

Annual Center Progress Report
Southeastern Center for Air Pollution and Epidemiology
Georgia Tech/Emory EPA Clean Air Research Center
August 1, 2011 – July 31, 2012

This Progress Report covers the work of the Southeastern Center for Air Pollution and Epidemiology (SCAPE) from August 1, 2011 – July 31, 2012. 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 developed a quality management structure, which is detailed in the EPA-approved Quality Management Plan. Functions of the quality management team over the past year are described below under Quality Assurance. The second annual meeting for SCAPE's eleven member Science Advisory Committee is scheduled for September 2012 in Atlanta. Multiple Center-wide and Project-specific meetings have been held throughout the year to ensure that research is coordinated and integrated among Projects and Cores.

1. Research Conducted and Results Generated

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 spatial distributions of key air quality parameters to inform the SCAPE modeling and health studies.

Research Conducted and Results Generated:

1. Prepared suite of instrumentation and sampling trailer at the Jefferson Street (JST) SEARCH site in Atlanta for a nominal two-year, paired sampling campaign.
2. Completed construction of a DCFH-ROS online instrument based on a mist chamber collector and syringe pump/external mixing vial analytical system capable of measuring ROS (total), ROS (gas) and particle-bound ROS by difference. Conducted pre-campaign testing.
3. Inter-compared an Aerosol Chemical Speciation Monitor (ACSM) with other online aerosol composition monitors prior to field deployments. Results showed significant discrepancies that change under different sampling conditions (results included in a manuscript submitted to *Environmental Science and Technology*, results to be presented at AAAR conference (Kotra et al. 2012)).
4. Developed expertise for quantifying ROS via DTT assay on filter extracts from both organic (methanol) and water-based solvents. Collected filters during pre-campaign testing at JST and analyzed via DTT-probe (manuscript submitted to *Environmental Science and Technology*, results to be presented at AAAR conference (Verma et al., 2012)).
5. Constructed an online DTT analytical system for high filter sample throughput, including in-vehicle filters collected as part of Project 2. This effort is in response to the first SAC review and entails substantial additional effort beyond the original proposed research.
6. Completed two months of field sampling with all instruments deployed at paired sites JST/JST and JST/Yorkville (rural SEARCH site) as the start of the two-year measurement campaign.

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

Objective: Examine the effects of exposure to particulate mixtures occurring during automobile commuting and within indoor, non-commuting microenvironments and corresponding measures of oxidative stress-mediated response.

Research Conducted and Results Generated:

1. Implemented several study design modifications including: added a surface street commute as an alternative control exposure setting to the clinic, extended the interval between exposure windows from two to seven days, and added dried blood spot collection to characterize biomarkers of inflammatory response.
2. Recruitment began in November 2011 and was completed in May 2012 with a surplus of healthy and asthmatic adults.
3. Pilot sampling was conducted in February and March 2012. Results validated selection of the clinic as a low exposure microenvironment in contrast to exposures during highway commutes.
4. Twenty (of 120 total) sampling sessions have been conducted, including completed protocols for ten subjects. Initial QAQC review of health and pollutant measurements indicates satisfactory data capture and completeness.

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. Analyzed the quality of the linkage of birth data and emergency department/hospitalization data using patients' unique longitudinal ID. Evaluation of inconsistencies in the longitudinal ID did not reveal any major issues that would have caused problems with the linkage.
2. Prepared analytic datasets.
3. Developing satellite-derived estimates of PM_{2.5} in Georgia at 10 km resolution, with calibration to the fixed site monitors using a Bayesian statistical model. Estimating biomass burning events using NASA remote sensing data and ground measurements collected in prescribed burn areas in southern Georgia.
4. Working on classification and regression tree (C&RT) approaches for examining complex joint effects of mixtures (Gass et al., ISES 2012)
5. Continued work on the effects of measurement error on the risk ratio estimates from time-series studies (Goldman et al., 2012; follow-up manuscript in draft form).

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:

1. Developed air quality monitoring database for the relevant study periods in each of the five cities.

2. Continued development of emergency department visit and hospital admissions databases for each of the cities. Data collection for Atlanta, Dallas, and St. Louis is complete. Data collection in Birmingham and Pittsburgh is nearing completion.
3. Continued single-city epidemiological analyses in Atlanta and St. Louis data, resulting in one in press publication (Darrow et al., in press) and two articles in review (Winquist et al., in review; Winquist et al., in review).
4. Developed and applied spatially-refined modeled estimates of ambient concentrations and population exposures in Atlanta epidemiologic analyses (Sarnat et al., ISES 2011). Several articles are in preparation from this work and will be included in a JSM 2012 (Waller et al., 2012) presentation.
5. Began work on applying self-organizing maps (SOMs) and classification and regression trees (C&RT) to our Atlanta data as approaches for detecting and analyzing air pollution mixtures (Gass et al., ISES 2012).
6. Began work on applying source apportionment outputs to epidemiologic analyses in St. Louis, comparing results among multiple source apportionment approaches (Sarnat et al., ISEE 2011).

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. Continued development of the MC Toolkit.
2. Applied receptor modeling approaches (CMB-based, PMF, ensemble) to data from Atlanta, Dallas, and St. Louis.
3. Completed application of the ensemble method to organic molecular marker data from St. Louis (manuscript in draft form).
4. Applied the ensemble approach to Atlanta SEARCH site data to characterize uncertainty in the various methods used in source apportionment analysis (Balachandran et al., 2012).
5. Conducted a simulation study using a spatio-temporal model to generate ambient air pollutant fields for Atlanta over six years and thereby quantify the amount and type of bias and error associated with ambient concentration data (Goldman et al., 2012).

Biostatistics Core

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

Research Conducted and Results Generated:

1. Supported Projects by providing guidance on design issues and assisting with development of analytic plans for data analysis.
2. Continued work on methods for identification of model mis-specification, particularly due to confounding (Flanders et al., 2011).
3. Continued work on the relative impact of Berkson and classical measurement error in exposure on estimated health effects and measurement error from uncertain geocoding locations (Goldman et al. 2011, Reich et al. 2012).

4. Began work on the use of classification and regression tree (C&RT) and self-organizing map (SOM) approaches for investigating pollutant mixtures (two manuscripts under development).
5. Assisted with coordination of the first CLARC Biostatistics Workshop.

2. Difficulties in Carrying out Mission of Center

During this second reporting period, the work of the Center has progressed as planned without any major difficulties in carrying out the proposed mission. Several changes were made to research plans based on feedback from the SAC during the 2011 annual meeting. These changes are described in the respective Project Summaries.

3. Absences or Changes in Key Personnel

Key personnel on all Projects and Cores have remained the same since the initial grant funding. Ten personnel have been added to the Center.

Project 1 added two personnel. Hongyu Guo was hired in the Earth and Atmospheric Sciences Department at Georgia Tech to fill a graduate student position on Project 1. Dr. Sally Ng was hired by Georgia Tech as an Assistant Professor with a joint position between Chemical and Biochemical Engineering and Earth and Atmospheric Sciences. Dr. Ng's expertise is in aerosol mass spectrometry and she is involved in Project 1 and Collaborative Project 1 (Chamber Characterization).

Project 2 added three personnel. Amit Raysoni was hired in the Environmental Health Department at the Rollins School of Public Health at Emory and works as a postdoctoral researcher on Project 2. Dr. Raysoni brings expertise in differential health panel studies and characterizing air pollution exposures and health effects. Two personnel were hired in the Civil and Environmental Engineering Department at Georgia Tech. Dr. Jaidevi Jeyaraman (postdoctoral researcher) brings expertise in measuring chemical and physical properties of aerosols. Chris Forehand (graduate student) works on in-vehicle sampling including data analyses and analytical measurements.

Three graduate students were hired at Georgia Tech to work on Projects 3 and 4. Xinxin Zhai works on source apportionment modeling for Project 3. Also on Project 3, Sheila Sororian works on spatial modeling across Georgia with fused observations and CMAQ model estimates. Mariel Frieberg works on spatial modeling in the Project 4 cities.

