Annual Center Progress Report
Southeastern Center for Air Pollution and Epidemiology
Georgia Tech/Emory EPA Clean Air Research Center
January 1, 2011 – July 31, 2011

This Progress Report covers the work of the Southeastern Center for Air Pollution and Epidemiology (SCAPE) from January 1, 2011 – July 31, 2011. Four Research Projects are supported by three Cores: an Administrative Core, an Air Quality Core and a Biostatistics Core. Summaries of the research conducted to date, results, and future activities for each Research Project and Research Core are provided below. More detailed information may be found in the Annual Research Project Summaries.

The Administrative Core provides overall oversight, coordination, and integration of the Center. Since initial funding of the Center, the Administrative Core has developed a quality management structure, which is detailed in the EPA-approved Quality Management Plan. A twelve member Science Advisory Committee was selected and the first annual meeting is scheduled for August 2011 in Atlanta. Multiple Center-wide and Project-specific meetings have been held to ensure that research is coordinated and integrated among Projects and Cores.

1. Research Conducted and Results Generated

Air Quality Core

Objective: Provide Center researchers the information and methods to comprehensively characterize air pollutant mixtures relevant to their Projects and to support Project activities by collecting and managing data, developing a "Mixture Characterization Toolkit" (MC Toolkit) for further analyses specific to the Projects, and providing the expertise and resources to facilitate the application of MC Toolkit components.

Research Conducted and Results Generated:

1. Developing the MC Toolkit for further analyses specific to the Projects.
2. Gathering air quality-related data for areas where studies are planned.
3. Applying various receptor modeling approaches to air quality data in Atlanta, Dallas, and St. Louis.
4. Applying a new, hybrid ensemble source apportionment approach to air quality data in Atlanta.
5. Developing and applying a new, hybrid chemical transport model-CMB based approach with results available for six cities.
6. Conducting analyses to develop a better understanding of how air quality observations can best be used to estimate population exposure and how exposure measurement error can impact epidemiologic results (Strickland et al., 2011).

Biostatistics Core

Objective: Provide statistical support to the Center and to the associated Projects.

Research Conducted and Results Generated:

1. Initiated conversations on the conceptual nature of mixtures across Clean Air Research Centers and completed a first draft of a manuscript to summarize these ideas.
2. Continued work on methods for the identification of model mis-specification, particularly due to confounding. A manuscript for application of the Core's approach to spatial studies, entitled "A method for detection of residual confounding in spatial and other observational studies" and led by Dr. Flanders, has been accepted in *Epidemiology*.

3. Considered the impact of Berkson type error and the relationship with use of the population weighted average to measure levels of an air pollutant. Identified clearly how bias occurs with Berkson error in Poisson regression (with the usual log-link function) and derived a correction approach for use with Poisson regression when one uses population weighted averages.
4. Provided support for Center Projects with regard to design issues.

Project 1: Development and Deployment of an Instrumentation Suite for Comprehensive Air Quality Characterization including Aerosol ROS

Objective: Develop method(s) for measuring ROS online and semi-continuously, acquire instrumentation, and organize measurement program. Undertake an extensive measurement campaign that will characterize aerosol spatial distributions of key air quality parameters to inform the SCAPE modeling and health studies.

Research Conducted and Results Generated:

The first reporting period for Project 1 focused on two major areas: 1) developing online semi-continuous methods to quantify ROS in aerosol particles, and 2) acquiring and preparing instrumentation for field studies in years 2 and 3. More specifically, the following tasks were undertaken:

1. Testing three different chemical probes (DCFH/HRP, Amplex Red, and DDT Assay) for ROS. Experiments have been completed for the DCFH probe and testing for the latter two probes will be completed this year.
2. Tested two methods for collecting ambient particles into water for ROS analysis, including a particle-into-liquid-sampler and a Mist Chamber. These experiments resulted in selection of the Mist Chamber, and two Mist Chambers have been constructed.
3. Preliminary ambient field testing of a Mist Chamber/DCFH system have been undertaken and first results suggest a viable online ROS method.
4. Various instruments have been acquired and assembled in preparation for the upcoming intensive field study.

Project 2: Examining In-Vehicle Pollution and Oxidative Stress in a Cohort of Daily Commuters

Objective: To examine the effects of exposure to particulate mixtures occurring during automobile commuting and within indoor, non-commuting microenvironments (μE's) and corresponding measures of oxidative stress-mediated response.

Research Conducted and Results Generated:

1. Evaluating protocol proof-of-concept based on the ongoing results from the Centers for Disease Control and Prevention-funded Atlanta Commuter Exposure (ACE) study. As a result of this initial evaluation, design modifications have begun for the vehicle pollutant sampler, pollutant analytical protocols, and database management systems to meet Project 2 research aims.
2. Commenced a sub-analysis examining in-vehicle noise as a potential confounder of any observed pollutant-related health effects.

Project 3: Novel Estimates of Pollutant Mixtures and Pediatric Health in Two Birth Cohorts

Objective: Explore the interplay between certain early life events, characterizations of air pollutant mixtures developed as part of the Center's Mixtures Characterization Toolkit, and a range of pediatric health outcomes using two large, population-based birth cohorts.

Research Conducted and Results Generated:

1. Obtained individual-level birth data from 1994-2006 from the Office of Health Indicators and Policy, Georgia Division of Public Health.
2. Obtained individual-level pediatric emergency department data from the Georgia Hospital Association for 1999-2010.
3. Evaluating data quality, creating analytic datasets, and describing the distribution of outcomes in space and time.

Project 4: A Multi-City Time-Series Study of Pollutant Mixtures and Acute Morbidity

Objective: Conduct a multi-city time-series study to clarify the impacts of air quality on acute cardiorespiratory morbidity in five US cities using novel mixture characterization metrics.

