UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

December 15, 1988

OFFICE OF
THE ADMINISTRATOR

The Honorable Lee. M. Thomas
Administrator
U.S. Environmental Protection Agency
401 M Street, S.W.
Washington, DC 20460

RE: Report on Acid Aerosol Research Needs

Dear Mr. Thomas:

We are pleased to transmit via this letter the advice of the Clean Air Scientific Advisory Committee (CASAC) concerning research needs for acidic aerosols. As part of its review of the potential health effects of acidic aerosols, the CASAC and its Acid Aerosol Subcommittee, reviewed the Acid Aerosol Issue Paper prepared by EPA and prepared this report to present its research recommendations for acid aerosols. A separate report has been prepared by the Committee concerning the potential health effects of acidic aerosols.

The research recommendations for acid aerosols are presented in four parts: characterization and exposure; animal toxicology; human exposure studies; and epidemiology. Recommendations are classified as high, medium and low.

The Committee appreciates this opportunity to present our views on acid aerosol research. We look forward to the Agency's response to our report.

Sincerely,

Roger O. McClellan, D.V.M.
Chairman
Clean Air Scientific Advisory
Committee

Mark J. Utell, M.D.
Chairman
CASAC Acid Aerosol Subcommittee

cc: Don Barnes
Erich Bretthauer
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EPA-SAB/CASAC-89-002

CLEAN AIR SCIENTIFIC ADVISORY COMMITTEE

SUBCOMMITTEE ON ACID AEROSOLS

REPORT ON

ACID AEROSOL RESEARCH NEEDS

FINAL SUBCOMMITTEE REPORT
OCTOBER 19, 1988

U.S. ENVIRONMENTAL PROTECTION AGENCY
SCIENCE ADVISORY BOARD
WASHINGTON, DC

ABSTRACT

Under Section 109 of the Clean Air Act, the U.S. Environmental Protection Agency (EPA) is required to periodically review national ambient air quality standards (NAAQS) and the criteria on which they are based. The Act also requires the Clean Air Scientific Advisory Committee (CASAC) to provide scientific advice on any additional knowledge that is required to evaluate existing, or setting new or revised NAAQS. To evaluate the health effects of the class of air pollutants known as acid aerosols, the Committee requested that EPA prepare an "Acid Aerosol Issue Paper". In reviewing this Issue Paper, the Committee developed a series of research recommendations for acid aerosols, prioritizing them as high, medium, and low. This report presents these research recommendations in four parts: 1) characterization and exposure, 2) animal toxicology, 3) human exposure, and 4) epidemiology.

Key Words: acid aerosols, acid particles, research needs, NAAQS

U.S. Environmental Protection Agency

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1.0 EXECUTIVE SUMMARY

1.1 Overview and Background

This is the third in a series of reports prepared by the Clean Air Scientific Advisory Committee (CASAC) providing recommendations to the U.S. Environmental Protection Agency (EPA) on research needed to develop and support national ambient air quality standards (NAAQS). The first report, issued in December 1983, provided research recommendations on four of the six criteria air pollutants: carbon monoxide, nitrogen oxides, particulate matter, and sulfur oxides. The second report, issued in September 1987, provided recommendations on the two remaining criteria air pollutants: ozone and lead. The present report presents research recommendations for acid aerosols, a class of air pollutants that are under consideration for possible listing as a seventh criteria pollutant.

The research recommendations for acid aerosols are presented in four parts: 1) characterization and exposure; 2) animal toxicology; 3) human exposure studies; and 4) epidemiology. This document is only concerned with the health risks of acid aerosols and does not consider potential welfare issues.

1.2 Major Recommendations

It should be noted that though we have used high, medium, and low priorities to define research needs as is customary in our reports, in most cases the use of the last two designations simply means that these projects should not be initiated until the high priority projects have a commitment for support.

The Committee has the following high priority research recommendations for acid aerosols:

1.2.1 Characterization and Exposure Research

- A program is needed to evaluate existing measurement methods, to improve them as needed, and to establish the precision and accuracy of the best methods.
- Quality assurance/quality control procedures should be developed with respect to outdoor monitoring networks, indoor characterization, and personal sampling.
- The spatial and temporal behavior of acid aerosols and gaseous ammonia should be characterized. This should include measurement of indoor/outdoor ratios.
- Population exposure estimates are needed for all microenvironments, not just outdoor air.

