DRAFT
January 19, 1981

Rebuttal Comments on the Scientific Issues in the Proposed Airborne Carcinogen Regulations

The EPA's proposed airborne carcinogen policy is based on a purported threat of carcinogenic hazard from industrial air pollution. Although air pollution can have some health related effects on the population, the scientific evidence simply does not support the assertion that ambient levels of air pollution cause cancer. Neither the documents referred to by EPA in its preamble to the proposal or in its supplemental materials nor the comments and studies on "community-based industrial disease" presented by EDF and NRDC have made the case that airborne carcinogens pose a significant health hazard to the general populace.

EDF and NRDC Comments

The comments submitted by EDF and NRDC assert that "the existence of cancer hazards in the extraplant environment has been demonstrated," and cite a group of what are termed "successful" studies showing hazards to community members from three industrial substances -- asbestos, vinyl chloride and arsenicals. The evidence from these studies, however, does not demonstrate a serious hazard to community members exposed to ambient air. A review of individual studies in the EDF and NRDC comments is attached (see Attachment A), but the sum of the

evidence presented in the papers does not support a conclusion of a detectable hazard to the general population from ambient levels of airborne carcinogens.

All of the studies are preliminary; none of them is characterized by the authors as a definitive demonstration of general airborne hazards. All of the studies, for example, are forced to assume past exposure of populations to airborne chemicals without having measurements of the levels of the suspected pollutants. None of the studies demonstrates a positive correlation between levels of pollutants and the incidence of cancer in the exposed population, a basic demonstration that would be necessary for a solid case for airborne carcinogenic hazard. On the contrary, many of the studies reason only negatively that, because no other explanation is readily apparent, slight statistical increases in the incidence of certain disease must be due to previous exposure to the substance under study. The studies are uncontrolled for a host of factors.

Several of the studies are better interpreted as meager evidence of occupational hazard rather than any evidence of a general airborne hazard. For example, studies which demonstrate that workers in industrial settings are at higher risk of particular diseases, are not relevant to the existence of a general airborne hazard. At the outset, workers may be exposed to substances under different conditions and at concentrations many orders of magnitude higher than ambient air concentration of the substance. In addition, the interpretation of the degree of

hazard presented even to workers by particular substances often is uncertain. Observations on health risks to workers, so often controversial in their significance for workers, cannot be stretched, in the absence of other data, to prove a hazard to the general populace.

Since it is recognized that exposures to very high levels of certain carcinogens in occupational settings can cause cancer, it is theoretically possible that in rare instances of accidental origin in close neighborhood associations persons may receive high level exposure to carcinogens in non-occupational circumstances. Demonstration of even a causal association between such exposure and an elevated cancer incidence would not establish a general airborne carcinogen hazard. While observations on non-occupational exposure may be important in formulating standards to regulate individual substances, such episodes, if found, cannot be extrapolated to constitute the entire case for a generic airborne carcinogen policy.

EDF and NRDC Studies

EDF and NRDC cite ten studies: three on asbestos, four on vinyl chloride, and three on arsenicals. The asbestos studies are very preliminary. One asbestos study obtained retrospective case histories from the relatives of 33 individuals who died of mesothelioma, a rare form of lung cancer linked to asbestos exposure. The paper reported that all of the affected individuals had lived at one time in the asbestos mining region

of South Africa although not all had histories of occupational exposure. A second retrospective asbestos study showed that of a group of 36 mesothelioma patients in a London hospital who did not have histories of occupational or domestic exposure to asbestos, 30.6% had lived within a half mile of an asbestos factory while only 7.6% of an unmatched control group of other patients from the hospital had lived in the area. A third review article discussed an experiment which found higher mesothelioma rates in the vicinity of a shipyard which, prior to World War II, emitted very high (even visible) levels of asbestos than were found in other areas of the city.

The inference from these preliminary studies of a connection between airborne exposure to ambient levels of asbestos and risk of mesothelioma are tentative at best. At most, they suggest possible risk to those living in immediate neighborhoods of asbestos plants emitting extremely high levels of asbestos. These findings must be considered, however, in light of other recent studies (see Hammond, et al. below) which show no increase of lung cancer in the neighborhood of U.S. asbestos factories.

The vinyl chloride studies are totally unconvincing on the danger of non-occupational airborne exposure. One study examines only the mortality of workers in a vinyl chloride plant. Another noted central nervous system mortality higher than the state levels in one of three Ohio cities with vinyl chloride facilities, but only among males in that city. A comparison of two communities, one with and one without a vinyl chloride

polymerization plant, showed elevated rates of cancer mortality, but again only in males. The fourth study was a retrospective survey of the case histories of 26 people with angiosarcoma, a rare cancer known to be associated with three toxic agents, vinyl chloride, arsenicals and thorotrast. ~~The study showed only that 5 of the 19 persons without known direct exposure to one of the three toxic agents had lived near vinyl chloride plants.~~

The arsenic studies also are too preliminary or too poorly controlled to demonstrate the existence of airborne arsenical hazards. An excess lung cancer rate noted among women in a Montana smelter community was attributed to an unknown airborne agent, but the observation was based on a very small number of women and the results were uncontrolled for smoking. A preliminary study of cancer mortality in the neighborhood of a chemical plant which produced arsenic containing products showed higher cancer mortalities only among males. A nationwide survey of mortality patterns for lung cancer found higher rates among males and females in the group of 36 U.S. counties with copper, lead or zinc smelting and refinery industries in comparison with the rest of the country. The data, however, were uncontrolled for both smoking and occupation.

These studies, discussed in greater detail in Attachment A hereto, do not establish a general carcinogenic hazard from ambient exposure to airborne substances.

EPA's Scientific References

AIHC's original comments analyzed each of the references cited by EPA in the preamble and supplementary statement to the proposed rule. These documents did not demonstrate the existence of a carcinogenic hazard to the general population from airborne pollutants. (See AIHC Comments, Legal, Appendix) The additional set of documents included in the docket by EPA as having been "used in the preparation" of the proposed rule, Section II-I of the docket, have also been analyzed for the extent to which they support the existence of a hazard. (See Attachment B hereto). These documents, like the first set, discuss a variety of tangential topics in the fields of carcinogenic identification and regulation but do not demonstrate a causal relationship between air pollution and cancer, and therefore add nothing substantial to support this proposal.

In addition to failing to demonstrate positively the existence of a general airborne hazard, EPA, EDF and NRDC ignore the currently available data which suggest that general air pollution does not contribute significantly, if at all, to human cancer incidence. For 25 years, epidemiologists have conducted studies designed to test the hypothesis that air pollution contributes to cancer incidence. (The speculation that there are substances in the air, albeit at low concentrations, which can induce cancer in test animals, apparently has raised the possibility in the eyes of the Agency that the presence of such substances contributes to human cancer incidence. However, none

of these studies has made a positive finding in this respect. AIHC Comments, Alternatives, Section V.)

The consensus resulting from all of the recent studies is that the maximum role all sources of air pollution combined can play in lung cancer is limited to a possible synergistic increase in the risk of cancer among smokers in the population, and even this is an unsubstantiated postulate. These studies do lead to the following conclusions: Smoking is the overwhelming cause of lung cancer, (the disease most likely thought to be the result of air pollution if there were a causal relationship). General air pollution, is not per se a significant factor.1/

These conclusions are supported by a large group of studies that show lower cancer rates in industrialized cities than in several large non-industrialized areas. Persons whose convictions prevent smoking or drinking, or who otherwise moderate their lifestyle have lower rates than their neighbors who do not practice these restraints. The male/female differential persists in urban and rural settings.

