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REVIEW

The Complexities of Air Pollution Regulation: the Need for an Integrated Research and Regulatory Perspective

Srikanth S. Nadadur,*,[1] C. Andrew Miller,† Philip K. Hopke,‡ Terry Gordon,§ Sverre Vedal,¶ John J. Vandenberg,* and Daniel L. Costa||

*National Center for Environmental Assessment, †National Risk Management Research Laboratory ORD, U.S. EPA, Research Triangle Park, North Carolina 27711; ‡Center for Air Resources Engineering and Science, Clarkson University, Potsdam, New York 13699-5708; §NYU School of Medicine, Tuxedo, New York 10987; ¶Department of Environmental and Occupational Health Sciences, University of Washington, Seattle, Washington 98105-6099; and ||ORD, U.S. EPA, Research Triangle Park, North Carolina 27711

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The Clean Air Act mandates the U.S. Environmental Protection Agency to periodically reassess existing and new science that underlie the regulation of major ambient pollutants—particulate matter (PM) and tropospheric ozone being most notable. While toxic effects have been ascribed individually to these and other pollutants in the air, it is clear that mixtures of these contaminants have the potential to interact and thereby influence their overall toxic outcomes. It follows that a more comprehensive assessment of the potential health effects of the air pollution complex might better protect human health; however, traditional regulatory drivers and funding constraints have impeded progress to such a goal. Despite difficulties in empirically conducting studies of complex mixtures of air pollutants and acquiring relevant exposure data, there remains a need to develop integrated, interdisciplinary research and analytical strategies to provide more comprehensive (and relevant) assessments of associated health outcomes and risks. The research and assessment communities are endeavoring to dissect this complexity using varied approaches Here we present five interdisciplinary perspectives of this evolving line of thought among researchers and those who use such data in assessment: (1) analyses that coordinate air quality-health analyses utilizing representative polluted U.S. air sheds to apportion source and component-specific health risks; (2) novel approaches to characterize air quality in terms of emission sources and how emission reduction strategies might effectively impact pollutant levels; (3) insights from present-day studies of effects of single ambient pollutants in animal and controlled clinical toxicology studies and how these are evolving to address air pollution; (4) refinements in epidemiologic health assessments that take advantage of the complexities of existent air quality conditions; and (5) new approaches to integrative analyses to establish the criteria for regulation of PM and other criteria pollutants. As these examples illustrate, implementing multi-disciplined and integrative strategies offer the promise of more realistic and relevant science, greater reductions in uncertainty, and improved overall air pollution assessment. The regulatory mandate may lag behind the science, but real gains both in public health benefit and the science to dissect complex problems will result.

Key Words: **Air pollution; criteria pollutants; PM; monitoring; toxicity; epidemiology; regulation.**

Air pollution is inherently complex, containing particulate matter (PM) of varied sizes and composition, inorganic gases, and myriad volatile organic compounds (VOCs) intermingled with biological materials such as pollens, spore fragments, viruses, and bacteria. These airborne constituents exist as a dynamic cloud interacting with sunlight and modified by its contemporaneous meteorology. The contaminants of ambient air arise from a variety of natural and anthropogenic sources. The latter are dominated by emissions from the combustion of fossil fuels that power our industrial economy and personal activities. Tail pipe emissions contribute carbon monoxide (CO), oxides of nitrogen (NO_x), VOCs (many of which are classified as hazardous air pollutants or HAPs), and nano-sized particles. Power plant emissions are responsible for most atmospheric sulfur dioxide (SO_2), significant quantities of NO_x, and a complex array of respirable PM, some directly emitted and others resulting from photochemical transformation of

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[1] To whom correspondence should be addressed at Cellular, Organs and Systems Pathobiology Branch, Division of Extramural Research and Training, National Institutes of Environmental Health Sciences, Mail Drop-EC-23, Research Triangle Park, NC 27709. Fax: (919) 541-5064. E-mail: Nadadurs@niehs.nih.gov.

VOCs. Ozone (O_3) is a secondary gaseous pollutant also produced by photochemical reactions involving NO_x and VOCs. Biomass combustion, as natural forest fires or agricultural burning, can contribute substantial levels of ambient PM and a wide range of partially combusted carbonaceous materials and various semivolatiles and gaseous products. The many anthropogenic air contaminants that coexist with naturally emitted biogenic VOCs and their transformation products ultimately define the character of urban air sheds around the country.

The U.S. Clean Air Act (CAA) originally passed in 1963 is the principal statute concerning regulation of ambient air quality in the United States. In 1970, the responsibility of administering the CAA and identifying pollutants that may reasonably be anticipated to endanger public health and welfare was codified with the establishment of the U.S. Environmental Protection Agency (EPA). Air quality management was mandated by the CAA to (1) identify goals for the protection of public health and the environment; (2) evaluate current conditions through monitoring and modeling to evaluate if the goals are being met; (3) identify emission sources contributing to problems; and (4) establish a coordinated system of federal, state and local measures to attain acceptable air quality.

