ADDENDUM II

Responses of Alcoa
of
THE NORTH CAROLINA SENATE JUDICIARY II
COMMITTEE HEARING

JULY 6, 2010

Responses made available
to
SENATE JUDICIARY II COMMITTEE
by
ALCOA

This is not an official record of the Committee, but is being included for informational purposes only.

ALCOA

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September 9, 2010

Honorable Fletcher L. Hartsell, Jr.
Chairman, Judiciary II Committee
North Carolina General Assembly
Room 518, Legislative Office Building
Raleigh, NC 27603

Dear Senator Hartsell:

Over the past several weeks, Alcoa has reviewed the video, questions and testimony from the July 6,2010 Senate Judiciary II Committee meeting in an effort to provide information that was requested by the Committee members. Alcoa has been a good corporate citizen for more than 120 years, including nearly 100 years in North Carolina, is proud of both its environmental and worker safety records and wants to ensure there is a fair exposition of the matters discussed by your Committee. We appreciate this opportunity to do that.

Alcoa's Environmental Leadership

Alcoa is recognized as a national and global leader on sustainability issues and has invested hundreds of millions of dollars in the generation of clean, renewable energy. Alcoa was named a founding member of the Dow Jones Sustainability Index, has been recognized as one of the "100 Most Sustainable Corporations in the World" and is ranked #1 by FORTUNE for "Social Responsibility" in the Metals industry. Alcoa is also a founding member of the US Climate Action Partnership, which supports reductions of greenhouse gas emissions, and is leading by example. Alcoa has voluntarily reduced greenhouses gas emissions by 44% (compared to 1990 levels) despite continuous growth. Alcoa is a major supporter of recycling initiatives across the country and has partnered with the Aluminum Association to increase the recycling rate of aluminum cans to 75% by 2015. Alcoa encourages employees to take an active role in protecting the environment. In 1998, Alcoa challenged employees to personally plant 1 million trees by 2010. We reached that goal in two years, and then started the "10 Million Trees" program. Alcoa employees remain on track to personally plant 10 million trees by 2020. For the past eight years, Alcoa has published a sustainability report, transparently reporting on its environmental, social and business performance. A copy can be viewed at www.alcoa.com.

Alcoa's Environmental Record at Badin Works

The Badin Works smelter began operations in 1917. During the ensuing decades, Alcoa's operation of the Badin smelter and Alcoa Power Generating Inc.'s operation of the Yadkin hydro project have provided many benefits to local communities and the state. During the smelting years, Alcoa's manufacturing operations had waste discharges and releases that we later realized would require investigation, analysis and, in some cases, remediation. Alcoa has worked closely with state and federal officials for more than 20 years to identify, investigate, and remediate old waste sites on its property in Stanly County. The company has already spent

more than $10 million to remediate old waste sites that were identified through the Resource Conservation and Recovery Act (RCRA), a federal program implemented by the State of North Carolina to regulate the management of industrial and hazardous waste and managed under the supervision of the NC Department of Environment and Natural Resources, Division of Waste Management (DWM).

During its RCRA investigation and under DWM oversight, Alcoa hired an independent consultant to test the groundwater on its property for a variety of contaminants. The results demonstrated that there is no imminent threat to human health or the environment associated with these sites, a conclusion with which DWM agrees. Alcoa is proactively working with the State of North Carolina to evaluate potential remedial options, if needed, for groundwater to meet applicable North Carolina standards.

In accordance with the RCRA process, Alcoa is working with DWM on a Corrective Measures Study that will specify any needed additional remedial measures and ongoing monitoring the company will perform beyond what has already been completed. Alcoa submitted a work plan to DWM outlining the conduct of the study. The plan involves additional sampling that will be conducted and the analysis used to evaluate additional remediation measures for six Badin plant waste sites. DWM recently approved that plan and Alcoa is now in the process of implementing it.

Finally, Alcoa, at Stanly County's request, has investigated additional sites reported by the County to be Alcoa waste sites. Those investigations were conducted with full transparency to the State and the County. Of these, one site was identified for further Alcoa action. Testing shows that chemicals found at the site are contained, have not impacted soil, groundwater or surface water and are unlikely to pose risk to human health or the environment. There are no suspected waste sites that have not been addressed through the RCRA program or North Carolina's Inactive Sites program.

Worker Safety and Health

With respect to our employees, Alcoa has a stellar worker safety and health record in North Carolina and throughout the United States and the world. Alcoa has been honored for its outstanding safety performance by N. C. Department of Labor for 37 consecutive years.

Senate Judiciary II Committee Meeting on J 6,2010

Alcoa has noted, as it has sought to understand the intentions of the committee, that the only official action taken by the committee pertaining to Alcoa was the issuance of subpoenas to UNC-TV and one of its employees, Eszter Vajda, for an unaired, unedited video attacking our company. Recent news articles have called into question the objectivity of the video and the motivations of its producer. Others opposed to APGI's relicensing (including private interests, members of the General Assembly as well as the executive branch) appear to have been directly involved with her efforts. A panel of journalism professors at the University of North Carolina at Chapel Hill who reviewed Ms. Vajda's work concluded that "the result was a series of stories proffering an apparent point of view unsupported by the facts" and that the report "not only tarnished the reputation of a valued state resource, UNC-TV, but, more importantly, presented an unbalanced and slanted view of this important public issue."

The issuance of the subpoena came about as you and certain state officials and private interests pursue a government takeover of Alcoa Power Generating Inc.'s private property and business. The committee meeting provided a forum for the proponents of a takeover to attempt to further their cause by using a now discredited video.

Further, having reflected on the prominent role in the video played by a plaintiffs personal injury attorney and the multiple questions pertaining to workers compensation and related litigation, all of which have nothing to do with the relicensing of the Yadkin project, it appears that this video and some of the related committee questions were driven by agendas other than relicensing. We understand that the public nature of this written response means that others outside of the committee will have access to any and all information that Alcoa provides. As the UNC journalism professors' review demonstrates, to an objective eye the heavy hand of an attorney actively engaged in litigation against Alcoa greatly influenced the video production. The release of partial records by UNC-TV has shown that many others, outside the journalism process, were actively involved in its production. As such, we respectfully decline to provide any information we believe is inappropriate to provide outside of privilege or that is part of or may potentially be part of a litigation process.

Responses to Committee Questions

With respect to questions raised by the committee members and information contained in this response, for ease of understanding we have categorized the documents and information as follows:

1. Alcoa Health Studies. Several questions were directed to health studies that Alcoa has commissioned. Of particular interest to the Committee were studies that Alcoa commissioned concerning potential kidney or bladder cancer effects of Alcoa's operations, specifically at our Badin smelter facility. These studies are:

    - Proportionate Mortality Study of Alcoa Workers (1980-1987), Rockette, H. E. and Arena, V.C., March 1990.
    - Case-Control Study of Kidney Cancer and Hydrocarbon Exposure in the Aluminum Industry, Rockette, H.E, and Arena, V.C., August 1993.
    - Re-Analysis of Kidney Cancer Case-Control Study Following Data Corrections, Checkoway, H, Alexander, B.H and Cullen, M.R., May 1996.

    All three studies were communicated to the federal Environmental Protection Agency. Copies of those studies are attached to this letter.

2. Information Related to Workers' Compensation Claims in North Carolina:

Much of the information requested with respect to worker injury claims is confidential. In particular, Alcoa is not authorized to supply information about amounts of any settlements. Additionally, a significant issue in occupational disease claims is in the conflicting science, or lack of science, to address what causes illness and disease--especially where personal habits and family history may also play a causative role. In other words, the number of claims filed and any settlements, individually or in aggregate, are not an accurate indication of

worker safety or the precautions put in place by the company to protect its workers, and Alcoa does not agree that settlement of these often highly disputed claims constitutes an acceptance that the claim was compensable or that the employee developed any work-related disease at Alcoa.

3. Fish Study and Posting of Fish Consumption Advisory:

There are small amounts of PCBs in the sediment in Badin Lake adjacent to the Badin Works plant. When Alcoa initially made this discovery in 1997, we immediately notified the appropriate officials within Stanly County and DENR. The PCBs levels are already similar to post-cleanup levels typically recommended by the federal Environmental Protection Agency. Alcoa has continued to monitor these sediments and recent testing (December 2008) confirms that the contaminated sediments remain isolated and are not migrating.
In 2009, APGI filed a petition for contested case hearing concerning the Fish Consumption Advisory issued by the N.C. Department of Health and Human Services, acting through its Division of Public Health, for Badin Lake. The advisory recommended limits on the amount of largemouth bass and catfish the public should eat from the lake.

APGI respects the DPH's responsibilities and duty to protect public health and inform the public of risks. However, APGI appealed the advisory because the State changed its own stated evaluation criteria, but only after the study was completed, and held Badin Lake to a different standard than other lakes and rivers in North Carolina.

Specifically, the State had never before issued a fish advisory based on the findings in a single fish with slightly elevated levels - and from a location far from the Badin plant outfall. And, even though the State had monitored similar levels of chemicals in fish caught in other waterways in North Carolina, it had not issued a fish advisory in those instances. The failure to use consistent evaluation criteria and apply fish advisories consistently across all waterways called into question the confidence the public will place in fish advisories issued by the State.

Importantly, APGI never vrotested or appealed the posting of signs. In fact, after working with DHHS on appropriate wording for the fish consumption advisory APGI worked with the appropriate agencies to post the signs on Badin Lake.

The presence of PCBs in fish is not an isolated issue affecting Badin Lake. In fact, the N.C. Division of Water Quality website indicates that fish in many other lakes and rivers across the state — including the Yadkin River near Mocksville, upstream of Badin Lake — have been found to have similar levels of PCBs. Health officials have suggested looking for upstream sources of contamination since a majority of fish with elevated PCB levels were caught in the northwest part of the lake, upstream of the Badin Works plant. There are more than 4,500 square miles that drain into the Yadkin Project, including discharges of approximately 100 outfalls from other industries or municipalities permitted by the State of North Carolina.

4. Naturally Occurring Arsenic in Stanly County:

Beyond an onsite landfill at the Badin site, there is no arsenic contamination in Stanly County attributable to Alcoa's operations. The arsenic identified in groundwater at the facility is more likely related to natural background conditions of the soils in the area than smelter operations. That arsenic associated with groundwater at Alcoa's Badin smelter is contained to the area of an onsite landfill. There simply is no plausible

way that elevated arsenic levels in well water across Stanly County could be associated with the smelter. Moreover, studies show no impact from Alcoa's Badin operations on water in Badin Lake or the groundwater in other parts of the County.

Arsenic naturally occurs in soils and can become more prevalent in groundwater if certain soil conditions are present. In fact, during a joint meeting between APGI and Stanly County that was held on September 19,2007, Vance Jackson, a State geologist pointed out that Stanly County soil contains high levels of arsenopyrite (a form of fools gold with which arsenic is associated) which is a natural explanation for the high levels of arsenic. Mr. Jackson told representatives from Stanly County that it is "unlucky" to be located in an area with large amounts of naturally-occurring arsenic. Mr. Jackson said a geological study would show that large natural concentration and that anyone would be hard-pressed to directly attribute it to a particular source - such as the Alcoa plant. (This meeting was attended not only by County and Alcoa officials, but also by representatives of several agencies of the state government and the General Assembly.)

Alcoa also tested the water in Badin Lake and Little Mountain Creek for elevated arsenic levels. These are the only bodies of water near the Badin Works site that could be affected by the groundwater at the onsite landfill. Arsenic was not detected. In addition, Alcoa tested the groundwater at other waste sites for elevated arsenic levels. Alcoa has conducted extensive testing of ground water at the Badin smelter site. Arsenic was detected in groundwater in a localized area, near the boundaries of two Badin plant landfills. These levels appear to be the result of naturally occurring soil arsenic levels that are made soluble by relatively higher pH and reducing chemistry conditions at the landfill/soil interface and do not persist very far from the landfill boundary. In particular, our sampling data demonstrates that the groundwater is not transporting arsenic off site to rivers or the lake.

5. Groundwater Monitors at the Badin Plant:

Alcoa has placed nearly 80 groundwater monitoring wells on the Badin site and taken approximately 270 discrete samples from them in the course of preparing its RCRA Facility Investigation report that was submitted to the state and EPA. Many of those wells still exist and others are being installed in preparation for the Corrective Measures Study. That study will provide for the long term management of existing identified waste sites. Again, this interaction with DENR is a transparent process.

Because the site groundwater has been found by the State to be stable and contaminants are not moving and do not pose a risk to human health or the environment, routine monitoring is not currently necessary, according to DENR.

6. Alcoa's Business Model

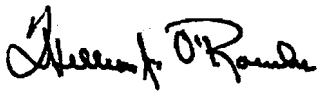
During the Committee's questions, one of the members observed that since Alcoa no longer operates the smelter at Badin, APGI it should no longer own and operate the Yadkin hydro facility and suggested that only regulated public utilities own and operate facilities that produce electricity which is sold onto the grid. Quite to the contrary, there are many private owners and operators of hydro-electric facilities and other electric generating facilities throughout the United States, including in North Carolina. These private owners generate and sell electricity at wholesale to utilities and provide an indispensible part of the nation's electric supply. The member also suggested that APGI had "recouped" its investment and would not suffer a loss if the new license

were not approved. APG1's existing project investment must continue to earn a return, whatever the past returns might have been, as is the case with any capital investment. Going forward, **APGI's** $240 million investment in the hydro-project for modernization of equipment and other upgrades will continue over ten years. That new investment creates a negative cash flow for the project during these years with a resulting need to borrow money to sustain operations. This investment also increases depreciation expense significantly, with potentially lower profitability dependant on power prices and water availability. It is investment in a business with probable long-term gains for which a long-term license is appropriate to ensure success.

Closing

We appreciated the opportunity for Alcoa to be heard before the J II Committee and to provide this supplemental information.

Sincerely,



William J. **O'Rourke**
Vice President, Sustainability, Environment, Health & Safety

Attachments

Cc: Judiciary II Committee

PROPORTIONATE MORTALITY STUDY

OF AL'COA WORKERS

(1980-1987)

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MARCH 1990

Acknowledgements - The authors wish to acknowledge Mrs. Bonnie Besseck for coding the death certificates, Mr. Rao Damaraju, Ms. Cora Wixey for coding employment histories and help in preparing the report, and Mrs. Betty Valentine for typing the manuscript. We would also like to thank Ms. Barbara Peterson for her diligence in obtaining the death certificates.

Background

This study provides an evaluation of the mortality patterns of workers in the aluminum industry that can b.e used with the information from the previously reported Tripartite Study to help assess potential health problems in the aluminum industry. The Tripartite Study was initiated in Hay 1978 and a report of study findings was made in November 1981. Progress of the study was reported quarterly throughout the duration of the contract period to a Tripartite Committee consisting of representatives of labor, management and government. The study population consisted of 21,829 men employed at least five years in a reduction operation in one of the 14 plants between January 1, 1946 and December 31, 1973 (1). Vital Status determination as of December 31, 1977 was made on 99.3% of the cohort and death certificates were obtained for 97.6% of the men believed to be deceased. The priorities which directed the analysis of the Tripartite data were as follows:

(1) Mortality patterns of workers in the potroom and/or carbon departments were given the most attention in the analysis.

(2) Respiratory cancer was to be investigated thoroughly and was the disease category given the highest priority.

(3) Lymphopoietic cancers were to be investigated and were second only to respiratory cancer as a disease category to be given special attention.

(4) For diseases other than respiratory cancer and lymphopoietic cancer, enough preliminary analysis was

done to identify any excess mortality that was associated with a particular plant or process.

(5) Causes of death associated with the aluminum reduction process in other studies were reinvestigated using the Tripartite data.

In order to satisfy these objectives, the mortality patterns of employees in the fourteen reduction plants was compared to the total U.S. male population for 59 selected causes of death. Analysis was done by plant, process, calendar time period, time since first employment and selected exposure measurements. Industrial hygiene measurements were available for total particulates, benzene solubles, benzo(a)pyrene, particulate polycyclic organic matter, sulfur dioxide and total fluorides. Based on these analyses and the previous research literature on mortality of reduction plant workers, some categories of disease were selected for more detailed investigation.

The major findings of the Tripartite Study were as follows:

(1) There were no strong associations of lung cancer mortality and work in the reduction plant. Overall the lung cancer SMR of the total cohort based on 272 observed deaths was 96.4. Formal tests of a dose-response relationship to cumulative years employment in the potroom and carbon departments, cumulative pears of employment in the reduction plant, and cumulative exposure to benzene solubles, particulate polycyclic organic matter, benzo(a)pyrene, total particulates, total fluorides and sulfur dioxide showed no statistically significant relationship.

There were two exceptions to the lack of an excess for lung cancer mortality. One plant, a horizontal Soderberg, had an SMR of 162.0 (pC0.05) for white males. However, the region in which the plant was located has a high lung cancer rate in the general population and when the data was reanalyzed using local rates, the SMR was below 100. The second excess was in the baked carbon department of one of the plants where there was an SMR of 266.8 ($p<0.05$) based on eight observed deaths. However, this excess was not observed in the baked carbon departments of the remainder of the prebake plants.

(2) The SMR for leukemia was 124.9 based on 43 observed deaths. This excess was not statistically significant. The SMR for the prebake process was 123.5 and for the Soderberg process was 130.2. The SMR for potroom workers in the Soderberg process was 169.1 and for potroom workers in the prebake process was 124.6. Analysis by duration of employment was not consistent by process with men in the prebake showing more excess with longer term employment and men in the Soderberg process showing greater excess with short term employment.

(3) The SMR for pancreatic cancer was 122.3 and was not statistically significant. However, there was a significant excess for men with more than 15 years employment in the potroom department in both the Soderberg (SMR=271.3, $p<0.05$) and prebake process (SMR=222.2, $p<0.05$).

(4) The SMR for kidney cancer in the prebakc process was 144.9. The excess was greater in men with less than 20 years employment and greater in men employed outside the carbon and potroom departments.

(5) Although the number of observed deaths was small there was an excess of bladder cancer in men employed 5 or more years in the potroom or carbon department of the Soderberg process.

(6) The only cause of death which was statistically elevated for an entire process was benign and unspecified neoplasms. For the prebake process the SMR for this cause was 193.5 ($p<0.05$) based on 14 observed deaths. The estimated risk was greater for men employed twenty-five or more years, and was higher outside the potroom and carbon departments.

(7) There was an excess of emphysema in the potroom and carbon departments of the Soderberg process (SMR=216.5, $p<0.05$; SMR=258.9, $p<0.05$). Although the excess in the prebake process was elevated, it was not statistically significant. The emphysema risk may have been understated in the prebake process because of a tendency to code many death certificates to "chronic obstructive lung disease" after 1970. If these cases were considered to be emphysema there would be a statistically significant excess in the prebake process. For men with more than 20 years employment in the prebake process there was an SMR of 260.2, ($p<0.01$) for asthma.

The present study is a PMR Study without detailed work histories and without exposure measurements available. Thus, the conclusions that can be drawn from this study are more limited than those that could be obtained from the Tripartite Study. Nevertheless, this study provides us with an independent data base on which to confirm the interpretation of some of the findings in the Tripartite Study and also provides a means of

obtaining a preliminary evaluation of mortality patterns of nonreduction plant workers. Specifically, the primary objectives of the present study are as follows:

(1) To obtain mortality data from aluminum reduction plants independent of the Tripartite cohort that can be used to further clarify the relationship of employment in aluminum reduction plants to excess mortality from cancer. Because the majority of ALCOA workers were employed in the prebake process, it is for workers in this process that we expect the most information to be obtained. The mortality patterns in the PMR study will be contrasted with those obtained from the Tripartite Study.

(2) To obtain a profile of the mortality experience of nonreduction plant workers. Little information is available on the mortality experience of nonreduction plant workers since most studies have focussed on exposure in the potroom and carbon departments. This part of the investigation is limited because of the lack of detailed coding within the nonreduction plants. However, by investigating the consistency of any excess among plants with similar processes we may identify potential associations for future investigation.

(3) On the basis of this PMR study, the Tripartite Study and a review of the literature of potential health hazards in the aluminum industry, we will make specific recommendations of studies we feel are necessary in order to determine the association of disease with exposure in the aluminum industry. Such studies will be primarily hypotheges testing as opposed to hypothesis generating.

Methods

The study population assembled by ALCOA consisted of all deaths known to the company as determined by insurance claims during the time period 1/1/80 through 12/31/87 in one of the 37 study plants. Any former employee whose beneficiary had either filed a claim or was receiving death benefits from the company was included in the study population. The initial list supplied by ALCOA was reviewed for duplicates and incomplete or inconsistent names. The resultant study population contains 6433 workers. Death certificates were obtained for all but 60 (0.9%) of the study population. These deaths were coded by a nosologist according to the ninth revision ICD and it is these 6373 death certificates on which the analyses in the present report are based. The frequencies of deaths for each cause are given in the Appendix.

Detailed work histories were not coded and analyzed for this study, since to provide such coding for such a large variety of plants and processes would have required considerable effort. For this report an employee was classified in the plant where he was last employed. Using this method of classification, 2777 workers were coded to one of the eight reduction plants. For these eight reduction plants we further coded whether they had ever worked in the potroom or carbon department as well as the department they spent the majority of time. Nine employees could not be included in this analysis because we did not have work histories. The departments in the reduction process used to classify majority of time were potroom, carbon, ingot, mechanical maintenance, electrical maintenance, and power. A total of 1320

employees in the eight reduction plants spent the majority of their time in a nonreduction process. We have done analysis separately for the 3596 employees in nonreduction plants, the 1320 employees in a nonreduction process of a reduction plant and the 1448 employees in the reduction process.

The proportionate mortality ratio was the primary summary index of risk. The analysis was done using the computer program OCMAP (2) and five year average annual age, race and sex-specific U.S. rates for the control group. As a secondary analysis we used a proportionate cancer mortality index (PCMR) (3). This index uses "all cancer mortality" as the base on which to base proportionate mortality rather than "all cause" mortality and is believed by many investigators to be less subject to the healthy worker effect.

Both the PMR and PCMR were adjusted for age, sex, race and calendar time. To meet the primary objectives of this study we completed the following analyses:

(1) The PMR and PCMRs were computed for 62 selected causes of death by race, sex, and race-sex combinations for the total cohort, for nonreduction plants, and for plants with a reduction process (reduction plants).

(2) For plants with a reduction process PMRs and PCMRs were computed for employees with a majority of their time in each of the following: a) nonreduction process, b) potroom department, c) carbon department, d) ingot department, e) mechanical maintenance, f) electrical maintenance, and g) power. Mortality indices were also

computed for employees "ever employed in the potroom department" and employees "ever employed in the carbon department".

(3) PMRs and PCMRs were computed for each plant for all 62 selected causes of death.

Because of the large number of comparisons we expect some statistically significant excesses as well as deficits. When interpreting our data we will give emphasis to the excesses, but when interpreting excesses we will take into consideration the consistency of the result with the Tripartite Study as well as the consistency with other plants that have a similar process. In most cases we have required that either the observed or expected number of deaths be 5 before we attempt to interpret results for a specific cause of death.

Population Characteristics

A total of 6373 death certificates was obtained and coded for the years 1980 to 1987 in the 37 study plants. A total of 6112 (95.9%) death certificates were for males and 5816 (91.3%) were for whites. Table 1 summarizes the distribution of deaths by year. The number of deaths were approximately equal for each of the seven years of the study. The age at death is summarized in Table 2. Fifty-one percent of the deaths occurred at ages 65-79.

The distribution of deaths for the 37 study plants is shown in Table 3. The eight plants with a reduction process contributed 44% of the total deaths and 28% of the total deaths were for employees who at one time were in a reduction process evaluated in the Tripartite Study. Of the 2777 workers in one

of the eight plants.with a reduction process, all but 9 had employment histories. Of the 2768 workers with employment histories, 1320 spent the majority of their .time in a nonreduction process. The distribution of the number of employees spending the majority of their time in a specific reduction department is given in Table 4. Of the 1448 employees with the majority of time in one of the reduction departments, 556 (36%) had the majority of their time in the potroom. The second largest group was mechanical maintenance which accounted for 433 (29.9%) of the deaths.

Table 1

Distribution of Employees
by Year of Death

Year	Frequency	Percent
1980	766	12.0
1981	772	12.1
1982	781	12.3
1983	824	12.9
1984	793	12.4
1985	759	11.9
1986	819	12.9
1987	859	13.5
TOTAL	6373	100.0

Table 2
Distribution of Employees
by Age at Death

Value Label.	Frequency	Percent
20 - 24	7	.1
25 - 29	19	.3
30 - 34	29	.5
35 - 39	41	.6
40 - 44	57	.9
45 - 49	80	1.3
50 - 54	172	2.7
55 - 59	293	4.6
60 - 64	573	9.0
65 - 69	1002	15.7
70 - 74	1261	19.8
75 - 79	1182	18.5
80 - 84	838	13.1
85 - 89	541	8.5
90 - 94	206	3.2
$\geq$95	72	1.1

Table 3

Distribution of Workers by Plant

Plant Name	Frequency	Percent,
Tennessee	1325	20.8
Vernon	210	3.3
Point Comfort	167	2.6
Massena	630	9.9
New Rensington	754	11.8
Cleveland	448	7.0
Cressona	231	3.6
Buffalo	7	.1
Vancouver	196	3.1
Warrick	116	1.8
chillicothe	54	.8
Richmond	74	1.2
Detroit	76	1.2
East St. Louis	145	2.3
Edgewater	282	4.4
Chicago	27	.4
Corona	12	.2
Bridgeport	36	.6
Edison	103	1.6
Davenport	247	3.9
Wentachee	88	1.4
Lafayette	355	5.6
Lancaster	31	.5
Marshall	11	.2
Logans Ferry	16	.3
Mobile	149	2.3
Lebanon	8	.1
Anderson	2	.0
Badin	152	2.4
Bauxite	148	2.3
Addy	8	.1
Atc	89	1.4
Fort Meade	4	.1
Franklin	23	.4
Rockdale	103	1.6
Rosiclare	36	.6
Tiffon	10	.2
Total	6373	100.0

Table 4
Department Where Reduction Plant Workers
Spent Majority of Time

Department	Frequency	Percent
Potroom	556	38.4
Carbon	140	9.7
Ingot	183	12.6
Mech Maintenance	433	29.9
Elec Maintenance	113	7.8
Power	23	1.6

Results

A. Mortality for Total Cohort

The cause-specific mortality for 62 selected causes of death is shown in Table 5. The PMR for the category "all malignant neoplasms" is 103.7 based on 1605 observed deaths. Five causes of death are significantly elevated. These are cancer of the kidney (PMR=158.1, $p<0.01$), all other malignant neoplasms (PMR=134.3, $p<0.01$), benign and unspecified neoplasm (PMR=195.6, $p<0.01$), nephritis and nephrosis (PMR=242.2, $p<0.01$) and cerebral vascular disease (PMR=111.4, $p<0.05$). Since males comprise 91% of the cohort, it is not surprising that when we restrict our analysis to the population of males (Table 6) the same causes of death show a significant excess. For females (Table 7), all other malignant neoplasms (PMR=240.2, $p<0.01$), benign neoplasms (PMR=600.5, $p<0.01$) and all other causes of death (PMR=135.1, $p<0.05$) show a statistically significant excess.