- If important routes of exposure other than outdoors are identified, a total exposure measurement study should be carried out to ascertain the contributions of each exposure route to different population subsets.

1.2.2 Animal Toxicology Research

- Develop more concentration times time (CxT) health and monitoring data.
- More delayed response studies are needed, as are studies which examine responses to short-term repeated exposures.
- Further evaluate the hypothesis that long-term exposure to low levels of sulfuric acid may cause bronchitis.
- More studies are needed which document the nature of the various health effects of acids.
- More effort is needed to improve animal to human extrapolations.

1.2.3 Human Exposure Research

- Studies are needed on the influence of ventilatory rates and concentration and duration of single and multiple exposures to acid aerosols on the magnitude and duration of respiratory function responses, airway hyperreactivity, and assays dependent on bronchoalveolar lavage in volunteers, and the influence of age, gender, pre-existing disease and endogenous ammonia excretion on these responses.
- Studies are needed on the influence of concentrations and durations of single and multiple exposure to acid aerosols on the magnitude and duration of mucociliary clearance function in healthy volunteers.
- Studies are needed on the separate and combined effects of acute exposures to ozone and acidic aerosols and vapors on respiratory function and assays of possible tissue injury, altered defenses, or inflammation, including epithelial permeability.

1.2.4 Epidemiology Research

- Studies that directly measure health outcomes among individuals are needed, rather than descriptive or ecological studies.
- Specific studies warranting highest priority are: Harvard Multicity; Chestnut Ridge or other areas of high acute exposure; and occupational studies of acid aerosol exposure.

2.0 INTRODUCTION

2.1 Overview

Under Section 109 of the Clean Air Act, the EPA is required to periodically review NAAQS as well as the air quality criteria on which they are based. When appropriate, the EPA is to update and revise these standards. New pollutants are to be listed if the Administrator concludes that they may reasonably be anticipated to endanger public health or welfare and are emitted by numerous or diverse mobile or stationary sources. The Administrator will consider the advice of his staff and the advice of the CASAC before making a decision. Adequate scientific information for such a decision must be available, including a rigorous data base which supports the basis for the decision. Additional research will be necessary where gaps exist in the data base.

A major responsibility of the CASAC, as established in the Act, is to provide scientific advice on additional knowledge that is required for evaluating existing, or setting new or revised NAAQS. Based on its review of Agency documents and relevant scientific literature and on discussions with Agency staff and the interested public, CASAC develops research recommendations designed to fill the gaps in existing research.

2.2 Purpose of this Report

On June 14-15, 1988, the CASAC Acid Aerosol Subcommittee met in Washington, DC to review the draft "Acid Aerosols Issue Paper" (EPA/600/8-88/005A) prepared by EPA's Office of Research and Development (ORD). The three main purposes of the meeting were as follows: to prepare a Subcommittee recommendation on the acid aerosol listing issue, to comment on the adequacy of the draft issue paper, and to identify research needs for acid aerosols. The Subcommittee recommendations were approved, with minor changes by the full CASAC at a public meeting in Washington, DC on October 6, 1988.

This report on acid aerosol research recommendations represents the first such CASAC report that evaluates research needs for a potential new criteria pollutant.

3.0 CHARACTERIZATION AND EXPOSURE RESEARCH NEEDS

3.1 Overview

This section recommends priorities for research to characterize acid species (i.e. to identify and quantify acids potentially in the breathing zones of U.S. citizens), and research to determine actual exposures in order to link these exposures to health end points obtained by animal, clinical, and epidemiological studies.

The foundation of any air quality standard is the measurement method, not only because the standard itself must specify the method, but equally important, because before establishing a standard, the contaminant must be fully characterized and exposure measurements made to correlate with health outcomes. Therefore, it is critical to have measurement methods which have been thoroughly validated. Often, necessary validation has not been done until the standard is about to be promulgated. Thus, much of the characterization and health effect data relies on measurement techniques which are not as rigorously validated as they are once the standard is set. This is part of the difficulty in competently establishing a standard in the first place. This difficulty is especially acute with respect to the development of an acid aerosol standard.

