81.71	100.00
77	33	140	173
	19.08	80.92	100.00
78	36	143	179
	20.11	79.89	100.00
79	37	133	170
	21.76	78.24	100.00
80	35	166	201
	17.41	82.59	100.00
81	31	161	192
	16.15	83.85	100.00
82	40	157	197
	20.30	79.70	100.00
83	39	155	194
	20.10	79.90	100.00
84	51	144	195
	26.15	73.85	100.00
Total	1003	1911	2914
	34.42	65.58	100.00

Table III-2

Number of subjects by outcome and job-history availability

	Job History			
	Available		Not available	
Outcome	Included	Total	no.	%
Orolx*	21	21	10	32
Esophagus	13	13	6	32
Stomach	19	19	8	30
Colon	60	60	22	27
Rectum	32	32	4	11
Livbil*	9	10	2	17
Pancreas	33	34	11	24
Lung	139	142	68	32
Prostate	58	60	26	30
Bladder	20	22	12	35
Kidney	12	12	4	25
Lymphomas*	15	16	5	24
Leukemias	22	23	17	43
Brainp*	16	16	9	36
Other cancers	53	53	24	31
Control causes	1202	1270	719	36
Excluded causes	--	107	71	40

*Abbreviations: Orolx = oral, laryngeal, pharyngeal
Livbil = liver, gallbladder, and biliary tract
Lymphomas = lymphosarcomas, reticulosarcomas
Brainp = malignant and unspecified brain tumors

Table III-3
Summary of continuous covariate distributions
(in years)

	Mean	Min	Max	Std. Deviation
Cases				
Year of birth	1909	1884	1955	12
Age at death	68	24	90	12
Year of death	1978	1969	1984*	4
Year of hire	1937	1909	1980	14
Year stopped work	1968	1946	1984*	8
Duration of employment (leaves excluded)	27.4	0.8	48.4	9.8
Time on retirement	8.2	0	31.9	7.5
Controls				
Year of birth	1907	1880	1956	12
Age at death	70	21	90	12
Year of death	1978	1969	1984*	4
Year of hire	1935	1903	1981	15
Year stopped work	1968	1946	1984*	8
Duration of employment (leaves excluded)	28.4	0.2	49.3	10.4
Time on retirement	9.5	0	28.2	7.9

*End of study period.

TABLE III-4
Summary of dichotomous-covariate distributions

	Percent positive	
	Cases	Controls
Foreign born	18%	15%
Vested 5 years before death?	93	92
Employed 5 years before death?	44	37

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TABLE III-5 NON-WINSORIZED SCORES AMONG CONTROLS (N=1202)

Exposure score	Mean	Std Dev	Minimum	Percentiles 90th	95th	97th	98th	Maximum
PYRANOL years								
at level 1	3.7	7.0	0	14.2	20.8	24.7	26.8	36.5
at level 2	0.7	2.9	0	0.4	3.5	8.7	10.8	27.3
at level 3	0.3	2.0	0	0.0	0.2	2.6	5.4	28.9
at level >0	4.6	8.1	0	18.0	24.7	27.3	28.9	36.5
at level >1	1.0	3.5	0	1.6	7.5	10.6	14.2	29.0
Pyranol L.S.[1]	5.9	11.2	0	21.5	30.2	34.6	39.2	86.7
TCE years								
at level 1	2.0	5.1	0	7.2	13.4	18.1	20.7	34.8
at level 2	0.1	0.9	0	0.0	0.0	0.3	1.2	18.9
at level >0	2.1	5.2	0	7.9	14.2	18.1	20.7	34.8
TCE L.S.[2]	2.3	5.5	0	8.3	14.6	18.3	22.0	37.8
BENZENE years								
at level 1	2.8	5.3	0	9.7	13.8	16.9	20.4	31.0
at level 2	0.6	2.6	0	1.1	3.6	7.1	10.0	30.8
at level >0	3.4	5.9	0	10.5	15.6	21.1	23.5	31.0
Benzene L.S.[2]	4.1	7.4	0	12.2	18.9	23.8	28.1	61.6
Other SOLVENTS years								
at level 1	11.9	11.4	0	29.0	33.3	36.2	40.6	48.2
at level 2	5.6	9.1	0	19.7	27.8	30.6	32.8	44.2
at level >0	17.4	12.9	0	34.9	39.4	42.1	43.1	48.2
Oth. solvents L.S.[2]	23.0	19.1	0	48.7	59.7	65.6	70.2	90.6
ASBESTOS								
years exposed	2.6	6.2	0	10.9	18.1	21.5	25.5	35.0
RESINS								
years exposed	1.5	4.6	0	4.6	11.1	16.6	20.0	31.4
MACHINING FLUIDS								
years exposed	6.2	9.7	0	22.3	28.6	31.9	34.3	46.7

[1] L.S. = Linear Score: sum (i*years at level i), i = 1,2,3
[2] L.S. = Linear Score: sum (i*years at level i), i = 1,2

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TABLE III-6
Summary of stratified analyses
EXPOSURE: Pyranol time at level >1 (pytimgt1)

