I. THE ROLE OF AIRBORNE POLLUTANTS IN THE INDUCTION OF CANCER

The World Health Organization as well as respected members of the scientific community have estimated that 60 - 90 percent of human cancers are associated with environmental factors. Support for this conclusion derives in part from the great variation in the incidence of most cancers, both from place-to-place and time-to-time; from the experience of migrants, among whom the risk of cancer changes to that of the adopted country in the course of one or two generations; and from the increasingly frequent demonstration of excessive cancer among various industrial groups.

Whereas some have suggested that lifestyle factors (diet, alcohol and cigarette smoking) are the major sources of environmental cancer, a recent NCI, NIEHS and NIOSH Report[1/] concluded that those estimates were based on the erroneous assumption that each cancer should be assigned to a single specific cause, were limited to the small number of known examples and were largely unsupported by documentation or critical review of data. In contrast, this NCI, NIEHS and NIOSH Report, the conclusions of which were considered by American Industrial Health Council consultants to be reasonable, estimated that in coming decades up to 20 percent and perhaps as much as 40 percent of cancer in the U.S. might be associated with occupational factors.[2/] While the possibility of overestimation has been raised regarding this report, it should be noted that the report only dealt with six substances instead of at least 18 substances known to be confirmed human occupational carcinogens. In arriving at these estimates, the NCI, NIEHS and NIOSH

1/ 45 Fed. Reg. 5031, 5033 (January 22, 1980).

2/ Ibid.

Report[1] noted:

> The initiation and development of cancer is a multi-phased, multi-causal process in which both external and internal factors act, probably at each of several stages, before frank, clinical cancer appears. It is likely that many, if not most, cancers are influenced by two or more different external factors acting simultaneously or sequentially. Thus, alcohol by itself appears to be a minor cause of cancer -- but alcohol combined with cigarette smoking leads to risks 15 times higher than those experienced by non-smoking non-drinkers. If a drinker smoker develops cancer of the oral cavity, to which 'cause' should it be attributed? Drinking or smoking? If we could correctly identify the proportions of cancer incidence 'attributable to' each of the classes of environmental factors considered by Wynder and Gori, the sum of these percentages would be considerably higher than 100. One of the best-studied examples of interaction between exogenous agents is that between asbestos and cigarette smoke in inducing lung cancer. Most lung cancers 'attributable to' asbestos are probably simultaneously 'attributable to'smoking. If current theories of a multi-causal process are correct, it seems likely that a large fraction of cancers which at first appear to be 'attributable to' smoking should also be 'attributable to' asbestos, radiation, and/or other occupational factors.

Of the six substances considered in the NCI, NIEHS and NIOSH Report, several including asbestos, arsenic and vinyl chloride have been emitted into or are present in the ambient air in such a way that significant human exposure results. Numerous studies have reported an excess of cancer among individuals residing in close proximity to industrial sources emitting each of these same three substances.

With regard to asbestos, Wagner's[2] study in South Africa, Newhouse's[3] studies in the United Kingdom and Bohlig's[4] study in Hamburg

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1/ NCI, NIEHS and NIOSH Institutes. Report. 1978, p. 3. OSHA Hearing Exhibit 224b.

2/ Wagner, J. C., Steggs, C. A. and Marchand, P. Diffuse pleural mesothelioma and asbestos exposure in the North-Western Cape Province. Br. J. Ind. Med. 17: 260-271, 1960.

3/ Newhouse, M. L., and Thompson, H. Mesothelioma of pleura and peritoneum following exposure to asbestos in the London area. Br. J. Ind. Med. 22: 261-269, 1966.

4/ Bohlig, H. and Hain. E. Cancer in relation to (cont'd on p. I-3).

reported that the risk of mesothelioma has spread beyond the factory, mine or asbestos mill gate. In 1964 Newhouse and Thompson[1] reported numerous cases of mesothelioma among individuals whose only identified asbestos exposure was associated with living one-half mile from an asbestos factory. This form of cancer only rarely is found in the absence of exposure to asbestos.

With regard to arsenic, three studies have shown an excess of lung cancer among inhabitants of communities with smelters emitting arsenic. Blot and Fraumeni[2] demonstrated that the 36 counties in the U.S. with copper, lead and zinc smelting and refining industries had a significantly higher lung cancer mortality among males ($p<0.001$) and females ($p<0.05$) than did counties in the rest of the U.S. Those 35 counties with industries processing nonferrous ores other than copper, lead and zinc showed no such excess of lung cancer mortality. According to the authors, the most likely explanation for the elevated lung cancer mortality was neighborhood air pollution from industrial sources of inorganic arsenic. In like manner, Newman, et al.,[3] demonstrated that the rate of lung cancer mortality among females resident in Anaconda, Montana, the site of a copper smelter known to be the point source for arsenic air pollution was significantly elevated (2.9/10,000 vs. 1.4/10,000; $p<0.05$).