There are two problems that are specific to an acid standard. First, current exposure science has advanced sufficiently since previous standards were set that it is no longer acceptable to characterize acids or determine exposures in only one microenvironment, viz. outdoor air. Rather their presence in other microenvironments must also be estimated, and in the case of acids, particularly indoor environments using kerosene heaters. Unfortunately, samplers developed for outdoor monitoring stations cannot always be used indoors because of size, noise, air flow, and cost (since the indoor environment requires more samples to characterize it). Secondly, there is some uncertainty at the present time regarding the specific acid species of concern. Thus, any research program must be flexible enough to accommodate species other than titratable H^+ and H_2SO_4, the currently accepted species of concern. Therefore, the recommendations given below rest on an uncertain foundation.

3.2 Method Evaluation

3.2.1 High Priority Research Needs

3.2.1.1 Evaluating Existing Methods

A program is needed to evaluate existing methods, to improve them as needed, and to establish the precision and accuracy of the best methods. The goal is to establish standardized methods so that research and monitoring carried out by different groups will be comparable. This effort should be of the same comprehensiveness and quality as that carried out for the present criteria pollutants. It is recommended that the program begin with the following three steps:

A. EPA should sponsor a scientific workshop to discuss what species should be emphasized (total titratable acidity, H_2SO_4, pH, other ions, NH_3, strong and weak acids, etc.), and to decide which are the best candidate methods presently available. Discussions should include the sampler, sampling time, sample preservation, precision and accuracy, as well as the analytical method itself. Discussion is required on sampling artifacts, including possible displacement and subsequent off-gassing of

volatile acids from the filter surface, potential penetration of particulate bases (e.g. soil derived carbonates) past the annular denuder with subsequent chemical neutralization of filterable acidity, and possible loss of acidity due to within-particle reactions of alkaline combustion particles with their acidic surface coatings.

B. An acid aerosol "shoot-out" should be conducted. EPA should fund any group with a promising measurement method as determined by the above workshop to participate in a week-long methods intercomparison study. Since the National Oceanographic and Atmospheric Administration (NOAA) is already sponsoring an ammonia "shoot-out", EPA should consider the results of that study before including ammonia in the acid aerosol "shoot-out".

C. Following the "shoot-out", a second workshop should be held to determine the causes of differences in the methods, to determine what modifications can be made to improve the methods, and finally to establish which of the methods should be standardized for acid aerosol and ammonia research and monitoring.

This is not only a high priority research component, but should be carried out before major field studies using untested methods are begun. Of course, if no existing methods perform adequately, an intensive effort must then be launched to develop new methods.

3.2.1.2 Quality Assurance/Quality Control

Quality assurance/quality control (QA/QC) procedures should be developed with respect to outdoor monitoring networks, indoor characterization, and personal sampling.

3.2.1.3 Transfer of Standards

EPA should develop suitable transfer standards for accuracy assessment and determination of experimental (sampling and analytical) precision targets. This would help assure compatibility of data among various research and monitoring groups.

3.2.2 Medium Priority Research Needs

Methods for acid fog need to be evaluated.

3.2.3 Lower Priority Research Needs

Methods must be evaluated for acidic gases, particularly for nitric acid, the predominant atmospheric species. This effort should be coordinated with the work of the California Air Resources Board (CARB).

3.3 Characterization of Acid Aerosols

3.3.1 Indoor and Outdoor Measurements

3.3.1.1 High Priority Research Needs

A. The spatial and temporal behavior of acid aerosols and gaseous ammonia should be characterized. Five or six urban areas in the country should be selected for this task. For example: one in the Northeast (Philadelphia), one in the Ohio Valley source region (Cincinnati), one in the Southeast (Atlanta), Houston, and Los Angeles. In each of these areas, six to ten monitoring sites should be established. They should be located upwind, downwind and within the urban centers. The networks should be operated for one year. At the end of the year, the data should be analyzed to determine the spatial distribution of acids, ammonia and products of neutralization, source-receptor relationships, seasonal patterns, and local and synoptic meteorological influences.