Two recent studies examine smaller, less diverse populations and consider cancer at a specific organ site (as EDF suggested in

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1/ Numerous recent reports support this conclusion. In addition to documents discussed in AIHC's initial comments, the Agency could refer to the Surgeon General's Report: "Smoking and Health" (19); The American Cancer Society, "1981 Facts and Figures" and "Cancer Prevention Study, 1959-1979"; a recent NCI monograph, "Persons at Low Risk of Cancer," NCI, Nov. 1980, v.65; or many public statements and papers by Drs. DeVita and Gori of the National Cancer Institute; "Cancer and the Environment," ~~Progs.~~, 1980.

its comments). These studies of populations living in the vicinity of industrial facilities support the conclusion that air pollution is not a significant factor in lung cancer incidence.

1. Asbestos. A study compared the lung cancer incidence in two matched neighborhoods in Patterson, New Jersey, one of which was the site of an asbestos factory which operated in the 1940's and 1950's. The incidence of lung cancer in non-occupationally-exposed males in the two neighborhoods was nearly identical. In fact, the lung cancer incidence was lower in the exposed neighborhood group although the difference was not statistically significant. (E. C. Hammond, I. J. Selikoff, L. Garfinkle and W. J. Nelson, Mortality Experience of Residents in the Neighborhood of an Asbestos Plant, Presented at a meeting of the New York Academy of Sciences, New York, June 25, 1978.)
2. General industrial pollution. A follow-up study found that occupational factors adequately explained differences in cancer rates for residents of South Central Los Angeles County, an area of high air pollution. The study refined the conclusion of a previous study which had "for lack of a clear smoking or occupational explanation for this regional excess" attributed a lung cancer excess to air pollution. The detailed follow-up study noted that no excess of lung cancer occurred in white females and then looked further

and found that occupational factors accounted for the observed differences in males. (M. C. Pike, J. S. Jing, I. P. Rosario, B. E. Henderson and H. R. Menck, Occupation: "Explanation" of an Apparent Air Pollution Related Localized Excess of Lung Cancer in Los Angeles County, in Energy and Health, Proceedings of a Conference sponsored by SIAM Institute for Mathematics and Society, N. E. Breslow and A. S. Whittemore, eds., Philadelphia, 1979.)

Considered in the context of all available epidemiological data, the studies provided by EDF and EPA do not make the case that air pollution constitutes a significant hazard. For example, EDF cites only one study to directly support the connection between general air pollution and cancer (Carnow, B.W., The "Urban Factor" and Lung Cancer: Cigarette Smoking or Air Pollution?, Environ. Health Pespectives, Vol. 22:17-21 (1978)). The paper admits that smoking is the overwhelming cause of lung cancer but goes ahead to summarize the studies suggesting air pollution may play a minor causative role. The evidence presented is very weak. For example, the article cites a regression analysis done to examine the relationship between air pollution and cigarette smoking as factors in cancer. The degree of air pollution was followed as the concentration of Benzo-[a]pyrene, a single chemical which, although commonly used, is of unknown value as a quantitative marker for air pollution. The cigarette consumption data was approximated by cigarette sales

data. Considering the weakness in methodology the finding that there appeared to be a 5% increase in lung cancer death rates in white males for each increase in pollution indexed by benzo-[a]pyrene is not convincing evidence of a hazard from air pollution. In addition, the study in the Carnow review that was highlited by EDF as demonstrating the link between lung cancer and pollution shows an increase in cancer rates in the population of counties with coke oven emission facilities, but only among men, not women, in comparison with rates in other counties in the state. Since both men and women breath the ambient air the observation of the differences in rates only among men would appear to support a role for occupational exposure, if anything.

Conclusion

Stationary sources are not even the major source of urban air pollution (Hammond, E.C. and Garfinkle, L., General Air Pollution and Cancer in the United States, Preventive Medicine 9, 1980) and the combined effects of air pollutants have not been shown to contribute a detectable fraction of lung cancer incidence. Accordingly, implementation of the proposed regulation is highly unlikely to produce any measurable impact on the lung cancer incidence in the United States.

Besides being ineffective, such a program, supposedly justified by its potential to prevent lung cancer, seriously misleads the public. By lulling the public into the belief that the expensive regulatory programs will have a significant impact

on lung cancer, the agency diverts attention away from the only actions likely to have major impact on the incidence of the disease, such as changes in lifestyle, which include smoking, drinking, dieting habits, and exposure to sunlight.

If convincing scientific evidence of carcinogenic hazard emerges in the case of a specific air pollutant, EPA already has adequate authority under existing statutory provisions of the Clear Air Act to regulate emissions of that substance. (See AIHC Comments, Legal.) In light of the lack of evidence for the existence of a widespread airborne carcinogenic hazard, the imposition of a generic carcinogen program on top of ~~the~~ existing substance-by-substance regulation seems an unwise use of resources.

We do not believe that the agency has demonstrated a need for its proposal, nor shown any substantial connection between the sources to be controlled and the disease which is to be prevented. Therefore, the Agency should withdraw this proposal.

REBUTTAL COMMENTS ON
INDIVIDUAL STUDIES
SUBMITTED BY EDF

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January 18, 1981

ASBESTOS

Wagner, Steggs and Marchand, Diffuse Pleural Mesothelioma and Asbestos Exposure in the North Western Cape Province, 17 Brit. J. Indust. Med. 260 (1960).

The purpose of this preliminary study was to establish a connection between exposure to crocidolite asbestos and a rare form of lung tumor, mesothelioma of the pleura. The study was a retrospective investigation of the life histories of the 33 histologically proven cases of mesothelioma which occurred over a four year period in the "Cape" asbestos mining region of South Africa. (The disease has only rarely been observed in South Africa outside the Cape asbestos field region studied by the authors.)

The histories were obtained from the patients' relatives, whose memories and access to information limit the quality of the data. The histories revealed that all but one of the 33 cases had been exposed to asbestos either occupationally (as a miner or in industry) or had grown up in the asbestos mining region.

The study provides good evidence linking the rare type of cancer to crocidolite asbestos exposure. The inference (not stated in the paper) that those persons not shown to be occupationally exposed developed cancer as a result of exposure to very low levels of asbestos in the ambient air, is, however, in the absence of positive data, at best suggestive. There is no evidence presented in this study on the mode or level of exposure

of those patients who had lived in the region but whose history contained no report of having worked with asbestos. It was reported, for example, that children in the mining districts played on dumps from asbestos mines and mills. This type of very high level exposure to asbestos has no relevance to ambient air pollution.

Newhouse and Thompson, Mesothelioma of Pleura and Peritoneum Following Exposure to Asbestos in the London Area, 22 Brit. Jour. Industri. Med. 261 (1965).

The authors studied the histories of a series of 76 patients in a London hospital with a diagnosis of mesothelioma for possible exposure to asbestos. Forty of the patients had histories of occupational or domestic (living with a worker) exposure. Neighborhood exposure was suggested as an additional factor in the disease based on the following single observation. Of those mesothelioma patients with no evidence of occupational or domestic exposure (36 patients), 30.6% had lived within one half mile of an asbestos factory, while only 7.6% of the control group, in-patients in the same hospital for other diseases, had lived within the half mile radius. A single observation on so few patients, especially where the authors admitted that the in-patient controls were not matched to the test cases on many important factors, contributes little to an understanding of the role of air pollution.