			LOGISTIC REGRESSION WITH BINARY EXPOSURES[3] (CUTPOINT AT 0) ADJUSTED FOR AGE AND YEAR OF DEATH						TEST FOR TREND (MANTEL EXTENSION) UNCATEGORIZED EXPOSURE[3] ADJUSTED FOR AGE AND YEAR OF DEATH	
			ADJUSTED FOR OTHER EXPOSURES			NOT ADJUSTED FOR OTHER EXPOSURES				
	N1[1]	N2[2]	ODDS RATIO	(95% LIMITS)	P[4]	ODDS RATIO	(95% LIMITS)	P[4]	P[4]	TREND SIGN
Controls	209	36								
Orolx[5]	4	0	0.88	(0.29, 2.71)	0.83	1.12	(0.37, 3.36)	0.84	0.69	(-)
Esophagus	2	1	0.68	(0.14, 3.19)	0.62	0.90	(0.20, 4.12)	0.89	0.06	(+)
Stomach	3	1	1.27	(0.35, 4.59)	0.71	0.89	(0.26, 3.08)	0.85	0.75	(+)
Colon	7	0	0.60	(0.26, 1.35)	0.22	0.63	(0.28, 1.41)	0.26	0.28	(-)
Rectum	5	0	0.98	(0.36, 2.65)	0.97	0.88	(0.33, 2.31)	0.79	0.32	(-)
Pancreas	6	2	1.02	(0.40, 2.58)	0.97	1.05	(0.43, 2.59)	0.91	0.90	(+)
Livbil[5]	3	2	2.46	(0.54, 11.2)	0.24	2.40	(0.59, 9.71)	0.22	0.10	(+)
Lung	24	2	0.89	(0.55, 1.43)	0.63	0.99	(0.62, 1.58)	0.96	0.32	(-)
Prostate	8	2	0.81	(0.37, 1.78)	0.60	0.80	(0.37, 1.71)	0.56	0.86	(+)
Bladder	2	0	0.52	(0.12, 2.35)	0.40	0.53	(0.12, 2.29)	0.39	0.35	(-)
Kidney	1	0	0.35	(0.04, 2.82)	0.32	0.43	(0.06, 3.35)	0.42	0.46	(-)
Lymphomas	6	1	3.02	(1.01, 9.02)	0.05	3.26	(1.14, 9.32)	0.03	0.41	(+)
Leukemias	2	0	0.46	(0.10, 2.04)	0.31	0.48	(0.11, 2.05)	0.32	0.31	(-)
Brainp[5]	3	1	0.83	(0.23, 3.03)	0.78	1.09	(0.31, 3.88)	0.89	0.82	(+)

Footnotes on next page

Footnotes for Table III-6

1 N1 = number of subjects with exposure >0 (For total number of subjects see Table III-2)

2 N2 = number of subjects with exposure > 97th percentile of controls 3 Exposure scores: Time exposed to Pyranol above level 1, TCE above level 0, benzene at level 2, other solvents at level 2, asbestos above level 0, resins above level 0, machining fluids above level 0

4 2-sided

5 Not adjusted for other exposures

6 Abbreviations: Orolx = oral cavity, larynx, and pharynx; Livbil = liver, gallbladder, and biliary tract; Brainp = brain and unspecified brain tumors

TABLE III-7
Summary of stratified analyses
EXPOSURE: TCE time at level >0 (tctimgt0)

	N1[1]	N2[2]	LOGISTIC REGRESSION WITH BINARY EXPOSURES[3] (CUTPOINT AT 0) ADJUSTED FOR AGE AND YEAR OF DEATH						TEST FOR TREND (MANTEL EXTENSION) UNCATEGORIZED EXPOSURE[5] ADJUSTED FOR AGE AND YEAR OF DEATH	
			ADJUSTED FOR OTHER EXPOSURES			NOT ADJUSTED FOR OTHER EXPOSURES				
			ODDS RATIO	(95% LIMITS)	P[4]	ODDS RATIO	(95% LIMITS)	P[4]	P[4]	TREND SIGN
Controls	407	36								
Orolx[6]	8	0	1.42	(0.52, 3.94)	0.49	1.26	(0.51, 3.08)	0.61	0.91	(+)
Esophagus	4	0	1.03	(0.27, 4.02)	0.96	0.95	(0.29, 3.17)	0.94	0.34	(-)
Stomach	5	1	0.71	(0.23, 2.16)	0.55	0.70	(0.25, 1.95)	0.49	0.42	(+)
Colon	18	1	0.99	(0.52, 1.88)	0.98	0.83	(0.47, 1.46)	0.51	0.24	(-)
Rectum	9	1	0.69	(0.29, 1.66)	0.41	0.78	(0.35, 1.69)	0.52	0.63	(-)
Pancreas	15	1	2.32	(1.00, 5.34)	0.05	1.64	(0.82, 3.29)	0.16	0.37	(+)
Livbil[6]	2	0	0.46	(0.08, 2.51)	0.37	0.54	(0.11, 2.63)	0.45	0.22	(-)
Lung	46	4	1.13	(0.73, 1.73)	0.59	1.01	(0.69, 1.47)	0.97	0.46	(+)
Prostate	17	1	0.81	(0.42, 1.56)	0.54	0.82	(0.46, 1.46)	0.50	0.44	(-)
Bladder	6	1	0.76	(0.26, 2.18)	0.61	0.85	(0.32, 2.23)	0.74	0.80	(-)
Kidney	4	0	0.73	(0.20, 2.73)	0.65	0.99	(0.30, 3.32)	0.99	0.82	(-)
Lymphomas	4	0	0.57	(0.16, 2.02)	0.38	0.76	(0.24, 2.42)	0.64	0.15	(-)
Leukemias	8	2	1.09	(0.41, 2.90)	0.87	1.10	(0.46, 2.66)	0.82	0.05	(+)
Brainp[6]	5	0	1.15	(0.34, 3.88)	0.82	0.93	(0.32, 2.69)	0.89	0.48	(-)

Footnotes are the same as in table III-6

TABLE III-8
Summary of stratified analyses
EXPOSURE: benzene time at level 2 (benztime2)

