Contains No CBI

Mary Jane Von Allmen **Texaco Inc**
Manager
Product Safety

PO Box 509
Beacon NY 12508
914 838 7294
914 838 7105 FAX

93 MAY 20 PM 2:05

23PP

A

May 11, 1993

FYI-93-000883
INIT 05/20/93

Document Processing Center
Attn: Section 8(e) Coordinator
Office of Toxic Substances
U.S. Environmental Protection Agency
401 M Street, S.W.
Washington, DC 20460

84930000021

SUBJECT: FOR YOUR INFORMATION

Dear Sir or Madam:

Attached is an updated cohort mortality study of male workers employed at least six months between 1943 and 1990 at a 1,3-butadiene production plant in Pt. Neches, Texas. This cohort has been the subject of two earlier published studies (Downs et al, 1987; Divine, 1990). The update examines mortality patterns with an additional five years of follow-up, new cohort members, and complete work history information.

The overall pattern of the results is essentially the same as previously reported. For the total cohort, the all causes SMR is 88 (95% CI 82-93); the all cancers SMR is 87 (95% CI 76-100). The elevated SMR for lymphosarcoma of 209 (95% CI 95-396) is still the major finding. For comparison, in the previous update (Divine, 1990) the lymphosarcoma SMR was 229 (95% CI 104-435). The SMR for all lymphohematopoetic cancers (all LHC) is also elevated in both the present study (SMR = 143, 95% CI 100-200) and the previous update (SMR = 130, 95% CI 84-192). For both lymphosarcoma and all LHC, the highest SMRs are seen in short-term workers and SMRs decrease with increasing length of employment, arguing against a causal relationship with 1,3-butadiene exposure. Lymphosarcoma and all LHC SMRs are based on comparison to national mortality rates, and would be lower if compared to local mortality rates.

This paper has also been forwarded to the organizers of the International Symposium on Health Hazards of Butadiene and Styrene. Selected results were presented in a platform session at that meeting on April 21, 1993. The abstract of that presentation is also enclosed.

CAS # 106-99-0

RECEIVED 12-9-93

1

These results are being forwarded to you for your information. If you have any questions, please contact Barbara J. Divine at (713) 752-6290.

Very truly yours,

Mary Jane Von Allmen

FAR:jra
far\8ecoor.ltr

Enclosures

Cancer mortality among workers at a butadiene facility

Divine, B. J., Wendt, J. K.
Texaco Inc.
P. O. Box 1404
Houston, TX 77251 U.S.A.

This is a cohort mortality study of 2749 male workers employed at least 6 months between 1943 and 1990 at a 1,3-butadiene facility. Most of this cohort was the subject of two earlier reports[1,2] both of which found a statistically significant deficit for all causes of death and lower than expected mortality for most of the leading causes of death. There was, however, a statistically significant excess of death from lymphosarcoma which was concentrated in those employed less than 10 years and first employed before 1946. The cohort was also divided into exposure groups based on their department codes, and exposure group mortality was examined. The lymphosarcoma deaths were concentrated in those employed in jobs with the potential for routine exposure. No excess of leukemia was seen for the cohort overall, but there was a nonsignificant elevation for the nonroutine exposure group.

The purpose of this update was to examine the patterns of mortality with 5 additional years of follow-up. In addition, we obtained copies of the complete work histories for the cohort members in an effort to characterize better the potential for exposure. Through meetings with long-term plant personnel and industrial hygienists we were able to develop a list of jobs having similar potential for exposure that should be grouped together and a history of the major changes in processes at the plant. These groupings and histories were used to develop subcohorts for analysis. We also added persons who had become eligible since the cohort was first assembled in 1979.

Of the 2749 males eligible for inclusion in the expanded cohort, 2624 were eligible for the cohort in the earlier reports. We have found additional original eligibles by rescreening all the plant personnel records, and we also removed a few people who were since determined not to meet the eligibility criteria. We were able to obtain vital status information on all but 2.3% of the cohort, and 1040 deaths were identified. Death certificates were obtained for all but 23 of the deaths (2.2%). The standardized mortality ratio (SMR) for all causes of death is 88 which is statistically significantly low and that for all cancer is 88 which is not significant. The SMR for all lymphohematopoietic cancers is 144 (95% confidence interval: 100-200) and that for leukemia is 113. There were no additional deaths from lymphosarcoma giving an SMR of 210 which is no longer statistically significant. Slight elevations were also seen for cancer of the larynx (SMR=140), cancer of the prostate (SMR=108), cancer of the kidney (SMR=144), Hodgkin's Disease (SMR=177), and cancer of other lymphatic tissue (SMR=127). None of these SMRs was statistically significant. Another SMR which was significantly elevated was that for ill-defined diagnoses such as "natural causes" (SMR=229).

1 Downs TD, Crane MM, and Kim KW. Mortality among workers at a butadiene facility. *Am J Ind Med* 1987; 12:311-329.
2 Divine BJ. An update on mortality among workers at a 1,3-butadiene facility - preliminary results. *Environ Health Perspect* 1990; 86:119

3

CANCER MORTALITY AMONG WORKERS AT A BUTADIENE FACILITY

by

Barbara J. Divine, Ph.D.
Judy K. Wendt, M.P.H.
Christine M. Hartman, Ph.D.

Texaco Inc.
P. O. Box 1404
Houston, TX 77251
(713)752-6290

Running head: Cancer mortality among butadiene workers

Key words: carcinogens, environmental, longitudinal studies, mortality, neoplasms, occupational diseases, rubber manufacturing, butadiene, lymphohematopoietic cancer

4

ABSTRACT

This is a cohort mortality study of 2749 male workers employed at least 6 months between 1943 and 1990 at a 1,3-butadiene facility. Most of this cohort was the subject of two earlier reports both of which found a statistically significant deficit for all causes of death and lower than expected mortality for most of the leading causes of death. However, both found a statistically significant excess of lymphosarcoma which was concentrated in those employed less than 10 years, first employed before 1946, and employed in the group with routine potential for exposure.

