Fresno Asthmatic Children's Environment Study (FACES)

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by

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Glossary

$(NH_4)_2SO_4$	ammonium sulfate
24-hr	24-hour
AADT	total annual average daily traffic volumes
ACCEPTABLE	at least 2 acceptable FEV1 measurements
ACE	acenapthene
ACY	acenaphthylene
AG	Silver
AGFG	Agricultural fungi
AIC	Akaike Information Criterion
AL	Aluminum
ALTE	Alternaria
AMB	Ambrosia
ANT	anthracene
ARB	California Air Resources Board
ART	Artemesia
AS	Arsenic
ASP	Aspergillus/Penicillium
ATS	American Thoracic Study
AU	Gold
BA	Barium
BAA	benz(a)anthracene
BAA	Benz(a)anthracene
BAM	beta-attenuation mass monitor
BAP	benzo(a)pyrene
BBF	benzo(b)fluoranthene
BC	black carbon
BET	Betulaceae
BGP	benzo(ghi)perylene
BIC	Bayesian Information criteria
BKF	benzo(k)fluoranthene
BlaG	Cockroach allergen
BR	Bromine
b_{sp}	light scattering coefficient of particles
BSVT	Burkard Seven Day Recording Volumetric Spore Trap
CA	Calcium
CalTrans	California Department of Transportation
canF	dog allergen
CD	Cadmium
CEL	Celtis
CHA	Chenopodiaceae/Amaranth
CHR	chrysene
CHS	Children's Health Study
CL	Chlorine
CLAD	Cladosporium
CO	carbon monoxide
Co	Cobalt

COPD	chronic obstructive pulmonary disease
Cr	Chromium
CRY	Chrysene
Cu	Copper
CUT	Cupressaceae and Sequoia
CV	coefficient of variation
DAG	directed acyclic graph
DAIB	"Data Adjusted for Instrument Bias"
DBA	dibenz(a,h)anthracene
DEP	diesel exhaust particles
DIDTEST	attempted an A.M. EasyOne session
DLG	USGS Digital Line Graph
DNA	deoxyribonucleic acid
DR	double robust estimator (MSM)
DRG	diagnostic related group
DRI	Desert Research Instititute
DSA	deletion/substitution/addition algorithm
EC	elemental carbon
EO	EasyOne®
ESRI	Environmental Systems Research Institute, Inc.
ETA	experimental treatment assumption
ETS	Environmental Tobacco Smoke (also called SHS in this report)
EU	endotoxin units
FACES	Fresno Asthmatic Children's Environment Study
Fe	iron
FEF_{25-75}	forced expiratory flow between 25% and 75% of vital capacity
FEF_{75}	forced expiratory flow at 75% of vital capacity
felD	cat allergen
FEV_1	forced expiratory volume in 1 second
FLT	fluoranthene
FLU	fluorene
FO	field office
FRM	federal reference method
FUSD	Fresno Unified School District
FVC	forced vital capacity
Ga	Gallium
G-comp	g-computation estimator (MSM)
GINA	Global Initiative for Asthma
GIS	geographic information systems
grains/m^3	grains per cubic meter
GST	glutathione s - transferase
HDV	heavy-duty vehicle fraction of traffic
Hg	Mercury
HRMSM	history restricted marginal structural models
HVAC	Heating, ventilation and air conditioning
I/O	indoor/outdoor ratio
IC	ion chromatography
ICP	indeno(1,2,3-cd)pyrene

ICS	inhaled corticosteroids
IDSW	inverse distance-squared weighted
IDWT	inverse distance-weighted traffic
IDWTH	IDWT multiplied by HDV
IgE	immunoglobin E
IL	interleukin
In	Indium
INFγ	interferon-gamma
IPTW	inverse probability of treatment weight estimator (MSM)
IQR	interquartile range
ISAAC	International Study of Asthma and Allergies in Childhood
IUATLD	International Union Against Tuberculosis and Lung Disease
JUG	Average Carya and Juglans
K	Potassium
KLARE	Kineteic Limulus Assay with Resistant-parallel-line Estimation
KP	Potassium
La	Lanthanum
LA	Lanthanum
LAL	Limulus amebocyte lysate
LDV	light-duty vehicle fraction of traffic
LIQ	Liquidambar
LPM	liters per minute
MEDUSE	rescue medication use in 1-hour before A.M. test (see Rmed)
MEMS	Microenvironmental Exposure Monitoring System
MG	Magnesium (qualitative only)
$\mu g/m^3$	micrograms per cubic meter
µL	microliters
µM	micrometers
MMAD	mass median aerodynamic diameter
Mn	manganese
Mo	Molybdenum
MOR	Morus
MSM	marginal structural models
NA	Sodium (qualitative only)
NAP	naphthalene
NAPCC	Napthalene from Chemcombs
NAPST	Napthalene concentration from Sorbent Tubes
NASCAUM	Northeast States for Coordinated Air Use Management
NHLBI	National Heart Lung and Blood Institute
NHS	Nurses Health Study
Ni	Nickel
NO	nitrogen oxide
NO_3	nitrate
NO_x	oxides of nitrogen
NO_y	Reactive nitrogen
NP	particle number
NRC	National Research Council
NUC	no unmeasured confounding assumption

O_3	ozone
OC	organic carbon
OLE	Olea, Fraxinus, and Ligustrum
OS	oxidative stress
P	Phosphorous
PAH	polycyclic aromatic hydrocarbon
Pb	Lead
Pd	Palladium
PEFR	peak expiratory flow rate
PH	Phosphorous
PHE	phenanthrene
PIS	Pistacea
PLA	Platanus
PM	particulate matter
PM_1	particulate matter with a mass median aerodynamic of 1 micron or less
PM_{10}	particulate matter with a mass median aerodynamic of 10 microns or less
$PM_{2.5-10}$	particulate matter with a mass median aerodynamic between 2.5 and 10 microns (coarse fraction)
$PM_{2.5}$	particulate matter with a mass median aerodynamic of 2.5 microns or less
PMPAH	particulate matter polycyclic aromatic hydrocarbons
POA	Poaceae (including Cerealea)
PPAH	particle-bound polycyclic aromatic hydrocarbons
ppb	parts per billion
pphm	parts per hundred million
ppm	parts per million
pRmed	rescue medication use 1 hour before evening sesion
PTEAM	Particle Total Exposure Assessment Methodology
PYR	pyrene
QA	quality assurance
QC	quality control
QUE	Quercus
Rb	Rubidium
RH	relative humidity
RMed	rescue medication use in 1-hour before A.M. test
ROS	reactive oxygen species
S	Sulfur
SAS	Statistical Analysis System software
Sb	Antimony
Se	Selenium
SHS	secondhand smoke
Si	silicon
SJV	San Joaquin Valley
SJVAQMD	San Joaquin Valley Air Quality Management District
Sn	Tin
SO_2	sulfur dioxide
SO_4	sulfate
SOPs	standard operating procedures
spores/m^3	spores per cubic meter

Sr	Strontium
SRA	sequential randomization assumption
STI	Sonoma Technology, Inc.
SU	Sulfur
T	temperature
TAMN	TeleAtlas MultiNet™ USA
TAP	triethylamine phosphate
TC	total carbon
Ti	Titanium
Tl	Thallium
TNF-α	tumor necrosis factor alpha
TOP	Total Pollen Grain
TOTFS	Total fungal spores
U	Uranium
ULZ	Ulmus/Zelkova
UR	Uranium
VA	Vanadium
VOC	volatile organic carbons
WD	wind direction
WHO	World Health Organization
WIM	weigh-in-motion sensors
WS	wind speed
XAD	polystyrene-divinyl benzene
Y	Yttrium
YT	Yttrium
Zn	Zinc
Zr	Zirconium

1. EXECUTIVE SUMMARY

1.1 PROJECT OVERVIEW

1.1.1 Background and Public Health Significance

Children, especially children with asthma, have long been recognized by air pollution control agencies as a population at particular risk of suffering the adverse effects of air pollution exposure. While there remains debate as to whether air pollution alone can *cause* asthma, there is no debate regarding the role short-term exposures to various air pollutants have in the exacerbation of asthma in people diagnosed with the disease. Among the pollutants that have received the most attention in recent years is particulate matter (PM). However, there is a paucity of data on which components of the complex PM mixture produce these effects and no data on the relationship between the responses to short-term-exposures and the long-term progression of asthma in children. Furthermore, few studies have specifically looked at the effects of PM in the context of the complex exposures people experience outdoors and indoors – exposures that include not only other pollutants, but biologically active agents such as endotoxin, fungal spores, pollens, and common indoor allergens.

Asthma is an airway disease, which is characterized clinically by reversible airway obstruction, non-specific airway hyperresponsiveness, and mucus secretion. Particulate and gaseous air pollutants contribute significantly to asthma burden by causing acute asthma-related symptoms and short-term declines in lung function. However, an effective public health policy to protect asthmatics from the acute adverse effects of air pollution, especially PM, has not yet been achieved due to insufficient information on which components of PM or other pollutants, at what concentrations and in what combinations are associated with which observed effects. Evidence is mounting that a key mechanism by which air pollutants and other airborne agents can adversely impact health is through the promotion or induction of oxidative stress and/or inflammation. Because a cardinal feature of asthma is persistent airway inflammation, it is biologically plausible that repeated exposures to oxidant pollutants, including components of PM, can lead to enhanced inflammation and more severe asthma. A better understanding is needed of the characteristics, both biological and exposure, that define subgroups of persons with asthma who are more/less acutely responsive to different pollutants, or who experience larger chronic effects associated with long-term exposures.

The Fresno Asthmatic Children's Environment Study (FACES) is focused on the determination of the effects of particulate matter (PM) air pollution, in combination with other ambient air pollutants and bioaerosols, on the natural history of asthma in young children who reside in Fresno, California. This community is notable for a high prevalence of asthma among an ethnically diverse population, and for high levels of ambient air pollution, especially PM, making it an appropriate location to address questions of air pollution's impact on this vulnerable population. A unique opportunity to address critical questions related to air pollution's effects on the long-term progression of asthma was presented by the U.S. EPA's enhanced air quality monitoring platform ("Supersite") in Fresno. This is the first, and to our knowledge, the only

study to date to investigate directly the relationship between adverse short-term air pollution health effects and the long-term progress of asthma. Consideration of all particle effects is in the context of the complex and seasonal patterns of air pollution mixtures, including bioaerosols, to which children are exposed.

The study was comprised of two fully integrated components: an epidemiological and clinical component and an exposure assessment component formerly referred to as Part A and Part B, respectively. The overall study was designed as a 66-month effort, including a 6-month protocol refinement period. The ARB agreed to fund the project in two project periods (36 months and 30 months), with the second period of funding being contingent on satisfactory progress during the first. This report provides detailed information on the work completed to date, both in the characterization of the pollutant exposures of the asthmatic children that have been recruited for the study and the assessment of the effect of these exposures on lung function.

1.1.2 Study Goal, Research Questions and Hypotheses

The overall goal of FACES was to investigate the effects of PM air pollution on the natural history of asthma in young children. To achieve this goal, the study was designed to address four key research questions:

1. What is the relationship between short-term exposures to specific size fractions or constituents of particulate air pollution, or other ambient air pollutants, and acute exacerbations of asthma, which may include changes in lung function, occurrence of symptoms, and usage of medications?
2. What are the critical exposures leading to the observed acute health effects? For example, at what concentrations are the effects occurring, is there an interaction with other outdoor and indoor pollutants (criteria pollutants, toxic air contaminants) or bioaerosols (pollens, spores, PM-associated endotoxins), and what specific sources of PM are more strongly associated with specific adverse effects?
3. Are there cumulative effects of repeated acute responses to short-term air pollution exposures that result in altered disease progression, e.g., asthma severity, or changes in other markers of health status, e.g., reduced lung function "growth"?
4. Among the general population of asthmatic children, what are the biologic characteristics (e.g., asthma severity, , nutrition) or exposure characteristics (e.g., activity patterns, housing characteristics) that define subgroups who are more (or less) responsive to given acute exposures, or who experience larger effects associated with long-term exposures?

The health-related hypotheses developed to address these questions and presented in our orginal application for funding were the following:

Short-term Effects:

Hypothesis 1: Chemical components of particle air pollution (PM) that have immuno-enhancing properties (i.e., polyaromatic hydrocarbons (PAH) in diesel exhaust) are associated with symptom onset and severity and short-term reductions in lung function in a seasonally dependent pattern.

Hypothesis 2: There are specific biologic components (e.g., endotoxin, fungal spores) and specific anthropogenic components (e.g., latex particles from road tire dust) in the $PM_{2.5-10}$ (coarse) fraction that are associated with exacerbations of symptoms and short-term, reversible decrements of lung function in a subset of asthmatic children and these associations are strongest during the months of April through September, when $PM_{2.5-10}$ constitutes a major fraction of the PM_{10} mass.

Hypothesis 3: Components of PM that are markers for the oxidative potential of PM (e.g., transition metals) are associated with more severe symptoms and short-term, reversible decrements in lung function in a subset of asthma children.

Medium-Term Effects (Expected over Four Years of observation):

Hypothesis 4: The subsets of asthmatic children who respond with short-term deficits in lung function to components of PM (alone and/or in conjunction with other ambient air pollutants) will show relatively slower age-sex-specific growth of lung function than asthmatic children who do not so respond.

Hypothesis 5: The subset of asthmatic children who respond either to the immuno-adjuvants in PM or the oxidizing properties of PM will have greater asthma-related morbidity {increased frequency and severity of attacks of asthma, more likely to be classified as severe asthma (e.g., NHLBI/WHO classification), and have more medical interventions (e.g., increased use of quick relief medications, higher doses of anti-inflammatory medication, need for medical care).

1.2 METHODS

1.2.1 Study Design and Population

To test the health-related hypotheses our study design includes two components: 1) a series of panel-studies, which allows an assessment of short-term (daily) exposure effects that occur in seasons with different air pollution and meteorological patterns, and; 2) a classical longitudinal component that allows an assessment of changes due to the cumulative effects of short-term-exposure-responses.

The original goal was to recruit up to 450 asthmatic children (ages 6-10 at enrollment) in nine months in Year 1. Shortly after their baseline examinations, children would participate in a 14-day panel involving daily follow-up. In Year 2, the children would participate in a 14-day health-monitoring period in each of three air pollution seasons, for each of the 3½ years of follow-up. For the longitudinal study component, all children would undergo detailed evaluations at baseline and every 6-months thereafter. Because of unanticipated difficulties in recruitment of asthmatic children, with approval from ARB, the original goal of 450 subjects was revised to 300 subjects (up to age 11 at enrollment). Recruitment continued through October 2004. By the close of recruitment, 315 children participated in the study. It is not believed that the above noted changes significantly impacted the ability to meet the study objectives, in that

both the size of the cohort and the number of follow-up observations accumulated already are larger than most published studies that have reported associations with air pollution and symptoms or reduced lung function.

1.2.2 Health Assessment

The primary health outcomes to evaluate the day-to-day impacts of air pollution include: asthma symptoms (e.g., wheeze, cough, etc.); lung function (e.g., forced expiratory volume in 1 second (FEV_1) and forced expiratory flow between 25% and 75% of vital capacity (FEF_{25-75}), and asthma medication use (a covariate in some analyses). Longer-term health outcomes of primary interest include: changes in classification of asthma severity over the study period; and changes in levels of lung function over the study period ("growth" of lung function).

As noted above, the panel component of the study involved the observation of children during 14-day panels. Participants were asked to provide daily data, including twice-daily (a.m. and p.m.) lung-function tests, symptoms, medication use, and information to determine location-time-activity patterns. The longitudinal component involved subject visits to the field office to undergo detailed evaluations at baseline and every 6-months that included a medical history, housing characteristics, medication use, lung function tests, allergen skin testing (at least once over the study period), dietary assessment (preferably twice, once in the warm season and once in the cool season), and measures of somatic growth. Beginning 3-months after baseline, then every 6 months thereafter, adults were asked about their child's symptoms, medication use and any changes to housing characteristics.

A large number of data collection procedures and instruments (such as eligibility screening, baseline and follow-up questionnaires, daily diary, home environment survey forms) were developed specifically for FACES. Where possible, we used or adapted instruments from other studies, including the Southern California Children's Health Study (CHS), National Cooperative Inner-City Asthma Study (NCICAS), the Nurses Health Study and the Harvard Six-City Study. Extensive effort went into evaluation of appropriate portable and clinic-based spirometers. The latter needed to serve as a "gold standard" that would allow comparisons among the children across time and between FACES and other studies, such as the CHS. This work has now been published (1).

Also developed was a strategy for classifying asthma severity, which is an important outcome for the longitudinal component of FACES. Asthma severity is an important determinant of both short-term and long-term responses of asthmatic children to air pollution exposures, and repeated exposures-responses in turn influence asthma severity. However, asthma severity is difficult to disentangle from asthma control and existing classification schemes commonly used in the clinical setting are not designed to isolate underlying asthma severity over the long-term. Therefore, we needed to develop a strategy suitable for an epidemiologic study of the effects of environmental exposures among a pediatric population. After evaluating a number of strategies, a multi-component approach was developed that adapts existing asthma severity classification schemes. This work has been submitted for publication.

1.2.3 Exposure Assessment

Central to the core study design and ultimately to the success of FACES, is the need to accurately define the exposure-response relationship(s) for each air pollutant of interest, with consideration of co-exposures. An underlying premise of FACES is that observed health effects are associated with specific exposures or sets of exposures, and that there are subsets of the population of asthmatic children who are more/less responsive to different exposures. To identify these subsets of children, and to define the exposure characteristics of the children who comprise the subsets, the exposure assessment program is targeted to accurately estimate the individual-level exposures. Thus the technical approach for exposure analysis is to build databases and models to generate individual exposure estimates, rather than community average exposure estimates. The individual-level, or personal exposure estimates are based on microenvironmental models adjusted for indoor, outdoor, and activity patterns. Resources were not available for making direct measurements of personal exposures; these would have enhanced the exposure models but are not critical to their development.

The selection of environmental factors to be measured in FACES was based on the project's health hypotheses. The air pollutants measured included: PM mass and chemical constituents of coarse and fine fractions, particle number for PM in the ultrafine size range ($\leq$0.1 microns), ozone (O_3), oxides of nitrogen (NO_X), including nitrogen dioxide (NO_2) and nitric oxide (NO), sulfur dioxide (SO_2), and carbon monoxide (CO). Of interest are different exposure metrics, including, but not limited to, daily 1-hour maximum, daily maximum 8-hour average, 24-hour average, and annual average. Environmental measurements were also made for other known risk factors for asthma exacerbation that could modify or confound the air pollution exposure-response relationship. Among the most important are common environmental indoor and outdoor antigens (allergens – pollens, fungi), endotoxin and second hand smoke (SHS). In addition, data were obtained for meteorological factors (temperature, relative humidity and barometric pressure), which may be important effect modifiers or potential confounders.

The U.S. EPA Supersite in central Fresno was designed to be the core long-term environmental monitoring element of the study. It provided highly time-resolved measurements for all exposures of interest over the entire study period. The data from the routine home measurements, the home-intensive substudy (described below), and from two mobile monitoring platforms (trailers) provided the ability to define the relationship(s) between air quality characteristics throughout the study area to the measurements at the Supersite. For FACES, five additional measurements were initiated at the Supersite: PM_{10}-associated endotoxin, metals, SO_2 (using a continuously reading instrument with a low limit of detection), bioaerosols, and polycyclic aromatic hydrocarbons (PAHs). The U.S. EPA Office of Transportation and Air Quality provided FACES resources to implement monitoring of PAHs, which have been strongly implicated in some adverse effects associated with diesel emissions and which are central to a number of our health-related hypotheses.

Although responsibility for Supersite measurements, quality control/quality assurance (QC/QA) and data management did not lay with FACES investigators, they assisted in a number of these activities. Most notably, Sonoma Technology, Inc. provided additional quality assurance for the continuous data required for this report.

An aeroallergen sampler was deployed to the Supersite; the UCB laboratory performed identification and counts of pollen and fungal spores on a bi-hourly basis for most days. These detailed measurements are rarely available and are critical to gaining an understanding of the effects of aeroallergens on asthmatics, independently and in combination with ambient air pollutants.

The routine home measurements that occurred during all 14-day panel periods at all homes included passive measures of nitrogen dioxide and nicotine (a measure of SHS), and ozone (during the high ozone season, outdoors and indoors). It should be noted that passive samplers provide time-integrated data on exposure that do not allow peak exposures to be assessed (e.g., high peaks of NO_2 associated with the use of gas-fired cooking appliances for heating). As part of the panel studies there was also a home characteristics survey, moisture measurements, collection of house dust samples from the child's bed and a composite sample from the kitchen and living room floors, and a set of exposure-related questions on the daily diary.

The home-intensive element of the exposure assessment program, which involved a more comprehensive set of measurements at a subset of homes, was conducted in 2002-2003. Approximately 100 home visits occurred, which included some homes being visited twice, once in the "warm" season and once in the "cool" season. For this effort FACES investigators designed and constructed a Pollutant Exposure Monitoring System, which consists of a freestanding rack that contains measurement devices for O_3, NO_2, nicotine, spores and pollen, PAHs, and a variety of PM-related measures. At each of up to two-to-five homes per panel, one unit was placed inside the home in the living room and one unit was placed outside the home.

An important element of the exposure monitoring program was the mobile monitoring trailers provided by the ARB. The two trailers allowed key measurements required to characterize exposures in different neighborhoods throughout the study area, and to relate those exposures to the measurements at the Supersite. The trailers were instrumented such that each duplicated, to the extent possible, the measurements relevant to FACES being made at the Supersite. Due to the labor intensity and costs of moving the trailers, only one of the trailers was moved to a new location in the study area about every six weeks, while the other one remained in one location for longer periods. Both were set-up on school grounds, which served to characterize exposures both in a neighborhood and at the specific schools.

1.2.4 Analytic Strategy

From the early conceptual stages of FACES, the research team recognized the need to advance the analytic methods commonly applied in epidemiologic studies that involve a repeated measures design where exposures or treatments vary over time. The key issue is that when one evaluates air pollution exposure-response relationships, simple adjustments for potential confounders such as "medication use" can lead to biased results because these confounders are time-dependent and are affected by previous treatment. In epidemiologic terms, if for example rescue medication is taken to alleviate symptoms induced by air pollution, then rescue medication is also on the causal pathway between air pollution exposure and pulmonary function. It is a fundamental concept in epidemiology that the control for factors on the causal

pathway can lead to biased results. Robins and colleagues (2) introduced marginal structural models (MSM) to address this analytic issue; however, few studies have applied this method in the context of a study like FACES.

A nucleus of FACES investigators have invested a substantial effort to develop the conceptual and computer programmatic framework needed to apply and evaluate this analytic approach, including a comparison with other methods. The first stage of this effort was to examine the impact of treatment (medications use) on occurrence of symptoms, without further complicating the analyses by inclusion of air pollutant variables. The results detailed in the Final Report clearly demonstrated that the MSM outperformed the other analytic models and provided unbiased results, i.e., results that were more consistent with clinical observations.

An important observation, that reinforced the need to use the MSM analytic method for our final analyses, arose during our work for the interim report, when we evaluated a model that included a main effect and an interaction term for "use of rescue medication in the hour before testing." The results suggested that rescue medication was associated with increased occurrence of symptoms during the night, and rescue medication use increased the association between air pollutant exposure and more frequent occurrence of symptoms. This is both counterintuitive and contrary to well established clinical observations. It provides a classic case of what can happen if one controls for a factor on the causal pathway. In this instance, rescue medication use is confounded, in a time-dependent manner, by the occurrence of previous symptoms. In other words, medication use does not "cause" symptoms, but children who are sicker are more likely to take medication and are more likely to have symptoms during the previous reporting period. Because of these observations, an additional discussion and demonstration of the merits of causal analyses is provided in the report (Section 3.6.2). In addition, a manuscript that presents this pioneering analytic work has been prepared and accepted for publication (3). The second stage of this analytic work involved the development of methods to implement the MSM approach for data analysis. There was no existing statistical software that could execute the MSM analyses. In addition, it required significant time and effort to apply to the FACES data a general cross-validated data-adaptive estimation/model selection procedure (Deletion/Substitution/Addition (DSA) Algorithm), recently developed by one of the investigators (van der Laan).

This procedure is preferred over more conventional methods to optimize model fit because of 1) the limitations of more traditional model selection procedures with missing data; 2) recent promising theoretical and practical results associated with this methodology; and 3) a recent real-data comparison between this approach and more traditional approaches in the literature based on the Akaike Information Criterion (AIC). One compelling argument for a model selection procedure based on cross-validation is the presence of missing data in observational studies. Model selection criteria like the AIC only allow comparison of models fitted on the same number of observations. This typically leads to an important loss of information. A cross-validation procedure allows comparisons of models fitted with different numbers of observations and, thus, can be used to better compare models without loss of information. For the analyses presented in the Final Report, a model selection procedure based on cross-validation methods combined with the DSA algorithm was used.

Our general approach in the Final Report was to conduct and present both conventional regression analyses and MSM causal analyses.

1.3 RESULTS

1.3.1 Study Population Characteristics

A total of 315 children with asthma entered the study. Through the period included in the health analyses presented in the Final Report (i.e., through March 2003), 236 children had completed a baseline interview. The age distribution of children at baseline ranged from 6 to 12 years (one child turned 12 between screening and study entry), with a median age of 8. The oldest children were 15 years by the time of the 54-month visit in July 2005.

The report provides extensive details of the cohort's demographic and health characteristics. Some key observations are highlighted here. The household incomes of families participating in FACES were similar to those of the Fresno population, with 45.4% of households reporting annual incomes of $30,000 or below. Relative to the larger community, high school degrees were reported more frequently by parents of FACES children; more than 90% of families had at least one parent with a high school degree. The percentage of participating households that owned their own home (56.5%) was identical to that of the Fresno population. Almost 87% of children were covered by health insurance (through employer or government), and 8.7% of children had coverage that was "self-paid". Only 4.2% of children in FACES were not covered by any insurance; this contrasts with the 10.7% of the general population of children ages 6-to-11 in Fresno who are without health insurance.

Seventy-two percent of the cohort (n=226) is composed of children with persistent asthma, based on generally accepted classification criteria. More than 50% of the cohort reported that an unscheduled medical or emergency room visit occurred in the 12 months prior to baseline. Over 20% have been hospitalized for their asthma at some time (7% in the 12 months prior to baseline interview), 57% have visited an emergency facility (27% in the 12 months prior to baseline interview). Only 5.7% of children had ever been put in the intensive care unit due to their asthma.

Almost 80% of the cohort was on at least one controller medication. A few (3.2%) were not taking any medications for their asthma, and 17.1% only took beta-agonists. Prednisone was taken at least once in the lifetime of 59.0% of the cohort and had been used by 37.5% of the cohort in the past 12 months. Despite the prevalence of reported recent prednisone use, 75.8% of the children in the study were classified as having mild intermittent or mild persistent asthma when the Global Initiative for Asthma (GINA) classification scheme for symptoms was applied to assess severity at baseline. Unfortunately, we have no data on the distribution of all children with asthma in the study area with which to compare this distribution of severity. Nevertheless, given the above-listed characteristics, it can be inferred that these asthmatic children include a good cross-section of disease severity, and therefore, provide an appropriate cohort from which to generalize about the effects of air pollutants on childhood asthma.

Of the 315 children who began the study, many had frequent symptoms. For those with a history of wheeze (92.7%), 37.3% had wheezed in the 2 weeks prior to the baseline interview. Wheeze interrupted sleep in the past 2 weeks for 64.4% of the cohort. Wheeze led to school absences in the previous two weeks for 12.5% of the children and missed work for 8.1% of

parents over the same time period. Persistent cough occurred in 72.6% of the cohort in the 12 months before baseline and for 32.8% in the past 2 weeks. Most children reported activity limitations in the past year. Coughing was common in the cohort. Almost one-third of participants had a cough, which lasted two or more days within the 2 weeks before the baseline interview.

As expected for a cross-section of children with asthma, baseline lung function was relatively close to percent predicted lung function values for their age, sex, height and race (4) and the majority had evidence of allergy (a diagnosis of allergic rhinitis or eczema was reported by 32.6% and 17.0% of parents, respectively, and 61% of the 266 children skin tested had a positive reaction to at least one allergen).

1.3.2 Exposure Characterization

Fundamental to the FACES study design was the requirement that there be sufficient temporal (day-to-day, diurnal) and spatial variation in pollutant and bioaerosols concentrations and mixes. The key observations from the exposure component are presented here.

The day-to-day variations in ambient concentrations were large for most pollutants and bioaerosols components in FACES, which provided the exposure variability needed to support the panel study design. The temporal and spatial variation of pollen grains and fungal spores are independent of other pollutants and agents measured in FACES; this provides an opportunity to independently evaluate their associations with health outcomes.

The seasonal variations were large for many pollutants and agents, with median monthly ambient concentrations varying by factors of 5-to-10 between the lowest and highest months. The seasonal patterns of variations differed considerably for the different pollutants and bioaerosols components. 1) Pollens were highest in the spring; 2) ozone was highest in summer; 3) endotoxin was highest in the summer or fall, 4) coarse PM was highest in the fall; and 5) $PM_{2.5}$, EC, NO_3, PAH, NO, and CO were highest in the fall or winter. Total fungal spores (but not necessarily individual types of spores) were lowest in winter.

Diurnal variations in ambient concentrations were relatively large. Four-to-five-fold differences between the lowest and highest average hourly concentrations were observed for ambient ozone, EC, PAH, CO, NO, pollen grains and fungal spores.

Spatial variations in daily ambient concentrations ranged from barely detectable to high, with the results for specific exposures of interest being consistent with most of our original hypotheses related to regional-scale and neighborhood-scale spatial variations in ambient concentrations. $PM_{2.5}$ mass, SO_4, black smoke particulates (bsp), and PM_{10} mass, potassium, iron, silicon, and calcium had mean daily spatial coefficients of variation less than 20% and were classified as pollutants with regional-scale variations. $PM_{2.5}$ OC, EC, NO_3; coarse PM; PM_{10} zinc, bromine, manganese, aluminum, strontium, copper, and cobalt; endotoxin; CO; NO_2; NOx; and ozone had mean daily spatial coefficients of variation between 20% and 35%, and were classified as pollutants with moderate neighborhood-scale variations. NO, SO_2, PAHs, fungal spores, pollens, and other measured trace elements were found to have large neighborhood-scale variations, with mean daily spatial coefficients of variation greater than 35%.

For the residences of FACES participants, mean indoor concentrations of most (55 of 70) pollutants and agents were lower indoors than outdoors. Notable exceptions were OC and naphthalene concentrations that were higher indoors, on average; endotoxin was higher indoors than outdoors in the winter (November-March), but lower in other seasons. However, about half of the measured compounds had higher maximum concentrations indoors than outdoors. For example, the maximum indoor concentrations of $PM_{2.5}$ mass, PM_{10} mass, OC, EC, total fungi, naphthalene, pyrene, flouranthene, iron, and aluminum exceeded the maximum outdoor observations. To date, we have not attempted to assess the potential effects of indoor peak exposures on any health outcomes.

Routine home measurements in FACES residences indicated dust mites and cockroach allergens were uncommon in floor and bed dust, while cat and dog allergens were very common even in homes without these pets. Measurable endotoxin levels were common in house dust; median levels of endotoxin were 64 EU/mg in floor samples and 52 EU/mg in bed samples. Two-week average nicotine levels were low (<1 μg/m3) in 95% of the homes. Two-week average NO_2 and ozone indoor concentrations averaged 13 ppb and 9 ppb, respectively.

Window position and heating or air conditioning system use explained 70% of the variance in the indoor-outdoor ratio for SO_4, an important tracer of pollution of ambient origin.

A personal microenvironmental exposure model was developed to estimate individual daily exposure to pollution and agents of ambient origin. It combined a model of spatial variations of outdoor concentrations with a single-compartment, steady-state indoor air quality model. Daily individual diary information on residence operating characteristics and subjects' activities was used along with ARB time-activity survey data to estimate time spent in various microenvironments each day.

Results of the microenvironmental exposure model indicate that on most days between-subject personal exposures vary by a factor of two for $PM_{2.5}$ mass and by a factor of three or more for other pollutants considered. The implication of this large between-subject variation in estimated personal exposure to pollutants of ambient origin is important. If one used central site ambient concentrations for individual exposure assignments it might result in considerable exposure misclassification and assignment error. The magnitude of the error in the model-based estimates is unknown because the personal exposure model performance has not been evaluated against personal exposure observations (due to insufficient funds for this activity).

The mean estimated personal exposure concentrations of pollutants of ambient origin are consistently lower than the central site ambient concentrations. On average, the mean personal exposure concentrations range from 15% of central site ambient concentrations for total pollens to 59% of central site ambient concentrations for $PM_{2.5}$ mass. The pollutant ranking (from highest to lowest) for mean ratio of personal exposure to central site ambient concentrations is $PM_{2.5}$ mass, endotoxin, EC, agricultural fungi, NO_2, $PM_{2.5-10}$, Alternaria, ozone, Cladosporium, and total pollen. The differences in personal exposure levels relative to central site ambient concentrations are primarily a result of lower indoor than outdoor concentrations caused by pollutant deposition on indoor surfaces and penetration losses; these losses from outdoors to indoors are also quite variable among the pollutants and bioaerosols, with median indoor to outdoor ratios ranging from 0.82 for EC to less than 0.02 for total pollen. Spatial differences in

ambient concentrations within the community and indoor chemical reactions also contribute to the differences.

The between-subject variations in personal exposure estimates are generally greater for biological agents than conventional pollutants. For example, on a day with relatively high pollen grain and fungal spore levels, the personal exposure estimates may range from 100-to-800 total pollen grains/m3 and from 10-to-250 Alternaria spores/m3. In contrast, on a day when conventional pollutant levels are high, the personal exposure estimates may range from 40-to-80 μg/m3 for $PM_{2.5}$ mass and from 8-to-25 ppb for NO_2. The variance among subjects for primary PM components, such as EC, is also considerably greater than the variance for $PM_{2.5}$ mass.

1.3.3 Health Effects Analyses

The overall goal of FACES is to evaluate the effects of PM air pollution, alone and in combination with co-exposures, on the natural history of asthma in young children. Requisite to beginning to meet that goal was the need to advance analytic methods such as MSM that could deal with the complex timing-dependent interplay between exposure and response in the short and long-term. We implemented marginal structural models (MSM), which are capable of dealing with time-dependent confounding. The time invested in these efforts was necessary and fruitful. However, the additional time/resource investments meant fewer specific hypotheses could be addressed before the end of the project contract period and the preparation of the project Final Report. Furthermore, those analyses that have been conducted have not been sufficiently exhaustive to make strong inferences based on the results obtained to date.

The Final Report considers two health outcomes (primarily FEV_1 and a few analyses of FEF_{25-75}) and the main effects of three pollutants ($PM_{2.5}$, NO, NO_2). Conventional and MSM methods were applied to evaluate short-term exposure effects. Conventional methods were used in a preliminary examination of the influence of short-term exposure-responses on lung function over the longer term, referred to as the chronic analysis.

Based on the conventional acute analyses conducted so far, there is no evidence of an association between morning measures of FEV_1 or FEF_{25-75} and $PM_{2.5,}$ regardless of whether we used $PM_{2.5}$ estimates based on central site data or personal exposure estimates. These analyses were restricted to the "winter" months (October-February). It is possible that restriction of the analyses to these months is responsible, in part, for the lack of association. Among the key reasons this seems unlikely are the facts that: 1) There is over a 10-fold range of variability in the daily levels of $PM_{2.5}$ during this period compared to an average of less than 3-fold variation during other months of the year; 2) During the winter months, $PM_{2.5}$ levels often exceed Federal standards and are, in general, much higher than levels in studies that have reported associations with measures of lung function; 3) We had over 3,000 repeated measures with valid exposure and lung function measures for FEV_1 and 2,800 for analyses for FEF_{25-75}. These latter numbers are in the range of those for studies that have shown positive associations. Furthermore, we found the same null results with both the longitudinal and point treatment MSM analyses.

As noted previously, the sources of wintertime $PM_{2.5}$ in Fresno are derived largely from mobile sources and wood burning. To determine if a more specific marker for mobile sources

would give different results, we carried out longitudinal and point-treatment MSM analyses with Central Site NO (estimated individual exposure data were not available at the time of this submission). In the longitudinal MSM, a 6-day moving average of 24-hour NO did enter the model for A.M. FEV_1; however, the sign of the coefficient was *positive* and not significant at $p < 0.05$. (Table 4.2.3-9). Point-treatment MSM did not reveal any significant associations with 24-hour Central Site NO concentrations at any moving average.

Our conventional analyses with NO_2, which were not restricted to a single season, did indicate an inverse association between Central Site 2-to-8 day moving averages and FEV_1. (We did not complete analyses for FEF_{25-75}). The estimated effect was between a 3-to-6% reduction in FEV_1 for a 10 ppb increase in the NO_2 2-to-8 day moving averages, conditional on fixing the other covariates in the model and at a population mean FEV1 of 1.50 L. The results suggest that each of the moving averages had a similar effect. We did not find any such associations with estimated personal exposure to NO_2.

When we forced NO_2 into the point treatment MSM, we observed inverse relations with the moving averages and FEV1 (we did not complete the analyses for FEF_{25-75}). The interpretation for these analyses is that, if contrary to fact, the population of asthmatic children were exposed to a 10 ppb lower level of NO_2 on any day, FEV_1 would be increased approximately 1.6-2.3%. The fact that the DSA algorithm did not select NO_2 at any lag or moving average imposes a note of caution on the validity of these findings.

A further suggestive piece of evidence in support of NO_2 as a marker of health-relevant air pollutants comes from a preliminary test of our hypothesis related to the relation between response to short-term increases in daily pollutant levels and growth of lung function over a six to twelve-month period. To our knowledge, no research has ever been presented on this question. We found that an inter-quartile decrease (more negative) in the parameter estimate for the association between daily increase in NO_2 and FEV_1 was associated, on average, with a 4.9% decline in FEV_1 growth over a given six- to twelve-month interval. These observations are consistent with those from the Children's Health Study on the relation between community levels of NO_2 and lung function growth. However, we reiterate our caution about the interpretation of these results. The possible association between exposures to NO_2 and reduced lung function will be explored further as we follow the cohort and carry out more detailed analyses on both morning and evening lung function.

Results from a cross-sectional, conventional analysis to evaluate the effects of exposure to highway traffic on lung function, indicated that lung function tended to be positively associated with longer distance-to-road and negatively associated with traffic measures that capture traffic intensity (count); however, few associations reached statistical significance. For example, percent-predicted FEV1/FVC% was diminished with increases in inverse distance-weighted traffic count (IDWT) and annual average daily traffic count, and tended to increase with greater distance-to-road. When we evaluated effect modification by FEF_{25-75}/FVC, a parameter that reflects small airway size, all lung function measures of flow were significantly inversely related to IDWT. These results indicate that residence proximity to highway traffic may be related to deficits in lung function among children with asthma. Additionally, smaller airway size appears to be an important modifier of the effect of traffic on lung function and thus a marker of greater susceptibility.

The summary of results from analyses of pollution effects on lung function should be viewed in the context of the following caveats. The analyses are viewed as preliminary by the research team due to limitations in the data available at the time that analyses for this report were conducted. For example, fully processed exposure data from the Central Site provided by ARB were available only through March 31, 2003, thus reducing the sample size. In addition, there was relatively limited duration of follow-up for many subjects. Furthermore, for neither the conventional nor the MSM analyses, did we fully exhaust the complex relationships that might exist between the outcome, exposure and covariates. The latter fact combined with limitations in software which is still under development, leads to the possibility that the final longitudinal MSMs were not optimally specified. Finally, there are many options for what health inputs to use to assess short-term exposure effects that could influence longer-term outcomes. For example, the current analyses have focused on morning FEV_1, with some limited exploration of FEF_{25-75}. We have not completed any analyses with FEF_{75}, FEF_{25-75}/FVC or symptom data. We have not analyzed any lung function or symptom data from the evening lung function sessions, nor have we analyzed morning-evening and within-session variability in relation to pollutant and bioaerosol exposures.

We have made major strides towards meeting the overall goal of the health component of FACES, to investigate the effects of PM air pollution on the natural history of asthma in young children. The hypotheses in the original application remain the guiding hypotheses for our research. They will be pursued fully with funding from three sources: 1) A several month extension of the original contract by ARB; 2) a new 4.5-year award from the National Institutes of Health (NIH) that should begin sometime in Spring 2006; and 3) a 3-year award from the Mickey Leland National Air Toxics Research Center to continue our PAH work. Summarized below is the status of our progress each hypothesis.

1.3.3.1 Short-term Effects:

Hypothesis 1: Chemical components of particle air pollution that have immuno-enhancing properties (i.e., polyaromatic hydrocarbons (PAH) in diesel exhaust) are associated with symptom onset and severity and short-term reductions in lung function in a seasonally dependent pattern (and sub hypotheses).

In pursuit of the aim, a number of elements have been addressed: 1) We have developed spatial maps for our PAH data (work funded through EPA) and received funding to obtain additional years of PAH data. We have developed estimated individual exposure estimates for EC—EC is a good marker for mobile source emissions and, in parts of our study area, for diesel emissions. Our analysis of traffic metrics that included the heavy duty vehicle fraction represents the beginning of this work. We have developed the algorithm for classification for asthma severity that will be required for analyses related to this aim. In addition, we have developed estimated individual exposure estimates for pollens and endotoxin that are likely to be important exposures to consider with respect to this aim. The work described in the Final Report does lay the ground work for addressing the overall hypothesis and the sub-hypotheses.

Hypothesis 2: There are specific biologic components (e.g., endotoxin, fungal spores) and specific anthropogenic components (e.g., latex particles from road tire dust) in the $PM_{2.5-}$

$_{10}$(coarse) fraction that are associated with exacerbations of symptoms and short-term, reversible decrements of lung function in a subset of asthmatic children and these associations are strongest during the months of April through September, when $PM_{2.5-10}$ constitutes a major fraction of the PM_{10} mass (and sub-hypotheses).

We have developed spatial maps and individual exposure estimates for the bioaerosols and $PM_{2.5-10}$ that are the focus of these analyses. The analyses for $PM_{2.5}$, NO_2 and NO included in the Final Report evaluated the possible contribution of the bioaerosols and coarse PM to any associations observed for these three pollutants. None was observed; however, we did observe associations between endotoxin and fungal spores and Central Site NO_2, observations that provide a justification for the inclusion of this hypothesis and further exploration of these potential associations.

Hypothesis 3: Components of particle air pollution that are markers for the oxidative potential of particle air pollution (e.g., transition metals) are associated with more severe symptoms and short-term, reversible decrements in lung function in a subset of asthma children (and sub-hypotheses).

We carried out initial analyses of the spatial distribution and indoor-outdoor distributions of these metals. These data lay the groundwork for analyses to address this hypothesis.

1.3.3.2 Medium-Term Effects (Expected over Four Years of Observation):

Hypothesis 4: The subsets of asthmatic children who respond with short-term deficits in lung function to components of particulate air pollution (alone and/or in conjunction with other ambient air pollutants) will show relatively slower age-sex-specific growth of lung function than asthmatic children who do not so respond (and sub-hypotheses).

We have made a preliminary test of this hypothesis with NO_2. These very preliminary results provide the very intriguing suggestion that this hypothesis might be supported when more complete analyses with a variety of pollutants and exposure combinations have been conducted for the panel data. If so, this would be the first report of a direct connection between acute responses to short-term fluctuations in ambient pollutant concentrations and long-term adverse effects on asthma. Test of this hypothesis will remain a priority for our future work.

Hypothesis 5: The subset of asthmatic children who respond either to the immuno-adjuvants in particulate air pollution or the oxidizing properties of particle air pollution will have greater asthma-related morbidity [increased frequency and severity of attacks of asthma, more likely to be classified as severe asthma (e.g., NHLBI/WHO classification), and have more medical interventions (e.g., increased use of quick relief medications, higher doses of anti-inflammatory medication, need for medical care)].