B. Indoor/outdoor ratios should be measured at one or more of the urban locations discussed above.

3.3.1.2 Medium Priority Research Needs

A. At one or more of the urban sites discussed above, intensive aerial measurements of acid-related species should be made so that acid plumes can be mapped. This will augment the information needed to define the spatial distributions and source-receptor relationships.

B. Measure acid particle size distributions, on a more localized, intensive scale than the monitoring network. This includes examination of the effect of relative humidity or presence of fog on size.

C. Measurement of ammonia surface fluxes (emission rates) are needed for subsequent modelling efforts.

3.3.1.3 Lower Priority Research Needs

A. If the indoor/outdoor data, the health data, and the total exposure estimates (discussed below) indicate a potential health risk, a nationwide monitoring network would need to be established. The criteria used to select the urban areas and the specific monitoring sites would be developed based on the information learned from the operation of the five or six-city monitoring networks.

B. The uncertainties in the chemical mechanisms and rate constants involved in the formation of acid aerosols need to be assessed. The key reactions which require better information must be identified. The appropriate experiments to obtain the information must then be designed and implemented.

C. Develop an acid aerosol climatology. If acid aerosols are found to only be a local problem, this task may not be necessary. If on the other hand, it is found to have an important regional componant like ozone and sulfates, then a regional scale rural monitoring network will be needed to obtain the data necessary to understand the formation mechanisms, behavior, and spatial distributions.

D. The co-occurrence of nitric acid vapor over the same acidic particle network should be characterized.

3.3.2 Total Exposure Measurements

3.3.2.1 High Priority Research Needs

If the microenvironmental measurements carried out above indicate potentially important routes of exposure besides the outdoors, a total exposure measurement study should be carried out to ascertain the contributions of various routes of exposure to different subsets of the population.

3.4 Modelling

3.4.1 High Priority Research Needs

3.4.1.1 Estimate of Population Exposure

A crucial part of the health risk assessment necessary to determine the need of a standard is the estimate of population exposure. The exposure estimates should be for all microenvironments, not just outdoor air. Thus, it will be necessary to examine the various exposure models, particularly the NAAQS Exposure Model (NEM), to establish which one will be most appropriate for estimating the exposure distributions for the various population groups. Clearly this should be establishsd before the indoor/outdoor measurement studies are designed and implemented to assure that the data collected will satisfy the input requirements of the model.

3.4.1.2 Exposure Distributions

The indoor/outdoor data base should then be used in the chosen exposure model to obtain exposure distributions to determine potential population subsets at risk.

3.4.2 Medium Priority Research Needs

3.4.2.1 Thermodynamic Equilibria of Ammonia

Using the data base which presently exists, an improved understanding of thermodynamic equilibria of ammonia with sulfuric and nitric acid systems should be developed.

3.4.2.2 Ammonia Diffusion/Reaction Kinetics

There is a need for the measurement of ammonia diffusion/reaction kinetics with actual atmospheric acid particles. This information, along with size distribution data will allow for better assessment of the potential for respiratory NH_3 neutralization during inhalation. The information is also needed for atmospheric models.

3.4.2.3 Ammonia Emissions Inventory

An ammonia emissions inventory is necessary input to all models which attempt to describe the formation of the acids.

3.4.3 Lower Priority Research Needs

A. an appropriate aerosol module for incorporation into an air quality model is needed. The scale of the model into which the aerosol kinetic model will be incorporated will depend on whether acid aerosols are a local, urban-scale, or regional-scale model.

3.5 Conclusions

Clearly the above recommendations represent an ambitious research plan. Nevertheless it must be implemented because the very foundation of the standard depends on good methods, characterization studies, and exposure assessments. Because of the present weakness in the measurement methodology for acid aerosols, it is particularly important that large field studies not be implemented until there is concurrence as to the most appropriate measurement methods, and reliable information is available on the accuracy and precision of the methods chosen. It should also be recognized that not all of the recommended studies can be carried out in parallel since the detailed design for many studies, and in some cases whether a study should be carried out at all, will depend on previous data obtained. Therefore it is recommended that EPA develop a comprehensive time-line strategy for all studies expected to be undertaken.

4.0 ANIMAL TOXICOLOGICAL RESEARCH NEEDS

4.1 Overview

The Subcommittee endorses the research needs identified by the EPA in the draft Acid Aerosols Issue Paper. We have modified these research needs and prioritized them into high and medium priorities.

