Theme Three: Source to Health Outcomes

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It is tempting to ask why "*Source to Health Outcomes*" is a topic at all, as it would seem obvious that the entire PM research program is intended to address this very issue. But even though that is indeed the case, our tendency as scientists is to reduce problems to their fundamental components. The structure of our organizations, our training, and more immediately, the recommendations of the NRC Committee on Research Priorities for Airborne Particulate Matter all reinforce our inclination to take a reductionist approach to addressing PM. However, nature does not respect our artificial segmentation of the health and environmental impacts of PM, and by attempting to fit our investigations into the relevant natural processes into boxes that conveniently match our scientific disciplines, we can overlook important parts of the continuum between human activities that emit materials into the atmosphere and the impacts those materials ultimately have.

But this is not simply a philosophical issue. There are important reasons why it is necessary for EPA to make "*Source to Health Outcomes"* a significant part of our efforts to address the PM issue. We will discuss some of those reasons below, and describe the differences and similarities to a strictly component-based approach. We will also show how our previous work has set the stage for the "Source to Health Outcomes" approach, and why it is also important to continue some efforts to evaluate the effects associated with specific components.

It is well understood that, unlike other criteria pollutants (CO, NO_2, SO_2, O_3, and Pb), PM is not a distinct chemical substance. One of the factors we must therefore address is whether there are some particles that are causing adverse health effects, or are causing worse health effects, than other particles. As it is often stated, are all particles equally toxic? To address this question, it is helpful to take a reductionist approach, but the challenge arises as to how we define the problem. Our initial approach has been to examine particles to see if we can find a particular component (or a limited number of components) that are more closely associated with PM toxicity than others. As we have progressed down this path, however, it appears less and less likely that we will find a reasonably small number of components that are causing these problems. Rather, it seems to be more likely that we are experiencing numerous specific health impacts caused by numerous components or combinations of components. Nearly every PM component or attribute tested has shown some degree of toxicity (albeit many at relatively high levels compared to ambient concentrations). Alternatively, no major component of ambient PM, with the possible exception of crustal material, has been entirely ruled out as *not* playing a role in causing adverse health impacts.

Even so, we know there are differences in particle toxicity. The recent reanalysis of the American Cancer Society study by the Health Effects Institute clearly illustrated variations in mortality risk vs. particle concentration in different locations across the US. At one level, we can assume that these differences are a consequence of variations in particle composition. However, if we ask why there are such variations in composition, the answer is usually that there are differences in the mix of sources that contribute to the ambient PM. Thus, we are also correct in assuming that the variations in particle toxicity are a consequence of variations in particle sources. In any case, it is important for us to understand why these variations exist and how we can reduce the risks associated with exposure to ambient PM. From a very practical perspective, then, understanding how particles from different sources impact the toxicity of PM provides us with a straightforward motivation for studying health outcomes as a function of particle source. Such understanding points us toward those sources that are contributing most to the adverse health effects and therefore opens a clear path toward targeted risk management approaches.

So how is a "source to health" approach different than what we have been doing to now? Perhaps we should begin by pointing out some of the similarities. The most important similarity is that a source to health outcome approach maintains ORD's successes in: (1) component-based research to evaluate health effects, mechanisms, and susceptibility through toxicological, clinical, and epidemiological studies; (2) studies of exposure to PM mass and components; (3) research into atmospheric chemistry, transformation, and measurements; and (4) source emission characterization. Source to health outcome research will draw upon the existing expertise and facilities available to ORD scientists and to our external partners. In sum, a source to health outcomes approach is based on a firm foundation of ORD's previous work on all aspects of PM-related science.

Where the source to health outcomes approach begins to distinguish itself from previous approaches is at first glance a change of emphasis rather than direction. Because most modern science is the result of incremental progress, we have been moving toward this approach for several years in several ways. The most noticeable change is a greater emphasis on multidisciplinary studies. Although these studies may have begun with informal consultations to clarify specific issues, current efforts under the source to health outcomes heading have been designed from the outset to incorporate (as appropriate to a given task) the expertise of engineers, atmospheric scientists, exposure researchers, and toxicologists, clinicians, and epidemiologists. Less noticeable, but as important, are the initially subtle changes in how experts in these fields are now thinking of their own specialties. As the interactions across disciplines grow, engineers consider how to collect source samples to ensure they can be used in toxicological studies, toxicologists recognize the need to know details of what fuels were used by sources and how those sources were operated, and epidemiologists look for methods to estimate actual exposure to PM. Although these factors were always known, the key difference is that these issues are now being considered as being an integral aspect of a study rather than as simply a factor to consider in the primary task.