Research Conducted and Results Generated:

Project 4 has focused on assessment of the specific cities to be included in the study and initiation of the health and air quality data collection phase of the project. Progress made on obtaining data for each city is described below:

1. For Atlanta, GA, existing emergency department (ED) visit and hospital admission (HA) databases covering the 1993-2004 time period were extended through 2009 with data acquired from the Georgia Hospital Association. These data are currently being processed and validated for use in epidemiologic analyses. Air quality (AQ) monitoring data for the extended time period have been acquired from state and federal monitoring networks, and data from local intensive monitoring programs has been requested.
2. For St. Louis, MO-IL, all ED visit, hospitalization, and AQ monitoring were acquired previously. The AQ data have been shared among the project team for use in the mixture characterization metrics development.
3. For Dallas, TX, negotiations with a central health data source have progressed and a data use agreement is currently under review. Data transfer to Emory investigators is anticipated by September 2011. All relevant AQ data for Dallas have been acquired and population-weighted metrics have been created.
4. For Pittsburgh, PA, progress has been made on developing the required collaboration with the University of Pittsburgh investigators and assessing the feasibility of including data from this study in the current project (e.g., with respect to anticipated data availability, timeline, and data sharing matters).
5. For Birmingham, progress has been made on acquiring the relevant AQ monitoring data and initiation of hospital recruitment activities.
6. Considering the feasibility of including a limited number of additional cities to this study.

2. Difficulties in Carrying out Mission of Center

During this first reporting period, the work of the Center has progressed as planned without any major difficulties in carrying out the proposed mission.

3. Absences or Changes in Key Personnel

Key personnel on all Projects and Cores have remained the same since the initial grant funding. Two personnel have been added to the Center. Howard Chang was hired in the Biostatistics Department at the Rollins School of Public Health. Dr. Chang will begin work on the Biostatistics Core, Project 3, and Project 4 in August 2011. Vishal Verma was hired by the School of Earth and Atmospheric Sciences at Georgia Tech to fill the postdoctoral position for Project 1.

5. Quality Assurance

SCAPE's Quality Management Plan was submitted to and approved by EPA in March 2011. Quality Assurance Project Plans (QAPPs) have been drafted for each of the four Projects and the Air Quality Core. QAPPs have been reviewed by the quality assurance team, including the Center Co-Directors, Quality Assurance Manager, and two Quality Advisors. Standard Operating Procedures (SOPs) have been drafted where required. For Project 1, SOPs for the 18 instruments/analysis methods to be deployed have been drafted. For Project 2, all SOPs, technician guidance documents and operation manuals to be used during the field collection and analysis phase of the project have been drafted.

The Quality Assurance Manager will perform technical systems audits for each Project and the Air Quality Core during the first year of research. Audit checklists are currently under development.

Quality Control Reviewers have been named for each Project and the Air Quality Core. The Quality Assurance Manager will maintain records of data quality audits performed by the Quality Control Reviewers, as specified in the QAPPs.

Finally, the data management plan for the Air Quality Core data at Georgia Tech is included within the Air Quality Core QAPP. Investigators from Emory have met to discuss data management practices for health and air quality data on the Emory server. An initial draft of this data management plan has been completed.

6. Planned Future Activities

<u>Air Quality Core</u>

1. Continue to collect relevant air quality-related data (e.g., air quality and emissions data), apply the various source apportionment approaches, and finalize the hybrid CTM-CMB approach.
2. Continue to build the air quality database to support Projects 3 and 4 with data obtained from EPA's AQS and STN and from the SEARCH and ARIES networks supported by EPRI.
3. Conduct descriptive analyses of the data and error analyses to support Projects 3 and 4.
4. Implement organic speciation methodology in support of Projects 1 and 2.

<u>Biostatistics Core</u>

1. Continue work on conceptualizing mixtures, measurement errors, and support of separate research projects in regard to design and analytic issues.
2. Work to adapt methods for analyses of time series based on LASSO and CART.

<u>Project 1: Development and Deployment of an Instrumentation Suite for Comprehensive Air Quality Characterization including Aerosol ROS</u>

1. Finish development of the ROS instrument, perform preliminary testing and validation, prepare manuscripts describing ROS instrumentation, and present results at meetings.
2. Continue acquiring/testing instrumentation necessary for field deployment.
3. Begin first year of roughly two continuous years of field measurements at sites within Atlanta.
4. Collect and quality check data from field studies and submit to data archive.

<u>Project 2: Examining In-Vehicle Pollution and Oxidative Stress in a Cohort of Daily Commuters</u>

1. Continue to finalize the sampling protocol and evaluate proof-of-concept based on the ACE study results throughout 2011 with a goal of beginning subject recruitment in November 2011.

2. Continue staffing throughout 2011 in anticipation of commencing actual field sampling in spring 2012. Hire a Project Manager at the postdoctoral level to begin working around October 2011.
3. Conduct the sub-analysis examining in-vehicle noise as a potential confounder of observed pollutant-related health effects during the July – September 2012 time period.

Project 3: Novel Estimates of Pollutant Mixtures and Pediatric Health in Two Birth Cohorts

1. Create final, clean, ready-to-use health datasets.
2. Work on analytic issues inherent in Project 3, particularly those related to mixtures and to the use of modeled exposure estimates in epidemiologic models.
3. Conduct empirical work characterizing mixtures that can be applied across Projects.