Bolilig and Hain, Cancer in Relation to Environmental Exposure in Bogovsik, Gilson, Timbrell, and Wagner, Proceeding on the Biological Effects of Asbestos

This is a review article on environmental (non-occupational) asbestos-induced malignant tumors. The article cites the South African study (above) on mesothelioma patient histories and also five other studies reporting higher incidences of lung cancer in the vicinity of asbestos ship-building factories. (The crocidolite asbestos, implicated in the South African study, is used extensively in ship insulation.) The authors also discuss a retrospective study in Hamburg, Germany, which reported an increased incidence of mesothelioma among persons living in the neighborhood of shipbuilding facilities as compared to the incidence of mesothelioma observed in the general population of the city. Patients reported that in the vicinity of this plant before World War II "a severe, visible snowfall-like air pollution was emitted from this factory..."

Where neighborhoods are exposed to "severe, visible snowfall-like air pollution," the exposure approaches occupational levels and constitutes, as do very high level exposures in occupational settings, a probable hazard. Such instances of non-occupational, but very high level exposure present different problems from the quality of the ambient air and are best dealt with in agency proceedings on individual substances. Increased cancer rates in these special situations are, like observations of cancer hazards in occupational settings, not persuasive evidence that the ambient air containing much lower concentrations of the same substances constitutes a

carcinogenic hazard. See, for example, the neighborhood study by Hammond, et al., cited above.

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VINYL CHLORIDE

Infante, Oncogenic and Mutagenic Risks in Communities With Polyvinyl Chloride Production Facilities. Annals New York Academy of Sciences.

(Most of the data collected by these authors concerned congenital malformations; only one part of the study concerned cancer.) In this study mortalities of three types of cancer whose rates are reported to be elevated among vinyl chloride workers, lymphoma, leukemia and CNS (central nervous system) tumors, were examined in the three communities in Ohio with vinyl chloride facilities.

The rates of death from lymphomas and leukemia in the three index cities were not significantly different from rates reported in the rest of Ohio. In contrast, rates of CNS tumors were higher than the rest of Ohio in the three cities combined. But when the deaths due to CNS tumors among males in one of the cities were eliminated from the data, "the differences between observed and expected deaths would not have been significant."

In summary, the study showed an increased incidence at only one of three suspected tumor sites (CNS tumors) and that increase was observed only among males in one of the three cities studied. This single observation supports, if anything, an occupational hazard among workers of that city. It provides no support for the hypothesis that airborned carcinogens [of any kind] in these cities posed a threat to the residents. The

Center for Disease Control reviewed this study and stated that it could not establish any association between the cases and vinyl chloride (Weekly Report 24 (29) 245 (1975)).

Waxweiler, Stringer, Wagoner, Jones, Falk and Carter. Neoplastic Risk Among Workers Exposed to Vinyl Chloride, 271 Ann. N.Y. Acad. Science. 40 (1976)

This study examines only exposed workers in facilities engaged in the polymerization of vinyl chloride. The study found that workers in these plants, exposed to vinyl chloride in the course of their work, were at increased risk of cancer of the liver, and there was suggestive evidence for risk at other sites. However, this study was too small to be conclusive on this point.

Although important for considerations of occupational exposure, these observations do not demonstrate any risk to populations exposed to ambient air pollution.

Brady, Liberatore, Harper, Greenwald, Burnett, Davis, Bishop, Polan, and Vianna, Angiosarcoma of the Liver: An Epidemiologic Survey, 59 Jour. Nat. Cancer Inst. 1383 (1977).

A survey of the histories of the 26 known cases of a rare type of cancer, angiosarcoma of the liver, occurring in New York outside New York City from 1958 to 1978 and reported in the Tumor Registry of the Cancer Control Bureau. Seven of the 26 persons were directly exposed to one of the three toxic substances associated with angiosarcoma, vinyl chloride (from production plants), arsenicals (from pesticides) or thorotrast (ThO_2) (from injection as part of a diagnostic procedure). Five of the others

in the group had lived within 500 to 4,000 feet of a vinyl chloride facility. For 14 of the 26 persons no residential or occupational information pertinent to known risk factors for angiosarcoma were discovered in the histories.

This is another preliminary study, not even mentioning air pollution. Caution in interpretation is emphasized by the authors. "These observations lend some indirect support to the hypothesis that exposure outside the industrial facility is an important factor, but the patients involved and the lack of information concerning air levels of monomer around their residences severely limit interpretation. Accordingly the issue must be considered unresolved at present." ~~(emphasis added)~~

Iturra, A Community Vinyl Chloride Mortality Analysis Study in Proceedings of Toxic Substances in the Air Environment Specialty Conference. Pittsburgh, 1976, pp. 96-113.

This study compares cancer mortality in a community with a vinyl chloride polymerization plant with another community matched for demography and industrialization but without a vinyl chloride facility.

The rates of cancer mortality at a variety of sites were determined over a ten year period in the two populations. The rates of cancer mortality differ only for males between the ages of 20 and 64, a result which is consistent with differences in the occupational hazards of the two communities.

The authors admit the limits of this preliminary study. "But since this study is a simple description of mortality and

cancer mortality in two towns, nothing can be concluded as to why the phenomenon exists." ~~(emphasis added)~~

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ARSENIC

Newman, Archer, Saccamano, Kuschner, Auerbach, Grondauhl and Wilson, Histologic Types of Bronchogenic Carcinoma Among Members of Copper-Mining and Smelting Communities. 271 Ann. New York Acad. Science 260 (1976).

This study examined the distribution of the histologic types of respiratory carcinomas occurring among the residents of two communities in Montana, one located near copper mines (Butte) and one near a larger copper smelter (Anaconda).

Cases were selected from the files of the regional pathology labs. Slides of the tissue from each case were classified according to histological type. Cases were divided in four groups: copper smelter workers, copper miners, "other" men (men involved in a variety of other occupations) and women who lived in the city of Butte. Smoking and occupational histories were obtained on the cases; the smoker histories were incomplete.

Although evaluating the effects of the air in the two communities was not a primary purpose of the study, two observations in the course of the study elicited a discussion of air pollution.

1. Copper smelter workers had a distribution of cancer types different from both copper miners and the "other men." The distribution was similar, however, to a reported series of arsenic poisoning victims. Because smelter workers are exposed to high levels of arsenic, among other metals,

arsenic was implicated as a factor in cancer among the smelter workers. The authors also report that there was a higher cancer incidence among women in Anaconda, the smelter community, compared to the rates of lung cancer in the rest of the state. The authors merely suggested that this increase among women as well as men was "best explained" by the exposure to a common agent, perhaps airborne arsenic.

The "excess" lung cancer among women which prompted the suggestion of an airborne agent was, however, a very tenuous observation. The difference in lung cancer incidence between Anaconda and all Montana women was based on only three deaths in Anaconda. The difference became significant at a 0.05 level only when the rates were extrapolated over a ten year period. The data were uncontrolled for smoking and based on a very small sample size.

There was, beyond the tenuous observation of a possible excess cancer rate among women, no information to suggest an air pollution hazard rather than an occupational hazard from arsenic. There was, for example, no data on the distribution of histologic types of cancer among the women to show that they were, in fact, experiencing the same arsenical-type cancer as experienced by the men.

2. A second observation suggesting air pollution was that, relative to the whole state, both the men and women of Butte (the copper mining community) showed a high incidence of respiratory cancer. The higher incidence of cancer among both men and women in the city could have suggested ~~as above~~ a common

airborne agent. But the observations on the Butte population not only fails to demonstrate the link between the increased disease and pollution from any source, but in no way implicates industrial air pollution. For, according to the authors, there is no industrial air pollution in Butte. The authors suggest as an alternative source of pollution that the increased rate of respiratory cancer in Butte might be due to the sanding compound used on the city streets in the winter to aid traction.

