

associated with an excess lung cancer risk when evaluated together with cumulative hexavalent chromium exposure. Mancuso [1997a] concluded that lung cancer risk increased with increasing cumulative trivalent chromium exposure, but cumulative trivalent chromium exposure correlated with increasing hexavalent chromium exposure in his study as it did in this study. There was no effort by Mancuso [1997a] to examine the effects of the two in a multiple regression. Mancuso [1997b] presents additional argument using autopsy results that trivalent chromium is carcinogenic although, again, the results may be confounded by the presence of hexavalent chromium. There is no evidence from the current study that trivalent chromium is carcinogenic. If trivalent chromium is indeed carcinogenic, it is much less so than hexavalent chromium. Cumulative hexavalent chromium exposure was also a significantly stronger predictor of lung cancer risk than was duration of work, suggesting that it was hexavalent chromium and not other exposures in the workplace responsible for the excess lung cancer risk.

Although the exposure data in the current study offers an advantage over that of previous studies, it has its limitations. The cumulative exposure of each individual in the cohort was compiled from their work history and average exposures specified by job title by calendar year. Variability in exposures between individuals with the same job title and across a year are not captured in the current analysis. These variabilities could reasonably be expected to be high. Conversely, it should be noted that clinical findings of hexavalent chromium exposure (e.g., nasal, skin, eye, and ear irritation) were not found to be significant predictors of lung cancer risk when included as variables with cumulative hexavalent chromium exposure and smoking status in the Cox model. If such clinical findings are the result of high, short-term, ambient exposures, as might be expected, this suggests that cumulative hexavalent chromium exposure is a stronger predictor of lung cancer risk than is high, short-term exposure.

The availability of extensive smoking data is unusual for any occupational study. The measure of smoking in the current study was yes/no at the time of beginning employment. Such a measure does not provide information on the amount smoked or the number of individuals who smoked at time of employment and who subsequently quit or the number of nonsmokers who became smokers.

Recognizing that the data developed by this study may be useful to risk assessors doing quantitative risk assessment, we have presented the number of observed and expected lung cancer cases and person-years of observation by age and cumulative hexavalent chromium exposure (Table V). Such information is usually lacking in epidemiologic papers. Age and exposure are critical variables for an exposure response assessment using epidemiologic data. It is hoped that future epidemiologic papers on the cancer

response to chemical carcinogens will also present information allowing the risk assessor to examine the concurrent effect of these two critical variables.

It should be noted that the current OSHA Permissible Exposure Limit (PEL) of $100 \text{ g CrO}_3/\text{m}^3$ [OSHA, 2000] and the American Conference of Government and Industrial Hygienists [ACGIH, 1999] threshold limit value of $50 \text{ g Cr}/\text{m}^3$ (equivalent to approximately $100 \mu\text{g CrO}_3/\text{m}^3$) for water-soluble hexavalent chromium would both fall into the fourth quartile of cumulative hexavalent chromium exposure in the current study (assuming OSHA's standard 45-year working lifetime). OSHA has been petitioned to set a new PEL of $0.5 \text{ g CrO}_3/\text{m}^3$ [Public Citizen's Health Research Group and the Oil, Chemical, and Atomic Workers International Union 1993]. The NIOSH [1975] Recommended Exposure Limit (REL) for hexavalent chromium is $1 \text{ g Cr}/\text{m}^3$ (approximately $2 \text{ g CrO}_3/\text{m}^3$). Both the REL and the PEL which has been petitioned for would fall into the third quartile of cumulative hexavalent chromium exposure in the current study, again using the standard OSHA assumption of a 45-year working lifetime. The lung cancer observed-to-expected ratios for both the third and fourth quartiles of the current study were both significantly elevated. The lung cancer observed-to-expected ratio in the second quartile was elevated although not statistically significant ($O/E = 1.42$, 95% CI = 0.95, 2.01).

ACKNOWLEDGMENTS

The authors wish to thank Dr. Donald Billmaier and Mr. John Turner of Allied Signal Corporation for their kind assistance in providing information, data, and advice for this study. Thanks also to Dr. Marcie Francis, currently of the Chlorine Chemistry Council, who participated in the exposure analysis portion of the study. We also wish to thank Dr. Richard Hayes of the National Cancer Institute who first assembled the cohort and provided much of the valuable information used in the current study. Thanks to Dr. Chao Chen of the U.S. EPA National Center for Environmental Assessment who provided expert statistical advice. Finally, we would like to thank all the States that provided death certificates for the study.

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