John Pearce was hired in the Biostatistics Department at the Rollins School of Public Health and works as a postdoctoral researcher for the Biostatistics Core. Dr. Pearce brings expertise in self-organizing maps (SOMs) and other multivariate analyses of air quality and climate indicators. Finally, Heather Holmes was hired in the Civil and Environmental Engineering Department at Georgia Tech and works as a postdoctoral researcher on the Air Quality Core, Project 3, and Project 4. Dr. Holmes brings expertise in air quality data analysis and numerical modeling.

4. Quality Assurance

SCAPE's Quality Management Plan (QMP) was submitted to and approved by EPA in March 2011. A minor addendum was added to the QMP and approved by EPA during the annual QMP review in March 2012. Quality Assurance Project Plans (QAPPs) for all four Projects and the Air Quality Core were initially approved by the quality assurance team (Center Co-Directors, Quality Assurance Manager, and two Quality Advisors) in 2011 and are reviewed annually. All necessary Standard Operating Procedures have been drafted and approved.

The Quality Assurance Manager meets with the designated Quality Control Reviewer for each Project on a semiannual basis to review all QA/QC procedures detailed in the Project QAPPs and data management plans, and to conduct annual project audits during the first year of research. Audits for Project 3 and Project 4 were conducted in February 2012. Audits for Project 1 and Project 2 are scheduled for summer 2012 and winter 2013, respectively. The Quality Assurance Manager maintains detailed meeting records and works with the PIs and Quality Control Reviewers to resolve any issues.

The Quality Assurance Manager also works with the PIs and Quality Control Reviewers on a regular basis to ensure that data are stored securely. The Quality Assurance Manager maintains a data access log detailing user access to all restricted folders stored on network drives. Finally, the Quality Assurance Manager works with the Quality Control Reviewers to maintain updated IRB approvals and inform the Project Officer of any amendments.

5. Planned Future Activities

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

1. Continue extensive field measurements with suite of instruments at paired sites in Atlanta. Conduct three weeks of measurements in St. Louis and Birmingham.
2. Determine the levels of particle-bound and gaseous ROS (e.g., typical ambient concentrations).
3. Perform extensive measurements of ROS oxidative potential via DTT assay on various filter extracts to determine sources and specific groups of organic species responsible for toxicity.
4. Explore other possible cellular based assays on a limited set of filters for comparison with acellular particle-bound ROS and DTT-ROS.
5. Determine if water-soluble redox active metals and hydrophobic organics (e.g., HULIS) synergistically combine to produce more ROS than either species alone based on authentic ambient aerosols.

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

1. Conduct a QAQC analysis for four weeks beginning in August 2012.
2. Continue data collection on enrolled subjects through fall 2013.

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

1. Initiate subcontract with Kaiser Permanente and begin work on development of birth cohort.
2. Conduct various epidemiologic analyses of the statewide data using both the routine data from fixed site monitors as well as model-based outputs from the MC Toolkit.
3. Continue work on measurement error in time-series studies.

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

1. Complete health data collection and data processing activities.
2. Begin epidemiologic analyses of Birmingham, Dallas, and Pittsburgh data.
3. Extend work on SOMs and possibly C&RT to other cities.
4. Apply source apportionment outputs for other cities (e.g., Atlanta and Dallas) in epidemiologic analyses.
5. Assess and compare the Census 2000 data among the five study areas.
6. Evaluate approaches for comparing epidemiologic results among the five cities.

Air Quality Core

1. Continue collection of relevant air quality-related data (e.g., air quality and emissions data).
2. Continue application of the various source apportionment approaches and the hybrid CTM-CMB approach.
3. Work on an approach to use CMAQ data for the continental US from 2001-2008 to provide spatially-resolved source impact estimates for major sources in an efficient fashion.

Biostatistics Core

1. Extend classification and regression tree (C&RT) and self-organizing map (SOM) techniques for characterizing air pollution mixtures.
2. Characterize measurement error in remotely sensed and modeled measures of air quality.
3. Detect and adjust for confounding in health effect models.
4. Characterize the impact of measurement error on estimates of health effects of air pollution.
5. Continue collaborations on the design and analysis of exposure measurements in Projects 1 and 2.
6. Continue collaborations on the design and analysis of health effect studies in Projects 3 and 4.

6. Collaborations

SCAPE supports in principle the four collaborative projects described below pending agreement on personnel and budget commitments with the other collaborative centers. SCAPE's proposed budgetary commitment is discussed above in the financial report. SCAPE investigators are currently working with the other centers to develop formalized agreements.

Collaborative Project 1: Chemical Characterization of Fresh and Aged Traffic Aerosols using Photochemical Chamber and Aerosol Chemical Speciation Monitor (ACSM) (Collaborators: Harvard and SCAPE)

The objective of this collaborative project is to obtain near real-time chemical characterization of Harvard's tunnel chamber aerosols with the use of an Aerosol Chemical Speciation Monitor (ACSM). The Harvard Center has developed an exposure generation system to investigate the health effects of fresh and aged traffic emission particles. The Harvard tunnel chamber has a comprehensive set of offline analyses for chemical characterization but currently does not have the capability for real time aerosol chemical characterizations. Georgia Institute of Technology (GIT) will operate the ACSM at the Harvard tunnel study from July 23rd – August 10th, 2012. Aerodyne Research Inc. (ARI) will provide the ACSM for this study, and GIT will be responsible for analyzing and providing quality controlled ACSM data, collecting filters for DTT analysis and conducting those analyses.

The ACSM will be operated simultaneously with animal exposures. It will provide complementary chemical data such as the near real-time determination of the contribution of aerosol sources (primary vs. secondary, others) and extent of oxidation over the course of each experiment. Furthermore, as numerous chamber studies have been conducted in laboratory settings to study SOA formation previously, this collaboration also provides a unique opportunity for linking the chemical properties of laboratory-generated chamber aerosols to ambient aerosols and their consequent health effects. Such information will be valuable for designing future laboratory chamber studies to mimic the ambient atmosphere for assessing relevant health outcomes.

Collaborative Project 2: Mobile Platform and Fixed-Site Monitoring in Atlanta: Combining CCAR and SCAPE to Characterize Vehicle Emissions (Collaborators: SCAPE, CCAR, and EPA)

The goal of this collaborative project is to compare instruments and methods for characterizing vehicle emissions, personal exposures and spatial distributions by deploying the CCAR measurement platforms and sampling protocols in Atlanta for a roughly one-month study. Both the Atlanta-based SCAPE and Washington/Washington State CCAR EPA Centers are investigating emissions and spatial distributions of mobile sources of urban traffic, with each center using a distinct approach. The project is proposed for September 2013, following CCAR measurements scheduled for Winston-Salem NC. Results will be presented at the CLARC meeting the following summer and subsequently at various professional society venues.

The study is proposed to include: (1) one week of simultaneous in-vehicle (SCAPE) and outdoor (CCAR) mobile platform measurements along commuter routes, as well as possible deployment of the EPA mobile platform; (2) outdoor (CCAR) mobile platform measurements at 10 selected fuzzy points per day in one of two sampling zones (20 total points) over a 2-3 week period; (3) co-located mobile platform (CCAR) and fixed site (SCAPE) measurements at Atlanta sites over a 2-3 week period to intercompare Center measurement methods; and (4) an EPA Chemvol will be deployed during this

period (sampling site to be determined based on electrical service) for collection of ultrafine, fine and coarse particles for detailed chemical analysis and possible distribution to other studies for toxicity testing.

Collaborative Project 3: Ambient PM_{2.5} Estimation Inter-Comparison (Collaborators: SCAPE, Harvard, CCAR, and EPA)

The goal of this effort is to summarize the strengths and limitations of current satellite-driven PM_{2.5} exposure models and CMAQ PM_{2.5} simulations, and to identify directions for future model development and applications in various population-based health effects studies. There are six candidate models to be evaluated: (1) Koutrakis group's mixed effects model, (2) Schwartz group's multi-level model, (3) Chang's spatial downscaler, (4) Liu group's mixed effects model, (5) Sampson's spatiotemporal model, and (6) Russell group's CMAQ PM_{2.5} simulation. We propose to design a modeling domain centered in North Carolina for the 2006 – 2008 time period.