Project 4: A Multi-City Time-Series Study of Pollutant Mixtures and Acute Morbidity

1. Finalize selection of cities to be included and continue data collection activities.
2. Compile ED visit and hospitalization data from all cities, which will entail a combination of hospital recruitment activities and negotiations and contracts to be initiated with centralized data sources or collaborators.
3. Compile air quality monitoring data for all cities and relevant study periods and compute population-weighted averages when possible.
4. Commence work on developing the proposed mixture characterization metrics, including source-resolved PM metrics in each city.
5. Develop focused hypotheses and epidemiologic approaches for the planned multi-city analyses.

7. Publications/Presentations List

1. Flanders WD, Klein M, Darrow LA, Strickland MJ, Sarnat SE, Sarnat JA, Waller LA, Winquist A, Tolbert PE. A method for detection of residual confounding in time-series and other observational studies. *Epidemiology* 22:59-67, 2011.
2. Flanders WD, Klein M, Darrow LA, Strickland MJ, Sarnat SE, Sarnat JA, Waller LA, Winquist A, Tolbert PE. A method for detection of residual confounding in spatial and other observational studies. *Epidemiology*, in press.
3. Goldman GT, Mulholland JA, Russell AG, Strickland MJ, Klein M, Waller LA, Tolbert PE. Impact of exposure measurement error in air pollution epidemiology: effect of error type in time-series studies. *Environmental Health* 10:61, 2011.
4. Strickland MJ, Darrow LA, Mulholland JA, Klein M, Flanders WD, Winquist A, Tolbert PE. Implications of different approaches for characterizing ambient air pollutant concentrations within the urban airshed for time-series studies and health benefits analyses. *Environmental Health* 10:36, 2011.
5. Upcoming Presentations:
    a. King L, Verma V, Weber R. "Refinement and testing of a fluorometric assay for continuous online ROS measurement and results from preliminary field deployments." American Association for Aerosol Research Annual Meeting. Orlando, FL. Oct. 2011.
    b. Sarnat JA, Greenwald R, Sarnat SE, Kewada P, Yip F, Boehmer TK, Bergin MH. "In-vehicle pollutant exposures and acute cardiorespiratory response in a cohort of healthy and asthmatic car commuters in the Atlanta Commuters' Exposure Study." International Society for Environmental Epidemiology Annual Meeting. Barcelona, Spain. Sept. 2011.
    c. Sarnat SE, Sarnat JA, Winquist A, Schauer JJ, Turner JR, Klein M, Tolbert PE. "Associations of source-resolved particulate air pollution mixtures and cardiorespiratory emergency department visits in St. Louis, MO-IL." International Society for Environmental Epidemiology Annual Meeting. Barcelona, Spain. Sept. 2011.

Date of Report: July 31, 2011
EPA Agreement Number: R834799
Center Name: Southeastern Center for Air Pollution and Epidemiology
Project Title: Air Quality Core
Investigator(s): PI -- Armistead Russell, PhD[1] (ted.russell@ce.gatech.edu); M. Talat Odman, PhD[1] (odman@gatech.edu); Yongtao Hu, PhD[1] (yh29@mail.gatech.edu); James Mulholland, PhD[1] (james.mulholland@ce.gatech.edu); Yang Liu, PhD[2] (yang.liu@emory.edu)
Institution(s) of PI(s): [1]Georgia Institute of Technology and [2]Emory University, Atlanta, Georgia
Research Category: Air Quality and Air Toxics
Project Period: 01/01/2011 – 7/31/2011

Objective of Research: The primary mission of the Air Quality Core (AQC) is to provide Center researchers the information and methods to comprehensively characterize air pollutant mixtures relevant to their Projects and to support Project activities by collecting and managing data, developing a "Mixture Characterization Toolkit" (MC Toolkit) for further analyses specific to the Projects, and providing the expertise and resources to facilitate the application of MC Toolkit components. An additional mission of the AQC is to facilitate transmission of atmospheric data and methods to potential users outside of the Center. The more comprehensive characterization is developed, first, by analyses of the detailed chemical and physical measurements produced by the Center along with those available from other routine and special studies. Further spatial and temporal characterization of the air pollutant mixtures, and the sources involved, will come from the use of extended receptor-oriented and chemical transport models (CTM) applied over multiple scales. MC Toolkit is being developed to include a range of both source- and receptor-oriented air quality models, regression approaches and hybrid methods. In support of the four Research Projects and other Cores within the Center, the AQC has six functions: 1) atmospheric data collection and management; 2) development of the MC Toolkit to support Center Projects; 3) support of Project teams using MC Toolkit, 4) application of the extended Models 3/CMAQ; 5) integration of satellite remote sensing into health studies and air pollutant mixture characterization; and 6) assessment of exposure misclassification. In addition to these functions, the AQC team assists in the preparation of reports and journal publications resulting from Center activities.

Progress Summary/Accomplishments: The AQC has been actively engaged in beginning the development of MC Toolkit and the foundational methods upon which the methods rely. Further, we are gathering air quality-related data for the areas where studies are planned, first concentrating on collecting air quality and emissions data for Georgia, Dallas, and St. Louis. A password-protected website has been established for sharing data between the research teams.

We have applied various receptor modeling approaches (CMB-based, PMF, ensemble) to Atlanta, Dallas, and St. Louis. We are further applying a new, hybrid, ensemble source apportionment approach to Atlanta with an emphasis on characterizing the level of uncertainty in the more traditional methods used. A new, hybrid, chemical transport model-CMB based approach has been developed and applied, with results available for six cities at present.