An algorithm has been developed for classification of asthma severity that will be required for these analyses. The data framework developed to address hypothesis 4 will be used for the specific analyses to address this hypothesis as well.

Overall Summary of Work on Hypotheses: We have carried out a large amount of the work that is necessary to test our original hypotheses. What remains is to process sufficient data collected over time for pollutant/bioaerosol exposures and health outcomes as well as to further refine the estimated individual exposures. Given the complexity of the analyses, this will take considerable time to complete, but we have obtained a large amount of long-term funding to complete this work as part of our ongoing collaboration with ARB.

1.4 CONCLUSIONS AND THE FUTURE OF FACES

The FACES investigative team has made great progress toward achieving our goal of investigating the potential relationship between short-term responses of asthmatic children to air pollutant exposures and their long-term growth of lung function and asthma severity. We have extensively characterized both the ambient pollutant exposures and the health of a cohort of asthmatic children living in Fresno. We have also successfully followed the cohort over several years' time. Exposure to multiple pollutants and bioaerosol components varies widely among the cohort. The severity of disease among the cohort appears to be reasonably representative of the population of asthmatic children in general. To date, the results of the analyses of exposures to $PM_{2.5}$ and lung function have not demonstrated an association. In contrast, analyses to date have suggested a potential association between exposure to NO_2 and both short and long-term reductions in lung function. Exposure to traffic may also be associated with reduced lung function. Whether NO_2 has an independent effect on lung function or is a surrogate for the traffic pollution mix remains to be determined. However, we reiterate that the results related to health effects presented in this report are preliminary.

As in most complex research endeavors, much work remains to be done to fully answer key questions. Due to recruitment difficulties and the need to implement new statistical methods for which no software was available, much of the large amount of data collected still requires analysis. We will be conducting additional analyses, both conventional and MSM, during a 9-month augmentation period supported by the ARB and over the next 4.5 years under continued funding by the Division of Lung Diseases, National Heart, Lung and Blood Institute (NIH). Therefore, the results presented in this report may be revised when a more extensive suite of analyses have been completed. Revised results will be available in a supplemental report to this document and we will continue to share results with ARB as the work continues over the next 4.5 years.

The extensive field and statistical analytical work supported to date by ARB has allowed the FACES investigative team to submit a successful application to the NIH for funding to continue to follow the cohort, as well as to receive an award from the Mickey Leland Foundation to better characterize exposures of FACES children to PAHs. This additional support will enable us to collect and analyze much more data and follow the children for two more years. An application to NIH for funds to do source apportionment has also been submitted. Potential tracers exist for several of the important sources of ambient pollution, including those for combustion sources (CO, NO, EC, and PAHs), soil dust (Si, Al, Fe, and Mn), and biological sources (endotoxins, fungal spores, and pollens) that potentially could support apportionment of health effects to sources.

Other work needs to be done, pending availability of future additional funds. Validation of the model for estimating personal exposure to pollutants measured at the Central Site was not possible, since sufficient funds were not provided for personal monitoring. We plan to seek additional funding to assess the validity of the model and to define the measurement errors (magnitude and sources) associated with model exposure estimates. The FACES team has also collected biological samples (buccal cells and blood) from many of our participants that will allow DNA to be extracted and analyzed. This bank of samples provides an opportunity to investigate genetic markers of risk for air pollution-associated health responses if sufficient funding can be obtained in the future.

We are very confident that FACES will ultimately yield important new information about the complex relationships between environmental exposures and both short-term and long-term effects in this highly vulnerable population of asthmatic children.

2. INTRODUCTION

2.1 BACKGROUND

In July 1999, Governor Gray Davis along with the California Legislature authorized the Vulnerable Populations Research Program (VPRP). The goal of this program was to evaluate the effects of air pollution on California's most vulnerable citizens defined as having increased biologic sensitivity or reduced resilience to an environmental insult, or a greater potential for exposure to environmental hazards. The Program is situated in the Populations Studies section of the Air Resource Board's (ARB) Research Division.

During this time, a group of researchers from the University of California at Berkeley and San Francisco, Sonoma Technology, Inc. and the ARB sought to investigate the health effects of air pollution on asthmatic children –a vulnerable population of particular interest to the VPRP. In February 2000, this group was awarded funding from the ARB Research Division and Board for their proposal Responses to Short-term Fluctuations in Particulate Air Pollution in Asthmatic Children: Implications for Asthma Natural History. The study is more conveniently known as the Fresno Asthmatic Children's Environment Study (FACES).

A review of the FACES study design has been presented in detail in the original application. The background has been subsequently updated in an Interim Report (IR) submitted to the ARB in August 2002. The present document contains an abbreviated form of the original background along with the most updated information including a rationale for the continued relevance and novelty of the FACES project. Here, we bring to light the importance of the principal purpose of FACES: to deduce the relationship between responses to acute changes in air pollution and long-term health outcomes, a novel inquiry into the causation of asthma that has recently been embraced by the scientific community and commands further study.

2.1.1 Background Presented in Original FACES Application, September 2000

Asthma is a complex, multi-factor condition, which requires the presence of a combination of factors for its development and its subsequent natural history (5). Genetic, environmental, dietary and socio-cultural components have been examined in detail (6). The specific role of each factor, as well as interaction between factors, is understood only incompletely both in terms of primary causation and natural history (i.e., the behavior of asthma over the long-term once the disease has become manifest). Current research indicates that the mechanisms for "getting asthma" (i.e., mechanisms that underlie etiology) and "getting attacks of asthma" (i.e., episodes of worsening asthma in persons with the diagnosis) may be quite different (6, 7). Although it is clear that asthma has a strong genetic component, it is almost certain that the rapid rise in the prevalence of asthma over the past two decade (6) is not attributable to genetic changes. Consequently, a major focus of current research efforts in relation to asthma goes beyond attempts to identify "asthma genes" to include the effects of the environment and gene-environment interactions (6). Since the economic impact of asthma on the medical system and society as a whole is substantial (8), the identification of these

environmental effects and their mechanisms has important public health implications for the prevention as well as the treatment of this disease.

A wide variety of environmental factors have been associated with the prevalence and severity of asthma. There is overwhelming evidence that common environmental antigens (allergens) play a major role in the onset and natural history of asthma. Indoor allergens (e.g., dust mite, cockroach, cat) have a strong causal relationship to asthma onset and natural history (9, 10). In addition, allergens such a fungal spores (11, 12) and pollens contribute importantly to asthma. Recent studies have suggested that bacterial products such as endotoxin also may have a role in the natural history of asthma that extends beyond the occupational setting (13). Among non-biologically derived exposures, there is epidemiologic evidence to link second hand smoke exposure both to onset of asthma as well as to exacerbations of the disease (14). Even among asthmatics who do not manifest evidence of atopy, there is a strong suspicion that unrecognized environmental allergens or microbial antigens that are part of the human flora are the inciting agents (15). The common immunopathology of atopic and non-atopic asthma (16) reinforces the concept that a disordered response-injury-repair mechanism to environmental antigens is at the root of most non-occupational asthma.

Current data provide convincing evidence that there may be a causal link between ambient, outdoor air pollutants produced as a consequence of human activities and short-term asthma morbidity manifest as increases in hospitalizations, emergency department visits, increased asthma symptoms and use of medications and decreases in several measures of pulmonary function (17-22). These effects have been documented in geographically and demographically diverse populations and with a variety of study designs. Few of these studies (23-25) have provided any data on the characteristics of the asthmatics who are "responders" to air pollution and who account for the effects observed in these studies. Recent analyses by Mortimer and colleagues (26) of data from the National Cooperative Inner-City Asthma Study indicate that asthmatic children who were premature or low birth weight accounted for most of the observed peak flow and symptom responses to summertime air pollution (estimated by ozone concentrations) observed in this study. These data highlight the need for better characterization of air pollution "responders" among asthmatic children in terms of the components of the ambient air pollution mixture to which various asthmatics respond and the similarities and differences between those who respond to the different components.

Although air pollution-related symptoms and decreases in lung function may be clinically relevant and burdensome to the asthmatic patient, there only is sparse evidence that air pollution is associated with the incidence of asthma – i.e. that it 'causes' asthma (27, 28). This relatively weak evidence for causation, however, may be due to inconsistencies in the definition and diagnosis of asthma, inadequate study designs, failure to study exposure during critical periods (e.g., perinatal period during which critical immunologic development is occurring (29)), inherent difficulties in studies of asthma incidence and incomplete/inaccurate exposure assessment. Moreover, there are virtually no data on the relationship between the acute responses to air pollutants and the natural history of asthma—i.e., whether these symptomatic and/or pulmonary function responses to daily fluctuations in ambient air pollution are markers for more severe disease over the long-term as assessed by symptoms, disability, need for medication and long-term adverse effects on lung function in persons with asthma (30).

Numerous studies (31, 32) have identified a need for additional research on the long-term effects of air pollution on the natural history of asthma, particularly among children. Examination of the effects of long-term exposure is essential to characterize more fully the air pollution-related costs in economic and public health terms. Current estimates of the social and economic costs of exposure to short-term increases in ambient air pollutants are likely to be inaccurate to the extent that: 1) they fail to account for potential relationships between short-term effects and the long-term natural history of asthma; and 2) they have not identified the sub-groups of asthmatics which actually respond to variations in air pollution.

Recent studies (33), have identified the need for an improved understanding of the interaction between a variety of environmental conditions (e.g., exposure to allergens, tobacco smoke, etc.) and ambient air pollution as they relate to asthma and allergic sensitization. The effects of air pollutants need to be studied with respect to the role that exposure (temporal patterns, types of pollutants) could play in the onset of asthma and the exacerbation of existing asthma, through amplification of the asthmatic response and/or enhancement of primary sensitization to other stimuli (e.g., allergens). (34). Currently available data suggest that there are several ways in which air pollution exposure could affect occurrence and natural history of asthma: a) inciters or triggers in airways that are already hyper-responsive, without themselves directly causing inflammation; b) inducement or augmentation of airway inflammation and hyper-responsiveness (35); c) direct toxic effect on respiratory epithelium resulting in inflammation and remodeling, hyper-responsiveness and the manifestations of asthma-like symptoms in previously normal subjects ; or d) augmentation or modification of the immune response to inhaled allergens such as to facilitate allergic sensitization or enhance the severity of allergic reactions in previously sensitized individuals (33, 36, 37).

The U.S. Clean Air Act Amendments of 1970 specify that air quality standards are to be set at values for the "attainment and maintenance of which in the judgment of the administrator, based on such criteria and allowing an adequate margin of safety, are requisite to protect the public health" (PL 91-604, December 31, 1970). The concept of "sensitive sub-populations" has become integral to the "margin of safety" component of the law; and persons with asthma are identified as one of the most important of such sub-populations along with children and the elderly (38). Among its research priorities to fill gaps in the extant scientific database on PM health-related effects, U.S. E.P.A. identified the need to "characterize the health effects of long-term PM exposure" (Research Need 4.4) and to "determine the relative public health burdens of long-term and short-term PM exposures" (Need 4.5) (31). Moreover, the Research Needs document went on to state, "In children, ambient PM effects … on asthma should be further assessed" (31). The State of California Health and Safety Code (CHSC) also specifies that ambient air quality standards be established that are protective of public health. The implementation of this mandate historically has included consideration of sensitive subgroups and the provision of an adequate margin of safety. The CHSC also requires the Air Resources Board (ARB) to carry out an effective research program in conjunction with its efforts to combat air pollution. For nearly a decade that program has placed significant emphasis on studying long-term exposure effects, as well as the effects of PM.

Although a relatively large body of data is available on acute respiratory effects of PM mass, there are relatively few data on acute effects attributable to specific PM mass components (PM_{10}, $PM_{2.5}$, $PM_{2.5-10}$, PM_1, ultrafines). Moreover, there are few studies that examine the acute

effects of non-mass measures (particle number, chemical constituents) of particulate air pollution (39, 40). Furthermore, the studies that have focused on asthmatics contain small samples of asthmatics (41) or contain relatively small numbers of asthmatics as part of more general population studies (42). The specific PM components that are relevant to health-effects and acute effects on asthma are largely unknown, although oxidative effects of transition metals (43), particle acidity (44), organic compounds, elemental carbon, biological materials (e.g., endotoxin, fungal spores) (11, 13, 45) and ultrafine diesel soot (39) and its polyaromatic hydrocarbon fraction (46) all are under active investigation. Most of the focus has been on the fine particle fraction of PM_{10}, but recent *in vivo* data suggest that components of the coarse fraction ($PM_{2.5-10}$) of PM_{10} may be an important source both of cyotoxicity and a stimulus to inflammation (endotoxin) (45) that could be relevant to asthma. Primary sensitization also may be related to man-made components of $PM_{2.5-10}$ as well (47). The biological effects of particles, alone and in combination with gaseous pollutants, are likely to be determined by the physical and chemical nature of the particulate mixture, the physics of the deposition in the respiratory tract, and the biologic events occurring in response to the particle exposure (5). These biologic effects include inflammation, diminished mucociliary clearance and macrophage function, and adverse changes in lung function, all of which would be expected to affect adversely the natural history of asthma. Particulate air pollution also may alter immune responses to allergens (37), which may be important in the onset of asthma as well as in its exacerbation (36, 37, 48). Finally, there is evidence that the poly-aromatic hydrocarbon component of diesel exhaust has immuno-adjuvant properties that could be important both for the onset and exacerbation of asthma (46). To date, the effects of the repetitive operation of these acute processes on the long-term natural history of asthma have not been studied.

Potential health effects due to long-term exposure to PM only can be ascertained through appropriate epidemiological studies. While there are a relatively few data on asthma, sufficient information does exist that relates PM exposure to respiratory symptoms to warrant concern for such long-term effects. One of the first studies to evaluate the association between long-term exposure to PM_{10} and respiratory symptoms in adults was the Swiss Study on Air Pollution and Lung Disease in Adults (49). The predicted effect of a 10 ug/m^3 increase in annual mean concentrations of PM_{10} was substantial: increases of 24% in the prevalence of chronic phlegm production, 27% in the prevalence of chronic cough or phlegm production, almost 50% for breathlessness during the day, 33% for breathlessness during the day or night, and 32% for dyspnea on exertion. No associations were found for wheezing, current asthma, chest tightness, or chronic cough (49). Jammes, *et al.*, (50) also found an association between exposure to outdoor air pollution (PM_{10} and NO_2) and the severity of airway obstruction and prevalence of bronchial hyper-responsiveness in sensitive adults patients who suffer from COPD or asthma. The CORD study, a large-scale comparison of lung function across different parts of Southern California suggested lower function levels and more rapid loss rates in adults living in more polluted communities (51). The Adventist Health Study reported an association between reduced forced expiratory volume one-second (FEV_1) in adult males with a family history of asthma or other chronic lung disease and 20-year level of exposure to PM_{10} (52). However, in this population, incident asthma in adult males only was associated with 20-year exposure to O_3 but not to particles (53). Effects on lung function in women were limited to peak flow ability (52). This latter study emphasizes the need to investigate possible PM health effects in the context of a strategy for the comprehensive measurement of the mix of air pollutants to which individuals are exposed.

The Six Cities Study (42) found a threefold increase of chronic cough in children with exposure to 59 versus 20 mcg/m^3 of PM_{15}, which was similar to the effect size noted in a Swiss study, which had lower levels of exposure (54). In these Six Cities data, the associations between bronchitis, chronic cough and chest illness and long-term exposure to PM were most pronounced in children with self-reported asthma (42). In the 24 Cities study, the predicted loss of lung function in children due to lifelong residence in the community with the highest strong acid particulate concentration, relative to the cleanest community was about 3% for FVC and FEV_1 (55) The Pollution Effects on Asthmatic Children in Europe (PEACE) project found little overall adverse effects of ambient air pollutants from PM_{10} on respiratory health of children (56). Based on a cross-sectional analysis in 12 communities in California, Peters, *et al*. found PM_{10} and $PM_{2.5}$ to be associated with lower FVC, FEV_1 and maximal mid-expiratory flow (57). However, this design could not distinguish between the acute reversible effects of recent air pollution exposures from the chronic effects of interest. Unpublished, cross-sectional data from this same study indicate that symptoms of phlegm and bronchitis are associated with community levels of PM_{10} and NO_2 in children with asthma but not in children who are asymptomatic or who report wheeze without a doctor's diagnosis of asthma. (58)

In general, the effects of PM in studies of both acute and chronic effects of air pollution on asthmatics have been relatively small. However, many of the studies have had limitations such as short-term follow-up, substantial loss to follow-up, inability to control for confounding or modifying factors such as biological exposures, incomplete measurement of exposure (e.g., lack of daily PM data) and failure to explore the optimal air pollution metrics in terms of assessment of health effects. The importance of the latter point is illustrated by the study of Delfino, *et al*. (41) which found substantially larger effects when exposure was defined by 1-hour and 8-hour maximum PM_{10} levels, as compared with the most commonly used standard metric of 24-hour average PM_{10}.

In summary, given that asthmatic children have been singled out as a group that warrants intensive research focus in terms of potential health effects of PM and gaseous pollutants, the current body of data for this group is seriously incomplete in at least 6 critical areas: **1**) the effects of long-term exposure on the natural history of asthma; **2**) the relationship between symptom and lung function responses to short-term fluctuations in air pollution and the natural history of asthma; **3**) the characteristics of asthmatic children who "respond" to different components/mixtures of air pollutants; **4**) the specific components of the mix of ambient air pollutants that may be responsible for health effects, which includes the relative contributions of the $PM_{2.5}$ and coarse fraction ($PM_{2.5-10}$, CF) components (and their chemical constituents) and particle number to health effects; **5**) the potential mechanisms that might be involved; and **6**) the optimal pollutant-specific metrics for the evaluation of health effects. Clarification of elements 1-4 above is essential inputs into any overall risk evaluation of the health impacts of ambient air pollution in persons with asthma.

The study carried out specifically addresses the data gaps noted above. The study will provide a more comprehensive and interpretable examination of the long-term effects of particulate air pollution on young children with asthma through tests of very specific hypotheses that relate exposure to air pollution with specific short- and medium-term responses in such children. Consequently, the data generated will provide for a more accurate and complete risk evaluation for the age group of children covered by the study.

2.1.2 Background Presented in Interim Report, July 2002

For the Interim Report we had searched the published literature to determine the extent to which the limitations that we identified have been addressed. We restricted our search to studies related to air pollution-related health effects in children with asthma that have been published since the preparation of our original proposal in 1999. With a few exceptions, we had excluded consideration of cross-sectional studies. We also had reviewed the relevant section (Section 8) of the latest draft of the E.P.A. criteria document for PM (59). We did not find any studies for any pollutants that address specifically the questions posed by our study. In fact the recent draft version of air quality criteria document for PM (59) contains the following quotes in Chapter 9 (Integrative Summary)

> "…little is yet known about the involvement of PM exposure in the progression from less serious childhood conditions, such as asthma and respiratory symptoms, to more serious disease endpoints later in life." (page 9-79 in (59))

> "In summary, host variability may come to be the most important factor in determining the response profile of any population exposed to PM. Studies to date suggest that certain subpopulations are indeed more acutely responsive to PM, perhaps due to differences in lung deposition (either in terms of dose and/or intrapulmonary distribution) or other biologic aspects of the cardiopulmonary system or disease thereof. The role of innate attributes of risk grounded in one's genetic code is largely unknown but potentially of great importance." (page 9-79 in (59)).

Thirteen potentially relevant new daily time series studies (not specifically related to residence near roadways) were identified that evaluated the occurrence of acute symptoms, hospitalizations and changes in lung function in relation to daily changes in air pollutants in persons with asthma (60-72). In relation to our previous review, these studies did not add important new insights into the nature and magnitude of the risk of exposure to air pollution. Selected studies were presented which appear most relevant.

Two studies from Seattle reported increased respiratory morbidity in children with asthma in relation to daily changes in air pollution (62, 65). Norris, ***et al.*** (62) observed an association between fine PM (at levels below the newly adopted NAAQS of 15 μ/m^3) and CO and daily emergency department visits for children with asthma. In a more extensive analysis, Yu and colleagues (65) reported increased risks for daily asthma symptoms related to CO, $PM_{1.0}$ and PM_{10} even after conditioning on the presence or absence of asthma symptoms on the previous day. These authors estimated a 31% increased risk for symptoms for a 10 μ/m^3 and 1 pphm increase in $PM_{1.0}$ and CO, respectively, in a two-pollutant model. Quantitatively, the CO effect was greater than that for $PM_{1.0,}$ and the authors interpreted the CO effect as a marker for traffic-related pollutant effects. Ostro, ***et al***. (71) presented results from a 13-week time series study for African-American children with asthma who lived in the Los Angeles area. New onset of cough was associated with PM_{10}, $PM_{2.5}$, 12-hour average NO_2, and mold (*Cladosporium* and *Alternaria*—see below for additional data) but not with O_3. However, daily O_3 was associated

with increased medication use as was daily PM_{10}. Severity of asthma (44% mild, 41% moderate, 15% severe) and use of controller medications did not affect the results.

Friedman and colleagues (72) studied the effects of reduced traffic-related air pollution and acute asthma events over the 17 days of the 1996 Olympic Games in Atlanta. Percentage decreases in air pollutants during the games were: peak O_3 28% (81 to 59 ppb), CO 18%, PM_{10} 16% and NO_2 7%. In contrast, SO_2 concentrations increased by 22%. Traffic counts decreased by 22% during the games and these decreases were correlated with decreases in peak O_3. Declines in three day average O_3 were associated with decreased odds for Medicaid claims for asthma events and pediatric emergency department visits. Similar effects also were seen for $PM_{10,}$ but the estimates were less precise than those for O_3. Another study of pediatric emergency department visits for asthma performed in Atlanta over the summers 1993-1995 also could not distinguish clearly independent effects for O_3 and PM_{10} (66).

Investigators from the PEACE study (Pollution Effects on Asthmatic Children in Europe) attempted to ascertain the components of PM that might be responsible for the effects of daily changes in PM concentration on asthma morbidity (PEFR and symptoms) (68). Over 1000 thousand children ages 6-12 years with asthma were observed daily for approximately 2 months during the winters of 1993/1994. Iron, nickel, zinc, vanadium, sodium, lead and silicon were evaluated in addition to PM_{10} mass. Changes in daily concentrations of most of the metals were not associated with either changes in PEFR or symptoms. Silicon and iron showed some association with the occurrence of phlegm, but the importance of this observation is unclear, given all of the evaluations that were conducted.

A study of 49 children with asthma from Finland followed for six-weeks is particularly relevant to this study. The PM to which these children were exposed was largely derived from re-suspended road dust (61). Various lags of $PM_{2.5}$, particle number in the range of 0.1-1.0 μm, PM_{10} and $PM_{2.5-10}$ were associated with decreased PEFR and increased occurrence of cough. Based on their results, the authors concluded (from abstract): *The present study demonstrates the highly variable size and number distribution and chemical composition of particles in Finland, and underlines the importance of measuring the size and chemical composition….*

A final acute effects study of interest is that of Thompson and colleagues who evaluated daily hospital admissions for children who presented for treatment for asthma in Belfast, Northern Ireland over the period 1993-1995 (70). PM_{10}, gases and benzene were evaluated. In two-pollutant models with benzene always included as one of the pollutants, previous day benzene concentrations remained significantly associated with hospital admissions in all models. Associations for PM_{10}, CO and NO_2 also were significant in the benzene+other pollutant models; O_3 was not significantly associated with admissions in a model with benzene. These authors interpreted the consistent effect of benzene and the two-pollutant models with PM, CO and NO_2 as evidence for traffic emissions as the source of the pollutants.

In summary, these acute effects time-series studies reinforce previously available data on the association of daily variation in concentrations of various criteria pollutants on changes in asthma morbidity. However, these studies do not provide any additional insights into either the mechanisms for the observed associations, nor do they address the specific components of PM

that might be most important or the identification of particular sub-groups of children with asthma who appear to be particularly sensitive to short-term fluctuations in daily concentrations of ambient pollutants.

Publications from the Children's Health Study (CHS) provide some evidence that is relevant to the present study, in terms of potential long-term effects of air pollution in children with asthma. A publication in 2000 reported evidence that increasing 4-year average levels of air pollutants across the 12 sites for the study were associated with decrements in expected growth of lung function (73). Overall, the effects were strongest for NO_2, $PM_{2.5-10}$, inorganic acid and $PM_{2.5.}$ No overall effect was seen for O_3. In analyses that evaluated effects in asthmatic children compared to non-asthmatic children, percentage decrement in FEV_1 growth was greater in asthmatic children in relation to O_3 and PM_{10} levels—the PM effect being greater than the O_3 effect. A cross-sectional analysis of the baseline lung function in this cohort (57) had observed significant effects for O_3 on FVC and FEV_1 levels in girls with asthma. A second publication related to the role of air pollutants to the new onset of asthma (74) is relevant indirectly to our study. This study observed that children who engaged in 3 or more high intensity sports and lived in "high ozone" communities (average 4-year 8-hour O_3 concentrations 56-69 ppb) had a three-fold increased risk of the occurrence of new onset asthma (74). Finally, cross-sectional data from this study also have shown that increasing community concentrations of PM_{10} and NO_2 are associated with increasing prevalence of bronchitis in children who reported a physician's diagnosis of asthma (58). Taken in aggregate, these data provide evidence that long-term exposure to ambient air pollution is likely to have long-term effects in children with asthma in terms potentially of worsening the excess loss of lung function that characterizes asthma in general and the increased occurrence of chronic symptoms. These data also provide support for our hypothesis that children who are responders to short-term changes in concentrations in ambient pollution may be the susceptible sub-set of children with asthma who are driving the responses observed in the CHS.

Our original application discussed the need to include measurements of selected components of the bioaerosol that contributes to overall PM complexity. One new study has been published which reinforces this need, in terms of the development of unbiased estimates of PM-related health effects on children with asthma. An Australian group of investigators reported a prospective study of a general sample of 399 school children average age 9 years who were observed up to five times over a two-year interval (75). These investigators observed an association between ambient concentrations of *Alternaria* in the previous month and the occurrence of airways hyperreactivity and increased use of bronchodilator rescue medication in children with skin test sensitivity to *Alternaria* but not in children without such sensitization. Although not all of the subjects in the study had asthma and air pollution effects were not ascertained, the study, along with studies cited in our previous application, points to the potential of exposure to fungal spores and acute and chronic symptoms in children with asthma. This inference is reinforced by a second study that evaluated the effects of the house dust (1→3) β-D glucan levels (marker for fungal exposure) on peak expiratory flow (PEFR) variability in children ages 7-11 years (76). PEFR variability was related to dust levels of (1→3) β-D glucan levels independent of the effects of endotoxin, other allergens and bacteria in dust. The association was strongest in children with asthma. No association was observed in children without respiratory symptoms; atopic children without asthma showed associations that were closer to children with asthma. Unfortunately, this study provided no data on potential effects of

either ambient or indoor air pollutant effects. In aggregate, these new studies leave unresolved the relative importance of exposure to fungal antigens and ambient air pollutants, particularly PM, to asthma morbidity and the long-term natural history of asthma.

The importance given to endotoxin as a potential contributor to health effects related to PM can be seen by the innumerable references made in the recent draft version of the update criteria document for PM to endotoxin effects *in vitro* and *in vivo* in humans (59). A recent *in vitro* study with alveolar macrophages has confirmed an independent and predominant role for endotoxin in stimulation of cytokine production by the insoluble fraction of PM_{10} derived from ambient air in Chapel Hill, NC (77). Cytokine stimulation was much lower in the soluble PM_{10} and insoluble $PM_{2.5}$ and undetectable in the soluble $PM_{2.5}$. These findings point to $PM_{2.5-10}$ as the important source for the asthma-relevant pro-inflammatory effect of PM. These data taken in conjunction with the identification of seasonal patterns in the concentration of endotoxin levels in outdoor and, to a lesser extent, indoor environments (78) point to the need to have ambient measurements, as well as indoor measurements, to distinguish effects on asthma related to the non-bioaerosol components of PM and to better clarify season-specific air pollution effects. A recent review of health effects related to endotoxin has highlighted the role of endotoxin as an agent that exacerbates asthma (79). Data from a birth cohort study have identified an association between levels of endotoxin in house dust and wheezing in the first year (80), which further points to a potential role of endotoxin in the aggravation of asthma in childhood. As with the fungal antigens, the relative importance of endotoxin as a contributor to associations between ambient PM and asthma remains poorly defined and much in need of further study. Given the new *in vitro* data noted above, it is particularly important that endotoxin effects be separated from PM health effects that are related to combustion sources of PM and PM effects that may be observed for the "coarse" fraction of PM ($PM_{2.5-10}$).

Attempts to identify the sources of PM that are related to health effects are the subject of considerable current research. For obvious reasons, motor vehicle sources, especially diesel exhaust, remain at the forefront of interest. Since the time of our summary in 1999, no new studies have been published that diminish the relevance of our hypotheses related to diesel exhaust exposures and oxidative potential of ambient pollutants. A review by Casillas, *et al*. (81) highlights the role of oxidant mechanisms to explain the effects of diesel exhaust particles on the immunology relevant to exacerbation and long-term effects on asthma. However, the data from epidemiological studies remain conflicting. A study conducted in San Diego County, CA found an association between higher traffic flows and increased medical care visits for asthma among children who received health insurance through Medi-Cal (California's Medicaid program) (82). A case-control study in London, UK failed to show any association between hospital admissions for asthma in children ages 5-15 and distance of residence from roadways (83), while a study from Erie County, NY showed an association for children ages birth-14 years between asthma hospitalization and intensity of traffic on residential streets (84). Two cross-sectional studies show the same conflicting results in relation to wheeze prevalence in children. One study did not find an association between traffic intensity in relation to the school of children 4-16 years (85). A study by the same authors found an association between wheezing in children 4-16 years who lived in the same area as the first study and nearness of family residence to a main road (86). Thus, many issues remain to be defined with regard to the best measures of exposure, the locations at which exposures should be assessed as well as the size of effects on respiratory morbidity related to asthma. A preliminary analysis of the association between distance from

roadways and baseline pulmonary function among FACES children [revised later] was completed for a UC Berkeley senior thesis.

In summary, the large body of research published since our original submission reinforces the synthesis that we provided in that application. Our selected review finds that all of the health-related hypotheses that we proposed to test are still relevant and have not been addressed by any study to date. Moreover, none of the issues related to the need to employ methods of causal analysis have been addressed in any study of which we are aware.

2.1.3 Updated Background from Interim Report to the Present

To carry out this update, the latest draft of Chapter 8 for the most recent draft of the EPA Criteria Document (87) and the ozone criteria prepared by ARB were reviewed (88). In addition a PubMed search was done for the years 2003-2005 for the following search categories all of which had "asthma and air pollution" as their root: 1) the root search; 2) root+"traffic"; 3) root+particles; 4) root+pollen; 5) root+endotoxin; 6) root+fungi; and 7) root+spores. References also were checked from the background section from a grant application to NIH (Division of Lung Diseases, NHLBI) for continued funding for FACES. We also have included some studies that were omitted from our previous background sections that should have been noted. We focus attention on short-term exposure studies that go beyond associations with $PM_{2.5}$ mass alone, since these really do not add any additional strength to the case that we already have made with respect to effects of such exposures. We found no studies that directly relate responses to short-term changes in air pollution and long-term progress of asthma symptoms and lung function in children with asthma. In fact, neither the ARB Ozone Criteria Document, nor the EPA PM Criteria Document even notes this connection in its relevant sections on health effects.

Several new studies (we include one from 2000) have address asthma-related outcomes in relation in relation to bioaerosols with varying degrees of sophistication (89-92). Independent associations for various pollutants, pollens and spores have been found for emergency room visits for asthma (89, 92) and peak expiratory flow rate (90). However, no studies have evaluated overall interactive effects or season-specific interactive effects. Moreover, these studies have been restricted to PM mass and gaseous pollutants without consideration of PM components or particle numbers. No studies have specifically address the associations between endotoxin and asthma outcomes in the context of ambient pollutants.

Several studies have gone beyond mass-based PM estimates to evaluate effects of volatile organic compounds (VOCs), usually in settings where mobile sources predominate (70, 93, 94), and one study evaluated a large panel of toxic air pollutants (95). Hagen, *et al*. (93) found that ambient benzene and formaldehyde concentrations were more consistently associated with hospital admissions for respiratory diseases, even in models that included PM_{10}. A time series of study of hospital admission of children with asthma in Belfast, Ireland found the relative risk estimates for benzene were greater than those for PM_{10}, NO_2, NO, NO_x and SO_2 in single pollutant models (70). However, the correlations between benzene and these pollutants were all greater than 0.80, which made it impossible to discern an independent benzene signal. Delfino, *et al*. studied a panel of 24 Hispanic children with asthma during the high VOC in east Los Angeles county (95). Twelve air toxics, along with PM_{10}, elemental carbon (EC), organic carbon

(OC) and gaseous pollutants were measured. EC and OC were strongly correlated with all VOCs, except formaldehyde. A variety of two pollutant models were evaluated. In two-pollutant models, EC, OC and VOCs all lead to a decrease in PM_{10} associations with asthma symptoms, while each showed a statistically significant association with increased symptoms. Similar findings were observed for SO_2 and NO_2. Although it is tempting conclude that there is an independent signal for the various VOCs, the high correlations renders interpretation of the magnitude of the coefficients uncertain and dependent on the variance of the exposure variables (96). In a second study in the same population, the same authors evaluated asthma outcome associations with exhaled breath and ambient VOC concentrations (same 12 VOCs as in (95)). The correlations between breath and ambient VOC concentrations ranged between –0.18 and +0.38 for all pairs and between -.14 and +0.31 for ambient/breadth concentrations for the same compound. In general, associations between concentrations and decreased peak flow were slightly greater for exhaled breath concentrations, although most were not statistically significant. This study really does not establish any causal connection between ambient VOC exposures, body burden and adverse asthma outcomes. The poor correlation between ambient and breath concentrations undoubtedly is due to lack of data on indoor sources. Finally, the Children's Health Study (CHS) evaluated the association between O_3, EC and OC, NO_2, organic acid and three mass fractions of PM (10, 2.5, 2.5-10) and other gaseous pollutants on the occurrence of bronchitic symptoms (97). Single-pollutant models that compared across the 12 communities in the study, EC had the largest association per unit, although the pollutant effects across the range of observed values were the same for all others, except for O_3. In the within-community analyses, the largest associations were seen for EC>OC, with all others being much lower. In two-pollutant models, OC was most consistently associated with the onset of bronchitic symptoms, followed by NO_2. Since the organic carbon fraction is rich in redox active compounds (polycyclic aeromatic hydrocarbons, quinones), these data would support and important role for this mix of PM constituents (97). However, OC was highly correlated with $PM_{2.5}$, NO_2, EC, O_3 and organic acid, which makes it difficult to assign a unique role to this fraction in these data.

A very large number of new studies have appeared that have explored the association between exposure to mobile sources and adverse outcomes, not all related to asthma in children. Most have used a variety of indirect measures (distance to roadways, weighted traffic counts or weak surrogates such as NO_2; for example see (98)). We focus on a few studies that have gone beyond these simple approaches; although none of the studies that we site address the questions being studied in FACES. A study in the Netherlands applied GIS-based estimates of traffic-associated pollutants at the residences of children (99, 100). Although the investigators focused only on $PM_{2.5}$, soot and NO_2, they did show that traffic-related variables explained 73% of the $PM_{2.5}$ concentrations in the Netherlands (100). These investigators could not find conclusive support for an association between residence-based traffic-related exposure and the diagnosis of asthma over the first 2-years of life (99). Although not related to childhood asthma nor based on individual-level data, a study by Janssen, *et al*. (98) is worth noting, since the investigators used vehicle emission source data and data on air conditioner prevalence to assess the contribution of exposure to traffic-related pollutants to hospitalization for COPD, pneumonia and cardiovascular diseases in 14 U.S. cities. Air conditioner use was inversely associated with effect estimates for PM_{10}. PM_{10} emissions from traffic were more closely associated with daily hospitalizations for cardiovascular diseases and pneumonia than with COPD. A cross-sectional German study used a combination of averaged daily traffic data, measurements of benzene, soot and NO_2 plus GIS to

estimate residential exposure to traffic-related pollutants for children who participated in ISAAC (101). Their model had an R^2 of 0.80, 0.80 and 0.77 for benzene, soot and NO_2 respectively. These authors found that current asthma was associated with benzene exposures and current wheeze with benzene and NO_2, as was high traffic counts. There was an interaction between exposure to second hand smoke and high traffic and the occurrence of allergic sensitization. However, the relative contribution of specific components to the increased risk was not investigated. In a cross-sectional study, investigators from the California EPA measured $PM_{2.5}$, PM_{10}, black carbon (BC) NO_x, NO_2 and NO for 11 weeks at 10 schools (age distribution of subject not given) in Alameda County, CA (102). Wind direction and proximity to traffic were also considered. Among children who had lived at their current residence for at least 1-year, school concentrations of NO_2, NO, and BC had the strongest association with bronchitic symptoms and physician-diagnosed asthma; however, the association was limited to females. Wind direction and location <300 meters from roadway gave similar effect estimates to those obtained with the pollutant measurements. Increasingly, oxidative stress has been recognized as one of the major pathways through which ambient pollutants damage the human host (103). The association between exposure to traffic-related air pollutants and oxidative damage was investigated in 47 female highway toll workers and 27 female office workers (104). Toll workers were found to have significantly higher urinary concentrations of 8-hydroxydeoxyguanosine, a marker of oxidative DNA damage. These findings are consistent with *in vitro* studies that have demonstrated that the quinines and aeromatic compounds in diesel exhaust particles and ultrafine PM cause damage to mitochondria (105, 106).

The contribution of coarse PM ($PM_{2.5-10}$) to morbidity in childhood asthma has not been well studied. In a recent review, Brunekreef identified only a single such study (107). This Canadian study case-crossover and time series design evaluated hospital admissions for asthma in children 6-12 years in Toronto from 1981-1993 (108). Only $PM_{2.5-10}$ at lags 5 and 6 days showed significant associations with hospitalizations in both designs. No such consistence was seen with PM_{10} or $PM_{2.5}$ at any lag. As in other studies noted above, the association was largest in girls, although a significant association was seen for males as well. This study did not evaluate any components of the course or fine fraction.

One new study has compared differences in the association between FEV_1 and particles between exposure estimates based on personal monitoring of $PM_{2.5}$ and estimates based on ambient measurements made indoors and outdoors at the homes of 19 subjects ages 9-19 with physician diagnosed asthma and at a central site (109). Percent changes in FEV_1 were larger with exposure estimates from personal monitoring than those derived from the ambient measurements. Of interest, for all measurements, associations were greatest for 4- and 5-day moving averages. Ambient measurements made indoors, outside the homes and at the central site had similar magnitude of association with decline in FEV_1. Exposure estimates based on a true microenvironmental model that used indoor-outdoor measures and time-activity-location data were not constructed to compare with the individual exposure estimates. Associations based on individual exposures were larger in boys who had positive skin prick tests to house dust mite antigen (no girls positive). No effect modification was observed with cat antigen positivity.

Our previous background sections discussed several studies that tried to evaluate air pollution related asthma outcomes in the context of medications used to treat asthma; and several additional studies on this issue have been published. In a panel study of children with asthma,

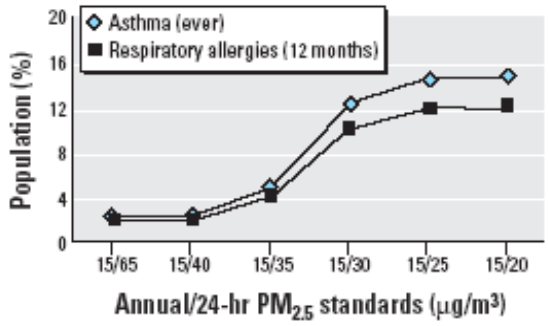
Delfino found that adverse associations of PM_{10}, NO_2, O_3, fungi and pollen with FEV_1 were largely confined to subjects who were not taking anti-inflammatory medications for their asthma (110). However, in a latter panel study with personal monitoring, these investigators did not observe effect-modification by use of anti-inflammatory therapy (109). Von Klot and colleagues conducted a 7-month panel study of 67 adults with asthma in Erfurt, Germany (111). Daily mean particle number concentrations (fine and accumulation modes) were the PM exposure metric, along with gravimetric measurements of PM_{10} and $PM_{2.5}$ as well as SO_2. The authors reported an association between cumulative 14-day number concentration (fine and ultrafine) and use of inhaled corticosteroids (ICS) and an association between rescue medication use ultrafine number concentration and fine mass concentration. However, in 2-pollutant models for use of ICS, fine mass concentration had more consistent association than did ultrafine number concentration. An 11-month longitudinal cohort of 149 children in Sydney, Australia with a history of wheeze were evaluated for association between 3 daily symptom variables, use of rescue medication, use of inhaled corticosteroids and doctor visits for asthma and daily concentration of O_3, NO_2, and PM_{10} (112). No associations were observed with use of either type of medication. Effect modification by medication use was not evaluated in the analyses of symptoms or visits to the doctor. The largest study of the association between exposure to ambient pollutants and symptoms and medication use in children with asthma was that of Gent, *et al*. (113). These investigators followed 271 children under age 12 years with physician-diagnosed asthma. Ozone and $PM_{2.5}$ were the only pollutants evaluated. Subjects were stratified into those who did and did not use maintenance medication throughout the 183-day study; respiratory symptoms were the outcome. The authors note that those on maintenance medication had more symptoms overall compared to those not on such medication. Among users, chest tightness and, to a lesser extent, breathlessness were associated with same and previous-day ozone but not with $PM_{2.5}$ in 2-pollutant models. An association between increased use of bronchodilators and same day O_3 was observed in non-users. In non-users, the point estimates for the association between same day O_3 and chest tightness and breathlessness were greater than for bronchodilator use but were estimated less precisely. While it is tempting to suggest that the differences between studies could be due solely to population differences or differences in exposure environments (not the case for the 2 Delfino studies), it is more likely that the estimates of medication effect from these studies potentially are severely biased to varying extents by different patterns of time-dependent confounding. This point is made clear in a recent publication from the FACES project (3). We demonstrated, based on data from the FACES cohort, that failure to consider the time-dependent confounding between medication use and symptoms in conventional analyses can lead to severely biased (in fact, counterintuitive) effect estimates. Moreover, even with the application of methods such as marginal structural models that can address time-dependent confounding, failure to specify a "correct" model can still result in severely biased effect estimates. Based on this latter publication, we believe that the question remains completely open as to the extent to which asthma medications alter the impact of air pollutants on adverse asthma outcomes and the extent to which ambient pollutants actually lead to increased use of rescue medication.

A final area that is relevant to the FACES study relates to effects of ambient pollution on lung function growth in children with asthma. Although other studies are available (e.g., see (114)), the one most relevant to FACES is a follow-up study of lung function growth over the ages 10-18 years in the Children's Health Study (115). The same pollutants noted for the previous discussion of the CHS (97) were used in this analysis. Results are presented in terms of

cross-community differences for each pollutant, with range between highest and lowest community being used for size of association. No estimates at the individual-level are provided. Except for O_3, which had little variability across the cities, PM_{10}, $PM_{2.5}$, NO_2, acid vapor, EC and OC all were associated with declines in FVC, FEV_1, and FEF_{25-75}, with the largest changes seen for the latter measure. The number of children with asthma (n=457) was too small to provide a precise estimate of association in children with asthma compared to children without asthma.

