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Document Processing Center (Mail Code 7407M)  
 Room 6428  
 Attention: 8(e) Coordinator  
 Office of Pollution Prevention and Toxics  
 U.S. Environmental Protection Agency  
 1201 Constitution Ave., NW  
 Washington, D.C. 20460



CONTAIN NO CBI

Dear 8(e) Coordinator:

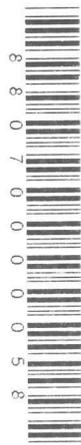
Acrylonitrile  
 CAS # 107-13-1

This letter is to inform you of the results of a recently completed epidemiology study entitled "Mortality Update for a Cohort of Acrylonitrile Workers Engaged in Fiber Production".

The study updated a retrospective cohort study (Wood, SM Scand J Work Environ Health 1998; 24(suppl 2):54-62) assessing all-causes and cancer mortality patterns of 2,548 male employees exposed for at least 6 months to acrylonitrile in fiber production at two plants that operated between 1944 and 1991. Since the two plants (May Plant, Camden, SC and Waynesboro, VA) ran identical processes using the same starting materials, data for workers at the two plants were combined to increase statistical power. Vital status follow-up was extended through December 31, 2002, and causes of death were obtained through the U.S. National Death Index (NDI *Plus*). Standardized mortality ratios (SMRs) were calculated using both U.S. population reference rates and rates based on regional DuPont workers. The regional DuPont reference population enabled us to reduce bias from the healthy worker effect and to control to some extent regional socio-cultural differences. Cox Proportional Hazards Modeling (CPHM) provided internal comparisons<sup>1</sup> for lung cancer using cumulative and peak exposure in separate statistical models.

An additional 385 deaths occurred in the cohort since 1991 (end of study for the last update); the total number of deaths was 839. SMRs for all causes of death combined (SMR = 69) and all malignancies combined (SMR = 73) were reduced when based on comparison to the U.S. general population, as would be expected due to the healthy worker effect. The use of rates based on DuPont Region 7 (DuPont employees in the states of Virginia, North Carolina, South Carolina, Georgia, Florida, Alabama, Mississippi, and Tennessee) returned somewhat higher SMRs, but both overall mortality and all cancer mortality remained decreased (SMR = 92 for both categories). The decrease of the all-causes of death SMR was statistically significant for p=0.05. SMRs for prostate, respiratory, central nervous system, and digestive cancers were not increased in comparisons to either U.S. or DuPont regional rates.

<sup>1</sup> Members of the study cohort still living at end of study or dying from other causes are used as controls.



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SMRs calculated using U.S. and DuPont regional rates stratified by cumulative exposure categories likewise showed no increases. When the exposure strata were based on peak exposure categories, lung cancer was significantly elevated in the highest peak category (30 ppm). Fifty of the 88 lung cancer deaths were in this category; the SMR was 144 (95% CI: 107-189).

Cox proportional hazards were calculated on both cumulative and peak exposure categories. Similarly to the SMR analyses, there were no increased risks seen with cumulative exposure, but the hazard ratio for the highest peak category, when compared to the lower three categories combined into one group (to provide adequate distribution of cases), was 1.94 (95% CI: 1.28-2.96).

The overall risk estimates based on this update are very similar to the Wood study findings published several years ago. The risks in the highest peak exposure category were increased in the earlier study, though not statistically significant; but did reach statistical significance with  $p=0.05$  in this update.

An important limitation of these analyses is the lack of data concerning tobacco use among study cohort members. Because the trend of increasing lung cancer with increasing peak exposure was largely driven by the data in the South Carolina plant, we compared reported state incidence rates for lung cancers among white males. These general population rates were: South Carolina: 104.9 per 100,000 (1995-1999); Virginia: 86.8 per 100,000 (1996-2000); and National SEER rate: 84.4 per 100,000 (1995-1999). The higher incidence of lung cancer in South Carolina may be a factor contributing to the inconsistency in respiratory cancer mortality between the two plants.

There are limitations to the interpretability for SMRs stratified by exposure categories due to the likelihood of differing demographic distributions among members of the categories. However, the proportional hazards analyses are designed to take these differences into account. Another limitation is the categorization of peak exposure. We did not consider the duration of time spent in the highest exposure category in either the SMR or proportional hazards analyses, but restricted categorization to the mean peak exposure for each of the four categories as was done in Wood, et al (1998). The duration of time spent in each subject's peak category was highly variable and was not always consecutive throughout the working career. In addition, the standard deviation of duration for each category except the lowest was larger than the mean. Because cumulative exposure is generally considered the more biologically meaningful exposure metric and there were no exposure-response trends seen using cumulative exposure, these results should be interpreted in that context.

A copy of the final report will be sent to the Agency when available.

Sincerely,



A. Michael Kaplan, Ph.D.  
Director – Regulatory Affairs and Occupational Health

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