To facilitate model cross-comparison, a common input dataset will be compiled by Liu group and distributed to all participating research teams. A common master modeling grid at 3-km resolution will also be developed by Liu group and shared by all teams. A set of common procedures and statistics will be jointly developed by all participating teams to evaluate model performance. After preliminary results are generated, each team will document their model development in sufficient detail for other teams to reproduce their results. The estimated deliverable of this project will be a manuscript to report evaluation results.

Collaborative Project 4: Measurement Error for Air Pollution Cohort Studies: Application and Comparison of Several Statistical Methods to Georgia Birth Cohort Data (Collaborators: CCAR, Harvard, SCAPE)

This collaborative project brings together existing biostatistics expertise to facilitate the application, extension, and comparison of state-of-the-art statistical methodology to a unified SCAPE dataset. Investigators will collaborate with an ongoing study of maternal exposure to air pollution and fetal growth in Georgia. The project will consider three statistical approaches to account for measurement error arising from spatio-temporal exposure prediction models: (1) parametric/parameter bootstrap (Szpiro, Sheppard); (2) regression calibration and simulation extrapolation (Alexeeff, Coull); and (3) Bayesian modeling (Chang, Waller). These statistical approaches will be developed and applied to examine linear associations between ambient PM_{2.5} concentrations and birth weight among full-term births using Georgia state-wide geocoded birth records for the period 2001-2005.

The collaboration project period is from January 2013-December 2014. Investigators expect to provide measurement error corrected findings to be incorporated in a substantive paper on the risks of air pollution and low birth weight, an area of increasing interest in reproductive epidemiology. Additionally, investigators expect to provide a statistical methodology paper comparing and contrasting several measurement error methods when applied to the Georgia birth cohort data and in related simulation studies.

7. Publications

1. Balachandran S, Pachon JE, Hu Y, Lee D, Mulholland JA, Russell AG. Ensemble-trained source apportionment of fine particulate matter and method uncertainty analysis. *Atmospheric Environment*, in review.
2. Brown MS, Sarnat SE, DeMuth KA, Brown LAS, Whitlock DR, Brown SW, Tolbert PE, Fitzpatrick AM. Residential proximity to a major roadway is associated with features of asthma control in children. *PLoS ONE* 7(5):e37044, 2012.
3. Darrow LA, Hess J, Rogers CA, Tolbert PE, Klein M, Sarnat SE. Ambient pollen concentrations and emergency department visits for asthma and wheeze. *J Allergy Clinical Immunology*, in press.
4. Flanders WD, Klein M, Darrow LA, Strickland MJ, Sarnat SE, Sarnat JA, Waller LA, Winquist A, Tolbert PE. A method to detect residual confounding in spatial and other observational studies. *Epidemiology* 22:823-826, 2011.
5. Goldman GT, Mulholland JA, Russell AG, Gass K, Strickland MJ, Klein M, Tolbert PE. Characterization of ambient air pollution measurement error in a time-series health study using a geostatistical simulation approach. *Atmospheric Environment* 57:101-108, 2012.
6. Pachon JE, Balachandran S, Hu Y, Darrow LA, Sarnat JA, Tolbert PE, Russell AG. Development of outcome-based, multipollutant mobile source indicators. *Journal of Air and Waste Management Association* 62(4):431-442, 2012.
7. Reich BJ, Chang HH, Strickland MJ. Spatial health effects analysis with uncertain residential locations. *Statistical Methods in Medical Research*, 2012, DOI: 10.1177/0962280212447151.
8. Verma V, Rico-Martinez R, Kotra N, King L, Liu J, Snell T, Weber R. Contribution of water-soluble and insoluble components and their hydrophobic/hydrophilic sub-fractions on the ROS-generating potential of fine ambient aerosols. *Environmental Science and Technology*, in review.
9. Winquist A, Klein M, Tolbert P, Sarnat SE. Power estimation using simulations for air pollution time series studies. *Environmental Health*, in review.
10. Winquist A, Klein M, Tolbert P, Flanders WD, Hess J, Sarnat SE. Comparison of emergency department and hospital admissions data for air pollution time series studies. *Environmental Health*, in review.

8. Presentations

1. Waller L, Chang H, Pearce J, Sarnat S, Tolbert P. "Spatial uncertainty estimation and public health data: air pollution epidemiology in Atlanta, Georgia." Oral presentation at the Joint Statistical Meetings. San Diego, California, July 2012.
2. 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, Florida, October 2011.
3. Kotra N, King L, Weber RJ. "Optimization of ROS measurement with Amplex Red." American Association of Aerosol Research Annual Meeting. Orlando, Florida, October 2011.
4. Sarnat J, Sarnat S, Isakov V, Baxter L, Crooks J, Özkaynak H, Mulholland J, Russell A, Kewada P, Tolbert P. Challenges in evaluating alternative exposure metrics in an epidemiologic setting: results from the Atlanta EPA COOP Study. International Society of Exposure Science Annual Meeting. Baltimore, Maryland, October 2011.
5. 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." International Society of Environmental Epidemiology. Barcelona, Spain, September 2011.

6. 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, September 2011.
7. 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, September 2011. *Environmental Health Perspectives* <http://dx.doi.org/10.1289/ehp.isee2011>.

Upcoming Presentations:

1. Darrow LA, Strickland MJ, Klein M, Tolbert PE. "Ambient air pollution and respiratory emergency department visits among children age 0-4 years." Oral presentation at the International Society for Environmental Epidemiology Annual Conference. Columbia, South Carolina, August 2012.
2. Gass K, Strickland MJ, Darrow LA, Klein M, Mulholland JA, Tolbert PE. "Short-term associations between ambient air pollutants and pediatric asthma emergency visits and the role of seasonal interaction." Poster presentation at the International Society for Environmental Epidemiology Annual Conference. Columbia, South Carolina, August 2012.
3. Pearce J. "Application of self-organizing maps to classify the spatiotemporal characteristics of multiple air pollutants." Oral presentation at the International Society for Environmental Epidemiology Annual Conference. Columbia, South Carolina, August 2012.
4. Greenwald R, Li W, Flanders WD, Kewada P, Bergin M, Sarnat JA. "Acute lipid peroxidation in breath and traffic pollution among a panel of commuters in Atlanta." Poster presentation at the International Society for Environmental Epidemiology Annual Conference. Columbia, South Carolina, August 2012.
5. Waller L. "Spatial uncertainty in regression associations." Oral presentation at the International Society for Environmental Epidemiology Annual Conference. Columbia, South Carolina, August 2012.
6. Holmes HA, Maier ML, Friberg M, Balachandran S, Hu Y, Russell AG, Mulholland JA, Sarnat SE, Sarnat JA, Winquist A, Klein M, Tolbert PE. "Development of a Mixtures Characterization Toolkit to estimate air pollution source impacts for time series epidemiologic analysis to investigate air quality and human health associations: Application to a High Biogenic and a High Industrial Emissions Areas." Poster presentation at the 12th International Global Atmospheric Chemistry Open Science Conference. Beijing, China, September 2012.
7. Ivey C, Holmes H, Hu Y, Russell A, Mulholland J. "Hybrid Chemical Transport-Receptor-Geostatistical Modeling for Spatial and Temporal Source Impact Assessment in Health Studies." Platform presentation at the 12th International Global Atmospheric Chemistry Open Science Conference. Beijing, China, September 2012.
8. Verma V, Rico-Martinez R, Kotra N, King L, Liu J, Snell TW, Weber RJ. "Contribution of water-soluble and insoluble species and their hydrophobic/hydrophilic sub-fractions in the toxicological properties of ambient atmospheric aerosols." Poster presentation at the International Global Atmospheric Chemistry Open Science Conference. Beijing, China, September 2012.