In summary, no existing studies that have published results to date have addressed the questions that are the main focus of this grant; and none have used the analysis methods that we have used to get directly to causal inference and to deal with problems of colinearity of various pollutants. Moreover, even for the short-term component of FACES, there are no other panel studies that include as many subjects with clinically diagnosed asthma and who have been followed for as long a time period as the FACES cohort. Thus, the study remains highly relevant scientifically. This conclusion is reinforced when one compares the research questions and the data being collected with the research priorities set in the 2004 (most recent) National Research Council report (see Box S-1, (116)). In whole or part, six of the 10 research priorities set out in this report are being addressed in FACES (numbers refer to Box S-1 (116)): 1) Outdoor measurements versus actual human exposure; 2) Exposure of susceptible sub-populations to toxic PM components; 5) Assessment of hazardous PM components; 7) Combined effects of PM and gaseous pollutants; 8) Susceptible sub-populations; and 10) Analysis and measurement.

Figure 2.2-1: Percentage of all Children that would Especially Benefit (Members of Subgroups with Pre-Existing Health Conditions) from Compliance with Alternative Annual/24-hr $PM_{2.5}$ (98^{th} percentile) Standards



2.2 PUBLIC HEALTH SIGNIFICANCE

Asthma is the most important chronic disease of childhood in terms of numbers affected, morbidity and health care costs (117). A recent NASCAUM impact assessment estimated that, in the Northeastern states, approximately 1.5 million persons under age 18 had asthma at some time (118). Figure 2.2_1 shows the estimated percentage of children (<18 years) with asthma and respiratory allergy who would benefit from various forms of the $PM_{2.5}$ standard (118). Even adherence to the current standard would lead to benefits for over 30,000 children with a history of asthma in this region. In Fresno (1st Street monitoring site), the 2002-2004 3-year average 98th percentile for $PM_{2.5}$ was 61μg/m^3 (National 24-hour standard = 65μg/m^3) (http://www.arb.ca.gov/adam/cgi-bin/db2www/adamtop4b.d2w/Branch). In addition, during 2004, there were 18 days that exceeded the Federal 8-hour average O_3 standard. A recent study conducted by the Allergy and Asthma Foundation in conjunction with the Research Triangle Institute rated cities with respect to a variety of factors related to asthma occurrence (prevalence, environmental triggers and asthma health care) (http://www.asthmacapitals.com/). Fresno was ranked 20th worst in the U.S. and worse than any other location in the San Joaquin Valley (e.g., Bakersfield was ranked 53rd). Fresno received the worst rating on air quality and an average rating on asthma prevalence. In 2003, Fresno County hospitals report 1,292 hospital discharges for the "asthma-bronchitis" diagnostic related group (DRG) in children between the ages 0-17 years (1.6% of all discharges) (http://www.oshpd.cahwnet.gov/HQAD/PatientLevel/Frequencies/Fresno/03DRGFresnoCounty.pdf). A recent study conducted in the Fresno Unified School District found that 13.5% (2,534/18,732) and 9.0% (3,935/43,781) of students enrolled in the high schools and elementary schools, respectively reported asthma on their emergency cards filed with the FUSD (http://www.calcleanair.org/documents/yes%20asthma%20research%20project%20FINAL.pdf).

In the 2004 review of the rationale for a revision of the California O_3 standard (88)**,** it was estimated that a 10 ppb increase in daily 1-hour maximum O_3 concentration was associated with a 2.3% (95% CI: 1.3-3.3%) increase in hospital admissions for asthma in children ages 0-18. The CHS reported a 68% (95% CI: 43-98%) increase in school absences for the combination of lower respiratory illness/wheeze/asthma for a 20 ppb increase in 8-hours O_3 (119). The incidence of lower respiratory illness with wheeze over the 6 months of the study was 0.3/100 child-days (approximately 1000 children/day at risk). In contrast, there was no increase associated with daily increases in PM_{10} or NO_2. The 2002 review of the California standard for particulate matter and sulfates (120) did not provide specific benefit estimates for children with asthma but did provide some estimates that are useful to assess potential impacts on children with asthma. It was estimated that, if the $PM_{2.5}$ annual average were lowered to a background of 5 μg/m^3, in California, a mean of approximately 33,000 hospitalizations for acute bronchitis would be saved in children ages 8-12 years (it reasonably can be assumed that many of these would have asthma) and a mean of 340,000 attacks of asthma would be prevented across all ages.

In summary, air pollution-related asthma morbidity is a major public health problem in the study area and in the state of California, and the nation as a whole. The San Joaquin Valley remains a non-attainment area for O_3, PM_{10} and $PM_{2.5}$

(http://www.arb.ca.gov/desig/adm/adm.htm). Fresno has a population of 425,000 and is one of the fastest growing cities (counties) in the state of California as of the 2000 census (http://factfinder.census.gov/home/saff/main.html?_lang=en). Given the continued burden of asthma in Fresno, there is a continued need to identify those children with asthma most at risk for short- and long-term asthma-related morbidity in the study community. The FACES study represents the most far-reaching research effort to-date to provide these data in the study community and the San Joaquin Valley overall.

A recent quantitative risk assessment estimated that the expected effect of planned reductions in air pollution between now and 2010 (121) would lead to 10,000 (4,000-20,000) fewer hospitalizations for asthma in U.S population under age 18 years and 40,000 (10,000-70,000) fewer emergency room visits for the population under age 16 years. This study addresses this burden and provides much needed data to identify the characteristics of children with asthma who are most susceptible to the long-term adverse effects of exposure to current levels of ambient air pollution.

2.3 BIOLOGICAL RATIONALE

We have discussed biological mechanisms to some extent in the background section. Here we present a brief review of the current thinking on the mechanisms through which ambient pollutants and bioaerosols are related to increased asthma morbidity. A number of mechanisms have been proposed to explain the epidemiological data. We focus on those mechanisms that have relevance to the FACES study.

Although the inflammatory component of asthma affects all airways of the lung, peripheral airway abnormalities are a particularly important component of the structural changes in asthma (122-124). Studies of 30-day-old rhesus monkeys sensitized to house dust mite antigen (HDMA) demonstrated that 6 months of cyclic exposure to O_3 markedly increased structural remodeling of terminal bronchioles, an effect not seen with 6 months of cyclic exposure to HDMA alone (125). The structural abnormalities persisted after animals were returned to clean air environments (C. Plopper, personal communication). Exposures to O_3 and NO_2 enhance allergic responses to inhaled antigens to which young adult subjects are susceptible (126-129).

Data have accumulated that diesel exhaust particles (DEP) not only produce inflammatory responses directly (130), but also serve as an important modulator of IgE immune responses (131). In studies of ragweed-sensitive individuals, DEP have induced IgE switching, as measured by increased numbers of IgE-producing cells (48), antigen-specific IgE, increased levels of mRNA that code for specific expressed IgE proteins, and decreased expression of mRNA for Th-1 cytokines {interferon-γ (INFγ)- and IL-2} and increased expression of mRNA for Th-2 cytokines (IL-4, 5 and 13) (37, 48). These effects can be duplicated with exposure to the polycyclic aromatic hydrocarbon (PAH), phenanthrene (46). Nasal instillation of DEP in humans sensitized to ragweed pollen leads to induction of IgE antibodies to keyhole limpet hemocyanin (KLH), a response not seen in the absence of DEP exposure. In this later study, IL-4 levels increased and INFγ levels decreased 29 days after KLH+DEP exposure but not after KLH exposure alone (132). A recent study has shown that this response to DEP is under specific

genetic control (133). Ragweed-sensitive subjects challenged with intranasal instillation of ragweed+DEP showed increases in nasal lavage IgE, IL-4 and histamine and a decrease in INFγ, responses not seen during ragweed challenge alone in the same subjects. Subjects who had the glutathione S-transferase (GST) M1 null or the GSTP1 wild-type genotype had the largest differences between DEP+ragweed and ragweed alone challenges for all markers. The largest differences were seen in those subjects with both the GSTM1 null and GSTP1 wild-type genotypes (133). Approximately 15-20% of the population can be expected to carry this combination of genes (133). GSTs are involved in phase 2 xenobiotic and reactive oxygen species (ROS) metabolism (134). GSTM1, which is found in the lung, plays an important role in the metabolism of redox active oxy-PAHs that are an important component of PM and gas phase air pollution (135). GSTP1 is found in high concentrations in the lung and is involved in detoxification of lipid peroxidation products (136). An important role of the GSTs is to protect the host from generation of toxic ROS that are capable of induction of inflammation, and damage to cell membranes and DNA (137, 138).

Reactive oxygen species are known to play a role in the adverse health effects related to exposure to ambient air pollutants (103, 139-141) and may be the final common pathway that leads to tissue damage in asthmatics (141). ROS and reactive nitrogen species generated by ambient air pollutants (e.g., PM-associated PAHs and transition metals, O_3, oxides of nitrogen and their photolytic reactions with organic species in ambient air pollution) can explain many of the observations summarized above with respect to the effect of air pollutants on asthma. (141). ROS initiate cell-signaling cascades that lead ultimately to activation of non-allergic and allergic inflammation, peroxidation of cell membranes, programmed cell death and cell necrosis (131, 139, 142, 143). The inflammatory process itself generates additional ROS that are part of normal cellular defense mechanisms (144-146) and down-regulates enzymes involved in the metabolism of ROS (147), thereby creating an ongoing cycle of cellular injury (148). Components of fine and coarse PM also lead to oxidant stress, either directly (105) or indirectly, through bioaerosol components (e.g., endotoxin) that are potent inducers of inflammation (149). These effects can be reduced or eliminated *in vitro* with anti-oxidants (150) or with the chelation of water-soluble transition metals that participate in the Haber-Weiss reaction (137). Several studies of ambient PM show that endotoxin may be as important a source of inflammation and ROS as are metals and organic components (77, 151, 152). Through interactions with specific lymphocyte receptors, endotoxin activates many of the same signaling pathways that are activated by organic components of PM created by the activities of man (153). The relevance of these *in vitro* data was provided in a randomized, controlled study of vitamin E and C supplementation in children with asthma in Mexico City which demonstrated that supplementation eliminated the reductions in FEF_{25-75} associated with previous day's O_3 concentrations (154). A follow-up publication showed that the effect of previous day's O_3 concentrations led to decrements in FEF_{25-75} only in children who carried the GSTM1 null genotype and that the effect of the antioxidant supplements was confined to this group (155). Controlled exposure studies also have demonstrated a protective effect of antioxidant supplementation on ozone-induced enhancement of bronchial reactivity in young adults with asthma (156).

No studies have evaluated joint or additive effects of daily changes in ambient pollutants and endotoxin. Endotoxin is ubiquitous in the environment, either adsorbed onto the surfaces of particles generated through combustion processes or as part of indoor dust created by human activity and tracking of soil into homes and the presence of animal or pets (78, 157, 158). *In*

vitro exposure of rat alveolar macrophages to urban air PM demonstrated that stimulation of inflammatory cytokines can be blocked by specific inhibitors of endotoxin (151) and that endotoxin in the $PM_{2.5-10}$ (coarse) fraction of ambient PM largely was responsible for the induction of pro-inflammatory cytokines (IL-6, IL-8) after *in vitro* exposure of human monocytes (45) and alveolar macrophages (77). Endotoxin exposure has a complex relationship with childhood asthma (79). Levels in dust have been associated with increased asthma severity (13, 159) and wheezing in the 1st year of life (80) but also with decreased skin prick test reactivity (158), decreased occurrence of atopic asthma and production of IL-10, IL-12 and TNF-α (160). The relevance of genetic polymorphisms in the CD14 receptor for asthma etiology and disease severity remains to be clarified (161-163). Very few data are available on the distribution of endotoxin concentrations in air (157).

Oxidative stress (OS) thus provides a link between the immunomodulatory effects of all oxidant species of the air pollution/bioaerosol mixture and the specific allergic mechanisms that underlie asthma (37, 48, 131, 132, 164-166). OS also provides a pathophysiological link to the airway inflammation and airway remodeling, which are hallmarks of asthma (124, 141).

2.4 HYPOTHESES (AS PRESENTED IN THE ORIGINAL APPLICATION)

The overall goal of this study is to determine the effects of particulate air pollution on the natural history of asthma in young children. To address this overall goal, a series of hypotheses will be tested in a cohort of asthmatic children who are 6-10 years of age (subsequently modified to 6-11) at intake into the cohort. The hypotheses are developed to evaluate the extent to which particle air pollution (mass, chemical constituents, particle number) acts both independently and as a modifier of other environmental exposures that can trigger asthma attacks (allergens, infectious agents, etc.) to influence the short and long-term patterns of occurrence of symptoms and the growth of lung function during the childhood years. Consideration of all particle effects will be in the context of the complex and seasonal patterns of air pollution mixtures to which children are exposed. The hypotheses are based on the premise that, within a population of asthmatic children, particle air pollution (specific constituents of PM) has effects on subsets of asthmatic children and these subset may differ in relation to different PM components and other air pollutants. The hypotheses will be tested through a series of panel studies and through a classical longitudinal, cohort study. Both the patterns of response to air pollution and the phenotypic characteristics (e.g., degree of sensitization to environmental allergens, degree of air way reactivity, etc.) of the responding subsets will be studied.

An implicit assumption of the hypotheses to be tested is that there are identifiable subsets of asthmatics whose asthma short and long-term natural history is influenced by ambient air pollution. These subsets are identified most readily by repeated physiologic measures and reports of symptoms

> (**NB**: One critical issue not addressed explicitly in the stated hypotheses/specific aims relates to the effects that individual-level cumulative exposures to particulates (alone and in combination with other ambient pollutants) may have on asthma natural history independent of any observed effects due to responses to short-term changes in air pollution levels. To address this question a relatively

high degree of individual-level variation in cumulative exposures will be required. It will not be known whether there is sufficient variation in cumulative exposures among the study cohort until the exposure assessment data has been collected and analyzed. In the absence of this information, we do not believe it is appropriate to state hypotheses related to this issue. However, in recognition of the importance and implications of this type of health effect, we have given substantial thought to how one could address the question analytically should we find that the required variation exists. Hence, our analytic plan does include a description of the approach we would take to answer the question.)

2.4.1 Short-term Effects

1. Hypothesis 1: Chemical components of particle air pollution that have immuno-enhancing properties (i.e., polyaromatic hydrocarbons (PAH) in diesel exhaust) are associated with symptom onset and severity and short-term reductions in lung function in a seasonally dependent pattern.
   a. A subset of asthmatic children who are sensitized to outdoor spring and early summer allergens and/or to fungal spores will have increased episodes of symptoms and short-term, reversible decrements in lung function that are related to markers of vehicle particle emissions, especially diesel particles {e.g., elemental carbon (EC), number of ultra-fine particles and particle size range} during the spring and summer months.
      i. These associations will be enhanced (additive or synergistic) by ambient ozone concentrations.
   b. A subset of asthmatic children who are sensitized to indoor allergens (e.g., dust mite, cockroach) will have an increased risk of episodes of symptoms and decrements in lung function that is related to markers of vehicle exhaust emissions that either will not have a seasonal component or, if seasonal, will be more strongly associated in the late fall and winter months.
      i. These associations will not be influenced by ambient ozone concentrations.
      ii. These associations will be not be detected in asthmatic children repeatedly exposed (passively or directly) to second hand smoke and/or wood burning smoke in their homes.
   c. The associations in **1a** and **1b** will be less evident in children with intermittent and mild asthma (NHLBI/WHO definitions) or in children with moderate asthma on inhaled anti-inflammatory medication.
   d. Specific chemical constituents (or classes thereof) are stronger determinants (i.e., larger estimate of association and/or more precise estimate) than particle size distribution of the associations in **1a** and **1b**.
   e. Particle effects that are identified under this hypothesis will be most pronounced (larger effect size) among children whose residences and/or schools are in closest proximity to major roadways with heavy traffic density.

2. Hypothesis 2: There are specific biologic components (e.g., endotoxin, fungal spores) and specific anthropogenic components (e.g., latex particles from road tire dust) in the $PM_{2.5-10}$

(coarse) fraction that are associated with exacerbations of symptoms and short-term, reversible decrements of lung function in a subset of asthmatic children and these associations are strongest during the months of April through September, when $PM_{2.5-10}$ constitutes a major fraction of the PM_{10} mass.

a. These associations will be less evident in children with intermittent and mild asthma (NHLBI/WHO definitions) or in children with moderate asthma on inhaled anti-inflammatory medication.
b. Endotoxin, fungal spore concentration and concentration of latex particles "explain" most of the association between $PM_{2.5-10}$ mass concentration and exacerbations and transient declines in lung function that are observed in asthmatic children during the dry season (May-October).

3. Hypothesis 3: Components of particle air pollution that are markers for the oxidative potential of particle air pollution (e.g., transition metals) are associated with more severe symptoms and short-term, reversible decrements in lung function in a subset of asthma children.
   a. These associations do not follow the same seasonal pattern of association as observed for vehicle exhaust markers.
   b. These associations also will be dependent (additive and or synergistic) on ambient ozone concentrations during the months of May-October.
   c. These associations will not be detected in asthmatic children repeatedly exposed to second hand smoke and/or wood burning smoke in their homes.

2.4.2 Medium-Term Effects (Expected over Four Years of observation)

4. Hypothesis 4: The subsets of asthmatic children who respond with short-term deficits in lung function to components of particulate air pollution (alone and/or in conjunction with other ambient air pollutants) will show relatively slower age-sex-specific growth of lung function than asthmatic children who do not so respond.
   a. The greatest deficits in growth of lung function will be observed in the subset of children whose short-term lung function decrements are associated with the markers for the oxidative potential of particle air pollution.
   b. Measures of particle mass (e.g., ultra fine, fine, coarse) and particle number are less strongly associated with relatively slower growth of lung function in these subsets of asthmatic children who are subject to this effect than are specific PM chemical constituents or groups of constituents.

5. Hypothesis 5: The subset of asthmatic children who respond either to the immuno-adjuvants in particulate air pollution or the oxidizing properties of particle air pollution will have greater asthma-related morbidity {increased frequency and severity of attacks of asthma, more likely to be classified as severe asthma (e.g., NHLBI/WHO classification), and have more medical interventions {e.g., increased use of quick relief medications, higher doses of anti-inflammatory medication, need for medical care}.
   a. The severity of symptoms also will be related to the relative deficits in the growth of lung function independent of effects of particle air pollution on symptoms

3. METHODS

3.1 INTRODUCTION

This section contains the methodologies for all but two of the methods used for the entire FACES project. Since the details are complex and better understood in relation to the results, the marginal structural model methods are presented in conjunction with the results of the statistical analysis (see Section 4.2.3). Additional details are provided in Appendix I. Also, the home intensive monitoring methods and quality assurance are found in Appendix F.

3.2 STUDY DESIGN

3.2.1 Overview and Rationale

The FACES cohort includes 315 asthmatic children with clearly defined asthma recruited as a convenience sample from Fresno and Clovis, CA through advertisements and referrals from local physicians. Fresno was selected because of: 1) the presence of an E.P.A. Supersite that permitted a much wider range of pollutant data than is available normally at routine area-wide monitoring sites; and 2) a high incidence of hospitalizations for asthma in children. Recruitment began in September 2000, and study visits began on November 2000.

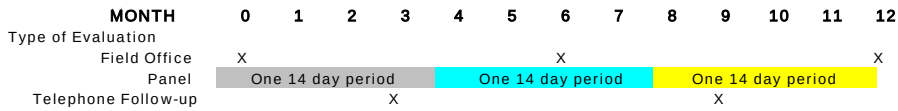
To address hypotheses listed above involving short term effects on long term health, the study design consists of a series of panel studies embedded within a longitudinal cohort study. Measurements of ambient air quality were also made at residences and schools in FACES (see Figure 4.1.6-1) to supplement those obtained at the central site and other routine air monitoring stations and to facilitate investigation of neighborhood- and urban-scale spatial variability in Fresno.

Figure 3.2.1-1 represents a typical 12-month cycle of health data collection. The field office (FO) visits and telephone surveys comprised the longitudinal cohort component of the study. At month 0, the first FO visit constituted the baseline evaluation where detailed asthma, general respiratory and family respiratory history, smoking and household characteristic data were obtained for each subject (Appendix A). Other data collected during this visit included height (sitting/standing), weight, pre and post-bronchodilator spirometry, skin prick testing, buccal cell collection and training on use of a portable spirometer (Appendix B). A FO visit collecting detailed respiratory history, pre and post-bronchodilator spirometry was conducted every 6 months following the baseline evaluation. Every 6-months, beginning at the third month following the baseline visit, a telephone follow-up survey with a parent of each FACES participant consisting of symptoms, medication use, health utilization and changes to the household was conducted.

The first 14-day panel was conducted within 1-month of the baseline visit. This panel included a detailed home inspection to evaluate indoor sources of pollution, evidence of excessive moisture, collection of dust samples for two dust mite allergens, cockroach, cat, and dog allergens and endotoxin levels. Passive samplers for NO_2 and nicotine were deployed for 14

days in the main living area (including O_3 samplers for the same two weeks in summer months of 2002, 2003 and 2004) of each home until environmental samples were collected once in each of the 3 seasons. Subjects completed twice-daily spirometry with an *EasyOne*® portable spirometer (described in 3.2.2.1.1 and Appendix C) (1) . At the end of each session, the instrument asks 5 questions related to symptoms and medication use (Appendix D). Sessions were time and date- stamped electronically to prevent "back-filling" of missed sessions. Parents and children were asked to complete a daily paper diary that assessed symptoms, medication use, location, and activity patterns (Appendix A).

Figure 3.2.1-1



Between February 2002 and March 2003, a special data collection occurred during panel visits for 80 participating households (see section 3.4.4.1 for details). For this effort, FACES investigators designed and constructed a Micro-environmental Exposure Monitoring System (MEMS) that consisted of a freestanding rack that contained measurement devices for O_3, nicotine, fungal spores and pollen grains, PAHs, and a variety of PM-related measures. For each participating household, one unit was placed inside the home in the living room and one unit was placed outside of the home. In 26 of these homes, the unit was used during two panel visits, once in the "warm" season and once in the "cool" season. These indoor and outdoor residential measurements were one component of models that were used to estimate daily individual exposure estimates for each child.

3.2.2 Health Assessment Protocols

Detailed protocols for every step of the study including enrollment, field office spirometry, panel assignments, home visit, spirometry, diary and environmental sample data collection, laboratory analysis and data entry are located in Appendix B. The protocols that were used as part of participant health assessment are described briefly below.

3.2.2.1 Assessment of Lung Function

3.2.2.1.1 *EasyOne*® Spirometry for Panel Visits

The EasyOne® portable spirometer was used for the 14-day panel visits. The EasyOne® is a small, portable device that uses ultrasound flow sensors to measure airflow through a hollow disposable mouthpiece. It has the ability to save hundreds of sessions of spirometric data in memory, which can later be uploaded easily to a computer database. The instrument time and date stamps all sessions electronically. The device has a screen that can display up to 40 characters of text as well as flow-volume curves. A numeric keypad allows the user to answer yes/no questions that are displayed on the screen. The device has no moving parts that require calibration although the calibration was checked prior to each panel visit.

A detailed description of the EasyOne® software and its use by the FACES cohort is included in Appendix C and in 3.5.1.1. In short, the devices were programmed with an alarm that is activated during the time windows of 7A.M.-9A.M. and from 7P.M.-10P.M. to remind children to perform the tests. No tests could be performed outside of these windows. The spirometers used the same acceptability criteria noted previously (Appendix B) to evaluate each effort. If a criterion was not met, the message prompted the child on how to improve the subsequent effort. Children were allowed six attempts to achieve three acceptable efforts (with a secondary target of at least two that were reproducible). Data were saved for each of the three best efforts, even if the acceptability criteria were not satisfied during the session. At the end of each session, children were prompted to answer a series of questions about asthma symptoms and medication use by entering "yes" or "no" on the spirometer keypad. For each session, 500 incentive points were awarded if three acceptable and at least two reproducible efforts were obtained and all questions were answered. If six attempts were made and all questions were answered but the efforts failed to meet either the acceptability criteria, the session was awarded 200 points. Over a 14-day period, a total of 14,000 points could be obtained. This point system was designed to encourage the participants to complete all the sessions to the best of their ability. We had planned on providing prizes based on these incentive points. However, after discussion with the field staff, it was reported that some children were upset when they got fewer points than their siblings and this discouragement led to their reluctance to complete the tests. For this reason, we did not pursue the implementation of the reward system. Since the original protocol was never implemented, the revision did not affect the study in any way. However, presumably, the revision did improve children's study retention over the years.

Before being delivered to a home, the *EasyOne*® was fit with new batteries and the calibration was checked with a 3-liter calibration syringe and a specially designed spirette. Next the field staff ensured the unit was fully functional by completion of a test run. Finally, the device was programmed to take the "3 best curves" and the time and date were checked. Once the unit passed all tests, the child's identification number and other information were entered into the device then it was delivered to the home.

When the device was returned, putting the portable unit into its cradle retrieved the spirometry data. The EasyWare software was used to load the data into the computer. Each test session was printed out and sent or faxed to Berkeley for review (see 3.2.2.1.3)

3.2.2.1.2 Spirometry During Field Office Visits

Standing height was measured in stocking feet with a wall-mounted stadiometer; sitting height was measured with a standard protocol. Weight was measured in stocking feet with a digital scale. (Appendix B).

Forced expiratory volumes were obtained in the sitting position (with nose clip) with a Morgan rolling seal spirometer attached to a microprocessor with an *Easy One* ® spirometer in tandem as a mouthpiece (1). Subjects were permitted 8 attempts to achieve 3 acceptable and reproducible tracings (Appendix B). Reproducibility was defined for this population as FEV_1 with less than 10% variability and PEFR with less than 20% variability. Immediately following baseline spirometry, subjects inhaled two puffs of albuterol from a metered dose inhaler (90

μg/puff) through a spacer fitted with a pediatric facemask. Spirometry was repeated 20 minutes after the second puff of albuterol. At the beginning of the study, the investigators trained the technicians who performed the testing. Instruments were calibrated daily with a 3-liter syringe in accordance with the manufacturer's instructions. Any calibrations outside of the acceptable range were reported immediately to the investigators. All calibration results were recorded into a logbook. Time- and flow-volume curves from the Morgan were reviewed on screen by two investigators (JB, IT) and subsequently by Lucas Carlton (LC), a staff person with extensive experience in administration and interpretation of spirometry. These individuals made the final judgment as to whether or not tracings were acceptable for analysis. The investigators and staff person repeatedly calibrated each other to assure consistent readings. Therefore, this protocol change should not reduce data quality for this part of the study. LC referred all equivocal tracings to IT or JB for final reading. Only sessions that contained at least two acceptable tracings were used for all analyses.

To obtain an objective evaluation of EasyOne's® reliability and validity, we made a direct comparison with the office-based rolling seal, volume spirometer (Morgan Scientific, Winchester, MA), based on an in-line technique to measure simultaneously forced expiratory maneuvers from both instruments. The details of this comparison have been published in (1) (Appendix C). Based on this evaluation, we concluded that the portable spirometer accurately and reliably measured lung function, relative to a "gold standard" clinic-based device. Despite the excellent agreement across measures, physician review of the curves revealed some limitations of the quality control software. These limitations are not unique to the *EasyOne*®; rather, they reflect the marked variability in lung function that can occur during an unsupervised test session for a child who may be symptomatic and is experiencing worsening asthma. Also, the end-of-test criteria differed slightly for each instrument that can lead to differences in the simultaneously collected mid-expiratory flows.

3.2.2.1.3 Quality Control/Quality Assurance for Lung Function Measures

Initially, it was expected that the QA/QC algorithms implemented by the Morgan and *EasyOne*® spirometers would be sufficient to provide high quality data. However, after a preliminary review of data from both spirometers, Drs. Ira Tager (IT) and John Balmes (JB) decided that every curve from both spirometers should be reviewed.

All spirometry data presented in this report have undergone the following QA/QC procedures.

- Review every time volume and flow volume tracing from the Morgan spirometer by recalling test data on the Morgan database. Since these data are obtained during a technician supervised sessions strict criteria are used for acceptability and are retained (See Appendix B for these criteria).

- Review each time- and flow-volume curve for all test sessions from the 14-day panel data obtained by the *EasyOne*® spirometers. Data from each test session are printed out on a standardized report form that includes both types of curves for at least 3 repetitions (if available) as well as numerical results for lung function measures of interest to the study

and quality assurance parameters (i.e., time to peak flow, end-of-test volume and back extrapolation volume). Until March 2004, these reviews were performed primarily by IT and to a lesser extent by JB. Beginning in 2004, under the supervision of IT, curves were screened by LC for acceptability. Curves that appeared to be unacceptable by LC were then reviewed by IT. The investigators and staff person repeatedly calibrated each other to assure consistent readings therefore, this protocol change should not reduce data quality for this part of the study. Since data were obtained in the homes of the children and without technical supervision, we implemented additional criteria to take into consideration that after a forced expiratory volume maneuver, subsequent maneuvers may show evidence of bronchoconstriction with changes in the shape of the time and flow-volume curves and the forced expiratory time: (**1)** coughing may occur during testing which reflects the clinical status of the child's asthma Therefore, curves with the obvious evidence of coughs were retained unless the cough precluded the calculation of at least peak expiratory flow rate (PEFR) or $FEV_;$ (**2)** some curves provide valid measures of peak flow and FEV_1 but not FEF_{25-75} or FEF_{75}, that are of interest to the study—peak flow and FEV_1 from such curves were retained; (**3)** curves produced in less than 2 seconds for which it was evident that the subject had completed a full forced expiratory maneuver were retained.

- To assure that there was consistency between the reviewers, curves for which the interpretation were not absolutely clear were read by a person who did not carry out the initial evaluation and was blinded as to the initial interpretation. In addition, JB, IT and LC met regularly to review criteria for difficult curves to be sure that each applied the agreed upon decision rules for certain recurring patterns that lead to problematic interpretation.

Tests conducted in the field office were included only if they met all ATS acceptability criteria. All tests that were used in analyses met all ATS acceptability criteria. We included tracings that had cough, provided that the coughs did not occur before peak flow. In the cases where reproducibility criteria were not met (in our case 10% for FEV_1, 20% for peak flow) but the subject could produce at least two acceptable tests, we did not eliminate these tests. This is consistent with the ATS recommendation not to eliminate tests solely for reasons of reproducibility (see ATS statement Am J Respir Crit Care Med 1995;152:1107-36). The reasons for this are obvious—as asthma worsens, within-test session variability increases. It should be noted that, unlike many other studies, we did not use a single maximum. We required two acceptable tracings per session as a criterion for inclusion of data in the analyses.

3.2.2.1.4 Bronchodilator Protocol

During the baseline visit and all subsequent FO visits (at 6-month intervals), children were asked to complete pre- and post-bronchodilator spirometry. Most asthmatics have been exposed to Albuterol and it is commonly used in clinical and research settings. As discussed in the original proposal, we decided that a methacholine challenge would not be performed for three reasons: **1**) methacholine testing is time consuming and has potential for side effects; **2**) Methacholine challenge would have been contraindicated in asthmatic children with low levels of lung function (e.g., FEV_1 <80% predicted); and **3**) repeated methacholine testing at 6-month

intervals was not likely to be acceptable to children or their parents. Thus, given the significant demands of the overall protocol, the additional information that could be gained from methacholine testing did not outweigh the practical and theoretical disadvantages. Physicians trained research staff on the proper administration of Albuterol. Details for bronchodilator administration are outlined in the Baseline Protocol (Appendix B).

3.2.2.2 Allergen Skin Test Panel

There is evidence to suggest that children who are allergic to indoor and outdoor allergens may respond differently to air pollutants than children who do not react to these allergens. To identify atopic children in our cohort, we included a panel of 14 aeroallergens in the baseline assessment (see Table 3.2.2.1 for a list of the allergens tested).

Children who were not tested at baseline were examined during either the 6 or 24-month visits or later at a subsequent clinic visit. The selection of allergens for baseline testing was determined though discussions with the Mobile Asthma Clinic at Valley Children's Hospital in Madera (a major pediatric hospital that serves the study area) with additional modifications from UCSF-affiliated allergists familiar with Fresno area aeroallergens.

Prior to administration of the skin test, each parent was asked whether their child had ever reacted to skin testing so severe that treatment was required (other than ointments or creams). If so, the test was not given to the child. The parent was also asked whether the child had recently had a cold or taken antihistamines. If so, this information was recorded on the form so that these data could be excluded, if necessary. The test was administered using a Multi-Test II allergy skin testing kit. The allergens, histamine, and saline controls were applied to the surface of the right and left arms using a Multi-Test II applicator (donate by Lincoln Laboratory, Decatur, IL). After 20 minutes, the allergens were wiped off and the field technician measured wheals (raised skin) and flares (redness) using a Multi-Test II slice chart. (See Appendix B).

In January 2002 penicillium antigen was replaced with chladosporium. Since most children completed only one round of skin testing, the change meant that we were missing information on chladosporium skin-test positivity for the 62 children who had been skin-tested by that point. Nevertheless, the decision to test for chladosporium was an important one, given the focus on fungal spores in other parts of the study.

3.2.2.3 Nutritional Assessment

To examine whether dietary antioxidants or other nutrients provide protective effects from air pollutants and to consider changes in nutrient intake with age and season, parents were asked to fill out a nutritional survey twice (initially at 6 and 24-month post baseline; after January 2004, at any two points at least six months apart). The nutritional survey was developed by the "Growing up Healthy" component of Nurses Health Study (NHS) and contains questions about the child's diet and use of vitamin supplements. Beginning 6 months after baseline, the survey was mailed to the household one-week prior to the next FO visit along with instructions (see nutrition letter in Appendix A) to complete the survey and bring it to the visit. Respondents were also told that assistance with the survey would be available at the FO visit. Coding of

nutrient intake will be carried out at the NHS at the Harvard School of Public Health with programs developed for this assessment tool.

3.2.2.4 Collection of Samples for DNA Testing

3.2.2.4.1 Blood Samples

Most participating children and their families were compliant with all aspects of the study. However, only 29% of participants who had completed a baseline interview as of May 2002 agreed to blood sampling. The original purpose for the blood collection was to obtain inflammatory markers and DNA for future genetic studies (e.g., C-reactive protein). Beginning in July 2002, blood collection was replaced by buccal cell collection. Participants who had submitted a blood sample also were asked for a buccal sample. Since all parents and children were asked for a buccal sample regardless of whether they had completed a blood sample, this protocol change did not affect data quality or the subsequent analysis in any way.

3.2.2.4.2 Buccal Cell Collection

Buccal cells were collected by swabbing the inside of the cheek with a cytobrush. Cells were shipped immediately to UC, Berkeley. Since samples were shipped at room temperature, but required processing within 48 hours, buccal cells were obtained only on Mondays, Tuesdays and Wednesdays. After informed consent was obtained from the responsible adult, participating children and biological parents who lived with the child were asked to give buccal samples at their next FO visit. To encourage completion of this part of the protocol, we provided two other opportunities for the parents to participate. We offered the option of having the FACES staff collect buccal cell samples during a home survey and also provided the families with the necessary instructions and materials to collect the samples themselves, refrigerate and have them picked up that same day by the FACES staff.

Table 3.2.2-1 Well Skin Test Solutions

Right Forearm	Left Forearm
Bermuda Grass	***Saline (Scratch Control)***
Standardized Cat Pelt	*Alternaria tenuis*
Standardized mite mix (der p and der f)	Dog hair and dander
Olive	*Cladosporium (*replaced penicillin)
Standardized Grass Pollen (Perennial Ryegrass)	Cockroach mix
Chinese Juniper	Common Privet
Oak Mix	Cedar, Mountain
Mugwort Sagebrush	***Histamine (1 mg/mL) (Positive Control)***

3.2.3 Questionnaires and Visits

3.2.3.1 Overview

The screening form and all adult questionnaires (baseline, telephone and FO) were translated into Spanish.

A baseline visit was scheduled after a child was screened, determined to be eligible and parental consent was obtained. Telephone, FO and panel visit "windows" for the duration of the study were calculated by the electronic data tracking system from the time the baseline was completed. FO, telephone and panel visit windows were six weeks in duration. A visit could be scheduled anytime during the window but not once the window was closed. Non-participation during a specific window did not preclude continued participation in the study.

Telephone surveys were conducted every six months and began three months after baseline. Field office visits were also conducted every six months beginning six months after baseline. At baseline, the child was assigned randomly to one of 8 groups. The child's panel visit schedule for the duration of this study was determined by the group assignment. Panel visits were scheduled once in each of three "seasons": Winter (October through January); Spring (February through May); and Summer (June through September). Panel visits included placement of NO_2 and nicotine samplers inside the home, a home survey, collection of a dust sample (to determine concentrations of household antigens and endotoxin), a 14-day daily diary, and twice-daily spirometry with the *EasyOne*®.

Questionnaires fell into four categories: baseline FO visit, follow-up telephone surveys (3-, 9-, 15-, 21-, 27-, 33-, 39-, 45- and 51-month visits.), follow-up FO visits (6-, 12-, 18-, 24-, 30-, 36-, 42-, 48- and 54-month visits), and home surveys. The follow-up FO visits were essentially identical with the exception of the 6- and 24-month adult clinic visit questionnaires that included special sections (see Table 3.2.3.5a). Questions were identical for each telephone survey. The same home survey was given at each panel visit. The content of each survey type is reviewed below.

3.2.3.2 Screening

The screening questionnaire included questions related to eligibility (diagnosed asthma, age, medication use, health care utilization, symptoms in the past 12 months, chronic conditions, behavioral problems, duration of residency in Fresno and address, plans to stay in the area for at least 2 years and willingness to have environmental samples collected in the home). In addition, the form included information on age at diagnosis, race/ethnicity of both the child and the mother and additional contact information for tracking purposes (see Table 3.2.3-1).

3.2.3.3 Baseline

At baseline, children and one adult relative (usually the mother) were each interviewed separately. The adult was asked about the child's birth history, health history, health utilization

in the past year, symptoms in the past year and 2 weeks, current medication use, history of oral steroid use, triggers, exposures in the home and at school, exposure to second hand smoke and demographic questions. (See Table 3.2.3-2)

The child's height and weight were measured. After training, the child performed up to 8 forced vital capacity maneuvers before and after administration of a bronchodilator (see descriptions of Morgan spirometry and bronchodilator protocols (sections 3.2.2.1.2 and 3.2.2.1.4) or the protocols themselves (Appendix B)**.** During the 20 minute waiting period required before post-bronchodilator spirometry, the child was asked questions about symptoms (wheeze and shortness of breath, then cough) in the past 12 months and past week, triggers, medications (currently used and used in the past week), and asthma management (use of a space, nebulizer, and peak flow meter). Each child who was at least 10 years old was asked whether s/he smoked. The child listened to a tape of the smoking questions with headphones then answered each question aloud and the interview recorded the child's answer. Finally, the child was skin tested; and buccal cells were collected. (Before July 2002, blood tests were taken). (See Table 3.2.3-2)

3.2.3.4 Telephone Questionnaire

The telephone questionnaire was administered only to an adult. The questionnaire included: 1) information on health utilization, symptoms and prescription medication use in the past 3 months or 2 weeks; 2) general exposures in the home and at school in past 3 months; and 3) exposure to second hand smoke (SHS) in the past 3 months. (See Table 3.2.3-4)

3.2.3.5 Field Office Visits

Every six-months, the child and a related adult or legal guardian came to the field office. The child completed spirometry and the same questions that were asked at baseline, except that symptom questions referred to the past 3 months and past week. Skin testing and buccal cells were collected, if still needed. The adult was asked all of the questions that were asked at the telephone survey and additional questions about changes to the home environment, second hand smoke (SHS) in the home, and the child's activities. During the FO visit, the adult was asked to fill out a nutritional survey, until two were completed. The adult, if related biologically to the child, was also asked to give a buccal cell sample, if one had not already been collected. (See Table 3.2.3-5a,b)

During the 6- and 24-month visits, two special modules were included. The 6-month questionnaire included a section on early life exposures both from residences in which the child had lived since birth and from occupational exposures of the mother and father during the mother's pregnancy.

3.2.3.6 Panel Visits

During the first year of the study, each participant was asked to complete a panel visit within one month of the baseline visit. As planned at the outset, beginning one year after the

baseline visit (November, 2001 for those who began at the start of data collection), participants completed three panel visits each year. Participants who enrolled after November 2001 were put immediately on a 3-visit/year schedule. The panel or "home" visit contained several components: 1) 2-week passive samples for nicotine/NO_2 both inside and outside of the home; 2) a home survey that contained both interviewer observations of the home and questions for an adult in the household; 3) a dust sample collected to measure indoor allergens and endotoxin; 4) 14 days of twice-daily spirometry (7-9 A.M., 6-10 P.M.); 5) completion of a two-page daily symptom and activity dairy by the parent and/or child for 14-days; and 6) 2-week passive samples for ozone both inside and outside of the home (summers of 2002, 2003 and 2004) (Table 3.2.3-7).

To reduce the burden on study participants, beginning in January 2003, a household was asked to provide the nicotine/NO2 and ozone (if applicable) samples, the home survey and dust collection at least once in each of the three seasons. The Easy One ® spirometry and completion of the daily diary were still scheduled three times per year. If a family moved to a new house, environmental samples were again collected for three seasons for the new home. The change was made to encourage participants to be part of the EasyOne and diary components of the panel visit. By January 2003, there were already many homes with two or more samples in a given season. Therefore, we are still able to compare concentrations of nicotine/NO2 and dust across seasons within selected households. While it would have been ideal to continue collecting the environmental samples, the positive (presumed) effects on study retention were more important to overall data quality.

Soon after this change was implemented, when environmental samples were not part of the visit we gave participants the option of having the *Easy One* ® and diary placed in a drop off container on their porch or other agreed-upon location. The *Easy One* ® and diary were placed in the same box for pickup at the end of the14-day panel visit. Most participants who were given this option, elected to use it.

3.2.3.6.1 Home Survey

The home survey was a modified version of the form used in the National Cooperative Inner-City Asthma Study (NCICAS). Some questions that were relevant only for east coast urban populations were deleted and additional questions, such as distance from agricultural fields, were added to make the form relevant for the FACES population. Most of the home inspection form was completed by visual inspection by field staff. Some questions were asked of the participant (i.e. how often is the fireplace used), and those questions were translated on the hardcopy of the form with standardized wording. In addition to the survey, FACES-specific forms were developed for *EasyOne*®, diary and nicotine/NO_2/ozone sampler tracking forms, dust collection and moisture measurements. The interviewers and data entry clerks who used these forms also used the health data forms; and, therefore, coding was consistent across the health and exposure instruments (e.g. 1=Yes, 2=No.). Variable naming conventions (see Appendix E), skip pattern rules, and data cleaning procedures are identical to those described in Section 3.2.5.

Since the study began, only minor revisions have been made to the home visit forms. All changes were such that data across forms was compatible.

3.2.3.6.2 Two-Week Diary

The original two-week diary was based on forms used in the ARB-funded University of Southern California Children's Health Study and several other large cohort studies. The diary included questions about symptoms (wheeze, cough, shortness of breath, runny nose), symptom severity, exposures in the home (e.g. gas stove use, vacuuming), ventilation in the home (time windows were opened for several time intervals), and time-location-activity questions for five time blocks that spanned the hours between 6:00 A.M. and 10:00 P.M. For each time block, participants were asked to fill out their activities; time spent doing each activity and its location (indoors our out, at home, school, or somewhere else). FACES investigators determined the appropriate time-intervals for reporting of activities (i.e. 6:00 A.M.-9:00 A.M., etc) based on information about patterns of air pollutants of interest and children's "typical" school schedules. A coding scheme was developed for daily activities (Table 3.2.3-8). Rather than enter detailed text, only an activity code and the amount of time spent doing the particular activity was recorded on the form. If an activity fell into multiple categories (e.g. "went out to dinner"), then up to two codes were entered in the field (see Table 3.2.3-8).