	N1[1]	N2[2]	LOGISTIC REGRESSION WITH BINARY EXPOSURES[3] (CUTPOINT AT 0) ADJUSTED FOR AGE AND YEAR OF DEATH: ADJUSTED FOR OTHER EXPOSURES: ODDS RATIO	(95% LIMITS)	P[4]	NOT ADJUSTED FOR OTHER EXPOSURES: ODDS RATIO	(95% LIMITS)	P[4]	TEST FOR TREND (MANTEL EXTENSION) UNCATEGORIZED EXPOSURE[5] ADJUSTED FOR AGE AND YEAR OF DEATH: P[4]	TREND SIGN
Controls	178	36								
Orolx[6]	3	1	0.65	(0.18, 2.36)	0.52	1.03	(0.30, 3.58)	0.96	0.99	(-)
Esophagus	2	2	0.73	(0.15, 3.66)	0.70	1.23	(0.26, 5.72)	0.80	0.03	(+)
Stomach	1	1	0.48	(0.06, 3.95)	0.50	0.32	(0.04, 2.42)	0.27	0.83	(+)
Colon	7	0	0.68	(0.29, 1.61)	0.38	0.74	(0.33, 1.66)	0.47	0.26	(-)
Rectum	4	2	1.24	(0.37, 4.22)	0.73	0.85	(0.29, 2.47)	0.77	0.72	(+)
Pancreas	3	0	0.70	(0.19, 2.57)	0.59	0.58	(0.18, 1.93)	0.38	0.21	(-)
Livbil[6]	3	0	4.79	(0.60, 38.0)	0.14	2.76	(0.68, 11.2)	0.15	0.49	(-)
Lung	12	0	0.47	(0.25, 0.89)	0.02	0.58	(0.31, 1.07)	0.08	0.04	(-)
Prostate	9	1	1.05	(0.46, 2.40)	0.90	1.02	(0.49, 2.12)	0.96	0.60	(-)
Bladder	3	2	0.83	(0.22, 3.20)	0.79	1.02	(0.29, 3.51)	0.98	0.58	(+)
Kidney	5	4	3.63	(0.85, 15.6)	0.08	4.29	(1.33, 13.8)	0.01	0.00	(+)
Lymphoma	2	1	0.59	(0.12, 3.00)	0.53	1.00	(0.22, 4.53)	1.00	0.26	(+)
Leukemias	3	1	0.76	(0.20, 2.85)	0.68	0.90	(0.26, 3.08)	0.87	0.54	(+)
Brainp[6]	4	2	1.45	(0.41, 5.12)	0.56	2.11	(0.66, 6.73)	0.21	0.00	(+)

Footnotes are the same as in table III-6

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TABLE III-9
Summary of stratified analyses
EXPOSURE: Other solvents time at level 2 (solvtime2)

			LOGISTIC REGRESSION WITH BINARY EXPOSURES (CUTPOINT AT 0) ADJUSTED FOR AGE AND YEAR OF DEATH						TEST FOR TREND (MANTEL EXTENSION) UNCATEGORIZED EXPOSURE[5] ADJUSTED FOR AGE AND YEAR OF DEATH	
			ADJUSTED FOR OTHER EXPOSURES[3]			NOT ADJUSTED FOR OTHER EXPOSURES				
	M1[1]	M2[2]	ODDS RATIO	(95% LIMITS)	P[4]	ODDS RATIO	(95% LIMITS)	P[4]	P[4]	TREND SIGN
Controls	654	36								
Orolx[6]	18	0	6.57	(1.79, 24.1)	0.00	5.32	(1.54, 18.3)	0.01	0.41	(+)
Esophagus	10	2	3.85	(0.90, 16.5)	0.07	3.60	(0.94, 13.8)	0.06	0.17	(+)
Stomach	9	0	1.04	(0.38, 2.83)	0.94	0.78	(0.31, 1.93)	0.59	0.97	(+)
Colon	34	4	1.40	(0.78, 2.51)	0.26	1.09	(0.65, 1.85)	0.74	0.34	(+)
Rectum	12	0	0.43	(0.18, 1.01)	0.05	0.51	(0.25, 1.06)	0.07	0.32	(-)
Pancreas	14	1	0.81	(0.37, 1.77)	0.60	0.61	(0.30, 1.24)	0.17	0.11	(-)
Livbil[6]	4	1	0.33	(0.05, 2.23)	0.26	0.69	(0.18, 2.60)	0.59	0.50	(-)
Lung	89	5	1.75	(1.16, 2.62)	0.01	1.57	(1.08, 2.27)	0.02	0.91	(+)
Prostate	29	0	0.90	(0.49, 1.65)	0.72	0.84	(0.49, 1.42)	0.51	0.09	(-)
Bladder	12	2	1.43	(0.53, 3.87)	0.48	1.21	(0.49, 2.98)	0.68	0.53	(+)
Kidney	8	1	0.80	(0.18, 3.60)	0.77	1.64	(0.49, 5.50)	0.42	0.28	(+)
Lymphomas	10	0	1.60	(0.48, 5.37)	0.44	1.97	(0.65, 5.95)	0.23	0.10	(+)
Leukemias	13	0	1.54	(0.59, 4.00)	0.37	1.26	(0.53, 2.99)	0.59	0.31	(-)
Brainp[6]	12	2	2.66	(0.74, 9.52)	0.13	2.65	(0.84, 8.36)	0.10	0.01	(+)

Footnotes are the same as in table III-6

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TABLE III-10
Summary of stratified analyses
EXPOSURE: time with any exposure to asbestos (asbtime1)

	N1[1]	N2[2]	LOGISTIC REGRESSION WITH BINARY EXPOSURES[3] (CUTPOINT AT 0) ADJUSTED FOR AGE AND YEAR OF DEATH: ADJUSTED FOR OTHER EXPOSURES ODDS RATIO	(95% LIMITS)	P[4]	NOT ADJUSTED FOR OTHER EXPOSURES ODDS RATIO	(95% LIMITS)	P[4]	TEST FOR TREND (MANTEL EXTENSION) UNCATEGORIZED EXPOSURE[5] ADJUSTED FOR AGE AND YEAR OF DEATH: P[4]	TREND SIGN
Controls	379	36								
Orolx[6]	6	0	0.69	(0.25, 1.89)	0.47	0.83	(0.32, 2.15)	0.70	0.47	(-)
Esophagus	6	1	1.58	(0.48, 5.18)	0.45	1.87	(0.62, 5.65)	0.26	0.26	(+)
Stomach	0	0	0.00	(0.00, 0.00)	0.00	0.00	(0.00, 0.00)	0.00	0.08	(-)
Colon	17	2	1.03	(0.55, 1.90)	0.94	0.89	(0.50, 1.58)	0.68	0.43	(-)
Rectum	12	1	1.49	(0.67, 3.33)	0.33	1.27	(0.61, 2.64)	0.52	0.95	(-)
Pancreas	9	1	0.95	(0.41, 2.18)	0.90	0.80	(0.37, 1.75)	0.58	0.72	(+)
Livbil[6]	3	0	1.09	(0.22, 5.51)	0.92	1.15	(0.28, 4.65)	0.85	0.40	(-)
Lung	48	4	1.03	(0.69, 1.54)	0.88	1.10	(0.76, 1.60)	0.62	0.44	(+)
Prostate	17	1	1.21	(0.64, 2.28)	0.56	1.02	(0.57, 1.83)	0.95	0.42	(-)
Bladder	6	0	1.10	(0.39, 3.12)	0.86	0.93	(0.35, 2.47)	0.89	0.76	(-)
Kidney	7	1	2.41	(0.68, 8.54)	0.17	2.99	(0.94, 9.56)	0.06	0.01	(+)
Lymphomas	7	1	1.57	(0.52, 4.81)	0.42	1.88	(0.68, 5.25)	0.23	0.57	(+)
Leukemias	6	0	0.92	(0.34, 2.53)	0.87	0.83	(0.32, 2.15)	0.70	0.85	(-)
Brainp[6]	7	1	1.47	(0.50, 4.33)	0.48	1.61	(0.59, 4.37)	0.35	0.06	(+)