When mortality patterns for the total cohort are

Table 5
observed and Expected Deaths and Proportionate Mortality Ratios for the Total Population

Cause of Death (ICDA 9th Revision Codes)	OBS	EXP	SPMR		95% Limits LOWER	UPPER
All Cruses of Math	6373	6373.00	100.0		---	---
Tuberculosis	4	8.18	48.9		18.7	127.6
All Malignant Neoplasms	1605	1548.32	103.7		98.4	108.1
Cancer of Buccal Cavity & Pharynx	18	33.56	53.6	**	34.1	84.4
Cancer of Digestive Organs b Peritoneum	385	381.80	100.8		91.5	111.1
Cancer of Esophagus	19	38.85	51.8	**	33.2	80.0
Cancer of Stomach	59	53.88	109.5		84.8	141.2
Camr of Large Intestine	186	151.98	108.2		94.0	120.9
Cancer of Rectum	30	29.70	101.0		70.7	144.3
Cancer of Biliary Passages b Liver	30	34.79	86.2		60.4	123.2
Cancer of Pancreas	74	75.10	98.5		78.6	123.8
Cancer of All Other Digestive Organs	7	10.85	63.9		30.7	133.2
Cancer of Respiratory System	568	545.75	104.1		96.3	112.5
Cancer of Larynx	7	17.89	39.1	*	19.2	79.8
Cancer of Bronchus, Trachea, Lung	558	522.98	106.7		98.8	115.4
Cancer of All Other Respiratory	3	4.88	61.5		20.1	188.5
Canter of Breast	13	14.29	91.0		53.8	153.9
All Uterine Cancers (Females only)	4	3.23	123.8		46.9	320.0
Cancer of Cervix Uteri (Ferules only)	1	1.33	75.2		10.8	524.4
Cancer of Other Female Genital Organs	4	4.17	95.9		38.4	252.9
Cancer of Prostate (Males only)	147	167.98	87.5		74.7	102.0
Cancer of Testes and Other Male Genital Organs	3	2.48	121.8		39.4	377.1
Cancer of Kidney	53	33.52	158.1	**	121.2	206.3
Curer of Bladder and Other Urinary Organs	48	48.32	103.6		78.2	137.4
Malignant Melanoma of Skin	18	16.88	112.6		71.8	170.3
Cancer of Eye	1	0.79	127.3		18.0	899.0
Cancer of Central Nervous System	24	29.12	82.4		55.3	122.7
Cancer of Thyroid & Other Endocrine Glands	4	3.42	116.9		43.9	311.1
Cancer of Bone	3	2.50	120.0		38.8	371.3
Cancer of All Lymphatic, Haematopoietic Tissue	147	129.45	113.6		96.8	133.2
Lymphosarcoma & Reticulosarcoma	16	13.74	116.5		71.4	188.9
Hodgkins Disease	7	4.78	146.6		70.2	305.9
Leukemia & Aleukemia	55	53.91	102.0		78.4	132.7
Cancer of All Other Lymphopoietic Tissue	69	57.03	121.0		95.7	153.0
All Other Malignant Neoplasms	164	122.11	134.3	**	115.5	158.2
Benign Neoplasms	29	14.82	195.6	**	136.9	279.5
Diabetes Mellitus	82	85.41	96.4		78.7	118.1
Cerebrovascular Disease	466	418.26	111.4	*	102.1	121.8
All Heart Disease	2555	2567.57	99.5		96.6	102.5
Rheumatic Heart Disease	14	22.81	61.4		36.8	103.0
Ischemic Heart Disease	1889	2217.28	85.2	**	82.2	88.3
Chronic Endocard. Dis.; Other Myocard. Xnsuff.	134	125.14	107.1		90.6	126.8
Hypertension with Heart Disease	52	82.35	63.4		63.7	109.2
All Other Heart Disease	466	461.67	100.9		92.5	110.1
Hypertension w/o Heart Disease	23	17.23	133.5		88.9	200.5
Non-malignant Respiratory Disease	462	560.81	82.4	**	75.5	89.8
Influenza b Pneumonia	153	198.70	77.0	**	66.0	89.9
Bronchitis, Emphysema, Asthma	73	88.50	82.5		65.7	103.5
Bronchitis	10	15.53	64.4		34.8	119.0
Emphysema	54	68.12	79.3		60.8	103.3
Asthma	9	5.80	155.3		81.2	286.8
Other Non-malignant Respiratory Disease	236	287.62	82.1	**	72.5	92.9
Ulcer of Stomach & Duodenum	22	19.09	115.2		76.0	174.8
Cirrhosis of Liver	58	90.49	81.9	**	47.8	80.0
Nephritis & Nephrosis	85	35.09	242.2	**	197.3	297.4
All External Causes of Death	268	285.28	100.9		90.9	112.1
Accidents	181	178.11	106.6		93.2	122.1
Motor Vehicle Accidents	80	69.53	115.1		93.2	142.0
All Other Accidents	111	111.10	99.9		83.2	120.0
Suicides	74	72.58	102.0		81.6	127.5
Homicides b Other External Causes	23	33.62	68.4		46.2	101.3
All Other Causes of Death	688	651.81	105.3		98.1	113.0
Unknown Causes (In All Causes Category Only)	0					

* Significant at 5% Level; ** Significant at 1% Level

Table 6
observed and Expected Deaths and Proportionate Mortality Ratios for Hales

Cause of Death (ICDA 9th Revision Cobs)	OBS	EXP	SPMR		95% Limits LOWER	UPPER
All Causes Of Death	6112	6112.00	100.0		---	---
Tuberculosis	4	7.98	50.1		19.2	130.8
All Malignant Neoplasms	1533	1482.52	103.4		98.0	108.0
Cancer of Buccal Cavity A Pharynx	18	32.69	55.1	*	35.0	86.7
Cancer of Digestive Organs A Peritoneum	387	385.61	100.4		90.9	110.8
Cancer of Esophagus	19	36.20	52.5	**	33.8	81.5
Cancer of Stomach	57	52.24	109.1		84.3	141.3
Cancer of Large Intestine	158	144.54	107.9		92.4	126.0
Cancer of Rectum	28	28.48	101.8		70.8	146.4
Cancer of Biliary Passages b Liver	28	33.15	84.5		58.4	122.2
Cancor of Pancreas	71	71.57	99.2		78.7	125.0
Cancer of All Other Digestive Organs	7	10.40	67.3		32.3	140.4
Cancer of Respiratory System	557	533.38	104.4		98.5	113.0
Cancor of Larynx	7	17.68	38.6	*	19.4	80.8
Cancer of Bronchus, Trachea, Lung	547	510.97	107.1		98.9	115.9
Cancer of All Other Respiratory	3	4.73	83.4		20.8	194.5
Cancer of Breast	0	1.83	---		---	---
All Uterine Cancers (Females only)	0	0.00	---		---	---
Cancor of Cervix Uteri (Females only)	0	0.00	---		---	---
Cancer of Other Female Genital O r -	0	0.00	---		---	---
Cancor of Prostate (Males only)	147	187.98	87.5		74.7	102.8
Cancor of Tortes and Other Male Genital Organs	3	2.46	121.9		39.4	377.1
Cancer of Kidney	53	32.42	163.5	**	125.3	213.3
Cancer of Bladder and Other Urinary Organs	48	45.38	105.7		79.8	140.2
Malignant Melanoma of Skin	19	16.19	117.4		75.0	183.7
Cancer of Eye	1	0.74	134.5		19.1	948.2
Cancor of Central Nervous System	21	27.68	75.9		49.6	118.1
Cancer of Thyroid & Other Endocrine Glands	4	3.16	126.5		47.8	338.2
Cancer of Bone	3	2.38	125.9		40.7	389.2
Cancer of All Lymphatic, Haematopoietic Tissue	141	123.81	114.1		96.9	134.3
Lymphosarcoma A Reticulosarcoma	16	13.03	122.8		75.3	200.1
Hodgkins Disease	7	4.55	153.9		73.9	320.9
Leukemia A Aleukemia	53	51.71	102.5		78.4	134.0
Cancer of All Other Lymphopoietic Tissue	65	54.32	119.7		94.0	152.4
All Other Malignant Neoplasms	151	116.70	129.4	**	110.5	151.5
Benign Neoplasms	24	13.99	171.5	**	115.8	254.6
Diabetes Mellitus	85	89.58	94.9		76.9	117.2
Cerebrovascular Disease	446	394.33	113.1	**	103.4	123.7
All Heart Disease	2467	2469.77	99.9		96.9	103.0
Rheumatic Heart Disease	13	20.40	63.7		37.2	109.1
Ischemic Heart Disease	1823	2137.37	85.3	**	82.2	88.5
Chronic Endocard. Dis.; Other Myocard. Insuff.	128	119.10	107.5		90.8	127.5
Hypertension with Heart Disease	52	59.04	88.1		67.2	115.4
All Other Wart Disease	451	443.35	101.7		93.1	111.2
Hypertension w/o Heart Disease	22	16.41	134.1		88.5	203.2
Non-malignant Respiratory Disease	451	543.17	83.0	**	76.1	90.6
Influenza & Pneumonia	149	190.83	78.1	**	66.8	91.3
Bronchitis, Emphysema, Asthma	72	85.91	83.8		66.7	105.4
Bronchitis	10	15.04	66.5		36.0	122.9
Emphysema	53	66.54	79.7		61.0	104.0
Asthma	8	5.36	188.1		88.1	320.6
Other Non-malignant Respiratory Disease	230	278.78	82.2	**	72.5	93.2
Ulcer of Stomach A Duodenum	20	18.29	109.3		70.8	169.4
Cirrhosis of Liver	55	87.23	63.1	**	48.7	81.7
Nephritis a Nephrosis	82	33.71	243.2	**	197.4	209.7
All External Causes of Death	278	275.54	100.9		90.7	112.3
Accidents	184	172.47	106.7		93.0	122.4
Motor Vehicle Accidents	75	66.87	112.5		90.5	139.9
All Other Accidents	109	(07.28	101.8		84.5	122.2
Suicides	71	70.79	100.3		79.9	120.0
Homicides 6 Other External Causes	23	32.29	71.2		48.1	105.6
All Other Curses of Death	845	821.26	103.8		B8.5	111.7
Unknown Causes (In All Causes Category Only)	0					

* Significant at 5% Level; ** Significant at 1% Level

Table 7
Observed and Expected Deaths and Proportionate Mortality Ratios for Females

Cause of Death (ICDA 9th Revision Codes)	OBS	EXP	SPMR		95% Limits LOWER	UPPER
All Causes of Death	261	261.00	100.0		---	---
Tuberculosis	0	0.20	---		---	---
All Malignant Neoplasms	72	65.80	109.4		00.3	132.1
Cancer of Buccal Cavity & Pharynx	0	0.17	---		---	---
Cancer of Digestive Organs & Portt——	18	10.19	111.2		71.2	173.7
Cancer of Esophagus	0	*0.85*	---		---	---
Cancer of Stomach	2	1.14	122.2		30.8	485.3
Cancer of Large Intestine	10	7.44	134.4		73.2	248.9
Cancer of Rectum	1	1.22	81.8		11.6	575.7
Cancer of Biliary Passages A Liver	2	1.14	121.7		30.6	483.2
Camr of Pancreas	3	3.53	84.9		27.7	280.7
Cancer of All Othrr Digestive Organs	0	0.55	---		---	---
Camr of Respiratory System	11	12.36	89.0		50.3	157.2
Cancer of Larynx	0	0.22	---		---	---
Cancer of Bronchus, Trachea, Lung	11	12.00	91.6		51.8	162.1
Camr of All Othrr Respiratory	0	0.14	---		---	---
Cancer of Breast	13	12.86	102.7		60.9	173.3
All Uterine Cancers (Females only)	4	3.23	123.8		48.9	326.6
Cancer of Cervix Uteri (Females only)	1	1.33	75.2		10.8	524.4
Cancer of Other Female Genital Organs	4	4.17	95.9		36.4	252.9
Cancer of Prostate (Males only)	0	0.00	---		---	---
Cancer of Testes and Other Male Genital Organs	0	0.00	---		---	---
Cancer of Kidney	0	1.10	---		---	---
Cancer of Bladder and Other Urinary Organs	0	0.93	---		---	---
Malignant Melanoma of Skin	0	0.89	---		---	---
Cancer of Eye	0	0.04	---		---	---
Camr of Central Nervous System	3	1.48	205.4		68.2	618.7
Cancer of Thyroid A Other Endocrine Glands	0	0.26	---		---	---
Cancer of Bone	0	0.12	---		---	---
Cancer of All Lymphatic, Haematopoietic Tissue	6	5.84	102.8		46.6	226.4
Lymphosarcoma & Reticulosarcoma	0	0.70	---		---	---
Hodgkins Disease	0	0.23	---		---	---
Leukemia & Aleukemia	2	2.20	90.8		22.9	360.8
Cancer of All Other Lymphopoietic Tissue	4	2.70	147.9		58.2	389.4
All Othr Malignant Neoplasms	13	5.41	240.2	**	142.7	404.2
Benign Neoplasms	5	0.83	600.5	**	278.8	1294.5
Diabetes Mellitus	7	5.86	119.5		57.5	248.3
Cerebrovascular Disease	20	23.93	83.8		55.2	128.4
All Heart Disease	88	97.80	90.0		78.8	105.8
Rheumatic Heart Disease	1	2.41	41.5		6.3	274.4
Ischemic Heart Disease	66	79.90	82.6		67.8	100.6
Chronic Endocard. Dis.; Other Myocard. Insuff.	6	6.04	99.4		45.2	218.8
Hypertension with Mart Disease	0	3.32	---		---	---
All Other Heart Disease	15	18.32	81.9		50.4	133.1
Hypertension w/o Mart Disease	1	0.82	121.8		17.3	858.8
Non-malignant Respiratory Disease	11	17.74	62.0		35.3	109.0
Influenza & Pneumonia	4	7.87	50.8		19.8	130.4
Bronchitis, Emphysema, Asthma	1	2.59	38.7		5.9	252.8
Bronchitis	0	0.49	---		---	---
Emphysema	1	1.58	63.4		9.2	439.2
Asthma	0	0.44	---		---	---
Other Non-malignant Respiratory Disease	6	7.84	76.6		34.9	187.8
Ulcer of Stomach & Duodenum	2	0.80	250.3		85.8	952.6
Cirrhosis of Liver	1	3.27	30.6		4.9	190.4
Nephritis & Nephrosis	3	1.38	217.8		72.5	654.7
All External Causes of Death	10	9.75	102.6		58.2	180.7
Accidents	7	6.64	105.3		52.0	213.4
Motor Vehicle Accidents	5	2.87	174.4		76.9	395.7
All Othr Accidents	2	3.83	52.3		13.8	201.1
Suicides	3	1.77	168.8		58.5	508.7
Homicides A Other External Causes	0	1.34	---		---	---
All Other Causes of Death	41	30.34	135.1	*	101.5	178.8
Unknown Causes (In All Causes Category Only)	0					

* Significant at 5% Level; ** Significant at 1% Level

Table 8
Observed and Expected Deaths and Proportionate Mortality Ratios for Whites

Cause of Death (ICDA 9th Revision Codes)	OBS	EXP	SPMR		95% Limits LOWER	UPPER
All Causes of Death	5816	5816.00	100.0		---	---
Tuberculosis	3	6.96	50.3		16.6	152.5
All Malignant Neoplasms	1438	1407.46	102.2		97.7	108.8
Cancer of Buccal Cavity & Pharynx	13	29.89	43.5	**	25.7	73.6
Cancer of Digestive Organs & Peritoneum	340	344.43	98.7		89.1	109.4
Cancer of Esophagus	17	30.51	55.7	*	34.9	88.9
Cancer of Stomach	48	48.47	99.0		74.2	132.0
Cancer of Large Intestine	153	140.84	108.6		92.9	127.0
Cancer of Rectum	28	27.60	105.1		73.1	151.1
Cancer of Biliary Passages & Liver	22	30.89	71.2		47.0	107.8
Cancer of Pancreas	86	88.29	96.7		76.0	122.8
Cancer of All Other Digestive Organs	7	10.17	68.9		33.0	143.7
Cancer of Respiratory System	520	499.48	104.1		96.0	112.9
Cancer of Larynx	7	15.91	44.0	*	21.4	90.3
Cancer of Bronchus, Trachea, Lung	510	479.07	106.5		98.0	115.8
Cancer of All Other Respiratory	3	4.49	66.8		21.7	205.3
Cancer of Breast	13	13.67	95.1		56.2	180.8
All Uterine Cancers (Females only)	3	3.04	98.8		32.2	303.6
Cancer of Cervix Uteri (Females only)	0	1.19	---		---	---
Cancer of Other Female Genital Organs	4	4.09	97.8		37.1	257.7
Cancer of Prostate (Males only)	123	143.49	85.7		72.0	102.0
Cancer of Testes and Other Male Genital Organs	3	2.23	134.8		43.7	418.0
Cancer of Kidney	48	31.56	152.1	**	115.0	201.3
Cancer of Bladder and Other Urinary Organs	44	43.56	101.0		75.3	135.8
Malignant Melanoma of Skin	18	16.65	108.1		68.2	171.4
Cancer of Eye	1	0.77	129.9		18.4	917.0
Cancer of Central Nervous System	22	28.05	78.4		51.8	118.8
Cancer of Thyroid & Other Endocrine Glands	4	3.22	124.2		46.7	330.2
Cancer of Bone	3	2.31	130.0		42.1	401.8
Cancer of All Lymphatic, Haematopoietic Tissue	132	120.58	109.5		92.5	129.6
Lymphosarcoma & Reticulosarcoma	13	13.13	99.0		57.5	170.4
ins Disease	7	4.51	155.1		74.4	323.3
emia & Aleukemia	50	50.88	98.7		74.9	130.0
Cancer of All Other Lymphopoietic Tissue	62	52.28	118.6		92.6	152.0
All Other Malignant Neoplasms	147	110.55	133.0	**	113.4	156.0
Benign Neoplasms	28	13.80	181.2	**	131.1	278.8
Diabetes Mellitus	73	84.63	86.3		68.7	108.3
Cerebrovascular Disease	422	373.12	113.1	**	103.2	124.0
All Wart Disease	2371	2371.79	100.0		96.9	103.1
Rheumatic Heart Disease	14	21.75	64.4		38.3	108.1
Ischemic Wart Disease	1777	2082.36	85.3	**	82.2	88.8
Chronic Endocard. Dis.; Other Myocard. Insuff.	128	113.89	112.4		94.7	133.4
Hypertension with Heart Disease	36	49.63	72.5		52.5	100.3
All Other Heart Disease	416	405.99	102.5		93.4	112.4
Hypertension w/o Heart Disease	20	14.42	138.7		89.7	214.4
Non-malignant Respiratory Disease	430	521.14	82.5	**	75.4	90.3
Influenza & Pneumonia	143	180.38	79.3	**	67.6	93.0
Bronchitis, Emphysema, Asthma	68	83.92	81.0		64.0	102.5
Bronchitis	10	14.87	67.2		36.3	124.3
Emphysema	50	65.12	76.8		58.3	101.1
Asthma	8	5.02	159.4		80.2	316.8
Other Non-malignant Respiratory Disease	219	269.47	81.3	**	71.4	92.4
Ulcer of Stomach & Duodenum	21	17.56	119.6		78.0	183.1
Cirrhosis of Liver	50	83.04	60.2	**	45.9	78.9
Nephritis & Nephrosis	75	29.89	251.0	**	201.8	312.1
All External Causes of Death	281	255.72	102.1		91.4	114.0
Accidents	174	160.98	108.1		93.8	124.5
Motor Vehicle Accidents	70	63.51	110.2		88.0	138.0
All Other Accidents	104	98.79	105.3		87.2	127.2
Suicides	70	70.11	99.8		79.4	125.6
Homicides & Other External Causes	17	24.85	89.0		43.4	109.5
All Other Causes of Death	828	583.52	107.3		99.6	115.5
Unknown Causes (In All Causes Category Only)	0					

* Significant at 5% Level; ** Significant at 1% Level

Table 9
Observed and Expected Deaths and Proportionate Mortality Ratios for Nonwhites

Cause of Death (ICDA 9th Revision Codes)	OBS	EXP	SPMR		95% Limits LOWER	UPPER
All Causes of Death	557	557.00	100.0		---	---
Tuberculosis	1	2.22	45.1		6.7	302.8
All Malignant Neoplasms	167	140.88	118.5	*	104.1	135.0
Cancer of Buccal Cavity & Pharynx	5	3.66	136.6		57.3	325.8
Cancer of Digestive Organs & Peritoneum	45	37.37	120.4		90.9	150.5
Cancer of Esophagus	2	6.34	31.6		8.8	116.0
Cancer of Stomach	13	7.41	175.5	*	103.0	299.1
Cancer of Large Intestine	13	11.15	116.6		68.1	199.6
Cancer of Rectum	1	2.11	47.5		7.0	321.2
Cancer of Biliary Passages & Liver	8	3.90	205.1	*	104.4	403.1
Cancer of Pancreas	5	8.81	117.4		59.0	233.6
Cancer of All Other Digestive Organs	0	0.78	---		---	---
Cancer of Respiratory System	48	46.27	103.7		78.3	135.7
Cancer of Larynx	0	1.98	---		---	---
Cancer of Bronchus, Trachea, Lung	48	43.90	109.3		83.5	143.1
Cancer of All Other Respiratory	0	0.38	---		---	---
Cancer of Breast	0	0.82	---		---	---
All Uterine Cancers (Females only)	1	0.19	513.2		90.6	2908.6
Cancer of Cervix Uteri (Females only)	1	0.14	697.7	*	132.1	3685.6
Cancer of Other Female Genital Organs	0	0.08	---		---	---
Cancer of Prostate (Males only)	24	24.48	98.0		68.4	144.7
Cancer of Testes and Other Male Genital Organs	0	0.24	---		---	---
Cancer of Kidney	5	1.96	254.5	*	109.5	591.9
Cancer of Bladder and Other Urinary Organs	4	2.78	145.0		54.9	383.2
Malignant Melanoma of Skin	1	0.23	435.8		72.5	2818.7
Cancer of Eye	0	0.02	---		---	---
Cancer of Central Nervous System	2	1.07	187.0		47.9	729.9
Cancer of Thyroid & Other Endocrine Glands	0	0.20	---		---	---
Cancer of Bone	0	0.19	---		---	---
Cancer of All Lymphatic, Haematopoietic Tissue	15	8.87	169.2	*	103.0	277.9
Lymphosarcoma & Reticulosarcoma	3	0.61	495.0	**	178.7	1371.1
Hodgkins Disease	0	0.26	---		---	---
Leukemia & Aleukemia	5	3.23	154.9		85.1	368.6
Cancer of All Other Lymphopoietic Tissue	7	4.77	146.8		70.5	305.5
All Other Malignant Neoplasms	17	11.58	147.1		92.2	234.7
Benign Neoplasms	3	1.22	245.3		82.2	732.1
Diabetes Mellitus	19	10.78	176.1	*	113.5	273.2
Cerebrovascular Disease	44	45.14	97.5		73.5	129.3
All Heart Disease	184	195.77	94.0		83.7	105.5
Rheumatic Heart Disease	0	1.07	---		---	---
Ischemic Heart Disease	112	134.92	83.0	*	70.7	97.4
Chronic Endocard. Dis.; Other Myocard. Insuff.	6	11.25	53.3		24.5	118.1
Hypertension with Heart Disease	16	12.72	125.8		77.6	203.9
All Other Heart Disease	50	55.88	89.8		69.1	116.8
Hypertension w/o Heart Disease	3	2.80	107.0		34.6	330.7
Non-malignant Respiratory Disease	32	39.77	80.5		57.7	112.2
Influenza & Pneumonia	10	18.32	54.6	*	30.0	99.3
Bronchitis, Emphysema, Asthma	5	4.57	109.3		45.7	281.5
Bronchitis	0	0.68	---		---	---
Emphysema	4	3.00	133.4		50.4	353.2
Asthma	1	0.78	128.8		18.3	908.1
Other Non-malignant Respiratory Disease	17	18.15	93.6		58.7	149.4
Ulcer of Stomach & Duodenum	1	1.52	65.8		9.4	457.6
Cirrhosis of Liver	6	7.45	80.5		36.8	176.8
Nephritis & Nephrosis	10	5.21	192.1	*	104.8	352.0
All External Causes of Death	27	29.57	91.3		64.8	128.7
Accidents	17	18.15	93.7		59.1	148.5
Motor Vehicle Accidents	10	6.02	166.0		90.8	303.3
All Other Accidents	7	12.31	56.9		27.7	116.8
Suicides	4	2.45	163.6		62.6	427.7
Homicides & Other External Causes	6	8.98	66.8		31.8	140.7
All Other Causes of Death	80	88.09	88.1		69.8	111.6
Unknown Causes (In All Causes Category Only)	0					

* Significant at 5% Level; ** Significant at 1% Level

investigated by race, the white population shows a similar mortality pattern to that observed for the total cohort (Table 8). For nonwhites, causes of death (Table 9) for which there were five observed or expected deaths and where there was a statistically significant excess were all malignant neoplasms (PMR=118.6, $p<0.05$), cancer of the stomach (PMR=175.5, $p<0.05$), cancer of the liver (PMR=205.1, $p<0.05$), cancer of the kidney (PMR=254.5, $p<0.05$), cancer of the lymphatic and haematopoietic tissue (PMR=169.2, $p<0.05$); diabetes mellitus (PMR=176.1, $p<0.05$), and nephritis and nephrosis (PMR=192.1, $p<0.05$).

B. Nonreduction Process

A total of 3596 employees worked in a plant that had no reduction process (Table 10). The overall PMR for these employees was 105.2. The only excess within the category of neoplasms was for "all other malignant neoplasms" where the PMR was 145.9 ($p<0.01$). Other causes of death showing a statistically significant excess were benign and unspecified neoplasms with a PMR of 227.3 ($p<0.01$), "all other heart disease" with a PMR of 117.2 ($p<0.01$), and "nephritis and nephrosis" with a PMR of 293.8 ($p<0.01$). Investigation separately for males and females indicated no causes of death other than those identified in excess for the total cohort. When we evaluated mortality patterns separately for race, in addition to the four causes of death in excess for the total group of nonreduction plant workers we found for whites a PMR of 122.8 ($p<0.05$) for cancer of the large intestine and a PMR of 135.4 ($p<0.01$) for chronic endocarditis and other myocardial insufficiency. For nonwhites, we found that

the excess of stomach cancer, liver cancer, lymphatic cancer and nephritis reported in the nonwhite population comprising the total cohort occurred in these nonreduction plants. The PMR for all malignancies for nonwhites in the nonreduction plants was 128.0 ($p<0.01$).

Of the 2777 workers in the 8 plants with a reduction process, 1320 spent the majority of their time in a nonreduction process. For this group of workers the PMR for all malignant neoplasms was 93.6. There were statistically significant excesses of cancer of the lymphatic and haematopoietic tissue (PMR=140.1, $p<0.05$), cerebrovascular disease (PMR=126.9, $p<0.05$), hypertension without heart disease (PMR=230.2, $p<0.05$) and nephritis and nephrosis (PMR=196.8, $p<0.01$). We also note the excess for asthma (PMR=331.0, $p<0.05$) based on only four observed deaths. There were only 56 females in this group of workers so the mortality pattern of the total group is essentially the *same* as that observed for males. For whites, the excesses were the same as that observed for the total group of 1320 workers. For nonwhites, excesses occurred in hypertension with heart disease (PMR=239.2, $p<0.05$) and "all other causes of death" (PMR=202.9, $p<0.01$).