An increased level of publication of articles coauthored by investigators across several disciplines is a very tangible measure of the greater integration inherent in the source to health outcome approach. However, it is those more subtle influences in how we approach the science that will have the longest-lasting and most profound impact on the ability of ORD science to maintain a leadership position in the science linking public health to air quality. As researchers expand their perspectives of what science is relevant to their studies, they become more open to collaboration, innovative approaches, and new ways to interpret unexpected results. These are the qualities of leading-edge science, and the Source to Health Outcomes session highlights examples of how ORD is leading the way in integrating science across organizations and disciplines.

Helen Suh outlines two excellent examples of this integration in her poster, and illustrates how a source to health outcome approach can increase our abilities to study the effects of PM exposure. The St. Louis Bus Study and the Care-related Occupational PM and Air Toxics Exposure to Patrolmen (COPP) Study both measure how people are affected by relatively short-duration exposures to roadway emissions. These two studies each showed that exposure to particles from mobile sources are associated with significant changes in cardiac and vascular function. Given the increasing amount of time people spend in traffic, these findings have important implications for their health. These findings may have particular importance to those who work on busy roadways – police, truck and taxi drivers, and others who spend several hours each day exposed to mobile source particles.

Although these are important results by themselves, they also demonstrate the strength of an integrated source to health outcomes approach. Some of these results showed that spikes in PM exposure that were only 1-2 hours in duration can have significant measurable adverse health implications. Concentration measurements at microenvironmental scales allow us to see the impacts of such short exposures, something that would be impossible if we were limited to use of existing data from central ambient monitoring sites.

By taking the integrated approach in a different direction, John Froines and his colleagues at the Southern California Particle Center and Supersite have shown how rapidly mobile source-related effects in mice drop off as distance from the roadway increases. These results are shown on two related posters (**Froines** et al**.** and **Siotas** et al.). Mice exposed to concentrated roadway emissions 50m from a heavily-trafficked Los Angeles Freeway exhibited significant increases in markers of pulmonary inflammation compared to mice exposed to concentrated particles 150m from the same freeway. This suggests that he effects of PM exposure can change significantly over a relatively short distance. Concurrent ambient measurements made at different locations verify that the nature of the aerosol changes significantly as one moves away from the freeway centerline. These findings have substantial implications for policy makers relative to siting schools, hospitals, and other facilities where potentially susceptible populations may frequent, or alternatively, implications for siting roadways.

Again, by combining expertise (in this case of health and atmospheric scientists), we are able to achieve important results that would not otherwise be possible. In both these examples, we have not only increased our scientific understanding of how exposures to PM impact health, we have also developed information that is of immediate use to policy makers.

The source to health outcomes approach can also be used in more controlled environments, and the results of such efforts are likely to be as important to policy development as the studies discussed above. The examples highlighted in the poster by Madden et al. illustrate that controlled exposures to PM and associated emissions from specific sources can cause adverse health responses in a variety of biological systems ranging from cell cultures to animal models of healthy and susceptible populations to human volunteers. These efforts demonstrate that exposures to diesel exhaust particles (DEP), coal fly ash, residual oil fly ash, and steel plant emissions all result in some degree of adverse health response. Those responses are similarly diverse, ranging from sensitization to allergens to alteration of cardiac function.

This work emphasizes the complexity involved in the question, "what attributes of PM are responsible for adverse health effects?" Although each example presented in the poster shows how exposure to PM from an individual source type can result in adverse health impacts, the larger picture is that there is a range of different health responses associated with a range of different source types. These results show that, rather than a few "silver bullets" being responsible for causing adverse health effects, there appear to be many bullets causing many different effects. Although there may be differences in the effects associated with specific source types, these results reiterate the need to effectively control particle emissions in general.