Footnotes are the same as in table III-6

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TABLE III-11
Summary of stratified analyses
EXPOSURE: time with *any exposure* to resins (resntime1)

			LOGISTIC REGRESSION WITH BINARY EXPOSURES[3] (CUTPOINT AT 0) ADJUSTED FOR AGE AND YEAR OF DEATH						TEST FOR TREND (MANTEL EXTENSION) UNCATEGORIZED EXPOSURE[3] ADJUSTED FOR AGE AND YEAR OF DEATH	
			ADJUSTED FOR OTHER EXPOSURES			NOT ADJUSTED FOR OTHER EXPOSURES				
	N1[1]	N2[2]	ODDS RATIO	(95% LIMITS)	P[4]	ODDS RATIO	(95% LIMITS)	P[4]	P[4]	TREND SIGN
Controls	257	36								
Orolx[6]	6	1	1.05	(0.38, 2.88)	0.93	1.42	(0.55, 3.71)	0.47	0.66	(+)
Esophagus	4	1	1.02	(0.27, 3.76)	0.98	1.66	(0.51, 5.48)	0.40	0.04	(+)
Stomach	2	0	0.65	(0.14, 2.89)	0.57	0.44	(0.10, 1.90)	0.27	0.39	(-)
Colon	11	2	0.78	(0.38, 1.57)	0.48	0.85	(0.43, 1.65)	0.62	0.72	(-)
Rectum	7	3	1.16	(0.47, 2.87)	0.75	1.02	(0.43, 2.38)	0.97	0.03	(+)
Pancreas	3	1	0.38	(0.11, 1.30)	0.12	0.36	(0.11, 1.20)	0.10	0.32	(-)
Livbil[6]	0	0	0.00	(0.00, 0.00)	0.00	0.00	(0.00, 0.00)	0.00	0.27	(-)
Lung	45	14	1.47	(0.97, 2.21)	0.07	1.72	(1.17, 2.52)	0.01	0.00	(+)
Prostate	7	0	0.54	(0.23, 1.24)	0.14	0.55	(0.24, 1.22)	0.14	0.07	(-)
Bladder	2	0	0.38	(0.08, 1.71)	0.21	0.41	(0.09, 1.78)	0.23	0.60	(-)
Kidney	3	0	1.05	(0.26, 4.19)	0.94	1.20	(0.32, 4.48)	0.79	0.76	(+)
Lymphomas	4	0	1.01	(0.30, 3.47)	0.98	1.34	(0.42, 4.26)	0.62	0.45	(-)
Leukemias	3	0	0.56	(0.16, 2.02)	0.38	0.59	(0.17, 2.02)	0.40	0.37	(-)
Brainp[6]	4	0	0.85	(0.25, 2.88)	0.79	1.18	(0.38, 3.71)	0.77	0.78	(-)

Footnotes are the same as in table III-6

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TABLE III-12
Summary of stratified analyses
EXPOSURE: time with any exposure to machining fluids (mflutime1)

			LOGISTIC REGRESSION WITH BINARY EXPOSURES[3] (CUTPOINT AT 0) ADJUSTED FOR AGE AND YEAR OF DEATH						TEST FOR TREND (MANTEL EXTENSION) UNCATEGORIZED EXPOSURE[3] ADJUSTED FOR AGE AND YEAR OF DEATH	
			ADJUSTED FOR OTHER EXPOSURES			NOT ADJUSTED FOR OTHER EXPOSURES				
	N1[1]	N2[2]	ODDS RATIO	(95% LIMITS)	P[4]	ODDS RATIO	(95% LIMITS)	P[4]	P[4]	TREND SIGN
Controls	707	36								
Orolx[6]	12	1	0.65	(0.24, 1.81)	0.41	0.98	(0.41, 2.36)	0.96	0.54	(+)
Esophagus	7	1	0.71	(0.19, 2.64)	0.61	0.96	(0.31, 2.96)	0.94	0.44	(+)
Stomach	12	0	1.75	(0.62, 4.96)	0.29	1.22	(0.48, 3.14)	0.68	0.52	(+)
Colon	31	1	0.69	(0.38, 1.26)	0.23	0.74	(0.44, 1.24)	0.25	0.45	(-)
Rectum	18	1	1.17	(0.52, 2.65)	0.71	0.92	(0.45, 1.88)	0.83	0.44	(-)
Pancreas	17	1	0.54	(0.23, 1.27)	0.16	0.75	(0.37, 1.49)	0.41	0.60	(-)
Livbil[6]	5	0	1.20	(0.27, 5.31)	0.81	0.86	(0.23, 3.24)	0.83	0.07	(-)
Lung	75	4	0.78	(0.52, 1.19)	0.26	0.86	(0.60, 1.23)	0.42	0.20	(-)
Prostate	33	1	0.96	(0.52, 1.77)	0.90	0.90	(0.53, 1.54)	0.70	0.42	(-)
Bladder	13	1	1.27	(0.45, 3.61)	0.65	1.27	(0.50, 3.21)	0.61	0.54	(-)
Kidney	9	2	1.68	(0.39, 7.25)	0.49	2.10	(0.56, 7.83)	0.27	0.00	(+)
Lymphomas	9	0	1.33	(0.41, 4.32)	0.64	1.19	(0.41, 3.43)	0.75	0.39	(+)
Leukemias	14	1	1.08	(0.40, 2.97)	0.88	1.24	(0.51, 2.99)	0.63	0.73	(+)
Brainp[6]	8	2	0.51	(0.16, 1.64)	0.26	0.73	(0.27, 1.98)	0.54	0.61	(+)