Work is continuing on developing a better understanding of how air quality observations can best be used to estimate population exposures and how exposure measurement error can impact epidemiologic results. One study was completed characterizing measurement error due to instrument imprecision and spatial variability as multiplicative (i.e., additive on the log scale) and modeling it over a range of error types to assess impacts on risk ratio estimates both on a per measurement unit basis and on a per

interquartile range basis in a time-series study in Atlanta. Building on this work, a second study simulated pollutant fields over a 6-year time period over the 20-county metropolitan Atlanta area. These pollutant fields were developed to mimic the statistical properties of the actual observations. Error type was characterized, and the impact of error on the epidemiologic analysis was predicted. Measurement error due to spatial variability alone was found to be largely Berkson, suggesting reductions in significance but minimal risk attenuation in time-series risk estimates due to this error source. However, total measurement error, consisting of spatial variability error and error associated with instrument imprecision and location, results in substantial attenuation of the risk estimate, particularly for primary pollutants.

Publications/Presentations:

1. Goldman GT, Mulholland JA, Russell AG, Strickland MJ, Klein M, Waller LA, Tolbert PE. Impact of exposure measurement error in air pollution epidemiology: effect of error type in time-series studies. *Environmental Health* 10:61, 2011.
2. Strickland MJ, Darrow LA, Mulholland JA, Klein M, Flanders WD, Winquist A, Tolbert PE. Implications of different approaches for characterizing ambient air pollutant concentrations within the urban airshed for time-series studies and health benefits analyses. *Environmental Health* 10:36, 2011.

Future Activities: Plans for 2011-2012 include continued collection of relevant air quality-related data (e.g., air quality and emissions data), application of the various source apportionment approaches, and finalization of the hybrid CTM-CMB approach. Building of the air quality data base to support Projects 3 and 4 will continue with data obtained from EPA's AQS and STN and from the SEARCH and ARIES networks supported by EPRI. Descriptive analyses of the data will be performed and error analyses conducted to support Projects 3 and 4. Organic speciation methodology in support of Projects 1 and 2 will be implemented.

Supplemental Keywords: Air Quality, Chemical Transport Modeling, Receptor Modeling, Exposure Measurement Error

Relevant Web Site: www.scape.gatech.edu

Date of Report: July 31, 2011
EPA Agreement Number: R834799
Center Name: Southeastern Center for Air Pollution and Epidemiology
Project Title: Biostatistics Core
Investigator(s): Co-PIs -- W. Dana Flanders, MD, ScD (wflande@emory.edu) and Lance Waller, PhD (lwaller@sph.emory.edu); Mitchel Klein, PhD (mklein@emory.edu)
Institution(s) of PI(s): Emory University
Research Category: Air Quality and Air Toxics
Project Period: 01/01/2011 – 7/31/2011

Objective of Research: The primary objective of the Biostatistics Core is to provide statistical support to the Center and to the associated Projects. The five primary functions of the Biostatistics Core are to: 1) provide guidance and support to all Projects for design issues; 2) provide guidance and support to all Projects for epidemiologic modeling, including identification and characterization of mixtures and their health effects; 3) perform methodological development, including identification of model misspecification, analyses of time series based on LASSO and CART, and identification of mixtures that associate with health outcomes; 4) develop and provide support and guidance for addressing the impact of measurement error; and 5) archive, document, and assure security of analytic data files.

Progress Summary/Accomplishments: In this first period, we have performed a number of activities.

1. We have considered the conceptual nature of mixtures. The goal is to clarify the different conceptual issues that are often raised in discussing mixtures so that they can be identified and addressed more clearly. We have initiated conversations across the EPA Clean Air Research Centers on this topic and written a first draft of a manuscript to summarize these ideas.
2. We have also continued our work on methods for the identification of model mis-specification, particularly that due to confounding. A manuscript on application of our approach to spatial studies is now accepted for publication in *Epidemiology*.
3. We have also made progress in considering the impact of Berkson type error, and the relationship with use of the population weighted average to measure levels of an air pollutant. We have identified clearly how bias occurs with Berkson error in Poisson regression (with the usual log-link function). We have also derived a correction approach for use with Poisson regression when one uses population weighted averages.
4. We have participated in meetings and have provided support for Center Projects with regard to design issues.

Publications/Presentations:

1. Flanders WD, Klein M, Darrow LA, Strickland MJ, Sarnat SE, Sarnat JA, Waller LA, Winquist A, Tolbert PE. A method for detection of residual confounding in time-series and other observational studies. *Epidemiology* 22:39-67, 2011.
2. Flanders WD, Klein M, Darrow LA, Strickland MJ, Sarnat SE, Sarnat JA, Waller LA, Winquist A, Tolbert PE. A method for detection of residual confounding in spatial and other observational studies. *Epidemiology*, in press.

Future Activities: Over the next period, we plan to continue our work on conceptualizing mixtures, measurement errors, and support of separate research projects in regard to design and analytic issues. We will also work to adapt methods for analyses of time series based on LASSO and CART.

Supplemental Keywords: measurement error, time series, spatial statistics, exposure misclassification, nonparametric methods, LASSO, CART, mixture models

Relevant Web Site: www.scape.gatech.edu

Date of Report: July 31, 2011
EPA Agreement Number: R834799
Center Name & Internal Number: Southeastern Center for Air Pollution and Epidemiology (R834799C001)
Project Title: Development and Deployment of an Instrumentation Suite for Comprehensive Air Quality Characterization including Aerosol ROS
Investigator(s): PI -- Rodney Weber, PhD[1] (rweber@eas.gatech.edu); Michael Bergin, PhD[1] (mike.bergin@ce.gatech.edu); James Mulholland, PhD[1] (james.mulholland@ce.gatech.edu); Athanasios Nenes, PhD[2] (nenes@eas.gatech.edu); Jeremy Sarnat, ScD[2] (jsarnat@emory.edu); Stefanie Sarnat, ScD[2] (sebelt@sph.emory.edu); Matthew Strickland, PhD[2] (mjstric@emory.edu)
Institution(s) of PI(s): [1]Georgia Institute of Technology and [2]Emory University, Atlanta, Georgia
Research Category: Air Quality and Air Toxics
Project Period: 01/01/2011 – 7/31/2011

Objective of Research: Develop method(s) for measuring ROS online and semi-continuously, acquire instrumentation, and organize measurement program. Undertake an extensive measurement campaign that will characterize aerosol spatial distributions of key air quality parameters to inform the SCAPE modeling and health studies.