4.2 High Priority Research Needs

4.2.1 Hazardous Chemical Species

There is a major need to identify all of the biologically active chemical species so that future epidemiology and

monitoring studies are properly directed and so that ultimately the proper causative species can be controlled. The relative potency of various acid species needs further study; most work has focused on H_2SO_4 but HNO_3 and/or NH_4HSO_4 may dominate ambient aerosol acidity at times. In addition, there is a need to understand the relative role of the cation and the anion associated with various acid species, and the toxicological effects of acidic particles compared to acidic gases. A more complex issue has arisen from recent research by Dr. Amdur and her colleagues. They found that H_2SO_4 adsorbed onto ultrafine zinc oxide particles was 3 to 10 times as potent in changing pulmonary function as an equivalent-sized aerosol of H_2SO_4 mist. This raises several questions, not only for H_2SO_4 but also for HCl since it is emitted from hazardous and municipal waste incinerators, in association with particles.

4.2.2 Concentration Times Time Relationships

Health effect outcomes are dependent on many factors, with exposure concentration and time (C x T) being among the major ones. Ambient air concentration patterns for acids, as for other pollutants, are not steady-state, so it is critical to determine which exposure patterns are of greater risk and hence must be monitored, and controlled if control is warranted. Given the paucity of C x T health exposure response data, it is important to develop a research strategy between both health and monitoring scientists so that the research of each may be made more efficient by the results of the other. The alternative is a less efficient integration of monitoring data and health risk data. Health studies must include a large variety of doses, endpoints and exposure times - much basic data is missing and needs to be generated. Such studies are not routine, so some flexibility and discretion on the part of the investigators is necessary.

4.2.3 Exposure-Response Patterns

This topic has elements in common with the C x T studies described above, but focuses more on the effects of timing of the pattern of exposure vis-a-vis pattern of response. Only rarely are delayed responses studied, although they can occur and may provide important guidance to design and interpretation of human clinical and epidemiological studies. In the Cincinnati dog study, in which dogs exposed to H_2SO_4 plus SO_2 were examined two years post-exposure, pulmonary function effects were progressive even after stopping the exposure, arguing further for the incorporation of delayed response studies in experimental designs. Another issue of importance to explore is the response to short-term repeated exposures. Over a week, the pattern of pulmonary function responses changes, in some cases worsening and in others plateauing. To interpret the degree of adversity, it is necessary to know whether there are 'silent' changes to one endpoint that progress while other endpoints adapt, as is the case with ozone.

4.2.4 Development of Chronic Lung Disease

There are sufficient data to hypothesize that long-term exposure to low levels of H_2SO_4 may cause chronic bronchitis. Because of the significance of these findings, it is essential to test the hypothesis. Several approaches are of interest. A few would include conducting studies similar to the rabbit study of Schlesinger et al. in at least two additional species; repeating the Schlesinger et al. study at a lower concentration; increasing the knowledge of the relationship between alterations in lung clearance and the development of chronic bronchitis; and applying state-of-the-art lung morphometric methods in a time-course study.

4.2.5 Classes of Effects

Generally, the literature on the health effects of acids is sparse, with the more useful findings resulting from the application of newer methods and technologies. Recently, low levels of H_2SO_4 have been observed to result in inflammatory responses and effects on alveolar macrophages. These changes have implications to the development of chronic lung disease. The alveolar macrophage effects and lung clearance effects may portend decrements in host resistance to infection, most probably viral infection since bacterial infectivity is apparently not affected. Taking the literature as a base, several findings require follow-up so that risk potential can be understood. As examples, is the influx of neutrophils associated with other inflammatory changes; are defenses against viral infection compromised?

4.2.6 Extrapolation

It is expected that animal studies will provide cause-effect data on the chronic effects of acids, mechanisms of effects, and the full range of effects, thereby providing information unavailable from epidemiological or human clinical studies. These animal data are therefore of great importance to risk assessment, but quantitative extrapolation to man is needed. To achieve the animal-to-human extrapolation, two primary factors must be considered: dosimetry and species sensitivity. Research on the relationship between concentration and delivered dose will be complex since 1) acids are frequently in hygroscopic aerosols for which more fundamental data are needed, 2) neutralization by breath ammonia and, in whole body exposure, ammonia from excrement, can be important, 3) tissue dose will be highly dependent on mucus buffering capacity, requiring data on mucus biochemistry, and 4) microdosimetry (i.e., dose within lung regions) is quite important since health studies on a single endpoint (i.e., clearance) show responses to be dependent on regional dose.