In accordance with the CAA, EPA has identified six air pollutants, PM, CO, NO_x, SO_2, O_3, and lead (Pb), as criteria pollutants because of their widespread occurrence and their potential to endanger public health. Regulation on the levels of these six criteria pollutants is carried out by establishing and periodic reviewing national ambient air quality standards (NAAQS) (Fig. 1). Two sections of the CAA (Sections 108 and 109) direct the Administrator of EPA to propose and promulgate (1) primary NAAQS for pollutants to protect public health with an adequate margin of safety and (2) secondary NAAQS to protect the public welfare from other adverse impacts associated with the presence of the pollutant. Welfare effects include deleterious impacts such as damage to crops and natural ecosystems, damage to man-made materials, reduced visibility, and climate change. The CAA also contains separate provisions related to acid deposition and stratospheric O_3 depletion, which relate to welfare.

Three of the six criteria pollutants (CO, SO_2, and Pb) can be directly monitored and controlled. NO_2 is controlled indirectly, primarily by reductions in nitrogen oxide (NO), which makes up the vast majority of total NO_x emissions and which further reacts in the ambient atmosphere to form NO_2. A portion of PM is directly controlled, but significant efforts are underway to control the major precursors to PM formed in the atmosphere from SO_2, NO_x, and organic compounds. O_3 is controlled only indirectly through reductions in its precursors, NO_x and VOCs.

Significant classes of noncriteria pollutants are the 188 chemicals identified in the 1990 Amendments to the CAA as HAPs. These HAPs represent more localized hazards (arising from industry or mobile source emissions). They are regulated in a two-phase process. In the first phase, a Maximum Achievable Control Technology (MACT) standard is set for each pollutant source category, e.g., refinery processes, chemical plant

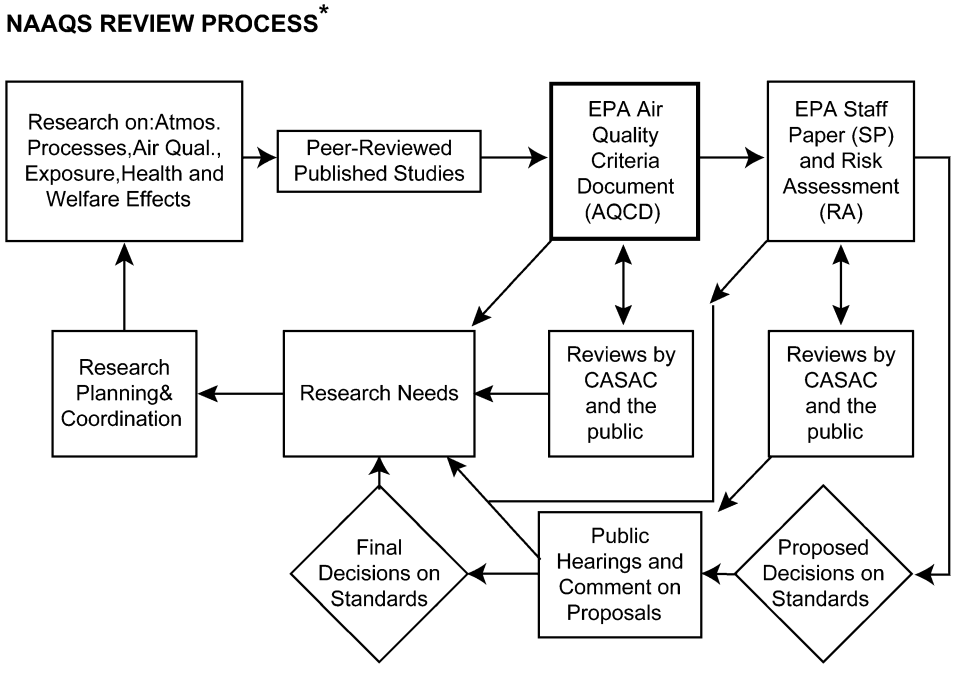

FIG. 1. Schematic presentation of the NAAQS setting process.

processes. The MACT standards are designed to reduce emissions of HAPs without considering the specific level of risk. The second phase is based on evaluating residual risk to health and/or the environment remaining after MACT measures are implemented to determine if further steps to control emissions are necessary to reduce residual risks to acceptable levels. EPA is currently developing regulatory and control approaches to address residual risk associated with exposure to HAPs.

The EPA has recently concluded a thorough review of the scientific literature and developed air quality criteria documents for ambient air PM (U.S. EPA, 2004), O_3 (U.S. EPA, 2006a), and Pb (U.S. EPA, 2006b). Based on these scientific assessments, policy perspectives of the science to support review of the NAAQS were developed in "Staff Papers" by the Office of Air and Radiation. These assessments were pollutant specific, and although they considered potential interactions with other pollutants, the significance of such interactions could only be assessed qualitatively and accounted for in the "margin of safety" evaluations.

