Exhibit 260

An Updated Study of Mortality among Workers at a Petroleum Manufacturing Plant

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This study evaluated mortality among 9796 white male workers at a petroleum-manufacturing plant. The main purpose was to examine recent patterns in leukemia mortality, for which an increase had been reported in an earlier investigation. Compared to U.S. white men, the cohort had an excess of leukemia in 1940–1979 (38 observed/23 expected; standardized mortality ratio = 168; 95% confidence interval = 119–230). In the 1980s, there was a deficit of leukemia (8 observed/14 expected; standardized mortality ratio = 55; 95% confidence interval = 24–108). However, this was balanced by an excess of myelofibrosis and myelodysplasia (4 observed, <1 expected). These results indicate that any occupational leukemogenic exposures at the plant have been reduced to a point at which they are insufficient to cause leukemia. Hourly workers also had an excess of deaths from mesothelioma in the 1980s (8 observed, about 2.5 expected), possibly because of exposure to asbestos in the past.

This report is a further investigation of the mortality experience of workers at a petroleum-manufacturing plant located in southern Illinois. The facility began operations in 1918 and currently includes crude oil refining and production of gasoline, aviation fuel, diesel fuel, lubricating oils, asphalt, and various petrochemical products, including benzene. Disease patterns among workers at the plant were evaluated previously in two retrospective follow-up studies,[1,2] in a case-control study of leukemia,[3] in a prospective investigation of general morbidity,[4] and in a program of medical surveillance for leukemia among active and retired employees.[5]

The most recent retrospective follow-up study, which examined mortality from 1940 through 1984, found that the cohort had a 68% increase in leukemia during 1940–1979, based on 38 observed and 23 expected deaths.[2] The excess appeared to diminish in 1980–1984, but observed and expected numbers of deaths were too small to be conclusive. The present study was undertaken primarily to evaluate more thoroughly the apparent disappearance of the earlier leukemia excess and to provide an update of the mortality patterns among the workers.

Methods

The study included white men who had worked at the plant for at least 6 months before 1990 and who were either hourly and actively employed at any time during 1942

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1076-2752/95/3702-0194$3.00/0

through 1989 or salaried and actively employed at any time through 1989. Hourly workers who left employment before 1942 and salaried employees who terminated before 1940 were not included because their records had not been retained consistently by the company.

Data files developed for previous follow-up studies of this cohort[1,2] served as the primary source of identifying and work history information. The files contained the name, Social Security number, race, gender, birth date, hire date, termination date, employment status (active, retired, terminated, transferred), and payroll status (hourly, salaried) of subjects employed in or before 1983. We used computerized data from the company's health surveillance system to update through 1989 the work history of subjects actively employed at the end of 1983 and to identify and obtain information on persons hired since 1983.

To determine the vital status of subjects as of January 1, 1990, we used data from the previous follow-up study,[2] from company records, from the Social Security Administration's Death Master file, and from the National Death Index (NDI), and records of the Illinois and Missouri divisions of motor vehicles. Death certificates of decedents were obtained from state vital records offices or from the company and were coded by a nosologist according to the ninth revision of the International Classification of Diseases (ICD). Subjects were classified as presumed living if they were actively employed or had active pension or division of motor vehicle records in or after 1979, the year in which the NDI was established, and if they did not have an NDI or other death record. Subjects not classified as deceased or as presumed living were considered as lost to follow-up on their employment termination date. All subjects lost to follow-up had terminated employment before 1979.

We compared the mortality rates of the subjects with the rates of the white male U.S. population, using the standardized mortality ratio (SMR) as the measure of association. The SMR is the ratio of the observed number of deaths among cohort members to the expected number, multiplied by 100. We computed expected numbers of deaths by multiplying the age- and calendar time-specific person-years (PY) of the study cohort by the corresponding U.S. population rates. For always salaried workers, PY accumulation began 6 months after the hire date or on January 1, 1940, whichever was later. For ever hourly workers, PY accumulation began 6 months after the hire date or on January 1, 1942, whichever was later. Follow-up ended on January 1, 1990, on the death date or on the date when the subject was lost to follow-up, whichever was earliest. We calculated 95% confidence intervals (CI) of the SMRs assuming a Poisson distribution for the observed numbers of deaths. The most recent version of a program developed by Monson[6] was used for most analyses. This program was supplemented with leukemia cell type-specific mortality rates, as described in our previous study,[2] except that we used 1985 leukemia cell type-specific mortality rates from the Surveillance, Epidemiology and End Results (SEER) program to estimate expected numbers for the 1980–1989 time period.