Footnotes are the same as in table III-6

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Table III-13 Summary of continuous logistic regression results

Site	Exposure	Levels[1]	OR[2]	95% CL[2]	P (2-sided)
Orolx[2]	Solvents	2	2.8 (1.8)[3]	0.68, 11	0.15 (0.41)[4]
Esophagus[5]	Benzene	2	1.9	0.82, 4.5	0.13
	Solvents	≥1	2.3 (3.9)	0.21, 25	0.50
	Resins		2.9	0.85, 9.5	0.09
Colon[6]	Solvents	2	1.6	0.72, 3.6	0.24
Rectum[6]	Resins		2.4	1.1, 5.3	0.03 (0.14)
Pancreas	TCE	≥1	1.4	0.51, 3.8	0.52
	Pyranol	≥1	2.4	0.86, 6.8	0.10
Livbil[2]	Pyranol	≥2	2.2	0.76, 6.5	0.15 (0.05)
Lung[7]	Asbestos		1.1	0.61, 2.1	0.71
	Resins		2.2	1.4, 3.6	0.001
Bladder	Benzene	L	2.3	0.79, 7.0	0.13
Kidney	Benzene	2	1.9	0.92, 4.0	0.08 (0.03)
	Solvents	2	11.5 (2.1)	0.37, 351	0.16
	Asbestos		1.5	0.37, 6.5	0.55
	Mach fl[2]		3.2	0.57, 18	0.19
Lymphomas	Pyranol	≥2	1.5	0.55, 4.3	0.42
	Solvents	2	4.5 (3.5)	0.99, 21	0.05
Leukemias	TCE	≥1	2.7	0.97, 7.7	0.06 (0.12)
	Benzene	2	1.4	0.64, 3.2	0.38 (0.93)
Brainp[2]	Benzene	2	2.1	1.00, 4.4	0.05 (0.37)
	Solvents	2	2.1	0.36, 12	0.41
	Asbestos		1.5	0.39, 5.7	0.56

Footnotes on next page.

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Footnotes for Table III-13:

[1]Code under "Level" is as follows: 2 = only time at level 2 was counted; ≥1 = time at levels 1 and above counted equally; ≥2 = only time at levels 2 and 3 count, and count equally (Pyranol only); L = linear combination of levels (time at level 2 counts double that of level 1, etc.)

[2]Abbreviations: OR = odds ratio; CL = confidence limits; Mach fl = machine fluids; Orolx = oral cavity, larynx, and pharynx.; Livbil = liver, gallbladder, and biliary tract; Brainp = brain including unspecified brain tumors (ICD8 238).

[3]Odds ratios are estimated risks for the 97th percentile of control exposure relative to no exposure. Odds ratios in parentheses are estimates after hire year is deleted from the model. Deletion of hire year did not alter any other estimate by more than 10%.

[4]P values in parentheses are P values after Winsorization of exposures. Winsorization did not alter other P values by more than a factor of 2.

[5]Odds ratios under a single site are from a single model containing age at death, death year, hire year, and the exposures listed under that site.

[6]TCE selected in stratified analysis but not entered in final model (or table) because it had a negative coefficient when the other selected exposure was entered.

[7]Solvents level 2 selected in dichotomous-exposure analyses but not entered in final model (or table) because it had a negative coefficient when asbestos and resins were entered.

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TABLE III-14

Summary of logistic regressions

with epoch-specific exposures[1]

Site	Exposure	Levels	Epoch[2]	OR[3]	95% CL	P (two-sided)
Rectum	Resins		1	1.8	0.16, 19	0.64
			2	2.5	0.92, 7.0	0.07
Lung	Resins		1	1.3	0.34, 5.0	0.70
			2	2.5	1.5, 4.3	<0.001
Kidney	Mach fl[4]		1	0.18	0.04, 8.6	0.38
			2	37	3.1, 426	0.004
Leukemias	TCE	≥1	1	1.5	0.14, 16	0.73
			2	3.3	0.62, 18	0.16

Footnotes:

[1]All models contain age at death and death year.