The recent National Research Council report "Air Quality Management in the United States" recognized the importance of mixtures and recommended that air quality management account for the health and ecological impacts of the mixtures of pollutants occurring in the ambient air (National Research Council, 2004). However, the science of pollutant mixtures is not well developed and needs stronger strategic underpinnings if more comprehensive assessments are to evolve. Any multipollutant air quality management strategy will need strong interdisciplinary support. Contemporary air pollution regulation strategies will evolve over time with impending reductions of sulfur emissions and inclusion of emissions from new fuel additives and alternate fuels; thus, the nature of air pollution itself is evolving.

This paper brings together the thinking of several prominent scientists representing disciplines involved in the full spectrum of air pollution assessment. Each section reflects a perspective of where the science is today and how it might be more beneficial in the assessment of human health risk if better integrated. Pollutants have to date largely been assessed singularly due in part to dominance in air concentration or toxicity. It has long been known that pollutants may interact altering the toxicity or impact of the mixture, but little is really known about mixtures and how to assess them. While many have tried approaches starting from single compounds and adding to the mix or starting from the reverse and breaking the mixture down in parts, no simple approach exists. If the desire is protection of public and environmental health, it may not be necessary to fully understand the mixture but to find a medium ground that can be used to derive assessments. One suggestion is to understand the prominent sources of air contaminants and use their profiles to evaluate their contribution to local air contamination and public risk. Various laboratories are exploring this approach. The contributing authors provide their views on the issue in the context of their expertise and how advances might be made.

AMBIENT AIR MONITORING, AIRBORNE CONSTITUENTS, AND SOURCE APPORTIONMENT

PM is unique among the criteria pollutants because it is a mixture rather than a single chemical compound. PM therefore provides a contemporary test of how to effectively address the challenges associated with complex mixtures of air pollutants. As the NAAQS for PM has evolved, it has become increasingly important to understand the spatial and temporal variability of PM characteristics and how that variability may be linked to health effects.

The NAAQS for PM were first established in 1971 for total suspended particulates (particles in the nominal size range of 25–45 μm). The review of the PM NAAQS in 1987 led to setting new standards for PM_{10} (particles with a mean aerodynamic diameter less than or equal to 10 μm). Significant revisions to the PM NAAQS were made in 1997 that included setting standards for $PM_{2.5}$ (particles with a mean aerodynamic diameter less than or equal to 2.5 μm) and the PM_{10} standards were retained for the purpose of regulating coarse particles (those greater than 2.5 μm and less than or equal to 10 μm).

Following the promulgation of the 1997 revisions to the NAAQS for airborne PM, EPA deployed several monitoring networks to determine the mass concentrations of particles with aerodynamic diameters of less than 2.5 μm ($PM_{2.5}$) as well as to obtain compositional information to provide the input data to source apportionment and health effects modeling. The data from these monitoring networks are now providing information on where problems of nonattainment of the NAAQS for $PM_{2.5}$ are and help in understanding the sources of those particles for air quality management strategy development and health effects studies. Networks of Federal Reference Method (FRM) samplers provide mass concentration measurements to evaluate attainment with the NAAQS. Along with the FRM networks, the Speciation Trends Network (STN) and Interagency Monitoring to Protect Visual Environments (IMPROVE) networks are providing a wealth of ambient PM compositional data across the United States.

Much of the aerosol mass of $PM_{2.5}$ is secondary in nature, meaning that these particles have formed from the reaction of gaseous precursors (SO_2, NO_x, VOCs) with atmospheric oxidants to form lower vapor pressure species that either form new particles or add mass to existing particles. The average composition of $PM_{2.5}$ in cities across the United States indicates significant compositional differences between various regions of the country (Fig. 2). Carbonaceous materials dominate the northwestern United States, while California has high nitrate concentrations in addition to carbon. In the southeastern United States, sulfate particles are the largest contributors to the $PM_{2.5}$ mass, while in the northeastern

FIG. 2. Average $PM_{2.5}$ compositions in urban areas across the United States as measured by the STN network (U.S. Environmental Protection Agency).

United States; there is a mix of sulfate and carbon with significant nitrate in the winter months. There are also urban–rural differences within regions. Figure 3 shows the average $PM_{2.5}$ compositions across the eastern United States as measured in the IMPROVE network. It can be seen that there is a smaller fraction of carbonaceous aerosol in these rural areas when compared to the comparable urban sites in Figure 2. It appears that there is an increment of carbonaceous aerosol in urban areas likely the result of mobile sources and building heating emissions. In spite of this variation in composition across the country, prior health effects modeling has not found large differences in the risk coefficients among the various regions, although there is a slightly higher average mortality risk from PM_{10} (respirable PM less than 10 μm) in the northeastern United States.