Every attempt was made to make the layout of the diary user-friendly, since this is one of the few self-administered forms used by FACES. The "front page" of the diary, which included questions about symptoms, school absences, and exposures that day in the home (e.g. vacuuming, use of the gas stove and time that windows were open) usually was completed. However, completion rates for the "back page" which included questions on time-activity portion of the diary were lower than desired. There were 2,776 diary-days for which the information on the back page was coded and entered. For the time questions, data were missing from at least one time block 52% of the time. Children had trouble assessing how much time they spent in a location or with each activity. The time spent on each activity was often both substantially less than or more than the total number of hours in the block. For the location questions, information was not available for the full day on 49.5% of diary days. Therefore the time-location-activity questions were revised into a much simpler form. Instead of five blocks of time, the diary contained only two time periods: A.M. and P.M. For each time period, the participants were asked to report medication use; rides in cars or buses, whether there was any physical activity during that period and whether the activity took place indoors or outdoors. Examples of physical activities were described as part of the diary instructions in the front of the packet. The revised form, although missing the potential detail on time-activity that the original had, has had high completion frequency. For example, the question on whether physical activities that made the participant "breathe hard" occurred was completed for both time blocks 90.4% of the time for indoor activities and 89.3% of the time for outdoor activities.

Given that the time-location-activity questions in the original diary were not completed 52% of the time, and that the revised, less-resolved time-location-activity questions were completed at a much higher rate (90% of the time), this change was important. However, the original time/location/activity questions were supposed to be used to come up with individual exposure estimates for each child on each diary-day. Because we did not have the more detailed time/location/activity data, we used answers to two "A.M." and "P.M." questions from the revised diary (Did you do any physical activity or sports outdoors?" and "Did you ride in a car or van") as modifiers of general activity estimates for children based on the CARB Children's Activity Patterns Study (167).

The diary has not been translated into Spanish. One of our eligibility criteria was that the child speak English and, therefore, is able to read the diary and the *EasyOne*® spirometer. We have very few Spanish-only speaking parents; and, to date, it has not been necessary to create a Spanish diary.

3.2.3.7 Development of Questionnaires

Before being used in the field, each questionnaire was designed or updated and translated into Spanish (adult questionnaires only). Next, data entry screens were created, and tested. A tracking system was used to identify children who were due to have a visit, and to identify procedures that were still needed for the child. The tracking database also was used to generate contact records and for logging the date/time of each attempted contact.

Small corrections were made to surveys when errors were detected, interviewers reported that questions were not clear to participants or questions were inadvertently omitted from the survey (e.g. a question about renting or owning the home was not included in the original questionnaires). Each time this occurred, the appropriate change was made to the English and Spanish versions and the version number of the hard copy and associated databases was changed. In November 2001, (between the 9- and 12-month surveys), revised versions of baseline, 3-, 6- and 9-month forms and daily diary were issued. These small changes were only made if questions or corresponding answer choices were incomplete or unclear. Thus, the revisions should have a positive effect on data quality.

The surveys and their start dates are listed in Table 3.2.3-9. Beginning in 2005, various questionnaires began to be phased out of the study. The telephone questionnaires ended in March 2005. Recruitment ended in October 2004. Screening continued for siblings of participants until April 2005. Baseline visits also ended in April 2005; and no more families were allowed to enter the study. In July and August 2005, all visit forms were revised to accommodate a new visit schedule. Participants are now asked to complete one FO and 2 panel visits each year. The panel visits no longer include environmental samples or the home survey.

Table 3.2.3–1: Content of Screening Questionnaire
Race/Ethnicity: Child and mother.
Eligibility-related questions: *Inclusion Criteria:* Diagnosed asthma, age, medication use in the past 12 months, duration of residency in Fresno and address, plans to stay in the area for at least 2 years and willingness to have environmental samples collected in the home. *Exclusion Criteria:* chronic conditions, behavioral problems
Consent (if eligible)
Alternative contact information: Workplace, e-mail, at least one friend/relative/neighbor. (Also an eligibility requirement)

Table 3.2.3-2: Content of Adult Baseline Visits
Birth History biological/adoptive; maternal age at birth; gestational age, city/state of birth; birth complications; birth weight; breast feeding history; vaccinations; day-care with 5+ children y/n for 1st 3 years of life.
Health History History of respiratory infections by the age of 2; respiratory infections after age 2; (age of diagnosis is asked at screening); hospitalization history; history of allergies, eczema, sinusitis; health history of each family member (asthma, eczema, allergic rhinitis; copd/emphysema/chronic bronchitis).
Health Utilization Hospitalizations, Emergency Room visits, unscheduled MD visits due to asthma (ever, in the past 12 months or 3 months)
Asthma Symptoms (wheeze/cough-variant asthma) in the past 12 months and 2 weeks. Symptoms in past 12 months and 2 weeks; school absences due to symptoms; symptoms with activity, emotion and during sleep.
Medications prescribed for child's asthma β-agonists; inhaled steroids/intal/cromolyn; other controller medicines asked about separately using chart with pictures of each medication; # times each medicine is supposed to be taken and actually taken when child is wheezing; or well; use of oral steroids ever/ past 12 months, most recently taken; use of alternative therapies
Exposures in the home and elsewhere. Distance from major roadways; number rooms; stuffed animals; child's bedding Household pets (time inside/outdoors; in child's room, child's bed; Pests; pesticides; gas stove presence and use; heating fuel; heating system; fireplace or woodstove; gas stove and oven; air conditioning type and use; Air cleaners, vaporizers/humidifiers; moisture/mold; pets;
Triggers in the past 12 months e.g. weather; pollens, grasses or trees; colds/flu; physical activity; outdoor smoke/fires; cigarette smoke; air pollution; cold air.
Smoking during each trimester of pregnancy (mother/father); currently among people who live with child; exposures in vehicles or when away from home.
Demographics Number of people in house; age and relationship to child; income; race/ethnicity; educational level of each parent; employment status of each parent; health insurance status of child;

Table 3.2.3-3: Content of Child Baseline Visits
Asthma Symptoms (wheeze/cough-variant asthma) in the past 12 months and 2 weeks. Symptoms ever and in past week; bad enough to stop talking; during play; school absences due to symptoms; symptoms with activity, emotion and during sleep. Triggers; presence of cough-variant asthma.
Medications prescribed for child's asthma β-agonists; inhaled steroids/intal/cromolyn; other controller medicines asked about separately using chart with pictures of each medication; # times each medicine is supposed to be taken and actually taken; use of nebulizers, inhalers, spacers, peak flow meters. Access to medication at school; Does child decide when to take medication.
Smoking Ever smoked; # times smoked (<10; 10-20; >20); Friends tried to smoke; with friends when they smoked

Table 3.2.3-4: Content of Telephone Survey (asked to adults only)
Health Utilization Hospitalizations; Emergency Room visits; Unscheduled MD visits due to asthma;
Symptoms (wheeze/cough-variant asthma) Symptoms in past 3 months and 2 weeks; school absences due to symptoms; symptoms with activity, emotion and during sleep.
Changes to medications prescribed for child's asthma in the past 3 months or since the last visit For medications reported at the previous visit, medication use in the past 3 months and most recent use; # times supposed to be taken ("as needed" was allowable answer); # times taken each day when well; # times taken each day when wheezing; Newly prescribed medications and their use patterns.
Medications for allergies
Exposures in the home and elsewhere. Pests; pesticides; moisture/mold; pets; smoking; school-related exposures; organized sports

Table 3.2.3-5a: Adult Field Office Visit Questionnaire
Health Utilization Hospitalizations; Emergency Room visits; Unscheduled MD visits due to asthma; Alternative methods to treat asthma
Symptoms (wheeze/cough-variant asthma) Symptoms in past 3 months and 2 weeks; school absences due to symptoms; symptoms with activity, emotion and during sleep.
Prescription medication use for asthma
Changes to medications prescribed for child's asthma in the past 3 months or since the last visit For medications reported at the previous visit, medication use in the past 3 months and most recent use; # times supposed to be taken ("as needed" was allowable answer); # times taken each day when well; # times taken each day when wheezing; Newly prescribed medications and their use patterns.
Exposures in the home and elsewhere. Pests; pesticides; moisture/mold; pets; smoking; school-related exposures; organized sports; Air conditioning type and use; Heat type and use; Air cleaners, vaporizers/humidifiers; use of dryers; fireplace or woodstove; gas stove and oven
Triggers in the past 3 months and 2 weeks.
Characteristics of new homes Type of housing; distance to major roadways; heating fuel; heating system; presence of gas oven, range or stove, presence of kerosene heater or space heater.
Occupations Occupation of mother/father; Exposures due to jobs or hobbies by anyone who lives with the child.
Nutritional Survey (until two completed; also could be completed at home by the parent before/after the FO visit).
Buccal cell collection (for biological parent, if not completed)

Table 3.2.3-5b: Child Field Office Visits Questionnaire
Questionnaire: Questions were identical to baseline visit except that asthma symptoms (wheeze/cough-variant asthma) referred to the past 3 months and past week.
Spirometry (pre- and post-bronchodilator use; up to 8 attempts for each)
Skin testing (if not yet completed)
Buccal cell collection (if not yet completed)

Table 3.2.3-6: Special One-time Components of Adult Field Office Visit Questionnaires	
6-month	**Residential History**
	Residences since child's birth; Occupations of mother/father during pregnancy of child
24-month	**Early-life & agricultural exposures**
	During first year of life, type of housing, exposure to dogs, cats, farm animals; live in urban/rural or other environments; Environment lived in from aged 3 to present age; parent worked on a farm.

Table 3.2.3-7: Content of Panel Visit
Nicotine and NO_2 samples; location, date/time opened; date/time closed
Ozone samples: (If during ozone collection period.) location, date/time opened; date/time closed
Dust Collection: Sample from kitchen/living area; sample from child's bedroom floor/ mattress & pillow
Home Survey: Where child sleeps; air conditioning, heat; vaporizer/humidifier use & frequency of use; gas stove presence / pilot / range hood / exhaust fan; presence of fireplace or woodstove; change in child's mattress in past 6 mo; pets -- y/n; in child's room/bed,; pests; distance to agricultural fields; physical characteristics of the home; number of rooms; farm animals close by; burning trash or leaves nearby; **For each room in the house:** floor coverings; heat type, AC type, fan use; air cleaner use; evidence of pets or pests; ashtrays, cigarette butts; GPS location of the house; overall condition and cleanliness in the home.
Household Sketch: Location of each room, location of samplers
Diary: For each day: symptoms (wheeze/shortness of breath/cough/chest congestion; runny or stuffy nose; cold or flu; sick; parent miss work; vacuumed; anyone smoked inside; with other smokers today; use of AC, Kerosene heater, wood stove, fireplace, candles, stove for frying or charring food, gas heater, oven cleaner; windows open more than 30 min.; windows open overnight; Stove burners on 10+ min.; gas oven on 10+ min; Out of Fresno/Clovis area; For AM and PM: medication use; Ride in car; bus; any physical activity; Indoors or out;
***Easy One* ®:** Twice-daily spirometry + questions about symptoms, use of medication before spirometry.

Table3.2.3-8: Original Time-activity codes for panel diaries	
Code	**Description**
1	Sleeping/napping
2	Sitting (reading, school work, eating)
3	Playing, visiting
4	Moderate activities (housework, yard work, shopping)
5	Strenuous activities (sports, exercise, physical labor)
6	Cooking or food prep
7	Travel
8	Other / not classifiable

Table 3.2.3-9 Data Collection Dates	
Visit / Protocol	**Start date**
Screening	September 2000
Baseline (Adult and child)	November 2000
Home panel (survey, 2-week monitoring, scheduled for 1 panel/yr/child)	November 2000
3-month telephone survey	February 2001
6-month clinic visit (adult and child)	May 2001
9-month telephone survey	August 2001
Revised versions of baseline, 3, 6, and 9-month forms and daily diary issued	November 2001
12-month clinic visit (adult and child)	November 2001
Home panels scheduled for 3 panels/yr/child	November 2001
15-month telephone survey	February 2002
18-month clinic visit (adult and child)	May 2002
Buccal cell collection (child and parents)	July 2002
21-month telephone survey	August 2002
24-month clinic visit (adult and child)	November 2002
27-month telephone survey	February 2003
30-month clinic visit (adult and child)	May 2003
33-month telephone survey	August 2003
Drop-off option first offered for visits with *EasyOne*® and diary only	August 2003
36-month clinic visit (adult and child)	November 2003
39-month telephone survey	February 2004
42-month clinic visit (adult and child)	May 2004
45-month telephone survey	August 2004
Recruitment ends	October 2004
48-month clinic visit (adult and child)	November 2004
Focus groups to improve retention	January 2005
51-month telephone survey	February 2005
Telephone Surveys end	March 2005
Screening ends	April 2005
Baseline Visits end	April 2005
54-month clinic visit (adult and child)	May 2005
New home visit schedule and protocol begins (1 FO/year, 2 home panels/year; no environmental samples taken)	July 15, 2005
Annual clinic visit begins, revised field office visit form.	August 1, 2005

3.2.4 Quality Assurance/Quality Control for Questionnaires

This section provides a discussion of the data management procedures for the health data and any exposure data that were obtained during the interview or home inspection process (other than Home Intensive interviews). It does not include the laboratory data from the samplers that were collected during those home surveys.

All of the interview data collected during clinic, telephone survey and home visits were recorded on hardcopy forms. Interviewers completed any coding that was needed (e.g. medication names) prior to submission of the forms for editing. The Field Coordinator reviewed all forms prior to data entry. If inconsistencies or missing data were noted, the family was called back within a day of the interview to retrieve the information. Only then were the forms forwarded to the data entry clerk. All data were entered directly into SAS data sets (Version 6.12 until December, 2003, Version 8.02, thereafter). All data sets can be linked through a series of identifiers (e.g. Child's identification number, home visit panel number, family identification number.) Data entry, with the exception of the two-week daily activity diaries and spirometry grades, was completed in the Fresno office. The diaries were sent to the Berkeley office and were coded by a research assistant and entered by a data entry clerk. Questions about particular coding problems were discussed with the Project Director or Principal Investigator prior to data entry.

In both offices, the data entry screens were programmed such that the screens looked identical to the hardcopies. The clerk was instructed to enter the data only as they appeared – if missing or incompletely coded information was found, s/he returned the form to the interviewer for resolution. For each data form, data were entered in batches. Every 10^{th} observation in a batch was double-entered into a separate data set. The data manager produced reports to compare the original and quality control samples. If a batch (10 observations) had an error rate of >0.5%, the entire batch was reentered. The data from each questionnaire were entered into a series of datasets. This system was implemented for several reasons. First, SAS has a limit to the number of variables that can be included in any one data set; and for many of our visits, the number of variables exceeded this limit. Second, given that different investigators were going to analyze the data, it was more efficient to split, for example, the smoking and skin test data into unique data sets to make the transfer and description of the coding schemes, etc, more efficient. In this way, investigators do not have to deal with data that are not relevant to their research question. Finally, because we knew that version changes would be necessary over time, it was felt that unique data sets would make it easier to keep track of changes between versions and to limit the need for reprinting a large number of pages of the forms (each section has the version number and data set name listed at the top).

The Fresno server is structured such that the hard drive used for data entry is mirrored with an identical drive, should that drive fail. In addition, each night, the server is backed up onto tape and the tapes are rotated and stored off-site. Once a week (and usually more often), copies of all data sets are copied onto the Berkeley server and archived. A copy is burned onto a CD for additional off-site storage. Files that are essential to the project (study form files, protocols, proposals, etc) also are copied onto the CD for archival and safe storage. The

Berkeley server has nightly tape back up. In addition, all files on the Berkeley server are continually saved to an external hard drive.

Data from the Morgan spirometer were collected on a separate computer linked to the Fresno server for storage. The Morgan produces a report of the "three best curves" which are filed in the child's chart. They were also sent by FAX to the Berkeley office for additional review and grading (see Section 3.2.2.1.3). The data files were transferred to the Berkeley server so that the tracings from all efforts (up to 8 each for pre and post-bronchodilator sessions) could be viewed by the physicians. The actual data files are in a proprietary format and cannot be retrieved in electronic form. Therefore, the data from each effort were entered manually into a database at the Berkeley office. Backup procedures were identical to those listed above for the interview data.

Data from the *EasyOne*® spirometer also was stored on the Fresno server. After each child's clinic visit, the data obtained by the *EasyOne*® (for the comparison to the Morgan spirometer's values) were uploaded to the server with a customized cradle connection into an Access database. A query was developed to compile all records into a common database. When an *EasyOne*® spirometer was returned after a 2-week home panel, the same procedures were used to synchronize the data. This common dataset was backed-up as described above. After the spirometry was graded, the data entry clerk in Berkeley entered the grade into a SAS dataset.

Study activity, tracking and quality control reports were written and continued to evolve to meet study needs. These reports could be run from the Fresno or Berkeley servers, which allowed both offices to have current information about study progress. For example, once a month, the Administrative Assistant in the Fresno office was instructed to run a report that identified all participants who were due for a visit during the following month. For each participant, these reports included current address information, windows for when visits were due, type of visit due, and key variables collected from previous visits that allowed the interview to proceed more quickly. Log sheets also were produced on which the interviewers recorded the time, date and disposition of every attempt to contact the family. These were reviewed periodically by the Field Coordinator to ensure that difficult-to-track participants were being called at a variety of times, including evening hours. The Data Manager created a weekly "Data Management Log" to summarize the status of all projects (e.g. new data entry screens, revisions to skip patterns, etc.) and distributed it to the Berkeley and Fresno offices so that everyone was aware of changes to the data management system.

The Project Director, Data Manager and Research Associates (all in Berkeley) are proficient in SAS and are involved in the editing, resolution and analysis of all data sets. The Project Director, Data Manager and Research Associates checked data sets routinely for errors or inconsistencies. Frequencies, cross-tabulations and distributions of variables were reviewed and errors or inconsistencies were sent to the Fresno office for resolution. The Field Coordinator then responds in writing to all requests for modification. Edits were made from the Fresno server, and those data were then copied back onto the Berkeley server for review. The copy on the Fresno system served as the 'master' version.

All study forms were pilot-tested before use on study participants. However, over the course of the study it occasionally was necessary to modify the forms to improve the wording of

questions, implement protocol modifications (e.g. change a skin test allergen), or fix skip pattern errors. When changes were made, new hardcopy forms were sent to Fresno and labeled with a new version number. At the same time, the Spanish version of forms and both the original and double-data entry systems were modified to include the new/modified questions and the version number. Electronic and hardcopies of all versions have been maintained for future reference.

3.3 STUDY POPULATIONS

3.3.1 Eligibility

The eligibility requirements are listed in Table 3.3.1-1. The age range chosen had to do with the children's ability to perform spirometry and to maximize the years during which it was very unlikely that children would be smoking cigarettes. The U.S. Environmental Protection Agency Supersite (Fresno First Street Site) was an essential part of the study design, hence the requirement to live no further than 20 kilometers from it and to have no plans to move out of the Fresno/Clovis area. Since measurements at the home also were part of the study design, it was important that the child slept in the home at least 5 nights each week and that the family be willing to have environmental samples collected in the home.

Children with certain medical conditions likely to interfere with their ability to carry out all elements of the protocol were excluded. Participating families were required to have an English-speaking child and English or Spanish-speaking parent/legal guardian.

These eligibility requirements include revisions made after receiving approval from the ARB management and staff for the original protocol in September 2001 (Table 3.3.1-2). Each of these revisions was made to increase the pool of eligible participants. In May of 2001, we expanded the original age range (6 to 10) to include 11-year-old children. We made this change in response to reports from the field office that a sizable number of callers were ineligible due to the upper limit of our age range. Originally, we did not plan to include 11-year-old children to minimize the probability of smoking. Given that no smoking was reported by any of the 10-year-old children we had recruited at the time of this change, we altered the age criterion. Although there were many parents who called with regard to children less than 6 years old, we did not feel it was useful to include these children due to the low probability of obtaining acceptable pulmonary function data on children younger than 6 years old. Originally, only one child per household was allowed into the study to maximize between-participant exposure variability. After May 2002, it was decided that increasing the number of participants was necessary and siblings of participants were allowed into the study. The residency requirement was initially one-year. This requirement was relaxed to 3 months. The final modification included an expansion of the geographic area from 10 to 20 kilometers from the First Street monitoring site. Analyses of the spatial distribution of target pollutants for FACES suggested that expansion of our eligibility area to 20 km would not appreciably change the representation of the ambient exposure assessment (Fred Lurmann, personal communication). This change was implemented in July, 2002. These revisions did not compromise the study objectives nor did they fundamentally change the study design. Rather, these modifications were instrumental to obtaining adequate recruitment and retention of participants.

Table 3.3.1-1: Eligibility Criteria for FACES
1. Self-report of physician diagnosis of asthma
2. Ages 6-11 years at entry
3. Use of asthma medication or symptoms or health care utilization in previous 12 months
4. Residence within 20 km of Fresno U.S.E.P.A. Supersite
5. Lived at current residence ≥3 months
6. No plans to move out of the Fresno/Clovis area in next 2 years
7. Sleep in home at least 5 nights/week
8. Parent speaks English or Spanish
9. Child speaks English
10. Child has no medical conditions that interfere with study objectives.
11. Willing to have environment samples (dust, NO_2 and SHS) collected in the home
12. Willing to give contact information

Table 3.3.1-2: Summary of Eligibility Criteria	
Original Criteria	**Modification**
Physician diagnosis of asthma	None
No other chronic disease	None
Current asthma symptoms	None
Medication use/prescription	None
Age 6-10	Age 6-11
Lived in house for 12 months	For 3 months
Residence within 10 km of 1st St.	Within 20km
No plan to move for 2 years	None
1 child per household	Siblings allowed

3.3.2 Development of the Cohort of Children with Asthma

3.3.2.1 Recruitment

3.3.2.1.1 Recruitment Strategies

There were several strategies that we could have employed to identify potential subjects for this study. Many studies of childhood asthma have relied on schools to identify potential subjects. The logistics of working with schools can be very complicated, labor intensive and are subject to selection bias and the whims of local school boards, principals and parent groups.

These relationships require a great deal of time and negotiation prior to the start of recruitment and are less suitable when study populations attend a wide range of schools. Given the age range of children in our target population, this approach would have involved relationships with kindergartens, grammar schools and possibly middle schools in two different school districts (Fresno and Clovis). The USC Children's Health Study (CHS) utilized a great deal of resources to complete school-based recruitment, but, unlike FACES, was not restricted to the small percent of students (10-15%) who have already been diagnosed with asthma. Other possible strategies included community-based advertising, use of pharmacy records, patient lists from physicians and health care facilities and contact with local community groups, such as coalitions and asthma camps. Each of these imposed a range of financial and time constraints, which we evaluated prior to our decision. Due to time constraints imposed on our project that were related to ARB's desire to have our project coincide to some extent with California Regional $PM_{2.5}/PM_{10}$ Air Quality Study (CRPAQS) in the San Joaquin Valley, we had only six months from the time of initial funding to the start of recruitment. During the proposal development period, we met with representatives from the San Joaquin Valley Health Consortium (SJVHC), Valley Children's Hospital (VCH), and the Mobile Asthma Care Program (MACP) to develop strategies to obtain names of children diagnosed with asthma. Several other physician groups and respiratory health programs expressed interest and a willingness to help in the identification of a sample of eligible children. This strategy had been used successfully in the past by several of the FACES investigators and was anticipated to be an efficient way for the identification of the target population.

Coincident with the time that the FACES study started recruitment, there was heightened public concern about patient confidentiality, and Human Subjects Committees nationwide became much more reluctant to release patient information to investigators. We applied to the Human Subject's committee at VCH and Community Hospital and met with a great deal of resistance, despite the support of the Chief of Pulmonology and several discussions with the Chair of the Human Subjects Committee. It should be noted that the pediatric pulmonary clinic of VCH was identified as a collaborator in our initial application, and we counted heavily on the assurances of the chief of that clinic that VCH would serve as a major source of subjects for FACES. One of the largest allergy practices in the area led by Dr. Malik Baz also changed its policy about the release of patient information and only after numerous meetings were we able to get them to send letters on our behalf to potential subjects. These letters were not sent out by Dr. Baz's office until Fall of 2001, nearly one-year after the start of the recruitment. We had numerous discussions with representatives from the Kaiser facility in Fresno to utilize their patient information for recruitment, and, after several meetings with one of their physicians, we were given a budget estimate for human subjects approvals and acquisition of patient names that far exceeded what FACES could afford at the time. Finally, upon closer examination of the population served by the Mobile Asthma Care Program; it became clear that the residential history of these families was much too unstable to meet the requirements of the FACES protocol.

Given these constraints, we were faced with the challenge of the development of an alternative recruitment strategy. After months of discussion, the largest provider in the area, Valley Children's Hospital, sent letters to patients in August 2001. However, this effort was only moderately successful, likely due to the lack of direct provider stake in FACES. Since our Field Coordinator had an extensive background in marketing, she was able to design and implement a community-based advertising campaign. Radio and television ads were produced

and aired on local network and cable channels in both English and Spanish. The Project Director completed a series a television interviews for local news stations. Print ads were run in English and Spanish newspapers. The staff attended numerous health fairs, community events and school functions to pass out study fliers and to recruit families. Fliers were distributed at all Fresno and Clovis day-care centers and schools that service children in the age range eligible for the study. The field coordinator established a strong relationship with the head of the school nurse program. She was very supportive of the project and encouraged the school nurses to distribute fliers and recruit children who frequently visited their offices for asthma care. FACES posters were hung in the school nurses' offices as a reminder. Staff presented information about the study at the Fresno/Madera Asthma Coalition meetings and enlisted their support. Several church groups allowed us to distribute fliers. Dozens of businesses agreed to display our fliers and donated gift certificates to be used as incentives for study participation. Over time, several health care providers (respiratory therapists and physicians) did develop an interest in the project and actively recruited participants.

There were several attempts to get stories about FACES covered by the local media, in part, as a means to advertise the study. During the course of recruitment, there were two articles in the Fresno Bee, one in May, 2000 before recruitment began, and another in September, 2003. In 2000, Dr. Kathleen Mortimer and a field staff member were interviewed for a local Spanish television station (Channel 21, the Univisio affiliate). In 2003, there was a 30-minute program dedicated to FACES (Channel 30, the local ABC affiliate) on which several of the senior investigators and the field coordinator appeared.

Later, when recruitment had slowed, we decided to pursue two strategies that had been considered earlier. In 2003, a special project was developed with Kaiser Permanente (Hal Farber, M.D.) through additional funding that was provided by ARB. As part of this project, Kaiser sent 560 letters to patients who were ages 6 to 11, lived in the Fresno/Clovis area and had an asthma diagnosis. At the same time, posters that advertised the study were placed in the pediatric asthma and allergy outpatient clinic(s) at Kaiser Permanente. In January 2004, flyers were distributed to all children in the target age group who attended schools in the Fresno Unified School district as part of a "backpack express" (flyers given to children in a special folder to be viewed by the parents).

The original goal was to recruit up to 450 asthmatic children in groups of approximately 50 children per month over a period of 9-10 months in Year 1 (nominally September, 2000 through August/September, 2001) of the study. It was planned that each of these groups of 50 subjects would, shortly after their baseline examinations, participate in a 14-day panel that involved daily follow-up. In Year 2, the 450 children were supposed to be reassigned randomly to nine reconstituted panels, the membership of which would remain fixed for the duration of the study. These panels were to each participate in one, 14-day health-monitoring period in each of three air pollution seasons for each of the 3½ years of follow-up. For the longitudinal study component, all 450 children were to undergo detailed evaluations at baseline and every 6-months thereafter. These evaluations were to include a medical history, housing characteristics, medication use, lung function testing, prick-skin testing and measures of somatic growth.

Because of the unanticipated delays in recruitment of children into the study, despite the best efforts of investigators, recruitment goals were revised and, as note above, eligibility

requirements were relaxed after approval from the ARB management and staff in September 2001. The new goal was to recruit 300 subjects until the goal was reached or until Summer/Fall 2002, whichever came sooner. From the approximately 300 children, eight panels, rather than nine, were formed. Recruitment was later extended to October 31, 2004. Baseline evaluations of screened children or siblings were allowed until May 2005.

Although the new strategies were far more labor intensive for the field team, the strategies did work, and we were able to recruit 315 participants into the study.

Television advertisements, while expensive, were the most effective form of recruitment resulting in more than one-fourth of total participants who underwent baseline evaluation. Television advertisements continued until March, 2004 (Table 3.3.2-1).

Recruitment from schools was also effective; more than 25% of participants were recruited through schools. Many of the early participants were referred to the study by this method. During the period of the "backpack express", at a point when recruitment had slowed considerably, 21 new children were screened, and ten underwent baseline evaluation.

Recruitment in doctors' offices, clinics and hospitals accounted for 66 participants. The letters sent by Kaiser Permanente yielded 17 screenings and 14 children who underwent baseline evaluation.

Recruitment efforts from health fairs (thousands of flyers distributed), 34 childcare centers, 70 businesses/community organizations and 41 churches) did not prove to be very effective. A total of 18 children were recruited by these means.

Friends, family and staff turned out to be an important source of participants. Seventy-seven participants came into the study through these referrals. Approximately one-half of these children were siblings of current participants (Table 3.3.2-1)

The 315 children that were recruited represent 70% of our original goal of 450 children. The original proposal included plans to recruit 450 children based on studies such as the National Cooperative Inner City Asthma Study (NCICAS), which involved a similar 14-day panel design and for which there was about a 60% compliance rate among participants in the FACES age-group. In contrast to the NCICAS compliance frequency, our study population has had a compliance frequency that is greater than 75%. Another important distinction between the two studies is FACES uses portable spirometers, which are far more sophisticated instruments to collect lung function data than the peak flow meters used in NCICAS. The instrument used in FACES provides a greater variety of more sensitive and precise measures of lung function. Other aspects of the FACES study design, most notably the significantly reduced exposure-related measurement error afforded by the enhanced environmental monitoring and exposure assessment, will also improve the precision of our estimates of air pollution associated health effects, thereby substantially diminishing the impacts of the reduced sample size.

3.3.2.1.2 Screening and Exclusions

When potential participants expressed interest in the study, they were asked questions from a *screening questionnaire* to determine their eligibility. The screening questionnaire was designed around the eligibility requirements of the study along with demographic information that would be useful for a comparison of screened, eligible and participants who completed the baseline evaluation (e.g. race/ethnicity of child, race/ethnicity of mother).

The age, doctor's diagnosis and residence requirements were listed on flyers and posters that advertised the study. Prior to answering the screening questionnaire, people were usually asked if the child had a doctor's diagnosis of asthma, was between ages six and 11 years = and if the family resided in the Fresno/Clovis area. Also, before starting a screening interview, the interviewers were instructed to determine that the child was age and zip code eligible to avoid wasting forms. For these reasons, only 76 of the 583 children screened were ineligible. The most common reasons for exclusion were medical conditions that were likely to interfere with the compliance with the study protocol, not sleeping in the home for at least five nights or living in the home for less than 3 months (a fraction of these children actually did not meet the original 1 year residency requirement but could not be contacted once the requirement changed) (Table 3.3.2-2).

Screening interviews began on September 5, 2000. Baseline evaluations began two months later on November 2, 2000. More than 11% of the cohort completed baseline evaluations within the first 2 months of the study. More than 40% of the cohort had been enrolled by the end of 2001. Both screening and baseline evaluations were reduced after that time, in part prompting the changes to eligibility and recruitment goals (Table 3.3.5). By 2004, nearly all new participants were due to special recruitment efforts through Kaiser Permanente and the Fresno Unified School district or by referrals from current participants. Recruitment stopped in October 2004. Between November, 2004 and April, 2005, all screening and baseline evaluation were either siblings or people who had been screened prior to October, 2004 but had not yet been had a baseline evaluation.

Initially, siblings were not eligible for enrollment. However, beginning in May, 2002, siblings that met other eligibility requirements were enrolled. To date, there are 34 families with two children in the study, and three families with three children, for a total of 37 siblings. Siblings are linked to the index child by the last 3 digits of their study identification (ID) number (Table 3.3.2-3). Since siblings are more likely to have similar susceptibilities, and similar individual estimates of exposure, the loss in efficiency was offset by gains in power from the 37 additional children who were added to the study.

Table 3.3.2-1 Evaluation of Recruitment Methods						
Type of Recruitment	***Screened (n=583)***		***Eligible (n=506)***		***Baseline (n=315)***	
	Number	**Percentage**	**Number**	**Percentage**	**Number**	**Percentage**
Television	172	29.5	147	29.1	81	25.7
Schools	174	29.8	142	28.1	80	25.4
Friends/Family/Staff	77	13.2	75	14.8	55	17.5
Doctor/Hospital/Clinic	66	11.3	63	12.5	47	14.9
Newspaper	46	7.9	44	8.7	33	10.5
Fair/Booth	26	4.5	19	3.8	10	3.2
Business Posting	6	1.0	6	1.2	5	1.6
Church	4	0.7	3	0.6	3	1.0
Radio	4	0.7	4	0.8	1	0.3
Walk-in	3	0.5	1	0.2	0	0.0
Other/DK	5	0.9	2	0.4	0	0.0

Table 3.3.2-2: Reasons for Ineligibility at Screening	
Reason for Exclusion	**Number Excluded**
Medical conditions	18
Sleep in same household fewer than 5 nights per week	15
Have not lived in their current home for at least 3 months	14
Not in eligible age range (6-11 years)	9
Plan to move out of study area in next 2 years	8
Refuse to give contact information	9
No asthma medication prescribed or used in the past 12 months	2
Child does not speak English	1
No asthma	0
Total Excluded	76

Table 3.3.2-3: Enrollment Over Time				
Year	***Screened (n=583)***		***Baseline Evaluation (n=315)***	
	Number	**Percentage**	**Number**	**Percentage**
Sep-Dec 2000	103	17.7	35	11.1
Jan-Dec 2001	191	32.8	102	32.4
Jan-Dec 2002	141	24.2	83	26.4
Jan-Dec 2003	87	14.9	51	16.2
Jan-Dec 2004	55	9.4	38	12.1
Jan-Apr 2005	6	1.0	6	1.9
Total	**583**	**100**	**315**	**100**

3.3.3 Characteristics of All Potential Participants Screened

A total of 583 children were screened, 507 of who were eligible. Of these, 315 had completed the baseline evaluation (Table 3.3.3-1). Information on household income and parent's educational level was not collected as part of the screening questionnaire and is only available for the subjects who completed the baseline evaluation.

The race/ethnicity, age and sex distributions were similar for the screened, eligible and the baseline populations. The small proportion of subjects of Asian descent is probably due to language requirements since the adult questionnaires were only administered in Spanish and English. Small differences in the age distribution, in part, are due to time elapsed between screening and baseline evaluations. Two children who were five years old at screening were admitted once they turned 6, and one child who was screened at age 11 was allowed into the study even though he was 12 years old at the time of the baseline interview.

Table 3.3.3-3: Description of Participants (Percentage)

		Screened (n=583)	*Eligible (n=507)*	*Baseline Evaluation (n=315)*
Race				
	Hispanic	40.7	40.9	39.7
	African-American	18.9	18.2	15.6
	White	37.1	37.4	41.9
	Asian	0.5	0.6	0.6
	Other/Missing	2.9	3.0	2.2
Age				
	5	1.54	0.20	0.00
	6	27.3	27.3	26.4
	7	17.3	17.8	15.6
	8	17.0	16.6	15.2
	9	18.0	18.8	19.4
	10	12.9	13.2	14.6
	11	5.8	6.1	8.6
	12	0.1	0.0	0.3
Male Sex		57.0	56.5	56.5

3.3.4 Participation Levels

Of the 315 participants, 75 are no longer enrolled because they refused to participate in future visits (n=27), moved out of the study area or became otherwise ineligible (32) or were lost to follow up (16). Of the 240 subjects who remain active in the study, 15 have not completed a visit of any type for at least one year (Table 3.3.4-1). After two years of inactivity, these participants will be placed in the "lost to follow-up category". However, if the contact information is current and the participant has not refused further participation, the families will continue to be contacted to schedule visits. The first two categories ("active" and "no activity in the past year") were used in the denominator for participation rates.

Table 3.3.4-2 shows the distribution of years in the FACES study after baseline. By March 31, 2003, on average children had been in the study for 1.30 years (median=1.35 years). The earliest participants had contributed information over 2.4 years. By June 30, 2005, the median number of years in the study was 2.7. Some participants had been in the study for more than 4.5 years.

The tables below give participation levels for follow-up field office, telephone interview and home visit for the 315 participants as of June 30, 2005 and for the 236 participants who had a baseline evaluation by March 31, 2003. The earlier time period is relevant for the analysis in this final report. Comparison with the later time period gives one an idea of the additional data that will be available for analysis once more recent air pollution data are available.

Based on data entered as of June 30, 2005, nearly all of the children have participated in at least one 14-day panel, and some have completed as many as thirteen 14-day panels. There have been 315 baseline evaluations, 1,083 follow-up field office visits, 1,096 telephone interviews and 1,652 panel visits. By March 31, 2003, 236 baseline evaluations, 346 follow-up field office visits, 477 telephone interviews, and 590 panel visits were completed.

3.3.4.1 Field Office Visits

As of March 31, 2003, 236 children had completed a baseline interview. By March 31, 2003, 147 children had completed both a baseline and 6-month visit, compared to 228 children by June 30, 2005 (see Table 3.3.4-3).

3.3.4.2 Telephone Interviews

Telephone interviews and field office visits both contain questions on symptom frequency, medication use and changes and health utilization over 3-month and 2-week periods. As of June 30, 2005, 1,096 telephone interviews had been completed by 315 participants. By March 31, 2003, 236 participants had completed 477 telephone interviews. (3.3.4-4)

For subjects who completed a baseline evaluation in November, 2000, there were 9 possible follow-up FO visits after baseline and 9 possible telephone interviews by June 30, 2005. By that date, 217 children had completed the baseline evaluation and at least 2 follow-up FO visits—i.e., up to 3 visits with spirometry (Table 3.3.4-5). There were a total of 1,087 follow-up FO visits. Participants had completed an average of 3.5 follow-up field office visits (71.9% of the possible number of visits), 3.5 telephone interviews (70.7% of possible) and 6.9 total follow-up visits (71.3% of possible). Children who entered the study at the beginning had completed up to 18 follow-up visits (follow-up FO visits and telephone interviews combined) (Table 3.3.4-6.)

As of March 31, 2003, only 4 opportunities for FO follow-up contacts had occurred for the 236 children who were then in the study (Table 3.3.4-7). Of these, 75 had not yet had a contact and only 97 had two or more contacts.

Participants had completed 346 follow-up FO visits, and 477 telephone interviews. On average, participants had completed 1.5 follow-up field office visits, 2.0 telephone interviews and 2.6 follow-up visits (follow-up FO and telephone interviews combined). (Table 3.3.4-8)

3.3.4.3 Field Office Spirometry

Spirometry was attempted at each FO visit. Each effort was evaluated by one of the investigators (JB or LC). All the Morgan data that were collected prior to December 31, 2003 have been entered into the database and graded. Due to the fact that we only have exposure data through March 2003, we have restricted the analyses to visits that occurred before September 30, 2003. This enables us to include any follow-up visit that would have occurred within 6 months of the last home panels for which we have acute exposure data. During the follow-up FO visits, we included only sessions for which our reviewers graded at least 2 curves as "acceptable". Spirometry data from 739 FO visits were available for the longitudinal analysis in this report. For these visits, there were 667 sessions that had at least 2 acceptable pre-bronchodilator curves (Table 3.3.4-9).
To estimate the number of sessions with 2 or more acceptable curves available by June 30, 2005, the percent with 2 or more acceptable curves at baseline (93.6%) and, on average, for follow-up FO visits (96.3%) were applied to the total number of baseline (315) and follow-up FO visits (1,083). Based on those percents, we estimate that there will be an approximately 1338 FO visits with acceptable pre-bronchodilator data as of June 30, 2005. The number of available FO visits may be even higher, since; as the children age, they become better at completing spirometry.

3.3.4.4 Completion of other Field Office Clinical Procedures

3.3.4.4.1 Buccal Cell Samples

We attempted to collect buccal cell samples from each child and each biological parent who lived with the child. Buccal cell samples need to be processed within 48 hours; therefore, samples could only be collected Monday through Wednesday.

At the time of this report, there are samples for 192 children, 170 mothers and 43 fathers (Table 3.3.4-10).

Samples were taken from parents if they were biologically related to and lived with the child. Otherwise, they were ineligible. Among the mothers and fathers whose eligibility was known, 61.7% of fathers were ineligible, compared to only 7.4% of mothers. This is reflected in the fact that samples were collected for a child and both parents only 11.7% of the time (Table 3.3.4-11).

Even though the sample collection is painless, some parents refused, possibly out of concern that the genetic information would be used improperly. On two occasions, letters were sent out to participants who had not provided a sample to reaffirm that the results would only be used to examine genetic markers that are thought to be related to asthma. Although some families did provide a sample after receipt of the letters and special Saturday collection hours were offered, we still have not collected samples from 37.1% of the children in the cohort.

3.3.4.5 Nutrition Survey

Originally, the nutrition survey was part of the 6-and 24-month FO visits so that changes in the child's diet with due to season and age could be captured. To obtain higher completion, beginning in January 2004, the survey was administered as part of any FO visit or telephone interview. Any two surveys were required to be at least six months apart. At least one nutritional survey has been completed by 66% of the cohort. Only 45.4% have completed both surveys (Table 3.3.4-12).

3.3.4.6 Allergy Skin Testing

Skin tests were completed by 266 of the 315 participants (84.4%). Nine children who reported having had a severe adverse reaction to skin tests prior to the study were not tested. Several young children refused. If the parents were willing, we tried again at a later visit. Initially, skin tests were offered at baseline, 6-, 12- and 24-months, although most children who were tested had the test done at baseline. In summer 2004, we attempted to get skin tests for all children who had not completed one. Of the people remaining in the study, all but a few either were tested, were ineligible for testing (had an adverse reaction) or refused the test. Skin testing ended in July 2005.

3.3.4.7 Participation for Follow-up Visits

Figure 3.3.4-3 shows the participation rates by visit. The denominator used for these percentages is the number of children who have had at least one visit in the past 2 years (excludes children who have moved out of the study area, refused further participation or been lost to follow up). Since there were 6-week visit windows, the denominator included all of those whose windows for that visit had closed by June 30, 2005. Since the earliest 51st and 54th-month visit windows had not closed by the time the telephone interviews and follow-up FO visits stopped, participation for these visits could not be calculated and are not included in the chart below. Participation for follow-up FO visits (the left side of the plot) was good, generally above 70% . Telephone interviews (the right side of the plot) had lower participation, but they were usually greater than 60% (see Figure 3.3.4-1).

3.3.4.8 Panel Visits

In the first year of the study, home visits were carried out once a year, usually within one motnh after the baseline evaluation was completed. Beginning in November 2001, three panel visits were scheduled each year. Environmental samples were collected at each panel visit until January 2003, when, to reduce the burden to study participants the samples were requested at least once for each "season". *EasyOne*® spirometry and the daily diary were part of each panel visit.

By March 31, 2003, 216 of 236 participants had completed at least one panel visit and 165 had completed 2 or more for a total of 590 panel visits. As of June 30, 2005, 293 of 315

children had completed at least one visit and 255 had completed 2 or more. There were 1,656 panel visits by this point in the study (Table 3.3.4-13).

Table 3.3.4-14 can be used to determine the participation percentage for panel visits in both periods. By March 31, 2003, participants had completed 590 panel visits, an average of 2.50 for each participant. There was an average of 3.14 visits expected, so the percent participation was 79.6%. By June 30, 2005, the mean number of expected panel visits was 6.50. On average 3.72 had been completed. Therefore the percent participation for home visits during this period was 80.6%.

Environmental samples were supposed to be obtained at least once in each study season for each home the child lived in during the study. Spring was defined as February through May. Summer was June through September and winter was October through February. Fifty-seven percent of the cohort completed samples in all three seasons. Twenty-four children never completed any environmental sampling. Of those not completing any environmental samples, 15 are no longer in the study (3 moved, 11 refused further participation and 1 was lost to follow up). (Table 3.3.4-15).

The percentage of samples obtained during the spring, summer and winter is presented in Table 3.3.4-16. For each season, we have samples from more than 70% of the cohort. Environmental sampling continued until July, 2005. The new protocol, which began at that time, did not include environmental samples.