Progress Summary/Accomplishments: The first reporting period of the project focused on two major areas: 1) developing online semi-continuous methods to quantify ROS in aerosol particles, and 2) acquiring and preparing instrumentation for field studies in years 2 and 3. Each aspect is discussed separately.

ROS Instrument Development

A number of tasks have been undertaken in the development of an online ROS method. This includes testing three different chemical probes and testing two methods for collecting ambient particles into water for ROS analysis. The three probes tested were:

1. DCFH/HRP – which is reported to provide a chemically comprehensive measure of ROS in ambient particles [*Venkatachari and Hopke*, 2008].
2. Amplex Red – which is reported to provide a more chemically specific measurement of ROS, specifically sensitive to H2O2 [*Yan et al.*, 2005].
3. DDT Assay – a probe that will provide a measure of the capability of ambient particles to oxidize cellular anti-oxidants and is referred to as a measure of oxidative potential/oxidative activity/redox activity [*Cho et al.*, 2005].

Our approach was to first test the characteristics of the three probes to various operational parameters by measuring response to H2O2 standards to determine suitability and requirements for the online system. The parameters tested were:

1. Chemical source (vendor) of probe (most important for DCFH).
2. Chemical stability of probes when in appropriate solutions needed for the measurement (i.e., how often do we have to make new solutions).
3. Considerations required for handling probe solutions (i.e., how light sensitive, what type of dark room is needed and what needs to be prepared in the dark).
4. Probe response to various concentrations of H2O2 as a function of method for mixing probe and standard (e.g., or ambient sample) through comparisons of online mixing schemes (e.g., super serpentine reactors of various length) vs. mixing in a vial.
5. Response as a function of mix incubation temperature.

6. Response as a function of mix incubation time.
7. A determination of the probe sensitivity to H2O2 (slope of response vs. H2O2 concentration).
8. Determination of method blanks and estimation of detection limits.

These experiments have been completed for the DCFH probe and are still in progress for the Amplex Red and DDT Assay; the latter two will be completed this year.

Two automated particle collection methods were tested; a PILS (particle-into-liquid-sampler) and a Mist Chamber. These experiments resulted in the selection of a Mist Chamber over the PILS for the following reasons:

1. The Mist Chamber operates in a batch mode and extensive mixing of probe and sample is achieved during sample collection. PILS operates in a continuous collection mode and requires mixing of probe and sample as a separate component. Thus, the Mist Chamber was operationally a simpler device.
2. Concerns associated with possible loss of volatile ROS components in the steam-based vapor condensation collection system of the PILS (sample heated to 100°C) compared to the scrubbing/wetted filter (which actually cools sample due to latent heat of evaporating water) approach of the Mist Chamber.
3. Potential for a smaller, simpler more robust design with the Mist Chamber.

Two Mist Chambers have been constructed by the Georgia Tech glass shop at a cost of roughly $100/collector. Preliminary ambient field-testing of a Mist Chamber/DCFH system has been undertaken. Difficulties with liquid pumping systems are currently being resolved, but first results suggest a viable online ROS method.

Field deployment preparation

In preparation for the upcoming intensive field study the following has been performed.

1. Development of Project 1 QAPP.
2. Writing of SOPs for the 18 instruments/analysis methods to be deployed.
3. Development of a preliminary deployment schedule.
4. Acquiring and assembling the various instruments.

Publications/Presentations:

King L, Verma V, Weber R. “Refinement and Testing of a Fluorometric Assay for Continuous Online ROS Measurement and Results from Preliminary Field Deployments.” American Association for Aerosol Research Annual Meeting. Orlando, FL. Oct. 2011.

Future Activities:

Project 1 planned activities for year 2.

1. Finish development of the ROS instrument, perform preliminary testing and validation, prepare manuscripts describing ROS instrumentation, present results at meetings.
2. Continue acquiring/testing instrumentation necessary for field deployment.
3. Begin first year of roughly two continuous years of field measurements at sites within Atlanta.
4. Collect and quality check data from field studies and submit to data archive.

Supplemental Keywords: Reactive oxygen species, ROS, oxidative stress, oxidative potential

Relevant Web Site: www.scape.gatech.edu

References:

1. Cho, A. K., C. Sioutas, A. H. Miguel, Y. Kumagai, D. A. Schmitz, M. Singh, A. Eiguren-Fernandez, and J. R. Froines (2005), Redox activity of airborne particulate matter at different sites in the Los Angeles Basin, *Environ. Res.*, *99*, 40-47.
2. Venkatachari, P., and P. K. Hopke (2008), Development and laboratory testing of an automated monitor for the measurement of atmospheric particle-bound reactive oxygen species (ROS), *Aerosol Sci. Tech.*, *42*, 629-635.
3. Yan, F., S. Williams, G. D. Griffin, R. Jagannathan, S. E. Plunkett, K. H. Shafer, and T. Vo-Dinh (2005), Near-real-time determination of hydrogen peroxide generated from cigarette smoke, *J. Environ. Monit.*, *7*, 681-687.