Table 10
Observed and Expected Deaths and Proportionate Mortality Ratios for Nonreduction Plant Employees

Cause of Death (ICDA 9th Revision Codes)	OBS	EXP	SPMR		95% Limits LOWER	UPPER
All Causes of Death	3596	3596.00	100.0		---	---
Tuberculosis	3	4.62	65.0		21.2	199.5
All Malignant Neoplasms	906	861.09	105.2		99.5	111.3
Cancer of Buccal Cavity & Pharynx	11	18.19	60.5		33.8	108.3
Cancer of Digestive Organs & Peritoneum	225	213.51	105.4		92.9	119.6
Cancer of Esophagus	11	20.10	54.7	*	30.7	97.7
Cancer of Stomach	36	30.13	119.5		86.4	165.4
Cancer of Large Intestine	103	85.59	120.3		99.5	145.6
Cancer of Rectum	20	16.64	120.2		77.7	186.0
Cancer of Biliary Passages & Liver	17	19.49	87.2		54.3	140.0
Cancer of Pancreas	35	41.81	83.7		60.3	116.3
Cancer of All Other Digestive Organs	3	6.17	48.6		16.1	147.0
Cancer of Respiratory Syatem	316	297.08	106.4		95.8	118.1
Cancer of Larynx	4	9.69	41.3		16.0	106.4
Cancer of Bronchus, Trachea, Lung	310	284.73	108.9		97.9	121.0
Cancer of All Other Respiratory	2	2.65	75.4		18.9	299.8
Cancer of Breast	9	10.45	86.1		45.8	161.8
All Uterine Cancers (Females only)	3	2.45	122.7		40.0	376.1
Cancer of Cervix Uteri (Females only)	0	0.98	---		---	---
Cancer of Other Female Genital Organs	2	3.16	63.3		16.3	246.3
Cancer of Prostate (Males only)	84	96.35	87.2		70.7	107.6
Cancer of Testes and Other Male Genital Organs	1	1.29	77.4		11.0	546.2
Cancer of Kidney	25	18.32	136.5		92.5	201.4
Cancer of Bladder and Other Urinary Organa	28	26.32	106.4		73.6	153.9
Malignant Melanoma of Skin	11	8.95	123.0		68.2	221.5
Cancer of Eye	1	0.44	229.1		34.1	1539.1
Cancer of Central Nervous System	14	15.51	90.3		53.6	152.1
Cancer of Thyroid & Other Endocrine Glands	4	1.89	211.7		81.3	551.4
Cancer of Bone	1	1.36	73.5		10.4	517.5
Cancer of All Lymphatic, Haematopoietic Tissue	72	71.84	100.2		79.7	126.0
Lymphosarcoma & Reticulosarcoma	6	7.54	79.6		35.9	176.7
Hodgkins Disease	2	2.51	79.8		20.0	317.7
Leukemia & Aleukemia	27	30.06	89.8		61.7	130.8
Cancer of All Other Lymphopoietic Tissue	37	31.74	116.6		84.6	160.6
All Other Malignant Neoplasms	99	67.83	145.9	**	120.2	177.2
Benign Neoplasm.	19	8.36	227.3	**	146.9	351.8
Diabetes Mellitus	55	54.16	101.6		78.1	132.0
Cerebrovascular Diaease	237	245.53	96.5		85.4	109.1
All Heart Disease	1477	1457.21	101.4		97.5	105.4
Rheumatic Heart Diaease	8	12.85	62.2		31.4	123.5
Ischemic Heart Disease	1038	1254.88	82.7	**	78.8	86.8
Chronic Endocard. Dis.; Other Myocard. Insuff.	95	73.19	129.8	*	106.5	158.2
Hypertension with Heart Disease	28	35.66	78.5		54.4	113.4
All Other Heart Disease	308	262.71	117.2	**	105.3	130.5
Hypertension w/o Heart Diaease	11	10.03	109.7		60.8	197.8
Non-malignant Respiratory Diaease	258	322.34	80.0	**	71.3	89.9
Influenza & Pneumonia	85	117.33	72.4	**	58.9	89.1
Bronchitis, Emphysema, Asthma	40	49.83	80.3		59.1	109.1
Bronchitis	4	8.85	45.2		17.4	117.2
Emphysema	34	38.27	88.8		63.6	124.1
Asthma	2	3.25	61.5		15.6	242.6
Other Non-malignant Respiratory Disease	133	163.39	81.4	*	69.0	96.0
Ulcer of Stomach C Duodenum	13	10.91	119.1		69.3	204.8
Cirrhosis of Liver	30	47.45	63.2	*	44.5	89.8
Nephritis & Nephrosis	60	20.42	293.8	**	231.0	373.6
All External Causes of Death	140	147.02	95.2		81.7	111.0
Accidents	99	93.90	105.4		87.3	127.4
Motor Vehicle Accidenta	43	34.82	123.5		92.6	164.8
All Mhar Accidents	56	59.93	93.4		72.2	120.9
Suicides	27	36.77	73.4		50.8	106.2
Homicides & Other External Causes	14	16.36	85.6		51.5	142.3
All Other Causes of Death	387	371.99	104.0		94.7	114.3
Unknown Causes (In All Causes Category Only)	0					

* Significant at 5% Level; ** Significant at 1% Level

Table 11
Observed and Expected Deaths and Proportionate Mortality Ratios for Employees in Reduction Plants Spending the Majority of Their Time in a Nonreduction Process

Cause of Death (ICDA 9th Revision Codes)	OBS	EXP	SPUR	95% Limitr LOWER	VPPCR
All Causes of Death	1320	1320.00	loo.0	---	---
Tuberculosis	0	1.63	---	---	---
All Malignant Neoplasms	302	322.52	93.6	85.0	103.2
Cancrr of Buccal Cavity & Pharynx	2	6.98	28.7	7.8	104.7
Cancer of Digestive Organs & Peritonrum	78	79.22	98.5	79.4	122.1
Cancer of Erophagum	1	7.56	13.2 *	2.5	69.3
Cancer of Stomach	15	11.09	135.2	81.9	223.4
Cancrr of Large Intestine	30	31.64	94.8	66.6	135.0
Cancer of Rectum	6	6.20	96.8	43.6	215.1
Cancer of Biliary Passages & Liver	6	7.20	83.4	37.6	185.0
Cancer of Pancreas	18	15.64	115.1	72.8	182.1
Cancer of All Other Digestive Organs	2	2.28	87.8	22.0	350.4
Cancer of Respiratory System	91	114.28	79.6 *	65.6	96.7
Cancer of Larynx	2	3.73	53.6	13.7	209.3
Cancer of Bronchum, Trachea. Lung	89	109.53	81.3 *	66.7	98.9
Cancer of All Other Respiratory	0	1.02	---	---	---
Cancer of Breast	4	3.10	128.9	50.2	331.4
All Uterine Cancers (Females only)	1	0.71	140.9	20.4	974.6
Cancer of Cervix Uteri (Females only)	1	0.32	314.6	49.7	1991.8
Cancer of Other Female Genital Organs	1	0.90	110.7	15.9	768.0
Cancer of Prostate (Males only)	32	34.15	93.7	66.6	131.8
Cancer of Testes and Other Hale Genital Organs	1	0.51	194.7	28.5	1332.3
Cancer of Kidney	11	7.05	156.1	87.0	280.0
Cancer of Bladder and Other Urinary Organs	10	9.61	104.1	56.2	193.0
Malignant Melanoma of Skin	3	3.59	83.5	27.0	257.8
Cancer of Eyr	0	0.17	---	---	---
Cancer of Central Nervoum System	3	6.21	48.3	16.0	145.6
Cancer of Thyroid & Other Endocrine Glands	0	0.72	---	---	---
Cancer of Bona	2	0.53	375.9 *	103.5	1364.5
Cancer of All Lymphatic, Haematopoietic Tissue	38	27.12	140.1 *	102.5	191.6
Lymphosarcoma & Reticulosarcoma	6	2.91	206.3	94.4	450.9
Hodgkins Disease	3	1.03	291.2	99.0	856.3
Leukemia & Aleukemia	13	11.31	115.0	66.9	197.4
Cancer of All Other Lymphopoietic Tissue	16	11.87	134.8	82.9	219.1
All Other Malignant Neoplasms	25	25.39	98.5	66.8	145.1
Benign Neoplasms	5	3.08	162.2	68.1	386.0
Diabetes Mellitus	15	19.66	76.3	46.2	125.9
Cerebrovamcular Disease	108	85.13	126.9 *	105.9	152.0
All Heart Disease	531	530.71	100.1	93.7	106.8
Rheumatic Heart Disease	4	4.81	83.1	31.3	220.7
Ischemic Heart Disease	422	460.01	91.7 *	85.0	99.0
Chronic Endocard. Dim.; Other Myocard. Insuff.	18	25.51	70.6	44.8	111.2
Hypertension with Heart Disease	11	12.55	87.6	48.7	157.6
All Other Heart Disease	76	94.56	80.4 *	64.8	99.7
Hypertension w/o Heart Disease	8	3.48	230.2 *	117.5	450.8
Non-malignant Respiratory Disease	103	115.44	89.2	74.3	107.2
Influenza & Pneumonia	39	40.23	96.9	71.3	131.8
Bronchitim, Emphysema, Asthma	17	18.47	92.1	57.4	147.5
Bronchitis	4	3.23	123.8	46.6	328.9
Emphysema	9	14.23	63.3	33.2	120.4
Asthma	4	1.21	331.0 *	131.4	833.2
Other Non-malignant Respiratory Disease	47	59.55	78.9	59.8	104.2
Ulcer of Stomach & Duodenum	3	3.93	76.3	24.7	235.3
Cirrhomir of Liver	15	19.05	78.7	47.8	129.6
Nephritis & Nephrosis	14	7.11	196.8 **	117.9	328.6
All Extrrnal Causes of Death	66	61.82	106.8	86.0	132.6
Accidents	44	38.34	114.8	86.8	151.8
Motor Vehicle Accident.	19	15.37	123.7	80.5	190.0
All Other Accidents	25	23.28	107.4	73.1	157.8
Suicides	21	15.70	133.8	88.1	203.0
Homicides & Other External Cause.	1	7.79	12.8 *	2.7	61.7
All Other Causes of Death	150	133.99	111.9	96.2	130.2
Unknown Causes (In All Causes Category Only)	0				

* Significant at 5% Level; ** Significant at 1% Level

C. Mortality for the Reduction Process

There were 1866 workers who had some employment in the reduction process. The overall PMR for cancer was 106.6 which was not statistically significant (Table 12). The PMR for lung cancer was 117.8 with a corresponding 95% confidence interval of (103.1, 134.5). Cancer of the kidney was also elevated with a PMR of 200.1 and a corresponding 95% confidence interval of (131.7, 303.8). The only nonmalignant cause of death with a statistically significant excess was cerebral vascular disease with a PMR of 135.3 and a corresponding 95% confidence interval of (116.0, 157.7). The PMR for the category ischemic heart disease was low [PMR=87.2 with corresponding confidence interval of (81.6, 93.2)]. Since only 6 women were employed in the reduction process, the mortality patterns in Table 12 are essentially the same for males. When analysis was done by race, some additional causes were in excess. For whites, in addition to respiratory and kidney cancer, there was an excess in cancer of the lymphatic and haematopoietic tissue (PMR=132.2, $p<0.05$). For nonwhites, the only excess was for diabetes where the PMR was 389.5 ($p<0.01$).

When the 62 causes of death were re-evaluated for men spending the majority of their time in the reduction process, the mortality patterns were similar to those "ever employed in the reduction process" but tended to be slightly increased for many of the malignancies (Table 13). The PMR for the category all malignant neoplasms increased from 106.6 to 109.5 ($p<0.05$). Similarly, the PMRs for cancer of the lung and kidney were

Table 12

Observed and Expected Deaths and Proportionate Mortality Ratios for Employees Ever Employed in a Reduction Process

Cause of Death (ICDA 9th Revision Codes)	OBS	EXP	SPMR		95% Limits LOWER	UPPER
All Causes Of Death	1866	1866.00	100.0		---	---
Tuberculosis	1	2.48	40.3		6.1	287.2
All Malignant Neoplasms	498	488.17	106.8		98.8	114.9
Cancer of Buccal Cavity & Pharynx	6	10.80	55.6		25.3	121.9
Cancer of Digestive Organs & Peritoneum	105	114.28	91.9		76.4	110.8
Cancer of Esophagus	7	11.86	59.0		28.5	122.4
Camr of Stomach	13	18.25	80.0		46.6	137.3
Cancer of Large Intestine	39	44.50	87.6		64.3	119.5
Cancer of Rectum	5	8.81	56.8		24.0	134.5
Cancer of Billary Passages & Liver	9	10.39	86.7		45.2	166.1
Cancer of Pancreas	29	22.88	127.9		89.2	183.4
Cancer of All Other Digestive Organs	3	3.21	93.5		30.2	289.5
Cancer of Respiratory System	197	172.88	114.0		99.9	130.0
Cancer of Larynx	1	5.76	17.4	*	3.1	97.8
Cancer of Bronchus, Trachea, Lung	195	165.57	117.8	*	103.1	134.5
Cancer of All Dther Respiratory	1	1.54	64.8		9.3	452.4
Cancer of Breast	0	1.00	---		---	---
All Uterine Cancers (Females only)	0	0.11	---		---	---
Cancer of Cervix Uteri (Females only)	0	0.05	---		---	---
Cancer of Other Female Genital Organs	1	0.18	543.6	*	120.0	3450.7
Cancer of Prostate (Males only)	39	47.68	81.8		60.1	111.3
Camr of Testes and Other Male Genital Organs	2	0.83	240.0		82.7	918.1
Cancer of Ktdney	21	10.50	200.1	**	131.7	303.8
Cancer of Bladder and Other Urinary Organs	14	13.26	105.8		62.7	177.9
Malignant Melanoma of Skin	7	5.59	125.2		58.9	261.7
Camr of Eye	0	0.24	---		---	---
Cancer of Central Nervous System	8	9.56	83.7		42.0	166.7
Camr of Thyroid & Other Endocrine Glands	0	1.04	---		---	---
Cancer of Bone	2	0.78	256.7		67.5	876.1
Cancer of All Lymphatic, Haematopoietic Tissue	50	39.07	128.0		97.4	188.2
Lymphosarcoma & Reticulosarcoma	5	4.22	118.5		49.4	284.0
Hodgkins Disease	3	1.59	188.9		62.2	574.3
Leukemia & Aleukemia	20	16.05	124.6		80.6	192.6
Cancer of All Other Lymphopoietic Tissue	22	17.21	127.8		84.4	193.6
All Other Malignrunt Neoplasms	47	37.12	126.6		95.5	167.9
Benign Neoplasms	5	4.33	115.5		48.1	278.9
Diabetes Mellitus	28	27.85	101.3		70.1	146.3
Cerebrovascular Disease	151	111.84	135.3	**	116.0	157.7
All Heart Disease	710	742.22	95.7		90.4	101.2
Rheumatic Heart Disease	3	6.62	45.3		15.1	136.2
Ischemic Heart Disease	561	643.10	87.2	**	81.6	93.2
Chronic Endocard. Dis.; Other Myocard. Insuff.	25	33.78	74.1		50.3	109.0
Hypertension with Heart Disease	17	18.13	93.8		58.5	150.4
All Other Heart Disease	104	133.89	77.7	**	64.6	93.4
Hypertension w/o Heart Disease	8	4.78	126.1		58.8	278.8
Non-malignant Respiratory Disease	126	156.88	80.3	**	68.0	94.8
Influenza & Pneumonia	42	52.52	80.0		59.5	107.5
Bronchitis, Emphysema, Asthma	22	25.71	85.6		56.5	129.5
Bronchitis	3	4.39	68.4		22.2	210.2
Emphysema	18	19.86	80.8		49.5	131.0
Asthma	3	1.72	174.7		57.2	533.7
Other Non-malignant Respiratory Disease	62	82.30	75.3	*	58.1	96.0
Ulcer of Stomach & Duodenum	7	5.42	129.2		61.8	270.1
Cirrhosis of Liver	15	31.08	48.3	**	29.8	78.7
Nephritis & Nephrosis	15	9.66	155.3		94.1	256.1
All External Causes of Death	105	98.28	106.8		90.0	126.8
Accidents	67	59.94	111.8		89.1	140.1
Motor Vehicle Accidents	25	24.84	101.4		69.8	147.8
All Other Accidents	42	35.77	117.4		87.3	157.9
Suicides	30	25.77	116.4		82.1	165.0
Homicides & Other External Causes	8	12.57	63.6		32.8	123.5
All Other Causes of Death	188	188.30	100.3		93.1	121.3
Unknown Causes (In All Causes Category Only)	0					

* Significant at 5% Level; ** Significant at 1% Level

Table 13
Observed and Expected Deaths and Proportionate Mortality Ratios for Employees Spending a Majority of Time in a Reduction Process

Cause of Death (ICDA 9th Revision Codes)	OBS	EXP	SPMR		95% Limits LOWER	UPPER
All Causes of both	1449	1449.00	100.0		---	---
Tuberculosis	1	1.93	51.9		7.6	355.1
All Malignant Neoplasms	397	382.63	109.5	*	100.6	119.1
Cancer of Buccal Cavity & Pharynx	5	8.34	60.0		25.3	142.2
Cancer of Digestive Organs & Peritoneum	82	88.56	92.6		78.1	114.2
Cancer of Esophagus	7	9.15	76.5		36.7	159.6
Cancer of Stomach	8	12.59	63.5		32.1	125.9
Cancer of Large Intestine	33	34.55	95.5		68.2	133.8
Cancer of Rectum	4	6.83	58.6		22.3	153.6
Cancer of Biliary Passages & Liver	7	8.06	86.9		41.5	181.8
Cancer of Pancreas	21	17.65	119.8		78.3	182.9
Cancer of All Other Digestive Organs	2	2.49	80.3		20.2	320.0
Cancer of Respiratory System	181	133.59	120.5	*	104.2	139.4
Cancer of Larynx	1	4.45	22.5		3.8	134.2
Cancer of Bronchus, Trachea, Lung	159	127.95	124.3	**	107.3	144.0
Cancer of All Other Respiratory	1	1.20	83.7		11.8	591.9
Cancer of Breast	0	0.73	---		---	---
All Uterine Cancers (Females only)	0	0.08	---		---	---
Cancer of Cervix Uteri (Females only)	0	0.04	---		---	---
Cancer of Other Female Genital Organs	1	0.11	948.9	**	195.9	4587.1
Cancer of Prostate (Males only)	31	37.27	83.2		58.9	117.5
Cancer of Testes and Other Male Genital Organs	1	0.65	153.1		21.9	1069.9
Cancer of Kidney	17	8.11	209.7	**	132.0	333.3
Cancer of Bladder and Other Urinary Organs	10	10.34	96.7		52.2	178.3
Malignant Melanoma of Skin	5	4.31	115.9		48.4	277.7
Cancer of Eye	0	0.18	---		---	---
Cancer of Central Nervous System	7	7.36	95.1		45.5	199.0
Cancer of Thyroid & Other Endocrine Glands	0	0.81	---		---	---
Cancer of Bone	0	0.60	---		---	---
Cancer of All Lymphatic, Haematopoietic Tissue	37	30.31	122.1		88.8	167.8
Lymphosarcoma & Reticulosarcoma	4	3.27	122.2		46.0	324.8
Hodgkins Disease	2	1.23	162.2		41.2	639.1
Leukemia & Aleukemia	15	12.47	120.3		72.7	198.9
Cancer of All Other Lymphopoietic Tissue	16	13.33	120.0		73.7	195.3
All Other Malignant Neoplasms	40	28.72	139.3	*	102.6	189.0
Benign Neoplasms	5	3.36	148.7		62.3	354.8
Diabetes Mellitus	22	21.48	102.4		67.7	155.1
Cerebrovascular Disease	121	87.15	138.8	**	117.0	164.7
All Heart Disease	545	576.37	94.6		88.6	100.9
Rheumatic Heart Disease	2	5.12	39.1		10.3	148.3
Ischemic Heart Disease	428	499.52	85.7	**	79.4	92.4
Chronic Endocard. Dis.; Other Myocard. Insuff.	20	28.28	78.1		49.4	117.2
Hypertension with Heart Disease	13	14.07	92.4		53.8	158.8
All Other Hurt Disease	82	103.83	79.0	*	64.2	97.2
Hypertension w/o Heart Disease	4	3.70	108.0		40.6	287.2
Non-malignant Respiratory Disease	99	122.38	80.9	*	67.1	97.6
Influenza & Pneumonia	28	40.89	68.5	*	47.7	98.3
Bronchitis, Emphysema, Asthma	16	20.08	79.7		49.1	129.5
Bronchitis	2	3.43	58.3		14.9	229.0
Emphysema	11	15.52	70.9		39.5	127.1
Asthma	3	1.33	225.5		75.0	677.7
Other Non-malignant Respiratory Disease	55	64.27	85.6		66.1	110.7
Ulcer of Stomach & Duodenum	6	4.22	142.2		64.2	314.8
Cirrhosis of Liver	11	23.88	46.1	**	26.1	81.3
Nephritis & Nephrosis	11	7.51	146.4		81.5	282.9
All External Causes of Death	82	78.20	107.8		88.7	130.6
Accidents	48	48.72	102.7		78.7	134.1
Motor Vehicle Accidents	18	19.30	93.3		59.9	145.1
All Other Accidents	30	27.78	108.0		76.1	153.3
suicides	28	20.01	129.9		89.4	188.8
Homicides & Other External Causes	6	9.46	84.5		43.1	165.8
All Other Causes of Death	145	144.85	100.1		85.8	118.8
Unknown Causes (In All Causes Category Only)	0					

* Significant at 5% Level; ** Significant at 1% Level

increased slightly (PMR=124.3 and 209.7, respectively). The remainder category "all other malignant neoplasms" is also significant with a PMR of 139.3 ($p<0.05$).

Since the primary departments of interest in the Tripartite Study were the potroom and carbon departments, we investigated mortality patterns separately for these two departments. There were 943 employees with some experience in the potroom department. The PMR for all malignancies was 106.8 with a corresponding 95% confidence interval of (96.1, 118.6) (Table 14). The PMR for cancer of the lung was 111.9 with a corresponding confidence interval of (92.6, 135.2). The only malignancy with five or more observed deaths and a statistically significant elevation was kidney cancer with a PMR of 297.9 and a corresponding 95% confidence interval of (187.1, 474.2). There was also an excess of ulcer of the stomach and duodenum based on six observed deaths and 2.69 expected (PMR=223.0, $p<0.05$). For employees with a majority of time in the potroom the PMR for all malignant neoplasms was 114.8 with a corresponding 95% confidence interval of (100.7, 130.9) (Table 15). Of those causes with more than 5 observed or expected deaths, cancer of the kidney and ulcer of the stomach were elevated (PMR=285.8, $p<0.01$ and PMR=317.2, $p<0.05$, respectively). Ischemic heart disease was significantly low (PMR=80.6, $p<0.01$).