Results

The Overall Cohort

The total number of PY of follow-up and the average number of years per subject were 300,991 and 31, respectively, with the present update adding 30,997 PY to the previous study. Of the total 9796 subjects, 5895 (60%) were classified as presumed living, 3627 (37%) were deceased, and 274 (3%) were lost to follow-up. Of the 3627 deaths, 747 (21%) occurred during the update period. The death certificate and, hence, the cause of death were obtained for 96% of all decedents. Seventy-nine percent of the cohort was ever hourly, 75% had a potential follow-up period of at least 30 years, and 53% had 10+ years of employment.

The SMR for all causes during the period 1940–1989 was 79, based on 3627 observed deaths; and the SMR for all cancers combined was 88, based on 868 observed deaths (Table 1). Both of these SMRs represent statistically significant deficits. For most noncancer disease categories, the observed number of deaths was appreciably lower than expected. The cohort did not have a statistically significant excess of any specific type of cancer.

The leukemia SMR for the overall study period was 123 (95% CI = 90–164). There was an excess of leukemia in 1940–1984 (44 observed/29 expected; SMR = 149, 95% CI = 108–200), as reported in the previous investigation of this cohort, but a deficit occurred in 1985–1989 (2/7.7; SMR = 26, 95% CI = 3–94).

Among workers with relatively long-term employment at the plant (ie, 10+ years), mortality patterns were similar to those observed for the overall cohort (all causes SMR = 76, 95% CI = 73–79; all cancer SMR = 84, 95% CI = 78–92). Also, the SMRs of men with relatively long potential induction time (ie, 20+ years since hire) did not indicate any unusual mortality experience (all causes SMR = 82, 95% CI = 80–85; all cancer SMR = 90, 95% CI = 84–96).

Hourly Workers

Hourly workers had lower than expected mortality from most causes of death (Table 2). For the entire follow-up period, there was only a 9% excess of leukemia deaths (SMR = 109, 95% CI = 76–152). The overall result reflects a 36% excess of leukemia in the 1940–1984 time period and a deficit in 1985–1989, when hourly workers had no leukemia death, compared to 6.3 expected.

TABLE 1
Observed Numbers of Deaths and SMRs for the Overall Cohort, 1940–1989

	Obs	SMR	95% CI*
All causes	3627	79	76–81
All cancer	868	88	82–94
Buccal cavity and pharynx	8	29	12–57
Digestive organs	215	80	69–91
Esophagus	15	66	37–108
Stomach	28	60	40–86
Large intestine and rectum	116	97	80–116
Liver	12	56	29–99
Pancreas	35	68	47–94
Larynx	10	73	35–134
Lung	280	86	76–97
Skin	19	114	69–179
Prostate	74	93	73–117
Bladder	26	86	56–126
Kidney	23	97	61–145
Central nervous system	22	86	54–131
All lymphopoietic cancer	104	114	93–138
Lymphosarcoma	14	89	49–149
Hodgkin's disease	9	106	48–200
Leukemia	46	123	90–164
Other lymphopoietic tissue	29	99	66–142
Other cancer	87	105	84–129
Benign and unspecified neoplasms	14	113	62–190
Diabetes mellitus	51	78	58–102
Blood diseases	10	86	41–157
Nervous system diseases	30	64	43–91
Circulatory diseases	1822	77	74–81
Respiratory diseases	203	63	54–72
Digestive system diseases	122	62	52–74
Genitourinary system diseases	39	56	39–76
External causes	249	73	64–82
Other specified causes	77	41	33–52
Unknown causes	142	(4% of total deaths)	

* 95% confidence interval of SMR.

Further details pertaining to leukemia mortality patterns are presented in a later section.