The purpose of this update was to examine the patterns of mortality adding 5 years of follow-up, new eligible cohort members, and complete work history information. We were able to obtain vital status information on all but 1.4% of the cohort, and 1051 deaths have been identified from 1943 to 1990. Death certificates were obtained for all but 15 of the deaths (1.4%). The standardized mortality ratio (SMR) for all causes of death is 88, and this low figure was statistically significantly while the SMR for all cancer was not statistically significant at 87. The SMR for all lymphohematopoietic cancers is 143 (95% confidence interval: 100-200). The SMR for leukemia is 112 (11 deaths), for lymphosarcoma the SMR is 209 (9 deaths), the SMR for other lymphomas is 126 (10 deaths), and that for Hodgkin's disease is 175 (4 deaths). None of these latter SMRs is statistically significant.

INTRODUCTION

This study reports on updated cause-specific mortality in a cohort of workers at a butadiene (BD) production plant. The plant was built during World War II in Port Neches, Texas to supply 1,3-butadiene to two adjacent rubber manufacturing facilities through the combined efforts of 5 local oil companies who operated it jointly during the war. In order to get the plant started, the

5

companies often lent experienced personnel from their refineries for short periods of time until the end of the war. This cohort was the subject of two earlier reports (Downs et al., 1987; Divine,1990) which covered the period from the opening of the plant through 1985. The original cohort consisted of all males who were employed at the plant for at least six months between the time the plant began operation in 1942 and the end of 1979.

The earlier reports found a 16 percent deficit for all causes of death and a 20 percent deficit for all cancers, both of which were statistically significant. Almost all the leading causes of death showed lower than expected mortality. Both earlier reports found a statistically significant excess of death from lymphosarcoma which was concentrated in those employed less than 10 years and first employed before 1946. The cohort was also divided into exposure groups based on their final department codes, and exposure group mortality was examined. The lymphosarcoma deaths were concentrated in those employed in jobs with the potential for routine or daily exposure to BD. No excess of leukemia was seen for the cohort overall or for the routine exposure group, but there was a nonsignificant elevation for the group exposed to BD on a non-routine basis.

The purpose of this update was to examine the patterns of mortality with five additional years of follow-up through December 31, 1990. In addition, 124 new persons have been added who worked at least six months at the facility since 1979 and before the end of follow-up, and copies of the complete work histories for all members of the cohort were obtained in an effort to characterize better the potential for exposure to BD.

METHODS

The study population includes those in the earlier reports (Downs et al., 1987; Divine, 1990). In addition, company computerized personnel records were searched for mention of persons who were employed at any time at the BD facility. The requirement for inclusion was at least six

6

months of employment between the time the plant went into operation and the end of 1990. The lists of cohort members were used to identify personnel records to be copied. At the same time the records were copied, other records in the files were scanned for additional eligible employees who may have been missed in the original cohort assembly. Demographic information on new cohort members, as well as complete work histories for the total cohort, were entered into a computer database.

Vital status follow-up through the end of 1990 was done on all persons without a death certificate who were not employed by the company as of December 31, 1990. Vital status information was obtained from the Social Security Administration death tapes, the National Death Index, the Health Care Financing Administration, Equifax, company pension records, and the Texas Department of Public Safety. Death certificates were obtained either from company files or from the state where the death was recorded. All death certificates were coded by a trained nosologist according to the Eighth Revision rules of the International Classification of Diseases.

Meetings were held with plant industrial hygienists and long-term employees to review each of the jobs and units mentioned on the work histories. The jobs and units were ranked according to their potential for exposure to BD. The ranks were then used to group jobs with similar potential for exposure into four groups; background, low, non-routine and routine exposure. The groups are similar to those used in the earlier reports on this cohort. Since the complete work history was used, it is possible for persons to have employment time in more than one exposure group. However, the background exposure group was restricted to those employed only in this group.

The **background exposure group** consists of those exposed at plant background levels including office, utilities, warehouse, and transportation employees. The **low exposure group** is composed of workers who spent time both on the operating units and also in the office or maintenance shops such as planners or engineers. This group also includes maintenance workers

with low potential for exposure such as welders, carpenters, and brickmasons.

The **non-routine exposure group** consists of maintenance workers who could have a high potential for exposure while working on the process units but whose jobs could also involve work in areas with limited potential for exposure. This group includes boilermakers, pipefitters, tinsmiths, instrument and electrical workers, and insulators. The **routine exposure group** includes workers who were potentially exposed to BD on a daily basis and were assumed to have the highest potential for exposure over time. This group includes the quality control laboratory, the process units, and receipt, storage, and transport. From a review of recent industrial hygiene sampling results and from discussions with plant personnel, it appears that the major difference between the routine and the non-routine exposure groups is in the frequency of exposure, not in intensity.

Analysis of mortality was performed using Monson's computer program (Monson, 1974) to compare the observed and expected number of deaths, with the U.S. white male population as the comparison group. Because there were only 198 blacks in the cohort and 51 persons with race unknown, all males were assumed to be white for the analysis. Person-years were accrued beginning when the person met the cohort eligibility criteria. Those persons with vital status unknown were assumed to be lost to follow-up on the date last observed. Analyses were performed for the cohort overall, for those employed at least 5, 10, and twenty years, for those first employed before the end of 1945 versus after, and for the four exposure groups, both those ever employed in the group regardless of length of employment and those employed ten years or more. In addition, mortality for all causes of death, all cancers, all lymphohematopoietic cancers, lymphosarcomas and reticulum cell sarcomas, other lymphomas, and leukemia was examined by latency and duration of employment in the above groups.