The carbon department had fewer workers than the potroom department. For the 489 employees with some employment in the carbon department, the PMR for all malignancies was 105.8 (Table 16). Both cancer of the kidney (PMR=250.7, $p<0.01$) and

Table 14
observed and Expected Deaths and proportionate Mortality Ratios for Employees Ever Employed in the Potroom Department

Cause of Death (ICDA 9th Revision Codes)	OBS	EXP	SPMR	95% Limits LOWER	UPPER
All Causes of math	943	943.00	100.0	---	---
Tuberculosis	0	1.34	---	---	---
All Malignant Neoplasms	256	239.81	106.8	96.1	118.8
Cancer of Buccal Cavity & Pharynx	5	5.67	88.2	36.9	211.1
Cancer of Digestive Organs & Peritoneum	51	58.46	87.2	66.9	113.7
Cancer of Esophagus	4	6.36	62.9	23.9	165.5
Cancer of Stomach	7	8.41	83.2	39.9	173.8
Cancer of Large Intestine	17	22.42	75.8	47.5	121.1
Cancer of Rectum	3	4.44	67.5	22.0	207.3
Cancer of Biliary Passages & Liver	6	5.35	112.2	50.5	249.0
Cancer of Pancreas	12	11.63	103.2	58.8	181.1
Cancmr of All Other Digestive Organs	2	1.61	123.9	31.1	493.8
Cancmr of Respiratory System	97	89.82	108.2	88.7	130.8
Cancer of Larynx	1	3.02	33.1	5.2	212.5
Cancer of Bronchus, Trachea, Lung	96	85.80	111.9	92.6	135.2
Cancer of All Other Respiratory	0	0.80	---	---	---
Cancer of Breast	0	0.26	---	---	---
All Uterine Cancers (Females only)	0	0.00	---	---	---
Cancer of Cervix Uteri (Females only)	0	0.00	---	---	---
Cancer of Other Female Genital Organs	0	0.00	---	---	---
Cancer of Prostate (Males only)	24	23.91	100.4	67.7	148.8
Cancer of testes and Ottmr Male Genital Organs	2	0.45	441.4 *	124.5	1584.5
Cancer of Kidney	18	5.37	287.9 **	187.1	474.2
Cancer of Bladder and Other Urinary Organs	8	8.51	92.2	41.8	204.6
Malignant Melanoma of Skin	3	2.88	104.2	33.7	322.1
Cancer of Eye	0	0.12	---	---	---
Cancer of Central Nervous System	1	4.97	20.1	3.5	118.9
Cancer of Thyroid & Other Endocrine Glands	0	0.54	---	---	---
Cancer of Bone	2	0.41	493.7 *	141.8	1720.8
Cancer of All Lymphatic, Haematopoietic Tissue	27	19.88	135.9	93.7	197.1
Lymphosarcoma & Reticulosarcoma	1	2.15	46.6	6.9	314.7
Hodgkins Disease	3	0.84	355.5 *	123.4	1024.2
Leukemia & Aleukemia	11	8.08	136.1	75.7	244.5
Cancer of All Other Lymphopoietic Tissue	12	8.79	136.5	77.9	239.2
All Other Malignant Neoplasms	22	19.09	115.2	78.2	174.2
Benign Neoplasms	0	2.18	---	---	---
Diabetes Mellitus	12	14.11	85.1	48.8	149.1
Cerebrovascular Disease	68	54.84	124.0	98.6	155.9
All Heart Disease	384	370.47	98.3	90.7	108.4
Rheumatic Heart Disease	2	3.34	60.0	15.3	235.6
Ischemic Heart Disease	278	319.30	87.1 **	79.2	95.7
Chronic Endocard. Dis.; Other Myocard. Insuff.	14	18.49	84.9	50.6	142.5
Hypertension with Heart Disease	10	9.55	104.7	56.6	193.8
All Other Heart Disease	80	88.15	88.0	69.0	112.3
Hypertension w/o Heart Disease	2	2.42	82.7	20.8	329.4
Non-malignant Respiratory Disease	68	76.81	88.5	70.6	111.0
Influenza & Pneumonia	20	25.28	79.1	51.5	121.5
Bronchitis, Emphysema, Asthma	13	12.71	102.2	59.6	175.4
Bronchitis	0	2.14	---	---	---
Emphysema	11	9.79	112.3	62.4	202.0
Asthma	2	0.89	223.7	58.1	861.6
Other Non-malignant Respiratory Disease	35	40.59	86.2	62.4	119.1
Ulcer of Stomach & Duodenum	8	2.89	223.0 *	102.4	485.5
Cirrhosis of Liver	7	16.45	42.5 *	20.9	86.4
Nephritis & Nephrosis	7	4.85	144.2	69.2	300.8
All External Causes of Death	54	54.64	98.8	78.2	124.8
Accidents	34	32.91	103.3	75.4	141.5
Motor Vehicle Accidents	13	13.99	92.9	55.4	156.0
All Other Accidents	21	19.18	109.6	72.2	168.4
Suicides	14	13.99	100.1	60.1	166.6
Homicides & Other External Causes	6	7.74	77.5	36.2	166.0
All Other Causes of Death	99	93.78	105.6	87.6	127.2
Unknown Causes (In All Causes Category Only)	0				

* Significant at 5% Level; ** Significant at 1% Level

Table 15
Observed and Expected Deaths and proportionate Mortality Ratios for Employees Spending a Majority of Time in the Potroom Department

Cause of Death (ICDA 9th Revision Codes)	OBS	EXP	SPMR	95% Limits LOWER	UPPER
All Causes of Death	558	556.00	100.0	---	---
Tuberculosis	0	0.82	---	---	---
All Malignant Neoplasms	163	141.98	114.8 *	100.7	130.9
Cancer of Buccal Cavity & Pharynx	4	3.35	119.5	45.1	318.8
Cancer of Digestive Organs & Peritoneum	33	34.83	85.3	58.5	132.5
Cancer of Esophagus	3	3.82	78.6	25.8	241.8
Cancer of Stomach	5	5.03	99.4	41.5	237.7
Cancer of Large Intestine	13	13.21	98.4	57.5	188.1
Cancer of Rectum	1	2.60	38.4	5.8	252.2
Cancer of Biliary Passages & Liver	4	3.18	125.7	47.4	333.2
Cancer of Pancreas	6	8.88	67.2	39.4	192.9
Cancer of All Other Digestive Organs	1	0.95	105.7	14.9	748.9
Cancer of Respiratory System	82	53.04	116.9	92.4	147.8
Cancer of Larynx	0	1.79	---	---	---
Cancer of Bronchus, Trachea, Lung	82	50.77	122.1	96.5	154.5
Cancer of All Other Respiratory	0	0.47	---	---	---
Cancer of Breast	0	0.16	---	---	---
All Uterine Cancers (Females only)	0	0.00	---	---	---
Cancer of Cervix Uteri (Females only)	0	0.00	---	---	---
Cancer of Other Female Genital Organs	0	0.00	---	---	---
Cancer of Prostate (Males only)	17	14.32	118.7	74.4	189.3
Cancer of Testes and Other Male Genital Organs	1	0.28	358.2	57.8	2241.7
Cancer of Kidney	9	3.15	285.8 **	153.4	532.5
Cancer of Bladder and Other Urinary Organs	2	3.80	52.6	13.5	204.5
Malignant Melanoma of Skin	2	1.68	119.2	30.0	474.3
Cancer of Eye	0	0.07	---	---	---
Cancer of Central Nervous System	2	2.91	68.7	17.4	271.1
Cancer of Thyroid & Other Endocrine Glands	0	0.32	---	---	---
Cancer of Bone	0	0.24	---	---	---
Cancer of All Lymphatic, Haematopoietic Tissue	17	11.73	144.9	90.8	231.3
Lymphosarcoma & Reticulosarcoma	1	1.26	79.5	11.3	560.8
Hodgkins Disease	2	0.50	398.9 *	110.3	1428.6
Leukemia & Aleukemia	8	4.75	168.3	85.1	333.0
Cancer of All Other Lymphopoietic Tissue	6	5.22	115.0	51.9	254.9
All Other Malignant Neoplasms	14	11.31	123.8	73.8	207.7
Benign Neoplasm	0	1.29	---	---	---
Diabetes Mellitus	8	8.39	95.3	47.9	189.8
Cerebrovascular Disease	41	32.28	127.1	94.8	170.7
All Heart Disease	202	216.80	93.2	83.7	103.7
Rheumatic Heart Disease	2	1.94	103.0	25.8	410.8
Ischemic Heart Disease	150	186.07	80.6 **	70.9	91.7
Chronic Endocard. Dis.; Other Myocard. Insuff.	7	9.63	72.7	35.0	150.8
Hypertension with Heart Disease	7	5.78	121.1	58.1	252.5
All Other Heart Disease	38	40.39	89.1	65.1	122.0
Hypertension w/o Heart Disease	1	1.44	69.3	9.9	485.1
Non-malignant Respiratory Disease	41	44.85	91.2	68.1	122.1
Influenza & Pneumonia	10	14.68	68.2	37.2	124.9
Bronchitis, Emphysema, Asthma	8	7.47	107.2	53.9	213.1
Bronchitis	0	1.24	---	---	---
Emphysema	6	5.75	104.4	47.1	231.2
Asthma	2	0.53	374.4 *	103.1	1359.3
Other Non-malignant Respiratory Disease	23	23.85	86.5	64.7	143.7
Ulcer of Stomach & Duodenum	5	1.58	317.2 **	138.5	728.4
Cirrhosis of Liver	5	9.62	52.0	22.2	121.5
Nephritis & Nephrosis	5	2.88	173.4	73.2	410.8
All External Causes of Death	34	33.38	101.9	78.2	136.3
Accidents	17	20.30	83.7	54.0	129.9
Motor Vehicle Accidents	7	8.88	78.8	38.3	158.1
All Other Accidents	10	11.56	86.5	47.3	158.2
Suicides	11	8.51	129.3	73.0	229.0
Homicides & Other External Causes	6	4.55	132.0	61.0	285.5
All Other Causes of Death	51	55.58	91.8	70.8	119.0
Unknown Causes (In All Causer Category Only)	0				

* Significant at 5% Level; ** Significant at 1% Level

cerebrovascular disease (PMR=136.2, $p<0.05$) were significantly elevated. There were only 140 men. spending the majority of their time in the carbon department (Table 17). Thus the statistical power to a true excess is limited. The only cause of death with a statistically significant excess is cerebrovascular disease with a PMR of 195.3 and corresponding 95% confidence interval of (124.6, 306.3).

The PMRs were also computed for the employees spending the majority of their time in mechanical maintenance, electrical maintenance, ingot and power. For most of these departments the number of employees was not sufficient to evaluate many of the specific cancer sites. Table 18 summarizes the observed and expected deaths and PMRs for all malignant neoplasms for employees with the majority of their time in each of the departments in the reduction plant. Those workers with the majority of time in the potrooms show an elevated PMR of 114.8 ($p<0.05$). The site-specific PMRs for cancer have already been discussed for the potroom and carbon departments. For the other four departments the only significant excess was for lung cancer in mechanical maintenance. The PMR was 138.3 with a corresponding 95% confidence interval of (107.2, 176.4).

Table 16
observed and Expected Deaths and Proportionate Mortality Ratios for Employees Ever Employed in the Carbon Department

Cause of Death (ICDA 9th Revision Codes)	OBS	EXP	SPMR	95% Limits LOWER	UPPER
All Causes of math	489	489.00	100.0	---	---
Tuberculosis	0	0.78	---	---	---
All Malignant Neoplasms	133	125.72	105.8	91.S	122.3
Cancer of Buccal Cavity & Pharynx	2	3.06	65.4	18.8	257.2
Cancer of Digestive Organs & Peritoneum	27	30.84	88.1	81.2	128.9
Cancer of Esophagus	1	3.59	27.9	4.5	172.7
Cancer of Stomach	5	4.52	110.7	48.3	284.8
Camr of Large Intestine	10	11.44	87.4	47.4	181.1
Cancer of Rectum	1	2.26	44.3	8.8	298.8
Cancer of Biliary Passages & Llvmr	3	2.84	105.7	34.2	328.4
Cancer of Pancreas	6	6.09	98.5	44.5	218.1
Cancer of All Othor Digestive Organs	1	0.82	121.4	17.2	657.5
Cancer of Respiratory System	51	47.16	108.1	83.5	140.1
Cancer of Larynx	0	1.82	---	---	---
Camr of Bronchus. Trachea, Lung	51	45.12	113.0	67.2	148.5
Cancer of All Othor Respiratory	0	0.42	---	---	---
Cancer of Breast	0	0.14	---	---	---
All Uterine Cancers (Females only)	0	0.00	---	---	---
Cancer of Cervix Uteri (Females only)	0	0.00	---	---	---
Cancer of Other Female Genital Organs	0	0.00	---	---	---
Camr of Prostate (Males only)	12	12.34	97.2	IS. 8	189.5
Camr of Testes and Other Male Genital Organs	1	0.28	359.4	63.4	2382.3
Cancer of Kidney	7	2.79	250.7 *	122.9	511.5
Cancer of Bladder and Othar Urinary Organs	3	3.19	94.1	30.5	290.8
Malignant Melanoma of Skin	2	1.55	128.9	32.5	61.1.5
Cancer of Eye	0	0.06	---	---	---
Cancer of Central Nervous System	0	2.65	---	---	---
Cancer of Thyroid & Other Endocrine Glands	0	0.28	---	---	---
Cancer of Bone	1	0.22	458.9	78.8	2717.1
Cancer of All Lymphatic, Hematopoietic Tissue	12	10.37	115.7	88.2	202.4
Lymphosarcoma & Reticulosarcoma	1	1.10	91.2	12.9	645.4
Hodgkins Disease	1	0.47	213.5	31.6	1444.0
Leukemia & Aleukemia	3	4.15	72.2	23.5	221.8
Cancer of All Other Lymphopoietic Tissue	7	4.65	150.5	72.4	313.0
All Other Malignant Neoplasms	15	10.12	148.2	90.1	243.7
Benign Neoplasms	1	1.14	87.9	12.4	621.6
Diabetes Mellitus	11	7.52	148.2	81.6	281.9
Cerebrovascular Disease	38	27.90	136.2 *	100.3	184.9
All kart Disease	190	187.93	101.1	90.5	112.9
Rheumatic Heart Disease	1	1.70	58.9	8.5	407.6
Ischemic Heart Disease	148	159.73	93.3	81.9	108.3
Chronic Endocard. Dis.; Othr Myocard. Insuff.	10	8.25	121.2	65.7	223.7
Hypertension with Heart Disease	3	5.37	55.9	18.5	169.1
All Other Heart Disease	27	36.11	74.8	52.1	107.3
Hypertension w/o kart Disease	1	1.29	77.2	11.0	543.8
Non-malignant Respiratory Disease	25	38.06	65.6 *	45.3	95.2
Influenza & Pneumonia	9	12.61	71.4	37.7	135.2
Bronchitis, Emphysema, Asthma	3	6.28	47.9	18.0	143.8
Bronchitis	0	1.03	---	---	---
Emphysema	1	4.77	20.9	3.8	122.2
Asthma	2	0.49	407.2 *	113.5	1481.2
Othr Non-malignant Respiratory Disease	13	20.10	64.7	38.2	108.5
Ulcer of Stomach & Duodenum	1	1.38	73.3	10.4	515.1
Cirrhosis of Liver	7	9.17	76.4	36.9	158.1
Nephritis & Nephrosis	4	2.55	157.1	59.8	413.8
All External Causes of Death	31	31.90	97.2	71.8	131.9
Accidents	17	19.10	89.0	57.2	138.5
Motor Vehicle Accidents	6	8.35	71.8	33.7	153.1
All Other Accidents	11	10.89	101.1	56.8	179.8
Suicides	12	8.03	149.5	88.7	257.8
Homicides & Other External Causes	2	4.77	41.9	11.5	152.3
All Other Causes of Death	47	49.22	95.5	72.9	125.1
Unknown Causes (In All Causes Category Only)	0				

* Significant at 5% Level; ** Significant at 1% Level

Table 17
Observed and Expected Deaths and Proportionate Mortality Ratios for Employees Spending a Majority of Time in the Carbon Department

Cause of Death (ICDA 9th Revision Codes)	OBS	EXP	SPMR	95% Limits LOWER	UPPER
All Causes of Death	140	140.00	100.0	---	---
Tuberculosis	0	0.25	---	---	---
All Malignant Neoplasms	38	35.48	107.1	81.5	140.7
Cancer of Buccal Cavity & Pharynx	0	0.88	---	---	---
Cancer of Digestive Organs & Peritoneum	8	8.78	91.2	46.7	178.1
Cancer of Esophagus	1	1.04	96.0	13.7	674.5
Cancer of Stomach	0	1.31	---	---	---
Cancer of Large Intestine	3	3.28	91.6	29.9	279.9
Cancer of Rectum	1	0.84	156.0	22.4	1086.9
Cancer of Biliary Passages & Ltvmr	0	0.82	---	---	---
Cancer of Pancreas	3	1.71	176.0	57.7	530.9
Cancer of All Other Digestive Organs	0	0.23	---	---	---
Cancer of Respiratory System	16	13.01	123.0	77.4	195.4
Cancer of Larynx	0	0.45	---	---	---
Cancer of Bronchus, Trachea, Lung	16	12.44	128.6	80.9	204.5
Cancer of All Other Respiratory	0	0.11	---	---	---
Cancer of Breast	0	0.04	---	---	---
All Uterine Cancers (Females only)	0	0.00	---	---	---
Cancer of Cervix Uteri (Females only)	0	0.00	---	---	---
Cancer of Other Female Genital Organs	0	0.00	---	---	---
Cancer of Prostate (Males only)	3	3.80	78.9	25.4	233.0
Cancer of Testes and Other Male Genital Organs	0	0.08	---	---	---
Cancer of Kidney	2	0.75	266.2	70.3	1001.3
Cancer of Bladder and Other Urinary Organs	1	0.95	105.5	15.0	743.4
Malignant Melanoma of Skin	0	0.37	---	---	---
Cancer of Eye	0	0.02	---	---	---
Cancer of Central Nervous System	0	0.56	---	---	---
Cancer of Thyroid & Other Endocrine Glands	0	0.08	---	---	---
Cancer of Bone	0	0.06	---	---	---
Cancer of All Lymphatic, Hematopoietic Tissue	3	2.86	105.0	34.3	321.5
Lymphosarcoma & Reticulosarcoma	0	0.29	---	---	---
Hodgkins Disease	0	0.11	---	---	---
Leukemia & Aleukemia	1	1.15	86.7	12.3	809.5
Cancer of All Other Lymphopoietic Tissue	2	1.30	153.7	39.1	804.1
All Other Malignant Neoplasms	5	2.84	175.8	74.7	413.7
Benign Neoplasms	1	0.32	309.5	48.3	1982.7
Diabetes Mellitus	3	2.19	136.9	44.8	418.8
Cerebrovascular Disease	17	8.70	195.3 **	124.6	306.3
All mart Disease	50	54.44	91.8	74.1	113.9
Rheumatic Heart Disease	0	0.46	---	---	---
Ischemic Heart Disease	40	45.89	87.2	67.8	112.1
Chronic Endocard. Dis.; Other Myocard. Insuff.	2	2.52	79.4	20.2	312.2
Hypertension with Mart Disease	0	1.65	---	---	---
All Other Heart Disease	8	10.69	75.5	38.9	146.5
Hypertension w/o Heart Disease	0	0.40	---	---	---
Non-malignant Respiratory Disease	5	11.52	43.4 *	19.3	97.8
Influenza & Pneumonia	0	3.91	---	---	---
Bronchitis, Emphysema, Asthma	0	1.85	---	---	---
Bronchitis	0	0.31	---	---	---
Emphysema	0	1.41	---	---	---
Asthma	0	0.14	---	---	---
Other Non-malignant Respiratory Disease	5	6.03	82.9	35.3	194.7
Ulcer of Stomach & Duodenum	0	0.40	---	---	---
Cirrhosis of Liver	2	2.34	85.5	21.9	334.9
Nephritis & Nephrosis	1	0.79	126.5	18.0	887.9
All External Causes of Death	9	7.43	121.1	67.0	218.8
Accidents	5	4.54	132.2	61.9	282.3
Motor Vehicle Accidents	4	1.81	221.4	67.9	557.5
All Other Accidents	2	2.77	72.2	18.7	279.2
Suicides	3	1.79	167.8	58.3	500.1
Homicides & Other External Causes	0	1.11	---	---	---
All Other Causes of Death	14	14.41	97.2	59.2	159.5
Unknown Causes (In All Causes Category Only)	0				

* Significant at 5% Level; ** Significant at 1% Level

Table 18
Observed and Expected Deaths and Proportionate Mortality Ratios by Department for All Malignant Neoplasms

	OBS	EXP	PMR	95% LOWER	UPPER
POTROOM	163	141.98	114.8*	100.7	130.9
CARBON	38	35.48	107.1	81.5	140.7
INGOT	44	44.33	99.3	76.9	128.1
MECH. MAINT.	117	108.00	108.3	92.7	126.6
ELECT. MAINT.	30	27.60	108.7	79.8	148.0
POWER	5	5.05	99.0	46.2	212.3

D, Selected Causes of Death

For those causes of death that were in excess or for which we have particular interest because of the Tripartite Study, we now present more detailed analysis.

(1) Kidney cancer - The PMR for kidney cancer for the total cohort is 158.1 based on 53 observed deaths and 33.52 expected. All cases of kidney cancer were in males and both white males and nonwhite males had an excess (PMR=157.5 and 257.8, respectively. Of the 53 employees with kidney cancer as a cause of death, 49 had more than 20 years employment. For those employees ever employed in the reduction process, the PMR is 200.1 based on 21 observed deaths and 10.5 expected and a corresponding 95% confidence interval of (131.7, 303.8). This compares to a PMR of 136.5 with a corresponding 95% confidence interval of (92.5, 201.4) for workers in nonreduction plants.

Further investigation within the reduction process indicates

that there is no particular area that appears to have a concentration of excess deaths (Table 19). The excess is not much affected when a PCMR is used instead of a PMR (Table 20). The investigation of kidney cancer by individual plant indicated no pattern for the excess although the distribution of only 53 observed deaths among 37 plants results in numbers too small to conclude that no clustering exists.

Table 19
Observed and Expected Deaths and Proportionate Mortality Ratios by Job Location for Kidney Cancer

	OBS	EXP	PMR	95% LOWER	95% UPPER
NONREDUCTION PLANT	25	18.32	136.5	92.5	201.4
REDUCTION PLANT	28	15.20	184.2**	128.1	265.0
NONREDUCTION PROCESS	11	7.05	156.1	87.0	280.0
REDUCTION PROCESS	17	8.11	209.7**	132.0	333.3
POTROOM	9	3.15	285.8**	153.4	532.5
CARBON	2	.75	265.2	70.3	1001.3
INGOT	2	.99	201.8	52.1	781.4
MECH. MAINTAIN.	4	2.48	161.1	61.2	423.7
ELECT. MAINTAIN.	0	.61	--	--	--
POWER	0	.11	--	--	--

Table 20
Observed and Expected Deaths and Proportionate Cancer Ratios
by Job Location for Kidney Cancer

	OBS	EXP	PMR	95% LOWER	UPPER
NONREDUCTION PLANT	25	19.25	129.9	88.2	191.1
REDUCTION PLANT	28	15.62	179.3**	125.0	257.2
NONREDUCTION PROCESS	11	6.60	166.6	93.5	296.9
REDUCTION PROCESS	17	9.01	188.6**	118.8	299.4
POTROOM	9	3.64	247.1**	132.4	461.2
CARBON	2	.84	237.9	63.1	897.5
INGOT	2	1.02	195.8	51.1	750.7
MECH. MAINTAIN.	4	2.74	146.2	55.8	382.7
ELECT. MAINTAIN.	0	.67	--	--	--
POWER	0	.10	--	--	--

(2) All other cancers - The PMR for the category "all other cancers" was 134.3 ($p<0.01$) with 164 observed deaths and 122.1 expected. The excess did not appear to be restricted to any particular race or sex. Of these, 138 were cancer of an unspecified site, 14 were cancer of multiple sites, and 12 were cancer of soft or connective tissue.

(3) Benign and unspecified neoplasms - The PMR for benign and unspecified neoplasms was 195.6 with a corresponding 95% confidence interval of (136.9, 279.5). The PMR was higher in the nonreduction plants than in the reduction plants (PMR=227.3, $p<0.01$) and PMR=154.7, respectively. The cases did not appear confined to any specific race or sex. The median age at death

for the 29 workers with this cause of death was 70.9. Of the 29 observed deaths, 2 were benign brain tumors and 10 were brain tumors of unspecified nature.

(4) Nephritis and nephrosis - The PMR for nephritis and nephrosis was 242.2 based on 85 observed deaths and 35.09 expected. The excess appeared in reduction as well as nonreduction processes and was not restricted to a specific sex or race group. This ICD classification is often a result of insufficient coding of the death certificate and a review of individual death certificates indicated "renal failure" as a frequent cause of death designated on the death certificates with this cause. Investigation of individual plants indicates that five plants accounted for 52 observed deaths when 13.95 were expected. These plants were both reduction and nonreduction plants.

(5) Cerebral vascular disease - The total cohort had approximately an 11% excess in cerebrovascular disease. This excess appeared restricted to white males where the PMR was 115.2 ($p<0.01$) based on 403 observed deaths and.349.8 expected and was higher in plants with a reduction process where the PMR was 135.3 ($p<0.01$) based on 151 observed deaths compared to a PMR of 98.9 for the remainder of the white male population. For reduction plant workers this represents 30 observed deaths in excess which is approximately the same as the deficit observed tor the category "all heart disease". Although the excess occurs in reduction plants it is not confined to the reduction process. The white males who spent the majority of their time in a nonreduction process had a PMR of 132.1 ($p<0.01$) compared to

138.8 ($p<0.01$) for the white males spending the majority of their time in a reduction process.

(6) Respiratory cancer - The primary hypothesis in the Tripartite Study was to determine if there was an excess of lung cancer in the potroom and carbon departments of the reduction process. The overall SMR for lung cancer in that study was 96.4 with a corresponding 95% confidence interval of (83.2, 105.9). The corresponding SMR of the plants in the Tripartite Study which have been included in this study is 91.7 with a corresponding 95% confidence interval of (78.4, 106.5).

For this study the PMR for lung cancer shows a slight excess. The PMR for lung cancer for employees in the reduction process is 124.3 with a corresponding confidence interval of (107.3, 144.0). This compares to a PMR of 108.9 for workers in plants with no reduction process and a PMR of 81.3 ($p<0.05$) for workers in a reduction plant that spent the majority of their time in a nonreduction process. Further investigation was conducted by department within the reduction process (Table 21). Workers spending the majority of their time in the potroom, carbon or ingot department all have excesses of 20%-30% that are not statistically significant. Workers spending the majority of time in mechanical maintenance have a significantly elevated PMR of 136.3 ($p<0.05$).

When the risk is estimated using a proportionate cancer mortality ratio ,(Table 22), the risk is slightly increased for employees in the nonreduction process of the reduction plant (PCMR=87.9) and decreased for employees in the reduction process

(PCMR=111.9). Neither of these is significantly different from 100. The only significant excess using the PCMR occurs for maintenance workers where the PCMR is 125.7 with a corresponding 95% confidence interval of (101.6, 155.6).

Table 21
Observed and Expected Deaths and Proportionate Mortality Ratios by Job Location for Cancer of Bronchus, Trachea and Lung

	OBS	EXP	PMR	95% LOWER	95% UPPER
NONREDUCTION PLANT	310	284.73	108.9	97.9	121.0
REDUCTION PLANT	248	238.24	104.1	92.5	117.1
NONREDUCTION PROCESS	89	109.53	81.3*	66.7	98.9
REDUCTION PROCESS	159	127.95	124.3**	107.3	144.0
POTROOM	62	50.77	122.1	96.5	154.5
CARBON	16	12.44	128.6	80.9	204.5
INGOT	19	15.13	125.6	82.0	192.4
MECH. MAINTAIN.	53	38.34	136.3*	107.2	178.3
ELECT. MAINTAIN.	8	9.53	83.9	43.5	162.0
POWER	1	1.69	59.2	9.4	372.4

Table 23
Observed and Expected Deaths and Proportionate Mortality Ratios for Lung Cancer by Plant

Plant	OBS	EXP	PMR	95% LOWER	95% UPPER
ADDY	3	.71	--	--	--
ANDERSON	1	.11	--	--	--
ALCOA	8	7.47	107.2	55.5	206.8
BADIN	12	12.19	98.5	57.5	168.7
BAUXITE	13	12.29	105.8	63.1	177.3
BRIDGEPORT	4	1.94	--	--	--
BUFFALO	0	.16	--	--	--
CHICAGO	3	2.45	--	--	--
CHILLICOTHE	6	4.87	123.2	57.8	262.6
CLEVELAND	42	36.63	114.7	86.0	152.8
CORONA	0	1.08	--	--	--
CRESSONA	23	23.53	97.8	66.5	143.8
DAVENPORT	29	23.39	124.0	88.0	174.8
DETROIT	2	4.39	--	--	--
EAST ST. LOUIS	5	7.99	62.6	27.1	144.5
EDGEWATER	17	18.26	93.1	59.0	146.8
EDISON	11	8.17	134.6	76.9	235.7
FORT MEADE	0	.31	--	--	--
FRANKLIN	2	1.95	--	--	--
LAFAYETTE	21	30.36	69.2	46.2	103.6
LANCASTER	5	2.69	185.5	81.8	420.8
LEBANON	2	.85	--	--	--
LOGANS FERRY	3	1.60	--	--	--
MARSHALL	3	1.09	--	--	--
MASSENA	47	53.08	88.5	67.5	116.1
MOBILE	22	13.65	161.2*	108.8	238.7
NEW KENSINGTON	54	52.96	102.0	79.0	131.5
POINT COMFORT	25	17.42	143.5	99.4	207.3
RICHMOND	4	5.94	67.3	26.7	170.0
ROCKDALE	5	9.58	52.2	23.1	117.7
ROSICLARE	5	2.45	204.4	89.9	464.8
TENNESSEE	107	109.3	97.9	81.7	117.2
TIFFON	1	.72	--	--	--
VANCOUVER	27	17.49	154.4*	108.3	220.1
VERNON	21	16.75	125.4	83.6	188.1
WARRICK	16	11.10	144.2	91.0	228.4
WENTACHEE	9	8.07	111.5	60.1	207.0

(7) Cancer of the Lymphatic and Haematopoietic Cancer - The PMR for the total cohort for lymphatic and haematopoietic cancer was 113.6 with a 95% confidence interval of (96.8, 133.2). The PMR for workers in nonreduction plants was 100.2 compared to a PMR of 130.2 ($p<0.05$) for workers in reduction plants. Within the reduction plants, those workers spending the majority of their time in a nonreduction process had a higher PMR than those in a reduction process [PMR=140.1, $p<0.05$ and PMR=122.1 (not significant), respectively]. The PCMR was 146.7 ($p<0.05$) for workers in the nonreduction process and 111.3 for workers in the reduction process. Analysis based on majority of time in individual departments yielded no statistically significant results. Potroom workers had a PMR of 144.9 with a 95% confidence interval of (90.8, 231.3) and electrical maintenance workers had a PMR of 217.3 with a corresponding 95% confidence interval of (93.3, 506.3). The only individual plant with a significant excess was Tennessee which had a PMR of 172.1 ($p<0.01$. The PMR for leukemia in the total cohort was 102.0. The PMR for those in reduction plants was 117.4 compared to 89.8 for those in nonreduction plants. The number of deaths was small on which to do an analysis by department. However, 8 of the 15 deaths occurred in the potroom with a subsequent PMR of 168.3 based on 8 observed deaths and 4.75 expected with a corresponding 95% confidence interval of (85.1, 333.0). The only individual plant with a significant excess was Edgewater with a PMR of 260.7 ($p<0.05$).