In addition to ~~Besides~~ failing to support the connection between industrial air pollution and cancer, the Butte situation graphically points up a danger inherent in "attributing" excess lung cancer incidence in a region to industrial pollution simply because no other candidate for a causal agent is apparent at that moment to investigators. Other, some perhaps important, potential causes of respiratory cancer escape notice. Had Butte had a smelter, the sand used on snow-covered streets would have received little consideration as a possible source of cancer-causing pollution.

Matanoski, Progress in a Community Arsenic Study, in Proceedings of Toxic Substances in the Air Environment Specialty Conference, Pittsburgh, 31 (1976).

This is a preliminary study of cancer mortality in the neighborhood of a chemical plant which produced insecticides, herbicides and other arsenic products.

The study shows only that the lung cancer mortality for males residing in the census tract in which the plant is located is significantly higher than for males in control tracts. A

similar comparison in females does not show an excess risk.

There is even some evidence in the study that suggests that excess cancers are not the result of airborne arsenic. Geographic plot of workers' homes who contracted lung cancer showed that their density, relative to other cancers, was highest in an area almost opposite that area which, based on prevailing wind direction, would have received the most arsenical dust. "This [observation] would not seem to correlate with the hypothesis that the lung cancers were arsenic related." p.

The report concludes, "At present the association between airborne arsenic and lung cancer is still only suggestive." (emphasis added) p.

Blot and Fraumeni, Arsenical Air Pollution and Lung Cancer, 2 Lancet 142 (1975).

This is an analysis of mortality patterns for lung cancer in U.S. counties where non-ferrous ores are refined and smelted. The study compares age-adjusted rates of lung cancer for males and females in U.S. counties with copper, lead or zinc smelting and refining facilities (the refining processes for these ores release inorganic arsenic) to rates of lung cancer in the rest of the U.S.

Lung cancer mortality was significantly higher among males, $p = 0.001$ and females 0.05, in the group of 36 counties with copper, lead or zinc smelting and refining industries when compared to the rest of the U.S. The mean increase in lung cancer mortality for these counties, corrected for demographic influences, was 17% for males and 15% for females.

This survey is very preliminary. The data is totally

uncontrolled for the two most important variables in any lung cancer study -- smoking and occupation. In addition, there are no data on the levels of arsenic or other metals in air during the relevant period. These data were inadequate, for example, to assess dose response relationships of arsenicals to lung cancer. There was no discussion of specific types of lung cancer [redacted]. Until some of these problems are addressed, the elevation in lung cancer rates noted in the selected counties cannot be confidently related to the levels of arsenic, or any other substance, in the air. See also the comments by ASARCO Co., (OAQPS-79-14-IV-D-155), on this subject.

DRAFT
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Attachment B

COMMENTS ON DOCUMENTS ALSO CONSIDERED IN THE DEVELOPMENT OF THE AIRBORNE CARCINOGEN PROPOSAL

The original AIHC comments included a set of analyses of the references cited in the text of the preamble and in the supplementary statement of the proposed airborne carcinogen rule. In addition to the references cited to support specific propositions, the agency provided another list of documents which had been considered in the development of the proposal. (Docket Section II-I-1) The following comments refer to these additional references.

Our comments focus on the listed documents which specifically assess the role of air pollution in causation of human cancer. The comments analyze the extent to which the documents support the agency's basic contention that air pollution contributes significantly to the incidence of human cancer.

Many of the references, however, do not concern air pollution but deal with general topics in carcinogen identification and regulation. These documents fall into three categories: a) magazine articles directed to the interested lay audience on regulation of toxic substances or carcinogens, b) Federal Register and other government documents setting forth general criteria for carcinogen identification and risk evaluation and c) scientific articles on various related topics: the presence of mutagens in the environment, short term

tests for bacterial mutagenicity, and theoretical models for carcinogen risk assessment. Comments have been included on selected documents from these groups.

A. REFERENCES ASSESSING THE ROLE OF AIR POLLUTION

1. Air Pollution and Cancer in Man (Ref. 1)

See previously submitted comments on the references cited in the text of the proposal, AIHC Comments, Legal Appendix, p. 19.

2. Epstein, Environmental Determinants of Human Cancer 34 Cancer Research 2425 (1974) (Ref. 5)

A general and somewhat dated article noting the presence of carcinogens in the environment and discussing the limits of the interpretation of animal bioassays and epidemiologic studies. The only reference to air pollution in the article states that the 25% excess incidence of lung cancer in the urban environment over the incidence of lung cancer in rural environment "is generally regarded as being due to air pollution." The statement is, however, unsupported; no studies linking air pollution to lung cancer are cited.

3. Cancer Mortality in the New Jersey Region, 1950-1969: Program on Environmental Cancer and Toxic Substances. State of New Jersey Department of Environmental Protection, January, 1979. (Ref. 8)

A preliminary study of cancer mortality in New Jersey relating cancer rates in the counties of New Jersey and some contiguous counties in other states to a

list of population characteristics differing among the counties in order to identify potential risk factors for cancer. The study was undertaken as a preliminary attempt to identify the areas most fruitful for further research. Because it was preliminary, the study was constrained by the limitation of data to existing sources and as a result analyses were often performed on incomplete data sets.

In its preliminary findings, the study found a strong association between rates of lung cancer in males and several risk factors associates with the "urban/industrial corridor," e.g., Polish and ethnic populations, chemical and transportation equipment industries and air pollution. (Rates of lung cancer in females were less strongly associated with the urban/industrial corridor. In fact high rates of lung cancer were found in several rural counties. Female status (divorced/married) appeared as a significant factor in female cancer.)

These observations, however, do not establish a causative relation between air pollution and lung cancer. The authors emphasized the poor and incomplete quality of the data, especially data used in identifying ambient risk factors. The most important deficiency in the study in evaluating risk factors for lung cancer was the complete absence of data on smoking. Without smoking data, the reported associations between air

pollution and cancer are not controlled for what is by far the major risk factor in the occurrence of lung cancer.

In addition the data available on air quality and air emissions in the studies counties were very poor. "[A]ir quality readings were deficient in time, place and parameter dimensions. The emissions inventory likewise was severely restricted in time parameters and reliability." p. 41. Also this study did not pose in a neutral manner the question of whether or not air pollution was associated with lung cancer but, in fact, assumed the correlation should be positive and used the assumption as a criterion to evaluate the data on possible risk factors.

Air emissions surrogates (i.e., mathematically adjusted air emission data) were retained because they did correlate positively with lung cancer rates, BUT "neither the 1953-57 nor the 1972-75 air quality variables correlated positively with lung cancer. The two air quality variables were eliminated...because the results were inconsistent and the expected correlations [with lung cancer] did not materialize." p. 130-31.

The authors of the study themselves severely limit the interpretation of data collected in this study:

-- "the degree on intercorrelation among the high risk lung cancer indicators makes it infeasible to

pull apart the separate contributions of personal, occupations and local ambient risk factors." p. 169.

-- "when combined with large size units of analysis, the poor quality of some of the data we were forced to use implies that the most important function of the study is to isolate disease-place combinations for further study by persons who will have access to better data." p. 64.

4. Boyland, Correlation of Experimental Carcinogens and Cancer in Man, International Symposium, 1967, in Progress in Human Research, 1969. (Ref. 9)

An old symposium presentation on chemical carcinogens topics includes a review of the ten current understandings of the cause of breast and kidney cancer, the use of drugs with carcinogenic potential and the occurrence of natural carcinogens. There is no discussion of air pollution.

5. Carcinogen Assessment Group's Preliminary Report on Population Risk to Ambient Coke Oven Exposure (1978) (Ref. 10)

This report presents an estimate of the possible number of excess deaths to be expected in populations living in the vicinity of coke oven facilities.