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environmental exposure, type of fibre, dose, occupation and duration of exposure, in Bogovski, P. Gilson, Jr., Timbrell, V. Wagner, J.C. (eds): Proceedings of the Conference on Biological Effects of Asbestos, Lyon.

1/ Newhouse and Thompson, op. cit.

2/ Blot, W. J. and Fraumeni, J. F. Arsenical air pollution and lung cancer. Lancet 2: 142-144, 1975.

3/ Newman, J. A., Archer, V. A., Saccamano, G., Kuschner, M., Auerbach, O., Grondauhl, R. D., and Wilson, J. C. Histologic types of bronchogenic carcinoma among members of copper mining and smelting communities. Ann. N.Y. Acad. Sci. 271: 260-268, 1976.

More recently, Matanoski[1] reported that the lung cancer mortality for males residing in the census tract in which an arsenical-producing insecticide plant is located was significantly higher than for males in control census tracts. Exclusion of lung cancer deaths of persons who had been employed in the plant did not alter the statistical significance of the excess risk. The female rate of lung cancer mortality in that same census tract was higher than most control tracts, but the numbers were too small to attach any statistical significance to it.

Regarding vinyl chloride, Infante[2] and Iturra[3] each have reported an excess of central nervous system (primarily brain) mortality among residents of communities having vinyl chloride monomer or polymerization plants. These studies, while based upon relatively small numbers, are consistent with results showing a statistically significant excess of brain cancer among individuals occupationally exposed to vinyl chloride.[4] More recently, Brady, et al.[5] reported the results of a study of 26 confirmed cases of liver angiosarcoma and a similar number of controls with an internal malignant tumor other than primary liver

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1/ Matanoski, G. M. Progress in a community arsenic study. Proceedings of Toxic Substances in the Air Environment Specialty Conference. Pittsburg, 1976, pp. 31-41.

2/ Infante, P. F. Oncogenic and mutagenic risks in communities with polyvinyl chloride production facilities. Ann. N. Y. Acad. Sci. 271: 49-57, 1976.

3/ Iturra, H. A community vinyl chloride mortality analysis study. Proceedings of Toxic Substances in The Air Environment Speciality Conference. Pittsburgh, 1976, pp. 96-113.

4/ Waxweiler, R. J. Stringer, W., Wagoner, J. K., Jones, J. Falk, H., and Carter, C. Neoplastic risk among workers exposed to vinyl chloride. Ann. N. Y. Acad. Sci. 271: 40-48, 1976.

5/ Brady, J., Liberatore, F., Harper, P., Greenwald, P., Burnett, W., Davis, J., Bishop, M., Polan, A., and Vianna, N. Angiosarcoma of the liver: an epidemiologic survey. J. N.C.I. 59: 1383-1385, 1977.

cancer. These controls were matched with the cases on the basis of age of diagnosis, race, sex and general place of residence. The authors noted that of 10 female cases of liver angiosarcoma (no direct occupational or therapeutic exposure to arsenic, vinyl chloride or thorium dioxide) five lived for prolonged periods of time within one mile of a VC polymerization plant or a PVC fabrication plant whereas none of their matched controls did so. This observation, according to the authors, lent support to the hypothesis that indirect modes of exposure to VC-PVC might be important in the etiology of liver angiosarcoma.

While the existence of cancer hazards in the extraplant environment has been demonstrated, it must be recognized that these community-based studies involving asbestos, arsenic and vinyl chloride were successfully completed only because of the relative rarity of the form of cancer under study, i.e., mesothelioma, liver angiosarcoma or brain cancer, all forms of cancer previously having been shown to be excessive in studies of occupationally exposed groups, or because of the emission of a single carcinogenic substance from predominantly isolated industrial facilities.

Therefore, given the high probability of multiple substance emissions associated with modern industrial processes and the limitations of sensitivity inherent in current epidemiological methods, it is unlikely that the true impact of cancer resulting from specific air pollutants can ever be fully documented. Nevertheless, epidemiological as well as experimental observations would indicate that the potential impact of air pollutants on cancer indication could be even more substantial. Studies of individuals occupationally exposed to asbestos or irradiation have indicated that in the presence of another

agent, cigarette smoking, the risk of lung cancer is more than additi or would appear within a shorter time period, i.e., reduced latent period. Experimental studies involving fast-neutron irradiation and carbon tetrachloride in like manner have demonstrated the interactive effects of several agents on carcinogenesis. These findings, both epidemiological and experimental, raise further concern for the interactive effects of multiple effluents from industrial sources.

It stands to reason therefore that a similar, while mitigated effect, of the various occupational and industry-related carcinogens present in the general air, especially of cities and industrialized regions, accounts for a substantial portion of cancers occurring in the general population.

The foregoing is merely an overview of the data supporting the regulation of airborne carcinogens. EDF and NRDC will submit additional materials on this subject in both supplemental and rebuttal comments.