(8) Pancreatic cancer - In this study, the PMRs for

pancreatic cancer did not show a significant excess for either reduction plant workers or workers spending the majority of their time in the potrooms (PMR=103.2 and 87.2). This compares to an SMR of 134.8 for workers in the potrooms of the Tripartite Study. The significant finding of the Tripartite Study was for potroom workers with more than 15 years employment, where the excess was more than twofold. With the data available in the present study a risk for longterm employees could not be obtained.

E. Analysis by Plant

Mortality for each of the 62 selected causes of death was done for each of the 37 study plants. Such analysis must be interpreted with caution since by random chance alone some plants would be expected to deviate from the average value. In addition, many of the plants did not have sufficient numbers for an individual analysis. Because of these limitations, we view the results as preliminary and any plants that are identified should be given consideration for a more detailed study (if feasible) in a second phase.

Table 24 summarizes the observed, expected deaths and Proportionate Mortality Ratios by plant. Of the 29 plants with sufficient sample size to compute a PMR, 14 had a PMR less than 100 and 15 had a PMR greater than 100. Four plants had a statistically significant excess, but one was based on only 5 observed deaths. One plant had a borderline excess of PMR=130.5 with a corresponding 95% confidence interval of (99.9, 170.4).

Numbers were often too small to do an analysis of individual plants for many of the specific cancers. Nevertheless, in reviewing the results from those plants we note the following

Table 24
Observed and Expected Deaths and Proportionate Mortality Ratios for All Malignant Neoplasms by Plant

Plant	OBS	EXP	PMR	95% LOWER	95% UPPER
ADDY	5	2.00	250.6*	123.2	509.9
ANDERSON	1	.37	--	--	--
ALCOA	21	22.02	95.3	66.1	137.6
BADIN	40	37.11	107.8	82.5	140.7
BAUXITE	34	36.16	94.0	70.4	125.5
BRIDGEPORT	12	7.04	170.5*	103.7	280.3
BUFFALO	0	.91	--	--	--
CHICAGO	5	7.06	70.8	33.5	149.4
CHILLICOTHE	16	14.98	106.8	70.8	161.0
CLEVELAND	138	110.16	125.3**	108.6	144.6
CORONA	1	2.85	--	--	--
CRESSONA	64	62.75	102.0	82.8	125.6
DAVENPORT	85	64.20	132.4**	110.5	158.6
DETROIT	14	16.17	86.6	54.6	137.3
EAST ST. LOUIS	28	29.04	96.4	69.5	133.9
EDGEWATER	60	61.07	98.2	78.7	122.6
EDISON	30	24.75	121.2	89.1	165.0
FORT MEADE	1	.88	--	--	--
FRANKLIN	5	5.85	85.4	40.4	180.5
LAFAYETTE	78	87.57	89.1	73.6	107.8
LANCASTER	7	7.83	89.4	47.4	168.3
LEBANON	3	2.16	--	--	--
LOGANS FERRY	5	4.36	104.7	54.5	24.7
MARSHALL	3	2.78	--	--	--
MASSENA	148	152.68	96.4	84.4	111.4
MOBILE	45	38.58	116.6	90.8	149.8
NEW KENSINGTON	160	168.55	94.9	83.0	108.6
POINT COMFORT	45	45.95	97.9	76.5	125.4
RICHMOND	19	19.81	95.9	65.6	140.1
ROCKDALE	23	26.44	87.0	61.4	123.2
ROSICLARE	10	7.78	128.5	74.7	220.9
TENNESSEE	330	323.35	102.1	93.0	112.0
TIFFON	4	2.33	--	--	--
VANCOUVER	52	49.27	105.8	83.6	133.2
VERNON	52	51.06	101.8	80.6	128.7
WARRICK	39	29.89	130.5	99.9	170.4
WENTACHEE	22	22.55	97.6	68.3	139.5

neoplasms which were in excess at particular plants:

(1) The Cleveland plant had PMRs of *280.5* for stomach cancer (based on 12 observed deaths, $p<0.01$), *298.8* for cancer of

the rectum (based on six observed deaths, $p<0.05$) and 464.7 for cancer of the breast (based on 4 observed deaths, $p<0.01$).

(2) The Cressona plant had a PWR of 247.4 for stomach cancer (based on five deaths, $p<0.05$), 261.9 for kidney cancer (based on four deaths, $p<0.05$), and 530.4 for melanoma (based on four deaths, $p<0.01$).

(3) The Davenport plant had a PMR of 177.0 for all digestive cancers (based on 27 observed deaths, $p<0.01$). The PCMR was not significantly elevated for this cause.

(4) The Edgewater plant had a PMR of 260.7 for leukemia (based on six observed deaths, $p<0.05$).

(5) The Hassena plant had a PMR of 283.2 for lymphosarcoma (based on 4 observed deaths, $p<0.05$).

(6) The Mobile plant had a PMR of 161.2 ($p<0.05$) for lung cancer. The PCMR was 135.3.

(7) The Tennessee (Alc) plant had a PMR of 172.1 (based on 46 observed deaths, $p<0.01$) for cancer of the lymphatic and haematopoietic tissue.

(8) The Vancouver plant had a PMR of 154.4 for lung cancer (based on 27 observed deaths, $p<0.05$) and a PMR of 356.1 (based on 4 observed deaths, $p<0.05$) for kidney cancer.

Summary

Conclusions from this study must be drawn more cautiously than was necessary for the Tripartite Study because of the inherent limitations of the PMR study design as well as the less specific job classification used in the present study. Furthermore, the large number of estimates of risk that were computed will result in a larger number of false positive findings than can be inferred from the p-values. Conversely, the small number of workers available for many of the estimates of risk precludes any strong statements in regard to those findings that were negative. With these limitations stated, we now summarize the findings we feel are most important. Consistent with the study objectives, we have given most attention in our summary to malignant neoplasms..

The PMR for malignant neoplasms for the total study population was 103.7 and was not significantly different from the total U.S. population. The only specific cancer site.which was significantly elevated was kidney cancer with a PMR of 158.1 and a corresponding 95% confidence interval of (121.2, 206.3). The nonspecific disease categories of benign and unspecified neoplasms, nephritis and nephrosis and "all other malignant neoplasms" were elevated and appeared to result from lack of complete specification of cause of death on the certificate. The only other disease category that was elevated for the total cohort was cerebral vascular disease with a PMR of 111.4 ($p<0.05$) and this was accompanied by a deficit in ischemic heart disease (PMR=85.2, $p<0.01$).

The analysis by work area yielded the following:

(1) For the combined group of workers in nonreduction plants the PMR for all malignant neoplasms was 105.2. The only statistically significant excesses occurred for nonspecific disease categories (i [illegible], nephritis, benign and unspecified neoplasms, all other cancers). Analysis by race indicated that whites had an excess of colon cancer and nonwhites had an excess of stomach, liver and lymphatic cancer.

(2) For the 1320 workers in a reduction plant who spent the majority of their time in a nonreduction process, the PMR for all malignant neoplasms was 93.6. The only specific neoplastic site with a significant elevation was cancer of the lymphatic and haematopoietic tissue (PMR=140, $p<0.05$).

(3) Workers with the majority of their employment in the reduction process had a PMR of 109.5 ($p<0.05$) for all malignant neoplasms. These workers had a PMR of 124.3 for lung cancer ($p<0.01$) and a PMR of 209.2 for kidney cancer ($p<0.01$). When a PCMR was computed, the estimate of risk for lung cancer was a nonsignificant 111.9 but remained significant for kidney cancer (PCMR=188.6, $p<0.01$). The workers spending the majority of their time in the reduction process had a significant excess for two of the study plants. Neither of these plants had an excess in the Tripartite Study. Workers spending the majority of their time in mechanical maintenance also had an excess of lung cancer.

(4) Although workers in reduction plants had a significantly elevated PMR of 130.2 ($p<0.05$), for cancer of the lymphatic and haematopoietic tissue it was greater in workers in the reduction plant spending the majority of their time in a

nonreduction process (PMR=140.1, p<0.05). No individual department had a statistically significant excess, although the small number of observed deaths when analyzed by department makes the results inconclusive.

(5) Analysis by plant is limited by small numbers and a further increase in the expected false positives due to the larger number of estimates of risk. Overall, 14 plants had a PMR for "all malignant neoplasms" below 100, 15 plants were above, and 8 had less than 5 observed deaths from neoplasms. Of plants with greater than 5 observed deaths for "all malignant neoplasms", three had a statistically significant excess and one had borderline significance. Eight of the plants had at least one specific site that showed a statistically significant excess. We could identify no consistent pattern in site-specific cancers among plants with similar processes, although such inferences are clearly limited by small numbers and lack of more detailed job classifications in plants with multiple processes.

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Appendix

Distribution of causes of death using 4 digit ICD codes

ICD	Freq.	ICD	Freq.	ICD	Freq.
88	1	1562	1	2008	4
119	3	1569	1	2019	7
189	1	1570	5	2020	1
310	1	1579	69	2021	1
360	1	1590	3	2024	1
381	3	1599	1	2028	41
384	7	1619	7	2030	25
388	1	1625	1	2040	5
389	54	1629	557	2041	8
419	1	1639	2	2049	2
498	1	1640	1	2050	17
499	1	1701	1	2051	6
539	1	1706	1	2080	9
543	1	1709	1	2081	1
703	2	1712	1	2089	7
1159	2	1713	1	2159	1
1169	1	1716	1	2169	1
1175	1	1719	9	2251	1
1179	2	1722	1	2252	1
1350	1	1725	2	2302	1
1363	2	1727	1	2373	1
1369	1	1729	15	2384	1
1409	1	1734	1	2387	4
1419	2	1749	13	2389	2
1449	1	1790	2	2390	2
1459	2	1809	1	2391	1
1460	2	1820	1	2395	1
1469	1	1830	4	2396	10
1479	3	1850	147	2398	1
1481	1	1869	1	2399	1
1490	5	1874	2	2429	1
1505	2	1889	47	2449	1
1509	17	1890	48	2500	72
1510	3	1891	1	2501	2
1519	56	1892	4	2502	2
1522	2	1899	1	2503	6
1529	1	1909	1	2504	1
1531	1	1910	1	2505	1
1532	2	1913	2	2506	6
1533	4	1916	1	2507	1
1534	2	1919	20	2509	1
1536	5	1930	1	2535	1
1539	152	1940	2	2554	1
1540	6	1946	1	2558	1
1541	24	1950	1	2599	1
1550	12	1990	14	2639	3
1551	2	1991	136	2651	1
1552	8	2000	5	2733	1

Table (continued)

Distribution of causes of death using 4 digit ICD codes

ICD	Freq.	ICD	Freq.	ICD	Freq.
1560	4	2001	6	2738	1
1561	2	2002	1	2754	1
2761	1	4049	4	4402	3
2762	2	4100	1017	4409	65
2765	4	4109	16	4410	4
2773	2	4110	11	4411	1
2780	1	4120	9	4412	1
2793	1	4130	1	4413	41
2810	1	4140	617	4414	3
2848	2	4141	1	4415	7
2849	2	4148	14	4416	3
2859	1	4149	203	4429	1
2866	2	4151	36	4439	8
2888	2	4160	3	4440	1
2898	1	4169	5	4449	5
2899	1	4210	3	4472	1
2900	4	4239	1	4479	1
2901	2	4240	5	4512	1
2910	1	4241	23	4519	2
3030	1	4249	6	4539	1
3089	1	4254	67	4549	1
3109	5	4255	2	4560	4
3229	1	4271	1	4578	1
3239	2	4273	3	4589	3
3240	1	4274	4	4590	5
3310	19	4275	164	4599	1
3312	1	4278	1	4660	1
3314	2	4279	19	4787	1
3319	2	4280	80	4809	1
3320	16	4281	2	4810	4
3334	3	4284	4	4820	3
3352	12	4289	14	4823	1
3400	3	4290	2	4824	1
3418	1	4291	1	4828	1
3419	1	4292	150	4829	1
3429	2	4299	4	4830	1
3481	3	4300	6	4850	35
3483	1	4301	5	4860	103
3485	1	4310	46	4870	1
3489	1	4321	6	4878	1
3561	1	4329	5	4900	3
3570	2	4330	1	4912	6
3760	1	4331	4	4919	1
3940	2	4340	49	4920	54
3941	1	4341	2	4939	9
3949	5	4349	27	4940	1
3959	1	4360	275	4960	141

Table (continued)

Distribution of causes of death using 4 digit ICD codes

ICD	Freq.	ICD	Freq.	ICD	Freq.
3980	1	4370	16	5000	18
3989	4	4371	1	5010	1
4019	11	4378	1	5020	1
4029	48	4379	15	5050	1
4039	12	4380	7	5064	1
5070	17	5715	34	8120	9
5109	3	5718	2	8121	1
5118	1	5719	3	8122	3
5119	4	5722	1	8129	16
5120	4	5724	3	8130	4
5130	3	5728	19	8147	6
5140	6	5733	4	8150	2
5150	13	5739	2	8159	2
5163	1	5742	2	8169	2
5168	2	5743	1	8190	7
5183	1	5750	3	8191	2
5184	2	5751	1	8192	3
5185	3	5754	1	8199	16
5188	9	5761	3	8209	1
5199	1	5770	5	8219	1
5301	1	5771	1	8220	1
5304	1	5789	11	8249	1
5309	1	5809	1	8259	1
5314	4	5829	4	8261	1
5315	2	5838	1	8300	1
5319	1	5839	2	8309	1
5324	2	5845	1	8329	1
5325	2	5849	12	8480	1
5326	1	5850	19	8682	1
5329	1	5860	45	8689	3
5334	6	5900	1	8698	1
5335	2	5901	2	8781	1
5339	1	5908	3	8782	2
5369	1	5920	1	8789	1
5400	1	5938	1	8799	5
5409	1	5939	4	8809	7
5532	2	5959	1	8810	4
5539	1	5990	25	8811	1
5560	1	6019	1	8820	1
5570	8	6029	1	8839	1
5579	1	6821	1	8849	2
5580	1	6829	1	8870	1
5601	1	6861	1	8880	10
5602	1	6954	1	8902	4
5608	1	7070	6	8903	2
5609	5	7101	1	8909	4
5621	5	7802	2	8920	1
5660	1	7855	6	8939	1

Table (continued)

Distribution of causes of death using 4 digit ICD codes

ICD	Freq.	ICD	Freq.	ICD	Freq.
5679	1	7860	1	9000	1
5698	4	7970	2	9053	1
5699	1	7981	5	9068	1
5710	1	7982	44	9102	1
5712	13	7991	41	9108	3
5713	2	7999	62	9110	4
5714	1	8109	2	9120	2
9138	1	9251	1	9571	1
9190	5	9289	15	9600	1
9192	1	9323	1	9651	1
9198	2	9345	1	9652	1
9199	2	9520	4	9654	7
9220	1	9530	5	9660	2
9221	1	9538	1	9689	2
9222	1	9540	1	9821	4
9229	5	9550	4	9830	1
9239	1	9551	4	9851	1
9240	1	9552	2	9854	2
9250	1	9554	52	9947	1

EXHIBIT 2

TRIPARTITE

FINAL REPORT

Case-Control Study of Kidney Cancer and Hydrocarbon Exposure in the Aluminum Industry

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* Analysis Based on Exposure Classification as of August 18, 1993.

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Carolyn Watkins is acknowledged for coding of the death certificates.

* Disclaimer: The authors do not take responsibility for the classification of jobs into exposure categories. As specified in the proposal Alcoa had responsibility for the exposure classification.' Subsequent to the analysis and preparation of this report an error in exposure 'classification was identified that could affect the results and/or conclusions of this study.

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Abbreviations Used in this Work

95% CI	95% confidence interval
IH	Industrial hygiene
ICDA	International classification of disease
P	Statistical significance level or α - level
p-value	Statistical significance level or a - level
PPOM	Particulate polycyclic organic matter
PMR	Proportionate mortality ratio
RR	Relative risk
SMR	Standardized mortality ratio

Summary

In March, 1990, a Proportionate Mortality Study was completed of 6373 deaths occurring in one of 37 Alcoa plants from 1980-1987. One of the goals of the original study was to provide a general assessment of mortality across all Alcoa plants and to identify potential problems requiring further research. Although the proportion of cancer deaths was not significantly greater than the proportion observed in the total U.S. population, the mortality from kidney cancer was 58% higher than expected. The present study is a follow-up to this previously reported Proportionate Mortality Study and its purpose was to investigate whether the excess was due to occupational exposure. One hypothesized cause of an excess of kidney cancer was exposure to some form of hydrocarbon. The primary purpose of the present study was to test the hypothesis of an association of kidney cancer and hydrocarbon exposure. The analysis was based on 71 observed kidney cancer deaths for workers in 26 plants in the aluminum industry from 1980 through 1990. These were matched to a control group consisting of individuals whose cause of death was not cancer or chronic nephritis.

We obtained a relative risk of 2.55 for those with high exposure to hydrocarbons as compared to those without high exposure ($p < .05$). Those with jobs classified as low or medium exposure did not have a significant excess risk. A significantly elevated risk remained after adjustment for nonoccupati'onal factors such as smoking, analgesic use and obesity. Given the suggestion of a relationship of hydrocarbon exposure and kidney cancer in several other occupationally exposed

groups we conclude that some of the excess of kidney cancer previously observed in this population of aluminum workers is likely due to hydrocarbon exposure. The number of jobs rated as high hydrocarbon exposure was small and many are no longer in existence. Estimates of risk were elevated for both high aliphatic and high aromatic exposure. However, since many employees had exposure to both types of hydrocarbons it is difficult to separate the effects of these two specific types of exposure,

It should be noted that the analysis and conclusions are based on the data for exposure groupings which we had as of August 18, 1993. On August 19, we became aware of some errors in the exposure classification given to us by Alcoa. This could have a major impact on the results, but there was insufficient time to incorporate these changes in classification into the report.

Introduction

In 1990, a Proportionate Mortality Study [1] was completed of all deaths known to Alcoa that occurred from 1980 through 1987 in one of 37 study plants. Any former employee whose beneficiary had either filed a claim or was receiving death benefits from the company was included in the study population. The resultant study population contained 6433 deaths and death certificates were obtained for all but 60 (0.9%) subjects. All but nine workers had employment histories. Detailed work histories were not coded and analyzed for this study, since coding for such a large variety of plants and processes was beyond the scope of the original proposal. Therefore, most of the analysis was presented by study plant. Employees were classified into the plant where they were last employed. One of the goals of the PMR study was to provide a general assessment of mortality across all Alcoa plants in order to identify potential problem areas. Previous mortality studies in the aluminum industry had focused primarily on workers in reduction plants.

The PMR study summarized the mortality experience for 62 causes of death for the total group and for selected subgroups based on race, sex, and a general characterization of job history. The only cancer-specific site which was significantly elevated for the total study population was kidney cancer with a PMR of 158.1 and a 95% confidence interval of (121.2, 206.3). Of the 6373 total deaths in the cohort, 2777 were for workers in one of the eight aluminum reduction plants. The PMR for kidney cancer for reduction plant workers was 184.2 ($p < .01$) based on 28 observed deaths with a 95% confidence interval of (128.1, 265.0). The corresponding PMR

in nonreduction plants was 136.5 based on 25 observed deaths and a corresponding 95% confidence interval of (92.5, 201.4).

Based on these findings, a review of the literature, and discussions with industrial hygienists, it was determined that some type of hydrocarbon exposure might be a cause of an excess kidney cancer risk. Two general classes of hydrocarbon exposure are aromatics and aliphatics. Polycyclic aromatic hydrocarbons are formed during the combustion of organic matter and the high temperature processing of crude oil, coke, coal and a variety of other industrial carbon compounds. Some of the members of this group of compounds have long been recognized as being carcinogenic. Occupational groups with exposure to aromatic hydrocarbons that demonstrate an excess cancer risk include workers in gas generation [2,3], coke oven workers [4,5], roofers [6,7] and aluminum reduction plant workers [8,9]. Excess lung cancer in coke oven workers had provided much of the motivation for the conduct of mortality studies of aluminum reduction plant workers. It is less well recognized that coke oven workers also have an excess kidney cancer risk [5].

Although in the aluminum industry investigations of hydrocarbon exposure have focused primarily on exposure to coal tar pitch volatiles in the potroom and carbon departments of reduction plants, there have been suggestions of a kidney cancer risk in other areas. The Tripartite Study [10] found a kidney cancer excess in prebake plants that was not confined to the potroom and carbon departments. The recently conducted PMR study [1], which included both reduction and nonreduction plants, also showed some excess for kidney cancer in nonreduction plants. Solvents. a class of

organic substances that includes members of both the aromatic and aliphatic group of compounds, have been considered as a possible carcinogen in several epidemiological studies. Occupational groups with solvent exposure for which an excess cancer risk has been reported include dry cleaners [11], commercial pressman [12] and painters [13]. Gasoline has been suggested as a possible kidney carcinogen [14]. Several cohorts of oil refinery workers, where there is exposure to both aliphatic and aromatic hydrocarbons have shown an excess of cancer [15-17], although in general estimates of cancer risks for this occupational group have been inconsistent [18].

Another source of aliphatic exposure in the aluminum industry are rolling and lubricating oils. The association of cancer of the skin with mineral oils was established in early epidemiological studies [19,20]. More recent studies have focussed on oil mists. Several investigators have shown a relationship of machining oils or mists to cancer [21-26]. Because of the evidence that hydrocarbons in the work environment that are not included in the class of aromatic compounds may be carcinogenic it was decided that the assessment of hydrocarbon exposure would include estimation of exposure to aliphatic as well as aromatic compounds.

Research Objectives

The current project is a case-control study of **71** cases and **283** controls. This study tests the association of hydrocarbon exposure with kidney cancer risk. Jobs were classified in regard to exposure to both aromatic hydrocarbons and aliphatic hydrocarbons. Information on nonoccupational factors which may be related to kidney cancer was obtained and investigated as possible causes of the excess risk of kidney cancer in this population.

Research Methods

Methods

The cases included 53 kidney cancer deaths occurring in the PMR Study and an additional **20** kidney cancer deaths identified in the time interval 1988 through **1990.** The two kidney cancer cases from the Detroit plant were excluded from the study because information on the employment histories did not identify the work areas or job titles held by the workers. Therefore, 71 cases were available for the analyses. For each kidney cancer case, four controls were randomly selected that were matched on race, sex, year of death and birth year (matched within five years). The control group excluded all deaths from other malignancies since employment in aluminum reduction plants has been associated with a variety of cancer sites including cancers of the lung, bladder, digestive system and haemolymphopoietic tissues. .In addition, deaths attributed to non-malignant kidney disease were excluded. Subsequent to the selection of the **284** controls, one subject was found to have died of cause of death

which made them ineligible as a control and was removed from the study. The distribution of the study population by cause of death is given in Appendix A.

The **354** study participants had a total of **9673** job entries. These were reviewed by industrial hygiene personnel at Alcoa and classified into **1931** potentially different categories of job exposure. Subsequently each of these was classified into one of the four categories; none, low, medium and high for both aromatic hydrocarbon exposure and for aliphatic hydrocarbon exposure. This resulted in identifying **649** jobs with exposure to either aliphatic or aromatic hydrocarbons, and, **1282** jobs considered to have insignificant exposures to these compounds. It was plann'ed that ,if sufficient industrial hygiene data were available, an assignment would be made of an appropriate quantitative aliphatic and aromatic hydrocarbon exposure for each of these **649** jobs. Otherwise, analysis would be based on the low, medium and high classification.

Conditional logistic regression was used to test the hypothesis of an association of hydrocarbon exposure and kidney cancer. Employing this analytical approach serves a twofold purpose. First, it preserves the matching used in the sampling of controls and leads to analyses with statistically more power. Second, the logistic regression is a multivariate technique and can incorporate adjustment for other covariates. Specifically, the effect of hydrocarbon exposure can be evaluated while simultaneously adjusting for potential confounders which were not matched during the sampling of the controls. Information on potential confounders was obtained from a questionnaire administered to a surrogate by telephone (Appendix B). Potential

confounders for kidney cancer include weight, smoking patterns and use of analgesics. Responses to the questionnaire were obtained for 301 (85.0%) of the 354 study participants. The response rates for the cases and the controls was 83.1% and 85.5%, respectively. The individual responding to the questionnaire was a spouse 63.8% of time and a child 27.9% of the time. There was no difference between the cases and controls in regard to the distribution of the relationship of the person responding for the study participant. The primary analysis will relate hydrocarbon exposure to kidney cancer for the total study group. Several exposure measures were used to investigate the primary hypothesis. These included estimation of risks: 1) for those ever exposed to hydrocarbons; 2) for those ever exposed to high levels of hydrocarbons; 3) by cumulative years of hydrocarbon exposure; and 4) by cumulative years of high hydrocarbon exposure. As a secondary analysis, we estimated risk separately for aliphatic and aromatic hydrocarbon exposure. To determine if exposure is related to disease outcome, the likelihood ratio test was used to determine whether the beta coefficient for exposure in the logistic model is equal to zero. A reanalysis, adjusting for potential confounders, was done for the subgroup responding to the questionnaire.

The .sample size estimates in the design of this study assumed a Type I error of .05, a proportion of exposed controls equal to 0.30 and a matching ratio of 1:4. Assuming a conditional logistic regression model, the sample size required for selected values of relative risk and statistical power are summarized in Table 1. We had planned to have reasonable power to detect a relative risk, of 2 to 2.5. At the time

we initiated the study we were unsure as to the exact number of kidney cancer cases since the number of kidney cancer deaths in 1988-1990 was unknown.

The actual number of kidney cancer cases was 71 which was in the expected range. However, the percentage of individuals with some exposure to hydrocarbons was 77%. This was because many of the workers in alurninum plants have at least low exposure to hydrocarbons, particularly aliphatics. With 71 cases and an exposure proportion of .77 there is 68% power of detecting a 2.5 relative risk and power of 80% of detecting a risk of 3.0. Overall, eleven percent of the workers were classified as having high exposure to hydrocarbons. High hydrocarbon exposure among the controls was nine percent. Assuming a conditional logistic regression model, the statistical power for relative risks of 2.5 and 3.0 were 68% and 85%, respectively [27].