Current controlled-exposure efforts are focused on relatively simple atmospheres that are composed almost entirely of emissions of gases and primary particles from a single source. This is true for several reasons, but to some extent because it is much more simple to generate primary particles from individual sources than to create more complex atmospheres in a controlled environment. Even so, a comprehensive source to health outcomes approach will incorporate the ability to create well-controlled, complex atmospheres that more closely simulate ambient conditions. **Tad Kleindienst's** poster describes how we can create these more realistic atmospheres that simulate formation of and exposure to secondary particles in a chemically complex mixture. Eventually, this approach will provide us with the ability to change specific primary and secondary components of a complex atmosphere and see how health responses are affected. This capability will significantly increase our ability to test different hypotheses of what sources, components, or mixtures may be most critical to health.

An alternative to generating particles for controlled exposure studies using actual sources is the use of concentrated ambient particles (CAPs). CAPs studies collect and concentrate ambient particles, either for immediate inhalation exposures or for future exposures via reentrainment in direct inhalation exposures, instillation, or use in *in vitro* studies. Unfortunately, use of CAPs removes the control we have over the composition of the particles. But by using source apportionment methods, it is possible to identify the sources of particles in a given sample. **Gary Norris** and his colleagues present methods that are being applied to tie CAPs used in controlled exposure studies to specific source types. Conventional source apportionment approaches provide a valuable means to identify the sources of particles and can therefore shed light on why differences in health measures may be occurring following exposure to different CAPs samples.

In some cases, we are able to use both controlled and natural exposures to develop a coherent picture of how sources are linked to effects. **Jan Dy**e and her colleagues present a classic example of such coherence in the poster describing the effects of exposure to Utah Valley dust. Epidemiological, toxicological, and clinical data all demonstrate the role of a single major source (a steel mill) in causing adverse health effects. The ability to take multiple approaches to demonstrate the impacts of a source requires that we have both air quality and health data necessary for conducted epidemiological studies, and that we have actual samples of the particles for use in more controlled exposures. This was possible in the Utah Valley case, and this series of studies serves as a model of how multidisciplinary efforts can substantially strengthen scientific conclusions and therefore lead to clearly defined policy implications based on those conclusions.

The Utah Valley example is relatively unique, however, in the strong dominance of a single source within the local airshed. Much more common are airsheds characterized by a diverse mix of sources. Although there are many similarities across different locations, it may well be the differences that are more important in determining the actual airshed-specific health risk associated with exposure to ambient PM. **Lucas Neas and Barbara Glenn** present an epidemiological approach to extracting information about which source types may be more strongly associated with adverse health effects. By combining source apportionment methods with epidemiologic statistical analysis, investigators have been able to indicate the types of sources that appear to be more strongly linked to adverse health end points, including mortality. These efforts require health and source apportionment data over long enough times and in enough locations to obtain statistically valid results. Interactions across the health and atmospheric science communities are critical to ensuring that the correct measurements are made and that the limitations of the data are clearly understood. This “multicity / multipollutant” approach can produce results of enormous importance, however. Consistent findings that repeatedly indicate specific source types emit particles that are relatively more toxic will result in strong pressures to reduce emissions from those source types, providing clear directions for regulatory actions.

To be able to link health effects to sources in multicity / multipollutant studies, we need to know how to identify the contributions of sources to the ambient samples that are used in the epidemiological studies. The poster by **Jamie Schauer and Prakash Bhave** illustrates the efforts being made to identify unique chemical markers that are unique to specific source types. These will be used in source apportionment models such as the Chemical Mass Balance (CMB) model to more accurately identify the source types that contribute to ambient PM concentrations. Although such methods are currently in use, the markers for many source types are relatively blunt, such as the elemental carbon/organic carbon ratio now used to distinguish between spark and compression ignition engine emissions. More detailed chemical markers hold the promise of allowing more accurate apportionment, and ultimately the development of risk management strategies that are more tightly targeted toward reducing emissions from source types that are most strongly associated with adverse health effects.