8

RESULTS

The cohort consists of 2,749 men who had worked for at least six months prior to the end of 1990. There are 2625 persons who were eligible for the original cohort, and 124 persons who since met the eligibility criteria. Several persons were removed from the original cohort because it was determined that they either were females or had less than six months of actual working time. Table 1 shows the demographic and other characteristics of the total cohort and of the four exposure cohorts described above. There were 83,591 person-years of follow-up, and the mean duration of survival from cohort entry was 30.4 years. There were 1051 deaths in the cohort through 1990, and death certificates were obtained for all but 15 (1.4%) of them. There were 1,660 persons still alive at the end of the study (60.0%) and 38 (1.4%) lost to follow-up.

Table 2 shows the SMRs for selected causes of death for the total cohort and for those employed less than 5 years, 5-19 years, and greater than 20 years. The SMR for all causes of death for the cohort is statistically significant at 88, but the SMR for all cancer deaths was not statistically significant at 87. Deficits are seen for almost all the leading causes of death, and in particular, large, but nonsignificant, deficits are seen for stomach cancer (SMR= 50) and liver cancer (SMR=18). However, there is a significantly increased SMR of 143 for lymphatic and hematopoietic cancer (LHC) which is almost entirely due to the increased SMR of 209 for lymphosarcoma and reticulosarcoma and the SMR of 175 for Hodgkin's disease, neither of which is statistically significant. The increase for lymphosarcoma is seen primarily in those employed fewer than 5 years (6 of 9 cases, SMR =286). The Hodgkin's disease excess is based on only 4 cases, all employed less than 20 years. The category of symptoms, senility, and ill-defined conditions (SMR=267) is significantly elevated and has increased since the last update. Cancer of the kidney is elevated for all employment groups except those employed fewer than 5 years, but is not statistically significant for any of them.

9

Table 3 shows the SMRs for selected causes of death for those first employed during World War II (war hire group) vs. those who were first employed after the war. The SMR is increased for LHC for both subcohorts, but neither is significant. Much of the excess for those first employed during the war is due to the significantly elevated SMR for lymphosarcoma (SMR=254). Four of the 7 war hire group's lymphosarcoma deaths were employed less than 5 years (SMR=308) as were 4 of the 7 leukemia deaths (SMR=143). Hodgkin's disease is also elevated for the war hire group (SMR=164). For those first employed after the war, elevated SMRs are seen for lymphosarcoma, Hodgkin's disease, and cancer of other lymphatic tissue. None of these is statistically significant, and the numbers of observed deaths are small. Kidney cancer is again elevated for both groups although the SMR is higher for the wartime hires.

Table 4 shows the SMRs for selected causes of death for each of the exposure groups for all in the subgroup and for those employed 10 years or more in the group. The **background exposure group** shows elevated SMRs for all cancers, cancer of the large intestine, all LHC, Hodgkin's disease, other lymphomas, and pneumonia for those ever in the group. Almost all of these SMRs are smaller for the subgroup employed 10 years or more in this category. For the **low exposure group**, elevated SMRs are seen for lung cancer, cancer of the kidney, other lymphomas, stroke, and pneumonia. The SMRs for kidney cancer, non-malignant respiratory disease, and pneumonia increase for those employed 10 years or more in this group.

The **non-routine exposure group** has a nonsignificant excess of LHC (SMR=180) which is primarily due to an increase in leukemia mortality (SMR=207). Only one of the six leukemia deaths was employed 10 or more years in this group (SMR=104). The other LHCs are also elevated although the numbers are small, and the elevations are not statistically significant. The LHC SMR is higher for the long-term employees, but there is only one death in each of five separate categories. The **routine exposure group** has a statistically significant excess for lymphosarcoma (SMR=452),

10

and all of the 6 deaths occurred in those employed less than 10 years. Elevated SMRs are also seen for cancer of the prostate and pneumonia. Elevations for cancer of the prostate, cancer of the kidney, and other lymphomas are also seen for those employed 10 years or more. None of these elevations is statistically significant.

The number of observed and expected deaths by years worked and latency for all deaths, all cancer deaths, all LHC deaths, lymphosarcoma, and leukemia were examined for all males and each of the exposure groups. For all deaths and all cancers, the SMRs are essentially unchanged as either latency or duration of employment increases. For all LHC deaths, the highest SMRs are seen for those with latency and length of employment fewer than 10 years, and the SMRs decrease with increasing employment. For lymphosarcoma, again the largest SMR is for those with the shortest employment and latency, and the SMRs decrease with increasing latency and with increasing length of employment. The pattern for the routine exposure group (Table 5) where most of the lymphosarcoma deaths are concentrated shows decreasing SMRs with increasing length of employment. The largest SMR is for those with both the shortest latency and length of employment. The SMRs for leukemia for the non-routine group (Table 6) increase and then decrease with both increasing length of employment and latency. For other lymphomas, no pattern is seen for any of the exposure groups.

DISCUSSION

The overall pattern of results seen for this update is essentially the same as those seen in the earlier reports on this cohort (Downs et al., 1987; Divine, 1990). There was a statistically significant reduction in expected mortality (SMR=88) when compared with the U.S. white male population which was primarily due to a reduction in deaths due to arteriosclerotic heart disease (SMR=72) and to mostly non-significant deficits in a few categories with smaller numbers of deaths.