Description of the Data Base

Of the 354 study participants, 349 (98.6%) were males and 329 (92.9%) were white. These characteristics as well as birth year and year of death were considered in the design by matching to assure comparability of cases and controls. Figure 1 shows the frequency distribution of year of birth for the study participants. The largest number of births occurred between 1911 and 1920, with very few births occurring before 1900 or after 1930. Year of death (Figure 2) was fairly evenly distributed among the 11 years of the study, and differences can be attributed to chance variation. The average age at death was 69.0 for cases and controls

combined. Figure 3 shows the frequency distribution of the average age at death for cases and controls. More than half (62%) of the deaths occurred between the ages of 60 and 75.

For the 85% of the study participants for whom there was a response to the questionnaire there was also information on smoking, weight, use of diuretics and use of analgesics. A comparison of the smoking patterns of cases and controls is shown in Table 2. Eighty-five percent of the study population were smokers or ex-smokers and 78% had smoked cigarettes. As expected, more detailed information on the amount and duration of past smoking was less complete. There is reasonably good agreement in the smoking patterns of the two groups. Although this might be considered surprising because smoking is a risk factor for kidney cancer, some of the causes of death in the control group are also associated with excess risk from cigarette smoking and would be expected to have an increased number of smokers.

A comparison of other selected characteristics is shown in Table 3. The proportion of patients using diuretics is higher in the control group. Information on the reason for usage was not available for most of the patients, but in those that did give a reason, blood pressure (46.3%) and heart disease (26.8%) were the most common reason. Since the control group contains a large number of deaths from cardiovascular disease it is not surprising that there would be a higher number of patients in the control group taking diuretics for a hypertensive or cardiovascular condition. Although the average weight is similar in the two groups the percentage of individuals classified by the surrogate as overweight throughout most of their adult

life is higher in the control group ($p < .05$). There is a tendency for a preference for aspirin rather than aspirin free products in the control group but the results are not statistically significant. The response on the duration and brand name of products used was not sufficiently complete to be useful in the analysis.

Work Environment

The study consists of 354 workers from 28 plants. Of this number, 56.2% are workers in aluminum reduction plants and 29.9% are from Alcoa, Tennessee (Table 4). Alcoa provided all of the information on exposure classification and was responsible for the coordination of this effort. Review of the jobs appearing on the work histories by Alcoa industrial hygienists resulted in a classification into 1931 potentially different categories of job exposure. Then blinded as to whether the job category was present on the work history of a case or a control, the 1931 job classifications were identified by company industrial hygienists as: a) none/insignificant; b) low; c) medium; and d) high for both aromatic and aliphatic exposure. This assessment was done through interviews with current industrial hygienists and process engineers with experience at the specific plants. For aromatic exposure the plant industrial hygienists were asked if specific jobs had exposure to coal tar pitch volatiles such as those in reduction operations, roofing or floor coatings; solvents containing chemicals such as benzene, xylene, toluene or other aromatic hydrocarbon; or paints or coatings containing aromatic hydrocarbons. For aliphatic

hydrocarbon exposure the plant industrial hygienists were asked whether the specific jobs had exposure to diesel or gasoline fumes, solvents containing aliphatic hydrocarbons, perchlorethylene, oil mists, or paints or coatings containing aliphatic hydrocarbons.

Pertinent industrial hygiene files were reviewed by Alcoa for the individual locations and when quantitative exposure assessments were available they were considered in the determination of the appropriate qualitative classification of job exposure. Table 5 summarizes the 1931 jobs cross-classified by aliphatic and aromatic hydrocarbon exposure. In the classification of aliphatics, six jobs were classified in an intermediate category of "low to medium" exposure. In analysis where the low and medium categories were distinguished these job categories were considered to have medium exposure. The cross-classification in Table 5 indicates that approximately 20% of the job categories with exposure have both an aliphatic and an aromatic component. However, since workers have been employed in multiple job categories the percentage of individuals with exposure to both aliphatics and aromatics is higher.

Table 6 summarizes the percentage of workers who had ever worked a job with some exposure to aliphatics or aromatics and those with at least one job at higher exposure levels. It is clear from Table 6 that the majority of workers have had some exposure to aliphatics. It is also clear that many workers have been exposed to both types of hydrocarbon exposure. All of the workers with exposure to aromatics also had some exposure to aliphatics. Forty-seven percent of the workers with exposure

to aliphatics had exposure to aromatics and sixty percent of the workers with high exposure to aliphatics had some exposure to aromatics.

The occurrence of both aliphatic and aromatic hydrocarbon exposure in the same individuals means it may not be possible to separate the effects of exposure to aliphatic and aromatic exposure. Therefore, as a first analysis we estimated risk associated with hydrocarbon exposure without regard to type. As a secondary analysis we will estimate risks separately for aromatic and aliphatic exposure.

We also considered the possibility of using industrial hygiene measurements in place of the qualitative classification. Unfortunately, since some operations either had substantial changes in exposure or were no longer in existence, we felt the data was too incomplete to attempt to link a numerical value with each specific job category. However, the data were useful in providing an indication of the average quantitative value associated with the qualitative categories and in providing an indication of the validity of the qualitative assessment. For aliphatics, measurements were taken on **161** exposure categories. For each of these categories we had quantitative estimates of exposure for aliphatic chains from length five to twenty (C_5 - C_{20}). The lowest quartile of quantitative exposure measures were all for job categories classified in the low or insignificant exposure category and for the second quartile **95%** of the measurements were for jobs in the low exposure category. In the third quartile (second highest quartile), 38% of the measurements were classified as medium exposure and the rest were classified as low or insignificant. The highest quartile based for the quantitative IH values contained all five of the jobs classified as high

exposure and a majority of the remaining jobs were classified as medium exposure. For aliphatic exposure there appeared to be reasonably good agreement between the quantitative measurement and the qualitative category.

For aromatic exposure a comparison between the qualitative categories and quantitative values was more problematic. First, the industrial hygienists did not consider any single quantitative measure for aromatic hydrocarbon exposure to be an adequate representation of the qualitative index since aromatic exposure includes both "pitch" and "non-pitch" exposure. Pitch exposure occurs primarily in the reduction plants and is primarily aromatics of three rings or higher. Solvents are one of the primary sources of "non-pitch" hydrocarbon exposure and consist primarily of the one ringed aromatics (benzene, toluene and xylene) and some two and three ringed aromatics. An individual ranking was not done of "pitch" and "non-pitch" hydrocarbon exposure so an appropriate comparison of qualitative and quantitative values could not be done. Second, the amount of quantitative data was limited. There were only 8 quantitative measurements available for jobs with exposure to only "nonpitch' aromatics.

Although there is more data for jobs associated with pitch, the range of values for present day operations is limited. Of the 152 jobs with an IH measure that had no exposure to 'nonpitch", aromatic hydrocarbons 130 (85.5%) were less than 30% below the PEL. This is a reflection of the improvements in levels of coal tar pitch in present day reduction plants but it provides little information for comparison to the qualitative categories where the assignment of "medium" and "high" often were based

on exposure representing historical conditions. In fact, there were no measurements taken for jobs classified as having high aromatic exposure since no comparable environments were available in current operations.

On August 18, we became aware of some errors in the exposure data given to us by Alcoa. These errors could impact on the results and conclusions of this report. However, there was not enough time to incorporate any changes which would result from a reanalysis of the data into this document.

Risk Associated with Hydrocarbon Exposure

The results of fitting a conditional logistic model with hydrocarbon exposure as an independent variable is summarized in Table 7. The estimated risk for those with some hydrocarbon exposure to those with no hydrocarbon exposure is 1.04. Those with low or medium exposure show no greater risk than those with no hydrocarbon exposure.. However, for those with high hydrocarbon exposure the estimated risk is 2.55 ($p = .02$). When a term for low to medium exposure and a term for high exposure are included in the model (Model 4) and compared to those with no hydrocarbon exposure, the association of kidney cancer and hydrocarbon exposure remains significant ($p = .05$). The risk is only evident for those with high hydrocarbon exposure and those with low to medium exposure actually have a risk that is slightly below the baseline group. Although high exposure is associated with kidney cancer risk there does not appear to be a relationship with duration of

exposure. There is no relationship of kidney cancer mortality with either cumulative years of hydrocarbon exposure (Model 5) or cumulative years of high hydrocarbon exposure (Model 6).

The same models summarized in Table 7 were fit to the data using aromatic hydrocarbon exposure as the independent variable (Table 8) and aliphatic hydrocarbon exposure as the independent variable (Table 9). Again, it is the high exposure categories that show the greatest risks for kidney cancer. For aromatic exposure, the relative risk of those ever exposed to high levels of aromatics to those never exposed to high levels was 1.61 ($p = .38$). When a term for low to medium exposure is added to the model (Model 4) the high exposure category has a risk of 1.67 compared to those never exposed and the p-value associated with the joint aromatic hydrocarbon coefficient remains nonsignificant. For aliphatics [Table 9) the relationship with kidney cancer is also strongest for those with high exposure ($RR = 4.10$, $p < .01$). There remains no association with length of time with aliphatic exposure (Model 5) or length of time with high aliphatic exposure (Model 6). Although the high aliphatic exposure category had increased risk, there appeared no increase with low or medium exposure.

When a dose-response relationship was tested using the relative weights of 0, 1, 2, 3 for none, low, medium and high exposure, respectively, neither aliphatic or aromatic hydrocarbon exposure showed a statistically significant excess. A reanalysis for aliphatics was done by selecting weights corresponding to mean values of the industrial hygiene measurements in the various exposure categories. This

corresponded to 3, 9, and 26 mg/m^3 for low, medium and high exposures, respectively. There was no significant trend of kidney cancer and exposure.

Adjustment for Nonoccupational Factors

Survey information was available for 59 cases and 242 controls. The primary purpose of the questionnaire was to control for potential confounding variables that may distort the relationship of exposure and risk of kidney cancer. A copy of the questionnaire appears as Appendix B. When the variables from the questionnaire are included in the analysis it must be done on the subset of patients with information available. The risk of kidney cancer due to high hydrocarbon exposure in the subgroup of patients responding to the questionnaire was 3.24, $p = .01$, which is similar to the estimated risk for the entire population (RR =.2.55, $p = .02$). A formal test was conducted to determine whether the risk of kidney cancer for those with high hydrocarbon exposure differed for those with a survey and those without a survey. The model used to test this hypothesis included a variable indicating whether a survey was done, a variable indicating high hydrocarbon exposure, and a variable measuring the interaction for these two factors. The variable for interaction was not significant, indicating there is no statistically significant difference in the risk of kidney cancer associated with high hydrocarbon exposure between those responding to the questionnaire and those not responding.

Logistic regression was used to test whether high hydrocarbon exposure was related to kidney cancer after adjusting for potential confounders. Potential confounders obtained from the questionnaire include smoking history, use of diuretics, use of aspirin analgesics, use of aspirin free analgesics and obesity. We measured obesity using the index weight/(height)^2 where weight was in kilograms and height was measured in meters. The model used a binary variable to characterize individuals that were overweight ($\geq$ 30.0 kg/m^2). In addition, adjustment for possible geographic variability was made by including an extra term in the model which controlled for plant location. This variable grouped together those plants which had jobs with high hydrocarbon exposure. Table 10 summarizes the effect of adjusting the risk of kidney cancer from high hydrocarbon exposure for various models. The estimated risk ranges from **2.74** to 3.37 when adjusted by single factors and in all cases the risk due to high hydrocarbon exposure remains statistically significant (Models 2 through **8).** The results remain unchanged when simultaneously adjusting by several factors. All of the models adjusting for multiple confounders have an estimated risk of high hydrocarbon exposure of at least 2.99 and all indicate the hydrocarbon effect is statistical significant. Model 13, which includes all the potential confounders, has an estimated relative risk of 4.28 **(p = .014)** for high hydrocarbon exposure. The corresponding 95% confidence interval is (1.31, 13.99). Both smoking and the use of aspirin-free analgesics also show increased risk of kidney cancer but including them in the model does not eliminate the risk due to hydrocarbon exposure. The inverse relationships of kidney cancer risk with diuretics usage and obesity probably occurs because these

factors have a stronger relationship with cardiovascular disease, a condition that is prevalent in the control group.

Table 11 summarizes the results of incorporating potential confounders in the model when the measure of exposure is high aromatic exposure. The estimates of kidney cancer risk associated with high aromatic exposure increase when adjustment is made for potential confounders. The estimated risk after adjustment for all potential confounders (Model 13) is 4.12 ($p = .08$). The corresponding **95%** confidence interval is (.80, 21.94).

Table 12 summarizes these same models applied to the exposure variable indicating high aliphatic exposure. The estimated risk of kidney cancer for those with high aliphatic exposure remains consistently above 3.0. When all potential confounders are included in the model (Model 13) the estimated risk for kidney cancer is **4.27** from high exposure to aliphatics ($p = .048$). The corresponding **95%** confidence interval is (1.01, 18.15).

Of the 22 workers with high exposure to aromatics, six (27%) died from kidney cancer. All were white males with an age at death ranging from 62-82 years. Several of the workers were in a high exposure area for only a short period of time, but all had long periods of time with hydrocarbon exposure (minimum 12 years). Three of the workers had at least 28 years of exposure to jobs with medium or high levels of aromatic hydrocarbon exposure. All of the jobs classified as having high exposure to aromatics had exposure to coal tar pitch volatiles that occurred in older reduction plant operations.

Of the 20 workers with high exposure to aliphatics 9 **(45%)** died from kidney cancer. All of the workers were white males with an age at death that ranged between 62 and 72. Five of the nine deaths were for workers at Massena. Only one of the workers had high exposure to aromatics and three were classified as having no aromatic exposure. The median length of time to aliphatic exposure was 19 years. Eight of these nine workers had employment in jobs with high aliphatic exposure in the wire, rod and bar or tube mills.

Discussion

The suggestion that there is a risk of kidney cancer from hydrocarbon exposure, is not a new one. Animal studies have shown a relationship of exposure to hydrocarbons and kidney cancer[28,29]. In addition, several epidemiological studies have demonstrated a risk of kidney cancer with hydrocarbon exposure identified as a possible causative factor. In a cohort study of coke oven workers, there was a relative risk of **7.49** based on **8** observed deaths [5,30]. Coke oven workers are exposed to aromatic hydrocarbons and much of the original concern with cancer in aluminum reduction workers is related to exposure to aromatic hydrocarbons. McLaughlin *et al.* [31] reported a relative risk of 1.6 for workers exposed to petroleum, tar and pitch products in a population based case-control study of renal carcinoma with **495** cases and **697** controls. In a population based case-control study with 210 cases and 210 matched controls, Kadamani et *al.* [32] reported a relative risk of 1.6 in males exposed

to hydrocarbons but no excess in females. Exposure was assessed by two industrial hygienists who assigned a subjective score of 0 to 5 for each job in the work history. Each individual then had a cumulative exposure score.

Cohort studies of aluminum workers have also identified excesses in kidney cancer although the results were not always statistically significant. Rockette and Arena [10] found an excess of kidney cancer in prebake plants (SMR = 151.3). However, excesses did not appear to be associated with potroom or carbon department jobs. In a large cohort of Norwegian reduction plant workers [33] there was an excess risk of kidney cancer of 20%..Two different studies of Canadian aluminum reduction plant workers [34,35] show excesses of 46% and 36%, respectively. Thus, there appears to be a consistent, although small, excess of kidney cancer in reduction plant workers. This consistent excess in kidney cancer was noted by Doll in a previous review of mortality patterns in aluminum reductionplant workers [36].

Although these studies as well as other have found excess cancer risk that may be due to hydrocarbon exposure, the investigators of some occupational groups with hydrocarbon exposure have produced inconsistent estimates of cancer risk. In particular, Harrington [18] considers 'the studies of exposure to gasoline to be inconsistent in regard to estimates of cancer risk. Savitz and Moure [37] attribute the inconsistent results in studies of oil refinery workers to methodological shortcomings. In particular, exposure is often not assessed, latency periods are not considered in many of the analyses, and there is often no attempt to adjust for potential confounding variables. In summary there have been many studies assessing the

association of hydrocarbon exposure and cancer risk, many of which have been positive and some of which have identified an excess of kidney cancer. However, a number of negative studies as well as methodological shortcomings in some of the studies which were conducted have prevented any general conclusions that a wide range of hydrocarbons result in an excess kidney cancer risk.

In regard to the excess kidney cancer risk found in the present study, there is always a possibility of bias in a case-control study. However, efforts were made to control bias. We matched on the factors age, race, sex, year of birth and death year to avoid possible confounding by these factors. The industrial hygienists were blinded in regard to whether the job entry was taken from the work history of a case or a control when making the exposure assessment. Therefore, misclassification errors were likely to be nondifferential between cases and controls. Errors of this type tend to lessen the chance of an association of outcome with exposure.

An attempt to control for nonoccupational confounders was done using questionnaire data. Several issues arise when incorporating data obtained from questionnaires, Information on confounders is usually difficult to obtain and there is usually a loss in statistical power due to exclusion of subjects from the analysis of those not responding. There is also the possibility that the subset of those who respond is not representative of the entire group. In this study, non-responders had a slight tendency to die in earlier years, however, there was not a sufficient difference to affect risk estimates. Furthermore, the estimates of risk from high hydrocarbon exposure were not significantly different in the group of responders and the group of

nonresponders. Smoking [38] has been associated with kidney cancer. The validity of smoking information obtained from surrogates has been discussed in the literature. For adults, Pickle et *al.* [38] report that the most complete information is collected when the subject's spouse or offspring is interviewed and when the data is consolidated into broad categories. In the present study, 91.7% of the respondents were a spouse or offspring of the decedent. An attempt was made not to have questions that were too specific in the interview because of the problems associated with surrogates providing detailed information on smoking habits. Age started smoking was categorized to the appropriate decade of life and estimates of the number of cigarettes per day were grouped into broad categories. Over ninety percent of those responding to the questionnaire indicated an age when the subject first started smoking and the amount of cigarettes smoked per day. Although the reliability of surrogate information is always an issue, Rojot and Redi [40] found that smoking information from next of kin was more reliable when deaths occurred recently. Telephone interviewing of the surrogates occurred within five years of the subjects death for 52% of the deaths in this study. None of the deaths occurred more than ten years prior to the interviews.

Even if one questions the validity of the smoking data, it is unlikely given the large number of smokers or ex-smokers and the magnitude of the estimated risk, that the risk for hydrocarbon exposure could be entirely due to confounding. Assuming the average risk of kidney cancer in a mixed population of smokers and ex-smokers is 3:0, and 85% of the controls are smokers or ex-smokers then even if 100% of the cases were smokers or ex-smokers the increase in risk estimate due to confounding

would result in an estimate of 1.15 [41], which is far below our estimates of risk due to hydrocarbon exposure.

Other nonoccupational risk factors for kidney cancer are less well established. Several investigators have suggested an association of obesity with an increased risk of kidney cancer [42-46]. Animal and human studies have shown a positive association between the ingredients found in diuretics and renal carcinoma [46,47]. Other studies have indicated an increase of kidney cancer in patients using certain based analgesic compounds [48-52]. Use of aspirin-free analgesics in the present study had an associated risk of kidney cancer of 1.96 (p.= .22) but there was no imbalance among cases and controls that would alter the elevated risk of those exposed to high levels of hydrocarbons. When aspirin-free analgesic usage was included in the model, the adjusted estimate of risk for high exposure to hydrocarbons remained significant.

When the risk for hydrocarbon exposure is adjusted for multiple factors the hydrocarbon risk remains statistically significant. Smoking and aspirin free analgesics are associated with excess risk of kidney cancer which is consistent with the literature. Weight and diuretic are inversely related to kidney cancer risk. This latter observation may be an artifact since these two factors would also be expected to be higher in individuals dying from cardiovascular disease. Cardiovascular deaths comprise a majority of the control group.

In addition to bias, excess risk sometimes occurs due to random variability. Over reliance on the p-value can lead to overemphasis of high relative risks in occupational mortality studies that test a large number of hypotheses. Due in part to

the Healthy Worker Effect, the effect of multiple comparisons on the probability of a false positive finding is greater in proportionate mortality studies [53]. This was a potential problem in the originally conducted PMR study [1]. However, in the present study which could be considered the "hypothesis testing" phase rather than "hypothesis generating" phase the probability of a false positive finding is more accurately reflected by the significance level associated with the risk

Although the present study indicates that individuals with high exposure to hydrocarbons are at excess risk from kidney cancer several limitations of the study should be noted. First, all studies of this type require estimates of exposure in some situations where actual measurements are presently unavailable. This is because operations and exposures have changed over time and present exposures may not be an adequate representation of historical ones. In the present study approximately 25.0% of the jobs had actual measurements taken. For those with measures there was reasonably good agreement between the a priori estimate of aliphatic exposure (classified as low, medium and high) and the quantitative measure. However, such estimates of exposure must always be viewed as an approximation. If the misclassification is nondifferential then the effect of poor estimates will make it harder to identify a dose-response. For aromatic exposure, there was more difficulty in comparing quantitative and qualitative values. Historically the reduction jobs had higher levels of aromatic exposures than current operations. Also, there is a possibility that some job classifications may not have adequately considered the lower ringed compounds since historically the aluminum industry has given emphasis to the

higher ringed compounds. Some of the hydrocarbon exposure included solvents. Exposure to solvents is particularly difficult to assess [54]. There may be large variations in an individual's exposure during the workday and there can be considerable variability among individuals even when performing the same task. It is common to use solvents in mixtures and exposure to specific ,solvents or even classes of compounds are often difficult to assess.

A second issue relates to delineating the risk for aromatic and aliphatic exposure. For many jobs both exposures are present and distinguishing risk is difficult. In the multivariate model both aliphatics and aromatics have an excess risk but only for aliphatics is the result statistically significant. Because of the confounding exposure occurring in the same job and because workers often held jobs with varying types of hydrocarbon exposure, it is difficult to separate the effects of risk of the aliphatic and aromatic compounds.

Even within the categories of aliphatic and aromatic hydrocarbons there can be considerable variability in job exposure. In this study the aromatic exposure was primarily coal tar pitch and the high category of coal tar pitch was assigned to jobs in the Soderberg process. Nonpitch aromatic exposure was due primarily to solvents. Since all the high exposure jobs were due to pitch the kidney cancer excess in the high aromatic category is probably due to pitch exposure.

In this study the higher categories of aliphatic exposure were primarily due to rolling and lubricating oils. There is increasing evidence that machining oils or oil mists [21-24,28,55] can cause cancer although the most frequently identified causes are

cancer of the skin and digestive cancer. In this regard cancer of the kidney has not been established as associated with machining oils and further investigation is needed.

Finally, there does not appear to be a dose-response relationship. Low and medium exposures show no excess risk. This could be due to a threshold or a result of some misclassification at the lower dose levels. Similarly, some of the workers with high hydrocarbon exposure had short exposure at these high intensities. Although it may be that high intensity is more important than cumulative dose, this is difficult to evaluate because those with high intensity hydrocarbon exposure tended to have long term aliphatic or aromatic exposure at lower levels.

In summary, epidemiological studies are always subject to limitations and investigations of hydrocarbon exposure are even more difficult because of the difficulties in measuring exposure. However, the conclusion that the high kidney cancer risk in the present study is related to high hydrocarbon exposure is strengthened by the following factors:

1) The magnitude of the risk is relatively high making it less likely to be induced by unknown confounders.

2) The risk remains significant even after controlling for potential nonoccupational confounders.

3) The quality of the exposure assessment is good compared to most previous studies of hydrocarbon exposure. The categorization was done blinded as to case or control status so errors are unlikely to introduce bias.

The foregoing analysis and conclusions is based on data we had available as of August 18, 1993. On August 19, we received information from Alcoa that there were some errors in the classification. Although the percentage of jobs misclassified is small, these errors could have an impact on the results and conclusions. In the short amount of time available, we could not assess the magnitude of the impact.