Although there was a 10% deficit of cancer during the overall follow-up period (SMR = 90; 95% CI = 84–97), the cancer SMR was higher in 1985–1989 (SMR = 102) than in 1940–1984 (SMR = 87). In 1985–1989, there were moderate increases in deaths from larynx cancer (5/1.9; SMR = 264, 95% CI = 85–617) and from cancer of other and unspecified sites (25/15; SMR = 172, 95% CI = 112–255). Further examination of larynx cancer mortality patterns indicated that the increases during 1985–1989 probably were not related to occupational exposure, because there was, overall, an inverse relationship with duration of employment. Larynx cancer deaths were increased among men with fewer than 20 years of employment (10/5.7), but a deficit (0/6.2) was present among men who worked for 20 or more years. Review of the death certificates of the 25 men who died of cancer of other and unspecified sites in 1985–1989 revealed four deaths from endocrine cancer, one death from connective tissue cancer, two deaths from mesothelioma, and 18 deaths from unspecified types of cancer.

The "all lymphopoietic cancer" category in Table 2 included six observed deaths from myelofibrosis or myelodysplastic syndrome (MF/MDS) in 1940–1989, two of which occurred in 1940–1984 and four in 1985–1989. An approximate expected number of MF/MDS deaths can be obtained by subtracting the sum of the expected numbers of lymphosarcoma, Hodgkin's disease, leukemia, and other lymphopoietic tissue cancer deaths from the expected number of deaths in the all lymphopoietic cancer category. The approximate expected number of MF/MDS deaths was less than 0.50 both for 1940–1984 and for 1985–1989 and less than 1.0 for the overall study period of 1940–1989, and the increases in observed over expected deaths were statistically significant for 1985–1989 and for 1940–1989. In addition to the MF/MDS deaths,

TABLE 2
Observed Numbers of Deaths and SMRs for Ever Hourly Subjects, 1942–1989

	Obs	SMR	95% CI
All causes	3257	82	79–85
All cancer	763	90	84–97
Buccal cavity and pharynx	6	25	9–55
Digestive organs	191	82	71–94
Esophagus	14	72	39–120
Stomach	23	56	35–84
Large intestine and rectum	106	102	83–123
Liver	10	54	26–100
Pancreas	30	67	45–96
Larynx	10	85	41–156
Lung	252	91	80–103
Skin	15	109	61–179
Prostate	64	91	70–116
Bladder	22	83	52–126
Kidney	21	104	64–158
Central nervous system	17	80	47–128
All lymphopoietic cancer	90	115	93–142
Lymphosarcoma	13	96	51–164
Hodgkin's disease	8	112	48–221
Leukemia	35	109	76–152
Other lymphopoietic tissue	28	112	75–163
Other cancer	75	106	83–133
Benign and unspecified neoplasms	13	123	65–210
Diabetes mellitus	47	83	61–110
Blood diseases	10	98	47–181
Nervous system diseases	27	68	45–98
Circulatory diseases	1661	80	77–84
Respiratory diseases	190	67	58–77
Digestive system diseases	105	63	51–76
Genitourinary system diseases	35	57	39–79
External causes	213	76	66–87
Other specified causes	71	45	35–56
Unknown causes	122 (4%)		

two hourly workers, dying in 1982 and 1989, had "myeloproliferative disease" (ICD code 238.7), specified by the ICD classification as a "neoplasm of uncertain behavior." Finally, three other men had MF (n = 2) or preleukemia (n = 1) reported as a contributing, rather than underlying, cause of death. All of the men who died of MF/MDS or myeloproliferative disease had started working at the plant in or before 1945. The subject with preleukemia was hired in 1955.

The finding of two mesothelioma decedents among hourly workers with "other and unspecified cancer" prompted us to review the death certificates of all other cohort members to determine if there were additional mesothelioma deaths, coded to other ICD categories. We found a total of nine mesothelioma deaths, eight of which occurred in or after 1980. The expected number of deaths could not be estimated because national mortality rates are not available for this type of cancer. However, using 1973–1980 and 1985–1988 SEER mesothelioma incidence rates and assuming that rates before 1970 were one-half the 1973–1980 rates or lower, the expected number of cases was about 0.5 for the 1942–1969 time period, 1.5 for 1970–1979, and 2.5 for 1980–1989. The SMR was 200 (CI = 92–380) overall and 320 (CI = 138–630) for the 1980s. These results may be underestimates of the true SMRs because in the general population, disease incidence rates are higher than mortality rates. All of the subjects with mesothelioma were hourly; all but two started working at the plant before 1950; and several had jobs that may have entailed exposure to asbestos (eg, pipefitter, insulator, carpenter) (Table 3).