4.3 Medium Priority Research Needs

4.3.1 Susceptible Subpopulations

Several subpopulations are known or suspected to be more susceptible to acid aerosols. While some of this research is discussed elsewhere in the report, further animal toxicological research on this topic is needed to supplement human studies to explore mechanisms more fully.

4.3.2 Acids and Co-occurring Pollutant Interactions

Acidity in association with other pollutants such as ammonium sulfate, ozone and NO_2 has been found to be additive, synergistic, antagonistic or non-influential, depending upon the endpoint, the co-pollutant, and whether the exposure was in sequence or in mixture. From a health risk perspective, understanding any possible synergism is of major importance. Such studies need to be designed to mimic ambient occurrences of H_2SO_4 and co-pollutant exposures, insofar as possible. For example, the temporal relationship and concentration ratios of O_3 and H_2SO_4 that actually occur should be investigated for effects using sensitive endpoints such as edema, lung clearance, and other endpoints as well, since there can be a dependence on endpoint. Once the phenomenon is understood better, mechanism studies are needed to enable predictions of interactions in risk assessments. Such predictions are important since it is not feasible to collect data on every potential interaction of interest.

5.0 HUMAN EXPOSURE RESEARCH NEEDS

5.1 Overview

Controlled human exposure studies can provide the best possible information on the relationship between acute exposures of humans to acid aerosols and transient responses to such exposures. Studies of the progression of effects during chronic exposures cannot be performed for both ethical and practical reasons, and standards designed to protect against the effects of chronic exposures must rely primarily on data from toxicological and epidemiological studies. However, controlled human exposure studies can provide valuable supplemental information to support the validity of extrapolations of such data. For example, the close correspondence of transient changes in lung clearance function between humans and animals following acute exposures supports the hypothesis that the persistent functional and structural changes that occur in chronically exposed animals would also occur in humans if they were similarly exposed. Furthermore, the kinds of chronic effects seen in the animal studies are consistent with the kinds of effects seen in human populations having chronic exposures to ambient acid aerosols.

Controlled human studies are best able to determine variations in transient responses associated with: 1) Pre-

existing diseases, such as asthma, 2) various combinations of concentration, composition, and duration of acid aerosol exposure; 3) joint actions of combined exposures to acid aerosols and irritant vapors such as ozone; and 4) endogenous ammonia excretion. Recently, using bronchoalveolar lavage brief ozone exposures have been shown to produce inflammation in the lower airways of humans; such information on effects of acid aerosols on inflammation, possible tissue injury, altered defense mechanisms, and mucus are needed. In the past, controlled human exposure studies have not generally provided much data on the temporal dynamics of transient responses, especially delayed responses. However, repeated measurements of function can generally be made during and following acute exposures and can, therefore, readily provide valuable data on the temporal aspects of delayed and/or persistent responses.

5.2 High Priority Research Needs

5.2.1 Respiratory Function Responses and Airway Hyperreactivity

Studies are needed on the influence of ventilatory rates and concentration and duration of single and multiple exposures to acid aerosols on the magnitude and duration of respiratory function responses, airway hyperreactivity, and assays dependent on bronchoalveolar lavage in volunteers, and the influence of age, gender, pre-existing disease and endogenous ammonia excretion on these responses. Such studies are critical for determining the need and possible exposure levels for a short-term standard (1 to 8-hr averaging time) to protect against acute respiratory function effects, especially in sensitive populations, such as asthmatics.

5.2.2 Airway Mucus and Mucociliary Clearance Function

Studies are needed to develop better methods for sampling and analyzing airway mucus, to develop better models of buffering capacity of airway secretions, and to examine the variation among population groups who may be especially susceptible to the effects of acid aerosols. Such studies are critical in understanding the mechanisms of effects of acid aerosols on mucociliary clearance. In addition, studies are needed on the influence of concentrations and durations of single and multiple exposure to acid aerosols on the magnitude and duration of mucociliary clearance function in healthy volunteers. Such studies are needed, in conjunction with coordinated studies in animals, to develop a basis for the quantitative extrapolation of chronic animal exposure studies' results to chronic symptom and disease effects in human populations, especially bronchitis prevalence and hospital admissions for respiratory diseases.