There are no epidemiologic studies showing an increase in cancer in populations living in the vicinity of coke ovens. The Carcinogen Assessment Group instead

has calculated a number representing its estimate of the excess risk to surrounding populations by extrapolating epidemiologic data collected on coke oven workers. The authors have obtained estimates of the levels of coke oven emissions at various distances from coke oven facilities and estimates of the size of populations from an assessment by the Stanford Research Institute. These estimates were assumed to be valid. According to their calculations, for persons exposed to high levels of emissions, there is a 0.2% to 0.6% excess chance of dying of lung cancer, while for the rest of the exposed population the air excess chance is 0.1%. Out of the exposed population of 15 million people, the total number of excess lung cancer deaths per year was calculated to be 150.

The report characterizes the estimate as "crude and conservative, i.e., probably on the high side." They note the substantial difficulties in predicting cancer risk. "As the emissions move away from the coke ovens, it is possible that the chemical composition and the associated carcinogenic potency of the material may change significantly." Also "unfortunately, there are no animal inhalation studies with coke oven emissions and consequently no evidence on the extent to which dilution and aging of emissions affects it carcinogenic effect."

Other factors also may affect the validity of a straight line extrapolation from high dose to which workers are exposed to the lower levels in ambient air. For example, smoking, the major factor in lung cancer incidence is not mentioned in the description of methods used to arrive at the estimate. Differences in the smoking habits between the occupationally exposed workers and the general populace could affect the expected excess incidence of lung cancer. It is important to know how or whether smoking was taken into account.

6. Health Effects of Air Pollution, Ad Hoc Committee on the Health Effects of Air Pollution, American Thoracic Society News, Spring, 1978 (Ref. 17)

An annual statement by the American Thoracic Society (ATS) summarizing the current scientific assessment of the adverse health effects of air pollution. The report reviews the effects of air pollution on the respiratory, cardiovascular and central nervous system functions as well as on the incidence of lung cancer.

After considering studies investigating the association between air pollution and cancer, ATS concludes: "There is no general agreement that urban air pollutants contribute to the development of lung cancer. The overwhelming contribution of cigarette smoking makes comparisons of lung cancer rates in areas

of heavy and light pollution meaningless unless adjustments are made for smoking habits in each population."

"On the basis of the evidence gathered thus far, the suspicion that air pollution leads to cancer remains neither proved nor disproved."

Criticizing a 1970 study by Lave and Seskin proposing that a 50% decrease in air pollution would be expected to result in a decrease of 15 per cent of the urban excess in cancer, the authors observe:

> "From these considerations, it would appear to be far beyond the quality of the data or the method of analysis to be able to attribute 25 to 50 per cent of the urban excess in lung cancer and other respiratory diseases to a given change in air quality. Too many strong determinants of these diseases were left unmeasured and therefore unanalyzed, and there determinants are very likely to be confounders of the apparent geographic association between air pollution and distance."

7. Air Pollution and Cancer: Risk Assessment Methodology and Epidemiological Evidence, Report of a Task Group, Karolinska Institute Symposium on Air Pollution and Cancer, March 8-11, 1977 (Ref. 18)

The report is the result of an international symposium which considered the current scientific

knowledge about carcinogenic substances in air as air pollutants.

The authors recognized that not all of the available epidemiologic evidence is consistent with an air pollution effect on cancer incidence. However, the authors, by taking into consideration all available evidence, excluding epidemiologic data, experimental studies, and the presence of carcinogenic substances in the ambient air, ... produced a "tentative estimate" that "combustion products of fossil fuels in ambient air, probably acting together with cigarette smoke, have been responsible for cases of lung cancer in large urban areas, the numbers produced being on the order of 5-10 cases per 100,000 males per year."

This estimate when considered along with the contradictory epidemiological data did not convince the American Thoracic Society (ATS). Although the ATS discussed the report in their summary of the health effects of air pollution, they nevertheless did not agree with the study that the weight of the evidence gathered so far supports the conclusion that air pollution is causally connected to lung cancer. See Ref. 17 above, p. 42.

8. American Cancer Society Calculation Showing That 80% of Lung Cancer is Caused by Cigarette Smoking (1977) (Ref. 24)

A letter from Lawrence Garfinkle, Assistant Vice President for Epidemiology and Statistics, American Cancer Society to R. P. Moore, M.D. containing a tabular presentation of the data supporting the claim that 80% of the lung cancer for the total U.S. population, including both men and women is caused by smoking.

9. Joan Arehart-Treichel, Chemical Carcinogens: Part of the Problem, 115 Science News 414 (1979) (Ref. 21)

A non-technical article reporting on a perspective on carcinogens somewhat different from that held in the early 1970's. Some scientists now maintain that chemicals, especially those artificially introduced into the environment are not the major culprits in human cancer causation. "Some chemical carcinogens, for instance, are known to be present in urban air. Yet as John Goldsmith of California Department of Health Services in Berkeley reports, when adjustments for cigarette smoking are made, one finds that the highest death rates for lung cancer are not in large cities with lots of air pollution but in smaller cities with less of it. Thus chemical carcinogens in the air do not seem to be a major cause of lung cancer.

"Yet another indication that air pollution is not a significant source of human cancer comes from the work

of Bernard Wagner of Columbia University College of Physicians and Surgeons. He and his colleagues examined pets in the highly industrialized regions of New Jersey and found no excess cancers among them." p. 414.

B. SCIENCE ARTICLES ON TOPICS OTHER THAN AIR POLLUTION

None of the articles discuss air pollution directly.

1. Environmental Mutagenic Hazards, 187 Science 503-14 (1975) (Ref. 3)

A description of screening methods for the detection of mutagens in the environment and proposal for the implementation of mass mutagen screening programs for old and new chemicals. Carcinogens are not discussed in this now dated treatment of chemical mutagens.

2. How to Assess Cancer Risk, 204 Science 811 (1979) (Ref. 6)

Discussion of Office of Science and Technology's proposal to centralize the authority over cancer risk assessment now dispersed among the regulatory agencies in the newly created National Toxicology Program.

3. Culliton, Toxic Substances Legislation: How Well Are Laws Being Implemented? Science (1978) (Ref. 12)

News analysis of toxic substance regulation. The article focuses on TSCA, its broad mandate and delayed implementation.

4. Maugh, Chemical Carcinogens: The Scientific Basis of Regulation, Science (1978) (Ref. 12)

A discussion for a lay audience of issues surrounding epidemiologic studies, animal bioassays and short term toxicity testing.

5. EPA and Toxic Substances Law: Dealing with Uncertainty, Science (19__)

A description of EPA's start up problems in setting up to administer TSCA.

6. Carter, Dispute Over Cancer Risk Quantification, Science ___, (19___ (Ref. 20)

News analysis of the decision by the Supreme Court to review the Fifth Circuit Court of Appeals rejection of the OSHA benzene standard.

7. Ames, Identifying Environmental Chemicals Causing Mutations and Cancer, __ Science ___ (19__) (Ref. 22)

Article proposes an important role for short term mutagenicity tests in identifying environmental mutagens as carcinogens.

8. Cornfield, Carcinogenic Risk Assessment, 198 Science 693 (1977) (Ref. 11)

A theoretical analysis of the interaction between a carcinogen and target showing that "even if carcinogesis is an irreversible one-hit phenomenon ... the existence of a no-effect or threshold level for the carcinogenic compound administer is not precluded." Proposal of the so-called "hockey-stick" model, describing a dose-

response relationship for carcinogens which predicts a threshold at low doses.

9. Models for Carcinogens Risk Assessment, 202 Science 1105 (1973) (Ref. 11)

An exchange of letters to the editor in Science between Cornfield and the critics of his article on the "hockey-stick" model.