Utilizing information on the source contributions to the $PM_{2.5}$ mass can aid in understanding the relationships between $PM_{2.5}$ exposures and the health effects reported in epidemiologic studies. Figure 4 shows the results of source apportionment intercomparisons with associated health effects modeling for two cities, Washington, DC and Phoenix, AZ (Thurston *et al.*, 2005). This figure shows percent excess deaths per 5th to 95th interquartile concentration increment for some of the major sources identified. Thus, data and tools are available to provide opportunities to explore relationships between particle composition, source contributions, and health effects. Identifying the most significant sources rather than the array of pollutants emitted may allow more effective management of air quality.

AIR POLLUTION SOURCES: STEPS TOWARD A MORE COMPLETE UNDERSTANDING

A focus on sources enables a more straightforward approach to air quality management, but if the relationships between sources and effects are to be fully understood, it is crucial to recognize how emission characteristics change across and within source categories. The characteristics of particles in emission streams can vary substantially due to operating conditions, engine design parameters, and even sampling methods. As discussed above, once particles are emitted into the atmosphere, they interact with coemitted pollutants, emissions from other sources, water vapor, and solar radiation, all under ever-changing meteorological conditions (Venkataraman and Friedlander, 1994; Fraser *et al.*, 2002). These and other changes in PM characteristics may have significant consequences for the ultimate health responses observed in toxicological studies. Because it is not yet known how these changes are related to PM toxicity (U.S. EPA, 2004) it is important to consider changes in physicochemical characteristics when striving to understand the potential health impacts of emissions from a given source type. For example, particle-bound reactive oxygen species (ROS) have been observed to be present on

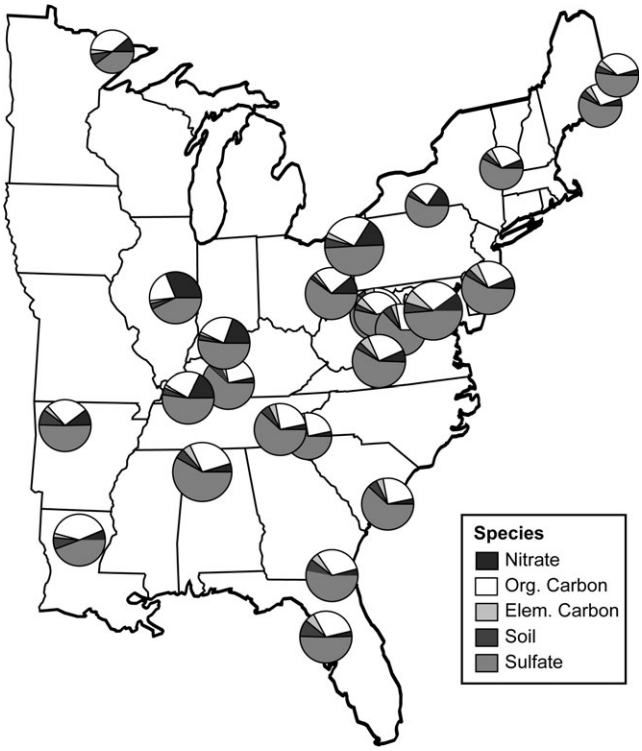

FIG. 3. Rural $PM_{2.5}$ composition across the eastern United States as measured in the IMPROVE network (US EPA).

particles in both summer (Venkatachari *et al*., 2005) and winter (Venkatachari *et al*. (2007). Since oxidative stress is considered important in inducing some of the observed effects, the role of particles as a transport vector for ROS must be considered.

One would expect particle characteristics to change across different source types and even from different sources within a given type. Such differences in characteristics make it possible to utilize source apportionment techniques to identify the contribution of specific source types to ambient PM concentrations (Hopke 1985), and it is well known that variability in fuel composition will affect the composition of particles from combustion sources (Miller *et al*., 1998; Linak *et al*. 2002). However, particle characteristics can also vary significantly even when emitted from a single source burning a single fuel, with the potential for significant differences in health responses. Figure 5 illustrates the variability in composition of coal particles generated from the combustion of a Powder River Basin coal in a pilot-scale combustor. Particles in the ultrafine fraction had much higher levels of iron, and generally higher levels of water-soluble metals, than did particles in the fine and coarse fractions generated at the same time. This size dependent variation is due to vaporization, nucleation, and condensation processes that form the ultrafine particles are significantly different than the fragmentation processes that generate the coarse, and to a large extent, fine particle fractions. Different coals would produce particles with different patterns of elemental composition. Thus, differences in the fundamental particle formation processes result in changes in particle composition that are independent of changes in fuel composition and operating conditions.

It has long been recognized (Cheng *et al*., 1984) that reporting specifics of source and particle characteristics is important to understand the biological responses. Yet, numerous animal toxicology studies that evaluated potential health effects associated with exposure to coal or residual oil fly ash or diesel exhaust particles failed to incorporate this information that might have significantly strengthened their value in health effects assessment. Attempts by investigators in two recently published toxicology studies (Gilmour *et al*., 2004; Singh *et al*., 2004) that compared responses to two samples of diesel exhaust particles having different characteristics highlighted the importance of linking source variability to differences in health.