The major finding is still the elevated SMR for lymphosarcoma (209) which is concentrated in those employed fewer than 10 years, first hired during World War II, and employed in a job with the potential for routine exposure. There were no additional cases since 1985 (0.4 expected), and the SMR is no longer statistically significant for the cohort as a whole. The fact that the SMRs decrease with increasing length of employment and are not elevated in the groups employed the longest (and presumably with the highest cumulative exposure) tends to argue against a causal relationship.

The original report by Downs *et al.* (1987) calculated SMRs using local rates (for a seven county area in the Texas Gulf Coast area) as well as national rates. The SMR for lymphosarcoma was about 22 percent lower using local rates. While national rates were used for all SMR calculations in this report, mortality rates for specific cancers from 1976-1989 were obtained from the Texas Department of Health, and the national and local rates for all malignant neoplasms, lung cancer, leukemia, and lymphosarcoma were compared. The local rates for all the above causes except lymphosarcoma were generally within 10 percent of the national rates. However, the local lymphosarcoma rates were 2-3 times the national rates. It is likely that this difference in rates is responsible for much of the increase in the lymphosarcoma SMRs seen in this cohort.

There were 10 additional deaths from all LHC that occurred in the additional 5 years of follow-up. Most of the increases were due to additional deaths from leukemia and Monson's "other lymphoma" category which includes lymphomas and multiple myelomas. Five of the deaths in the other lymphoma category were multiple myelomas, 3 of which occurred since the last update. Three of the multiple myeloma deaths were employed about 30 years or more, 2 in the routine exposure group and 1 in the non-routine group, and 2 were employed less than one year. All were first employed in the 1940's. Rates from the local seven county area were used to calculate the expected number of multiple myelomas from 1975-1990. There were 5 observed deaths and 2.2 expected

12

giving a nonsignificant SMR of 222.

Although the leukemia SMR is not elevated for the cohort overall, it is nonsignificantly elevated for the non-routine exposure group. Seven of the 11 leukemia deaths in this cohort occurred in persons who were first employed during the war and 8 of the 11 in those employed less than 5 years. Again, the fact that the SMR decreases with length of employment and that no elevation is seen in the longest exposed group argues against a causal relationship.

The elevated SMRs for lymphosarcoma and leukemia are concentrated in those persons in the war hire group who were employed less than 5 years. The way the plant was staffed in the early years, i.e., using a number of experienced personnel from the 5 companies operating the facility for short periods of time, may have had an effect on the mortality results for this subcohort. Obviously these experienced persons had a number of other occupational exposures both before and after their time at the BD monomer plant. No information about these and any other confounding factors is available.

The increased SMRs for Monson's category "symptoms, senility, and ill-defined conditions" is not readily explainable. The increase is concentrated in persons who were employed fewer than 20 years, but is seen for all exposure groups and regardless of time first employed. The number of deaths in this category would decrease if more specific cause of death information was available from the attending physician. The increase seen for pneumonia for many subgroups of this cohort may also be due to the lack of specificity in cause of death information.

Two other studies have examined mortality in cohorts exposed to 1,3-butadiene although both cohorts consisted of persons engaged in the manufacture of styrene-butadiene rubber (SBR) and so had the opportunity for multiple exposures. The first study (Matanoski and Schwartz, 1987; Matanoski *et al.*, 1990; and Santos-Burgoa *et al.*, 1992) covered males who had worked at 8 SBR manufacturing facilities in the U.S. and Canada. The overall SMR (81) was similar to that seen for

the current study. There were elevated SMRs for esophageal cancer in whites; stomach cancer in blacks; arteriosclerotic heart disease in blacks, especially maintenance workers; LHC in black but not white production workers; digestive cancers in maintenance workers; and rheumatic heart disease for the category of other work areas. No overall excess was seen for LHC or for leukemia, and there was a deficit for lymphosarcoma. The excesses seen in blacks and in job specific categories are questionable because of problems in enumerating the denominators for the SMRs. A nested case-control study (Santos-Burgoa *et al.*, 1992) of LHC using regression analysis reported a strong association between exposure to BD and leukemia, with an odds ratio of 9.36. No association was reported between any of the other LHCs and BD exposure, nor were any associations seen with styrene. In addition, no association was seen between leukemia and jobs in process or maintenance which have the highest exposures to BD. Cole *et al.* (1993) have stated that the Santos-Burgoa *et al.* study can not be interpreted as showing a causal relationship because of the discrepancy between the cohort and the case-control study.

The second study by Meinhardt *et al.* (1982) covered persons employed at the two SBR plants supplied by the facility in the current study. The Meinhardt study reported an elevated SMR for leukemia which was significant for those persons hired during the war and which was concentrated in those having short latency and length of employment. Elevated SMRs for lymphosarcoma were also seen although they were not statistically significant and were not as high as those seen in this study. One major problem with comparisons between the Meinhardt study and the present one is the overlap between the study cohorts, including at least one of the leukemia deaths and one of the lymphosarcoma deaths. The increases for each of these populations and the LHCs may be exaggerated because of this, and the double counting of some deaths has not been acknowledged in summaries which have grouped the data from the different studies.

There appear to be major inconsistencies among the diseases reported in excess for each of

the three prior studies of BD workers. One study (Meinhardt *et al.*, 1982) found an excess of leukemia in workers employed during World War II; another study (Downs *et al., 1987*; Divine, 1990) found an excess of lymphosarcoma, primarily in short-term workers first employed during World War II; and the third study (Matanoski *et al.*, 1990) found an excess leukemia in black production workers but not in white production workers. The case-control study (Santos-Burgoa *et al.*, 1992) also showed a strong association between leukemia and BD exposure, a result which is not compatible with the cohort results of 22 observed and 23 expected leukemias (Cole *et al.*, 1993). The Cole *at al.* review combined the data from the three studies (Meinhardt *et al.*, 1982; Matanoski *et al.*, 1990; Divine, 1990) and concluded that the SMRs for leukemia, lymphosarcoma, and other forms of LHC were all very similar. The SMRs were also very similar when mortality was examined by length of employment. Cole *et al.* (1993) concluded that "these data support the absence of a causal relation between employment in the styrene-butadiene rubber industry and LHC."