3.3.4.8.1 Daily Diary Data:

A 2-week diary was distributed along with an *EasyOne*® for each panel visit. Because of problems with both data quality and completion rates of earlier versions of the daily diary (described in Sections 3.2.3 and 3.4.6.2.1), the time-location-activity questions were simplified, and a new version was released in November 2002. By March 31, 2003, there were 5,181 diary-days with the original version of the diary and 2,140 diary-days for the revised version (Table 3.3.4-17).

3.3.4.8.2 *EasyOne*® Data

At each panel visit, the child was asked to use the *Easy One* ® twice a day for 14 days. Each curve was graded by one of the investigators (IT or LC). All curves collected up through March 31, 2003 (the period for which we have exposure information) have been graded. As of March 31, 2003 there were 6,902 A.M. sessions and 7,621 P.M. sessions. Since mean FEV_1 is the primary outcome used in this report, at least 2 curves with acceptable FEV_1 values are required for each observation used in the analysis. There were 6,366 A.M. sessions and 7,012 P.M. sessions that met this requirement (Table 3.3.4-18).

To determine the number of sessions with 2 or more acceptable values of FEV_1 since March 31, 2003 (the point beyond which most sessions are not graded), we used the following procedure: First, we determined the number of sessions with 2 or more acceptable values for FEV_1. For graded spirometry tracings, 92.7% of AM sessions had at least two acceptable results

for FEV_1. When these percents were applied to the ungraded data, we predict that there should be approximately 9,597 additional sessions with at least 2 acceptable tracings for FEV_1 (Table 3.3.4-19).

Of the 12,131 PM sessions that have not been graded, we expect that approximately 11,235 will have at least two acceptable FEV_1 measures. Adding this to the sessions that already are graded, we expect to have a total of 17,412 AM sessions and 18,461 PM sessions once air pollution data are available through June 30, 2005.

Table 3.3.4-1: Activity Levels (N=315)		
Activity Level	**Number**	**Percentage**
*Active**	225	71.4
No activity in past year	15	4.8
Refused	27	5.6
Moved out of study area	32	10.2
*Lost to follow-up***	16	5.1

* Active participants have participated in at least one follow-up field office visit, telephone interview or home visit in the past year.

**Participants who are lost-to-follow up either do not have current contact information or have not participated in any visit in two years.

Table 3.3.4-2. Distribution of Years in the Study after Baseline							
	Mean	**S.D.**	**Min**	**25%**	**50%**	**75%**	**Max**
as of March 31, 2003	1.30	0.72	0.19	0.74	1.35	1.92	2.41
as of June 30, 2005	2.64	1.33	0.19	1.45	2.73	3.89	4.66

Table 3.3.4-3. Field Office Visit Participation Levels			
Field Office Visit	**Number Completed June 30, 2005 (N=315)**	**Number Completed March 31, 2003 (N=236)**	**Percentage Completed by March 31, 2003***
Baseline	315	236	74.9
6-month	228	147	64.5
12-month	195	91	46.7
18-month	173	67	38.7
24-month	149	41	27.5
30-month	119	---	0.00
36-month	97	---	0.00
42-month	65	---	0.00
48-month	45	---	0.00
54-month	16	---	0.00

*This column represents the percentage of visits completed by March 31, 2003 out of the total completed on June 30, 2005. For example, by March 31, 2003, 147 6-month visits were completed, 64.5% of the total completed by June 30, 2005.

3.3.4-4: Telephone Interview Participation Levels*			
Telephone Interview	**Number Completed June 30, 2005 (N=315)**	**Number Completed March 31, 2003 (N=236)**	**Percentage Completed by March 31, 2003****
3-month	266	192	72.2
9-month	230	136	59.1
15-month	155	79	51.0
21-month	113	50	44.2
27-month	118	20	16.9
33-month	100	---	0.0
39-month	54	---	0.0
45-month	40	---	0.0
51-month	20	---	0.0

*Telephone interviews ended in March 2005.
**This column represents the percentage of visits completed by March 31, 2003 out of the total completed on June 30, 2005. For example, by the earlier date, 192 3-month visits were completed, 72.2% of the total.

Table 3.3.4-5: Total Number of Follow-up Contacts Completed for Each Child by June 30, 2005				
	Clinic Visits		***Telephone Interviews***	
	Number	**Percentage**	**Number**	**Percentage**
0	58	18.4	28	8.9
1	40	12.7	39	12.4
2	38	12.1	2	19.7
3	36	11.4	40	12.7
4	27	8.6	43	13.7
5	29	9.2	37	11.8
6	41	13.0	30	9.5
7	20	6.4	19	6.0
8	26	8.3	10	3.2
9	---	---	7	2.2

3.3.4-6. Distribution of Number of Contacts by June 30, 2005						
	Mean of Possible Contacts	**Mean of Contacts Completed**	**S.D**	**Min**	**Median**	**Max**
Field Office (n=1,087)	4.8	3.5	2.7	0	3	9
Telephone Surveys (n=1,096)	4.9	3.5	2.3	0	3	9
All Follow-Up (n=2,183)	9.7	6.9	4.8	0	6	18

Table 3.3.4-7: Total Number of Follow-up Contacts Completed for Each Child by March 31, 2003

	Field Office		*Telephone Surveys*	
	Number	**Percentage**	**Number**	**Percentage**
0	75	31.8	35	14.8
1	64	27.1	60	25.4
2	38	16.1	53	22.5
3	30	12.7	51	21.6
4	29	12.3	27	11.4
5	---	---	10	4.2

3.3.4-8. Distribution of Number of Contacts by March 31, 2003

	Expected Mean	**Actual Mean**	**S.D**	**Min**	**50%**	**Max**
Clinic (n=346)	2.08	1.45	1.37	0	1	4
Telephone (n=477)	2.56	2.02	1.38	0	2	5
All follow-up (n=823)	4.63	3.49	2.61	0	3	9

3.3.4-9: Field Office Spirometry Data as of September 30, 2003

Clinic Visit	**Number of Visits Expected by September 30, 2003**	**Number with Morgan Data Entered and Graded by September 30, 2003**	**Number Acceptable**	**Percent Acceptable**
Baseline	256	256	204	93.6*
6-month	227	174	166	95.4
12-month	182	117	110	94.0
18-month	134	92	89	96.7
24-month	92	65	64	98.5
30-month	53	35	34	97.1
Total	**944**	**739**	**667**	**95.1**

* A leak in the Morgan was detected on February 6, 2001. Spirometry data for 38 baseline evaluations that had been completed by that date were not valid and the percentage acceptable has been adjusted accordingly. After this date, the *EasyOne*® was used inline with the Morgan. On 13 occasions before September 30, 2003, the Morgan malfunctioned, and the spirometry results from the *EasyOne*® were used instead.

3.3.4-10: Number of Buccal Cell Samples for Children, Mothers and Fathers										
	Completed		***Refused***		***Not Biologically Related***		***Doesn't Live with Child***		***No Record***	
	Number	Percentage	Number	Percentage	Number	Percentage	Number	Percentage	Number	Percentage
Child	192	61.0	6	1.9	----	----	----	----	117	37.1
Mother	170	54.0	5	1.6	13	4.1	1	0.32	126	40.0
Father	43	13.7	3	0.95	13	4.1	61	19.4	195	61.9
* Parents of siblings are double-counted in this table.										

Table 3.3.4-11: Buccal Cell Completion for Each Family		
	Number	**Percentage**
Child only	19	6.0
Child and mother	131	41.6
Child and father	5	1.6
Child and mother and father	37	11.7
Mother only	1	0.3
Mother and father, no child	1	0.3
No buccal samples	121	38.4
* Parents of siblings are double-counted in this table.		

Table 3.3.4-12: Number of Nutrition Surveys Completed		
	Number	**Percentage**
None	106	33.7
One	66	21.0
Two	143	45.4

Table 3.3.4-13: Total Number of Panel Visits Completed by Each Participant				
	Prior to June 30, 2005		*Prior to March 31, 2003*	
Number of Panel Visits Completed	**Number Completed**	**Percent Completed**	**Number Completed**	**Percent Completed**
0	22	7.0	20	8.5
1	38	12.1	51	21.6
2	35	11.1	46	19.5
3	30	9.5	57	24.2
4	26	8.3	38	16.1
5	19	6.0	20	8.5
6	22	7.0	4	1.7
7	28	8.9	---	---
8	22	7.0	---	---
9	20	6.4	---	---
10	28	8.9	---	---
11	12	3.8	---	---
12	10	3.2	---	---
13	3	1.0	---	---

3.3.4-14: Percentage Participation for Panel Visits					
	Expected		*Actual*		*Percentage*
	Mean	**SD**	**Mean**	**SD**	***Participation***
Until March 31, 2003	3.14	1.68	2.50	1.49	79.6%
Until June 30, 2005	6.50	3.72	5.26	3.60	80.9%

Table 3.3.4-15: Number of Seasons of Environmental Samples		
Number of Completed Seasons	**Number of Children**	**Percentage**
0	24	7.6
1	51	16.2
2	61	19.4
3+	179	56.8

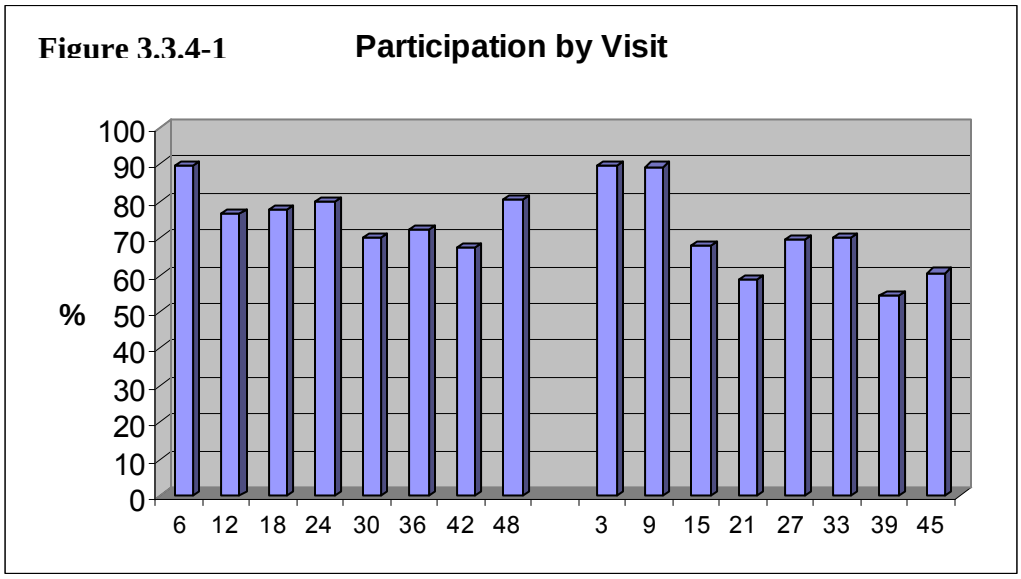
Table 3.3.4-16: Number of Homes with Environmental Samples for Each Season		
Season	**Number Completed**	**Percentage of Total**
Spring	248	78.7
Summer	233	74.0
Winter	229	72.7

Table 3.3.4-17: Data Completion for the Daily Diary			
	Original Version	***Revised Version***	
	November, 2000 to October, 2002	**November, 2002 to March, 2003**	**November, 2002 to December, 2004**
Number of 14-DayPackets	371	159	762
Percentage of Panel Visits with 10+ Days Filled Out (front and back)	-----*	89.3%	91.7%
Percentage of Panel Visits with 10+ Days Filled Out (front)	86.5%	90.6%	92.8%
Number of Observations	5181	2140	10666
Number of Diary-Days with No Data	309 (6.0)	78 (3.6)	711 (6.7)

* The time/location/activity questions in Version 1 of the diary suffered both from poor data quality and poor completion rates. Therefore, data from these questions were no longer entered after November 2001.

Table 3.3.4-18: Summary of Panel Visit Spirometry Data Quality				
	Morning Session		***Evening Session***	
	Number	**Percentage**	**Number**	**Percentage**
Number of Acceptable Blows				
0	358	5.2	413	5.4
1	178	2.6	196	2.6
2	581	8.4	665	8.7
3	5785	83.8	6347	83.3
Total Number of Sessions	6902	100	7621	100
Number of Sessions With 2 or More Acceptable Tracings	6366	92.2	7012	92

Table 3.3.4-19: Number of Sessions Expected for Analysis as of June 30, 2005		
	AM	***PM***
Number of Observations Since March 31, 2003	10,351	12,131
Percentage with at Least 2 Acceptable tracings before March 31, 2003	92.7	92.6
Projected Number of Acceptable Tracings from April 1, 2003 to June 30, 2005	9,597	11,235



3.4 EXPOSURE ASSESSMENT METHODOLOGY

3.4.1 Exposure Assessment Study Design

The overall goal of this study is to determine the effects of different components of particulate matter (PM), in combination with other ambient air pollutants, on the natural history of asthma in young children residing in the Fresno County region of California. Fresno County has an ethnically diverse population, a high prevalence of asthma, and high levels of ambient air pollution, especially PM, making it an appropriate location to address questions of how air pollution impacts this vulnerable population. The exposure assessment portion of the project is aimed particularly at the development of estimates of each child's exposure to each pollutant and possible bioaerosol co-factors, such as pollen grains, fungal spores, and endotoxin, on each day of the study. This task was approached with a combination of daily regional monitoring, routine monitoring in all homes for a subset of agents, periodic monitoring inside and outside a subset of homes, collection of home-specific data through questionnaires, home surveys, and diaries, and modeling to combine the measurements with observed relationships to develop daily exposure estimates specific to each child for air pollutants of concern.

Numerous air pollutants are suspected of influencing the health of asthmatic children. Exposure to the "criteria" pollutants such as particulate matter (PM), ozone, and nitrogen dioxide (NO_2), to toxic mixtures of pollutants such as second hand smoke (SHS), and to bioaerosols such as pollen grains, fungal spores, and endotoxin may influence the incidence, severity, and evolution of asthma in children. In this study, we assessed the exposure of asthmatic children in Fresno, California, to all these contaminants. Particulate matter is a complex mixture; and when we refer to PM, we mean not only the mass of PM but also its chemical composition and the particle sizes (or size distributions). In the absence of adequate mechanistic understanding of PM health effects, there is strong interest in determining which chemical components and/or

particle size range may be associated with adverse health effects in sensitive children (if they exist). Table 3.4.1-1 presents the agents which are being measured and studied in FACES; these include PM and its constituents, pollutant gases, and bioaerosols.

The ambient pollutants of concern in this study are known to have, or are suspected of having, strong temporal variability (hour-to-hour, day-to-day, and season-to-season changes). This variability is primarily caused by fluctuations in meteorological conditions and is caused secondarily by the temporal variations of emissions (168). The ambient concentrations also vary spatially. The extent of spatial variation depends on the pollutant and proximity to source emissions. For most secondary pollutants, such as $PM_{2.5}$ sulfate, nitrate, ozone, and secondary organics, ambient concentrations vary on an urban scale (i.e., 4-100 km) rather than on a neighborhood scale (0.5-4 km) (169, 170). Ambient concentrations of directly emitted species often have large spatial gradients near sources. Pollutants emitted by combustion sources [NO_x, SO_2, CO, $PM_{2.5}$ elemental carbon (EC), and $PM_{2.5}$ organic carbon (OC)] and resuspended PM from roadways, construction activities, and agricultural activities both are expected to have neighborhood-scale spatial variations. Likewise, the outdoor concentrations of pollens, fungal spores, and endotoxin are likely to depend on the local source strength and vary considerably across a city such as Fresno.

Human beings spend the majority of their time inside buildings. Both children and adults spend, on average, 70 to 90 percent of their lives indoors. Pollutants of outdoor origin infiltrate buildings and coexist with pollutants emitted indoors. Indoor pollutant concentrations may depend on a large number of factors that include the types of indoor sources, indoor source use patterns, building air exchange rate, building volume and room design, type of HVAC system, types of surfaces, reactivity of pollutants, and concentrations immediately outside of the building. There are pollutants for which there are no usual indoor sources, such as ozone and $PM_{2.5}$ sulfate; the indoor concentrations of these species depend on outdoor concentrations, air exchange rates, and indoor loss rates (to deposition or chemistry). (Note, occasionally there are homes with certain types of air cleaners and photocopying machines that are indoor sources of ozone.) Indoor concentrations of other pollutants, such as second hand smoke (SHS) and house dust allergens, are almost solely determined by their indoor source strengths. Many common pollutants have indoor and outdoor sources that contribute to their indoor concentrations. Thus, another spatial scale of importance for exposure assessment is the residential scale. Characterization of human exposure to pollutants of potential relevance for asthmatics should account for exposures in different locations, including indoors, and the amount of time individuals spend in various microenvironments.

Knowledge of the spatial scales of pollutant variability is essential for characterization of exposures. The hourly and daily Central Site air monitoring data collected at the Fresno Supersite during this study are well suited to specification of the ambient concentrations of pollutants that vary only on the urban scale. Ambient concentrations of $PM_{2.5}$ sulfate, nitrate, ammonium, and secondary organic compounds throughout the Fresno study area are expected to go up and down as indicated at the Central Site (Fresno Supersite). Ozone concentrations at many outdoor locations in Fresno are expected to be similar to those at the Central Site monitoring station.

Ambient concentrations of pollutants with neighborhood-scale variability may be biased from the Central Site, yet they often exhibit temporal variability similar to that at the Central Site. For example, ozone concentrations may be the same as the Central Site everywhere except near major roadways. Ambient NO/NO_2, $PM_{2.5}$ EC (elemental carbon), $PM_{2.5}$OC (organic carbon), PM_{10} geologic material (road dust and soil dust), pollen grains, fungal spores, and endotoxin concentrations are likely to be modulated on the neighborhood scale by the local source strengths. Previous neighborhood-scale studies of criteria pollutants in the San Joaquin Valley (171, 172) provide assurance that the within-community variations in species like PM_{10} and ozone are typically within ±30 percent of central-site measurements. Much less is known with regard to the spatial variability of biological aerosols and other components of PM. There is tremendous diversity in vegetation throughout a city like Fresno, and large spatial and temporal variations in pollen releases are expected. The heterogeneity of pollen releases and their relatively short atmospheric lifetimes (before removal by gravitational settling) suggests there could be very significant local scale variability in these species. Too few ambient endotoxin measurements exist to know the appropriate spatial scale of variability. Likewise, ambient particle number densities are expected to be high near busy roadways and to fall off rapidly (more rapidly than primary gaseous pollutants) with distance from the roadway because of coagulation of the huge number of tiny particles emitted by motor vehicles. Such phenomena have not been adequately characterized in the neighborhood-scale studies, and the FACES measurements were designed to help understand the phenomena and ultimately to develop models to estimate concentrations on these scales accurately.

Certain pollutants vary from house to house in a manner that strongly depends on the activities, operating characteristics, and materials in the individual houses. Important residential scale variations in concentrations can be captured with a combination of housing questionnaires and indoor and outdoor measurements at the homes of interest. FACES measurements were collected for the less frequently measured compounds such as pollen grains, fungal spores, endotoxins, house dust allergens, and other chemical components of indoor PM. This conceptual model of pollutant variability in Fresno leads to the exposure hypotheses described in Section 2.4.

Many epidemiologic investigations of associations between air pollution and health effects (1) rely on ambient air quality data from one or more central stations alone to assign exposures and (2) consider only criteria air pollutants. Typically, all individuals in a community the size of Fresno are assigned identical exposure values for ozone, NO_2, SO_2, CO, and PM_{10} mass on each day of the year. The technical approach for FACES was designed to overcome both of these limitations by using a more comprehensive approach to exposure assessment. The technical approach for the exposure analysis was to build databases and models to generate individual exposure estimates, rather than use community average exposure estimates. The individual exposure estimates were based on microenvironmental models adjusted for indoor and outdoor concentrations combined with personal activity patterns to estimate individual exposures.

The technical approach involves measurements of gases and both the chemical components and physical characteristics of PM that are beyond those conventionally measured for compliance monitoring. The groups of measurements incorporated into the study design are as follows (see also Table 3.4.1-2):

1. The Fresno Supersite provided the central site measurements of ozone, NO/NO_2, SO_2, particle number density, detailed particle size distributions, $PM_{2.5}$ mass, $PM_{2.5}$ sulfate, $PM_{2.5}$ nitrate, $PM_{2.5}EC$, $PM_{2.5}OC$, $PM_{2.5}$ metals, $PM_{2.5}$ polycyclic aromatic hydrocarbons (PAH), PM_{10} mass, and PM_{10} metals throughout the study period. Samplers were added to measure endotoxin, pollen grains, and fungal spores.
2. The ARB developed and deployed two mobile air monitoring trailers that measured selected agents at schools and in selected neighborhoods in Fresno; these agents included pollen grains, fungal spores, PM_{10} endotoxins, ozone, NO/NO_2, SO_2, CO, particle number density, $PM_{2.5}$ mass, $PM_{2.5}$ sulfate, $PM_{2.5}$ nitrate, $PM_{2.5}EC$, $PM_{2.5}OC$, PM_{10} mass, and PM_{10} metals. These measurements were made between May, 2002, and August, 2003.
3. During the two-week health panel studies, from 2000 through 2005, integrated NO_2, nicotine, and house dust allergen and endotoxin samples were collected inside participants' homes and integrated ozone samples were collected outside participants' homes. Ozone measurements were confined to the extended ozone season (May-October).
4. Between February, 2002 and February 2003 intensive air quality measurements were made during the panel studies at the homes of 80 participants. Two to five homes from each panel were sampled for ozone, light scattering by $PM_{2.5}$, $PM_{2.5}$ sulfate, $PM_{2.5}$ nitrate, $PM_{2.5}EC$, $PM_{2.5}OC$, PAHs (funded by US EPA), PM_{10} mass, PM_{10} metals, PM_{10} endotoxins, pollen grains, fungal spores, and nicotine. All agents except nicotine and NO_2 were measured concurrently inside and outside the homes. Separate 24-hour samples were collected on 3 weekdays and 2 weekend days. A subset of houses (26) was sampled in two seasons. Another 58 houses were sampled in one season, for a total of 110 sets of home visits.
5. Ongoing monitoring programs provided supplemental data. The National Weather Service (NWS), ARB, and SJVUAPCD monitoring programs provided meteorological data. Traffic count data were provided for state and county roadways by CALTRANS.

All the measurements made by UCB/STI were quality-controlled and quality-assured in accordance with generally accepted monitoring practices. All these data were acquired and implemented in a Microsoft ACCESS database for use by all study participants.

The analyses of data collected in the study focused on characterization of the exposure concentrations to which the study participants are subjected, as indicated by measurements in their homes, schools, and from the central air-monitoring site. These data were analyzed to characterize the within-community variability in concentrations of the different agents included in the study. Relationships between agents were explored to identify indicator species and metrics.

Table 3.4.1-3 and Figure 3.4.1-1 illustrate the relationship of among sample types collected from various locations during a typical two-week health panel during the FACES Study. Two-week integrative samples for NO_2, ozone and nicotine were collected in the home of each child who participated in the health panel; each day of that panel data were collected on the child's locations and activities, and activities in the home which might affect concentrations in the home (time location activity diary); hourly and daily samples were collected at the Central Site and the trailers; 24 hour samples and continuous light scattering data were collected indoors

and outdoors on five days at 2-5 homes from the health panel‘s part of the Home Intensive sampling. A map of the sampling locations is shown in Figure 4.1.6-1.

The data were analyzed to characterize relations (1) between pollutant concentrations at the Central Site and those outside participants’ homes and schools, and (2) between indoors and outdoors at the participants’ homes. The spatial variability in concentrations was evaluated. These analyses led to microenvironmental exposure models with parameters for selected agents of concern in the study. The database, models, and model estimates were delivered to the health team.

Table 3.4.1-1: Target Agents for Exposure Assessment in FACES
PM_{10}
Mass
Metals
Endotoxin
$PM_{2.5}$
Mass
Ions (nitrate and sulfate)
Organic carbon and elemental carbon (OC/EC)
NO_2
NO
SO_2
Ozone
Polycyclic Aromatic Hydrocarbons (PAHs)
Second Hand Smoke (SHS)
House dust
Endotoxin
Allergens (dog, cat, cockroach, dust mites)
Pollen grains
Fungal spores

Table 3.4.1-2: Agents Sampled and Sample Duration at Various Locations						
	Central Site	**Routine Home[2]**		**Home Intensive[3,4] (selected homes)**		**Schools (using 2 trailers)**
Location	***Fresno Supersite (on-going)***	***Inside Homes***	***Outside Homes***	***Inside Home***	***Outside home***	***Selected sites[5]***
Year(s) of Study	2000 – 2005	2000-2005	2001-2004	2002-2003	2002-2003	2002-2003
Collected	2000 – 2003	2000–2005	2001-2004	2002-2003	2002-2003	2002-2003
Analyzed						
Agent						
NO_2	H[1]	2W			2W	H[5]
NO	H[1]					H[5]
SO_2	H[1]					H[5]
Ozone	H[1]		2W	D – 8hr	D – 8hr	H[5]
PAHs[6]	H[1] D[6]			D[6]	D[6]	H[5] D[6]
Particle Number	H[1]					H[5]
Nicotine		2W		D		
House dust allergens& endotoxin		G				
Pollen Grains	2H, D[2]			2H,D	2H,D	2H,D[5]
Fungal Spores	2H, D[2]			2H,D	2H,D	2H,D[5]
PM_{10} endotoxin	D[2]			D	D	D[5]
Particle scattering	H[1]			H	H	H[5]
$PM_{2.5}$ mass	H[1]			D	D	H[5]
$PM_{2.5}$ sulfate & nitrate ions	H[1]			D	D	H[5] (sulfate: only 1 trailer)
$PM_{2.5}$ OC/EC	H[1]			D	D	H[5] (only 1 trailer)
PM_{10} mass	H[1]			D	D	H[5]
PM_{10} metals	D[5]			D	D	D[5]
PM black Carbon	H[1]					H[5]

Sample duration: H = hour, 2H = bihourly, D = 1 day (24 hour, midnight to midnight until February, 2002; then 8 p.m. to 8 p.m.), G = grab, 2W = 2-week

[1] Operations & data provided by DRI, ARB, and EPA

[2] Samples collected for 5 years during years 1-5; only first 2 years were to be analyzed; analyzed samples collected through March 2003

[3] 5 daily (D) samples collected during 2 weeks as follows: Wednesday 8 p.m. to Thursday 8 p.m., Friday 8pm to Saturday 8 p.m., Monday 8 p.m. to Tuesday 8 p.m., Wednesday 8 p.m. to Thursday 8 p.m., Saturday 8 p.m. to Sunday 8 p.m.; ozone samples collected from 10 a.m. to 6 p.m.; 2W samples collected from sampler setup to sampler takedown.

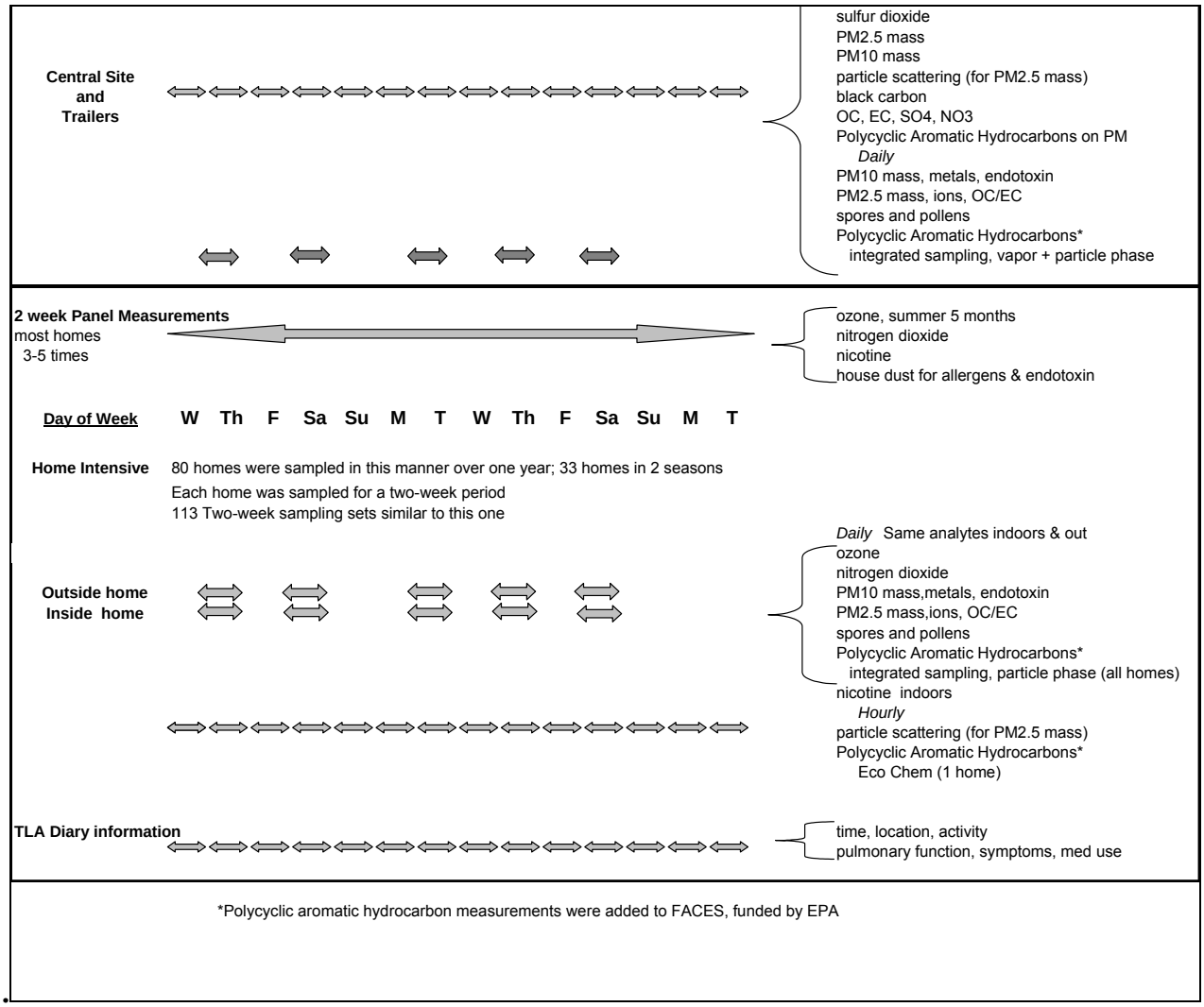
[4] As part of two-week panel measurements

[5] Operations & data provided by ARB

[6] Hourly particulate-PAH monitors for trailers and PAH sampling and analysis for selected days sponsored by U.S. EPA. Daily samples with analysis of 16 individual PAHs.

Table 3.4.1-3: Exposure Assessment for FACES				
Outdoor Samples			***Indoor Samples***	
Central Site	**Schools**	**Homes**	**Homes**	**Homes**
Supersite	Trailers	Home Intensive	Home Intensive	Panels
Hourly & Daily	Hourly & Daily	24 Hour	24 Hour	2 Weeks & Grab
Daily November 2000 – September 2005 (analyzed through March 2003)	Daily May 2002 – August 2003 (7 schools, 1 continuously)	5 days in 2 weeks February 2002 – February 2003 80 homes (33 homes twice)	5 days in 2 weeks February 2002 – February 2003 80 homes (33 homes twice)	Nearly all 300 homes at once per season
All target agents	All target agents	All PM agents (except black carbon, 8 hour ozone)	All PM agents (except black carbon, 8 hour ozone, nicotine)	NO_2, nicotine, house dust for allergens and endotoxin, outdoor O_3, moisture, home survey

Figure 3.4.1-1:Time scale for sampling of air pollutants and biological agents during one home's two-week panel study.
Arrows indicate the length of the samples (one day, for example).



3.4.2 Measurement Methods at the Central Site, Schools, and other Fixed Sites

This section discusses the measurements conducted at the Central Site (Fresno First Street) by the ARB, by Desert Research Institute (DRI) as part of the EPA Supersite program, and by the FACES exposure team. These same measurement methods were used by ARB in the trailers located at schools during 2002 and 2003. The same measurement methods for ozone and nitrogen oxides and for PM mass were used by the San Joaquin Valley Unified Air Pollution Control District (SJVUAPCD) at the routine sites they operate in the Fresno area.

3.4.2.1 Aerometric Measurements Conducted by ARB and DRI

The ARB has operated the site at 3425 First Street in Fresno since 1990. As part of the EPA Supersite program, DRI has supplemented the measurements at the site. The site, its surroundings, and the aerometric measurements being conducted by ARB and DRI at the Central Site are summarized by Watson et al., (173), and shown in Table 3.4.2-1. These measurements include gases, continuous PM mass and chemistry, particle number counts, continuous light scattering and light absorption, and meteorological measurements. Identical methods to those shown in Table 3.4.2-1 were used by ARB to collect data from two trailers located at various schools in the Fresno area. Additional measurements for FACES have been added to the Central Site by ARB. They include hourly SO_2 (from an API-100A instrument); 24-hr average filter samples for PM_{10} metals and endotoxin (using an R&P 2025 sampler); and samples for pollen grains and fungal spores (using a Burkard BVST). Table 3.4.2-2 lists the elements, including the metals, which were determined by DRI's x-ray fluorescence analysis of Teflon filters collected by ARB at the Central Site. The endotoxin and bioaerosol analyses were conducted by UCB (methods discussed below). STI also operated a PAH sampler for determining 24-hr average gas-phase and particle-phase PAHs on an intermittent schedule to coincide with the home intensive measurements; the PAH laboratory analysis methods performed by UCB are discussed below.

3.4.2.2 Endotoxin Measurement Methods

Airborne endotoxin was collected on Teflon filters with a PM_{10} inlet. Initially, the samples were collected at a nominal flow rate of 8.33 lpm for 24 hours. Initially, the samples were collected at the Central Site from 8 pm to 8 pm to coincide with the home intensive samples. Samples were returned to the laboratory, where they were analyzed using the Kineteic Limulus Assay with Resistant-parallel-line Estimation (the KLARE) Method, as developed by Dr. Donald Milton of Harvard School of Public Health (see Protocols and SOPs for details of the method).

The Limulus amebocyte lysate (LAL) test was used to determine the presence of endotoxin in both air filter and dust samples. The LAL method is an *in vitro* biological assay in which LAL is activated in the presence of endotoxin. In this chromogenic reaction, the LAL enzymes cause the release of a chromophore, which is detected by a spectrophotometer.

The samples were extracted by sonication in 5 ml of triethylamine phosphate (TAP) buffer for one hour. After extraction, the sample was diluted serially in endotoxin-free test tubes and

placed in a polystyrene microplate. Control standards and blanks were also loaded on the microplate for each assay. LAL was then added to each well, and the plate was monitored every 30 seconds for a period of 120 minutes. The absorbance wavelength was 405 nm, and the incubation temperature was 37 ^{o}C. The concentration of endotoxin is proportional to magnitude of the reaction and the color change. The standard and sample dilution curves were compared with an estimated parallel-line bioassay analysis to determine the validity of the assay.

Two sets of standard endotoxin solutions and one set of reagent blanks were run on each endotoxin plate, which also contained 13 samples. Both laboratory and field blanks were analyzed for endotoxin samples, as collected at the central site and trailers (47 mm filters). No endotoxin was detected on the 130 laboratory blanks (<0.00001 EU/m^3), while the 165 field blanks had a mean level comparable to a concentration of 0.01 EU/m^3. Of the 165 field blanks, the maximum blank had an equivalent of 0.5 EU/m^3 and the second largest was less than 0.1 EU/m^3.

3.4.2.3 Pollen Grain and Fungal Spore Measurement Methods

3.4.2.3.1 Sampling of Pollen Grains and Fungal Spores at Central Site and Trailers

A new, Hirst-type sampler (174, 175) (Seven-Day Recording Volumetric Spore Trap; Burkard Manufacturing Co. Ltd., Rickmansworth, UK) was used to measure regional pollen grains and spore concentrations at the Central Site and the Trailers. The performance of the Burkard Seven Day Recording Volumetric Spore Trap (BSVT) is slightly improved from the original Hirst sampler (174). This means that particles that have an aerodynamic diameter of 5 μm and above will be separated from the air-stream with efficiency greater than 90 per cent. The Hirst-type spore trap is considered a reference sampler for measurement of ambient aeroallergens and is used around the world in aerobiological studies (176). The spore traps have 2- × 14-mm slit inlets and were operated at an airflow rate of 10 L min^{-1}. In the 7-day sampler, particles impacted onto a 33.6-cm length of transparent, adhesive-coated tape (Melinex®, 200 gauge; Burkard Manufacturing Co. Ltd., Rickmansworth, UK) affixed to a rotating drum that completed one revolution in one week.

Three different adhesives for the deposition surface on the rotating drum were used during the first year of sampling at the CARB First Street station:

1. Lubriseal adhesive (November 2000 –February 2001) produced very thick and optically unsatisfactory deposition surface for pollen grains and fungal spores.
2. Mixture of Vaseline and Paraffin in Toluene (9:1:10) (February 2001 –May 2001) is considered as a standard adhesive on the polyester Melinex tape (Burkard Manufacturing Co. Ltd., Rickmansworth, UK). However, this adhesive does not tolerate high temperatures and was replaced in May, 2001 with

3. Silicon grease, Dow Corning 280A (Dow Corning, UK; diluted in xylene). This has greater particle collection efficiency than other adhesives and is stable in temperatures up to 500^{o}F (177).

The height of the orifice was 10.7 meters above the ground level on the roof of the ARB First Street station. This is not quite above the top level of the highest oak trees on the east side of the building, but the pollen grains collected are considered to be representative of the regional flora, since the prevailing winds at the sampling location are from northwest through southeast.

The 7-day tapes were cut into 24-hour segments and affixed to glass slides. Cover slips were mounted on all slide samples with unstained glycerin gelatin from May 2001 (178[Kearns, 1993 #213). Saffranine stained Gelvatol was used for mounting from November 2000 to February 2001; unstained Gelvatol from February 2001 to May 2001. The optical quality of the slides was noticeably improved when Gelvatol was replaced by Glycerin gelatin in May 2001.

3.4.2.3.2 Analysis of collected samples for pollen grains and fungal spores (same for both Central Site and home intensive samples)

The daily samples were examined by reading the particle traces transversely at 2-mm intervals. This procedure has been found to be more accurate than a single, longitudinal traverse (179). For pollen grains, transverse reading resulted in 12, evenly spaced, 7-mm^2 continuous fields that corresponded to 15-min periods every second hour (180). For fungal spores, because of the higher magnification, only 20, evenly spaced, 92.2-µm^2 fields were counted in each traverse (180). Daily air concentrations were reported as 2- and 24-hour average pollen grains and spore counts per cubic meter of air. Time discrimination below one hour is not possible given the slit width (2 mm) and rate of slide movement (2 mm h^{-1}) (179).

Particles were examined with a bright-field microscope (Nikon Eclipse 400; Nikon Instruments Inc., Melville, NY) at 400× magnification for pollen grains (in critical cases 1000× magnification with oil immersion was used), and with oil immersion and 1000× magnification for fungal spores.

3.4.2.3.3 Pollen Grains and Fungal Spore Identification

Pollen grains were identified at species or genera level. Reference slides and available reference manuals (181) were used for identification. However, no reference literature in airborne pollen grain identification for California or the southwestern United States is available; therefore, an extensive pollen grain reference collection for the area investigated has been prepared to facilitate the correct and reliable identification.

The different pollen grain types identified in Fresno are listed in Table 3.4.2-3 (182). Of the 124 pollen grain types identified, approximately 50% belong to wind pollinated plants. About 80% of these plants are known to produce pollen grains causing allergies and might promote asthma.

The epidemiologic analysis could not include all plant taxa that were observed. Therefore, 15 plant groupings (P1 through P15) were selected based on current knowledge of the allergenicity and immunological cross-reactivity of pollen grain allergens, and presence of ecological sources in the study area, as summarized in Table 3.4.2-3 (182).

From 2000–2001, 66 fungal spore types were identified (Table 3.4.2-4). The detailed data that were collected in the first part of the study allowed the FACES aerobiology team to evaluate the types of fungi in the study region and their concentration ranges. For subsequent periods, the time required to read slides was decreased by elimination of the 54 less common spore types and recording only the 12 categories in the four indicator groups (F1–F4) along with hyphal fragments and algae (F6 and F7) (Table 3.4.2-4). In this agricultural setting, separate consideration of crop-related fungi will allow study of the relations between the major contributors to this group (i.e., smuts and *Ustilago* spp.) and morbidity in our subjects. Additional advantages of the proposed fungal grouping are that spores can be categorized more reliably, and the inclusion of less-informative broad groups (such as Ascomycetes, Basidiomycetes, colorless spores, and unknown spores) is avoided. While some genera within the excluded groups have been implicated in seasonal allergy and epidemic asthma (183), they contain thousands of species with different ecological niches. The concentrations of Ascomycetes and Basidiomycetes were relatively high during the summer months in Fresno, but overall the relative concentration of all eliminated spore types was low (<15%).

3.4.2.3.4 Calculation of the pollen grain and fungal spore concentrations collected with Burkard sampler

Burkard continuous sampler allows timed sample collection to follow fluctuations over 24-hr interval. The air is sucked into the trap through a slit at a rate of 10 liters per minute ($\pm$ 1.5 L), and the pollen grain and other particles are captured on a prepared adhesive tape or microscopic slide, which is passing the slit at a set rate (2mm/hr).

For each 24-hour period, 12 transverse strips are analyzed each of which corresponds to 15 minutes exposure every second hour. This enables us to study the diurnal as well as the daily and seasonal pattern of the atmospheric concentration of airborne pollen grains. The counts are converted to represent the average 24-hour mean pollen grain concentration per cubic meter of air based on the following equation:

$$C = \left(\frac{N}{A}\right)\left(\frac{T}{B}\right)$$

Where C = pollen grain concentration in pollen grains per cubic meter
N = Number of pollen grains counted
A = Total air volume sampled per 24 hr (=14.4 m^3)
B = Analyzed tape area
T= Total exposed tape area (= 672 mm^2)

To get the best estimate of pollen grain and/or fungal spore concentration (m^{-3} of air) for shorter time intervals, the recorded number of pollen grains/fungal spores is divided by the number of counted transects times the flow rate times the number of minutes counted per transect. Based on the microscope and magnification used, the number of minutes counted per each 2-hr interval varies. The number obtained is multiplied by 1000 L $m^{-3, \text{which}}$ gives N number of pollen grains/fungal spores m^{-3} of air.

3.4.2.3.5 Time Resolution

Counting airborne pollen grains and fungal spores in 2-hour increments also allowed FACES to better characterize and compare regional, neighborhood, and home-specific concentrations and to construct the following concentration intervals to match the time periods for which the participants reported symptoms or during which other environmental measurements were made:

- 6 a.m.–12 noon (morning)
- 12 noon–8 p.m. (afternoon)
- 8 p.m.–6 a.m. (night)
- 8 p.m.–8 p.m. total (24-h total)
- 8 a.m.-8 a.m. total (24-h total)
- Maximum 2-hour concentration

For this study, the time intervals corresponded primarily with human activities rather than plant- or fungi-specific behavior. However, the above time periods also differentiated relatively well the main time blocks that were associated with pollen grains and fungal spore production and release (Table 3.4.2-5). In addition, this level of data analysis makes construction of other time periods possible for ecological research on pollination and sporulation patterns. The proposed groupings were based on three years of data to more completely identify the range of taxa that may be observed as well as their seasonal patterns and concentration ranges (182).

3.4.2.3.6 Data Quality Control

A trap and a field blank for each Burkard Drum were sent to and from Fresno. The field blank was removed from its container momentarily while the normal drum was loaded and unloaded. During different occasions, two Continuous Recording Air Samplers were operated at the Supersite next to the Burkard 7-day sampler.