Comprehensive knowledge of PM characteristics such as source type, operation, design, and sample collection methods along with the influence of atmospheric chemistry on PM characteristics is critical to gain an accurate understanding of how sources and effects may be linked. If toxicology studies fail to account for differences in particle characteristics, it will not be possible to develop the most effective control strategies. Particle characteristics that are relatively most toxic may be common to several source types, or are specific to a single source type or operating condition. In either case, this understanding can lead to control strategy development that targets those sources or conditions that are the largest contributors to particles causing adverse health outcomes.

TOXICOLOGICAL PROFILES OF AMBIENT PM AND GASES

Exposure to ambient PM is associated with myriad cardiopulmonary health effects. Traditional animal toxicology studies have utilized exposure regimens wherein animals, typically rodents, are exposed to individual air pollutants. To test the hypothesis that different components of size-fractionated PM or gaseous pollutants produce different adverse effects at the cellular and whole organism levels, additional exposure regimens have been added to the inhalation toxicologist's arsenal. For PM exposures, animal models of disease can be exposed to atmospheres containing real ambient PM (concentrated) using realistic concentrations of the PM mixture, durations, and routes of exposure.

Regardless of recent advances, the challenge for inhalation toxicologists is still to provide useful information to regulatory agencies using either simple or complex exposure atmospheres. Therefore, an integrated research approach is needed that combines toxicology and exposure assessment. One early example of this integrated approach has been reported for the cardiovascular effects of concentrated ambient PM in a dog model of ischemia (Wellenius *et al*., 2003). During a 5-min coronary occlusion period, a consistent increase in the

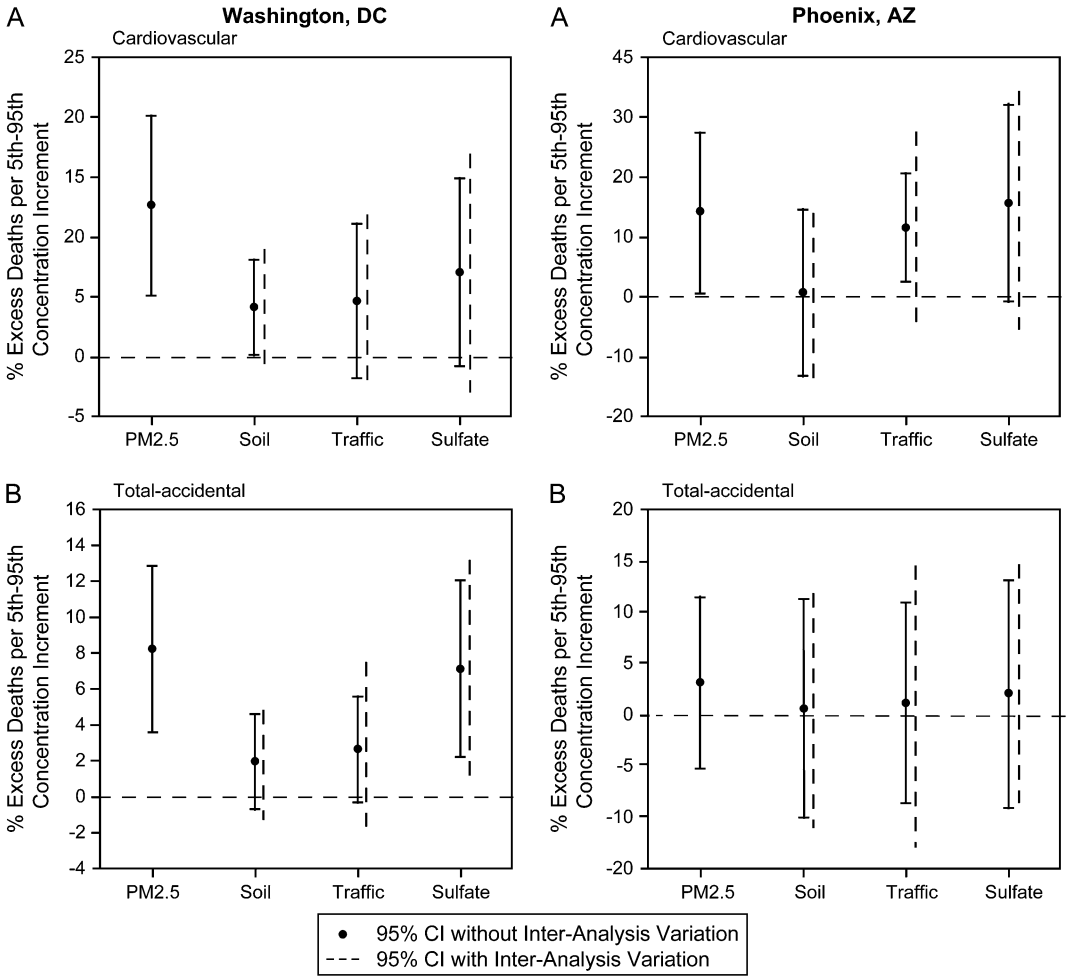

FIG. 4. City-specific mortality associations based on source-apportioned $PM_{2.5}$.