Salaried Workers

Salaried workers had fewer deaths than expected for all major disease categories. There was a small increase in lymphopoietic cancer deaths, because of a statistically significant excess of leukemia (11 observed/5.1 expected; SMR = 216, 95% CI = 108–386), which was

TABLE 3
Characteristics of Subjects with Mesothelioma

Year of death	Age at death	ICD code*	Employment dates	Plant job titles
1972	56	199.1	1937–1967	Pipefitter
1981	63	199.1	1956–1981	Carpenter, maintenance
1984	68	228.0	1942–1971	Instrument repairman
1986	67	163.9	1941–1980	Yardman, insulator
1986	73	162.9	1938–1966	Various jobs, lube comp. and ship; laborer and yardman, engineering field; drum reconditioner and other jobs, compounding
1987	67	199.1	1947–1954	Fireman helper, boiler house; extra man, lube filters; extra man, clay handler and clay burner; operator helper, lube-oil filters
1987	82	162.9	1935–1962	Tester, control lab, experimental lab
1987	70	163.9	1945–1946	Fireman helper; boiler washer
1988	57	199.1	1953–1958	Pipefitter helper

* Code assigned by nosologist.

restricted to the 1940–1984 time period (9 observed/3.7 expected; SMR = 242, 95% CI = 110–460).

Leukemia, Mortality, Patterns

As shown in Table 4, the slight overall increase in leukemia among hourly workers was concentrated among subjects who were under 45 years of age at the time of death (SMR = 211, 95% CI = 77–460), who died before 1970 (SMR = 188, 95% CI = 115–290), who were hired before 1940 (SMR = 123, 95% CI = 74–192), who worked at the plant for 10+ years (SMR = 123, 95% CI = 81–179), and who died 10–39 years after starting work (SMR = 154, 95% CI = 102–222). All six of the men who were under 45 years of age at the time of death died before 1970, five of them before 1960 (SMR = 303, 95% CI = 98–707). The increase in leukemia among salaried workers was concentrated among men who died at age 45 and older (SMR = 256, 95% CI = 128–459), who were hired before 1950 (SMR = 275, 95% CI = 132–505), who worked for 10+ years (SMR = 306, 95% CI = 123–630), and who died 10+ years after hire (SMR = 236, 95% CI = 118–422).

For the overall cohort, all of the leukemia excess occurred before 1980 (SMR = 168; 95% CI = 119–230). For the period 1980–1989, there were fewer observed than expected leukemia deaths (SMR = 55, 95% CI = 24–108). The deficit was due to the occurrence of only four leukemia deaths among hourly workers, compared to 12 expected. Salaried workers had slightly more leukemia deaths than expected in 1980–1989 (4/2.4), but this difference was based on small numbers. When leukemia mortality in 1980–1989 was examined by cell type, again, there were no excesses. Cell type-specific observed/expected numbers were 3/4.5 for lymphocytic leukemia (including one subject with hairy cell leukemia), 4/6.1 for myelocytic leukemia, 4/4.1 for acute myelocytic leukemia, and 1/3.9 for unspecified leukemia.

Discussion

The results of the present study and of other investigations of petroleum industry workers consistently indicate that such workers have overall mortality rates that are moderately lower and cancer rates that are slightly lower than the rates of the general population.[7] This pattern may be attributable in part to the employment of relatively healthy individuals by the industry and to socioeconomic benefits associated with employment. However, the persistence of the low rates even after long periods of follow-up and the consistency and strength of the observed mortality deficits suggest that petroleum refinery and related workers are not exposed to strong or pervasive health hazards.