The results of the study reported here are also not consistent with the risk assessment done by Dankovic *et al.* (1991) using tumor incidence data from a low dose BD mouse bioassay. The Dankovic risk assessment predicted 5.97 excess cancers per 100 workers per lifetime assuming 2 ppm exposure for 45 years. The war hire group has now been followed for 45 years and had an average length of employment of 12.7 years. Using the NIOSH risk assessment results and assuming an average exposure of 10 ppm (which is the company's internal standard) would predict 255.3 total cancers (observed=139), 140.7 lung cancers (observed=49), and 103.3 LHCs (observed=22). The probabilities that these are the true risks given the observed numbers of deaths for each cause are all less than 10^{-14}.

There are several weaknesses in the current study. Although complete work histories are now available, there are no industrial hygiene sampling data for all but the last 10 years of the

15

study. Over half of the cohort worked fewer than 5 years at the BD monomer facility and obviously spent considerable working time elsewhere. Thus they have the possibility for numerous other exposures. As mentioned above, it is this portion of the cohort in which the increased SMRs are concentrated. Finally, the cohort size is small, and the numbers become even smaller for the exposure group analyses. The causes of death of concern are rare, and the small numbers make interpretation difficult.

However, the cohort is one of the largest groups of individuals involved solely in the manufacture of butadiene and has been followed for 48 years. It includes all those with 6 months or more employment since the plant began production; the numbers with vital status unknown (1.4%) and without cause of death information (1.4%) are extremely small; and qualitative measures of exposures were available. Consequently, it is an important cohort for the evaluation of the potential health risks of BD.

REFERENCES

Cole P, Delzell E, and Acquavella J (1993): Exposure to butadiene and lymphatic and hematopoietic cancer. *Epidemiology* 4:96-103.

Dankovic DA, Smith RJ, Seltzer J, Bailer AJ, Stayner L (1991): A quantitative assessment of the risk of cancer associated with exposure to 1,3 butadiene, based on the low dose inhalation study in $B_6C_3F_1$ mice. NIOSH.

Divine BJ (1990): An update on mortality among workers at a 1,3-butadiene facility - preliminary results. *Environ Health Perspect* 86:119-128.

Downs TD, Crane MM, and Kim KW (1987): Mortality among workers at a butadiene facility. *Am J Ind Med* 12:311-329.

Matanoski GM and Schwartz L (1987): Mortality of workers in styrene-butadiene polymer

16

production. *J Occup Med* 29:675-680.

Matanoski G M, Santos-Burgoa C, and Schwartz L (1990): Mortality of a cohort of workers in the styrene-butadiene polymer manufacturing industry (1943-1982). *Environ Health Perspect* 86:107-117.

Meinhardt TJ, Lemen RA, Crandall MS, and Young RJ (1982): Environmental epidemiologic investigation of the styrene-butadiene rubber industry: Mortality patterns with discussion of the lymphohematopoietic and lymphatic malignancies. *Scand J Work Environ Health* 8:250-259.

Monson R. R. (1974): Analysis of relative survival and proportionate mortality. *Computer Biomed Res* 7:325-332.

Santos-Burgoa C, Matanoski GM, Zeger S, and Schwartz L (1992): Lymphohematopoeitic cancer in styrene-butadiene polymerization workers. *Am J Epidemiol* 136:843-854.

17

Table 1. Demographic, employment, and other characteristics of the study population and exposure cohorts.

Cohort	Total	Background exposure	Low exposure	Non-routine exposure	Routine exposure
Number of persons	2749	347	958	865	1056
Percent of total	(100.0%)	(12.6%)	(34.8%)	(31.5%)	(38.4%)
Mean age of entry, years	30.8	31.6	34.6	30.2	27.9
Mean year of entry	1954	1953	1954	1955	1956
Number hired between 1940-45	1050	176	492	339	374
Percent of cohort	(38.2%)	(50.7%)	(51.4%)	(39.2%)	(35.4%)
Mean years of employment	12.0	11.5	12.9	12.3	13.1
Number of lost to follow-up	38	7	19	13	7
Percent of each cohort	(1.4%)	(2.0%)	(2.0%)	(1.5%)	(0.7%)
Number of person-years	83591	10606	27196	26204	32864
Number of deaths	1051	151	419	296	302
Percent of deaths in each cohort	(38.2%)	(43.5%)	(43.7%)	(34.2%)	(28.6%)
Number without death certificates	15	3	2	4	6
Percent of deaths	(1.4%)	(2.0%)	(0.5%)	(1.4%)	(2.0%)
Mean age at death, years	65.6	66.9	67.3	65.7	61.8
Mean year of death	1975	1975	1974	1976	1977
Mean duration of survival, years	30.4	30.6	28.4	30.3	31.1

Table 5. Observed and expected deaths from lymphosarcoma by years worked and latency in the routine exposure group.

Years worked		Latency, years 0-9	10-19	20-29	30+	Totals
Routine exposure						
<5	Observed	2	0	1	2	5
	Expected	0.1	0.1	0.2	0.3	0.7
	SMR[a]	3333	--	476	714	725
5-19	Observed	1	0	0	0	1
	Expected	0.0	0.1	0.0	0.0	0.2
	SMR[a]	--	--	--	--	455
20+	Observed	--	--	0	0	0
	Expected	--	--	0.2	0.2	0.4
	SMR[a]	--	--	--	--	--
Totals	Observed	3	0	1	2	6
	Expected	0.1	0.3	0.4	0.5	1.3
	SMR[a]	3333	--	250	385	452

[a]SMR, standardized mortality ratio

Table 6. Observed and expected deaths from leukemia by years worked and latency in the non-routine exposure group.