ST-segment elevation of the electrocardiogram (EKG) waveform was observed in concentrated ambient PM-exposed dogs compared to filtered air control dogs. Detailed characterization of the concentrated ambient PM provided information on parameters including mass and number, sulfate, black carbon, elemental carbon, organic carbon, and trace element concentrations. Regression analysis of EKG waveform parameters with individual exposure parameter measurements provided a clear association of ST-segment effects with silicon, suggesting that crustal material may play a role in the observed cardiac effects.

At present, there are still only a limited number of similar examples of integrated toxicology studies trying to address the complex nature of exposure to ambient PM and the diverse health effects associated with such exposures. For example, Morishita *et al*. (2004) could correlate significant increases in allergy related endpoints such as lavage fluid eosinophil numbers with vanadium and lanthanum. However, earlier studies by this group using a similar model and repeated exposures

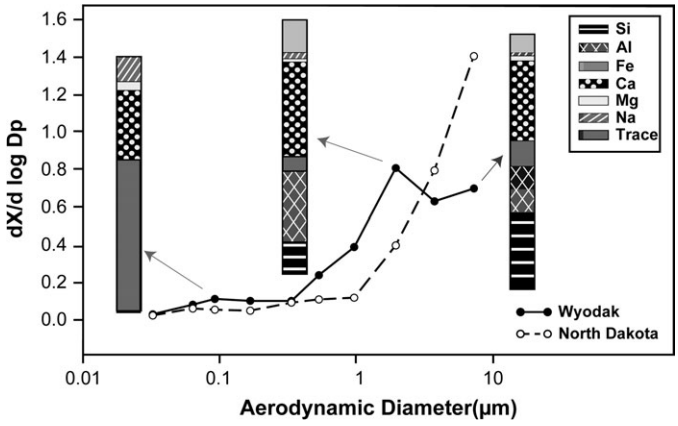

FIG. 5. Particle size distributions of PM emissions from the combustion of a Wyodak subbituminous coal and North Dakota lignite. The bars are the relative compositions of particles from Wyodak coal PM (Linak *et al*., 2002).

to concentrated ambient PM of a different makeup indicated depressed allergic asthma endpoints. (Harkema *et al*., 2004)

Another study that significantly demonstrated the importance of utilizing meteorological and speciation data comes from three subchronic animal studies in which ApoE knockout mice were exposed daily to concentrated ambient PM for 5–6 months in the rural environment of Tuxedo, NY (Hwang *et al*., 2005). In one of these studies, the investigators found sporadic yet significant increases in heart rate (HR) and decreases in heart rate variability (HRV), indicators of increased cardiac risk. Surprisingly, back trajectory analysis of the weather patterns demonstrated a wind from the northwest on all 14 of these days. Moreover, trace metal analyses found significant increases in nickel, chromium, and iron even though the concentrated ambient PM concentration was markedly reduced on these 14 days. In searching for a source contributing to these airborne metals, using a 72-h back trajectory analysis, the air mass passed by the largest nickel refinery plant in North America, thus suggesting a potential source for the observed changes in HR and HRV in mice.

Animal toxicology studies utilizing controlled exposure conditions and concentrations can be integrated with PM speciation data to precisely dissect the contribution of particulate air pollution's individual components and sources to adverse health effects. These findings and their association with various constituents may be informed by the results of studies using whole combustion mixtures which may yield analogous exposure or biologic response profiles (McDonald *et al*., 2004; Seagrave *et al*., 2006). How these varied approaches can be integrated remains to be seen, but the use of complimentary data and models that may link pollutant/source groups to toxicity will provide important information for regulation or mitigation strategies. Such animal toxicology studies will also benefit the interpretation of adverse cardiopulmonary effects to acute and chronic exposure to PM reported in epidemiologic studies.

AIR POLLUTION HEALTH EFFECTS: INPUT TO REGULATIONS

The CAA specifies that air quality regulations must be based on scientific evidence. It is clear that scientific evidence has played a central role in both developing and revising the NAAQS. However, the extent to which science is being used and the role it is playing in the NAAQS setting process are not widely appreciated.