As opposed to identifying sources that are the most significant contributors to ambient PM samples (e.g. source apportionment approaches), the ability to attribute exposure to biologically active particles from specific source types based on emissions, meteorology, and atmospheric chemistry (i.e., from dispersion air quality models) would provide additional details on spatial and temporal distributions of the particles of greatest interest, and may ultimately provide a tool that could predict times and locations of greatest concern from a health perspective. **Mike Kleeman's** poster presents an approach to developing more advanced air quality dispersion models that would allow the tracking and prediction of particles concentrations, including more detailed chemical composition information. Although the practical application of such a tool will require significant additional work, both in the modeling as well as in the model inputs, this work represents a strong initial step toward a more comprehensive approach to air quality management – an approach that looks beyond ambient concentrations to ultimate health impacts. As with the previous efforts, achieving this outcome can only occur when we bring together experts from across the different disciplines involved.

The work presented in this and the two previous poster sessions is of importance only to the extent that it is applied. The poster by **Rich Baldauf** clearly illustrates how these research efforts are being applied to regulatory actions designed to improve health and environmental quality. A study in Kansas City aims to improve our understanding of emissions from on-road vehicles, particularly those known as "high emitters." OTAQ is also using ORD science to better understand the next link in the chain between emissions and health outcomes – how people are exposed to engine emissions. In an evaluation of emissions and exposure to small engine exhaust, and in the T-REX study of near-roadway emissions, OTAQ and ORD are working together to ensure that the most up-to-date scientific information is incorporated into regulatory approaches. By designing studies that account for the full continuum of emissions, atmospheric transformation and transport, exposure, and effects, ORD and OTAQ are able to develop data that not only improve our understanding of the complexities of engine emissions, but also improve our ability to reduce those emissions through well designed and focused regulatory programs.

The final poster in this session is perhaps the most striking illustration of why a source to health outcomes approach is critical to the ultimate success of the PM research program. By its very nature, the emerging issue of accountability requires that we link changes in health outcomes to changes that have been required in source emissions. Accountability in this instance (addressed by the **Stone and Bachmann** poster) is an evaluation of whether (and if so, how much) EPA's regulatory programs have improved public health and environmental quality. The regulatory programs almost exclusively address source emissions, and to now have almost exclusively relied upon changes in ambient concentration or aggregated emissions as a measure of effectiveness. Accountability goes to the next step, and attempts to determine the changes in public health or environmental quality that can be ascribed to reduced emissions or other regulatory actions. Given the other changes in lifestyle, diet, medical care, and other factors outside EPA's mission, this is a complex challenge that will require participation by experts in all facets of ORD's PM and ozone Research Program. Reasonable estimates of the health impacts of EPA regulatory programs will require a coordinated effort that brings together expertise in source emissions, atmospheric chemistry and transport, ambient measurements, exposure, dosimetry, toxicology, and epidemiology.

Conclusions

ORD's PM and ozone Research Program has been moving toward a source to health outcomes approach in various ways during the course of the Program, and we intend to continue emphasizing an integrated approach to studying PM and its effects. That does not mean that studies that are focused on health mechanisms and PM components are unnecessary; on the contrary, these focused studies are critical to the success of a source to health outcome approach and must continue to be supported. Similarly, research on source emissions, atmospheric chemistry and modeling, and ambient monitoring will continue to be key to the Program's ultimate success. Even so, a source to health outcome approach gives us the ability to: (1) extend the spatial and temporal range of natural exposure studies; (2) identify sources differently (such as roadways rather than vehicles); (3) tie together natural and controlled exposure results into a coherent picture of PM effects; (4) develop a more complete understanding of the relative differences in toxicity of different source emissions; and most importantly (5) develop more targeted and more effective strategies for managing risks associated with exposure to ambient particles.

ORD's evolution toward a source to health outcomes approach is possible only because of the solid foundation of high quality, peer-reviewed research in the diversity of research areas needed to link source emissions to ultimate health effects. But this approach is possible not only through an integrated scientific approach; through our continuous and close partnerships with OAR, Regions, and states, ORD's efforts are guided by the ultimate goal of improving public health. These partnerships reinforce our realization develop science that can be applied to implement strategies to achieve this goal.

This is an ambitious effort, but one in which we have clearly made progress. In comparison to 1997, our understanding of the science and our ability to implement solutions has improved tremendously. We will never achieve perfect knowledge of the science. But with the resources we have in facilities, partnerships, and people, we are making significant strides and have every confidence that our efforts are making a difference in the lives of our ultimate stakeholders.