C. REGULATORY & POLICY DOCUMENTS

1. The Relation of Biossay Data on Chemicals to the Assessment of the Risk of Carcinogens for Humans Under Conditions of Low Exposure. Draft report of the Subcommittee on Environmental Carcinogenisis to the National Cancer Advisory Board. (Ref. 3)

A statement requested by the Chairman of the President's Career Panel setting forth the difficulties and limitations of biossay and epidemiologic data in the assessment of risk for humans under conditions of low exposure.

In the estimation of human risk, the report states: "[t]he importance of relating actual risk estimates to the real human situation cannot be overemphasized. On the basis of such determinations, regulations governing such agents should be established in order to ensure the safety of specific population groups on the one hand, while at the same time modifying

such regulations for populations where the risk is truely relatively negligible." (emphasis added) p. 36.

2. Memorandum to the Scientific Committee and to Contributors to the Reply to the Estimates Paper (Ref. 25)

The reference includes four documents obtained from NIOSH in response to a Freedom of Information Request for documents relating to the EPA documents "Estimates of Fraction of Cancer in the United States Attributable to Occupational Factors." (For analyses of the 'Estimates' paper see previously submitted documents, p. ___.) The documents are:

a. Bredbord, K., M.D., "Threshold or No Threshold for Carcinogens in the Workplace," A paper prepared by Dr. Bredbord and presented in 1975 at the nineteenth meeing of the Interagency Collaborative Group on Environmental Carcinogens.

b. A letter to Dr. Kenneth Bredbord from Dr. Donald Lassiter, Environmental Health Associates, Inc., suggesting the 'Estimates' paper had overstated the risk of cancer to occupationally exposed workers.

c. A memo from Marvin Schnederman (1978) written as a possible reply to the industry criticisms of the 'Estimates' paper.

d. A letter to Dr. Kenneth Bredbord from J. H. Weisburger, Naylor Dana Institute, criticizing the

'Estimates' paper's failure to take into account smoking and lifestyle factors in cancer incidence.

3. Remarks of Joseph A. Califano, Jr., Department of Health, Education and Welfare to the AFL-CIO National Conference of Occupational Safety and Health (1978) (Ref. 15)

   A speech to the AFL-CIO explaining HEW programs dealing with problems of occupational exposure to asbestos and radiation.

4. Nicholas Ashford, Ph.D., J.D., Federal Control of Toxic Substances in the Workplace and General Environment: Legal, Regulatory and Scientific Complexities (19__) (Ref. 16)

   An overview in policy terms of the toxic chemical regulatory legislation of the 1970's, the paper discusses the Occupational Health and Safety Act, the Consumer Products Safety Act and the Toxic Substances Control Act (TSCA).

5. Regulatory Analysis of a Proposal Policy for the Identification, Classification and Regulation of Toxic Substances, (1978) (Ref. 19)

   An analysis of the proposed OSHA policy for carcinogens in the workplace by the Regulatory Analysis Review Group (RARG).

6. Identification, Characterization and Control of Potential Human Carcinogens: A Framework for Federal Decision-Making. Office of Science and Technology

Policy, Executive Office of the President (1979). (Ref. 30)

A framework for decision-making proposed by the Office of Science and Technology to stimulate the development of uniform decision-making by the various agencies concerned with carcinogen regulation. The proposal suggests that regulatory decisions on carcinogens should be made independently of scientific assessments of the hazard posed by the substances.

D. SUMMARY OF REVIEW OF ADDITIONAL EPA REFERENCES

The majority of the papers cited by EPA as having been used in the preparation of the airborne carcinogen proposal discusses topics other than air pollution. Many deal with general topics of carcinogen identification and regulation, and a substantial number relate specifically to occupational exposure to carcinogens.

It is appropriate, of course, in the formulation of air carcinogens policy that EPA should refer to background articles on carcinogens and should have scanned both academic and governmental sources for regulatory programs or proposals in related fields. The experience obtained in regulating occupational exposure to carcinogens could be useful in many ways in making policy decisions with airborne carcinogens. But in assessing whether or not airborne carcinogens pose a risk of cancer to human populations the dicussion of known occupational carcinogenic hazards must be kept distinct from the possibility of ambient air pollution hazard. The danger of occupational

exposure to high levels of some carcinogens is unquestioned. But recognition that occupational hazards exist does not address the question whether exposure to carcinogens at vastly lower concentrations that may be present in the ambient atmosphere also poses a danger.

Only a few of the supplementary references presented by EPA discuss specifically the data available on the question of the association between air pollution and cancer: a) a "crude" estimate of the cancer hazard presented by coke oven emissions obtained by straight line extrapation of occupational coke emission data, b) the Karolinska report which estimates excess male deaths in Europe, c) the American Thoracic Society report which finds that in spite of studies looking for a causal link between air pollution and lung cancer, the evidence supporting the contention has not been produced, d) a 1974 review article containing only a single unsupported statement attributing cancer to air pollution, and e) a recent preliminary report on a study of cancer mortality in the New Jersey region, uncontrolled for smoking habits, whose authors disclaim the use of the data for more than identification of areas of further research.

These additional references do little to buttress the case that air pollution is a human cancer hazard. Although many of the references contain useful background material, evidence contained in the references does not support the assertion made in the original EPA proposal that in fact the "dimension of the problem posed by air carcinogens remains significant."

BEFORE THE
ENVIRONMENTAL PROTECTION AGENCY

In the Matter of

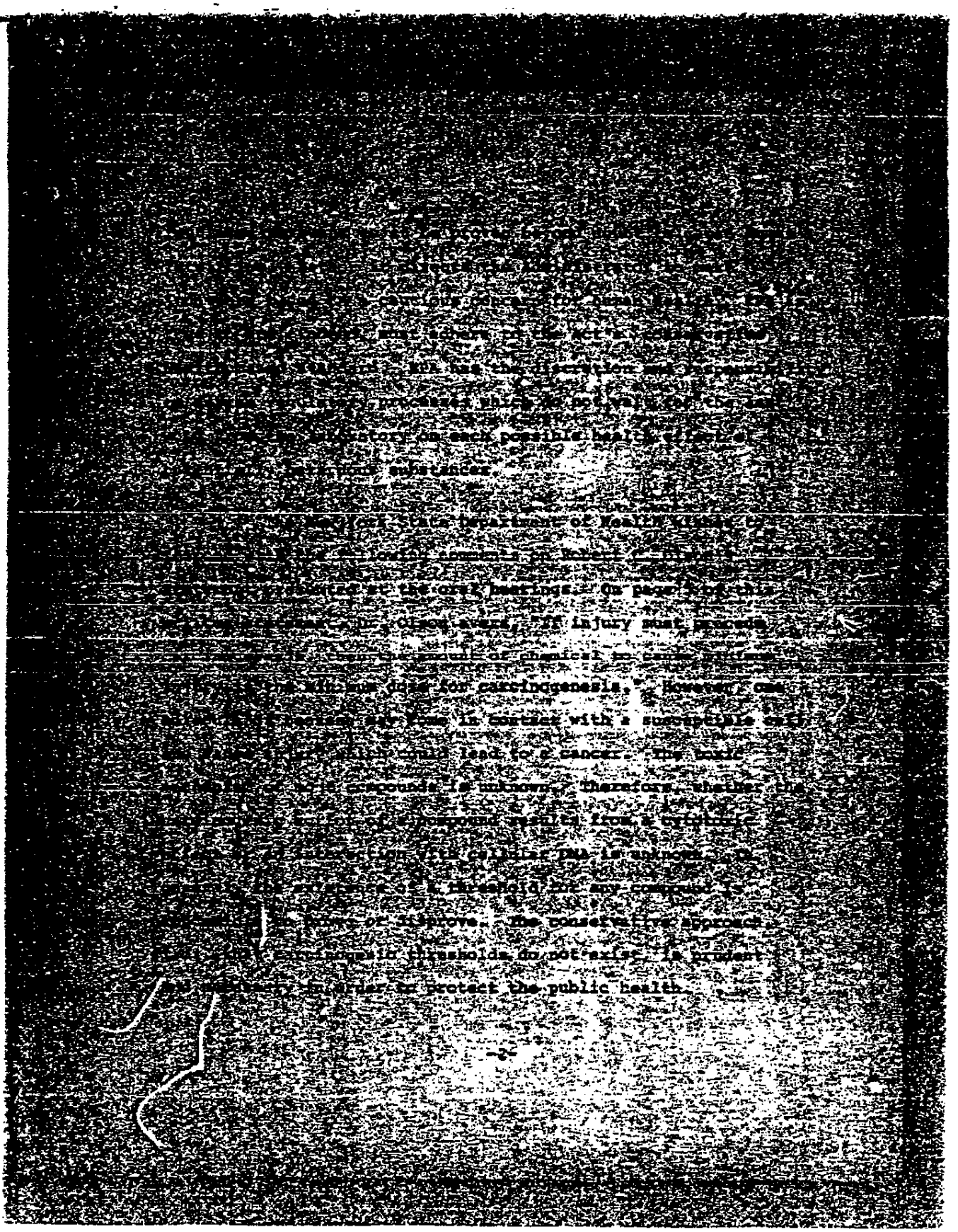
National Emission Standards for Hazardous Air Pollutants; Policy and Procedures for Identifying and Regulating Pollutants Posing a Risk of Significant Harm; Notice of Proposed Standards, Federal Register, Vol. 45, No. 197, p. 58642 et seq.