It might be insightful to consider some points regarding the use of science in regulatory actions. First, it is generally well appreciated that science and policy are different. Science is almost always characterized by uncertainty, but this does not preclude making policy based on this science. In fact, making policy in the face of uncertainty is unavoidable. The argument that policy should not be made because the science is too uncertain is itself arguing for a policy, albeit a policy of no action. However, action should be tempered by recognition of the potential consequences of possible deficiencies in the underlying science. Second, while science informs policy, policy sometimes influences science. In the air pollution arena, this manifests itself in at least four ways. The first is what one might refer to as "criteria pollutant science" in which the scientific questions being asked are framed by the policy needs to focus on individual criteria pollutants as opposed to air pollution more generally. The second issue is the influence of the policy agenda on the timing of publication of scientific findings. For example, a rash of publications on O_3 health effects at a time when the O_3 NAAQS was under review appeared to be no coincidence. Third, science does not present itself in an undiluted form. The U.S. EPA gets most of its science from the published biomedical literature, a literature that is widely acknowledged to suffer from a publication bias of preferentially reporting positive findings (Bell *et al*., 2005; Anderson *et al*., 2005). Fourth, and finally, it is clear that recently some types of health science have been more influential in deliberations to revise the NAAQS than others. Specifically, revisions to both the PM NAAQS, and now the possible revisions to the O_3 NAAQS, are based to a greater extent on observational epidemiology than on either toxicology or experimental work in humans.

What is this observational air pollution science now telling us? The finding that has the most direct relevance to the setting of the NAAQS is that the concentration–response relationship between air pollutant concentrations and adverse health effects is relatively linear with, most importantly, there being little evidence of a concentration below which effects are not seen. That is, there is no obvious threshold concentration using aggregated population data, the type of data used in most such observational studies. This has been a somewhat surprising finding. There is good reason to suspect that for some pollutants, such as O_3, where exposure measurement error is considerable, any threshold concentration would be obscured as a result of measurement error. For other pollutants, such as $PM_{2.5}$, where measurement error is much less, this is not a likely explanation for the inability to observe a threshold (Brauer *et al*., 2002). Experimental studies have not always been helpful in this regard, because the higher concentrations of pollutants used and the small number of animals used in toxicology studies may not have the statistical power to shed light on the issue of threshold concentrations. Despite these deficiencies, animal toxicology studies provide biological plausibility, chronic effects, and potential to link sources to effects.

The apparent absence of threshold concentrations has implications for how a level of the standard is viewed. In the language of the CAA, standards are intended to protect the public with an "adequate margin of safety." With no obvious threshold concentrations, an adequate margin of safety cannot be taken to mean the absence of risk, since almost any level

chosen will still allow risk at concentrations lower than that level. Further, it is not clear how one would decide on the appropriate level without using some external criteria, since at face value; there are health gains to be realized with ever lower levels of the standard. Since EPA is constrained from using cost considerations in setting the NAAQS, a cost–benefit analysis cannot be used in helping to determine the appropriate level. Other criteria that might be used include detecting that concentration below which the uncertainty in estimated risk is too large to make such an estimate meaningful or identifying the lowest concentration that is technologically feasible to achieve.

How then is observational science used in setting standards? The EPA in its 2005 PM Staff Paper took two approaches, a so-called evidence-based approach and a risk-based approach. The evidence-based approach attempted to use the most reliable science in directly informing the level of the standard. As an example of use of this approach, some argued that the current level of the annual fine PM standard was too high, since in several studies in several cities, short-term effects of fine PM were estimated to occur, even though the annual fine PM concentrations in these cities were below the level of the current NAAQS. The evidence-based approach, then, seemed to be useful in arguing for a change in the 1997 standards but does not provide much insight into the range of levels that might be appropriate. The risk-based approach used a risk analysis to estimate quantitative improvements in health for different scenarios of standard-related reduction in fine PM in cities with different PM concentrations. This has the advantage of being able to assess beneficial effects of reductions in standards of different averaging times in tandem, or of reductions in each alone (e.g., for a 24-h average standard and an annual average standard for fine PM). Unless estimated benefits to health stop increasing at some lower concentration, even the risk-based approach does not provide information on where to set the level of the standard.

The World Health Organization (WHO) found that expressing its air quality guidelines in the form of a risk function, as was attempted for PM in 2000, was not well accepted by users of the guidelines. In 2005, the WHO returned to the practice of specifying specific concentration levels for its guidelines, using a procedure reminiscent of the EPA evidence-based approach in its deliberations on the standards.

Science, at this point, then, is limited in identifying the specific requisite level of a PM standard. Instead, science is providing information that is critical in considering various levels of the standards. The current emphasis on observational study findings and the apparent absence of threshold concentrations has necessitated placing great weight on a risk analysis approach to informing the selection of standard levels. Factors other than science, however, come into play in the actual selection of the specific levels of the standards. Some of these factors enter into the policy judgment that, in the end, is required to come to a final decision on these specific levels.