This study found persuasive evidence that the leukemia excess observed among the workers during the period 1940–1979 was no longer present in the 1980s. In fact, a deficit of leukemia was observed for the latter time period among hourly workers. The recent deficit does not appear to be attributable to incomplete vital status ascertainment, inasmuch as there was no consistent pattern of lower SMRs in 1980–1989, compared with 1940–1979. Instead, the apparent leukemia deficit may be due to chance or to problems with certifying leukemia as the underlying cause of death, as discussed later in relation to MF/

TABLE 4
Observed/Expected Leukemia Deaths among White Men by Selected Characteristics

	Observed/expected deaths		
	Hourly	Salaried	Total
Overall	35/32	11/5.1*	46/37
Age at death			
<45	6/2.8	0/0.8	6/3.6
45–54	4/3.7	3/0.8	7/4.5
55–64	8/7.4	2/1.3	10/8.7
65+	17/18	6/2.2*	23/20
Period of death			
<1960	9/4.6	2/0.5	11/5.1*
1960–1969	11/6.1	0/0.8	11/6.9
1970–1979	11/9.2	5/1.4*	16/11
1980–1989	4/12*	4/2.4	8/14
Period of hire			
<1940	19/15	6/1.8*	25/17
1940–1949	12/13	4/1.9	16/15
1950+	4/3.3	1/1.4	5/4.7
Years worked			
0.5–9	8/10	4/2.8	12/13
10–19	7/5.9	3/0.9	10/6.8
20+	20/16	4/1.4	24/17
Years since hire			
<10	1/1.6	0/0.5	1/2.1
10–19	7/3.1	2/0.7	9/3.8*
20–29	8/5.9	2/1.0	10/6.9
30–39	13/9.2	3/1.4	16/11
40+	6/12	4/1.6	10/14

* $P < 0.05$.

MDS. On balance, the results for leukemia imply that any occupational leukemogenic exposures that might have been present at the plant have been reduced to the point at which they are insufficient to cause leukemia.

Five follow-up studies among petroleum workers, in addition to this study, have reported increased leukemia SMRs (Morgan and Wong, unpublished observations).[8,9–11] The SMRs ranged from 110 to 246, with the excess being statistically significant in only one of the studies (Morgan and Wong, unpublished observations). Eight additional studies have reported leukemia mortality rates that are similar to or lower than the rates of the general population (Hornstra, unpublished observations).[12–18] None of the other studies with positive results for leukemia covers the entire 1980–1989 decade. Therefore, it is not possible to determine if the trend of reduced leukemia mortality in the 1980s observed in the present study is generalizable to other groups of petroleum industry workers.

Some petroleum industry studies have reported excesses of various cancers other than leukemia, including central nervous system cancer, kidney cancer, skin cancer, lymphosarcoma, and "other lymphopoietic tissue" cancer.[7] The present investigation did not find any consistent excess of any of these cancers. Kidney cancer deaths were slightly elevated among hourly workers in 1985–1989, but the increase was limited to short-term workers.

The present study confirms an earlier report,[5] which suggested that the employees have a higher rate of MF/MDS than expected. The increase appears to be related to the same time period of employment as the leukemia excess, but the reason for the excess is unknown. MF/MDSs share some clinical and pathological features with certain types of leukemia, and some cases of MF/MDS have been reported to coexist with or to progress to leukemia.[19,20] Thus, MF/MDS and leukemia may be part of a single disease process. In addition, there may have been a local shift in diagnosis or reporting practices in the 1980s, with some persons

designated as having MF/MDS, who, if diagnosed in earlier time periods, would have been designated as having leukemia. This interpretation is supported by the fact that in the 1980s, the excess of MF/MDS (4 observed/0 expected) was closely balanced by the deficit of leukemia (8 observed/14 expected) during the same decade. That is, if leukemia and MF/MDS are considered as a single disease category, the combined observed number of deaths is approximately equal to the expected number. Another follow-up study of workers from various petroleum refineries reported 3 observed compared to 1.5 expected MF deaths in the time period before 1981.[18] Other investigations of petroleum industry workers have not reported results separately for MF or MDS.

Whereas only one death from mesothelioma occurred among the employees in the period 1940–1979, there were eight such deaths, constituting an apparent excess, in the 1980s. The job histories of the men with this cancer indicate that several of them had potential for exposure to asbestos during their employment, and the observed excess may be due to this agent, which is an established cause of mesothelioma. Two other investigations also have reported what appears to be an unusual number of mesothelioma deaths among petroleum industry workers (Hornstra, unpublished observations).[18]

Acknowledgment

This study was supported by a contract with the Shell Oil Company.

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