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FIGURE 1
Year of Birth for Study Participants

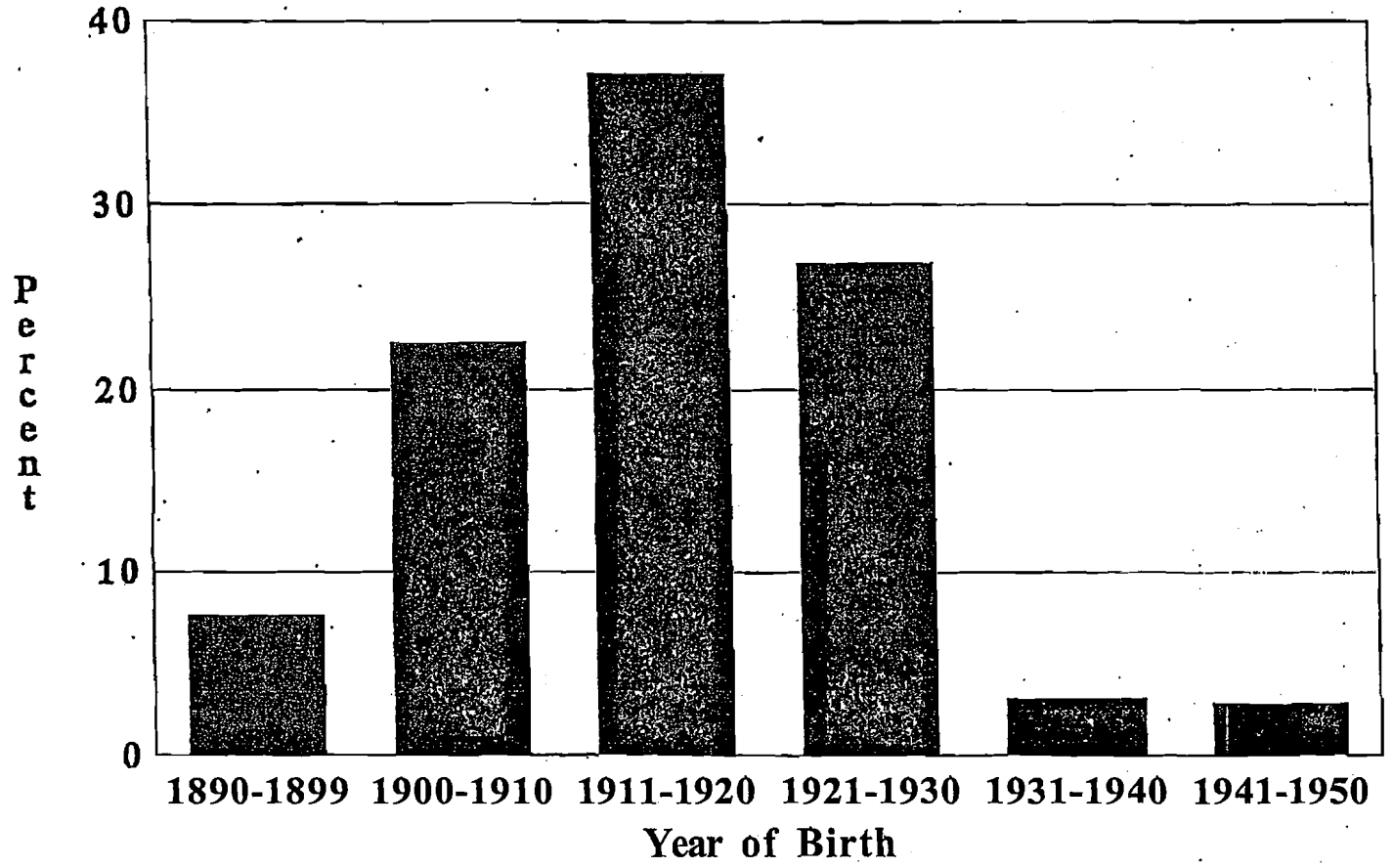

FIGURE *2*
Year of Death for Study Participants

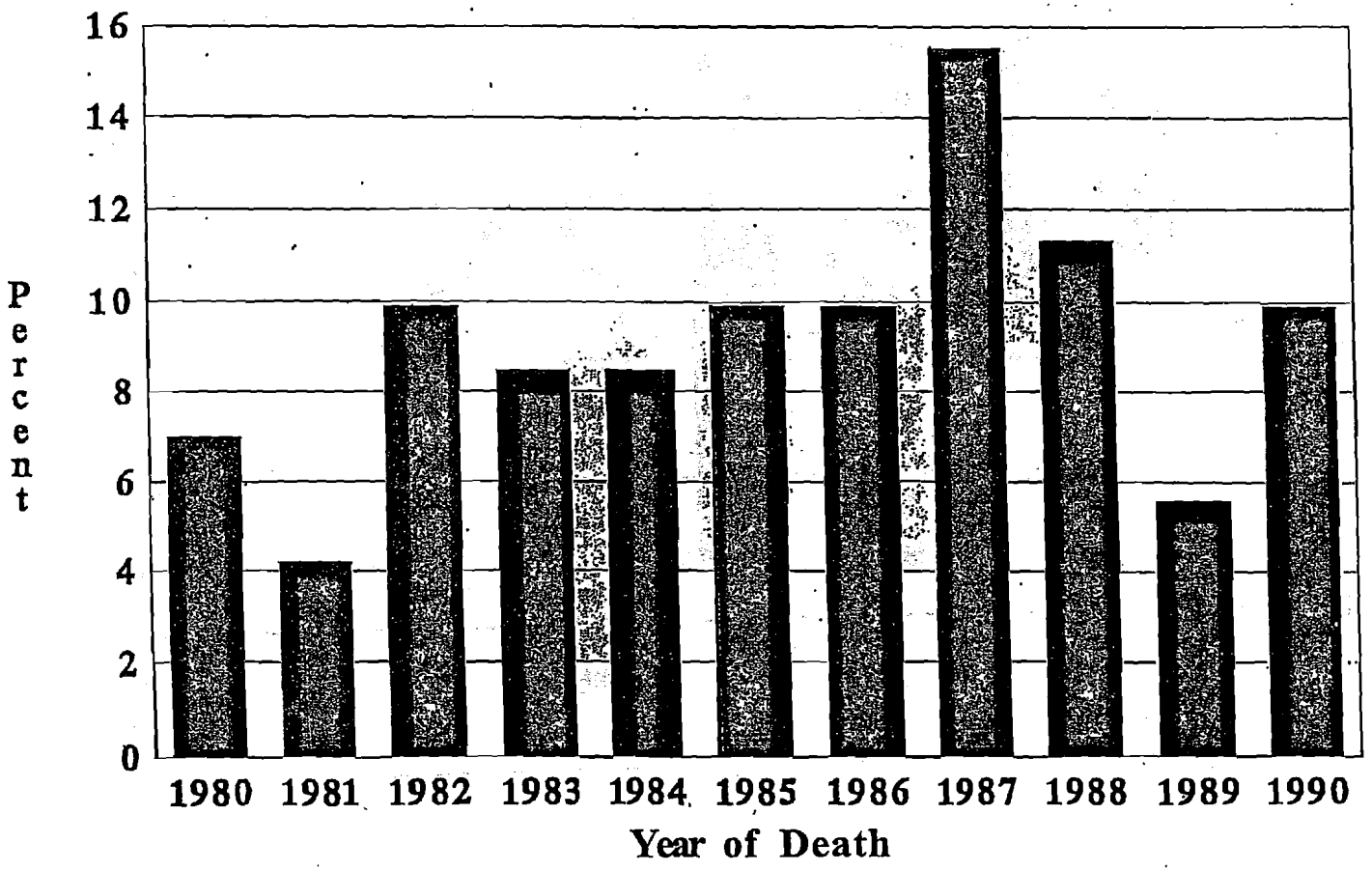

FIGURE 3
Age at Death for Study Participants

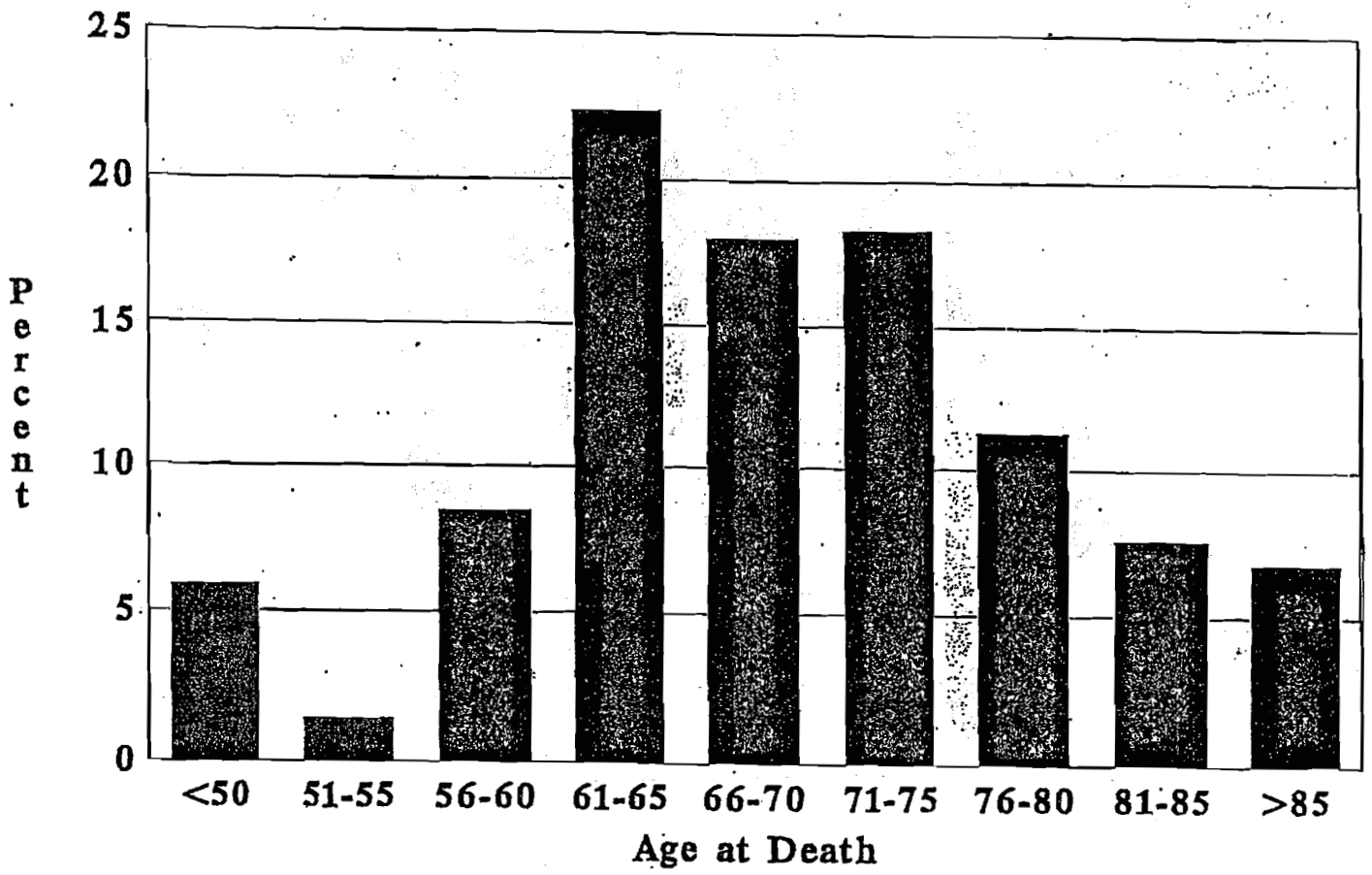

Table 1

Number of Matched Sets Needed to Achieve a Specified Power and Relative Risk Assuming a Two-Sided $\alpha = .05$ Test, A Matching Ratio of 1:4 and the Proportion of Exposed Controls Is 30%

	Power		
Relative Risk	80%	90%	95%
2.0	87	117	144
2.5	49	66	82
3.0	35	46	57

Table 2

Smoking Patterns of Study Population

	Number of Respondents	Cases §	Control §
Ever smoked	294	84.8	85.4
Ever smoked cigarettes	301	74.6	78.9
Ever smoked a pipe	298	25.4	30.1
Ever smoker cigars	300	15.2	12.4
Age stopped smoking	160	53.7	52.3
Started smoking in teens	213	77.3	63.9
Smoked more than pack/day	212	38.5	34.7

* $p < .05$
** $p < .01$
§ Numbers presented are for percentages of cases and controls with the specified characteristic,
Age stopped smoking is given in years.

Table 3

Comparison of Selected Patient Characteristics

	Number of Respondents	Cases	Control
Age (years)	354	69.0	69.0
Weight (pounds)	282	181.9	176.7
Overweight (percent) *	295	16.9	33.0
Aspirin use (percent) +	285	10.3	21.6
Aspirin-free analgesic use (percent)	287	10.3	6.6
Diuretics use (percent) **	269	16.7	35.4
Height (inches)	299	70.1	69.5

\+ $p < .10$
* $p < .05$
** $p < .01$

Table 4

Distribution of Deaths by Plant

Plant	Frequency	Percent
ALCOA	106	29.9
ATC	2	.6
BADIN	8	2.3
BAUXITE	8	2.3
BRIDGEPORT	1	.3
CHILLICOTHE	1	.3
CLEVELAND	18	5.1
CORONA	1	.3
CHESSONA	15	4.2
DAVENPORT	16	4.5
EAST ST. LOUIS	4	1.1
EDGEWATER	11	3.1
EDISON	6	1.7
FRANKLIN	2	.6
LAFAYETTE	16	4.5
LOGANS FERRY	1	.3
MARSHALL	1	.3
MASSENA	34	9.6
MOBILE	7	2.0
NEW KENSINGTON	29	8.2
POINT COMFORT	17	4.8
RICHMOND	7	2.0
ROCKDALE	11	3.1
ROSICLARE	3	.8
VANCOUVER	10	2.8
VERNON	6	1.7
WARRICK	10	2.8
WENATCHEE	3	.8

Table 5

Distribution of Aliphatic Exposure Level by Aromatic Exposure Level
For the Classified Job Categories

Aphatic Eposure Level	Aromatic Exposure Level				
	None	low	ium	High	tal
No	1282 (66.4)§	4 (2)	--	-	1 6 6.)
Low	328 (17.0)	52 (2.7)	45 (2.3)	2 (1)	4Z7 (Z2.1)
Low / Mediu m	6 (.3)	-	-	--	6 (.3)
Mediu m	3 18.4)	3 [2)	8 (.4)	12 (6)	186 (9.6)
H'gh	20 (1. 0)	4 (2)	-	2 (1)	26 (1 .4)
Total	1799 (93.2)	63 (3.3)	53 (2.7)	16 (8)	1931 (100.0)

§ Percentages are shown in parentheses

Table 6

Distribution of Hydrocarbon Exposure in Study Population

Type of Hydrocarbon Exposure	Percent of All Subjects
Aliphatics	76.8
Aromatics	36.7
Aliphatics or Aromatics	76.8
Medium to High Aliphatics	46.0
Medium to High Aromatics	22.0
Medium to High Exposure to Aliphatics or Aromatics	52.8
High Aliphatics	5.6
High Aromatics	6.2
High Exposure to Aliphatics or Aromatics	11.3

Table 7'

Relationship of Kidney Cancer to Hydrocarbon Exposure

Model	Variable	β	S.E.	RR	p-value	95% CI
1	Ever Hydrocarbon / Never	.043	.330	1.04	.90	(.55, 2.00)
2	Ever Medium or High Hydrocarbon / Never	-.040	.281	.96	.88	(.55, 1.67)
3	Ever High Hydrocarbon / Never	.935	.377	2.55	.02	(1.22, 5.34)
4	No Hydrocarbon '(baseline)			1.0	.05	
	Low / Medium Hydrocarbon	-.108	.342	.90		(.46, 1.76)
	High Hydrocarbon	.852	.460	2.34		(.95, 5.77)
5	Years Of Hydrocarbon Exposure	.840 E-2	.011	1.00	.45	(.99, 1.03)
6	Years Of High Hydrocarbon Exposure	-.014	.046	.99	.76	(.90, 1.08)

Table 8

Relationship of Kidney Cancer to Aromatic Exposure

Model	Variable	β	S.E.	RR	p-value	95% CI
1	Ever Aromatic / Never	.153	.287	1.16	.59	(.66, 2.04)
2	Ever Medium or High Aromatic / Never	.039	.333	1.04	.91	(.54, 2.00)
3	Ever High Aromatic / Never	.478	.526	1.61	.38	(.58, 4.52)
4	No Aromatic (baseline)			1.0	.65	
	Low / Medium Aromatic	.081	.304	1.08		(.60, 1.97)
	High Aromatic	.510	.539	1.67		(.58, 4.79)
5	Years Of Aromatic Exposure	.020	.015	1.02	.20	(.99, 1.05)
6	Years Of High Aromatic Exposure	-.038	.060	.96	.48	(.86, 1.08)

Table 9

Relationship of Kidney Cancer to Aliphatic Exposure

Model	Variable	β	S.E.	RR	p-value	95% CI
1	Ever Aliphatic / Never	.043	.330	1.04	.90	(.55, 2.00)
2	Ever Medium or High Aliphatic / Never	-.056	.283	.95	.84	(.54, 1.65)
3	Ever High Aliphatic / Never	1.410	.514	4.10	.007	(1.50, 11.22)
4	No Aliphatic (baseline)			1.0	.025	
	Low / Medium Aliphatic	-.054	.337	.95		(.49, 1.83)
	High Aliphatic	1.37	.582	3.92		(1.25, 12.27)
5	Years Of Aliphatic Exposure	.808 E-2	.011	1.00	.47	(.99, 1.03)
6	Years Of High Aliphatic Exposure	.079	.097	1.08	.43	(.90, 1.31)

Table 10

Effect of Confounding Factor on Kidney Cancer Risk From High Hydrocarbon Exposure

Model	Covariates in Model	Risk for Confounder	High Hydrocarbon Risk			observations +	
			RR	95% CI	p-value	n	sets
1	No covariates	--	2.55	(1.22, 5.34)	.016	354	71
2	Ever Any Smoking.	1.14	3.20	(1.29, 7.96)	.012	298	58
3	Ever Cigarette Smoking	.81	3.13	(1.27, 7.73)	.014	301	58
4	Plant *	.62	3.18	(1.42, 7.091	005	354	71
5	Diuretics	.33	2.91	(1.08, 7.80)	.034	269	52
6	Aspirin Analgesics	.44	3.37	(1.31, 8.65)	.011	288	57
7	Aspirin-free Analgesics	2.18	3.21	(1.30, 7.91)	.011	287	57
8	Obesity	.81	2.74	(1.04, 7.22)	.042	281	53
9	'Ever Any Smoking	1.98	3.70	(1.27, 10.76)	.015	258	51
	Diuretics	.33					
	Aspirin Analgesics	.48					
	Aspirin-free Analgesics	3.52					

Model	Covariates in Model	Risk for Confounder	High Hydrocarbon Risk			observations +	
			RR	95% CI	p-value	n	sets
10	Ever Cigarette Smoking	1.39	3.46	(1.21, 9.89)	.020	258	51
	Diuretics	.33					
	Aspirin Analgesics	.47					
	Aspirin-free Analgesics	3.62					
11	Ever Any Smoking	2.59	3.30	(1.09, 10.05)	.033	246	48
	Diuretics	.36					
	Aspirin Analgesics.	.50					
	Aspirin-free Analgesics	2.74					
	Obesity	.86					
12	Ever Cigarette Smoking	1.60	2.99	(1.02, 8.81)	.045	246	48
	Diuretics	.35					
	Aspirin Analgesics	.48					
	Aspirin-free Analgesics	3.04					
	Obesity	.77					

Model	Covariates in Model	Risk for Confounder	High Hydrocarbon Risk			observations +	
			RR	95% CI	p-value	n	sets
13	Ever Any Smoking	3.02	4.28	(1.31, 13.99)	.014	246	48
	Diuretics	.37					
	Aspirin Analgesics	.48					
	Aspirin-free Analgesics	3.11					
	Obesity	.86					
	Plant *	.52					
14	Ever Cigarette Smoking	1.93	3.90	(1.22, 12.48)	.020	246	48
	Diuretics	.36					
	Aspirin Analgesics	.45					
	Aspirin-free Analgesics	3.44					
	Obesity	.80					
	Plant *	.52					

§ . significance level of aliphatic exposure after adjusting for other covariates in the model
+ number of subjects and matched sets in the model
* **Alcoa, Cressona, Massena,** Point Comfort and New Kensington combined verses remaining plants

Table 11

Effect of Confounding Factor on Kidney Cancer Risk From High Aromatic Exposure

Model	Covariates in Model	Risk for Confounder	High Aromatic Risk			observations +	
			RR	95% CI	p-value	n	sets
1	No covariates	--	1.61	(.58, 4.52)	.375	354	71
2	Ever Any Smoking	.98	2 1 2	(.57, 7.89)	.269	298	58
3	Ever Cigarette Smoking	.74	2.20	(.59, 8.20)	.250	301	58
4	Plant	.74	1.92	(.64, 5.74)	.255	354	71
5	Diuretics	.35	2.56	(.63, 10.41)	.190	269	52
6	Aspirin Analgesics	.43	2.70	(.66, 11.02)	.168	288	57
7	Aspirin-free Analgesics	1.99	2.24	(.60, 8.34)	.236	287'	57
8	Obesity	.78	2.66	(.66, 10.70)	.169	281	53
9	Ever Any Smoking	1.81,	3.63	(.74, 17.83)	.104	258	51
	Diuretics	.35					
	Aspirin Analgesics	.48					
	Aspirin-free Analgesics	3.22					

Model	Covariates in Model	Risk for Confounder	High Aromatic Risk			observations +	
			RR	95% CI	p-value	n	sets
10	Ever Cigarette Smoking	1.32	3.37	(.70, 16.13)	.121	258	51
	Diuretics	.35					
	Aspirin Analgesics	.47					
	Aspirin-free Analgesics	3.31					
11	Ever Any Smoking	[illegible]	3.64	(.73, 18.13)	.104	246	48
	Diuretics	[illegible]					
	Aspirin Analgesics	.50					
	Aspirin-free Analgesics	2.59					
	Obesity	.71					
12	Ever Cigarette Smoking	1.50	3.29	(.69, 15.64)	.127	246	48
	Diuretics	.38					
	Aspirin Analgesics	.48					
	Aspirin-free Analgesics	2.86					
	Obesity	.66					

Model	Covariates in Model	Risk for Confounder	High Aromatic Risk			observations +	
			RR	95% CI	p-value	n	sets
13	Ever Any Smoking	2.42	4.12	(.80, 21.94)	.081	246	48
	Diuretics	.39					
	Aspirin Analgesics	.51					
	Aspirin-free Analgesics	2.61					
	Obesity	.68					
	Plant *	.75					
14	Ever Cigarette Smoking	1.65	3.88	(.76, 19.71)	.094	246	48
	Diuretics	.38					
	Aspirin Analgesics	.50					
	Aspirin-free Analgesics	2.88					
	Obesity	.65					
	Plant *	.72					

§ significance level of aliphatic exposure after adjusting for other covariates in the model
\+ number of subjects and matched sets in the model
* Alcoa, Massena and Point Comfort combined verses remaining plants

Table 12

Effect of Confounding Factor on Kidney Cancer Risk From High Aliphatic Exposure

Model	Covariates in Model	Risk for Confounder	High Aliphatic Risk			observations +	
			RR	95% CI	p-value	n	sets
I	No covariates	.--	4.10	(1.50, 11.22)	.007	354	71
2	Ever Any Smoking	1.07	4.27	(1.35,13.47)	.012	298	58
3	Ever Cigarette Smoking	.77	4.10	(1.30,12.93)	.015	301	58
4	Plant *	.64	4.94	(1.74, 14.05)	.003	354	71
5	Diuretics	.33	3.18	(.92, 10.96)	.069	269	52
6	Aspirin Analgesics	.44	4.84	(1.39, 16.86)	.010	288	57
7	Aspirin-free Analgesics	2.17	4.23	(1.34,13.30)	.013	287	57
8	Obesity	.78	3.61	(.99, 13.13)	.050	281	53
9	Ever Any Smoking	1.75	4.34	(1.13,16.56)	.030	258	51
	Diuretics	.33					
	Aspirin Analgesics	.47					
	Aspirin-free Analgesics	3.45					

Model	Covariates in Model	Risk for Confounder	High Aliphatic Risk			observations +	
			RR	95% CI	p-value	n	sets
10	Ever Cigarette Smoking	1.28	4.18	(1.10, 15.87)	.034	258	51
	Diuretics	.33					
	Aspirin Analgesics	.46					
	Aspirin-free Analgesics	3.53					
11	Ever Any Smoking	2.21	3.59	(.88, 14.61)	.074	246	48
	Diuretics	.35					
	Aspirin Analgesics	.50					
	Aspirin-free Analgesics	2.75					
	Obesity	.82					
12	Ever Cigarette Smoking	1.45	3.37	(.84, 13.51)	.086	246	48
	Diuretics	.35					
	Aspirin Analgesics	.47					
	Aspirin-free Analgesics	3.00					
	Obesity	.75					

Model,	Covariates in Model	Risk for Confounder	High Aliphatic Risk			observations +	
			RR	95% CI	p-value	n	sets
13	Ever Any Smoking	2.53	4.27	(1.01, 18.15)	.048	246	48
	Diuretics	.37					
	Aspirin Analgesics	.47					
	Aspirin-free Analgesics	3.05					
	Obesity	.77					
	Plant *	.60					
14	Ever Cigarette Smoking	1.64	3.47	(.95, 16.55)	.057	246	48
	Diuretics	.37					
	Aspirin Analgesics	.45					
	Aspirin-free Analgesics	3.33					
	Obesity	.70					
	Plant *	.61					

§ significance level of aliphatic exposure after 'adjusting for other covariates in the model
+ number of subjects and matched sets in the model
* Alcoa, Massena, Cressona, and New Kensington combined verses remaining plants

Appendix A: Distribution of Deaths by ICDA Codes

Appendix A

Distribution of Deaths for All Subjects by Four Digit International Classification of Disease Codes

ICDA	Frequency	Percent
11.9	2	.6
38.9	2	.6
189.0	66	18.6
189.1	1	.3
189.2	4	1.1
250.0	8	2.3
250.1	1	.3
289.9	1	.3
303.0	1	.3
331.0	4	1.1
332.0	2	.6
333.4	1	.3
335.2	1	.3
402.9	1	.3
410.0	79	22.3
412.0	1	.3
414.0	34	9.6
414.8	2	.6
414.9	14	4.0
415.1	4	1.1
423.9	2	.6
425.4	6	1.7
426.8	1	.3
427.3	2	.6
427.5	9	2.5
427.9	2	.6
428.0	7	2.0
429.2	10	2.8
431.0	3	.8
432.1	1	.3
434.0	1	.3
434.9	3	.8
436.0	12	3.4
437.0	2	.6

ICDA	Frequency	Percent
437.1	1	.3
437.9	1	.3
438.0	1	.3
440.9	1	.3
441.1	1	.3
441.3	4	1.1
441.5	1	.3
443.9	1	.3
454.9	1	.3
485.0	1	.3
486.0	6	1.7
490.0	1	.3
492.0	3	.8
496.0	9	2.5
513.0	1	.3
514.0	1	.3
518.8	2	.6
532.9	1	.3
533.4	1	.3
557.0	1	.3
560.1	1	.3
572.8	1	.3
578.9	1	.3
737.3	1	.3
785.5	2	.6
798.2	1	.3
799.1	1	.3
799.9	6	1.7
812.9	1	.3
816.0	1	.3
819.0	1	.3
819.9	1	.3
910.8	1	.3
928.9	1	.3
955.0	1	.3
955.4	3	.8
965.1	1	.3

Appendix B: Telephone Interview Questionnaire

DATE: _____

Aluminum Workers Health Study
Questionnaire

Worker's name:

Social Security Number:

Please fill in the name and phone number of the person answering the questions

Spouse _____

Child _____

Sibling _____

Other relative _____

Other _____

Phone number: ( ) _____

Please circle correct responses.

1. How tall was he?

   Feet _____ Inches _____ Unknown

2. Throughout most of his adulthood, what was his usual weight?

   Lbs. _____ Unknown

3. Throughout most of his adulthood, how would you classify his weight?

   Under-weight
   Slightly under-weight
   Just right
   Over-weight
   Very much over-weight
   Unknown

4. Did he ever take prescription diuretics or water pills?

   Yes
   No
   Unknown

5. The following are several reasons for taking diuretics. Did he take medication for any of the following reasons.

   To lower blood pressure
   For heart disease
   To lose weight
   To reduce swelling
   Did not take medication (If NO, go to question 7)

6. How many years did he take diuretics on a regular basis?

   Less than 6 months
   6 months to 2 years
   2 years to 5 years
   5 years to 10 years
   Greater than 10 years

The following lists several brand names of diuretics. Please circle any that he took.

Aldactazide
Aldactone
Diuril
Dyazide
Enduron
Esidrix
Hydrochlorothiazide
Hydrodiuril
Hygroton
Lasix
Metahydrin
Oretic
Zaroxolyn
Other _____

7. Did he smoke at least 5 packs of cigarettes in his lifetime?

Yes
No (If NO, go to question 12)
Unknown

8. How old was he when he first started to smoke cigarettes regularly?

Age started _____

(If you are uncertain, would you guess he was)

In his teens?
In his twenties?
In his thirties?
Older than thirties?
Unknown

9. Did he smoke cigarettes at the time of his death?

Yes (If YES, go to question 11)
No
Unknown

10. How old was he when he stopped smoking cigarettes?

Age stopped_____
Unknown

11. When he did smoke, approximately how many cigarettes did he smoke a day?

Less than one
1/2 pack or less
Between 1/2 to 1 pack
Between one to two packs
More than two packs
Unknown

12. Did he ever smoke a pipe?

Yes
No
Unknown

13. Did he ever smoke cigars?

Yes
No,
Unknown

14. Did he ever take any aspirin containing products such as Bayer aspirin or Bufferin on a regular basis? (A regular basis means at least 2 or more times a week for one month or longer.)

Yes
No (If no, go to question 16.)
Unknown

What brand aspirin product did he use? _____
(see next page for some examples)

15. How many years did he take aspirin containing products on a regular basis?

Less than 6 months
6 months to 2 years
2 years to 5 years
5 years to 10 years
Greater than 10 years

16. Did he ever take any aspirin-free products such as Tylenol or Datril on a regular basis? (A regular basis means at least 2 or more times a week for one month or longer.)