The blank slides for pollen grains and fungal spores (Field and Trip blank) from Central Site have been analyzed for the first 13 months period (November 2000-December 2001). The number of airborne pollen grains and fungal spores in each of the Field blanks has been extremely low--< 2 pollen grains or fungal spores per slide. The trip blanks have been completely empty. During 2002 and 2003, about 5% of the Field blank slides were analyzed; the daily concentration of pollen grains and fungal spores was under 0.5 pollen grains or fungal spores m^{-3} air.

Replicate microscopic analysis has been conducted. Approximately, 3% of pollen grains and fungal spore analyzed have been counted and identified a second time. The results are within

the range of variability for such analysis. The differences in numbers are > ± 5% for each transverse, since 12 transverse strips are analyzed for each slide, this has little effect on the final result (less than 3%). In the fungal spore analysis, the difference for the daily total spore count for each species can be closer to 5%, since the count is done in separate fields on the transverse (20 fields per each of the 12 transverse strips). The pollen grains analysis is done for the whole length of each of the 12 transverse strips, and the difference between replicate counts becomes very small. It is normal that slight differences between different counts can be observed, due to the fact that neither pollen grains nor fungal spores are homogeneously distributed on the deposition surfaces.

Replicate analyses were made for 45 pollen grain samples, and an independent reader analyzed an additional 25 samples. The differences in calculated concentrations and number of observed taxa were less than 3%. The comparison pollen grain counts were performed from material collected in March–April, which was the period of highest pollen grain concentration and greatest diversity of plant taxa. Forty-five fungal samples were analyzed independently by two readers and counts agreed within 5%. Variation among other readers has been found to be random and relatively small, accounting for 2–13% of total uncertainty (184).

3.4.2.4 Polycyclic Aromatic Hydrocarbons

Polycyclic Aromatic Hydrocarbons (PAH) in were measured in ambient air at selected fixed locations (the US EPA Supersite in Fresno, CA, and two California Air Resources Board Trailers located at schools in Fresno) and inside and outside selected homes. PAHs were collected at the central site and the schools with denuders and filters, all coated with XAD-4, to enable the separate determination of vapor phase and particle phase PAHs. At the homes, total PAHs were collected on the MEMs with similar filters coated with XAD-4. All samples were collected from 8 pm one day to 8 pm the following day, at 10 l/min with a $PM_{2.5}$ inlet. Samples were analyzed by gas chromatography/mass spectrometry/selected ion mode for 16 PAHs: naphthalene NAP, acenaphthylene ACY, acenapthene ACE, fluorene FLU, anthracene, ANT, phenanthrene PHE, fluoranthene FLT, pyrene PYR, benz(a)anthracene BAA, chrysene CHR, benzo(b)fluoranthene BBF, benzo(k)fluoranthene BKF, benzo(a)pyreneBAP, indeno(1,2,3-cd)pyrene ICP, dibenz(a,h)anthracene DBA, benzo(ghi)perylene BGP.

3.4.2.4.1 Naphthalene

Naphthalene is the most volatile of the 16 EPA priority PAHs and exhibited breakthrough in the Chemcombs which held three denuders followed by three filters (see section 3.4.2.4.3 below); therefore, a separate method for collection and measurement of naphthalene in ambient air was developed using sorbent tubes. Naphthalene was collected at a flow rate of 0.2 L/min with sorbent tubes that contained XAD-2 resin (SKC 226-30-06) in separate front (400 mg) and back (200 mg) sections, which can be extracted and analyzed separately to evaluate possible breakthrough. The average breakthrough observed in the back section of the tubes was less than 10%. The contents of the XAD tubes were placed in glass vials and extracted with 2 ml dichloromethane on a developing vibrator and analyzed with gas chromatography/mass

spectrometry with selected ion mode detection; the standard curve is linear in the analysis range, 2 to 250 ng/ml.

Unlike other methods used to sample naphthalene, sorbent tubes are able to collect naphthalene without breakthrough problems. They are also inexpensive, easy to extract, and provide good sensitivity in environmental sampling (the analytical limit of detection in the FACES study was 4 ng per sample). Naphthalene samples were collected daily at the Fresno EPA Supersite, stored in a freezer, and shipped weekly to the University of California, Berkeley for analysis.

3.4.2.4.2 Coating Filters and Denuders

Styrene divinylbenzene polymer resin XAD-4 beads were prepared for coating filter and denuder sampling media (185). The beads were ground in an agate ball mill with a planetary grinder. The resulting XAD powder was cleaned by sonication, first in methanol and water, then methanol and dichloromethane, followed by filtration in Alundum (Al_2O_3) thimbles. Quartz fiberglass filters (Pallflex Corporation) were coated with XAD for sample collection. The filter diameter was 37mm for the MEMS samplers and 47mm for the Chemcomb samplers. Dried and coated filters were stored in a glass jar with a Teflon lined cap. The inner surfaces of the glass denuders were coated with XAD that was applied from an n-hexane slurry. After the denuders had been sampled and extracted for 5 iterations, they were re-coated with XAD.

3.4.2.4.3 Sample Collection

At the Supersite and trailers, samples were collected at 10 l/min for 24 hours with ChemComb Model 3500 Speciation Sampling Cartridges (Rupprecht & Patashnick). These were configured to contain a $PM_{2.5}$ impaction inlet followed by three honeycomb denuders and three filters. Each denuder is 47 mm in diameter, 38 mm long and has 212 hexagonal flow channels that are 2 mm on a side; the internal surface area is 508 cm^2 for each denuder. The three filters were contained in the Teflon filter pack. The denuders and filters were coated as describe above.

3.4.2.4.4 Sample Storage and Shipment

Coated filters were stored in glass jars with Teflon lined caps prior to use. Coated denuders were stored by wrapping in clean aluminum foil prior to use. Filters and denuders were stored at room temperature. Chemcombs were assembled in the laboratory on the day of shipment to Fresno by Federal Express, where they were stored at 0 ^oC. After sampling, Chemcombs and home intensive filters were stored at 0 ^oC. They were shipped to the laboratory by Federal Express, and then stored at -20 ^oC. Denuders usually were extracted and analyzed within 7 days of collection and always within 30 days.

3.4.2.4.5 Sample Extraction

The denuders were extracted with two aliquots of dichloromethane of approximately 70 mL each. The extracts were reduced under vacuum rotary evaporation to a volume of approximately 10 mL and filtered under vacuum with a 0.45 uM Millipore Type FH filter. The extracts were quantitatively transferred to a 15 mL glass centrifuge tube and blown down under nitrogen to less than 300 uL. The extract was measured and collected using a 250-uL syringe, and the final volume was recorded. For selected samples, the front and middle denuders were extracted and analyzed separately; for the remainder, the front and middle denuders were combined for extraction and analysis. The back denuder was extracted and analyzed separately for all samples. The filters were removed from the Chemcombs and underwent ultrasonic extraction in dichloromethane and filtered under vacuum with a 0.45 uM Millipore Type FH filter. The filtered extract was blown down under nitrogen to less than 300 uL. The extract was measured and collected with a 250-uL syringe, and the final volume was recorded. For selected samples, the front and middle filters were extracted and analyzed separately; for the remainder, the front and middle filters were combined for extraction and analysis. The back filter was extracted and analyzed separately for all samples.

3.4.2.4.6 Analysis

Standard solutions were prepared from standards purchased from Supelco Corporation (BAA, ICP, DBA, BGP), Chem Service (NAP, ACE, FLU, ANT, PHE, FLT, PYR, CHR, BKF, BAP, ICP), and Sigma-Aldrich (NAP, ACY, ACE, FLU, ANT, FLT, PYR, CHR, BAP). Dilutions from the stock solution were prepared for each 2-week period of analysis, and a full set of standards was run at least once on each day of analysis

All analyses were performed on a Hewlett Packard model 6890 gas Chromatograph equipped with a 5972 Mass Selective detector (MSD). A 30 m (50%-Phenyl)- methylpolysiloxane fused silica capillary column was used. The inlet temperature was 305 °C and the MSD temperature was 280 °C. The initial oven temperature was 65 °C, and then increased at 5 °C per minute to 280 °C, which was held for 20 minutes, and then the temperature program rate was increased to 10 °C per minute to a final temperature of 310 °C, which was held for 5 minutes. The MSD was operated in the selected ion-monitoring mode for enhanced sensitivity. Mass ions were selected by analyzing each PAH using the MSD in Scan mode, and selecting ions with the greatest abundance. Table 3.4.2-5 presents the mass ions chosen and the retention time for each PAH.

3.4.2.5 Quality Assurance and Quality Control

Standard solutions were prepared and run during each analysis for PAHs. Solvent blanks and laboratory blanks (filters, denuders, sorbent tubes) were also run routinely. Field blanks were collected and analyzed, and the sample results were corrected for the field blanks.

Table 3.4.2-1: Aerometric measurements conducted by ARB and DRI at the Central Site for FACES
(Excerpted from Table 1, Summary of air quality and meteorological measurements at the Fresno Supersite, by Watson et al.)

Observable and Method	Size Range	Average Time	Period
Gases			
Nitrogen oxides (NO/NO_x) (TEI 42 chemiluminescence w/internal converter)	Gas	1 hr	1990 onward[a]
Ozone (API 400 UV absorption)	Gas	1 hr	1990 onward[a]
Carbon monoxide (Dasibi 3008 infrared gas filter correlation)	Gas	1-hr	1990 onward[a]
Reactive nitrogen (NO_y) (TEI 42C chemiluminescence with external converter)	Gas	1-hr	12/15/99 to 3/31/03
Continuous Particle Mass and Chemistry			
$PM_{2.5}$ mass (ambient temperature Met One 1020BAM)	<2.5 µm	1 hr	5/15/99 onward[a]
PM_{10} mass (ambient temperature Met One 1020 BAM)	<10 µm	1 hr	5/15/99 onward[a]
$PM_{2.5}$ NO_3^- (R&P/ADI flash volatilization with NO_x detector)	<2.5 µm	1-hr	9/23/99 to 3/31/03
$PM_{2.5}$ SO_4^{-2} (ADI flash volatilization with SO_2 detector)	<2.5 µm	1-hr	9/23/99 to 10/28/99 2/7/00 to 3/31/03
$PM_{2.5}$ organic and elemental carbon (R&P Series 5400 thermal evolution, OC at 275ºC, EC at 600ºC)	<2.5 µm	1-hr	12/15/99 to 3/31/03
PM Particle-bound PAH (EcoChem Analytics PAS2000 w/UV radiation and photoelectric aerosol sensors)	<1 µm	1-hr	9/30/99 to 3/31/03
Particle Number (TSI Model 3010)	<1 µm	1-hr	9/30/99 to 3/31/03
Continuous Light Scattering and Light Absorption			
Total particle light scattering[c] (Radiance M903nephelometer with smart heater at 530 nm)	<~30 µm	1 hr	2/15/00 to 3/31/03
Single-wavelength light absorption[d] (McGee AE 14U aethalometer at 880 nm)	<2.5 µm	1-hr	5/15/99 to 3/31/03
Seven-wavelength light absorption[d] (Andersen AE30S multi-color [350, 450, 570, 590, 615, 660, 880, and 950 nm] aethalometer)	<2.5 µm	1-hr	5/15/99 to 3/31/03
Meteorology			
Temperature (Met One CS500L platinum resistance sensor)	NA[b]	1 hr	5/15/99 onward[a]
Relative humidity (Met One CS500L capacitance sensor)	NA[b]	1-hr	5/15/99 onward[a]

[a] Part of the California ARB's compliance monitoring network.
[b] Not applicable.
[c] For b_{sp}
[d] For black carbon

Table 3.4.2-2: Elements determined in x-ray fluorescence analysis of Teflon filters collected at the Central Site

Element	Chemical Symbol	Atomic No.	Atomic Wt.	DRI Symbol
Aluminum	Al	13	26.982	AL
Silicon	Si	14	28.086	SI
Phosphorous	P	15	30.974	PH
Sulfur	S	16	32.065	SU
Chlorine	Cl	17	35.453	CL
Potassium	K	19	39.098	KP
Calcium	Ca	20	40.078	CA
Titanium	Ti	22	47.867	TI
Vanadium	V	23	50.942	VA
Chromium	Cr	24	51.996	CR
Manganese	Mn	25	54.938	MN
Iron	Fe	26	55.845	FE
Cobalt	Co	27	58.933	CO
Nickel	Ni	28	58.693	NI
Copper	Cu	29	63.546	CU
Zinc	Zn	30	65.390	ZN
Gallium	Ga	31	69.723	GA
Arsenic	As	33	74.922	AS
Selenium	Se	34	78.960	SE
Bromine	Br	35	79.904	BR
Rubidium	Rb	37	85.468	RB
Strontium	Sr	38	87.620	SR
Yttrium	Y	39	88.906	YT
Zirconium	Zr	40	91.224	ZR
Molybdenum	Mo	42	95.940	MO
Palladium	Pd	46	106.420	PD
Silver	Ag	47	107.868	AG
Cadmium	Cd	48	112.411	CD
Indium	In	49	114.818	IN
Tin	Sn	50	118.710	SN
Antimony	Sb	51	121.760	SB
Barium	Ba	56	137.327	BA
Lanthanum	La	57	138.906	LA
Gold	Au	79	196.967	AU
Mercury	Hg	80	200.590	HG
Thallium	Tl	81	204.383	TL
Lead	Pb	82	207.200	PB
Uranium	U	92	238.029	UR

Table 3.4.2-3: Pollen grains and fern spores in air samples from Fresno, California, with identification of the proposed 14 pollen-grain groups (P1–P14) that were analyzed separately from total pollen grain concentration (P15 = sum of all 124 taxa). Known allergenic pollen-grain groups shown in bold.

Group	Taxon	Family * Genus species
		Aceraceae (maple family)
	1	*Acer* spp.
		Anacardiaceae (sumac family)
P10	2	*Pistacia* spp.
	3	*Rhus* spp.
	4	***Schinus* spp.**
	5	Apiaceae (carrot family)
		Aquifoliaceae (holly family)
	6	*Ilex* spp.
	7	**Arecaceae** (palm family)
		***Asteraceae** (aster family)*
P1	8	***Ambrosia* spp.**
P2	9	***Artemisia* spp.**
	10	*Cirsium*-type
	11	*Senecio*-type
	12	*Taraxacum*-type
	13	*Xanthium*-type
	14	Other Asteraceae
P3		**Betulaceae** (birch family)
	15	***Alnus* spp**.
	16	***Betula* spp**.
	17	***Carpinus* spp**.
	18	***Corylus* spp**.
	19	***Ostrya* spp**.
		Boraginaceae (borage family)
	20	***Echium* spp**.
	21	*Myosotis* spp.
	22	Brassicaceae (mustard family)
	23	Cannabaceae (hemp family)
		Caprifoliaceae (honeysuckle family)
	24	*Lonicera* spp.
	25	*Sambucus* spp.
	26	*Viburnum* spp.
	27	Caryophyllaceae (pink family)
		Casuarinaceae (she-oak family)
	28	***Casuarina* spp**.
P4	29	Chenopodiaceae/Amaranthaceae (goosefoot and amaranth families)
		Cistaceae (rock-rose family)
	30	*Helianthemum* spp.
	31	Other Cistaceae

Table 3.4.2-3: Pollen grains and fern spores in air samples from Fresno, California, with identification of the proposed 14 pollen-grain groups (P1–P14) that were analyzed separately from total pollen grain concentration (P15 = sum of all 124 taxa). Known allergenic pollen-grain groups shown in bold.		
Group	**Taxon**	**Family** [*] **Genus species**
	32	Clusiaceae (St. John's-wort family)
	33	Convolvulaceae (morning-glory family)
	34	Cornaceae (dogwood family)
P5	35	**Cupressaceae** (cypress family)
	36	Cyperaceae (sedge family)
		Ephedraceae (mormon-tea family)
	37	*Ephedra* spp.
	38	Ericaceae (heath family)
		Euphorbiaceae (spurge family)
	39	*Euphorbia* spp.
	40	*Sapium* spp.
		Fabaceae (pea family)
	41	***Acacia* spp**.
	42	***Prosopis* spp**.
	43	Other Fabaceae
		Fagaceae (beech family)
	44	*Castanea* spp.
	45	*Castaneopsis* spp.
	46	***Fagus* spp**.
P13	47	***Quercus* spp**.
		Geraniaceae (geranium family)
	48	*Geranium* spp.
		Ginkgoaceae (maidenhair-tree family)
	49	*Ginkgo biloba*
		Hamamelidaceae (witch-hazel family)
P7	50	*Liquidambar* spp.
		Hippocastanaceae (horse-chestnut family)
	51	*Aesculus* spp.
P6		**Juglandaceae** (walnut family)
	52	***Carya* spp**.
	53	***Juglans* spp**.
		Juncaceae (rush family)
	54	*Luzula pilosa*
	55	Lamiaceae (mint family)
		Lauraceae (laurel family)
	56	*Cinnamomum* spp.
	57	Other Lauraceae
		Liliaceae (lily family)
	58	*Tofieldia* spp.
	59	Other Liliaceae
		Linaceae (flax family)

Table 3.4.2-3: Pollen grains and fern spores in air samples from Fresno, California, with identification of the proposed 14 pollen-grain groups (P1–P14) that were analyzed separately from total pollen grain concentration (P15 = sum of all 124 taxa). Known allergenic pollen-grain groups shown in bold.		
Group	**Taxon**	**Family** [*] **Genus species**
	60	*Linus usitatissimum*
		Lythraceae (loosestrife family)
	61	*Lagerstroemia* spp.
		Magnoliaceae (magnolia family)
	62	*Liriodendron* spp.
	63	*Magnolia* spp.
		Moraceae (mulberry family)
P8	64	***Morus* spp.**
	65	Myricaceae (bayberry family)
		Myrtaceae (myrtle family)
	66	*Callistemon* spp.
	67	*Eucalyptus* spp.
		Nyctacinaceae (four-o'clock family)
	68	*Bouganvillea* spp.
P9		**Oleaceae** (olive family)
	69	***Fraxinus* spp**.
	70	***Ligustrum* spp**.
	71	***Olea* spp**.
	72	*Jasminum* spp.
	73	*Syringa* spp.
	74	Papaveraceae (poppy family)
		Pinaceae (pine family)
	75	*Cedrus* spp.
	76	*Larix* spp.
	77	*Picea* spp.
	78	*Pinus* spp.
	79	*Pseudotsuga* spp.
	80	*Tsuga* spp.
		Pittosporaceae (pittosporum family)
	81	*Pittosporum* spp.
		Plantaginaceae (plantain family)
	82	Plantago lanceolata
	83	***Plantago major***
	84	*Plantago* spp.
		Platanaceae (plane tree family)
P11	85	***Platanus* spp**.
P12		**Poaceae** (grass family)
	86	**Cerealia** (cultivated grasses)
	87	**Other Poaceae**
		Podocarpaceae (podocarps family)
	88	*Podocarpus* spp.

Table 3.4.2-3: Pollen grains and fern spores in air samples from Fresno, California, with identification of the proposed 14 pollen-grain groups (P1–P14) that were analyzed separately from total pollen grain concentration (P15 = sum of all 124 taxa). Known allergenic pollen-grain groups shown in bold.

Group	Taxon	Family * Genus species
		Polygonaceae (buckwheat family)
	89	***Rumex acetosa/acetosella***
	90	***Rumex* spp.**
	91	*Polygonum* spp.
		Ranunculaceae (buttercup family)
	92	*Thalictrum* spp.
	93	Other Rannunculaceae
		Rhamnaceae (buckthorn family)
	94	*Rhamnus* spp.
		Rosaceae (rose family)
	95	*Adenostoma* spp.
	96	*Amelanchier* spp.
	97	*Prunus* spp.
	98	*Pyracantha* spp.
	99	*Pyrus* spp.
	100	Other Rosaceae
	101	Rubiaceae (madder family)
	102	Rutaceae (rue family)
		Salicaceae (willow family)
	103	***Populus* spp**.
	104	***Salix* spp.**
		Saxifracaceae (saxifrage family)
	105	*Saxifraga* spp.
	106	Scrophulariaceae (figwort family)
		Simmondsiaceae (jojoba family)
	107	*Simmondsia* spp.
	108	Solanaceae (potato family)
		Sparganiaceae (burr-reed family)
	109	*Sparganium* spp.
		Taxaceae (yew family)
P5	35	*Taxus* spp. (here included in Cupressaceae count)
		Taxodiaceae (bald-cypress family)
P5	110	*Cryptomeria* spp./*Sequoia sempervirens/Sequoiadendron giganteum*
		Tiliaceae (linden family)
	111	*Tilia* spp.
		Typhaceae (cat-tail family)
	112	*Typha angustifolia*-type
P14		**Ulmaceae** (elm family)
	113	***Celtis* spp**.
	114	***Ulmus spp.***/*Zelkova* spp.
		Urticaceae (nettle family)
	115	*Urtica* spp./***Parietaria* spp**.
	116	Verbanaceae (vervain family)
		Vitaceae (grape family)

Table 3.4.2-3: Pollen grains and fern spores in air samples from Fresno, California, with identification of the proposed 14 pollen-grain groups (P1–P14) that were analyzed separately from total pollen grain concentration (P15 = sum of all 124 taxa). Known allergenic pollen-grain groups shown in bold.

Group	Taxon	Family * Genus species
	117	*Vitis vinifera*
	118	Zygophyllaceae (caltrop family)
		Unknown and unidentifiable pollen grains
	119	Inaperturate
	120	Monolete
	121	Other
		Pteridopsida – Ferns
	122	Lycopodiaceae (club-moss family)
	123	Polypodiaceae (polypody fern family)
	124	Other Pteridopsida

* Nomenclature and systematics follow The Jepson Manual (186), International Code for Botanical Nomenclature (18 (188).

Table 3.4.2-4: Fungal spores and algal cells observed in air samples from Fresno, California, with identification of the proposed four spore groups (F1–F4) that were identified if considered separately from total indicator spore concentration (F5).

Group	Taxon	Fungal group * Genus
		Ascospores
	1	*Chaetomium* spp.
	2	*Leptosphaeria* spp.
	3	*Leptosphaerulina* spp.
	4	*Pleospora* spp.
	5	*Venturia* spp.
	6	*Xylaria* spp.
	7	Ascomycetes general (1–2 cell, multi-cellular, colored, hyaline)
		Basidiospores
	8	*Agrocybe* spp.
	9	*Boletus* spp.
	10	*Botrytis* spp.
	11	*Coprinus* spp.
	12	*Ganoderma* spp.
	13	*Gyrenospora* spp.
	14	*Inocybe* spp.
	15	*Perenospora* spp.
	16	*Pithomyces* spp.
	17	Phycomycetes
	18	*Pyrenospora* spp.
	19	*Rhizopus* spp.
	20	*Sordaria* spp.

Table 3.4.2-4: Fungal spores and algal cells observed in air samples from Fresno, California, with identification of the proposed four spore groups (F1–F4) that were identified if considered separately from total indicator spore concentration (F5).

Group	Taxon	Fungal group * Genus
	21	*Spegazzinia* spp.
	22	*Sporidylocladiella* spp.
	23	*Sporomiella* spp.
	24	*Tilletia* spp.
	25	Basidiomycetes general (1–2 cell, multi-cellular, colored, hyaline)
		Anamorphic fungi
	26	*Acrodictys* spp.
F2 (F5)	27	*Alternaria* spp.
	28	*Arthinium* spp.
F3 (F5)	29	*Aspergillus* spp./*Penicillium* spp.
	30	*Asperisporum* spp.
	31	*Beltrania* spp.
	32	*Cercospora* spp.
F1 (F5)	33	*Cladosporium* spp.
	34	*Corynespora* spp.
	35	*Curvularia* spp.
	36	*Dichotomophthora* spp.
	37	*Diplococcium* spp.
	38	*Endophragmiella* spp.
	39	*Exosporium* spp.
	40	*Fusariella* spp.
	41	*Fusarium* spp.
	42	*Fusicladium* spp.
	43	*Geotrichum* spp.
	44	*Gliomastic* spp.
	45	*Helicomyces* spp.
	46	*Monodictys* spp.
	47	*Nigrospora* spp.
	48	*Periconia* spp.
	49	*Pestalotiopsis* spp.
	50	*Phoma* spp.
	51	*Septonema* spp.
	52	*Sporodesmium* spp.
	53	*Stemphylium* spp.
	54	*Torula* spp.
	55	Fungi Imperfecti general
F4 (F5)		***Agricultural fungi***
	56	*Epicoccum* spp.
	57	Exserohilum group (*Bipolaris* spp., *Exserohilum* spp., and *Helminthosporium* spp.)
	58	*Oidium* spp./*Erysiphe* spp.
	59	*Puccinia* spp.
	60	Rust
	61	Smut

Table 3.4.2-4: Fungal spores and algal cells observed in air samples from Fresno, California, with identification of the proposed four spore groups (F1–F4) that were identified if considered separately from total indicator spore concentration (F5).

Group	Taxon	Fungal group * Genus
	62	*Ustilago* spp.
	63	Other fungi: unknown and unidentifiable spores
		Protozoa
	64	**Myxomycetes**
F6	65	Fungal hyphae
F7	66	Algae

* Nomenclature and systematics follow Kirk et al. (189).

Table 3.4.2-5: Medians of 24-hour Average Concentrations of Proposed Indicator Pollen and Fungal Groups in Fresno, CA							
		Regional 2000–2003	**Neighborhood (Trailer 1) 2002–2003**	***Residential***		**Flowering or Peak Season†**	**Peak Time of Day (Outdoor residential) 2002–2003**
				Outdoor 2002–2003	**Indoor 2002–2003**		
Pollen Indicator Group*		**(N = 505)**	**(N = 414)**	**(N = 284)**	**(N = 284)**		
P1	*Ambrosia* spp.**	**0** 2	**1** 4	**1** 7	**1** 1	**March–April** **September**	10–12 8–10
P2	*Artemisia* spp.	1	1	1	0	August–October	10–12
P3	Betulaceae **	14 10	30 14	38 14	<1 <1	January March/April	12–14 8–10
P4	Chenopodiaceae/ Amaranthaceae	2	7	4	<1	July–October	12–14
P5	Cupressaceae, *Taxus* spp., *Cryptomeria* spp./*Sequoia sempervirens*/ *Sequoiadendron giganteum*	53	29	21	<1	January–February	12–14
P6	Juglandaceae	14	11	18	<1	March/April	14–16
P7	*Liquidambar* spp.	22	24	9	<1	March/April	12–14
P8	*Morus* spp.	264	498	352	4	March/April	12–14
P9	Oleaceae **	**30** **37**	**20** **53**	**35** **21**	**4** **1**	**January/February** **–March/May**	10–12 10–12
P10	*Pistacia* spp.	**67**	**44**	**50**	**1**	**March/April**	8–10 and 14–16
P11	*Platanus* spp.	**31**	**124**	**50**	**1**	**March–April**	10–12
P12	Poaceae	**14**	**15**	**22**	**<1**	**March–August**	8–10

Table 3.4.2-5: Medians of 24-hour Average Concentrations of Proposed Indicator Pollen and Fungal Groups in Fresno, CA							
		Regional 2000–2003	**Neighborhood (Trailer 1) 2002–2003**	***Residential*** **Outdoor 2002–2003**	**Indoor 2002–2003**	**Flowering or Peak Season†**	**Peak Time of Day (Outdoor residential) 2002–2003**
P13	*Quercus* spp.	15	50	42	1	March–May	10–12
P14	Ulmaceae	127	277	877	58	September	14–16
Fungi Indicator Group		**(N = 678)**	**(N = 403)**	**(N = 255)**	**(N = 255)**	**Peak season**	**Peak Time of Day (all locations) 2000-2003**
F1	*Cladosporium* spp.	**3591**	**3260**	**4354**	**648**	**November/ December**	16–18
F2	*Alternaria* spp.	**67**	**94**	**229**	**68**	**March-May**	18–20
F3	*Aspergillus* spp./ *Penicillium* spp.	**324**	**256**	**256**	**95**	**November– December**	8–10 and 12–14
F4	Agricultural fungi	**432**	**486**	**1512**	**243**	**April-May**	18–20

* Median pollen concentration calculated for the time period in which 98% of the annual total was observed (177); median concentrations were reported because the data were log-normally distributed.
** Two values are reported for families including species that release pollen at different times of year.
† Months separated with / indicate that the pollen or spore season began or ended in that month.
†† Median fungal spore concentration calculated for all analyzed samples for all location; median concentrations were reported because the data were log-normally distributed.

Table 3.4.2-6: The mass ions chosen and the retention time for each PAH analyzed during FACES		
PAH	**SIM Mass Ions**	**Retention Time (minutes)**
Naphthalene	128, 102	11.6
Acenaphthylene	153,152,151,150	19.4
Acenaphthene	153,152,151,150	20.0
Fluorene	166	22.4
Phenanthrene	188,184,178,152	27.6
Anthracene	188,184,178,152	27.7
Fluoranthene	212,202,184,156,101	33.5
Pyrene	212,202,184,156,101	34.9
benz(a)anthracene	228,113	40.8
Chrysene	228,113	41.2
benzo(b)fluoranthene	253,252,250,125,126	46.7
benzo(k)fluoranthene	253,252,250,125,126	46.9
benzo(a)pyrene	253,252,250,125,126	49.5
indeno(1,2,3-cd)pyrene	279,278,276,139,138	61.2
dibenz(a,h)anthracene	279,278,276,139,138	61.6
benzo(ghi)perylene	277,276,138,137	65.2

3.4.3 Routine Home Exposure Measurement Methods

During each of the panel studies, several measurements and evaluations were conducted to assess home specific factors that might affect the exposure assessment. These included

- Home survey
- Exposure related questions on the daily diary
- Moisture measurements
- Collection of dust for measurement of allergens and endotoxin. The dust was collected in two locations:
  - The child's bed
  - The kitchen and the living room floors (one mixed sample)
- Passive measurements over the two weeks for:
  - Nitrogen dioxide
  - Nicotine (a marker for second hand smoke)
  - Ozone (indoors during the ozone season, with some outdoor samples)

These measurements and evaluations were made to classify homes and distinguish them from each other based on emissions within the home and home specific factors such as air

exchange rates. An attempt was made to collect at least three sets of samples and surveys from each home, one assessment in different seasons.

3.4.3.1 Moisture Protocol

A household survey was developed to gather information about each home, such as type of stoves, smoking policy, windows in the home, signs of mold, etc. During each home panel, two home inspectors visited the home. One home inspector collected survey data about housing characteristics, while a second home inspector used a no-pins moisture meter (Professional Equipment, model #CT100, Hauppauge, NY) to measure wall moisture in the living room and the child's bedroom. The meter measures moisture content in the wall with which it is in contact on a scale of 0-30%. In each home, the moisture meter was placed on three walls in the living room and in the child's bedroom at the horizontal midpoint, 18-24 inches from the floor. Priority was given (1) to external walls, (2) walls adjoining a bathroom, kitchen or laundry room, and (3) walls shared with a bedroom, the living room, or dining room. The maximum of these three measurements was used in the data analysis. The median of the maxima values from the living rooms and the bedrooms was used to dichotomize the data: in a bedroom or living room where the maximum moisture measurement was less than this median, the value was categorized as "lower moisture;" conversely, in a bedroom/living room where the maximum measurement was above this median, the value was categorized as "higher moisture." The home characteristics survey that was completed by the second home inspector included detailed questions about visual evidence of moisture, mildew, and leaks in the home. During the first year of the home visits, each home was visited once. During subsequent years of the study, the goal was to sample each home through a year, so that each home was to be visited three times a year during different seasons so that at least one survey/sampling set was conducted per season from each home.

3.4.3.2 NO_2 Measurement Methods

Passive samplers were collected in a home during the two-week panel study. The passive samplers were clipped to a plastic picture frame, which was then placed on top of a television or a coffee table in the living room or activity room where the child spent the most time while awake.

Nitrogen dioxide was collected with a standard passive sampler (Palmes tube) in which three screens coated with triethanolamine are placed at the end of a plastic tube. The samples were then analyzed colorimetically by Harvard School of Public Health.

3.4.3.3 Ozone Measurement Methods

Ozone was collected with a standard passive sampler (Ogawa sampler) in which filters are treated with nitrite, which ozone oxidizes to nitrate. The nitrate was then analyzed by ion chromatography in the laboratory. Ozone was measured outdoors at each home by placing the Ogawa samplers under a protective cap that was mounted on a tripod and placed in the backyard or some outdoor location belonging to the families. Outdoor samples were not collected for homes that did not have access to outdoor space. The laboratory analyses were performed by

three different laboratories – the Harvard School of Public Health laboratory for samples collected during the summer of 2001, the Johns Hopkins Bloomburg School of Public Health for the samples collected during the summer of 2002; and the RTI laboratory for samples collected during the summers of 2003 and 2004.

3.4.3.4 Nicotine Measurement Methods

Second-hand smoke (SHS) was sampled by collection of nicotine gas as a tracer. Nicotine was collected by passive diffusion to a filter treated with sodium bisulfate, with which the nicotine reacts. The sampler itself consists of a modified industrial hygiene sampling cassette with a Teflon coated glass fiber filter impregnated with sodium bisulfate and a windscreen. The sampler is approximately 1.5 inches in diameter and 1 inch high, made of plastic, and weighs half an ounce.

The nicotine was extracted from the filter in ethanolic water, the pH adjusted with sodium hydroxide to free the nicotine molecule, which was then concentrated by liquid extraction into heptane. A small aliquot of the heptane layer was then injected into a gas chromatograph with a nitrogen selective detector. Standards (0.01 ug/ml through 10 ug/ml) were run on each analysis day, as were a solvent blank, a blank filter (laboratory blank), and 3 filters spiked with known amounts of nicotine. Recovery must average at least 90% with a coefficient of variation less than 5 % before field samples may be analyzed. Under routine analysis conditions, the laboratory limit of detection for the 2-week samples was 0.02 ug/m^3, although greater sensitivity is possible if needed. This method was developed in the UCB laboratory and has been used in hundreds of homes in California and thousands of homes across the United States. The method has been tested successfully against other methods in an inter-comparison study of several methods, and, in fact, was the only passive sampler to perform effectively (190).

On each day of analysis, standard solutions of 0.01 to 10 ug/ml were prepared and run, along with solvent blanks and lab blanks. Three spiked filters also were prepared and extracted prior to sample analysis. Altogether, 12 lab blanks (all with less than 0.001 ug of nicotine) and 45 field blanks (with a mean level of 0.008 ug of nicotine, which corresponds to an air concentration of 0.017 ug/m^3 for a two week sample) were run.

3.4.3.5 Household Dust Collection Weighing, and Storing

A new method was developed to collect household dust. This method uses a commercial handheld vacuum cleaner (a Shark) connected to a modified industrial hygiene sampling cassette. The cassette contains window screening on the front to sieve out large particles; dust is collected on a cellulose support pad. Dust was collected on one sample by vacuuming the kitchen floor for two minutes and the living room or activity room floor for another two minutes. Dust was collected on a second sample by folding down the bed covers and sampling for 4 minutes on the child's bed. The full details of the collection method are given in the Protocols and SOPs. The sampling time was increased from 2 minutes per sample to 4 minutes per sample in August 2001.

The dust samples were stored in the refrigerator until they were returned to the laboratory. In the laboratory, the samples were weighed and aliquoted, 50 mg for allergen assays (stored in the freezer), 50 mg for endotoxin assay (stored in the freezer), and the remainder stored for future assays.

3.4.3.6 Dust Allergens Measurement Methods

Five allergens were analyzed: dog, cat, cockroach, and two kinds of dust mites (*D. farinae*, *D. pteronyssinus*). Enzyme-linked immunosorbent assays (ELISA) were performed to determine the concentrations of allergens in house dust samples. The dust samples (~ 50 mg) were extracted in 5 ml of phosphate buffered saline with 0.05% Tween 20 (PBS-T) on an orbital rotator for two hours and then centrifuged for 20 minutes at 2500 rpm. A microplate was coated with a capture monoclonal antibody (mAb) and placed in a refrigerator overnight. Allergen standard and dust extracts were added to the microplate and diluted serially with PBS-T by a multi-channel pipet on the plate. After incubation at room temperature, a detector mAb was added to the plate. Streptavidin peroxidase (for cat and mite allergens) or Peroxidase conjugated Goat anti Rabbit (for dog and cockroach allergens) was added to the plate after incubation. Finally, color development solution was added to the plate. The intensity of the color developed in each well is proportional to the amount of the allergen present. The plate was read at 405 nm by a spectrophotometer. The allergen concentration in the sample was calculated by based on the standard curve.

3.4.3.7 Dust Endotoxin Measurement Methods

The Limulus amebocyte lysate (LAL) test was used to determine the presence of endotoxin in both air filter and dust samples. The LAL method is an *in vitro* biological assay in which LAL is activated in the presence of endotoxin. In this chromogenic reaction, the LAL enzymes cause the release of a chromophore, which is detected by a spectrophotometer.

The dust samples were extracted by sonication in 5 ml of triethylamine phosphate (TAP) buffer for one hour. After extraction, the sample was serially diluted in endotoxin-free test tubes and placed in a polystyrene microplate. Control standards and blanks also were loaded on the microplate for each assay. LAL was then added to each well, and the plate was monitored every 30 seconds for a period of 120 minutes. The absorbance wavelength was 405 nm, and the incubation temperature was 37 ^{o}C. The concentration of endotoxin is proportional to magnitude of the reaction and the color change. The standard and sample dilution curves were compared based on an estimated parallel-line bioassay analysis to determine the validity of the assay.

3.4.4 Home Intensive Study Measurement Methods

The Home Intensive Study for FACES was conducted between February 6, 2002, and February 10, 2003. The Home Intensive Study sampling involved collection of both integrated and continuous air quality data at the homes of FACES participants. Sampling equipment was installed inside and outside their homes during two-week panels. The Home Intensive Study included sampling for $PM_{2.5}$ mass, $PM_{2.5}$ ions, $PM_{2.5}$ organic carbon (OC), $PM_{2.5}$ elemental

carbon (EC), PM_{10} mass, PM_{10} endotoxins, nicotine as an indicator of second-hand smoke (SHS), PM_{10} metals, PM_{10} PAHs, light scattering by particles (b_{sp}), ozone (O_3), pollen grains, and fungal spores. The FACES Home Intensive Study and PAH report by Vaughn *et al*. (Appendix F) provide more detail on sampling, panel reports, standard operating procedures, and audits. Additional details of the PAH portion of the Home Intensive Study are provided in Hyslop *et al*. (191) and Lurmann *et al*. (192). The following sections discuss the Home Intensive Study sampling strategy and home selection; introduce the sampling system designed for the FACES Home Intensive Study and the Microenvironmental Exposure Monitoring System (MEMS); and summarize the measurement methods used.

3.4.4.1 Sampling Strategy and Home Selection

The Home Intensive Study was designed to: 1) collect five 24-hr integrated samples at each selected home; 2) distribute the samples among weekdays and weekend days; 3) allow for filter media changes and flow checks and calibrations between samples; and 4) perform the sampling during the same two-week panel used for the health portion of the study. Sampler preparation and setup were performed on Tuesday and Wednesday, and samples were collected for 24 hours starting Wednesday night and Friday night of the first week and Monday, Wednesday, and Saturday nights of the second week. Sampler removal was performed the following Monday and Tuesday, and another sampling cycle was started. The nephelometers (for light scattering by particles) operated continuously during the two-week period, while a two-week sample was collected for ozone outside during the summer season.

Two to five homes typically were sampled during each two-week panel, and some MEMS were operated as collocated samplers at homes or comparison samplers at the Central Site. Homes were selected from among the participants to meet a range of criteria that included a distribution of homes across the spatial extent of the FACES, homes with acceptable outdoor locations, and participants agreeable to the six visits needed to perform the five days of sampling. Between February 2002 and February 2003, intensive air quality measurements were made during the panel studies at the homes of 80 participants. A subset of houses (26) was sampled in two seasons. Another 58 houses were sampled in one season, for a total of 110 sets of home visits.

3.4.4.2 Microenvironmental Exposure Monitoring System (MEMS)

The MEMS was used to perform air quality sampling inside and outside the homes of FACES participants. The MEMS was designed to: 1) collect several integrated samples with the use of five Harvard-type Impactors; 3) provide continuous 5-minute average monitoring of light scattering due to particles with a nephelometer (as a surrogate for continuous $PM_{2.5}$ mass); and 3) collect pollen grain and fungal spore samples over 24 hours with a mini-Burkard, a smaller version of the large Burkard used at the Central Site. The MEMS (see Figure 3.4.4-1 for an indoor MEMS) consisted of a frame on wheels that held the five Harvard-style impactors that faced downward, the nephelometer mounted inside a toolbox, the mini-Burkard mounted inside a second toolbox, and a sound-insulated box with a pump and a timer/controller. The pump was quiet enough to be placed inside a home and not bother the residents. The MEMS could be

moved easily into place either inside a home (as shown) or outside, plugged into a wall plug, and operated for the two-week panel. The MEMS has a footprint of 80 cm x 60 cm and a height of 150 cm. The outdoor MEMS is identical the indoor MEMS except that it has an opaque Plexiglas roof and a Mylar cover over the pump box on the bottom for rain and sun protection.

The filter sampling system consisted of a pump, a timer, a flow manifold, and five Harvard-type impactors. The impactors used Teflon cassettes to secure the filter media in place. The cassettes were loaded with filters at the Fresno office inside a glove box with filtered air. Stainless steel screens and Teflon spacer rings provided separation between stacked filters. Polyolefin drain disks supported the filters, particularly when abrupt changes in pressure occur. The Harvard-type impactors were selected for use in the Home Intensive Study sampling, because their performance is comparable to the Federal Reference Method (FRM) (193) and they are well characterized for indoor and outdoor sampling (194). Medo manufactures the pumps used in the filter sampling system; this brand of pump was selected for several technical reasons related to its unique pump-driving mechanism. The pump piston is driven by magnetics, not a motor. With the motor eliminated, there are fewer moving parts, which translates into a quieter, smaller, and more reliable pump that requires less maintenance than a motor-driven equivalent. The pump is capable of delivering over 50 LPM, and the flow rate of 10 LPM to each of the five impactors was set with precise needle valves. The flow rates have been characterized extensively and were stable throughout a broad range of temperatures and filter particle loadings. The impactor flow rates were checked before and after each filter sample was collected with Gilmont rotameters, which had been calibrated against a primary standard. The average of these two measurements was used to calculate the total volume that passed through each filter sample. The seven-day timers, which controlled the filter sampling pump and the Burkard, are mechanical and were chosen for their ease of programming. The filter sampling systems have proven to be robust and reliable.

Five 24-hr integrated samples were scheduled for each panel for filter-based collection of $PM_{2.5}$ mass, $PM_{2.5}$ ions, $PM_{2.5}$ OC, $PM_{2.5}$ EC, PM_{10} mass, PM_{10} endotoxins, SHS, PM_{10} metals, and PM_{10} PAHs; Table 3.4.4-1 lists the filters used and the preparation and analysis methods.

3.4.4.2.1 PM Mass, Inorganic Ions, Carbon, and Trace Metals

$PM_{2.5}$ and PM_{10} mass filters were conditioned and pre- and post-weighted in the Hammond Laboratory at UCB using standard protocols. $PM_{2.5}$ filters were extracted and measured for sulfate, nitrate, and ammonium ions using ion chromatography (IC) in the Hammond Laboratory at UCB. Samples for OC and EC were sent to the DRI Laboratory for analysis using the same procedures as for samples from the Central Site. PM_{10} endotoxin samples collected on Teflon filters were analyzed using the same KLARE Method as for samples collected at the Central Site (see Section 3.4.2.2). Samples for second-hand smoke (SHS) were analyzed using the same methods as described above for samples from the Home Intensive Study (see Section 3.4.3.4). PM_{10} metals samples were analyzed by DRI using the same methods as for the Central Site.