5.2.3 Mixed Pollutant Studies

Studies are needed on the separate and combined effects of acute exposures to ozone and acidic aerosols and vapors on respiratory function and assays for possible tissue injury,

altered cell function, or inflammation, including epithelial permeability. Such studies are needed to determine whether the substantially greater functional effects of ozone seen in field studies in comparison to chamber studies is attributable to enhanced lung permeability or other mechanisms resulting from exposures to acidic aerosols.

5.3 Medium Priority Research Needs

5.3.1 Measurement of Small Airway Response

Development of methodologies for non-invasive measurement of small-airway response are needed to permit improved sensitivity for the detection of early or minimal responses.

6.0 EPIDEMIOLOGY RESEARCH NEEDS

6.1 Overview

The Subcommittee endorses the introductory statement on research needs for epidemiologic studies of acid aerosols in the draft Acid Aerosols Issue Paper. We wish to particularly emphasize the need for concurrent measurements of acid aerosols and other important ambient pollutants, so that the independent effects of acid aerosols can be directly assessed instead of inferred or assumed from other measurements. This is a major deficiency in almost all of the existing epidemiologic studies, and seriously limits their value for this issue.

6.2 High Priority Research Needs

The highest priority should be for epidemiologic studies that directly measure health outcomes among individuals, and not descriptive or ecologic studies. The latter are useful for their ability to look at large populations in a cost effective manner, but generally provide less evidence of causal association, and are less able to control for potential significant confounding factors.

Health outcomes of highest priority for study are acute and chronic pulmonary function and respiratory symptoms. Pulmonary function studies provide important objective data, and are of value in relating to exposure chamber studies of pulmonary function. Studies of acute (e.g. daily) changes in pulmonary function should be directed towards locations with high levels of ambient acid aerosol exposure. Asthmatics and other subjects with hyperreactive airways may be an 'efficient' population for these studies. The inflammatory effects of acid aerosols and preliminary data consistent with an effect on 'bronchitis' confirm the need to study acute and chronic effects on cough and phlegm production.

In view of these considerations, the studies warranting the highest priority are:

6.2.1 Harvard Multi-city

This study has the best prospect of looking at chronic effects of acid aerosols on respiratory symptoms and function, with a range of other exposures to allow evaluation of the independent effects of acid aerosols.

6.2.2 Chestnut Ridge or Other Areas of High Acute Exposures

Study design for an acid aerosol study in this area is unknown. High daily peaks in acid aerosols with frequent fluctuation would allow epidemiologic studies of acute effects. Potential chronic effect studies would depend on available current and historical data on chronic acid aerosol exposures in the area, and the divergence of acid aerosols from other ambient pollutants. Absence of such a divergence might prevent useful conclusions about the independent effects of acid aerosols. Other study areas with high acute exposures to primary downwind acid aerosols should also be a high priority for study.

6.2.3 Occupational Studies of Acid Aerosol Exposure

Many occupational settings exist with acid aerosol exposures in a range that includes the highest current ambient exposures. This situation gives the greatest potential for assessing acute dose-response relationships.

6.3 Medium Priority Research Needs

6.3.1 New York Hospital Admissions

This study may provide useful data on exposure-response relationships for acute effects associated with inhalation of secondary acid aerosols over wide regions, but has some of the limitations noted above for observational studies.

6.3.2 Indoor Exposures

The Yale research on indoor acid aerosols from high-sulfur kerosene heaters may provide a useful opportunity to study acute and chronic effects, although the effects may be associated with other indoor pollutants (e.g. NO_2). Other studies of indoor acid aerosol exposures if identified provide a controlled environment for studying exposure-response relationships.

6.3.3 Assistance to Foreign Studies

Support for studies in foreign countries may provide unique opportunities, including assessment of exposures to higher ambient concentrations of acid aerosols than are seen in this country. These studies should be evaluated on an individual basis.