MIXTURES WE BREATHE: IMPLICATIONS FOR AIR QUALITY ASSESSMENT AND MANAGEMENT

Air quality management programs have historically established goals, evaluated ambient conditions and estimated potential health risks, and developed risk reduction strategies one pollutant at a time. In observational and controlled experimental studies and in health risk assessment activities, the focus has been on characterizing the health effects of exposures to single pollutants, copollutants have been treated as modifying or confounding factors whose influence characterize to the extent possible, minimize. Similarly, nonpollutant factors such as stress associated with socioeconomic conditions and urbanization are rarely considered, though they are related to and may result in disparities in public health linked also to air pollution. Emerging scientific developments on the importance of interactions among air pollutants on health, coupled with emerging strategies to approach air quality management strategies less focused on single pollutants and more targeted to key emissions sources and/or pollutant combinations and in consideration of other stressors affecting public health, suggest the promise of more holistic approaches to science and management.

Important steps have been made with the goal of better interdisciplinary integration as a foundation for studies of relevant ambient air pollution mixtures. There have been meetings such as the American Association for Aerosol Research Colloquia on PM and Health (2002) was designed with integration in mind, where researchers were encouraged by the meeting format to listen and discuss topics of mutual interest. The recent Request for Application (2005) defining the recompetition and awards for the EPA sponsored PM Centers focused on air quality to health science linkages and required communication and interactions between these science communities. Other organizations, such as the Electric Power Research Institute has sponsored studies of complex mixtures involving ambient air (Aerosol Research and Inhalation Epidemiology Study conducted in Atlanta, GA, with epidemiological assessments) and light transformed real-world combustion sources (Toxicological Evaluation of realistic Emissions of Sources—photolyzed power plant emission with rodent exposures). Organizations such as the Health Effects Institute have also recently (2007) awarded studies involving multiple locales to make use of diverse urban air pollution profiles that could be linked to epidemiological and animal toxicologic data. EPA itself has also begun to think in this integrative paradigm. Its research program has adopted a work strategy that is moving to a multipollutant design and the regulatory office for air pollutants (Office of Air Quality Planning and Standards) has reorganized to allow for "sector" (source) based evaluations as a basis for some air pollution control measures. So there are clear signs that the field of air pollution studies is integrating and making inroads into the complexity of such atmospheres.

There remain barriers, however. Funding agencies often make it difficult to develop successful proposals that bring in research partners from outside the core area for which funding is being offered. Similarly, it can be more difficult to find journals in which to publish cross-disciplinary work, given that most of the journals' reviewers tend to be focused on specific specialties. Measurements of emissions and ambient concentrations almost always focus on regulatory requirements, usually because the measurements are usually funded by the states, which cannot afford to take measurements that might be of greatest interest from a health perspective. And lastly, scientists themselves have to open to the challenge and risks of multidiscipline, mixture research. The move to this goal involves some education and of course the lure of funding opportunities.

Such promise may best be supported by coordinated development of new science, assessment, and management programs utilizing broad-based interdisciplinary teams of experts. The result of such scientific approaches may well lead to an improved foundation for air quality management programs under the current CAA and also provide a basis for creative legislative approaches in the future.

SUMMARY

Air quality management strategies are devised to reduce health risks associated with air pollution. For more than 30 years, the focus of air quality management has largely been to address one pollutant at a time, with the assumption that some pollutants dominate risk. This guiding principle has been adhered to despite knowledge that air pollution exists as a mixture, but with the mandate for single major pollutant regulation and the complexities of mixtures science, this approach has been retained for more than 35 years. Indeed, there has been considerable success with the approach but there is a growing feeling that as overall air quality improves, the importance of the mixture concept is likely to emerge as a major driver for health outcomes. Moreover, the major reductions in emissions as a consequence of current regulations coupled with changes in industrial and transportation technologies will make it increasingly difficult to achieve further substantial reductions in specific pollutants from a relatively small set of major sources. The subsequent reductions in ambient levels of specific pollutants may require that air quality be considered in terms of ambient air pollution mixtures, posing a greater challenge than the current single-pollutant approach. Hence, future control strategies may well be most effective in terms of improving public health and welfare when targeted to address the mixtures of emissions that are most harmful. Epidemiological studies often consider mixtures but mostly as copollutants impart confounding. Experimental sciences require strategies for approaching mixtures. In this context of mixtures, experimental, and observational research studies have to recognize and implement novel strategies that aid in the interpretation and extrapolation of results across the disciplines. This issue is complicated more by the fact that particle and smog formation are dynamic physicochemical processes that need to be better understood. Exposure sciences need better composition profile characterizations, as do sources and downstream ambient measurements. Modeling temporal and spatial variations also become important needs of health researchers if they are to define the responses to air pollution. While some advances are being made in this kind of integration, progress has been modest. Education as to the benefits to air pollution assessment science and encouragement with augmented funding for such research are needed to make the next major move forward. When researchers across disciplines interact more fully, it will be possible to develop a level of understanding of how air quality as we experience it each day may affect health and how adverse impacts may be best prevented or mitigated.

Not well understood

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