RECEIVED
ENVIRONMENTAL PROTECTION AGENCY
APR 16 1980
CENTRAL DOCKET SECTION

REPLY COMMENTS OF THE ATTORNEY GENERAL FOR THE STATE OF NEW YORK AND THE NEW YORK STATE DEPARTMENT OF HEALTH

New York State wishes to stress that the precautionary mandate in Section 112 of the Clean Air Act must be EPA's guide in this proceeding. The Act directs the Administrator to designate as a "hazardous air pollutant" any air pollutant which causes or contributes to air pollution which may be reasonably anticipated to result in an increase in mortality or an increase in serious irreversible or incapacitating reversible illness." 42 U.S.C. § 7412(a)(1).

The standard set by § 112 is therefore a broad one, which includes all pollutants which pose significant health risks. Section 112 does not require that each pollutant



On page 8 Dr. Olson states, "During exposures of man to benzene levels in the air of 10 parts per million or less, the metabolic detoxification reactions maintain benzene levels sufficiently low in the blood to be below the threshold for any effect on the bone marrow." However, to our knowledge this statement has not been proven and Dr. Olson offers no proof of this statement. Dr. Olson also states, "To my knowledge, there is no case of a human subject exposed to 10 part per million of benzene in the air or less who has developed any hematologic complications to benzene exposure." If the incidence were less than 1 in 1000, no one would see it at statistically significant levels. Most workplace exposure to benzene has involved males; females are known to be more sensitive to benzene toxicity than males.

On page 10 Dr. Olson claims, "A threshold exists for benzene." However, no proof of this statement is set out in the statement. Moreover, most benzene exposure has involved an 8 hour work day. Benzene can be exhaled when exposure levels are reduced. Exposure-free periods to ambient concentrations do not exist for the general population.

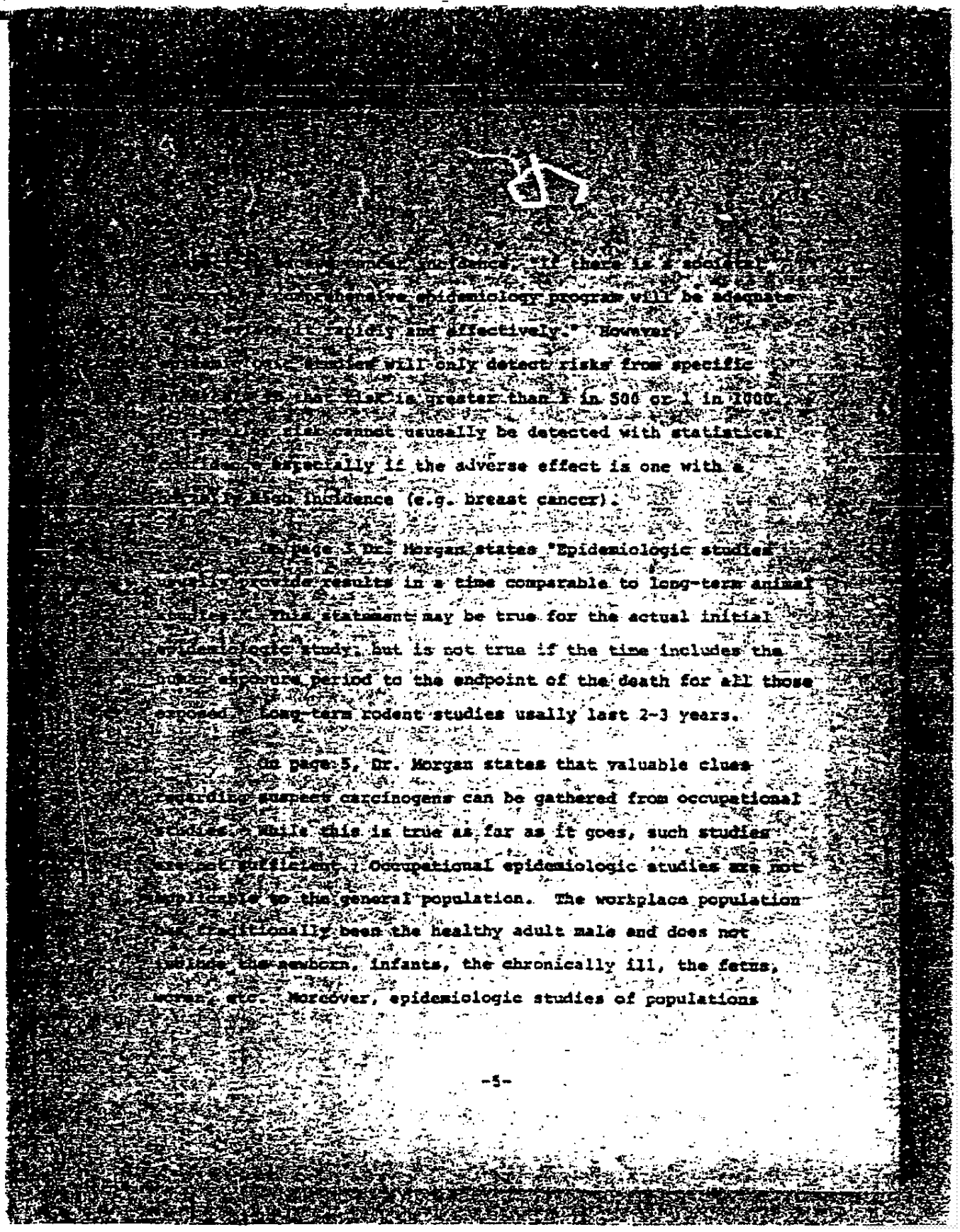
On page 11 of Dr. Olson's statement, in paragraph 19, Dr. Olson discusses rodent experiments with perchlorethylene. Carcinogenic experiments with tetrachloroethylene and trichloroethylene involve Osborne-Mendel rats. This strain of

[redacted] results with chloroform whose carcinogenicity [redacted] this same strain of rats have used [redacted] experiments, the result is not surprising since [redacted] rats may not be sensitive to halogenated [redacted] hydrocarbons.