Years worked		Latency, years 0-9	10-19	20-29	30+	Totals
Non-routine exposure						
<5	Observed	0	1	1	2	4
	Expected	0.2	0.3	0.4	0.9	1.8
	SMR[a]	--	385	244	217	225
5-19	Observed	0	0	2	0	2
	Expected	0.1	0.2	0.2	0.2	0.6
	SMR[a]	--	--	1333	--	333
20+	Observed	--	--	0	0	0
	Expected	--	--	0.1	0.4	0.5
	SMR[a]	--	--	--	--	--
Totals	Observed	0	1	3	2	6
	Expected	0.3	0.4	0.7	1.5	2.9
	SMR[a]	--	227	441	132	208

[a]SMR, standardized mortality ratio

Table 4. (cont'd) Observed and expected deaths and SMRs for selected causes for cohort members by exposure group and length of employment.

Cause of death (8th ICDA[a])	Non-routine exposure group n=865, p-y=26204				Non-routine exposure group employed ≥ 10 yrs n=223, p-y=5358				Routine exposure group n=1056, p-y=32864				Routine exposure group employed ≥ 10 years n=343, p-y= 9199			
	Observed deaths	Expected deaths	SMR[a]	95% CI[a]	Observed deaths	Expected deaths	SMR	95% CI	Observed deaths	Expected deaths	SMR	95% CI	Observed deaths	Expected deaths	SMR	95% CI
All causes	296	348.9	85	75-95	81	117.8	69	55-85	302	359.9	84	75-94	107	136.8	78	64-95
All cancers (140-209)	58	76.1	76	58-98	17	25.9	66	38-105	72	82.6	87	68-110	26	32.9	79	52-116
Cancer of digestive system (150-159)	10	20.3	49	24-90	2	7.0	29	3-103	17	21.1	81	47-129	7	8.4	84	34-173
Cancer of stomach (151)	0	3.4	0	0-108	0	1.1	0	0-326	4	3.3	122	33-311	1	1.3	80	1-444
Cancer of large intestine (153)	6	7.1	85	31-185	2	2.5	80	9-289	5	7.4	67	22-157	3	3.0	101	20-294
Cancer of pancreas (157)	3	4.0	76	15-222	0	1.4	0	0-270	4	4.2	95	26-243	2	1.7	118	13-426
Cancer of lung (162-163)	19	25.5	74	45-116	4	8.6	47	13-119	20	29.2	68	42-106	7	11.9	59	24-121
Cancer of prostate (185)	6	5.9	102	37-223	3	2.4	126	25-369	9	5.4	168	77-319	5	2.2	224	72-524
Cancer of bladder (188)	1	2.2	45	1-251	1	0.8	120	2-665	1	2.1	48	1-265	0	0.9	0	0-432
Cancer of kidney (189)	2	1.9	108	12-389	0	0.6	0	0-600	2	2.1	97	11-349	2	0.8	243	27-877
Lymphatic and hematopoietic cancer (200-209)	13	7.2	180	96-308	5	2.4	213	69-498	12	8.0	151	78-263	2	3.0	66	7-240
Lymphosarcoma and reticulosarcoma (200)	2	1.2	164	18-592	1	0.4	256	3-1426	6	1.3	452	165-984	0	0.5	0	0-730
Hodgkin's disease (201)	1	0.7	145	2-808	1	0.2	623	8-3468	1	0.8	123	2-687	0	0.2	0	0-1530
Leukemia (204-207)	6	2.9	207	75-450	1	1.0	104	1-581	3	3.1	97	19-283	0	1.2	0	0-317
Other lymphatic tissue (202,203,208)	3	2.4	127	25-370	1	0.8	122	2-676	2	2.7	74	8-269	2	1.1	182	20-658
Arteriosclerotic heart disease (410-413)	95	122.6	78	63-95	30	43.7	69	46-98	82	122.8	67	53-83	31	48.8	64	43-90
Vascular lesions of CNS (430-438)	22	21.7	101	64-154	5	8.3	60	19-141	15	18.8	80	45-132	5	7.3	69	22-160
Nonmalignant respiratory disease (460-519)	19	24.1	79	47-123	6	9.1	66	24-144	19	23.7	80	48-125	5	9.5	53	17-123
Pneumonia (480-486)	8	8.2	98	42-193	3	3.1	96	19-281	10	7.5	133	64-245	3	2.9	105	21-305
All external causes (800-998)	22	28.8	77	48-116	3	6.3	47	10-138	28	34.5	81	54-117	10	9.7	103	49-189

[a]8th ICDA, 8th International Classification of Diseases; SMR, standardized mortality ratio; 95% CI, 95% confidence interval

Table 4. Observed and expected deaths and SMRs for selected causes for cohort members by exposure group and length of employment