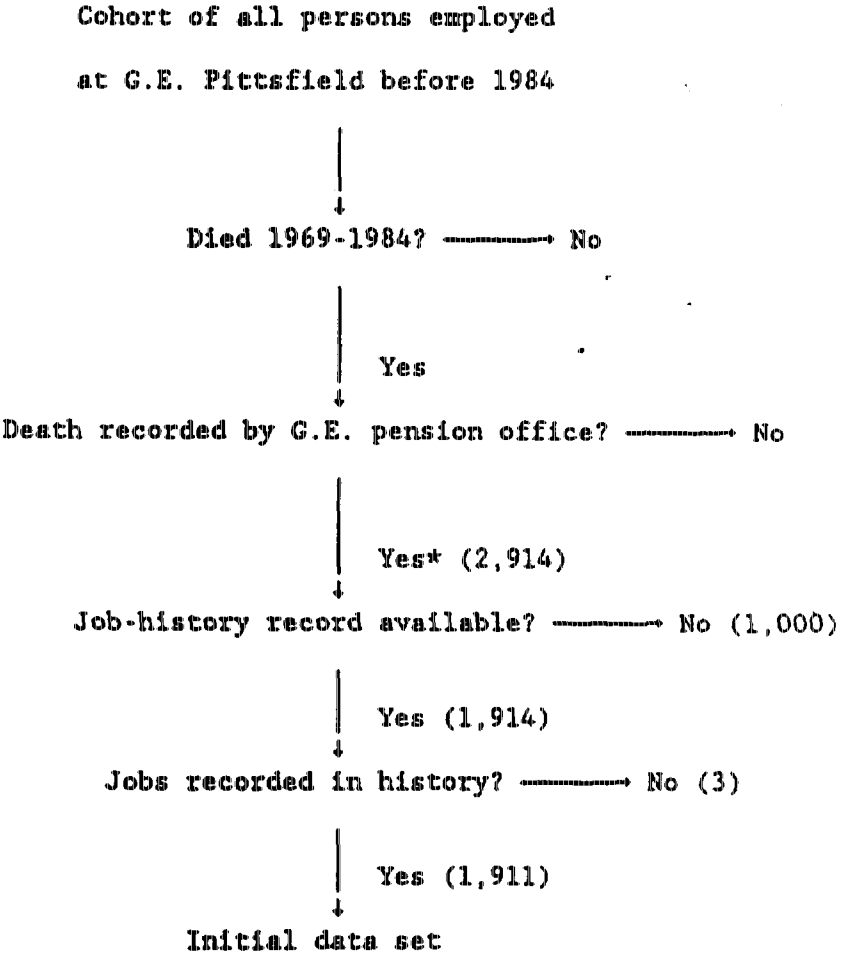
[2]1 = Through 1950, 2 = after 1950.

[3]Odds ratios are estimated risk for exposure at the 97th percentile of total (epoch 1 + epoch 2) control exposure relative to no exposure.

[4]Model also contains a single (control) term for benzene.

Figure III-1

Origin of study subjects.



*Requires that benefits be claimed for the death. This requires: 1) A surviving claimant and 2) the death be eligible for benefits. The latter requires that the person who died was either vested in the G.E. pension fund or employed by G.E. at time of death.

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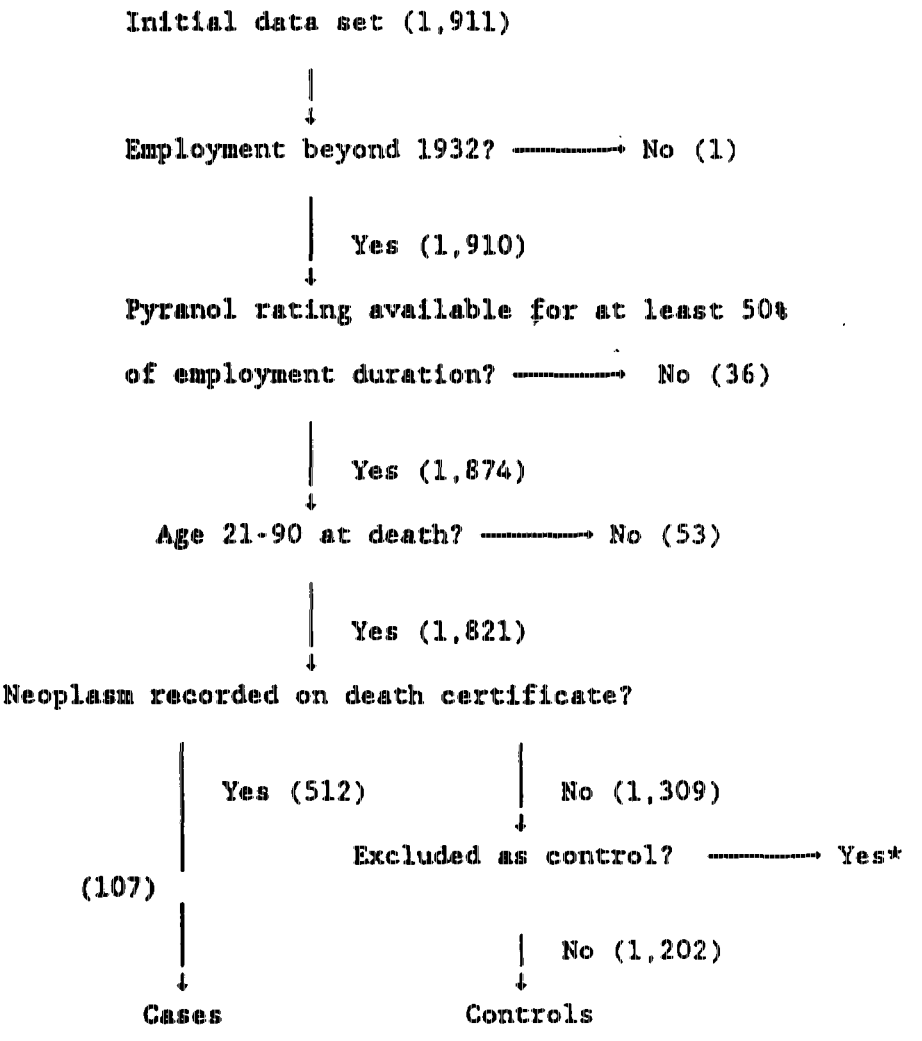
Figure III-2

Further data restrictions



*Excluded causes of death (ICD8 numbers in parentheses):
Diseases of blood and blood-forming organs (280-289)
Mental disorders (290-315)
Diseases of the digestive system (520-577)
Genitourinary diseases (580-629)
Ill-defined conditions (780-796)

FIG. III-3 Logistic regression on 7 binary exposures
n=98; covariates:age,deathyr