3.4.4.2.2 Polycyclic Aromatic Hydrocarbons

For the home intensive, napthalene samples were collected and analyzed in the same manner as for the Central site samples, as discussed in Section 3.4.2.4 above. The home intensive samples for the other PAHs were collected at 10 l/min for 24 hours with MEMS configured to contain a $PM_{2.5}$ impaction inlet followed by two filters. PAHs were collected on 37 mm quartz fiberglass filters coated with XAD-4 in the same manner as described in Section 3.4.2.4 above. For these home intensive samples, handling, shipping, extraction, and analysis procedures were the same as for the Central site samples, as discussed in Section 3.4.2.4 above.

3.4.4.2.3 Light Scattering by Particles Measured With a Nephelometer

The Radiance Research Model M903 nephelometer obtained a 5-minute average particle light scattering value, instrument temperature measurements, and relative humidity (RH) measurements. The nephelometers were stored in weather-tight containers with a fan to ventilate the enclosure and a heater to dry the air stream when necessary. The heater was controlled by RH measurements and was set to start heating the incoming air stream when the outgoing air stream exceeded approximately 60% RH. The amount of heating increased as the RH increased, and this setting resulted in a maximum RH of approximately 70% for the air stream passing through the nephelometer. Heating prevents water droplets from dominating the light scattering measurement and protects the instrument from moisture damage. Heating the air stream may result in some volatilization of particles, and the heater operation must be considered when the data are analyzed. The nephelometers stored approximately fourteen days of data. Particle light scattering values were calculated by measurement of atmospheric scattering and subtraction of Rayleigh scattering. Rayleigh scattering was adjusted for temperature measurements and the local average pressure. Nephelometer calibrations were checked before each measurement panel. The nephelometer zero values were first checked by passing the ambient air stream through a filter to eliminate the particles. Acceptable light scattering values for this filtered ambient air were $0 \pm 0.20 \times 10^{-6}$ $1/Mm^{-1}$. A precision point was then checked with a hydrofluorocarbon (HFC-143a) refrigerant, which has a moderate, approximately 90 Mm^{-1}, light scattering value.

The environmental enclosure for the nephelometer was a modified toolbox bolted to the MEMS scaffold. The design of the MEMS nephelometer enclosure was based on the enclosures used at Fresno First Street and on the FACES trailers. Sample air entered the enclosure through a 2-inch diameter ABS plastic pipe with a bulkhead-type mount to a screen-covered port in the side of the box. The ABS elbow and 12-inch extension promoted condensation of water vapor before air entered the shelter to avoid condensation in the shelter and potential damage to the nephelometer electronics. Air in the enclosure was continuously purged with a muffin fan, located at the top of the enclosure, which pulls 30 CFM (849 LPM) of air through the box. The enclosure volume is 41 liters, and approximately 75% of the space is occupied by equipment. Therefore, the air exchange rate inside the enclosure was approximately 85 exchanges per minute, which is more than adequate and greater than that in the Fresno First Street and FACES trailer enclosures. Although inlet effects are not a major concern with this instrument, the inlet diameter was large to minimize contact with the surfaces. Inlet effects were not a major concern because particle light scattering is dominated by particles with diameters less than 2.5 μm, and

particles of this size maneuver like gases. The enclosure configuration was modified slightly after July 2002 to increase the separation between the inlet and outlet of the nephelometer enclosure.

3.4.4.2.4 Endotoxins

For endotoxin quality control, two sets of standard endotoxin solutions and one set of reagent blanks were run on each endotoxin plate, which also contained 13 samples. Both laboratory and field blanks were analyzed for endotoxin samples as collected in the home intensive sampling (37 mm filters). No endotoxin was detected on the 135 laboratory blanks (<0.00001 EU/m^3), while the 34 field blanks had a mean level comparable to a concentration of 0.0021 EU/m^3. Of the 165 field blanks, the maximum blank had an equivalent of 0.005 EU/m^3.

3.4.4.2.5 Pollen Grains and Fungal Spores

Twelve smaller slit impactors (Continuous Recording Air Sampler for Glass Slides, Model 9100; Burkard Manufacturing Co. Ltd., Rickmansworth, UK) were used to measure daily indoor and outdoor home-specific concentrations. The efficiency of the 24-hour sampler has been observed to be similar to that of the 7-day spore trap (195). The spore traps have 2- × 14-mm slit inlets and were operated at an airflow rate of 10 L min^{-1}. In the 24-hour sampler, particles were collected onto an adhesive-coated glass slide that advanced at the same rate as the 7-day sampler (2 mm h^{-1}), thus the impaction area (particle trace) for each day's sample was 14 × 48 mm for both samplers (182).

Each 24-hour impactor was incorporated into a Microenvironmental Exposure Monitoring System (MEMS) unit. Daily indoor and outdoor home-specific pollen grains and fungal spore concentrations were measured at 1.5 m height.

The analysis method for the home intensive pollen grains and fungal spores was identical to the method used for the samples collected at the Central Site previously discussed in Section 3.4.2.3.

Sampling for pollen grains and fungal spores with the Burkard Continuous Recording Air Sampler for Glass Slides (mini-Burkard, Burkard Manufacturing Company Limited, Cat. No. 9100) followed the same schedule as the 24-hr filter-based MEMS samples. This sampler possesses the same sampling properties as the larger Burkard used at the Central Site, and the measuring results are known to be comparable (195). This sampler has a flow rate of 101 min^{-1} and collects the airborne material directly onto the adhesive-coated microscopic slide. The slide travel was adjusted to 48 mm in 24 hours, which is equivalent to the speed of the drum in the larger Burkard. The analysis method for the Home Intensive Study pollen grain and fungal spore samples was identical to the method used for the samples collected at the Central Site, as previously discussed in Section 3.4.2.3.

3.4.4.2.6 Ozone and NO_2

Two-week ozone and NO_2 samples were collected outside using the same sampling and analysis methods as described for the routine home measurements in Section 3.4.3.2. ozone samples were collected in the warm season.

3.4.4.2.7 Nicotine Measurement Methods (See Appendix F)

Nicotine was collected on the same medium and analyzed by the same methods as described in section 3.4.3.4. However, instead of being collected passively, nicotine was collected actively by the MEMS by drawing air through the sodium bisulfate coated filter at 10 lpm for 24 hours.

3.4.4.2.8 Home Intensive Study House Activity Survey

A house activity survey was developed and implemented as part of the Home Intensive study. The main purpose was to collect activity data for indoor pollution sources related activities that might explain the measured concentrations during the sampling period. A parent completed the questionnaire on each intensive sampling day. The questionnaire was explained to the parent on the first home visit and then collected and reviewed by a technician during each subsequent home visit. Incomplete or ambiguous responses were corrected based on discussion with the parent, typically within 8 hours of the end of the sampling period.

The questionnaire requested activity information for seven time periods: 8 pm - 10 pm, 10 pm - 6 am, 6 am - 9 am, 9 am -Noon, Noon - 3 pm, 3 pm - 6 pm, 6 pm - 8 pm. The questions were:

1. Was a vacuum used?
2. Did anyone smoke tobacco products (cigarettes, cigars or a pipe)?
3. Were any windows or doors open for more than 30 minutes?
4. Was a gas stove burner on for more than 10 minutes?
5. Was a gas oven on for more than 10 minutes?
6. Was a kerosene heater used?
7. Was a wood stove used?
8. Was a fireplace used?
9. Were candles burned?
10. Was incense burned?
11. Was an oil lamp used?
12. Was a stove used for frying?
13. Was a stove used for charring food?
14. Was an oven used for automatic cleaning?
15. Was a wall or floor gas heater used?
16. If the heating system was controlled by a thermostat, what was the temperature setting?
17. If the heating system was controlled manually, was it turned on and off?
18. If the air conditioning system was controlled by a thermostat, what was the temperature setting?

19. If the air conditioning system was controlled manually, was it turned on or off?
20. Were there any unusual activities or conditions?
21. Describe unusual activities (using up to 10 lines of text).

Participants filled out the questionnaire consistently, which resulted in a high completion percentage. The in-person follow up is believed to have contributed significantly to completeness and validity of the data. All of the questionnaire data are contained in the FACES exposure database.

Table 3.4.4-1: Filter arrangement and specifications for the five impactors in the MEMS

Leg	Filters	Pollutants	Filter Types and Cassette Arrangement from Upstream to Downstream	Pretreatment	Prep→ Collect→ Analysis Path[b]
L1	Front	$PM_{2.5}$ Mass, NO_3, SO_4	Teflo Membrane	Preweigh	UCB→ STI/Fresno→ UCB
	Back	NO_3	Stainless Steel Disk Teflon Ring PallFlex Tissue Quartz Polyolefin Drain Disk	Coat with Na_2CO_3	
L2	Front	$PM_{2.5}$ EC/OC	PallFlex Tissue Quartz Polyolefin Drain Disk	Acceptance test/bake @DRI	DRI→ STI/Fresno→ DRI
L3	Front	PM_{10} Mass/Endotoxins	Teflo Membrane	Preweigh	UCB→ STI/Fresno→ UCB
	Back	SHS	Stainless Steel Disk Teflon Ring Pallflex Teflon coated glass fiber Polyolefin Drain Disk	Coat with sodium bisulfate	
L4	Front	PM_{10} Metals	Teflo Membrane Polyolefin Drain Disk	Acceptance testing	DRI→ STI/Fresno→ DRI
L5	Front	PM_{10} PAH[a]	PallFlex Tissue Quartz (2 stacked) Polyolefin Drain Disk	XAD4 Coating	UCB→ STI/Fresno→ UCB

[a] PAH sampling was funded by the EPA Office of Transportation and Air Quality.
[b]This column indicates who is responsible for each phase: preparation, collection, and analysis; the entries for each row indicate the organization responsible; thus, UCB → STI/Fresno→UCB indicates that UCB prepared the samples and sent them to STI in Fresno, who were responsible for collection; the samples were then shipped back to UCB for analysis.

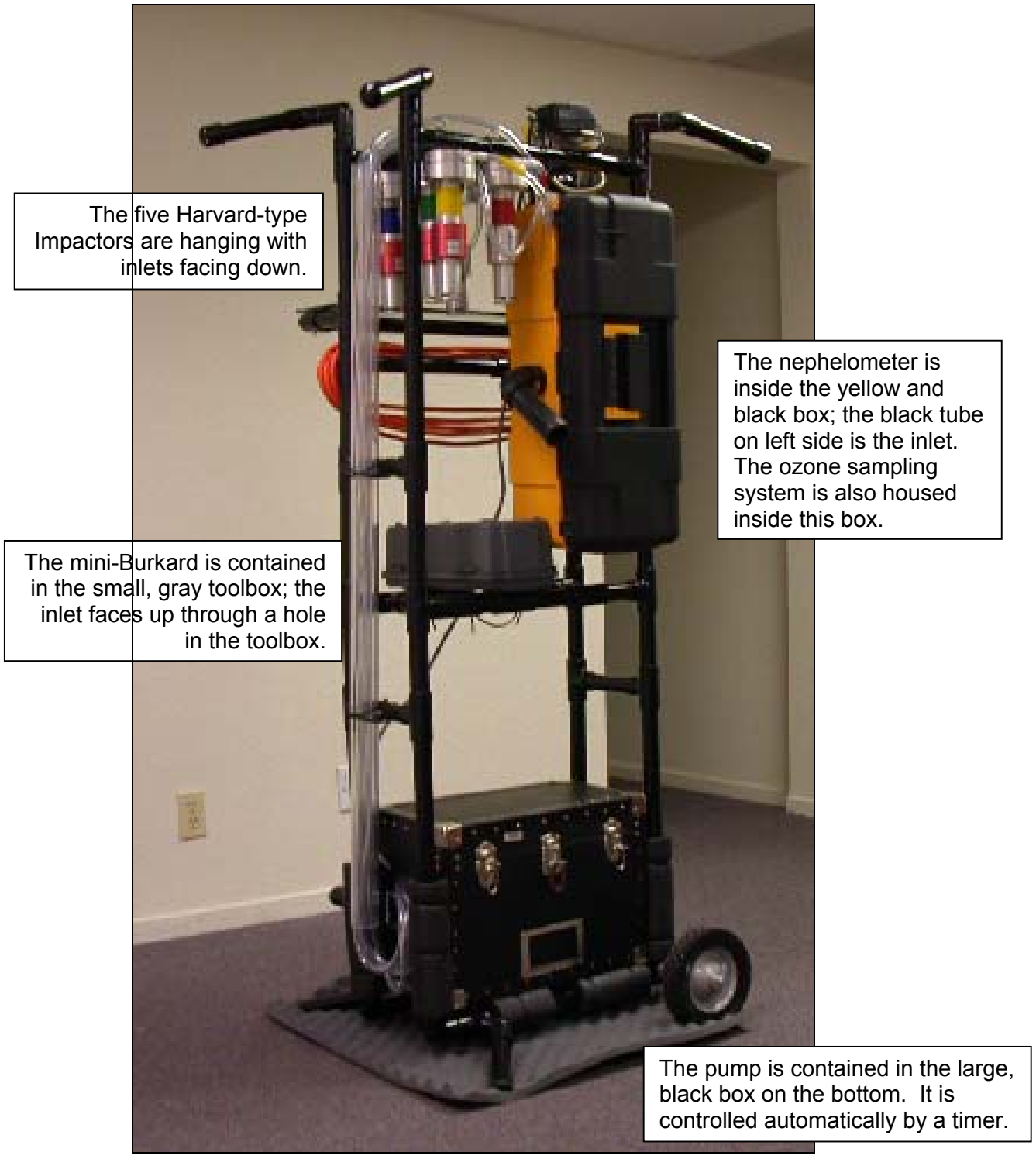


Figure 3.4.4-1. Microenvironmental Exposure Monitoring System (MEMS)

3.4.5 Quality Assurance and Quality Control Summary

This section summarizes the quality assurance (QA) and quality control (QC) activities for the exposure components of FACES. Significant additional documentation of these activities and results can be found in measurement Standard Operating Procedures (SOPs), Quality Assurance Plans, and audit reports by the independent auditor (David Bush) (see Appendix G for audits); that documentation is not repeated here.

Section 3.4.5.1 discusses data validation activities, data evaluations, and data adjustments for the FACES fixed-site continuous data. Section 3.4.5.2 discusses the sampling and laboratory procedures to provide QC data for the FACES data. Section 3.4.5.3 presents a summary of precisions estimates for the FACES exposure data.

3.4.5.1 Data Validation and Adjustments for the Fixed-Site Continuous Data

3.4.5.1.1 Background

The fixed site continuous database for FACES includes data from the centrally located Fresno First Street site, from the two trailers (Fremont School and the roving trailer), and from three other air quality sites within Fresno (Drummond, Sierra Sky Park, Clovis) for November, 2000 through March, 2003. The pollutants and meteorological parameters are ozone (O_3), oxides of nitrogen (NO, NO_2, and NO_x), carbon monoxide (CO), sulfur dioxide (SO_2), particle-bound polycyclic aromatic hydrocarbons (PPAH), light extinction coefficient from scattering by particles (b_{sp}), particulate mass for particles of 10 μm aerodynamic diameter or less (PM_{10}), particulate mass for particles of 2.5 μm aerodynamic diameter or less ($PM_{2.5}$), particulate mass for particles between 2.5 μm and 10 μm aerodynamic diameter ($PM_{2.5-10}$), number of particles (NP), wind speed (WS), wind direction (WD), temperature (T), and relative humidity (RH). Data for some pollutants required significant evaluation and adjustments--data for total carbon (TC), organic carbon (OC), elemental carbon (EC), sulfate (SO_4), and nitrate (NO_3) from all sites. These evaluations and adjustments are discussed separately at the end of this section. As part of the adjustments for the PM carbon data, EC data were estimated from measured Aethelometer™ black carbon (BC) data (see discussion in this section); thus, the BC data quality is often discussed below.

The specific pollutants and measurement time periods are summarized by site in Table 3.4.5-1. The resultant database consists of multiple daily exposure metrics for each pollutant and includes 24-hr average, 8-hr maximum, 1-hr maximum, 12-hr nighttime, and 12-hr daytime average values. The exposure metrics used in the final database are discussed in Section 3.4.8. The metric calculation methods and data reporting conventions are discussed in the Resulting Continuous Database section.

As part of the validation procedure, STI reviewed the results from the intercomparison experiment conducted by the California Air Resources Board (ARB) in May, 2002 when the trailers were located adjacent to First Street. The experiment aimed to establish a comparative data set that would provide estimates of precision, accuracy, and bias between the trailers' and First Street instruments. These comparative data are required for a meaningful interpretation of

the analyses of spatial variations in air pollution in Fresno. Our assessment of the ARB intercomparison data is presented in the Comparison of the Central Site and Trailer Data section.

3.4.5.1.2 Data Validation Procedures

The FACES fixed-site continuous data from First Street and the two trailers were first reviewed by the ARB. STI's role was to act as a secondary reviewer of the data and to compile the exposure data for use in the health effects analysis. STI's procedure for ensuring that the quality of the data was suitable for the FACES health analysis included the following elements:

- Review of time series plots of the hourly data on weekly, monthly, and annual basis. STI performed range checks and "reality checks" on the data, based on expected diurnal and annual trends for each pollutant. The time series plots helped to identify data outliers and changes in the baseline of the pollutant measurements.

- Comparisons of multi-variable time series plots of parameters that are expected to behave in either a proportional or inversely proportional manner (e.g., $PM_{2.5}$-to-b_{sp} and T-to-RH, respectively).

- Review of time series plots for consistency between the First Street, Fremont School trailer, and mobile trailer data.

- Review of the $PM_{2.5}$ and PM_{10} data for consistency between mass measurements. All PM_{10} mass concentrations less than the $PM_{2.5}$ concentrations were assumed to be equal to the $PM_{2.5}$ mass value.

- Review of data resolution. For example, CO data with ppm resolution were not considered acceptable for the calculation of monthly, or even annual, averages and were invalidated.

Limited data validation procedures were performed on the data from the Drummond, Clovis, or Sierra Sky Park monitoring sites, which were downloaded from the EPA Air Quality System (AQS), formerly the Aerometric Information Retrieval System (AIRS).

3.4.5.1.3 Central Site PPAH Monitor Calibration

The EcoChem PAS 2000 PPAH monitors deployed in the FACES trailers were factory-calibrated to yield concentrations in ng/m^3. No calibration factor was available for the PPAH monitor installed at the Central Site. The three instruments are used to characterize the spatial variability of PPAH concentrations in Fresno during FACES. The PPAH data need to be presented in common units for use in any spatial analysis. It is not possible to compare PPAH data in fA units, because the flow rates of the instruments differ.

Because the data from the First Street EcoChem PAS 2000 PPAH monitor were available only as fA, an experiment was conducted in August 2003 to translate the fA data to concentration units. The two trailer and the First Street EcoChem instruments were collocated at

the First Street location and allowed to sample PAH-laden air through a single inlet, distributed by a manifold, for three hours. A candle and wooden matches were used to generate PAHs in varying concentrations.

The coefficient of determination between the two calibrated monitors was very high (r^2 = 0.994). Regression of the average of the two calibrated trailer PPAH data on the First Street fA data yielded a coefficient of 0.94 ng/m^3/fA with an r^2 = 0.997.

3.4.5.1.4 Comparison of the Central Site and Trailer Data

The Central Site data were compared to the data from the two trailers in May 2002, prior to the deployment of the trailers for field measurements at schools, to analyze the relationships between the trailers' and First Street instruments. The comparison was performed and data analyzed by the ARB[1]. The comparison yielded acceptable results for O_3, NO_x, BAM PM_{10}, and ambient temperature, RH, and wind speed, but unacceptable results for many other pollutants and wind direction. The ARB report indicated numerous parameters considered essential for the planned spatial analysis ($PM_{2.5}$ mass, BC, EC, OC, nitrate, sulfate, and wind direction) were not measured well enough to use in quantitative analysis. The poor quality of the trailer data for so many parameters of major importance for the FACES study required significant further evaluation and analysis. In the following discussion, we summarize our re-analysis of the inter-comparison data and the results of our additional analyses and resultant adjustments to the data set. To understand the repercussions of the ARB's inter-comparison results, STI undertook additional review of the data included in the inter-comparison analysis. Only data collected under northerly to westerly winds were included to minimize the biases due to differences in proximity to local sources and obstructions. Heights between the inlets of the two trailers and the Central Site also differed. Overall, STI's initial results were not significantly different from those of the ARB. Table 3.4.5-2 lists STI's interpretation of the intercomparison results by pollutant. An assessment of the credibility or usefulness of the comparison is also included.

The comparison results for the BAM $PM_{2.5}$ data suggest that the BAM instruments were not functioning properly during the May, 2002 inter-comparison. In contrast, the data from the Central Site and Trailer 1, after it was deployed to the Fremont site from June through September, 2002, show a stronger correlation (r^2 = 0.60) than during the inter-comparison. When all valid data from June, 2002 through March, 2003 at First Street and Fremont are analyzed, the correlation is even stronger (r^2 = 0.81). The ARB's Monitoring and Laboratory Division (MLD) serviced the Trailer 1 BAM $PM_{2.5}$ instrument at the end of the inter-comparison period, which may help explain why the correlations were higher after the inter-comparison than during the comparison itself. Furthermore, the Trailer 2 $PM_{2.5}$ BAM instrument was replaced and calibrated by MLD at the end of the intercomparison period. This renders the comparisons of the First Street and Trailer 1 $PM_{2.5}$ BAM to Trailer 2 $PM_{2.5}$ BAM mass concentrations irrelevant. The ARB inter-comparison results for the BAM $PM_{2.5}$ data are not believed to be representative of the performance of these instruments during the FACES study and are thus being ignored.

[1] An Analysis of the FACES Intercomparison Study of 2002. Clint Taylor, June 2003.

The ARB inter-comparison results also are poor for CO. The Central Site reports data with a tenth of a ppm resolution, while the trailers report data with ppb resolution. This difference in resolution of the data greatly affects the comparison results, since all CO concentrations were far less than 1 ppm during this period. The Central Site's low-resolution CO data, combined with the low concentrations observed, render the inter-comparison results invalid for CO.

The SO_2 concentrations between the two trailers are adequately correlated, but the SO_2 data from both trailers show no relation with the Central Site data. All Central Site SO_2 data are reported as 0, 1, or 2 ppb during the inter-comparison while the trailer SO_2 data vary continuously, with decimal ppb resolution, from 0 to 4 ppb. No attempt was made to adjust the SO_2 data from the trailers to agree more closely with one another based on the intercomparison results. Again, the lack of resolution in the Central Site's SO_2 data, combined with the low concentrations observed, render the inter-comparison results between trailer and Central Site SO_2 data invalid.

The PPAH concentrations from the Central Site and the two trailers were strongly correlated with very little bias in STI's August2003 collocated experiment. ARB's inter-comparison results do not appear to be representative of the instruments' performance. This may be due in part to the differences in inlet location during the ARB inter-comparison that caused slightly different air masses to be sampled between the Central Site and trailers.

ARB's inter-comparison results are poor for nitrate, sulfate, and TC. For these pollutants either the correlations were less than 75%, the biases greater than 10%, or both. These data are discussed below.

The vector winds were compared between the two trailers and First Street. The inter-comparison report found the wind direction results to be unacceptable based on comparisons of the scalar wind direction data between the three sites. The biases of both wind components are greater than 10% between the trailers and First Street. The bias is greater in the v component, north to south, of the winds. This bias could be accounted for by the difference in inlet heights and proximity to potential obstructions. No adjustments were made to the wind data from any of the three sensors based on these results.

The inter-comparison results were used to adjust trailer data collected during FACES to agree with the First Street data when the R^2 value was higher than 75% and the bias between data sources was greater than 10% for a given pollutant. Table 3.4.5-3 lists the adjustments made to the FACES data based on the ARB's inter-comparison. We elected to adjust the trailer data, rather than First Street data, because the First Street data were considered as the long-term reference data for FACES (even though there were a few cases where the trailer instruments appeared less biased that First Street instruments). Notable parameter adjustments follow.

- The Fremont trailer b_{sp} data were adjusted based on the comparison to the First Street b_{sp} data.
- The Fremont trailer NO data were adjusted based on the comparison to First Street data. In the case of NO, we used the regression equation with the First Street data as the independent variable and solved for X to derive the adjustment equation applied to the Fremont NO data. The regression equation that resulted from inversion of the X and Y

axis (using Microsoft Excel) caused the Fremont NO data to be over-adjusted compared to the Trailer 2 NO data.

- The BC data from both trailers were adjusted based on the comparison with First Street data. The adjustments again were derived from the equations with First Street data as the independent variable and solving for X. Use of the First Street versus trailer regressions may have introduced a bias between the BC concentrations of the two trailers.
- The particle count data from the two trailers were adjusted to match one another by effectively splitting the bias between the two instruments. Data from Trailers 1 and 2 were adjusted by +5% and -5% respectively.

Table 3.4.5-4 summarizes comparisons between First Street and trailer data during the ARB inter-comparison period based on the adjusted data. In all cases, the biases are well within 10% with reasonable intercepts. For particle number (NP), the data from the trailers (with a TSI model 3022) were still significantly different from the data from the First Street site (with a TSI model 3010 with an SMPS). These instruments have different particle diameter cut point and counting methods, and because we could not adequately reconcile the differences, we did not make any further corrections to the data.

3.4.5.1.5 Continuous Database

All exposure metrics are calculated from the validated hourly data (reported as begin hour, PST). The 24-hr period from 8 p.m. to 8 p.m. PST was used. Twenty-four-hour-based exposure metrics, i.e. daily maximum or 24-hr average, are reported on end date. Hour-specific metrics, like wind direction at 10 a.m., are reported as start time PST. All valid and suspect data are included in the averaging. A 75% data completeness criterion was required for all metric calculations. Table 3.4.5-5 summarizes the calculation method by exposure metric category.

Table 3.4.5-6 summarizes the data completeness by site and pollutant from November, 2000 through March, 2003. Since the total possible data available vary by site (see Table 3.4.5-1), the total number of expected days is also listed by site in Table 3.4.5-6. Percent data availability is based on the available 24-hr average metric except for the wind direction which is based on the 10 a.m. value. All sites and parameters with less than 90% data completeness are discussed below:

- Nearly half of the b_{sp} data from both trailers was invalidated, from July 26, 2002 to January 9, 2003, due to a data logging error. All data were truncated at ~ 200 Mm^{-1}. Although the data recorded below this cutoff are likely valid, they are not useful for calculation of daily metrics because daily averages would be biased downward due to truncation of all higher values.
- All ppm resolution CO data from the Forkner and Holland Schools sites were invalidated.
- NP data from Viking were missing from August 2, 2002 to August 22, 2002.
- Data for most pollutants were missing for approximately three or four days near the end of the Burroughs School data period.
- $PM_{2.5-10}$ data are less available than PM_{10} or $PM_{2.5}$ data, because, if either of these PM measurements were missing or invalid, $PM_{2.5-10}$ was not calculated.

- Nearly half of the SO_2 data from First Street is missing (all prior to January 1, 2002). The SO_2 data from Viking and Copper Hills Schools are also missing for multiple blocks of time.
- RH data from Copper Hills are missing from December 27, 2002 to January 5, 2003.

The continuous data were collected at the First Street site and trailers to assess the within-Fresno variation of specific pollutant concentrations. The data to quantify properly the precision of the data are not available.

3.4.5.1.6 Data Adjustments Applied to FACES Continuous Carbon, Nitrate, and Sulfate Data

All nitrate, sulfate, TC, and OC data were withheld initially due to data quality issues. The inter-comparison results showed large biases in the nitrate data between sites and showed no relation between the First Street and Trailer 2 sulfate data. A significant portion of the First Street TC and OC data were invalidated by ARB, and there are suspicious inconsistencies between the TC and BC data at First Street and Trailer 2. The following evaluations and adjustments eventually were made, and appropriate additions were made to the final FACES exposure database.

TC data from the R&P 5400 instruments were adjusted in two steps. First the Trailer 1 and Trailer 2 TC data were adjusted to the First Street TC data, based on the May, 2002 inter-comparison (data from Clint Taylor). This adjustment is referred to as "Data Adjusted for Instrument Bias" or "DAIB" (Figure 3.4.5-1). Following this, all the 5400 TC data were adjusted to equivalence with the filter-based MEMS data that were collected at First Street (Figure 3.4.5-2). This allows direct comparison between the First Street data and the data collected throughout Fresno in the Home Intensive study. These data are referred to as "Data Adjusted for Method Bias", or "DAMB".

EC data were derived from Aethelometer BC measurements. Trailer 1 and Trailer 2 BC data were first adjusted to equivalence with First Street BC data (see Table 3.4.5-3). Additionally, the First Street BC data were compared to filter-based FRM EC data from the FRM sampler at First Street (Figure 3.4.5-3), and all continuous BC data were adjusted upward by a factor of 1.19 to arrive at an estimate of EC.

Organic carbon was calculated as TC – EC after all adjustments were made. The trailer nitrate data were adjusted to be equivalent to First Street data using the regressions that Clint Taylor developed from the April/May, 2002 inter-comparison (Figure 3.4.5-4 and 3.4.5-5). All continuous nitrate data were then adjusted to be equivalent to the MEMS data (1.45x) based on the First Street comparison (Figure 3.4.5-6). The combined adjustment equations are

$$\{T1\text{-corrected}\} = (1.45/2.16)\{T1\text{-uncorrected}\} - 0.3/2.16$$

$$\{T2\text{-corrected}\} = (1.45/2.04)\{T2\text{-uncorrected}\} - 0.4/2.04$$

No sulfate measurements were made in Trailer 1 (Fremont). Sulfate data from Trailer 2 were so poorly correlated with First Street sulfate data during the May 2002 intercomparison that

all Trailer 2 sulfate data were invalidated. First Street sulfate data compared favorably with FRM data (Figure 3.4.5-7) and were left unadjusted.

3.4.5.2 Sampling and Laboratory Procedures to Provide Quality Control Data

In order to provide QC data for the FACES continuous measurements, several intercomparisons were performed. The trailer-Central Site intercomparison was discussed in Section 3.4.5.1, as was the intercomparison of the continuous particulate PAH monitors.

As part of the Home Intensive Study, and of the PAH and supplemental bioaerosol sampling at the Central Site and the trailers, several types of QC activities were performed, including blanks, sampling duplicates, duplicate analyses, and calibrations. Details may be found in the various SOPs.

Field and laboratory blanks were prepared and analyzed as part of the routine analyses of exposed field samples; laboratory duplicate analyses were also performed. These results are summarized in the individual paragraphs on the measurement methods in Sections 3.4.2, 3.4.3, and 3.4.4, above.

As part of the Home Intensive Study, several types of sampling QC activities were also performed. Two MEMS were operated side by side at a few homes to collect QC samples. Duplicate MEMS were installed outside five homes, and duplicate MEMS were installed inside two homes. Duplicate MEMS were also operated at the Central Site throughout four separate panels. A single MEMS was operated at the Central Site for seven summertime panels; nephelometer data were collected continually, but filter samples were obtained only once a week when the supplemental PAH samples were collected. A continuous seven-day Burkard was operated outside three homes at different times of the year to provide comparison data with the small Burkard 9100 sampler that was part of the MEMS design. The results from these sampling intercomparisons are summarized in Section 3.4.5.3 below.

3.4.5.3 Summary of Precision Estimates for the FACES Exposure Data

A combination of approaches was used to estimate measurement precision and arrive at a decision "rule" for evaluation of whether spatial differences are real. Statistics are based on collocated samplers. Collocated samplers include

- MEMS at homes and First Street, all variables
- MEMS versus BAM for $PM_{2.5}$ and PM_{10} at First Street
- MEMS versus R&P 2025 for endotoxin and PM_{10} at First Street
- MEMS versus estimated EC (from Aethelometer™) and OC (as 5400 TC–EC) at First Street
- BAM versus R&P 2025 for PM_{10} at First Street

Table 3.4.5-7 summarizes the results. The table is modeled on the format used by Watson and Chow in their paper on comparison of carbon measurements at the Fresno Supersite. Scatter plots for most of the comparisons are shown in Figures 3.4.5-8 through 3.4.5-26.

Regression slopes and intercepts are given with their standard errors, the correlation coefficient (r), and the number of pairs in the comparison. Also given are the averages of *y/x* and standard deviations of the average ratios. The average of the paired differences ($y - x$) are presented along with the associated standard deviation of the paired differences, an estimate of the standard error (SE) of the paired differences ($StDev/n^{1/2}$), and the average CV (%) of differences over all pairs. A Student's *t* test for paired sample means was used to test the statistical hypothesis that the difference between samplers *x* and *y* is zero. The probability (*P*) for a greater absolute value of Student's t statistic is given in Table 3.4.5-7. If the P value shown is less than 0.05, it can be inferred that the measurements in the collocated comparison are different between the two samplers.

The endotoxin samples were initially problematic—the July through September 2002 MEMS and 2025 comparisons yielded poor results. However, after data values run on a suspect assay plate were eliminated, the collocated results were acceptable (see Table 3.4.5-7)

Table 3.4.5-1: Time Periods and Pollutants Available by Site			
Site	**Begin Date**	**End Date**	**Pollutants**
First Street	11/1/00	3/31/03	O_3, NO_x[a], CO, SO_2, PPAH, b_{sp}, BC, $PM_{2.5}$, PM_{10}, $PM_{2.5-10}$, WS, WD, Temp, RH
Clovis	11/1/00	3/31/03	O_3, NO_x, CO, WS, WD, Temp, RH
Drummond	11/1/00	3/31/03	O_3, NO_x, CO
Sierra Skypark	11/1/00	3/31/03	O_3, NO_x, CO, WS, WD, Temp
Fremont, Trailer 1 (T1)	6/10/02	3/31/03	O_3, NO_x[a], CO, SO_2, PPAH, b_{sp}, BC, $PM_{2.5}$, PM_{10}, $PM_{2.5-10}$, NP, WS, WD, Temp, RH
Bullard, Trailer 2 (T2)	6/10/02	7/25/02	
Viking, T2	7/26/02	9/27/02	
Burroughs, T2	10/1/02	11/19/02	
Copper Hills, T2	11/24/02	1/8/03	
Forkner, T2	1/9/03	2/19/03	
Holland, T2	2/20/03	4/2/03	

[a] NO, NO_2, and NO_x data are reported.

Table 3.4.5-2: Results from STI's Re-Evaluation of ARB's Comparison Between Central Site and Trailer Instruments

Parameter	Comparison (Y vs. X)	Slope	Intercept	R^2	Assessment
BAM $PM_{2.5}$	T1 vs. First	0.18	12.58	0.02	Results not believed to be representative of actual performance
	T2 vs. First	0.21	5.84	0.01	
	T2 vs. T1	0.50	-0.04	0.21	
BAM PM_{10}	T1 vs. First	0.92	9.76	0.72	Acceptable results
	T2 vs. First	1.00	5.43	0.77	
	T2 vs. T1	0.97	-1.11	0.81	
PPAH	T1 vs. First	1.37	0.25	0.62	Results not believed to be representative of actual performance
	T2 vs. First	1.15	0.47	0.69	
	T2 vs. T1	0.79	0.40	0.98	
b_{sp}	T1 vs. First	1.25	-3.24	0.95	Use results to adjust trailer data
	T2 vs. First	0.96	0.32	0.89	Acceptable results
	T2 vs. T1	0.73	3.62	0.85	Re-assess with adjusted T1 data
BC	T1 vs. First	0.75	44.63	0.92	Use results to adjust trailer data
	T2 vs. First	0.78	75.31	0.87	
	T2 vs. T1	0.99	50.33	0.84	Re-assess with adjusted trailer data
NP	T1 vs. First	1.93	0.38	0.81	Not acceptable results
	T2 vs. First	2.07	0.93	0.74	
	T2 vs. T1	1.12	-0.58	0.99	Use results to adjust trailer data
NO_3	T1 vs. First	1.93	0.54	0.78	Not acceptable results
	T2 vs. First	1.91	0.59	0.66	
	T2 vs. T1	1.03	-0.05	0.86	
SO_4	T1 vs. First				No SO_4 data from T1
	T2 vs. First	0.84	1.56	0.04	Not acceptable results
	T2 vs. T1				No SO_4 data from T1
NO	T1 vs. First	1.14	-0.11	0.89	Use results to adjust trailer data
	T2 vs. First	1.04	-0.88	0.91	Acceptable results
	T2 vs. T1	0.88	-0.74	0.97	Re-assess with adjusted T1 data
CO	T1 vs. First	1.00	0.10	0.25	Not acceptable results
	T2 vs. First	0.54	0.15	0.13	
	T2 vs. T1	0.28	0.15	0.20	
O_3	T1 vs. First	1.08	0.09	1.00	Acceptable results
	T2 vs. First	1.03	-1.55	1.00	
	T2 vs. T1	0.96	-1.77	1.00	

Table 3.4.5-2: Results from STI's re-evaluation of ARB's comparison between Central Site and trailer instruments (continued)

Parameter	Comparison (Y vs. X)	Slope	Intercept	R^2	Assessment
NO_x	T1 vs. First	1.04	-0.42	0.97	
	T2 vs. First	1.03	-1.43	0.97	Acceptable results
	T2 vs. T1	0.98	-0.86	0.99	
SO_2	T1 vs. First	0.93	0.20	0.16	
	T2 vs. First	0.68	0.54	0.02	Not acceptable results
	T2 vs. T1	1.12	0.31	0.84	
TC	T1 vs. First				No TC data from T1
	T2 vs. First	1.11	-0.68	0.74	Not acceptable results
	T2 vs. T1				No TC data from T1
Winds_u	T1 vs. First	0.81	0.25	0.81	Not acceptable results
	T2 vs. First	0.89	0.37	0.89	
	T2 vs. T1	1.02	0.31	0.94	Acceptable results
Winds_v	T1 vs. First	0.73	0.59	0.72	Not acceptable results
	T2 vs. First	0.75	0.52	0.72	
	T2 vs. T1	1.00	-0.10	0.97	Acceptable results

Table 3.4.5-3: Parameter adjustment equations used to improve comparability with First Street measurements. The revised parameter estimates are denoted by an asterisk (*)

Parameter	Equation	R^2
b_{sp}	$T1\_b_{sp}^{*} = 0.76(T1\_b_{sp}) + 3.51\ Mm^{-1}$	0.95
BC	$T1\_BC^{*} = 1.33(T1\_BC) - 59.32\ ng/m^3$	0.92
	$T2\_BC^{*} = 1.28(T2\_BC) - 96.38\ ng/m^3$	0.87
NP	$T1\_NP^{*} = 1.05(T1\_NP)$	0.99
	$T2\_NP^{*} = 0.95(T2\_NP)$	0.99
NO	$T1\_NO^{*} = 0.877(T1\_NO) + 0.096\ ppb$	0.89

Table 3.4.5-4: FACES May 2002 Inter-Comparison Results after Adjustments were Made				
Parameter	**Comparison (Y vs. X)**	**Slope**	**Intercept**	**R^2**
b_{sp}	T1 vs. First	0.95	1.06	0.95
	T2 vs. T1	0.96	0.23	0.85
BC	T1 vs. First	1.00	-3.54	0.91
	T2 vs. First	1.01	-4.08	0.87
	T2 vs. T1	0.95	22.92	0.85
NO	T1 vs. First	1.00	0.00	0.89
	T2 vs. T1	1.01	-0.85	0.97

Table 3.4.5-5: Calculation method by exposure metric category. All metrics are calculated from the 24-hr period spanning 8 p.m. on the sample start date to 8 p.m. on the sample end date.		
Type[a]	**Metric Category**	**Description**
AQ/Met	1-hr maximum	Maximum 1-hr concentration or scalar
AQ/Met	24 hour average	Average 24-hr concentration or scalar
AQ	8-hr maximum	Maximum average 8-hr concentration of all possible contiguous 8-hr segments within the 24-hr sample period
AQ	12-hr Daytime	Average concentration from 8 a.m. to 8 p.m.
AQ	12-hr Nighttime	Average concentration from 8 p.m. to 8 a.m.
Met	1-hr Minimum	For T and RH, minimum 1-hr average
Met	10 a.m.	Average WS or WD at 10 a.m.
Met	2 p.m.	Average WS or WD at 2 p.m.
Met	8 p.m.	Average WS or WD at 8 p.m.
[a] AQ = air quality parameters; Met = meteorological parameters		

Table 3.4.5-6: Percent data completeness by site and pollutant. The total number of expected days is also listed.											
	First Street	***Trailer 1 Fremont***	***Trailer 2 Bullard***	***Trailer 2 Viking***	***Trailer 2 Burroughs***	***Trailer 2 Copper Hills***	***Trailer 2 Forkner***	***Trailer 2 Holland***	***Sierra Sky Park[a]***	***Clovis[a]***	***Drummond[a]***
Total Days	**881**	**295**	**46**	**64**	**50**	**46**	**42**	**42**	**881**	**881**	**881**
	----------Data Availability (%)----------										
BC	87.3	98.6	91.3	96.9	92.0	95.7	95.2	95.2	NA	NA	NA
bsp	93.0	40.7	97.8	Invalid	Invalid	Invalid	83.3	95.2	NA	NA	NA
CO	99.2	91.2	97.8	95.3	86.0	89.1	Invalid	Invalid	98.9	99.3	99.3

NO	99.4	97.6	95.7	96.9	86.0	95.7	95.2	92.9	96.6	96.1	88.6
NO_2	99.4	97.6	95.7	96.9	86.0	95.7	95.2	92.9	96.6	96.0	88.6
NO_x	99.4	97.6	95.7	96.9	86.0	95.7	95.2	92.9	96.6	96.1	88.8
NP	Pending	93.9	97.8	65.6	86.0	95.7	95.2	95.2	NA	NA	NA
O_3	99.0	97.6	95.7	96.9	86.0	95.7	95.2	95.2	99.1	98.2	99.1
PM_{10}	97.2	94.9	95.7	92.2	84.0	91.3	95.2	95.2	NA	NA	NA
$PM_{2.5}$	92.8	97.3	93.5	96.9	86.0	91.3	92.9	95.2	NA	NA	NA
$PM_{2.5-10}$	89.7	92.5	93.5	92.2	84.0	84.8	92.9	92.9	NA	NA	NA
PPAH	100.0	98.3	97.8	96.9	86.0	95.7	95.2	95.2	NA	NA	NA
RH	96.5	90.2	97.8	96.9	86.0	73.9	95.2	95.2	NA	98.0	NA
SO_2	51.0	89.2	95.7	78.1	86.0	71.7	95.2	90.5	NA	NA	NA
T	99.5	96.6	97.8	96.9	86.0	95.7	95.2	95.2	99.2	97.5	NA
WD	90.6	97.3	95.7	93.8	90.0	91.3	92.9	95.2	99.5	99.2	NA
WS	96.4	96.6	95.7	93.8	86.0	95.7	95.2	95.2	99.5	97.3	NA

[a] Aerometric Information Retrieval System (AIRS) data

Table 3.4.5-7: Collocated Comparison Statistics for FACES PM, Carbon, and Endotoxin Samples