Cause of death (8th ICDA*)	Background exposure group n=347, p-y=10606				Background exposure group, employed ≥ 10 yrs n=137, p-y=3504				Low exposure group n=958, p-y=27196				Low exposure group, employed ≥ 10 years n=313, p-y= 6767			
	Observed deaths	Expected deaths	SMR*	95% CI*	Observed deaths	Expected deaths	SMR	95% CI	Observed deaths	Expected deaths	SMR	95% CI	Observed deaths	Expected deaths	SMR	95% CI
All causes	151	168.4	90	76-105	63	78.5	80	62-103	419	475.6	88	80-97	163	176.0	93	79-108
All cancers (140-209)	39	35.64	109	78-150	16	17.2	93	53-151	85	100.4	85	68-105	34	37.7	90	62-126
Cancer of digestive system (150-159)	10	9.8	102	49-187	3	4.7	64	13-188	12	28.0	43	22-75	4	10.5	38	10-98
Cancer of stomach (151)	1	1.7	58	1-322	0	0.8	0	0-479	1	5.0	20	0-112	0	1.8	0	0-208
Cancer of large intestine (153)	6	3.4	177	65-386	2	1.7	121	14-436	5	9.6	52	17-122	2	3.7	54	6-196
Cancer of pancreas (157)	1	1.9	53	1-298	0	0.9	0	0-403	4	5.3	76	20-194	2	2.0	99	11-358
Cancer of lung (162-163)	10	11.6	87	41-159	6	5.7	105	38-229	39	32.3	121	86-165	12	12.2	98	51-171
Cancer of prostate (185)	1	3.0	33	0-186	1	1.6	64	1-358	9	8.7	104	47-197	6	3.6	167	61-364
Cancer of bladder (188)	1	1.1	90	1-498	0	0.6	0	0-658	1	3.2	31	0-173	1	1.3	78	1-433
Cancer of kidney (189)	1	0.9	117	2-652	1	0.4	245	3-1366	4	2.4	167	45-428	3	0.9	340	68-994
Lymphatic and hematopoietic cancer (200-209)	6	3.3	181	66-395	1	1.6	64	1-358	9	9.3	97	44-184	4	3.4	118	32-303
Lymphosarcoma and reticulosarcoma (200)	0	0.6	0	0-645	0	0.3	0	0-1373	2	1.7	120	14-435	1	0.6	169	2-940
Hodgkin's disease (201)	2	0.3	661	74-2387	1	0.1	908	12-5052	0	0.8	0	0-457	0	0.2	0	0-1606
Leukemia (204-207)	1	1.4	73	1-409	0	0.6	0	0-578	3	3.8	79	16-230	1	1.4	71	1-397
Other lymphatic tissue (202,203,208)	3	1.1	283	57-828	0	0.5	0	0-687	4	3.0	135	36-346	2	1.1	176	20-634
Arteriosclerotic heart disease (410-413)	39	60.2	65	46-89	13	29.3	44	24-76	127	171.8	74	62-88	49	66.6	74	54-97
Vascular lesions of CNS (430-438)	9	11.5	78	36-148	7	5.5	126	51-260	42	33.5	126	90-170	18	13.1	137	81-216
Nonmalignant respiratory disease (460-519)	10	11.9	84	40-155	3	6.0	50	10-147	34	33.9	100	69-140	22	13.6	162	102-245
Pneumonia (480-486)	6	4.2	143	52-312	2	2.0	98	11-355	16	12.1	132	76-215	11	4.8	232	116-415
All external causes (800-998)	15	12.2	123	69-203	3	4.2	72	14-209	26	31.8	82	53-120	5	8.5	59	19-137

*8th ICDA, 8th International Classification of Diseases; SMR, standardized mortality ratio; 95% CI, 95% confidence interval

Table 3. Observed and expected deaths and SMRs for selected causes for all cohort members by time first employed

Cause of death (8th ICDA[a])	Employed < 1946 (war) n= 1050, p-y = 35061				Employed ≥ 1946 (postwar) n=1699, p-y = 48531			
	Observed deaths	Expected deaths	SMR[a]	95% CI[a]	Observed deaths	Expected deaths	SMR	95% CI
All causes	719	806.1	89	83-96	332	392.8	85	76-94
All cancers (140-209)	135	167.2	83	70-98	88	92.3	95	76-117
Cancer of digestive system (150-159)	24	47.6	50	32-75	21	22.6	93	57-142
Cancer of stomach (151)	2	8.6	23	3-84	4	3.4	118	32-302
Cancer of large intestine (153)	12	16.3	73	38-128	8	7.9	101	43-199
Cancer of pancreas (157)	5	8.9	56	18-131	6	4.6	130	47-283
Cancer of lung (162-163)	49	52.6	93	69-123	28	33.6	83	55-120
Cancer of prostate (185)	17	15.8	108	63-172	4	4.7	85	23-219
Cancer of bladder (188)	3	5.8	52	10-152	1	2.0	51	1-282
Cancer of kidney (189)	6	3.9	154	56-335	3	2.4	125	25-366
Lymphatic and hematopoietic cancer (200-209)	22	15.2	145	91-219	13	9.3	140	74-239
Lymphosarcoma and reticulosarcoma (200)	7	2.8	254	102-523	2	1.5	131	15-472
Hodgkin's disease (201)	2	1.2	164	18-590	2	1.1	188	21-680
Leukemia (204-207)	7	6.3	111	44-228	4	3.5	113	30-290
Other lymphatic tissue (202,203,208)	5	4.8	104	34-243	5	3.1	160	52-374
Arteriosclerotic heart disease (410-413)	212	297.1	71	62-82	94	127.1	74	60-91
Vascular lesions of CNS (430-438)	63	59.7	106	81-135	16	17.2	93	53-151
Nonmalignant respiratory disease (460-519)	54	60.4	89	67-116	22	22.8	96	60-146
Pneumonia (480-486)	29	21.6	134	90-193	9	7.1	127	58-241
All external causes of death (800-998)	43	44.3	97	70-131	36	49.0	74	51-102

[a]8th ICDA, 8th International Classification of Diseases; SMR, standardized mortality ratio; 95% CI, 95% confidence interval

Table 2. Observed and expected deaths and SMRs for selected causes for cohort members by length of employment