Date of Report: July 31, 2011
EPA Agreement Number: R834799
Center Name & Internal Number: Southeastern Center for Air Pollution and Epidemiology (R834799C002)
Project Title: Examining In-Vehicle Pollution and Oxidative Stress in a Cohort of Daily Commuters
Investigator(s): Jeremy Sarnat, ScD[1] (jsarnat@emory.edu); Michael Bergin, PhD[2] mike.bergin@ce.gatech.edu); W. Dana Flanders, MD, ScD[1] (wflande@emory.edu); Lou Ann Brown, PhD[1] (lbrow03@emory.edu); Andrea Winquist, PhD[1] (ldarrow@emory.edu); Anne Fitzpatrick, PhD[1] (amentro@emory.edu); Roby Greenwald, PhD[1] (roby.greenwald@emory.edu); Randy Guensler, PhD[2] (randy.guensler@ce.gatech.edu); Cherry Wongtrakool, MD[1] (cwongtr@emory.edu)
Institution(s) of PI(s): [1]Emory University and [2]Georgia Institute of Technology, Atlanta, Georgia
Research Category: Air Quality and Air Toxics
Project Period: 01/01/2011 – 7/31/2011

Objective of Research: The primary aim of Project 2 is to examine the effects of exposure to particulate mixtures occurring during automobile commuting and within indoor, non-commuting microenvironments (μE's) and corresponding measures of oxidative stress-mediated response.

Progress Summary/Accomplishments: Work on Project 2 during the first reporting period has focused on: a) developing and finalizing the project QAPP, SOPs, and technician manuals; b) establishing proof-of-concept for the measurement methods to be used during field sampling; and c) conducting a targeted sub-analysis aimed at examining the potential for confounding in the commuter study.

A draft of the Project 2 QAPP has been written and reviewed by the quality assurance team. In addition, we have written and compiled all SOPs, technician guidance documents and operation manuals to be used during the field data collection and analysis phase of the project. During this reporting period, we have continued to evaluate protocol proof-of-concept based on the ongoing results from our Centers for Disease Control and Prevention-funded Atlanta Commuters Exposure (ACE) study. The ACE study concluded field sampling during June 2011. In total, there were 40 subjects (20 physician-diagnosed adult asthmatics and 20 healthy adults) who participated in ACE. While the hypotheses and design of Project 2 differ from the ACE study in its focus on pollutant mixtures and oxidative stress-associated mechanistic pathways, the ACE study has served as a critical means of evaluating the proposed Project 2 protocol and methods. As a result of initial proof-of-concept evaluation from the ACE study, we have begun to design modifications to the in-vehicle pollutant sampler used in the ACE study, the pollutant analytical protocols, and database management systems to meet the Project 2 research aims. Specifically, the Project 2 in-vehicle sampler will use two DC-powered rocking piston pumps instead of the vacuum pumps used for ACE. These pumps will provide similar flow rates (100 LPM) while emitting less noise during the commutes. Using our initial ACE results as a guide, we have also switched our proposed method for characterizing particle count concentrations from a TSI P-TRAK Ultrafine Particle Counter to a TSI Condensation Particle Counter (Model 3006).

Few previous studies have quantified concurrent in-vehicle noise levels and corresponding pollutant concentrations. This is a significant omission for understanding the link between traffic exposures and human health, given results showing strong associations between traffic noise and numerous health endpoints, including cardiovascular outcomes[1-3]. This finding has led some to claim that health effects attributed to PM may be confounded by factors such as noise. To address this issue, we have commenced a Project 2 sub-analysis examining in-vehicle noise as a potential confounder of any observed pollutant-related health effects. During July - September 2012, we will be conducting

sampling in a variety of commuter exposure settings to characterize correlation patterns between measured noise and corresponding in-vehicle concentrations of size-resolved particle mass, particle counts, black carbon, and particle-bound polycyclic aromatic hydrocarbons.

Publications/Presentations: To date, we have not submitted any publications for Project 2. An abstract will be presented as a platform presentation at the upcoming ISEE meeting in September 2011. These results have direct relevance to Project 2 in showing elevated concentrations of many pollutant concentrations existed during the ACE commutes. We also observed significant ($p < 0.0001$) increases in post-commute exhaled nitric oxide (eNO) indicative of pulmonary inflammation. During the 4 post-commute measurement periods, mean eNO levels ranged from 12-16% above corresponding pre-commute levels and were typically highest at the 1h post-commute measurement period. C-reactive protein (CRP) levels, indicative of systemic inflammation, were also elevated, although not significantly, at each of the post-commute periods. CRP levels were highest (15% higher than pre-commute levels) immediately after the commute ($p = 0.07$). Associations between pre- and post-commute lung function were negligible. These preliminary ACE study results showed significant elevations in several biomarkers of acute pulmonary and systemic inflammation following a realistic morning commute and provide indication that sub-clinical changes, consistent with inflammation, may be occurring in our cohort. Future work for Project 2 will examine the role of specific particle mixtures and potential confounding by stress and noise. [Sarnat JA, Greenwald R, Sarnat SE, Kewada P, Yip F, Boehmer TK, Bergin MH. "In-vehicle pollutant exposures and acute cardiorespiratory response in a cohort of healthy and asthmatic car commuters in the Atlanta Commuters' Exposure Study." International Society for Environmental Epidemiology Annual Meeting. Barcelona, Spain. Sept. 2011.]

Future Activities*:* We expect to continue finalizing the Project 2 sampling protocol and evaluating proof-of-concept based on the ACE results throughout 2011 with a goal of beginning subject recruitment in November 2011. Project 2 staffing will also continue throughout 2011 in anticipation of commencing actual field sampling in spring 2012. We expect to hire a Project Manager (at the post doc level) to begin working on the project in October 2011. A qualified candidate has been identified and we expect to receive a signed offer letter soon.