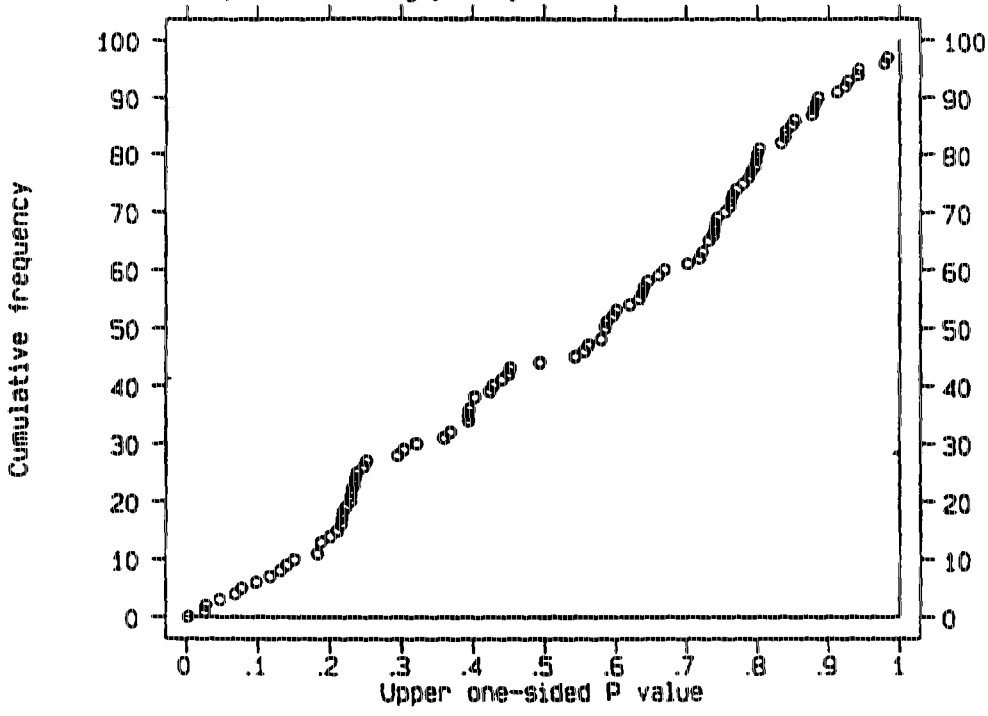
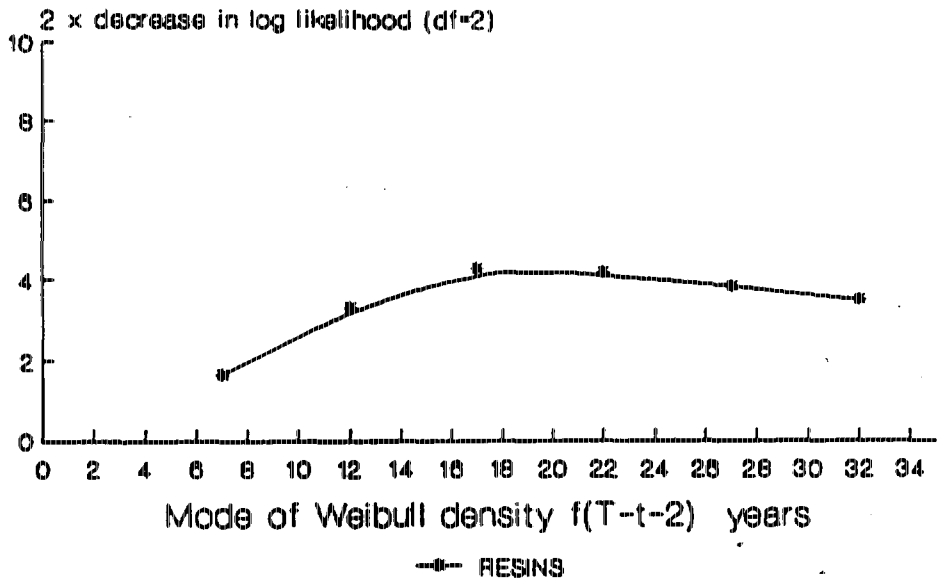
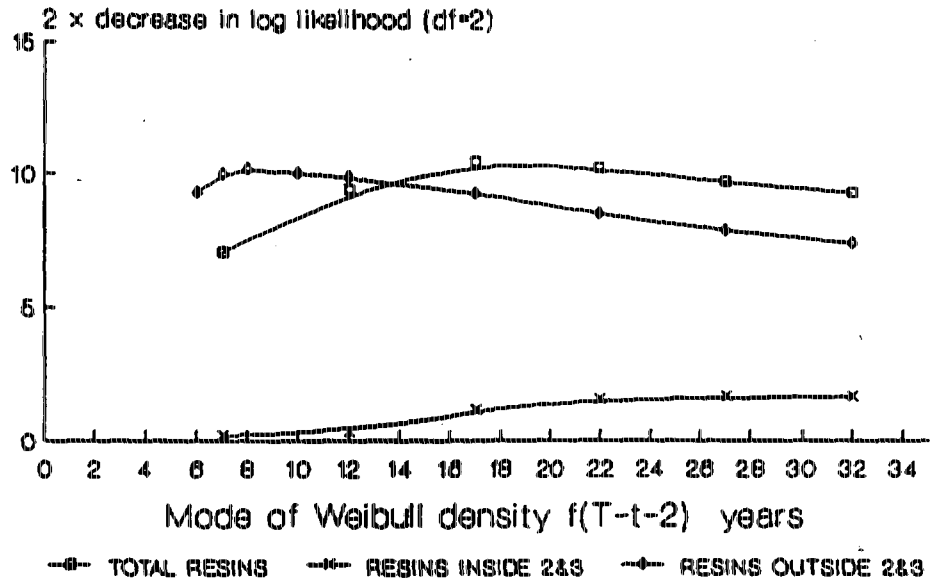


FIGURE III-4 RECTAL CANCER
INDUCTION-LATENCY ANALYSIS
covariates: age, year of death