9. Balachandran S, Baumann K, Pachon J, Mulholland J, Russell A. "Verification of Fire Weather Forecasts Using PM2.5 Sensitivity Analysis." Poster presentation at the American Association of Aerosol Research Annual Meeting. Minneapolis, Minnesota, October 2012.
10. Balachandran S, Chang H, Mulholland J, Russell A. "A Bayesian – Based Ensemble Technique for Source Apportionment of PM2.5." Platform presentation at the American Association of Aerosol Research Annual Meeting. Minneapolis, Minnesota, October 2012.
11. Chen J, Greenwald R, Johnson, BA, Sarnat JA. "Associations between In-Vehicle Noise and Speciated Pollutant Exposures in a Commuting Microenvironment." Platform presentation at the International Society for Exposure Science Annual Conference. Seattle, Washington, October 2012.
12. Goldman G, Mulholland J, Russell AG, Gass K, Strickland M, Tolbert P. "Characterization of Ambient Air Pollution Measurement Error in a Time-Series Health Study using a Geostatistical Simulation Approach." Platform presentation at the American Association of Aerosol Research Annual Meeting. Minneapolis, Minnesota, October 2012.
13. Greenwald, R, Li W, Yip F, Boehmer T; Sarnat JA. "Increased airway lipid peroxidation following a 2-hour commute in Atlanta." Platform presentation at the International Society for Exposure Science Annual Conference. Seattle, Washington, October 2012.
14. Ivey C, Holmes H, Hu Y, Russell A, Mulholland J. "Improving Particulate Matter Source Apportionment: A Hybrid Approach Utilizing Chemical Transport and Receptor Models with Geostatistical Methods." Poster presentation at the American Association of Aerosol Research Annual Meeting. Minneapolis, Minnesota, October 2012.
15. King L, Verma V, Weber RJ. "Semi-continuous online measurements of reactive oxygen species in the particle and gas phase." Oral presentation at the American Association of Aerosol Research Annual Meeting. Minneapolis, Minnesota, October 2012.
16. Kotra N, Verma V, Liu J, Surratt JD, Edgerton E, Ng NL, Weber RJ. "Performance Evaluation of a Recently Developed Aerosol Chemical Speciation Monitor (ACSM)." Poster presentation at the American Association of Aerosol Research Annual Meeting. Minneapolis, Minnesota, October 2012.
17. Verma V, Kotra N, King L, Liu J, Rico-Martinez R, Snell TW, Weber RJ. "Comparative analysis of the contribution of water-soluble and insoluble PM components in the toxicological properties of ambient atmospheric aerosols." Oral presentation at the American Association of Aerosol Research Annual Meeting. Minneapolis, Minnesota, October 2012.
18. Gass K, Klein M, Flanders WD, Chang H, Sarnat SE, Strickland MJ. "The use of recursive partitioning techniques for identifying complex patterns of multipollutant joint effects." Oral presentation at the International Society of Exposure Science Annual Meeting. Seattle, Washington, October 28-November 1, 2012.

Date of Report: July 31, 2012

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

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Institution(s) of PI(s): ¹Georgia Institute of Technology and ²Emory University, Atlanta, Georgia

Research Category: Air Quality and Air Toxics

Project Period: 08/01/2011 – 7/31/2012

Objective of Research: To provide a chemically comprehensive data set on ambient particle composition at various sites relative to roadway emissions that will be used by other SCAPE Projects. As a part of this effort, our goal is to develop new instruments and analytical methods to quantify concentrations of particle-bound reactive oxygen species (ROS) and the ability of aerosols to catalyze the production of ROS through interactions with antioxidants to determine their sources.

Progress Summary/Accomplishments:

1. **Design and testing of the particle-bound ROS system:** Construction of an ambient ROS instrument to be extensively deployed during SCAPE was completed during this reporting period. The system is based on collection of total (gas + particle) ROS and gas ROS by a mist chamber scrubber. Particle ROS is determined by difference. This method was chosen following tests that showed gas phase ROS concentrations were substantially higher than particle phase (factor of 10 or so), and no suitable coating was found for effective gas denuding. This makes exclusive particle collection systems (e.g., PILS) susceptible to substantial positive bias due to artifacts from gas interferences. In addition to the particle collection system, the ROS analytical method was finalized and was based on a syringe pump system with external mixing vial. This was a change from the original design based on mixing within the mist chamber, which experiments showed led to substantial chemical contamination due to carry-over between successive mist-chamber sample runs. This instrument underwent trial testing in February 2012 and to date has been running for two months as part of the SCAPE Project 1 field sampling. Continued refinements are being made to the instrument.
2. **Assessment of ACSM performance through two ambient inter-comparisons studies:** An Aerodyne Inc. Aerosol Chemical Speciation Monitor (ACSM) was purchased for deployment during SCAPE to measure particle composition. As this is a relatively new instrument, an assessment of the instrument's quantitative performance during two seasons (August 2011, February 2012) was undertaken through comparisons with other online aerosol composition monitors (i.e., PILS-IC for anions/cations, Sunset Labs OCEC for organic matter). The results showed significant discrepancies existed and that these differences change under different sampling conditions (seasons). Part of this is due to the ACSM measuring PM_{1.0}, whereas all other instruments measure PM_{2.5}, as per EPA standards. Other factors are related to variability in the AMS collection/measurement efficiency. The results of these tests suggest that the ACSM data will need to be checked and possibly scaled to other traditional measures of aerosol composition when deployed during SCAPE. A poster on this topic will be presented at the Oct

2012 AAAR conference (Kotra et al., 2012). Selected results are also included in a paper currently under review (Verma et al., 2012).

3. ***Development of a ROS system for quantifying the ability of particles to catalyze ROS production based on the DTT assay:*** Following suggestions from SCAPE's Science Advisory Committee, an additional ROS analytical system was developed and tested. In contrast to the online particle-bound ROS system described in Part 1 above, this instrument was designed for analysis of filter extracts. This acellular assay, in contrast to the particle-bound measurement, quantifies the ability of particles to generate ROS by interactions with antioxidants and is based on the dithiothreitol (DTT) assay. Substantial effort was required to develop and verify a DTT ROS measurement protocol. The method was extended from published approaches to include analysis of methanol filter extracts (i.e., non-water soluble species) and the hydrophobic and hydrophilic organic aerosol sub-fractions of both water and methanol filter extracts. As a preliminary study prior to our intensive SCAPE sampling, filters collected at the Jefferson Street SEARCH site (JST) during January-February 2012 were analyzed. The results are summarized in a manuscript submitted to Environmental Science and Technology (Verma et al., 2012) and will be presented at the October 2012 AAAR conference (Verma et al., 2012).
 - a. Key findings from this study include: Methanol filter extracts, which include water-insoluble and some fraction of the water-soluble aerosol components, have substantially higher PM_{2.5} mass-normalized DTT activity relative to water-soluble extracts. Thus, there are insoluble aerosol species that are DTT active. A correlation analysis indicated that the DTT activity of both extracted fractions were linked to organic species since the methanol extracted DTT activity was correlated with the water-insoluble organic carbon mass fraction, whereas the water-soluble DTT activity was correlated with the water-soluble organic carbon mass fractions. Overall, these results demonstrate the importance of both insoluble and soluble organics as potential aerosol toxic species through their ability to generate ROS. Further identification of possible DTT active organic species responsible for this potential toxicity was assessed through the isolation of hydrophobic and hydrophilic fractions. For both extracts (i.e., methanol or water extracts) the hydrophobic fraction (based on separation via C-18 SPE column) contained compounds that were the most DTT active. This result is consistent with aromatic compounds being exclusively associated with the hydrophobic fraction, which includes PAHs and quinones, both thought to be toxic through their ability to participate in REDOX reactions. For the water-soluble extract, however, additional soluble organics other than aromatics appear to be DTT active either by themselves or associated with some other component (e.g., possible organic-metal complex) since a non-trivial component of the overall DTT activity was associated with hydrophilic organics.
 - b. Since extensive DTT analysis of Project 1 filters is now planned, construction of an automated DTT analytical system was undertaken during this performance period. Equipment has been purchased (see section 4 below) and construction and testing of a DTT-ROS analytical system for high filter sample throughput has been undertaken. It is anticipated that this analysis system will be an integral part of Project 1 and Project 2.
4. ***Start of Project 1 Ambient Sampling Program:*** The main goal of Project 1 is to provide roughly two years of detailed ambient aerosol characterization. An existing Georgia Tech sampling trailer was acquired and retrofitted this spring to serve as our mobile sampling platform. The table below lists the various instruments deployed in the paired sites (fixed site and satellite site). In addition to the preliminary January-February 2012 deployments. Two months of

Project 1 paired measurements have been completed (JST fixed site and trailer co-located at JST; JST fixed site and trailer at Yorkville SEARCH site (YRK)). Preparations for near-road and road-side deployments are underway.