Supplemental Keywords: health effects, oxidative stress, inflammation, human health, susceptibility, vulnerability, PAHs, PM2.5, organics, elemental carbon, metals, ozone, oxidants, PAH, sulfates, source characterization, mobile sources, Georgia, GA

Relevant Web Site: www.scape.gatech.edu

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Date of Report: July 31, 2011
EPA Agreement Number: R834799
Center Name & Internal Number: Southeastern Center for Air Pollution and Epidemiology (R834799C003)
Project Title: Novel Estimates of Pollutant Mixtures and Pediatric Health in Two Birth Cohorts
Investigator(s): PI -- Matthew Strickland, PhD[1] (mjstric@emory.edu); Lyndsey Darrow, PhD[1] (ldarrow@emory.edu); Mitchel Klein, PhD[1] (mklein@emory.edu); Yang Liu, PhD[1] (yang.liu@emory.edu); Lance Waller, PhD[1] (lwaller@sph.emory.edu); Randy Guensler, PhD[2] (randy.guensler@ce.gatech.edu); James Mulholland, PhD[2] (james.mulholland@ce.gatech.edu); Armistead Russell, PhD[2] (ted.russell@ce.gatech.edu); Robert Davis, MD[3] (robert.l.davis@kp.org)
Institution(s) of PI(s): [1]Emory University and [2]Georgia Institute of Technology, Atlanta, Georgia (Collaborating Institutions: [3]Kaiser Permanente-Georgia, Atlanta, Georgia)
Research Category: Air Quality and Air Toxics

Objective of Research: *In utero* and early life experiences affect physiological development and can influence sensitivity to environmental factors throughout life. In this Project we will explore the interplay between certain early life events, characterizations of air pollutant mixtures developed as part of the Center's Mixtures Characterization Toolkit, and a range of pediatric health outcomes using two large, population-based birth cohorts. One cohort consists of roughly 2.3 million Georgia birth records that have been geocoded and linked with pediatric emergency department visits by staff at the Georgia Department of Human Resources. Using this statewide birth cohort, we will investigate acute effects of air pollution mixtures on respiratory health outcomes and ear infections in children, and we will assess whether children who were born premature or low birth weight are more sensitive to ambient air pollutant concentrations than their counterparts. Further, we will use the statewide birth cohort to investigate whether ambient air pollutant mixtures during pregnancy are associated with the risk of preterm delivery or reduced birth weight. The second birth cohort is comprised of children who were members of the Kaiser Permanente Georgia Health Maintenance Organization in metropolitan Atlanta. In this birth cohort, where comprehensive medical and residential histories are available for each study subject, we will examine whether air pollutant mixtures during the first year of life are associated with the incidence of childhood asthma.

Progress Summary/Accomplishments: We have been successful in obtaining the health data for this project. In June 2011 we received individual-level birth data from 1994-2006 from the Office of Health Indicators and Policy, Georgia Division of Public Health. These statewide data have daily temporal resolution, are geocoded to the 2000 Census Block Group level, and have a longitudinal ID that can be linked to the emergency department data. In July 2011 we received individual-level pediatric emergency department data from the Georgia Hospital Association for 1999-2010. These data have daily temporal resolution and are geocoded to the ZIP code level. To this point we have not used any of these data in air pollution analyses. Our focus has been to evaluate the quality of the data, create analytic datasets, describe the distribution of outcomes in space and time, etc.

Several different products from the Center's Air Quality Core will be available for use in Project 3. Efforts have been made to collect all the air quality and emissions data from Georgia. Various receptor modeling approaches are under development using these Georgia data. Work on the consequences of measurement error in time-series studies (using data from Atlanta) is ongoing and includes both simulation-based work as well as theoretical work.

Publications/Presentations:

1. Strickland MJ, Darrow LA, Mulholland JA, Klein M, Flanders WD, Winquist A, Tolbert PE. Implications of different approaches for characterizing ambient air pollutant concentrations within the urban airshed for time-series studies and health benefits analyses. *Environmental Health* 10:36, 2011.
2. Goldman GT, Mulholland JA, Russell AG, Strickland MJ, Klein M, Waller LA, Tolbert PE. Impact of exposure measurement error in air pollution epidemiology: effect of error type in time-series studies. *Environmental Health* 10:61, 2011.

Future Activities*:* Howard Chang will begin a faculty position in biostatistics in August 2011 and will work on many of the analytic issues inherent in Project 3, particularly those related to mixtures and to the use of modeled exposure estimates in the epidemiological models. We recruited a student (Chao Yu) to work closely with Center investigator Yang Liu to collect and analyze satellite data for the Air Quality Core and Project 3. We plan to do some empirical work characterizing mixtures that can be applied across the different Projects (including Project 3). We will create final, clean, ready-to-use datasets so that we will be ready to analyze the various air quality estimates when they become available.

Supplemental Keywords: ambient air, atmosphere, health effects, human health, susceptibility, vulnerability, sensitive populations, infants, children, risk, dose-response, cumulative effects, epidemiology, exposure, public policy, air quality modeling, monitoring, measurement methods, aerosol, particulates, PM2.5, organics, elemental carbon, metals, ozone, oxidants, PAH, sulfates, source characterization, mobile sources, Georgia, GA, Southeast

Relevant Web Sites: www.scape.gatech.edu

Project Period: 01/01/2011 – 7/31/2011
Date of Report: July 31, 2011
EPA Agreement Number: R834799
Center Name & Internal Number: Southeastern Center for Air Pollution and Epidemiology (R834799C004)
Project Title: A Multi-City Time-Series Study of Pollutant Mixtures and Acute Morbidity
Investigator(s): PI -- Stefanie Sarnat, ScD[1] (sebelt@sph.emory.edu); Lyndsey Darrow, PhD[1] (ldarrow@emory.edu); Mitchel Klein, PhD[1] (mklein@emory.edu); Paige Tolbert,PhD[1] (tolbert@sph.emory.edu); Andrea Winquist, MD[1] (awinqui@emory.edu); James Mulholland, PhD[2] (james.mulholland@ce.gatech.edu); Armistead Russell, PhD[2] (ted.russell@ce.gatech.edu);
Institution(s) of PI(s): [1]Emory University and [2]Georgia Institute of Technology, Atlanta, Georgia
Research Category: Air Quality and Air Toxics
Project Period: 01/01/2011 – 7/31/2011