Cause of death (8th ICDA[a])	Total cohort n=2749, p-y=83591				Employed < 5 YEARS n=1393, p-y=48838				Employed 5-19 years n=556, p-y=23455				Employed ≥ 20 years n=800, p-y=14298			
	Observed deaths	Expected deaths	SMR[a]	95% CI[a]	Observed deaths	Expected deaths	SMR	95% CI	Observed deaths	Expected deaths	SMR	95% CI	Observed deaths	Expected deaths	SMR	95% CI
All causes	1051	1198.8	88	82-93	525	567.0	93	85-101	266	286.7	93	82-105	260	345.1	75	66-85
All cancers (140-209)	227	259.5	87	76-100	115	121.2	95	78-114	44	54.1	81	59-109	68	84.2	81	63-102
Cancer of buccal cavity and pharynx (140-149)	6	7.3	82	30-179	2	3.5	57	6-206	2	1.5	133	15-481	2	2.3	89	10-321
Cancer of digestive system (150-159)	45	70.2	64	47-86	26	32.8	79	52-116	6	15.9	38	14-82	13	21.5	60	32-103
Cancer of esophagus (150)	3	6.0	50	10-145	3	2.8	107	22-313	0	1.2	0	0-306	0	2.0	0	0-184
Cancer of stomach (151)	6	12.0	50	18-109	5	5.7	88	28-205	0	3.2	0	0-115	1	3.1	32	0-179
Cancer of large intestine (153)	20	24.3	82	50-127	8	11.2	71	31-141	4	5.2	77	21-197	8	7.9	101	43-199
Cancer of rectum (154)	3	7.0	43	9-125	1	3.3	30	0-169	1	1.8	56	1-309	1	1.9	52	1-289
Cancer of liver (155-156)	1	5.5	18	0-100	1	2.6	38	1-214	0	1.2	0	0-306	0	1.7	0	0-219
Cancer of pancreas (157)	11	13.5	81	41-146	7	6.2	113	45-233	1	2.9	34	0-192	3	4.4	69	14-201
Cancer of respiratory sys. (160-163)	83	90.6	92	73-114	43	42.2	102	74-137	14	16.6	84	46-142	26	31.8	82	53-120
Cancer of larynx (161)	6	3.6	167	61-364	6	1.7	353	129-768	0	0.7	0	0-524	0	1.2	0	0-320
Cancer of lung (162-163)	77	86.2	89	70-112	37	40.1	92	65-127	14	15.7	89	49-150	26	30.4	85	56-125
Cancer of bone (170)	1	0.9	106	1-592	1	0.4	250	3-1391	0	0.3	0	0-1223	0	0.2	0	0-1805
Cancer of skin (172-173)	4	4.6	88	24-225	2	2.2	91	10-328	0	1.1	0	0-333	2	1.3	151	17-544
Cancer of prostate (185)	21	20.5	103	63-157	6	9.1	66	24-144	7	4.5	156	62-321	8	6.9	116	50-229
Cancer of bladder (188)	4	7.7	52	14-133	2	3.5	57	6-206	0	1.8	0	0-204	2	2.4	82	9-297
Cancer of kidney (189)	9	6.3	143	65-272	3	3.0	100	20-292	2	1.3	154	17-555	4	2.0	197	53-504
Cancer of brain & central nervous system (191-192)	4	6.9	58	16-150	1	3.4	29	0-164	2	1.6	125	14-451	1	1.9	52	1-287
Lymphatic and hematopoietic cancer (200-209)	35	24.5	143	100-200	20	11.7	171	104-264	8	5.5	145	63-287	7	7.3	96	38-197
Lymphosarcoma and reticulosarcoma (200)	9	4.3	209	95-396	6	2.1	286	104-622	2	1.1	182	20-656	1	1.1	90	1-500
Hodgkin's disease (201)	4	2.3	175	47-448	2	1.2	167	19-602	2	0.7	286	32-1032	0	0.4	0	0-908
Leukemia (204-207)	11	9.9	112	56-200	8	4.7	170	73-335	2	2.3	87	10-314	1	2.9	35	0-194
Other lymphatic tissue (202,203,208)	10	7.9	126	60-232	4	3.6	111	30-284	2	1.4	143	16-516	4	2.9	139	37-356
Benign neoplasms (210-239)	4	3.3	123	33-314	1	1.6	63	1-348	2	0.8	250	28-903	1	0.9	113	1-630
Diabetes mellitus (250)	13	17.0	76	41-131	6	8.0	75	27-163	4	4.0	100	27-256	3	5.0	60	12-175
Arteriosclerotic heart disease (410-413)	306	424.2	72	64-81	143	194.6	73	62-87	91	103.1	88	71-108	72	126.5	57	45-72
Vascular lesions of CNS (430-438)	79	76.9	103	81-128	39	34.9	112	79-153	22	21.5	102	64-155	18	20.5	88	52-139
Nonmalignant respiratory disease (460-519)	76	83.3	91	72-114	32	38.1	84	57-119	25	18.2	137	89-203	19	27.0	70	42-110
Pneumonia (480-486)	38	28.7	133	94-182	15	13.3	113	63-186	12	7.3	164	85-287	11	8.1	136	68-243
Emphysema (492)	12	15.8	76	39-133	7	7.0	100	40-206	2	3.8	53	6-190	3	5.1	59	12-174
Cirrhosis of liver (551)	15	25.7	58	33-96	8	12.5	64	28-126	4	5.9	68	18-174	3	7.3	41	8-121
All external causes (800-998)	79	93.3	85	67-106	46	50.9	90	66-121	16	25.9	62	35-100	17	16.5	103	60-165

[a]8th ICDA, 8th International Classification of Diseases; SMR, standardized mortality ratio; 95% CI, 95% confidence interval