List of instruments installed and operation at the Jefferson Street (JST) fixed site and the mobile trailer site	
Trailer (Satellite) Site	Jefferson Street (Fixed Site)
Met Station	Met Station*
TEOM (PM2.5)	TEOM (PM2.5)
Compact OPC (PM2.5,PM10)	Compact OPC (PM2.5,PM10)
OCEC (Sunset labs)	TC (Sunset labs)*
BC (7 lambda aeth.)	MAAP
WSOC and brown carbon	WSOC and brown carbon
AMS (HR-ToF-MS or ACSM)	AMS (ACSM)*, ACSM at GIT
ROS-DCFH (total, gas)	none
SMPS (size dist.)	SMPS (size dist.)
Ozone	Ozone
NOx	NOx *
High Volume Sampler	High Volume Sampler
2-Channel Filters (PCM)	2-Channel Filters (PCM)
VOC Whole Air Canisters	VOC Whole Air Canisters
*Instruments/data as part of SEARCH network.	

Publication:

1. Verma V, Rico-Martinez R, Kotra N, King L, Liu J, Snell T, Weber R. Contribution of water-soluble and insoluble components and their hydrophobic/hydrophilic sub-fractions on the ROS-generating potential of fine ambient aerosols. *Environmental Science and Technology*, in review.

Presentations:

1. King L, Verma V, Weber RJ. "Semi-continuous online measurements of reactive oxygen species in the particle and gas phase." Oral presentation at the American Association of Aerosol Research Annual Meeting. Minneapolis, Minnesota, October 2012.
2. Kotra N, Verma V, Liu J, Surratt JD, Edgerton E, Ng NL, Weber RJ. "Performance Evaluation of a Recently Developed Aerosol Chemical Speciation Monitor (ACSM)." Poster presentation at the American Association of Aerosol Research Annual Meeting. Minneapolis, Minnesota, October 2012.
3. Verma V, Kotra N, King L, Liu J, Rico-Martinez R, Snell TW, Weber RJ. "Comparative analysis of the contribution of water-soluble and insoluble PM components in the toxicological properties

of ambient atmospheric aerosols.” Oral presentation at the American Association of Aerosol Research Annual Meeting. Minneapolis, Minnesota, October 2012.

4. Verma V, Rico-Martinez R, Kotra N, King L, Liu J, Snell TW, Weber RJ. “Contribution of water-soluble and insoluble species and their hydrophobic/hydrophilic sub-fractions in the toxicological properties of ambient atmospheric aerosols.” Poster presentation at the International Global Atmospheric Chemistry Open Science Conference. Beijing, China, September 2012.
5. 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, Florida, October 2011.
6. Kotra N, King L, Weber RJ. “Optimization of ROS measurement with Amplex Red.” American Association of Aerosol Research Annual Meeting. Orlando, Florida, October 2011.

Future Activities:

1. Continue extensive field measurements with a suite of instruments at paired sites, including JST as the main site and satellite sites (trailer-based measurements) at YRK, near-roadside and roadside. Three weeks of measurements will also be conducted in other cities: St. Louis and Birmingham.
2. Determine the importance of particle-bound ROS (e.g., typical ambient concentrations).
3. Perform extensive measurements of ROS oxidative potential via DTT assay on various filter extracts to determine specific groups of organic species responsible for toxicity. Also, determine if water-soluble redox active metals and hydrophobic organics (e.g., HULIS) synergistically combine to produce more ROS than either species alone based on authentic ambient aerosols.
4. Explore other possible cellular assays on a limited set of filters for comparison with acellular particle-bound ROS and DTT-ROS.
5. Present results at meetings and prepare and publish manuscripts.

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

Relevant Web Sites: www.scape.gatech.edu

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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

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Institution(s) of PI(s): ¹Emory University and ²Georgia Institute of Technology, Atlanta, Georgia;
³Environmental Protection Agency

Research Category: Air Quality and Air Toxics

Project Period: 08/01/2011 – 7/31/2012

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: Based on feedback from SCAPE SAC members as well as the initial results from our Atlanta Commuters Exposure (ACE) Study, we implemented several study design modifications including:

1. The addition of a surface street commute as an alternative control exposure setting to the clinic. All 60 subjects will now conduct a scripted highway, as originally designed, with half of the subjects randomly assigned to either a surface street commute or clinic visit;
2. A seven-day interval between the two exposure periods for each participant, rather than 2 consecutive days of participation; and
3. Dried blood spot collection at the pre- and five post-exposure measurement period for characterizing levels of specific chemokines and cytokines and other biomarkers of inflammatory response.

The following is a summary of specific Project 2 tasks completed during the previous reporting period:

1. *Recruitment.* We received positive response to our Project 2 recruitment efforts. Recruitment began in November 2011 and was completed in May 2012 with a surplus of healthy and asthmatic candidates for potential enrollment. Of these candidates, all are affiliated with either Emory Healthcare or the Rollins School of Public Health as students, employees or research staff and live within close proximity (within 1 - 5 miles) from our laboratory facility.
2. *Pilot sampling and μE characterization.* During February – March, 2012, we conducted pilot sampling aimed at establishing a proof-of-concept demonstration for the Commuter Study sampling platform and characterizing our clinic μE . The clinic, in addition to the surface street in-vehicle, sampling serves as control μE 's for this protocol. Results from the clinic pollutant characterization showed very low concentrations for all of the measured pollutants, including fine PM, black carbon and particle number concentrations (Table 1). (Ambient pollutant concentrations measured concurrently are provided for comparison.) These results validate our selection of the clinic as a low exposure μE to be analyzed in contrast to exposures occurring during highway commutes.

3. *Data collection.* As of August 2012, twenty (of 120 total) sampling sessions have been completed for Project 2, which includes completed protocols for ten subjects. Each subject successfully participated for the entire two-day study protocol. Ten sampling sessions have been highway commutes, four surface street commutes, and six clinics, with each subject completing a highway commute and randomly assigned either a clinic or surface street μE . Our initial QAQC review of the health and pollutant measurements indicate satisfactory data capture and completeness. For all the measured parameters, data have been collected above the designated 90% data capture objective. Project 2 staff will conduct a month-long QAQC characterization that will begin in August 2012 (detailed below). We anticipate that Project 2 data collection will continue through fall 2013.

Presentations:

1. Chen J, Greenwald R, Johnson, BA, Sarnat JA. "Associations between In-Vehicle Noise and Speciated Pollutant Exposures in a Commuting Microenvironment." Platform presentation at the International Society for Exposure Science Annual Conference. Seattle, Washington, October 2012.
2. Greenwald, R, Li W, Yip F, Boehmer T; Sarnat JA. "Increased airway lipid peroxidation following a 2-hour commute in Atlanta." Platform presentation at the International Society for Exposure Science Annual Conference. Seattle, Washington, October 2012.
3. Greenwald R, Li W, Flanders WD, Kewada P, Bergin M, Sarnat JA. "Acute lipid peroxidation in breath and traffic pollution among a panel of commuters in Atlanta." Poster presentation at the International Society for Environmental Epidemiology Annual Conference. Columbia, South Carolina, August 2012.
4. 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, September 2011.

Future Activities: For four weeks beginning in August 2012, Project 2 staff from Emory and Georgia Tech will conduct extensive sampler collocations with the aim of characterizing sampler accuracy and precision for all the measured pollutants. The sampling platform will be deployed at a near roadway location. During this time no subjects will be enrolled in the study with data collection continuing upon completion of the collocations.

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

Relevant Web Sites: www.scape.gatech.edu

Table 1. Pilot study measurements of select pollutant parameters in the Emory Clinic microenvironment and at an adjacent ambient location.