Objective of Research: Although associations between ambient air pollution and acute cardiorespiratory outcomes have been observed in numerous studies, questions remain about the degree to which these findings are generalizable between locations and whether the observed health effects are due to the individual pollutants measured or to pollutants acting in combination with other pollutants. In Project 4, we are conducting a multi-city time-series study to clarify the impacts of air quality on acute cardiorespiratory morbidity in five US cities using novel mixture characterization metrics. Our overarching hypothesis is that factors related to air pollution mixtures, seasonality and climate, concentration-response functions, exposure measurement error, and population susceptibility and vulnerability can help explain apparent between-city heterogeneity in short-term associations between air quality measures and cardiorespiratory emergency department (ED) visits and hospitalizations.

Progress Summary/Accomplishments: During the current reporting period (1/1/2011-7/31/2011), work on Project 4 has focused on development of the project QAPP and associated data management activities, assessment of the specific cities to be included in the study, and initiation of the health and air quality data collection phase of the project. The specific cities proposed for this study were largely chosen based on availability of at least two years of daily speciated particulate matter (PM) data and availability of individual-level ED visit and/or hospitalization data for the corresponding time period. We have ongoing studies in Atlanta, GA; Dallas, TX; and St. Louis, MO-IL that meet these criteria. Data collection for these cities has progressed throughout the reporting period. For **Atlanta, GA**, existing ED visit and HA databases covering the 1993-2004 time period were extended through 2009 with data acquired from the Georgia Hospital Association. These data are currently being processed and validated for use in epidemiologic analyses. Air quality (AQ) monitoring data for the extended time period have been acquired from state and federal monitoring networks, and data from local intensive monitoring programs [e.g., the SouthEastern Aerosol Research and Characterization (SEARCH) network] has been requested. For **St. Louis, MO-IL**, all ED visit, hospitalization, and AQ monitoring data have been acquired previously. The AQ data have been shared among the project team for use in the mixture characterization metrics development. For **Dallas, TX**, negotiations with a central health data source have progressed and a data use agreement is currently under review. Data transfer to Emory investigators is anticipated by September 2011. All relevant AQ data for Dallas have been acquired and population-weighted metrics have been created. **Pittsburgh, PA** was selected as a city of interest because of a relevant ongoing study conducted by the University of Pittsburgh. Progress has been made on developing the required collaboration with the University of Pittsburgh investigators and assessing the feasibility of including data from this study in the current project (e.g., with respect to anticipated data availability, timeline, and data sharing matters). Finally, **Birmingham, AL** was proposed as a city of

interest due to its contrasting pollution mix from Atlanta, availability of detailed daily speciated AQ measurements conducted as part of the SEARCH network, and feasibility of ED visit and HA data collection from hospitals. Progress has been made on acquiring the relevant AQ monitoring data and initiation of hospital recruitment activities. These five cities may be characterized as distinct, non-coastal major urban population centers with varying degrees of contribution from traffic, industrial sources, coal-fired power plants, and secondary pollutant formation. We are considering the feasibility of including a limited number of additional cities in this study, which may provide increased power and generalizability of study findings.

Publications/Presentations: In this reporting period, several manuscripts have been published or have been accepted as part of Project 4 (Flanders et al., 2011; Flanders et al., in press; Goldman et al., 2011; Strickland et al., 2011). We also have several manuscripts in preparation, which include an examination of speciated fine PM and ED visits for cardiorespiratory diseases, a comparison of medical visit types and impacts on observed associations with air pollution, an analysis of the impact of daily pollen levels on ED visits for asthma, and an assessment of power in air pollution time-series studies.

A Project 4-related abstract has also been accepted for an oral presentation at the upcoming 2011 International Society for Environmental Epidemiology conference as part of a symposium on "Challenges and Opportunities for Using Data for Multiple Pollutants in Air Pollution Epidemiological Studies". In this presentation, we will present on associations of source-resolved particulate air pollution mixtures and cardiorespiratory ED visits in St. Louis. These analyses will be an important lead into further source- and mixtures-related work planned in Project 4. [Sarnat SE, Sarnat JA, Winquist A, Schauer JJ, Turner JR, Klein M, Tolbert PE. "Associations of source-resolved particulate air pollution mixtures and cardiorespiratory emergency department visits in St. Louis, MO-IL." International Society for Environmental Epidemiology Annual Meeting. Barcelona, Spain. Sept. 2011.]

Future Activities*:* Over the coming year, we will finalize the selection of cities to be included in this study and will continue with data collection activities. Specifically, ED visit and hospitalization data will be compiled from all cities, which will entail a combination of hospital recruitment activities and negotiations and contracts to be initiated with centralized data sources or collaborators. Air quality monitoring data for all cities and relevant study periods will be compiled and population-weighted averages will be computed when possible. Work will commence on developing the proposed mixture characterization metrics, including source-resolved PM metrics in each city. Throughout the coming year, we will also develop focused hypotheses and epidemiologic approaches for the planned multi-city analyses.

Supplemental Keywords: ambient air, health effects, sensitive populations, dose-response, cumulative effects, epidemiology, exposure, air quality modeling, $PM_{2.5}$, organics, elemental carbon, metals, oxidants, sulfates, source characterization

Relevant Web Site: www.scape.gatech.edu