Yes
No
Unknown'

What brand aspirin-free products did he use? _____
(see next page for some examples)

17. How many years did he take aspirin free products such as Tylenol or Datril on a regular basis?

Less than 6 months
6 months to 2 years
2 years to 5 years
5 years to 10 years
Greater than 10 years

Examples of aspirin and aspirin-free medications

Please circle any that apply.

A.P.C. tablets sometimes called "a perfect cure"
Alka Seltzer
Anacin-3 Maximum
Anacin-3 Regular Strength
Arthritis Strength **Bufferin**
Arthritis Pain Formula Anacin
ASA Compound
Aspirin-Free Anacin
Azolid/-A
BC powder or tablets
Bromoseltzer
Buffered aspirin such as **Bufferin** or Ascriptin
Butazolidin
Darvocet
Darvon Compound
Darvon
Doan's Pills
Empirin **Compound** not including Empirin **w/Codeine**
Empirin with Codeine
Excedrin
Excedrin P.M. or Aspirin-Free Excedrin
Extra strength aspirin such as Maximum Bayer
Extra Strength Datril
Extra Strength Tylenol
Generic acetaminophen
Indocin
Midol
Motrin
Naprosyn
P.A.C.
Percocet
Percodan
Phenylbutazone
Regular aspirin, such as Bayer Aspirin
Regular Strength Datril
Regular Anacin
Regular Strength Tylenol
Stanback, either as a powder or tablet
Tylenol with codeine
Vanquis

FINAL REPORT

Re-Analysis of Kidney Cancer Case-Control Study Following Data Corrections

Report to:

Aluminum Company of America

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EXECUTIVE SUMMARY

In 1993, researchers from the University of Pittsburgh Department of Biostatistics reported findings from a case-control study of kidney cancer among Alcoa workers from 26 U.S. plants. The study was prompted by a proportionate mortality ratio analysis in which an excess of kidney cancer mortality was observed. The case-control study findings suggested risk elevations related to the highest exposures to hydrocarbons, especially aliphatic hydrocarbons. A weaker, but still elevated risk was found with the highest exposures to aromatic hydrocarbons. At the conclusion of the study, some inadvertent data errors were found which called into question the validity of the results. These errors were the result of miscoding of some potroom jobs at one reduction facility. Uncertainty regarding the type of smelting technology, Soderberg or pre-bake, was the main cause of the coding errors.

Following discovery of these errors, the Alcoa industrial hygiene staff obtained corrected information for most of the data errors. We obtained from the University of Pittsburgh researchers the data from their case-control study, and performed analyses on the corrected data to determine whether the associations with hydrocarbon exposures persisted. Our re-analysis included data for all 71 kidney cancer deaths (cases) and the 283 deaths from other causes, excluding cancer and chronic kidney disease (controls). Data on non-occupational risk factors for kidney cancer, smoking, medication use, and obesity, that might have confounded the observed relations with hydrocarbon exposures were incorporated into the re-analysis. This information had been obtained previously by the University of Pittsburgh investigators from questionnaires administered to study subjects' next-of-kin.

Our re-analysis confirmed the observed association with aliphatic hydrocarbons. Workers who had ever been exposed to the highest levels of aliphatic hydrocarbons had roughly 4 times the risk of kidney cancer mortality as workers who had never been exposed to these chemicals. The association with aliphatic hydrocarbons was diminished somewhat, but remained elevated (2.5 times), when exposure was defined as at least 1 year rather than ever. In contrast, no association was detected with aromatic hydrocarbons after analysis of the corrected data. Confounding by smoking, medication use, or obesity was not a likely explanation for the observed association with aliphatic hydrocarbons.

The study had some notable limitations. The control group was not necessarily representative of the Alcoa workforce insofar is it was composed of roughly 75 percent of workers who had died from circulatory system diseases. Another significant limitation that hinders a clear interpretation of findings is the absence of quantitative data for specific chemicals, especially aliphatic hydrocarbons. The results of the re-analysis cannot confirm or refute specific causal hypotheses, but do offer some guidance for future assessments of kidney cancer in the aluminum industry.

BACKGROUND

In 1991, Alcoa commissioned researchers from the University of Pittsburgh Department of Biostatistics to conduct a case-control study of occupational risk factors for kidney cancer. The motivation for this new initiative was a finding by Rockette and Arena (1990) of a kidney cancer mortality elevation, of approximately 60 percent greater than national rates, among the Alcoa production workforce during the years 1980-87. This finding was based on proportionate mortality ratio (PMR) analysis which compared the percentage distribution of deaths, by cause, in the Alcoa workforce with the corresponding percentage distribution among U.S. males. Kidney cancer excesses have been found in some other aluminum industry worker studies (Rockette and Arena, 1983; Spinelli et al., 1991), although no excesses have been reported from others (Ronneberg and Anderson, 1995). The 1990 PMR kidney cancer results were considered to be suggestive of a consistent trend for Alcoa that was first noted in the Tripartite Study (Rockette and Arena, 1983).

The goal of the case-control study was to determine whether exposures to aromatic or aliphatic hydrocarbons during employment at Alcoa facilities were related to kidney cancer, while taking into consideration known or strongly suspected non-occupational risks factors (e.g., cigarette smoking). As stated in the original protocol for this case-control study (Rockette and Arena, 1990-91), aromatic hydrocarbons were of greater prior interest than aliphatics. This emphasis apparently evolved from earlier findings of a kidney cancer excess among reduction plant workers in the Tripartite Study, and the known associations of various polycyclic aromatic hydrocarbons with kidney cancer. Aliphatic hydrocarbons had been linked inconsistently with kidney cancer risk mainly from studies of workers exposed to gasoline and solvents.

Details of the study, including the study design, methods of data collection and analysis, original results, and discussion are provided in a report by Rockette and Arena (1993) from the University of Pittsburgh. This report is henceforth referred to as the "original report." At the time of its submission in August; 1993, all parties agreed that it should appropriately be regarded as a preliminary report, in view of the changes that would likely ensue following data corrections. The findings from the original report indicated elevated kidney cancer risks related to hydrocarbon exposures; a relative risk of 2.55 was noted for high exposures. This association was mainly due to an apparent excess risk concentrated among workers with the highest exposures to aliphatic hydrocarbons, for which the relative risk

was 4.10. The association with high aromatic hydrocarbon exposures (relative risk of 1.61) was considerably weaker.

Upon submission of their report to Alcoa in August, 1993, Drs. Rockette and Arena noted inconsistencies in some of the job assignment codings that may have resulted in erroneous classifications, and hence incorrect epidemiologic findings. The original report was therefore considered as a preliminary report, and the conclusions were disavowed by the investigators until errors could be corrected. Alcoa explored with researchers from another university the feasibility of having a new, more detailed exposure assessment for specific hydrocarbons and other workplace agents; however, this proved not to be feasible because of the enormous effort and resources that would have been required to locate and synthesize data relevant to historical exposures spanning back as far as the 1930s.

We agreed to oversee the Alcoa industrial hygienists' efforts to make corrections to the work history and exposure data sets, and to analyze the corrected case-control data following the same approaches taken by Rockette and Arena (1993). Drs. Rockette and Arena assisted us by providing data that they had analyzed in the original report, and by performing confirmatory data analyses that took into account possible effects of non-occupational risk factors (i.e., potential confounders, such as smoking).

METHODS

Original Study

Descriptions of the research design and study subjects are contained in the original report (Rockette and Arena, 1993). Thus, only a brief synopsis will be provided here. We will, however, provide details on the procedures that we followed in this re-analysis.

The case group included 71 of the 73 kidney cancer deaths (ie., cases) that occurred during 1980-90 among Alcoa workers from 26 plants. The 73 cases were 53 kidney cancer deaths included previously in the PMR study and 20 deaths identified during 1988-90. Two (2) of the 73 kidney cancer deaths were not included because their employment history records did not identify their past work areas and jobs (Rockette and Arena, 1993). Controls were a sample of deaths whose causes of death were attributed to diseases other than cancer or chronic nephritis during the same 1980-90 time period. Controls were individually matched to cases on race, gender, year of death and year of birth within 5

years. Rockette and Arena selected 283 controls who met these criteria According to Rockette and Arena (1993), deaths from cancers of sites other than the kidney were not eligible because of the possibility that some of the same exposures that may relate to kidney cancer might be associated with other cancers. Thus, the study included a large proportion of deaths (74%) from cardiovascular and other circulatory system diseases.

Cases' and controls' work history records were obtained and computerized for linkage with exposure information. Jobs held by cases and controls were classified according to separate exposure rating schemes for aliphatic and aromatic hydrocarbons. Jobs were classified as entailing "none," "low," "medium," or "high" exposures to either aromatic or aliphatic hydrocarbons. The exposure ratings for cases' and controls' jobs were provided by Alcoa industrial hygienists. Historical exposure information, industrial hygiene monitoring data from surveys performed during recent years, and industrial hygiene judgments formed the basis of the exposure ratings. The ratings were conducted without knowledge of where cases and controls had worked, i.e., blindly.

In order to address the concern that non-occupational risk factors (e.g., smoking) might confound observed associations detected with hydrocarbons, Rockette and Arena administered a telephone questionnaire to surrogate respondents (next-of-kin) of study subjects. Data were elicited for a history of smoking, obesity, and use of diuretics and analgesics.

Relative risk estimates (RR) were derived from logistic regression analyses for case-control data. RRs were estimated for any exposure to hydrocarbons, as well as for ordered levels of exposure: 'none, low/medium, high. Analyses were also performed separately for aliphatic and aromatic hydrocarbons.

Correction of Job/Exposure Classification Errors

The erroneous job and exposure coding assignments were identified as having resulted from ambiguities in the types of potroom technology that had been operated at one Alcoa facility. In particular, some potroom assignments during the 1930s-1950s had been erroneously classified as Soderberg potroom jobs when in fact they had been in pre-bake potrooms. These errors and the ensuing hydrocarbon exposure re-classifications were made by Alcoa hygienists. As before, the exposure classifications were made without knowledge of case or control status of the affected work history records.

In addition, there remained 23 potroom jobs held by 16 workers at this facility for which there was insufficient information to determine whether they were in Soderberg or pre-bake technologies. As will be described subsequently, we performed two sets of analyses in which these indeterminate potroom jobs were alternately classified as Soderberg and pre-bake.

Re-analysis of Case-Control Data

The first step in our re-analysis was to verify the results from the uncorrected data presented in the original report. Drs. Rockette and Arena provided us with a computer file of these data. Our analysis followed the procedures described in the original report, and we were able to replicate the earlier findings on the uncorrected data. Next, we received from the Alcoa industrial hygiene staff a list of corrected job/exposure assignments. The corrected list included new exposure codes for aliphatic and aromatic hydrocarbons (none, low, medium, high) for jobs where it was clear that pre-bake potroom jobs had been erroneously classified as Soderberg potroom jobs. Potroom jobs that could not be identified unambiguously as pre-bake or Soderberg were given alternative sets of aliphatic and aromatic hydrocarbon exposure ratings, one assuming that all of these were in a pre-bake potroom, and the other assuming all were in the Soderberg technology.

We analyzed the corrected data to generate relative risk estimates for hydrocarbon exposures, following the procedures of Rockette and Arena. Data on smoking, obesity, and medications (i.e., "confounders") were obtained from subjects' next-of-kin with the understanding that this information, that could potentially be linked to individual workers; would not be shared with parties outside of the University of Pittsburgh. In order to assess possible confounding by these non-occupational factors, we provided the corrected data set to Drs. Rockette and Arena for analyses that included these potential confounders. Their approach for statistical control of confounders (conditional logistic regression modeling) was identical to the methods used in their original report. Thus, we were able to estimate relative risks related to ever exposure to varying levels of hydrocarbon exposures that included control for the potential confounders.

The designation of "exposed" used in the original analysis by Rockette and Arena was made without reference to duration of exposure. Thus for example, ever exposed to high hydrocarbons included any duration of employment in a job classified as high exposure.

We performed an additional set of analyses in which "exposure" was defined as greater than 1 year. The purpose of this additional analysis was to evaluate possible dose-response relations in somewhat more depth than had been done previously.

RESULTS

The original and corrected exposure classifications for all, aliphatic, and aromatic hydrocarbons are shown in Table 1. There are two sets of reclassifications: Reclassification 1 placed the indetexminate potroom jobs in the Soderberg technology, and Reclassification 2 placed these jobs in pre-bake technology. Table 2 displays the corrected and uncorrected exposure classifications based on a minimum of 1 year exposure. The re-classification of aliphatic exposures, especially in the 'high' exposure group were minimally affected by data corrections. High aromatic exposures, however, were changed more profoundly. Based on the original classification, the percentages of cases and controls with high aromatic hydrocarbon exposures of any duration were 8.5 and 5.7, respectively, whereas the corresponding percentages under Reclassifications 1 and 2 were: 8.5 and 11.3; and 5.6 and 6.7 (Table 1). The classifications of high aromatic exposures under a 1 year minimum exposure duration criterion (Table 2) changed slightly as well, although a higher prevalence of exposure among controls than cases persisted throughout. It should be appreciated that high aromatic hydrocarbon exposures involved only a small number of cases and controls; thus, the overall classification of hydrocarbon exposures remained largely unaltered.

The relative risk estimates [odds ratios (OR)] associated with levels and types of hydrocarbons are given in Table 3, based on the original exposure classification and on Reclassifications 1 and 2. Following either exposure reclassification, there is no longer an excess apparent for the high compared to no aromatic hydrocarbon exposure; the OR was reduced from 1.76 to 0.79 or 0.89, depending on the classification of generic potroom jobs. The explanation for this change is that, following Reclassification 1, the cases' high exposure classifications were not changed, but 16 (5.7%) controls previously classified as having had low/medium aromatic hydrocarbon exposure were re-classified into the high category (Table 1). Following Reclassification 2, 2 (2.8%) cases were moved from high to low/medium aromatic hydrocarbon exposure, and 3 (1.1%) controls changed from the low/medium to high category. In contrast, re-classification had very little effect on the ORs for high aliphatic hydrocarbon exposure. The reduction of OR for the combined high

hydrocarbon category (from an original value of 2.34 to 1.40 or 1.76) was due to the change in the risk estimate for high aromatic hydrocarbon exposures.

The possible bias caused by confounding from non-occupational exposures was examined by computing adjusted relative risk estimates, and comparing these with unadjusted values. The results for the OR. associated with high hydrocarbon exposures, high aliphatic exposures, and high aromatic exposures, with and without adjustment for potential confounders, are summarized in Table 4. The adjusted analyses involved statistical control for ever cigarette smoking, use of diuretics, use of aspirin- and non-aspirin analgesics, and obesity (Model 14 from the original report). With several isolated exceptions, the adjusted and unadjusted ORs were reasonably close, which suggests that there was little evidence for important confounding by these factors. It is noteworthy that there were no instances where the direction of association changed from positive (OR>1.0) to negative (OR<1.0), or vice versa, after control for potential confounders.

When 1 year was set as the minimum duration of exposure, the ORs for high aliphatic hydrocarbon exposure were reduced somewhat from those based on an ever exposed classification, although the relative risk estimates remained elevated (Table 5). Thus in the corrected data set, we estimated an OR of 2.52 for high aliphatic exposure of 1 year or longer (Table 5), as contrasted with an OR of 3.70 for ever exposed (Table 3). The results based on the corrected data for aromatic hydrocarbons did not change materially when the 1 year minimum was imposed.

Review of the high aliphatic exposure jobs held by the cases and controls revealed that these jobs occurred at three plant locations, Cressona, Massena, and New Kensington, during the years 1934-1971. The jobs involved work in Merchant and Blooming Mills at Massena, and in the Tube Mills at Cressona and New Kensington Characterization of the highest aliphatic exposures to a small number of plant locations and specific jobs suggests that any elevation of kidney cancer risk related to aliphatic hydrocarbons, if one did indeed exist, was not widespread throughout the industry. It is also noteworthy that the high aliphatic exposures terminated in the early 1970s on cases' and controls' work history records. This may be due to the requirement of a prolonged latency interval for disease manifestation; alternatively, it may reflect exposure reductions that have taken place during the past 30 years. More detailed historical exposure data would be needed to evaluate the likelihood of the second explanation.

DISCUSSION

Findings from our re-analysis of the corrected data suggest that there remains a statistical association of hydrocarbons with kidney cancer risk (Rockette and Arena, 1993). The association pertains to aliphatic hydrocarbons rather than aromatic hydrocarbons. The original report indicated apparent elevated risks with both classes of hydrocarbons, but with a more prominent association for the aliphatics. The seeming disappearance of the relation with aromatic hydrocarbons, following data corrections, is not especially surprising because the original result was numerically dependent on only 6 cases and 16 control in the high exposed category (see Table 1). The findings for aliphatic hydrocarbons were and remain more numerically stable, and were thus altered only minimally after data corrections were made. However, evidence for a dose-response gradient with aliphatic hydrocarbon exposure and kidney cancer was weakened somewhat when a 1 year minimum exposure duration was imposed instead of an ever/never classification. Confounding from non-occupational risk factors, including cigarette smoking, use of diuretics or analgesics, and obesity, is very unlikely to be a meaningful explanation of the observed association with aliphatic hydrocarbons.

Interpreting the findings from this study should be made with due consideration given to some notable limitations of study design and quality of information. The most suitable control group would have been workers, either living or dead, from the same plants as the cases, who were free of kidney cancer at the times when the cases deaths occurred. Because it was not possible to enumerate the cohort that would have been necessary for this type of control selection scheme, Rockette and Arena (1993) selected controls from among other deaths that occurred at the same plants where the cases worked. The decision to eliminate cancer deaths, and to a lesser extent, chronic renal disease deaths, from the pool of eligible controls resulted in a large majority of circulatory system disease deaths in the controls (nearly 75%). This imbalance in the control group may have produced a bias if mortality from cardiovascular or other circulatory diseases was related to particular workplace agents or specific jobs in the smelter. For example, it cannot be determined whether the observed association with high aliphatic hydrocarbon exposures reflects a truly causal effect, or whether this is merely an artifact of unmeasured associations of aliphatics with cardiovascular diseases. In fact, Ronneberg (1995) reported increasing risk gradients for atherosclerotic disease mortality with cumulative exposure to tar and for cerebrovascular disease mortality with tar and pot emissions in a prebake smelter. In any event, the

potential effect of such bias on the findings cannot be evaluated because associations of occupational exposures in Alcoa facilities with circulatory system disease mortality have not been investigated previously.

Another important limitation of this study is the absence of quantitative exposure estimates for specific agents. This problem, while certainly not unique to this epidemiologic study, restricts the type of inference that can be drawn from the findings. Aliphatic hydrocarbons encompass many agents, ranging from solvents to machining fluids. Determining specificity and quantification of these exposures was especially complex in this study because the cases' and controls' relevant periods of exposure extended back as far as 50-60 years into the past and may have varied from plant to plant. Chemical usage by type and amount, and the extent of contamination with potential carcinogens, including some aromatic hydrocarbons (e.g., polycyclic aromatic hydrocarbons), undoubtedly have changed greatly in the 26 plants during this time interval. Documentation describing most of these changes, unfortunately, was not readily available to the investigators. As a result of these information shortcomings, exposure classification relied chiefly on industrial hygiene judgments regarding the potential and relative magnitude of exposure. to the non-specific groupings of aromatic and aliphatic hydrocarbon.

As reviewed recently by Smith and Liu (1995), there are many unresolved questions regarding etiologic associations between hydrocarbons and human kidney cancer. Much of the evidence from animal studies is conflicting, and more significantly, no consistent patterns of risk related to either broad categories or specific hydrocarbons have emerged from epidemiologic research. Taken in this context, the results from the present study neither support nor refute any previous epidemiologic associations with hydrocarbons. Our re-analysis of the data revealed that the observed association with presumably the highest aliphatic hydrocarbon exposures persisted after data corrections and control for potential confounders. This finding is consistent with a suspected occupational association with kidney cancer, and thus should provide some direction to further epidemiologic assessments of kidney cancer risks in the aluminum industry.

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Table 1. Hydrocarbon Exposure Classification Before and After Data Corrections

	Original Report				Reclassification 1*				Reclassification 2¶			
	Cases		Controls		Cases		Controls		Cases		Controls	
	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)
Any hydrocarbon												
None	16	22.5	66	23.3	16	22.5	66	23.3	16	22.5	66	23.3
Low/medium	41	57.7	191	67.5	41	57.7	175	61.8	43	60.6	188	66.4
High	14	19.7	26	9.2	14	19.7	42	14.8	12	16.9	29	10.2
Aromatic												
None	43	60.6	181	64.0	43	60.6	181	64.0	43	60.6	181	64.0
Low/medium	22	31.0	86	30.4	22	31.0	70	24.7	24	29.3	83	33.8
High	6	8.5	16	5.7	6	8.5	32	11.3	4	5.6	19	6.7
Aliphatic												
None	16	22.5	66	23.3	16	22.5	66	23.3	16	22.5	66	23.3
Low/medium	46	64.8	206	72.8	47	66.2	207	73.1	47	66.2	207	73.1
High	9	12.7	11	3.9	8	11.3	10	3.5	8	11.3	10	3.5
Total	71		283		71		283		71		283	

* Reclassification of generic potroom job codes as Soderberg
¶ Reclassification of generic potroom job codes as Prebake

Table 2. Hydrocarbon Exposure Classification Before and After Data Corrections : Minimum 1 Year Exposure Criterion

	Original Report				Reclassification 1*				Reclassification 2¶			
	Cases		Controls		Cases		Controls		Case		Controls	
	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)
Any hydrocarbon												
< 1 year	22	31.0	86	30.4	22	31.0	86	30.4	22	31.0	86	30.4
Low/medium ≥ 1 year	42	59.2	177	62.5	40	58.7	166	56.3	42	59.2	174	61.5
High ≥ 1 year	7	9.9	20	7.1	9	12.7	31	11.0	7	9.9	23	8.1
Aromatic												
< 1 year	46	64.8	209	73.9	46	64.8	209	73.9	46	64.8	209	73.9
Low/ medium ≥ 1 year	22	31.0	60	21.2	20	28.2	49	17.3	22	31.0	57	20.1
High 1 year	3	4.2	14	4.9	5	7.0	25	8.8	3	4.2	17	6.0
Aliphatic												
< 1 year	22	31.0	86	30.4	22	31.0	86	30.4	22	31.0	86	30.4
Low/medium ≥1 year	45	63.4	191	67.5	45	63.4	191	67.5	45	63.4	191	67.5
High ≥ 1 year	4	5.6	6	2.1	4	5.6	6	2.1	4	5.6	6	2.1
Total	71		283		71		283		71		283	

* Reclassification of generic potroom job codes as Soderberg
¶ Reclassification of generic potroom job codes as Prebake

Table 3. Relative Risk Estimates for Hydrocarbon Exposure: Original Report and Corrected Exposure Assessment

Type of hydrocarbon exposure	Original Report		Reclassification*		Reclassification¶	
	OR	(95% CI)‡	OR	(95% CI)‡	OR	95% CI)‡
Any Hydrocarbon						
Never	1.0	—	1.0	—	1.0	—
Low/medium	0.90	(0.46-1.76)	0.97	(0.50-1.90)	0.96	(0.49-1.86)
High	2.34	(0.95-5.77)	1.40	(0.59-3.29)	1.76	(0.71-4.40)
Aromatic						
Never	1.0	—	1.0	—	1.0	—
Low/medium	1.08	(0.60-1.97)	1.33	(0.72-2.43)	1.23	(0.68-2.21)
High	1.67	(0.58-4.79)	0.79	(0.30-2.06)	0.89	(0.28-2.84)
Aliphatic						
Never	1.0	—	1.0	—	1.0	—
Low/medium	0.95	(0.49-1.83)	0.97	(0.50-1.87)	0.97	(0.50-1.87)
High	3.92	(1.25-1.27)	3.70	(1.15-11.94)	3.70	(1.15-11.94)

* Reclassification of generic potroom job codes as Soderberg
¶ Reclassification of generic potroom job codes as Prebake
‡ Odds ratio (95% confidence interval)

Table 4. Relative Risk Estimates for High Hydrocarbon Exposures Before and After Data Corrections, with and without Control for Potential Confounders

Exposure	Original Report		Reclassification*		Reclassification 2¶	
	OR	(95% CI)‡	OR	(95% CI)‡	OR	(95% CI)‡
High any hydrocarbon						
Not adjusted	2.55	(1.22-5.34)	1.43	(0.72-2.84)	1.83	(0.86-3.87)
Adjusted[5]	3.90	(1.22-12.5)	1.25	(0.46-3.40)	1.52	(0.48-4.87)
Aromatic						
Not adjusted	1.61	(0.58-4.52)	0.71	(0.28-1.80)	0.83	(0.27-2.57)
Adjusted[5]	3.88	(0.76-19.7)	0.67	(0.19-2.40)	0.61	(0.11-3.44)
Aliphatic						
Not adjusted	4.10	(1.50-11.22)	3.80	(1.36-10.67)	3.80	(1.36-10.67)
Adjusted§	3.47	(0.95-16.6)	2.96	(0.70-12.5)	2.96	(0.70-12.5)

* Reclassification of generic potroom job codes as Soderberg
¶ Reclassification of generic potroom job codes as Prebake
‡ Odds ratio (95% confidence interval)
§ Adjusted for cigarette smoking, diuretic use, analgesic use, obesity, and plant.

Table 5. Relative Risk Estimates for Hydrocarbon Exposure with Minimum 1 Year of Exposure: Original Report and Corrected Exposure Assessment

Type of hydrocarbon exposure	Original Report		Reclassification 1*		Reclassification 2¶	
	OR	(95% CI)‡	OR	(95% CI)‡	OR	(95% CI)‡
Any hydrocarbon						
<1 year	1.0	—	1.0	—	1.0	—
Low/medium ≥ 1 year	0.93	(0.51-1.69)	0.94	(0.51-1.72)	0.94	0.52-1.71)
High ≥1 year	1.36	(0.50-3.66)	1.13	(0.46-2.75)	1.20	(0.45-3.20)
High ≥1 year§	1.43	(0.59-3.49)	1.17	(0.53-2.60)	1.25	(0.51-3.07)
Aromatic						
< 1year	1.0	—	1.0	—	1.0	—
Low/medium ≥1 year	1.69	(0.93-3.07)	1.89	(1.00-3.53	1.82	(0.99-3.37)
High ≥1 year	0.99	(0.27-3.61)	0.91	(0.33-2.53	0.78	(0.21-2.81)
High ≥1 year§	0.85	(0.24-3.06)	0.77	(0.28-2.11)	0.68	(0.19-2.45)
Aliphatic						
< 1year	1.0	—	1.0	—	1.0	—
Low/medium ≥1 year	0.93	(0.52-1.68)	0.93	(0.52-1.68)	0.93	(0.52-1.68)
High ≥1 year	2.52	(0.66-9.66)	2.52	(0.66-9.66)	2.52	(0.66-9.66)
High ≥1 year§	2.67	(0.75-9.45)	2.66	(0.75-9.45)	2.67	(0.75-9.45)

* Reclassification of generic potroom job codes as Soderberg
¶ Reclassification of generic potroom job codes as Prebake
‡ Odds ratio (95% confidence interval)
§ Ever exposed compared to never exposed