Clinic						
Pollutant	# Sessions	N (min)	Mean	SD	Median	Max
PM2.5 (ug/m3)	8	1,045	1.2	0.6	1.0	2.6
BC (ug/m3)	14	3,857	0.60	0.45	0.43	1.83
PNC (#/cc)	14	1,209	2062	2908	1296	12005
Ambient (8th Floor Terrace)						
Pollutant	# Sessions	N (min)	Mean	SD	Median	Max
PM2.5 (ug/m3)	3	425	16.1	2.6	15.2	19.1
BC (ug/m3)	4	523	0.81	0.41	0.96	1.11
PNC (#/cc)	5	470	16863	8440	17734	26553

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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

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Institution(s) of PI(s): ¹Emory University and ²Georgia Institute of Technology, Atlanta, Georgia (Collaborating Institution: ³Kaiser 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 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 1.7 million Georgia birth records that have been geocoded to the Census block level and linked with pediatric emergency department visits by staff at the Georgia Department of Human Resources. Using this statewide birth cohort, we are investigating acute effects of air pollution mixtures on respiratory health outcomes and ear infections in children, and we are assessing whether children who were born premature or low birth weight are more sensitive to ambient air pollutant concentrations than their counterparts. Further, we are using 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 1,705,130 individual-level birth records from 1994-2006 for Georgia. We have 8,252,996 individual-level emergency department visits among children age 0-18 years during 2002-2010 for Georgia and we have 2,458,950 individual-level hospital records for children age 0-18 years during 1999-2010 for Georgia. We have linked the birth record data with Census 2000 data to bring in a variety of socioeconomic variable that can be used in the analyses.

The birth data and the ED/hospitalization data are linked via a unique longitudinal ID, and we have devoted significant effort to examine the quality of this linkage. Although the ID should be unique (it is based on letters from the first name, last name, birth date, and sex), for 18,921 (1.1%) of the birth records this longitudinal ID is not unique. For 6,880 records this is because twins had similar first names. The remaining 12,041 instances appear to be unrelated individuals born on the same day with similar names. We then linked these data with the ED data based on longitudinal ID. When an ED record linked with multiple birth records we used ZIP code to determine which record to link to; if the zip code was the same (as in the case for twins) then we randomly selected which twin to assign that ED visit to. In total 3,700,003 ED records link with a birth record. We evaluated whether there were inconsistencies in

the longitudinal ID that might have caused a problem with the linkage (e.g., a missing apostrophe, such as ONeill instead of O’Neill, would cause all of the characters to be shifted to the right one spot) but did not find any major problems. There were several potential links that were suggestive but not definitive (e.g., the longitudinal ID matched on all characters save for one), but ultimately we chose not to create many new linkages based on longitudinal IDs that did not match.

Significant progress has also been made on the development of satellite-derived estimates of PM_{2.5} at 10 km resolution in Georgia, with calibration to the fixed site monitors using a Bayesian statistical model. Multiple years of satellite remote sensing data, gridded meteorological and land use variables have been collected and processed as input data to the Bayesian model. Work is ongoing to estimate biomass burning events using high resolution remote sensing data from multiple NASA satellites. Through collaboration with Georgia EPD and the Tall Timbers Research Station in Florida, we have collected ground measurements of prescribed burn areas in southwestern and southern Georgia. Customized satellite data processing procedures are being developed to better extract burn scar signals.

Analytic datasets have been prepared, and an abstract on the association between outdoor pollutant concentrations (population-weighted average from fixed site monitors) has been accepted for the August 2012 International Society for Environmental Epidemiology conference (Gass et al., 2012). We have also been working on classification and regression tree approaches for examining complex joint effects of mixtures, which was presented at the annual CLARC meeting and has also been accepted as a presentation at the October 2012 International Society for Exposure Science conference (Gass et al., 2012). Work on the effects of measurement error on the risk ratio estimates from time-series studies has been ongoing, with a new publication appearing in *Atmospheric Environment* (Goldman et al., 2012) and a follow-up paper that is in draft form that will be submitted later this summer.

Publications:

1. Goldman GT, Mulholland JA, Russell AG, Gass K, Strickland MJ, Klein M, Tolbert PE. Characterization of ambient air pollution measurement error in a time-series health study using a geostatistical simulation approach. *Atmospheric Environment* 57:101-108, 2012.
2. Reich BJ, Chang HH, Strickland MJ. Spatial health effects analysis with uncertain residential locations. *Statistical Methods in Medical Research*, 2012, DOI: 10.1177/0962280212447151.

Presentations:

1. Gass K, Klein M, Flanders WD, Chang H, Sarnat SE, Strickland MJ. “The use of recursive partitioning techniques for identifying complex patterns of multipollutant joint effects.” Oral presentation at the International Society of Exposure Science Annual Meeting. Seattle, Washington, October 28-November 1, 2012.
2. Gass K, Strickland MJ, Darrow LA, Klein M, Mulholland JA, Tolbert PE. “Short-term associations between ambient air pollutants and pediatric asthma emergency visits and the role of seasonal interaction.” Poster presentation at the International Society for Environmental Epidemiology Annual Conference. Columbia, South Carolina, August 2012.

Future Activities: The subcontract with Kaiser Permanente begins in 2013, and this fall we will begin working with them on development of that birth cohort. Various epidemiologic analyses of the statewide data will be conducted, with some analyses being more or less “conventional” (e.g., single pollutant and two-pollutant models) and others focusing on innovative approaches for characterizing mixtures (e.g., regression trees and/or cluster analyses). Continued work on measurement error in time-

series studies will be conducted, with a view towards extending our current work (which focused on pollutants one-at-a-time) to the situation where there are two pollutants in the model.

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

Date of Report: July 31, 2012

EPA Agreement Number: R834799

Center Name & Internal Number: Southeastern Center for Air Pollution and Epidemiology

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

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Institution(s) of PI(s): ¹Emory University and ²Georgia Institute of Technology, Atlanta, Georgia

Research Category: Air Quality and Air Toxics

Project Period: 08/01/2011 – 7/31/2012

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 (Atlanta, GA; Birmingham, AL; Dallas, TX; Pittsburgh, PA; St. Louis, IL-MO) 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 hospital admissions (HAs).

Progress Summary/Accomplishments: During the current reporting period (8/1/2011-7/31/2012), work on Project 4 has focused on data collection and management activities, epidemiologic analyses in Atlanta and St. Louis, and development of approaches to studying air pollution mixtures. **Air quality data.** Air quality monitoring data for the relevant study periods in each of the five cities were acquired by the Air Quality Core from state and federal monitoring networks, and data from local intensive monitoring programs [e.g., the SouthEastern Aerosol Research and Characterization (SEARCH) network]. Data were processed, data formats and variable labeling approaches were standardized, and the approach for computing population-weighted averages for all cities was finalized. Data for Atlanta (1993-2009) are final and have been posted to the SCAPE private site for sharing among Center investigators. Data for the other cities are being finalized and will be available by August 2012. As described by the AQ Core, work has also commenced on developing the proposed mixture characterization metrics, including source-resolved PM metrics in each city. **Health outcome data.** Progress on ED visit and HA data collection in each of the five cities was also made. For **Atlanta**, existing ED visit and HA databases covering the 1993-2004 time period were extended through 2009 with data acquired from the Georgia Hospital Association and processing of these data was completed over the past year. For **Birmingham**, hospital recruitment activities were initiated in September 2011. Sixteen acute care hospitals with emergency departments in the 7-county Birmingham study area were approached for participation to provide ED visit and HA data for the 1999-2010 time period. To date, 12 of 16 hospitals have agreed to participate and corresponding data use agreements or hospital-specific Institutional Review Board protocols have been approved; of these, 7 hospitals have provided full data sets and 4 hospitals have provided partial data to Emory investigators. Processing is underway for these data sets. Recruitment of the 4 remaining (non-participating) hospitals is anticipated to continue into fall