On page 14, Dr. Olson concludes that perchlorethylene is producing tumors in the B6C3F1 mouse by a nongenetic mechanism. However, even if tetrachloroethylene does act by a nongenetic mechanism, a threshold may not exist, or may be too low to be meaningful. Without data which substantiates the existence of a threshold and quantitifies it for the exposed population, there is no rational way to establish a meaningful regulatory threshold.

Dr. Olson also discusses the usefulness of the threshold concept in the field of occupational medicine. Work-place exposure involves an acceptance of some voluntary risk. Exposure of the general population to risks from drinking water and ambient air involve involuntary risks. These two types of risk cannot be equated and different precautionary measures are required to address each one.

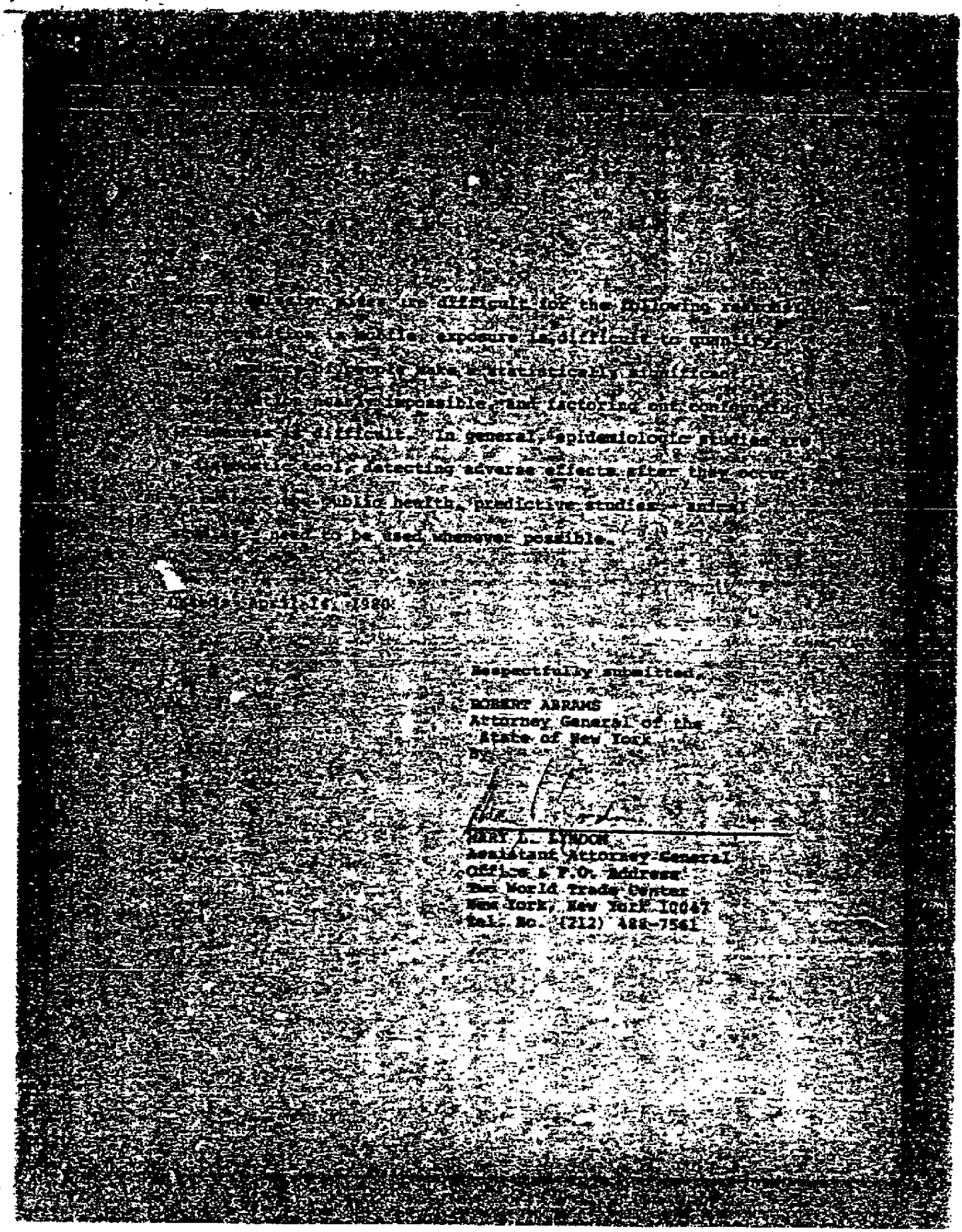
In response to the statement of Robert W. Morgan of ABMC, presented at the oral hearing on March 10, 1980, the New York State Department of Health makes the following comments. On page two of his written statement Dr. Morgan claims that with



[illegible] incidence. If there is a societal [illegible] comprehensive epidemiology program will be adequate [illegible] it rapidly and effectively." However, [illegible] studies will only detect risks from specific [illegible] so that risk is greater than 1 in 500 or 1 in 1000. [illegible] risk cannot usually be detected with statistical [illegible] especially if the adverse effect is one with a [illegible] high incidence (e.g. breast cancer).

On page 3 Dr. Morgan states "Epidemiologic studies usually provide results in a time comparable to long-term animal [illegible]." This statement may be true for the actual initial epidemiologic study, but is not true if the time includes the human exposure period to the endpoint of the death for all those exposed. Long-term rodent studies usally last 2-3 years.

On page 5, Dr. Morgan states that valuable clues regarding suspect carcinogens can be gathered from occupational studies. While this is true as far as it goes, such studies [illegible] sufficient. Occupational epidemiologic studies are not applicable to the general population. The workplace population has traditionally been the healthy adult male and does not include the newborn, infants, the chronically ill, the fetus, women, etc. Moreover, epidemiologic studies of populations



[illegible] are difficult for the following reasons:

[illegible] exposure is difficult to quantify.

[illegible] is statistically significant.

[illegible] impossible [illegible] confounding [illegible]

[illegible] difficult. In general, epidemiologic studies are [illegible] detecting adverse effects after they occur.

[illegible] public health, predictive studies [illegible] need to be used whenever possible.

[illegible], April 15, 1980

Respectfully submitted,

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By: /s/

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CAGPS 79-19

II-F-3-3

Regulating Airborn Substances Posing a Risk of Cancer

Comments on Proposed EPA Regulations

(44 Fed. Reg. 58642 Oct. 10, 1979)

and

Proposed Generic Standards

(44 Fed. Reg. 58662 Oct. 10, 1979)

Richard Wilson

Harvard University

Written at the Request of

American Industrial Health Council

Presented Wed., March 12, 1980

9:00 a.m.

Draft

a forthcoming book by

Edmund Crouch

and

Richard Wilson

Risk-Benefit analysis & Decision Making

Ballinger Press

DRAFT

Comments on Proposed Rule for

Vinyl Chloride Emissions

August 1, 1977

EPA

Richard Wilson

THE FDA CRITERIA FOR ASSESSING CARCINOGENS

Richard Wilson

Harvard University*

*Written for the American Industrial Health Council. The views expressed are not necessarily the views of either Harvard University or the American Industrial Health Council.

Submitted to FDA in response to request for comment in the Federal Register.

5457

Health Effects of Fossil Fuel Burning

Assessment and Mitigation

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