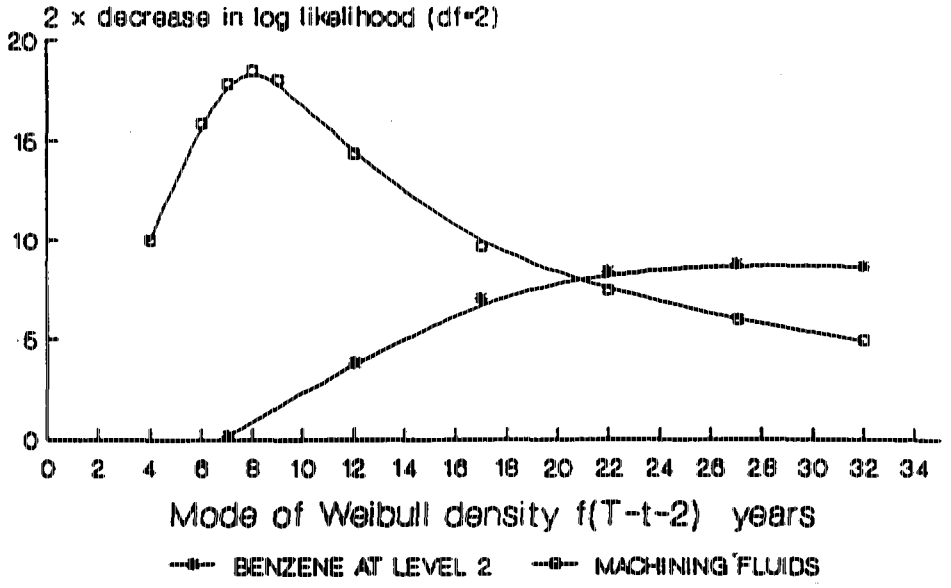
T = age at death; t = age at exposure.
Shape parameter of Weibull is 2.
Reference model has age, deathyr only

FIGURE III-6 LUNG CANCER
INDUCTION-LATENCY ANALYSIS
covariates: age, year of death



T = age at death; t = age at exposure.
Shape parameter of Weibull is 2.
Reference model has age, deathyr only

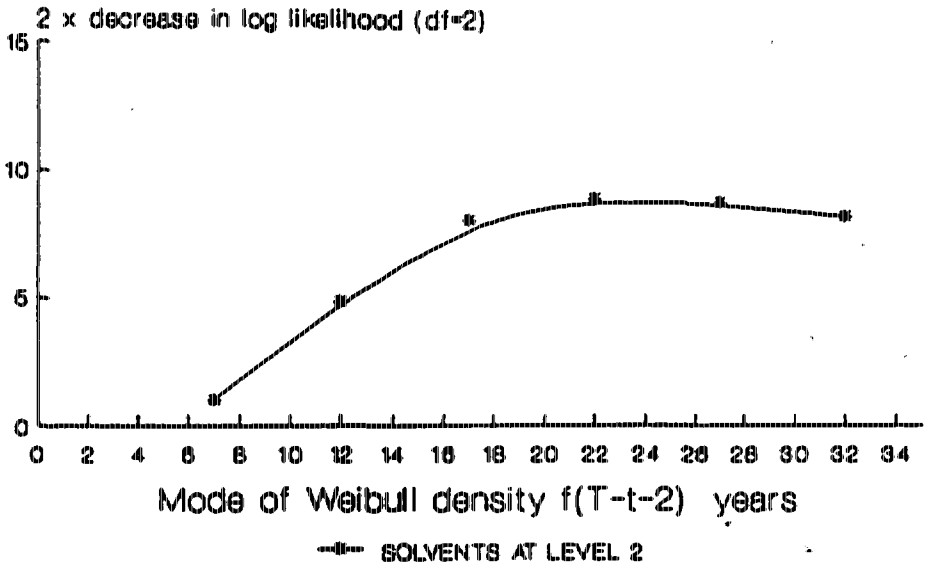
FIGURE III-6 KIDNEY CANCER
INDUCTION-LATENCY ANALYSIS
covariates: age, year of death



T = age at death; t = age at exposure.
Shape parameter of Weibull is 2.
Reference model has age, deathyr only

FIGURE III-7 RETICULUM-CELL SARCOMA INDUCTION-LATENCY ANALYSIS

covariate: year of hire



T = age at death; t = age at exposure.
Shape parameter of Weibull is 2.
Reference model has hireyr only

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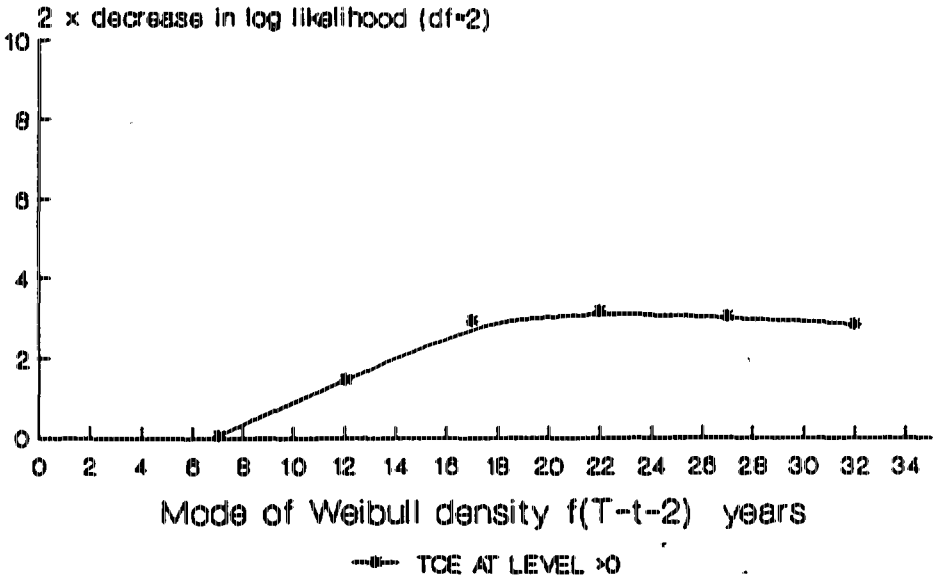
FIGURE III-8 LEUKEMIAS
INDUCTION-LATENCY ANALYSIS
covariates: age, year of death



T = age at death; t = age at exposure.
Shape parameter of Weibull is 2.
Reference model has age, deathyr only