2012. For **Dallas**, a data use agreement between Emory and the Dallas-Fort Worth Hospital Council Foundation was finalized and data were transferred to Emory investigators in fall 2011. These data are currently being processed and a final analytic dataset is anticipated by August 2012. The feasibility of including data from the **Pittsburgh** ARIES study in the current project was assessed over the past year. University of Pittsburgh investigators have begun setting up data sharing procedures, such as revision of data use agreements with Pittsburgh hospitals to include Emory investigators. Data sharing is anticipated to take place by fall 2012. For **St. Louis, MO-IL**, all ED visit, hospitalization, and AQ monitoring data were acquired previously and data analyses are continuing. **Other data.** To compare population and other characteristics among the 5 cities, data on socioeconomic measures and race/ethnicity were acquired from Census 2000 at the ZIP code tabulation area level. The Townsend deprivation score was calculated as a composite measure of relative socioeconomic status. Sources for crime data are also being considered. **Data analyses.** A number of analyses using these data were conducted over the project period: 1) Atlanta ED visit data for 2005-2009 were examined in preliminary epidemiologic time-series analyses with air pollution and results compared to analyses of 1998-2004 data; 2) ambient pollen concentrations were examined in association with asthma/wheeze ED visits in Atlanta; 3) daily ZIP code level measures of ambient PM and gaseous pollutants were applied in epidemiologic analyses of the Atlanta ED data and epidemiologic results among multiple exposure metrics were compared; 4) an extensive power estimation analysis for air pollution time-series studies was conducted using a subset of our observed Atlanta data, with a comparison of results using simulations and standard power software; 5) with the Biostatistics Core, work was begun on applying self-organizing maps (SOMs) and classification and regression trees (C&RT) to our Atlanta data as approaches for detecting and analyzing air pollution mixtures; 6) in St. Louis, we conducted a comparison of ED visit and HA data for use in air pollution time-series studies; and 7) St. Louis source apportionment outputs were finalized and were applied to preliminary epidemiologic analyses, comparing results among multiple source apportionment approaches.

Publications: These analyses have led to several manuscripts published and in preparation. In this reporting period, two manuscripts were published or have been accepted (Darrow et al., in press; Brown et al., 2012) and two manuscripts are in review (Winqvist et al., in review; Winqvist et al., in review). Several manuscripts are in preparation based on the exposure metrics work discussed above, including: 1) a comparison of modeling approaches for spatiotemporal exposure assessment of multiple air pollutants in Atlanta; 2) an assessment of these spatiotemporal metrics of air pollution exposure in Atlanta epidemiologic time-series analyses, and 3) assessment of spatiotemporally-resolved air exchange rate as a modifier of acute air pollution-related morbidity.

1. Brown MS, Sarnat SE, DeMuth KA, Brown LAS, Whitlock DR, Brown SW, Tolbert PE, Fitzpatrick AM. Residential proximity to a major roadway is associated with features of asthma control in children. *PLoS ONE* 7(5):e37044, 2012.
2. Darrow LA, Hess J, Rogers CA, Tolbert PE, Klein M, Sarnat SE. Ambient pollen concentrations and emergency department visits for asthma and wheeze. In press at *Journal of Allergy and Clinical Immunology*.
3. Winqvist A, Klein M, Tolbert P, Sarnat SE. Power estimation using simulations in air pollution time-series studies. In review at *Environmental Health*.
4. Winqvist A, Klein M, Tolbert P, Flanders WD, Hess J, Sarnat SE. Comparison of emergency department and hospital admissions data for air pollution time-series studies. In review at *Environmental Health*.

Presentations: Data and concepts from our exposure metrics work were presented at ISES 2011 (Sarnat et al., 2011) and will also be presented at the 2012 Joint Statistical Meetings as part of a broader presentation on spatial uncertainty estimation through the Biostatistics Core (Waller et al., 2012). Preliminary epidemiologic results using St. Louis source apportionment outputs were presented at the 2011 International Society for Environmental Epidemiology conference (Sarnat et al., 2011). We have also submitted an abstract to present our work on C&RT at the 2012 International Society of Exposure Science conference as part of a symposium on “Multipollutant exposure metrics and their application to air pollution epidemiological studies” (Gass et al., 2012).

1. Gass K, Klein M, Flanders WD, Chang H, Sarnat SE, Strickland MJ. “The use of recursive partitioning techniques for identifying complex patterns of multipollutant joint effects.” Oral presentation at the International Society of Exposure Science Annual Meeting. Seattle, Washington, October 28-November 1, 2012.
2. Waller L. “Spatial uncertainty in regression associations.” Oral presentation at the International Society for Environmental Epidemiology Annual Conference. Columbia, South Carolina, August 2012.
3. Sarnat J, Sarnat S, Isakov V, Baxter L, Crooks J, Özkaynak H, Mulholland J, Russell A, Kewada P, Tolbert P. Challenges in evaluating alternative exposure metrics in an epidemiologic setting: results from the Atlanta EPA COOP Study. International Society of Exposure Science Annual Meeting. Baltimore, Maryland, October 2011.
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, September 2011. *Environmental Health Perspectives* <http://dx.doi.org/10.1289/ehp.isee2011>.

Future Activities: Over the coming year, we anticipate completing our data collection and data processing activities, particularly the health data for Birmingham, Dallas, and Pittsburgh. Manuscript preparation will begin and/or continue for analyses conducted over the past year. New analyses are also planned, in particular: 1) epidemiologic analyses of Birmingham, Dallas, and Pittsburgh data; 2) our work on SOMs and possibly C&RT will be extended to other cities; 3) source apportionment outputs for other cities (e.g., Atlanta and Dallas) will be applied in epidemiologic analyses; 4) the Census 2000 and possibly crime data will be assessed and compared among the five study areas; and 5) approaches for comparing epidemiologic results among the five cities will be evaluated.

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 Sites: www.scape.gatech.edu

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Center Name: Southeastern Center for Air Pollution and Epidemiology

Project Title: Air Quality Core

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Research Category: Air Quality and Air Toxics

Project Period: 08/01/2011 – 7/31/2012

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 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 monitoring networks 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. A range of both source- and receptor-oriented air quality models, regression approaches, and hybrid methods are being developed. 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 the 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 is continuing the development of an MC Toolkit through data collection and development of methods and the application of methods for data analysis, including source apportionment. A password-protected website is used to store data and share data between the research teams.

We have applied various receptor modeling approaches (CMB-based, PMF, ensemble) to Atlanta, Dallas and St. Louis. The ensemble approach application to St. Louis involved using both traditional data (e.g., typically available from CSN network monitors), as well as organic molecular marker data available for a limited period. The application of the ensemble method to the period where the molecular marker data were available has been completed, and a manuscript is in draft form describing that work. These results were supplied to the health effects researchers for use in their epidemiologic analyses. We are now extending those results to the full period. Using the extensive data available from the Atlanta SEARCH site, the ensemble approach was also utilized to characterize uncertainty in the various methods used in source apportionment analyses. This work was described in a manuscript submitted for publication and, following favorable reviews, is now in revision (Balachandran et al., 2012).

Work continues to better understand how air quality observations can best be used to estimate population exposures and how exposure measurement error can impact epidemiologic results. Following on work described in last year's progress report, a simulation study was conducted using a spatio-temporal model to generate ambient air pollutant fields for Atlanta for six years. The simulation was designed to accurately capture the statistical distributions of measurement data, particularly the temporal and spatial autocorrelations. The resulting fields are used to quantify the amount and type of bias and error associated with the availability of ambient concentration data. A manuscript describing this work was recently accepted for publication (Goldman et al., 2012).

Publications:

1. Balachandran S, Pachon JE, Hu Y, Lee D, Mulholland JA, Russell AG. Ensemble-trained source apportionment of fine particulate matter and method uncertainty analysis. *Atmospheric Environment*, in review.
2. Goldman GT, Mulholland JA, Russell AG, Gass K, Strickland MJ, Klein M, Tolbert PE. Characterization of ambient air pollution measurement error in a time-series health study using a geostatistical simulation approach. *Atmospheric Environment* 57:101-108, 2012.
3. Pachon JE, Balachandran S, Hu Y, Darrow LA, Sarnat JA, Tolbert PE, Russell AG. Development of outcome-based, multipollutant mobile source indicators. *Journal of Air and Waste Management Association* 62(4):431-442, 2012.

Presentations:

1. Balachandran S, Baumann K, Pachon J, Mulholland J, Russell A. "Verification of Fire Weather Forecasts Using PM2.5 Sensitivity Analysis." Poster presentation at the American Association of Aerosol Research Annual Meeting. Minneapolis, Minnesota, October 2012.
2. Goldman G, Mulholland J, Russell AG, Gass K, Strickland M, Tolbert P. "Characterization of Ambient Air Pollution Measurement Error in a Time-Series Health Study using a Geostatistical Simulation Approach." Platform presentation at the American Association of Aerosol Research Annual Meeting. Minneapolis, Minnesota, October 2012.
3. Ivey C, Holmes H, Hu Y, Russell A, Mulholland J. "Improving Particulate Matter Source Apportionment: A Hybrid Approach Utilizing Chemical Transport and Receptor Models with Geostatistical Methods." Poster presentation at the American Association of Aerosol Research Annual Meeting. Minneapolis, Minnesota, October 2012.
4. Holmes HA, Maier ML, Friberg M, Balachandran S, Hu Y, Russell AG, Mulholland JA, Sarnat SE, Sarnat JA, Winquist A, Klein M, Tolbert PE. "Development of a Mixtures Characterization Toolkit to estimate air pollution source impacts for time series epidemiologic analysis to investigate air quality and human health associations: Application to a High Biogenic and a High Industrial Emissions Areas." Poster presentation at the 12th International Global Atmospheric Chemistry Open Science Conference. Beijing, China, September 2012.
5. Ivey C, Holmes H, Hu Y, Russell A, Mulholland J. "Hybrid Chemical Transport-Receptor-Geostatistical Modeling for Spatial and Temporal Source Impact Assessment in Health Studies." Platform presentation at the 12th International Global Atmospheric Chemistry Open Science Conference. Beijing, China, September 2012.

Future Activities: Plans for 2012-2013 include continued collection of relevant air quality-related data (e.g., air quality and emissions data), application of the various source apportionment approaches, and further application of the hybrid CTM-CMB approach. We are currently obtaining CMAQ data for the continental U.S. for 2001-2008 to provide increased spatial information not available from monitors and

are working on an approach to use these fields to provide spatially-resolved source impact estimates for major sources in an efficient fashion.

Supplemental Keywords: air quality, chemical transport modeling, receptor modeling, exposure measurement error

Relevant Web Sites: www.scape.gatech.edu

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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); Howard Chang, PhD (howard.chang@emory.edu); Mitchel Klein, PhD (mklein@emory.edu)

Institution(s) of PI(s): Emory University

Research Category: Air Quality and Air Toxics

Project Period: 08/01/2011 – 7/31/2012

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 C&RT, 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:

1. Coordinated the first CLARC Biostatistics Workshop with other CLARC Biostatistics Cores. Provided forum for discussion of analytic issues across CLARCs.
2. Continued work on methods for the identification of model mis-specification, particularly due to confounding. A publication relating to this issue appeared in press (Flanders et al. 2011)
3. Continued collaboration with Center investigators regarding the relative impact of Berkson and classical measurement error in exposure on estimated health effects (in particular, within a Poisson regression model) as well as measurement error that arises from uncertain geocoding locations. Two publications appeared in the literature (Goldman et al., 2012, Reich et al., 2012,).
4. Initial investigations into the use of classification and regression tree (C&RT) and self-organizing map (SOM) approaches for investigating pollutant mixtures. Two posters of preliminary work were presented at the annual CLARC meeting and both are being developed into manuscripts.
5. Initial collaborations regarding the assessment of statistical measurement error in the use of satellite remote-sensing measurements of air quality. This CLARC collaboration was conceptualized at the Biostatistics Workshop and a formal proposal was prepared.
6. Provided continued support for Center Projects with respect to design issues and development of analytic plans for data analysis.

Publications:

1. Flanders WD, Klein M, Darrow LA, Strickland MJ, Sarnat SE, Sarnat JA, Waller LA, Winquist A, Tolbert PE. A method to detect residual confounding in spatial and other observational studies. *Epidemiology* 22:823-826, 2011.
2. Goldman GT, Mulholland JA, Russell AG, Gass K, Strickland MJ, Klein M, Tolbert PE. Characterization of ambient air pollution measurement error in a time-series health study using a geostatistical simulation approach. *Atmospheric Environment* 57:101-108, 2012.
3. Reich BJ, Chang HH, Strickland MJ. Spatial health effects analysis with uncertain residential locations. *Statistical Methods in Medical Research*, 2012, DOI: 10.1177/0962280212447151.

Presentations:

1. Balachandran S, Chang H, Mulholland J, Russell A. "A Bayesian – Based Ensemble Technique for Source Apportionment of PM_{2.5}." Platform presentation at the American Association of Aerosol Research Annual Meeting. Minneapolis, Minnesota, October 2012.
2. Holmes HA, Maier ML, Friberg M, Balachandran S, Hu Y, Russell AG, Mulholland JA, Sarnat SE, Sarnat JA, Winquist A, Klein M, Tolbert PE. "Development of a Mixtures Characterization Toolkit to estimate air pollution source impacts for time series epidemiologic analysis to investigate air quality and human health associations: Application to a High Biogenic and a High Industrial Emissions Areas." Poster presentation at the 12th International Global Atmospheric Chemistry Open Science Conference. Beijing, China, September 2012.
3. Darrow LA, Strickland MJ, Klein M, Tolbert PE. "Ambient air pollution and respiratory emergency department visits among children age 0-4 years." Oral presentation at the International Society for Environmental Epidemiology Annual Conference. Columbia, South Carolina, August 2012.
4. Gass K, Strickland MJ, Darrow LA, Klein M, Mulholland JA, Tolbert PE. "Short-Term Associations between Ambient Air Pollutants and Pediatric Asthma Emergency Visits and the Role of Seasonal Interaction." Poster presentation at the International Society for Environmental Epidemiology Annual Conference. Columbia, South Carolina, August 2012.
5. Pearce J. "Application of self-organizing maps to classify the spatiotemporal characteristics of multiple air pollutants." Oral presentation at the International Society for Environmental Epidemiology Annual Conference. Columbia, South Carolina, August 2012.
6. Greenwald R, Li W, Flanders WD, Kewada P, Bergin M, Sarnat JA. "Acute lipid peroxidation in breath and traffic pollution among a panel of commuters in Atlanta." Poster presentation at the International Society for Environmental Epidemiology Annual Conference. Columbia, South Carolina, August 2012.
7. Waller LA. "Spatial uncertainty in regression associations" Oral presentation at the International Society for Environmental Epidemiology Annual Conference. Columbia, South Carolina, August 2012.
8. Waller L, Chang H, Pearce J, Sarnat S, Tolbert P. "Spatial uncertainty estimation and public health data: air pollution epidemiology in Atlanta, Georgia." Oral presentation at the Joint Statistical Meetings. San Diego, California, July 2012.
9. 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." International Society of Environmental Epidemiology. Barcelona, Spain, September 2011.
10. 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, September 2011.
11. 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, September 2011.

Future Activities: Biostatistics Core members are involved in analytic aspects of all Center Projects. In addition to the scheduled presentations listed above, Core collaborations for 2012-2013 include:

1. Extension of classification and regression tree (C&RT) and self-organizing map (SOM) techniques for characterizing air pollution mixtures (Core members Klein, Waller, Pearce).
2. Collaborations regarding characterization of measurement error in remotely sensed and modeled measures of air quality (Core member Chang).
3. Continuing collaborations regarding the detection and adjustment for confounding in health effect models (Core members Flanders, Klein, Waller, and Chang).
4. Continuing collaborations on the impact of measurement error on estimates of health effects of air pollution (Core members Flanders, Klein, Waller, and Chang).
5. Continuing collaborations on the design and analysis of exposure measurements in Projects 1 and 2.
6. Continuing collaborations on the design and analysis of health effect studies in Projects 3 and 4.

Supplemental Keywords: biostatistics, data analysis, study design

Relevant Web Sites: www.scape.gatech.edu