Observable	Location	Sampler *y*	Sampler *x*	Regression Slope ± Standard Error	Intercept ± Standard Error	Correlation (r)	Number of Pairs	Average Ratio of *y*/*x* ±Standard Deviation	Average Difference of *y* - *x*, ug/m3	Collocated StdDev of *y* - *x*	Precision: Collocated SE of *y* - *x*	Precision: Average CV(%)	*P*
PM_{10}	Outside	MEMS 1	MEMS 2	1.02 ± 0.02	-0.08 ± 0.66	0.99	39	1.00 ± 0.11	-0.55	1.98	0.32	6.3%	0.09
	Inside	MEMS 1	MEMS 2	0.75 ± 0.03	5.68 ± 1.27	0.99	10	1.02 ± 0.11	1.77	6.01	1.90	5.1%	0.38
	First Street	MEMS	BAM	0.89 ± 0.03	-0.99 ± 1.30	0.98	43	0.87 ± 0.12	-5.76	4.47	0.68	9.6%	1.35E-10
	First Street	MEMS	RP2025	1.18 ± 0.13	-5.76 ± 6.55	0.98	6	1.05 ± 0.09	2.63	5.00	2.04	4.8%	0.25
	First Street	BAM	RP2025	0.85 ± 0.04	17.25 ± 2.48	0.93	60	1.29 ± 0.36	9.96	8.91	1.15	19.5%	4.30E-12
$PM_{2.5}$	Outside	MEMS 1	MEMS 2	0.99 ± 0.01	0.38 ± 0.42	0.85	40	1.02 ± 0.17	0.27	1.65	0.26	7.5%	0.31
	Inside	MEMS 1	MEMS 2	0.94 ± 0.20	-0.97 ± 3.13	0.85	10	0.84 ± 0.22	-1.82	3.71	1.17	5.1%	0.16
	First Street	MEMS	BAM	0.97 ± 0.03	-0.04 ± 0.85	0.99	46	1.04 ± 0.18	0.79	3.50	0.52	12.1%	0.13
EC	Out & In	MEMS 1	MEMS 2	0.97 ± 0.03	0.09 ± 0.06	0.99	21	1.05 ± 0.15	0.04	0.15	0.03	8.4%	0.20
	First Street	MEMS	EC_Calc	2.63 ± 0.14	-1.84 ± 0.31	0.98	15	1.40 ± 0.56	1.33	1.96	0.51	25.4%	0.02
Outliers removed	First Street	MEMS	EC_Calc	1.44 ± 0.19	-0.38 ± 0.26	0.93	11	1.11 ± 0.26	0.20	0.33	0.10	15.2%	0.07
OC	Out & In	MEMS 1	MEMS 2	1.03 ± 0.02	-0.19 ± 0.14	1.00	21	0.99 ± 0.07	0.00	0.37	0.08	3.6%	1.00
	First Street	MEMS	OC_Calc	Only 1 matching OC_Calc datapoint from R&P 5400 TC minus EC_Calc									

Table 3.4.5-7. Collocated Comparison Statistics for FACES PM, Carbon, and Endotoxin Samples Continued

Observable	Location	Sampler *y*	Sampler *x*	Regression Slope ± Standard Error	Intercept ± Standard Error	Correlation (r)	Number of Pairs	Average Ratio of *y*/*x* ±Standard Deviation	Average Difference of *y* - *x*, ug/m3	Precision: Collocated StdDev of *y* - *x*	Precision: Collocated SE of *y* - *x*	Precision: Average CV(%)	*P*
Endotoxin	Out & In	MEMS 1	MEMS 2	0.97 ± 0.05	0.13 ± 0.14	0.96	38	1.32 ± 0.88	0.10	0.74	0.12	25.5%	0.43
	First Street	MEMS	RP2025	0.54 ± 0.05	0.34 ± 0.19	0.89	27	0.83 ± 0.34	-0.72	1.37	0.26	28.2%	0.01
W/O suspect plate	First Street	MEMS	RP2025	1.10 ± 0.15	-0.17 ± 0.14	0.88	18	0.90 ± 0.38	-0.09	0.30	0.07	27.5%	0.23
NO_3Tot	Out & In	MEMS 1	MEMS 2	0.73 ± 0.25	2.34 ± 1.98	0.66	13	1.36 ± 1.40	0.34	2.93	0.58	17.5%	0.62
Two outliers removed	Out & In	MEMS 1	MEMS 2	0.96 ± 0.04	0.33 ± 0.30	0.99	11	1.04 ± 0.45	0.21	0.63	0.12	4.0%	0.72
SO_4	Out & In	MEMS 1	MEMS 2	0.99 ± 0.04	0.02 ± 0.05	0.99	13	1.02 ± 0.09	0.01	0.08	0.02	4.4%	0.68
Metals													
Al	Out & In	MEMS 1	MEMS 2	0.84 ± 0.06	0.02 ± 0.05	0.97	12	1.16 ± 0.38	0.01	0.08	0.02	13.8%	0.79
Si	Out & In	MEMS 1	MEMS 2	0.94 ± 0.02	0.07 ± 0.03	1.00	12	1.00 ± 0.06	-0.03	0.09	0.03	2.7%	0.32
Fe	Out & In	MEMS 1	MEMS 2	0.94 ± 0.02	0.02 ± 0.01	1.00	12	1.01 ± 0.06	-0.004	0.02	0.01	3.0%	0.56
Mn	Out & In	MEMS 1	MEMS 2	0.87 ± 0.07	0.001 ± 0.001	0.97	12	1.03 ± 0.23	-0.0002	0.0013	0.0004	12.7%	0.65
Kp	Out & In	MEMS 1	MEMS 2	1.01 ± 0.03	-0.01 ± 0.01	0.99	12	0.98 ± 0.05	-0.01	0.01	0.01	2.8%	0.39

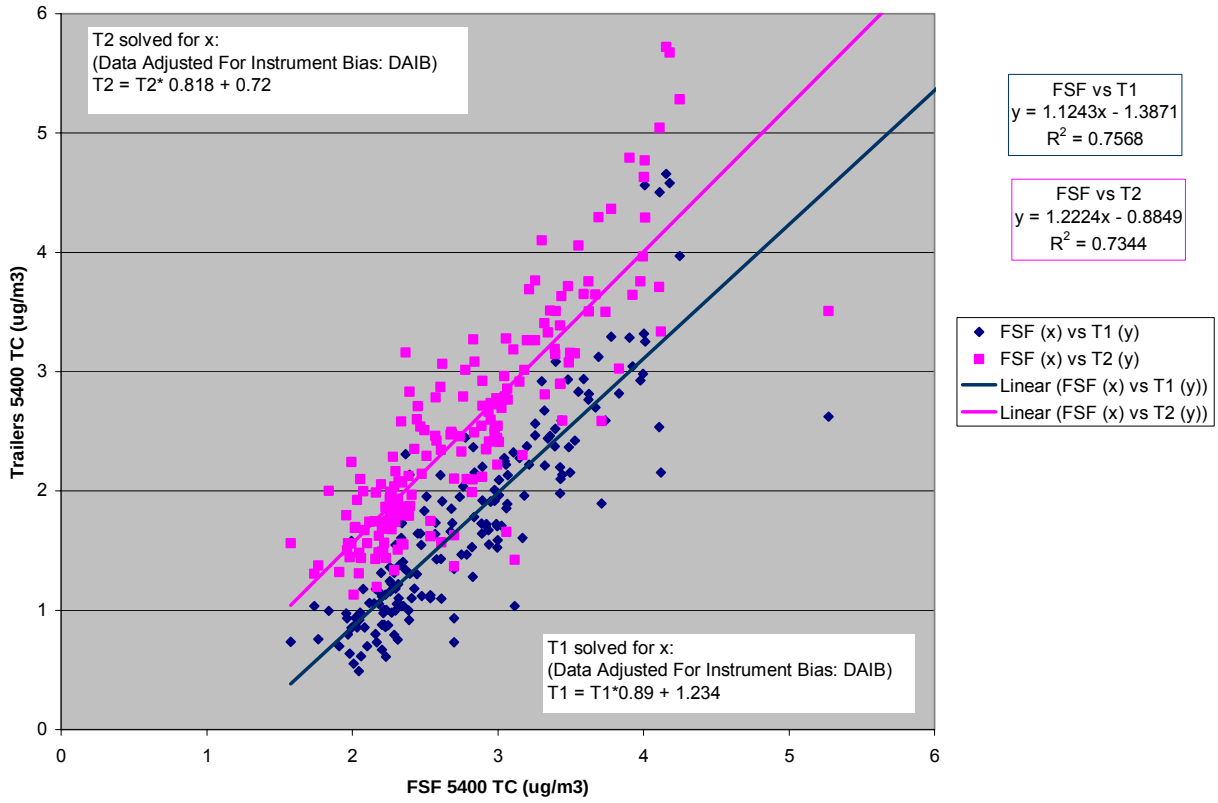


Figure 3.4.5-1. FACES trailer TC data were adjusted to the First Street 5400 data based on the May 2002 intercomparison.

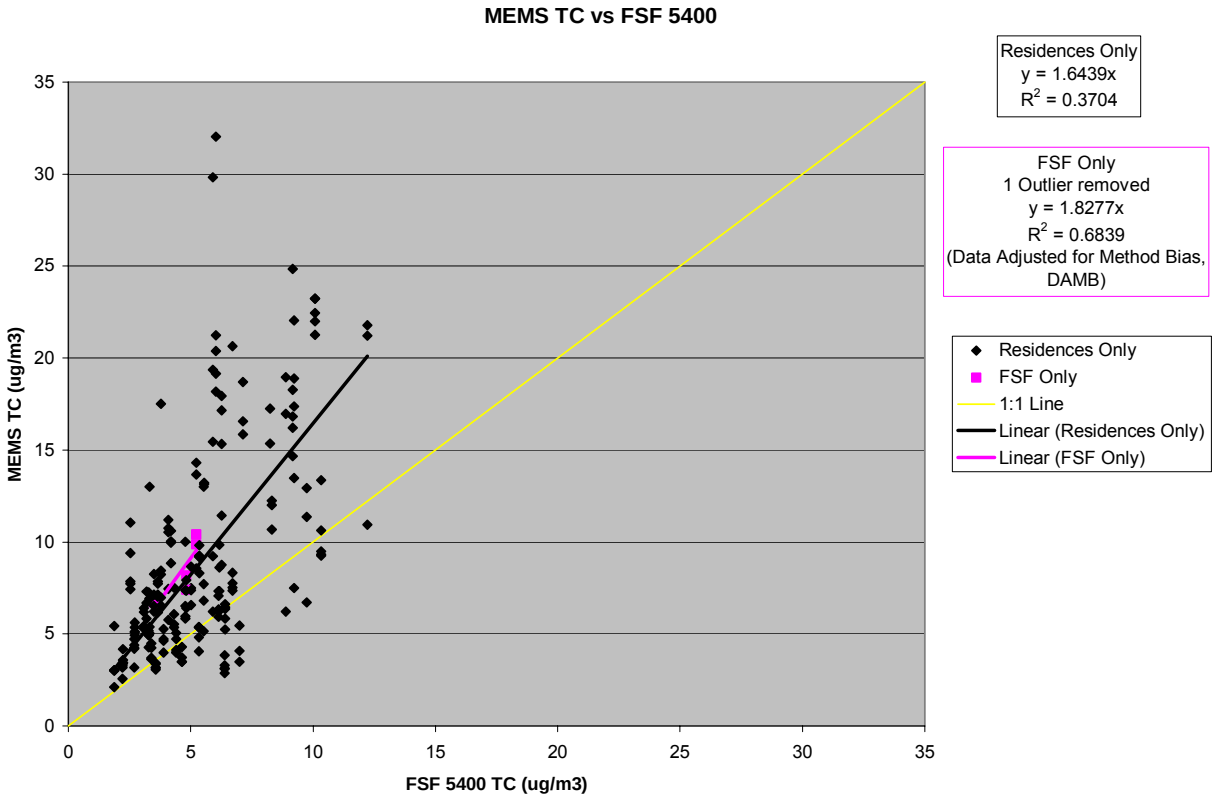


Figure 3.4.5-2. In a second adjustment, all R&P 5400 TC data were adjusted to equivalence with filter-based MEMS data by multiplying by a factor of 1.83.

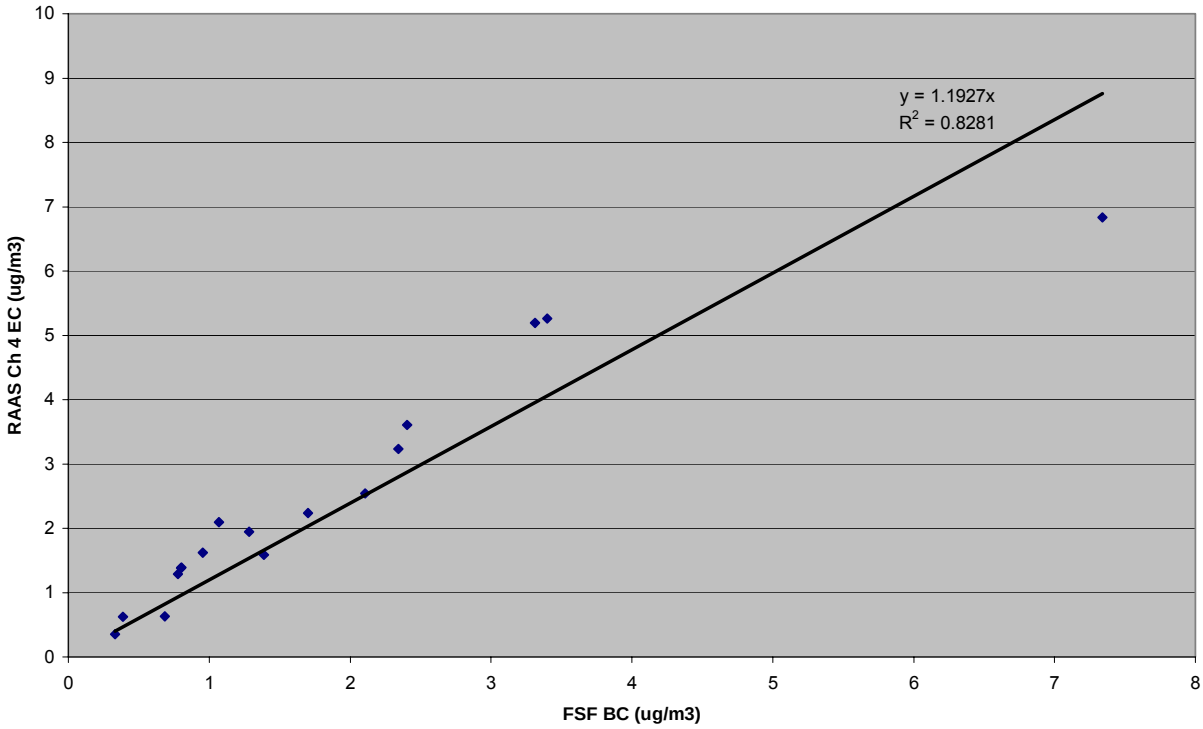


Figure 3.4.5-3. FRM EC data were regressed on 24-hr average continuous BC data. The resulting slope was applied to all continuous BC data.

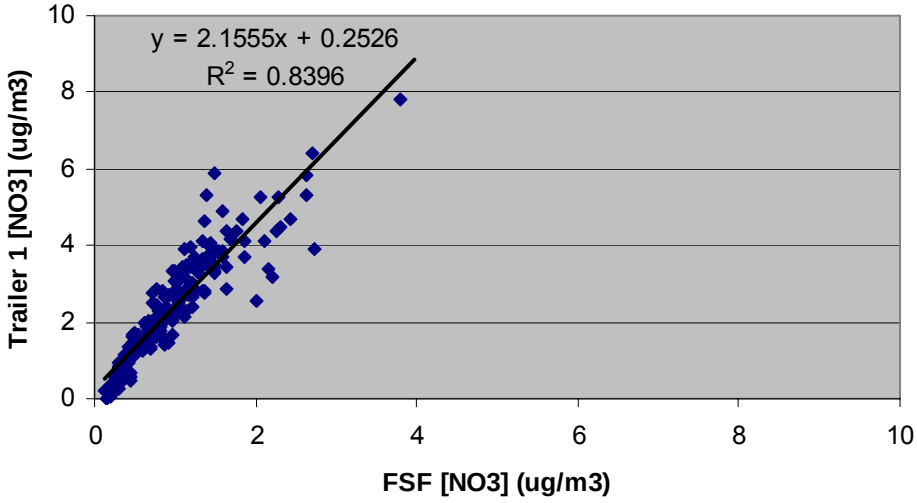


Figure 3.4.5-4. Regression of Trailer 1 nitrate data on First Street nitrate data, May 2002 intercomparison.

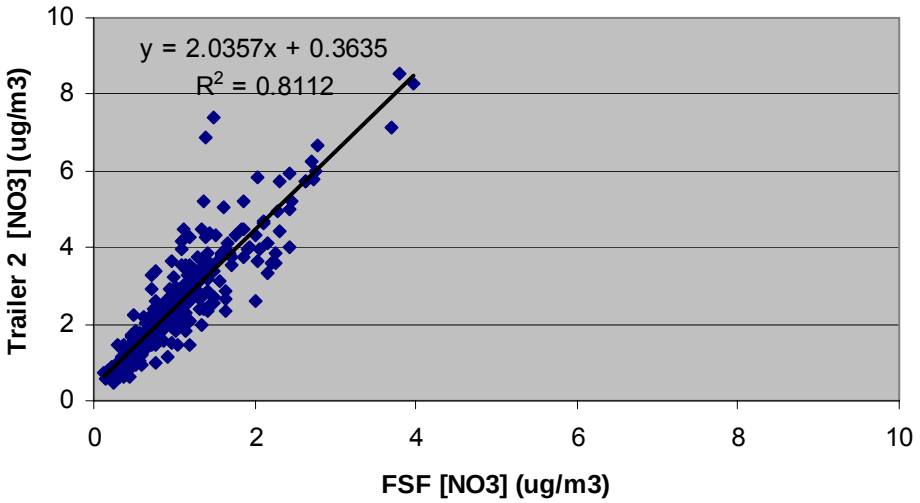


Figure 3.4.5-5. Regression of Trailer 2 nitrate data on First Street nitrate data, May 2002 intercomparison.

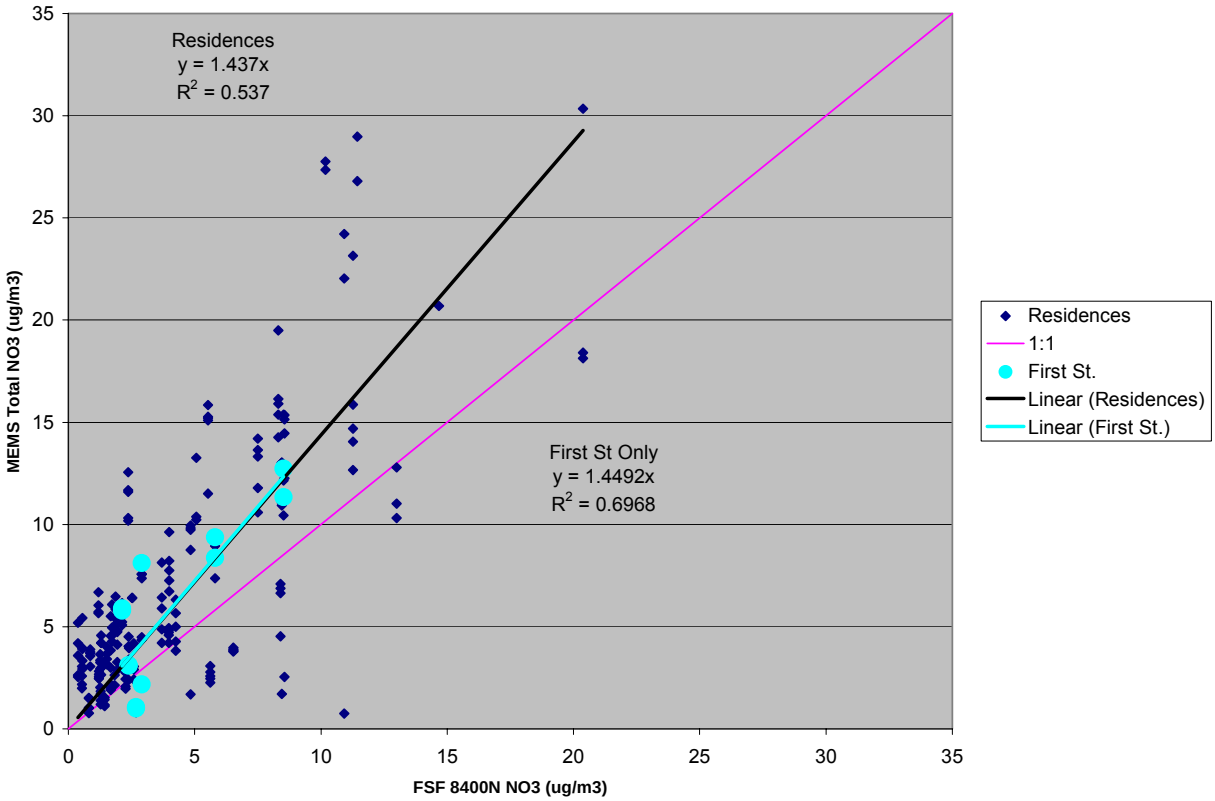


Figure 3.4.5-6. The slope of the regression of First Street MEMS total nitrate versus First Street 8400N total nitrate was applied to all continuous nitrate data.

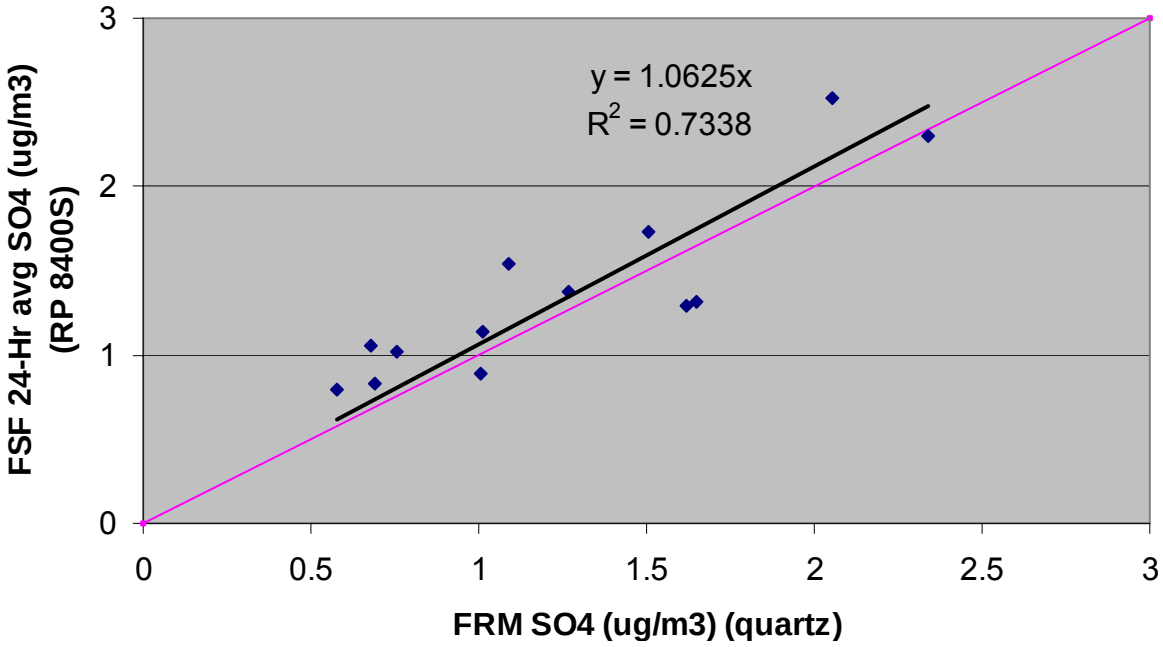


Figure 3.4.5-7. First Street continuous sulfate compared well with FRM sulfate data.

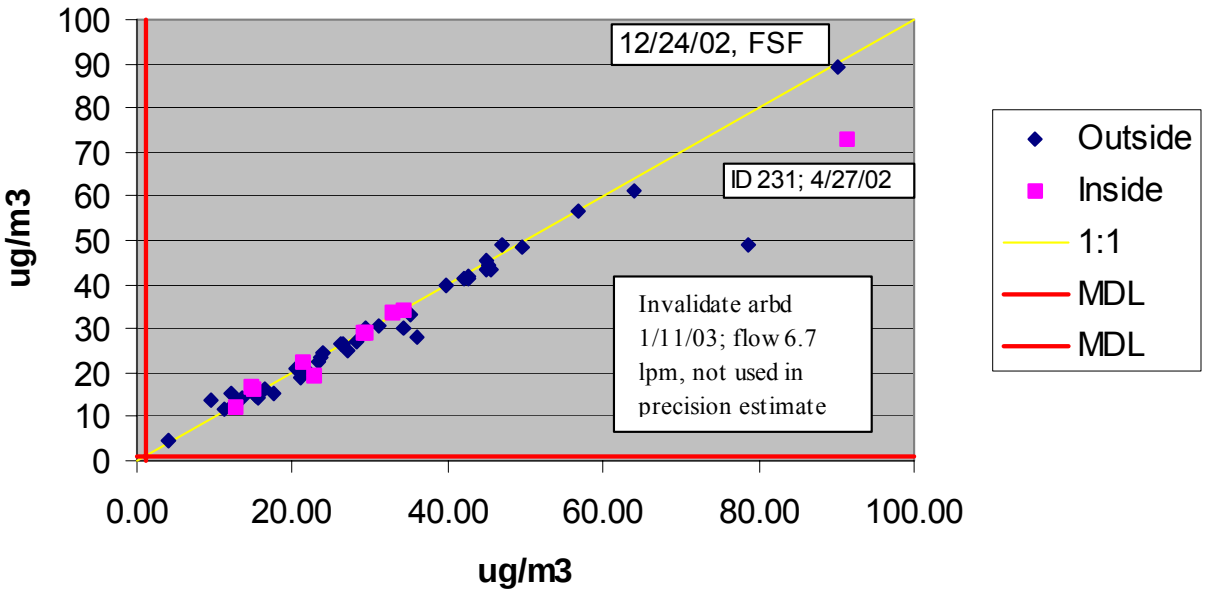


Figure 3.4.5-8. Scatter plot of MEMS duplicate PM_{10} samples.

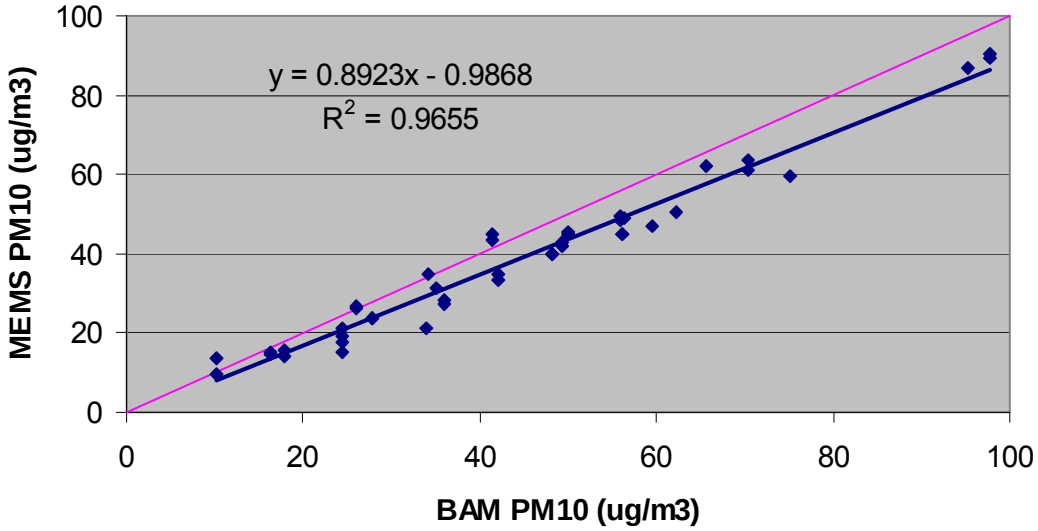


Figure 3.4.5-9. Scatter plot of MEMS versus BAM duplicate PM_{10} samples.

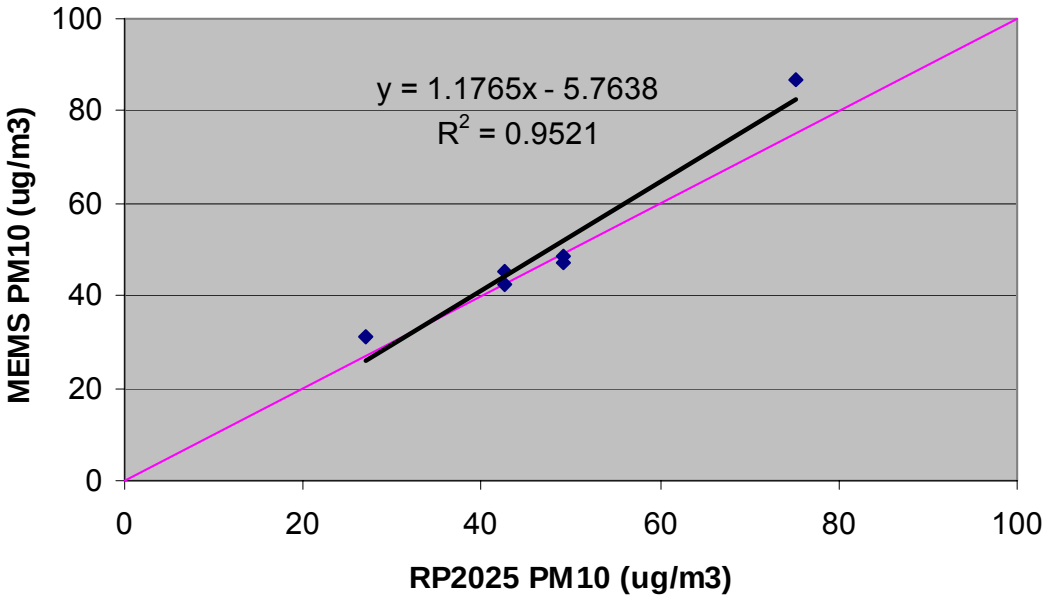


Figure 3.4.5-10. MEMS versus RP 2025 PM_{10} at First Street.

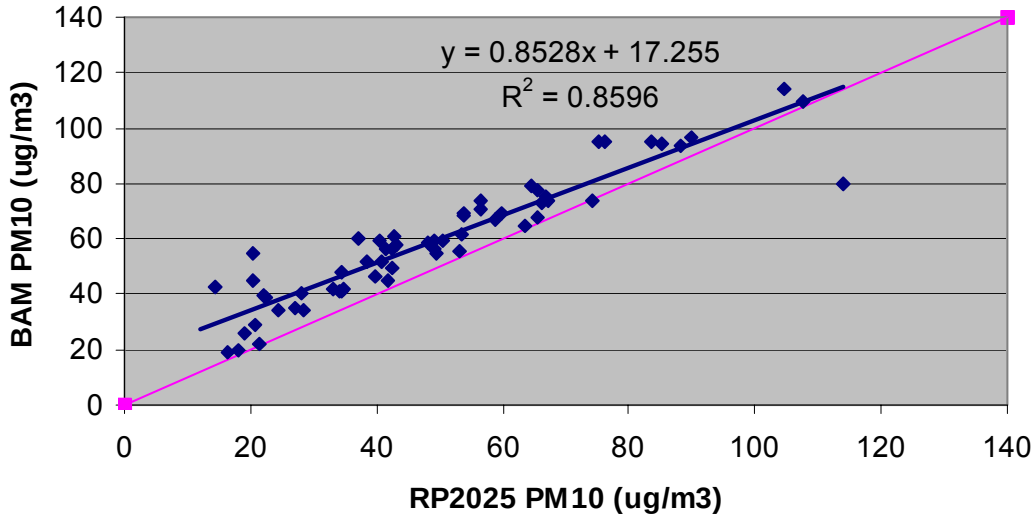


Figure 3.4.5-11. RP 2025 versus BAM PM_{10}.

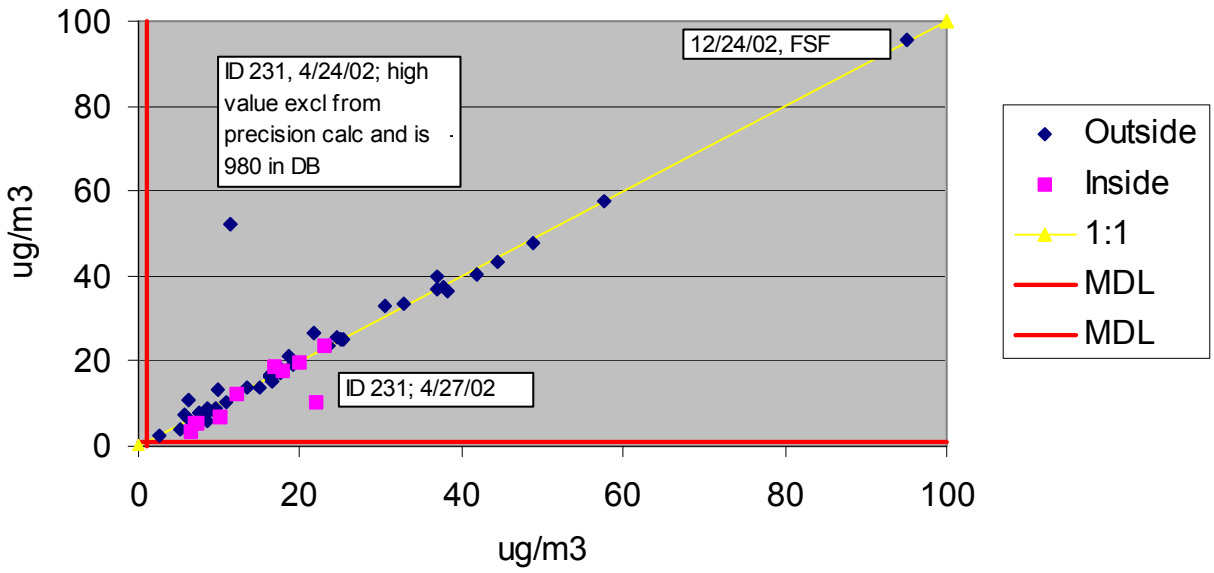


Figure 3.4.5-12. Scatter plot of MEMS duplicate $PM_{2.5}$ samples.

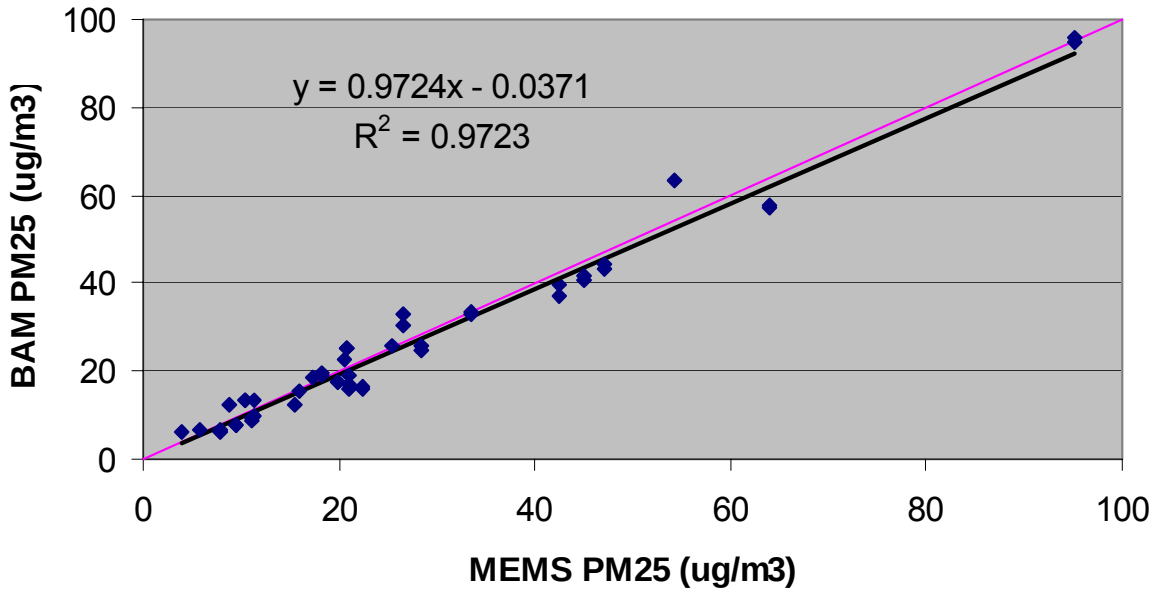


Figure 3.4.5-13. Scatter plot of MEMS versus duplicate BAM $PM_{2.5}$ samples.

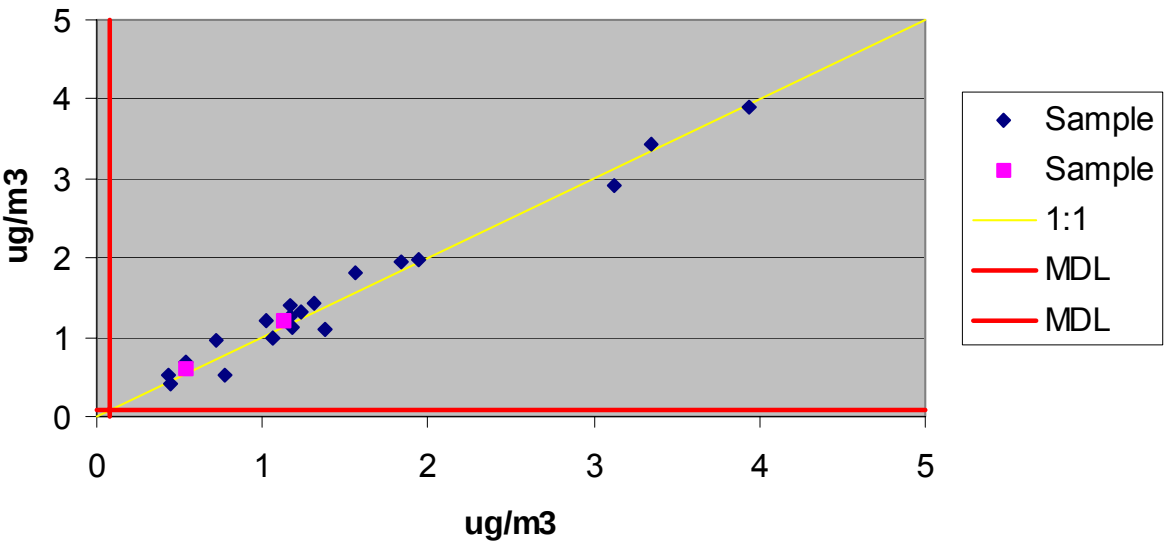


Figure 3.4.5-14. Scatter plot of MEMS duplicate EC samples.

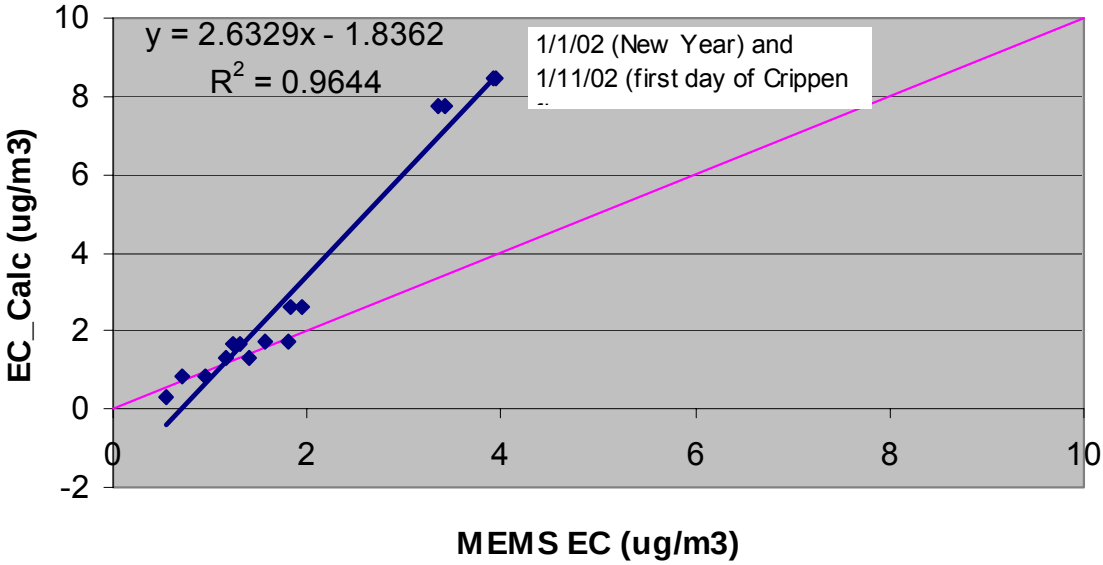


Figure 3.4.5-15. Scatter plot of MEMS versus EC_Calc duplicate samples. EC_Calc is derived from the 7-wavelength Aethelometer BC multiplied by a factor of 1.19. It is suspected that the Aethelometer was picking up some "blue carbon" not detected in the filter samples. See also Figure 3.4.5-16.

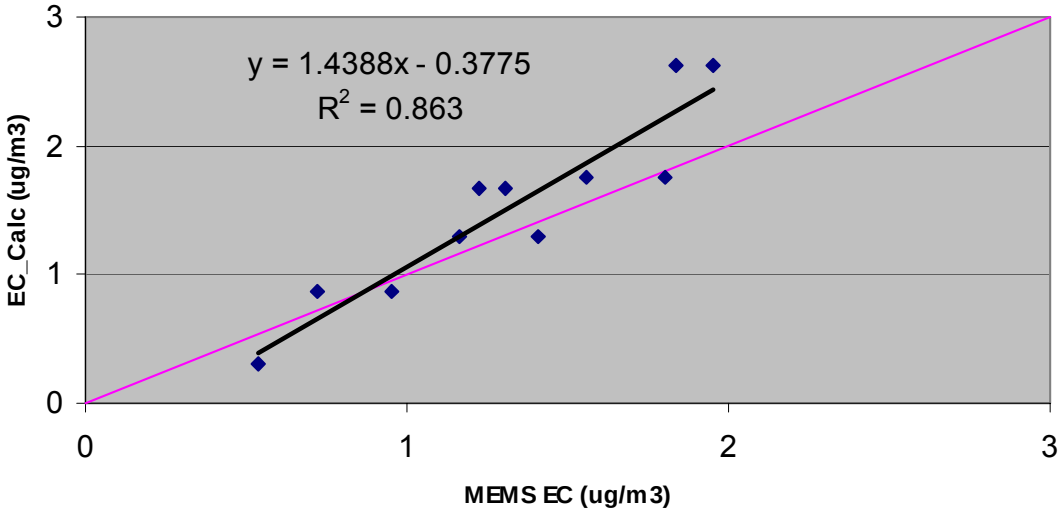


Figure 3.4.5-16. Scatter plot of MEMS versus EC_Calc duplicate samples, with the January 1, 2002, and January 11, 2002, outliers removed. EC_Calc is derived from the 7-wavelength Aethelometer BC multiplied by a factor of 1.19.

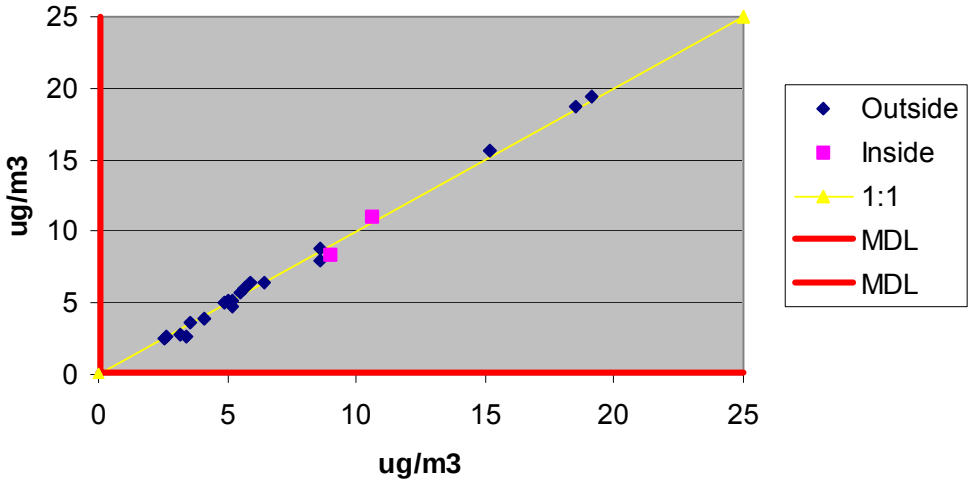


Figure 3.4.5-17. Scatter plot of MEMS duplicate EC samples.

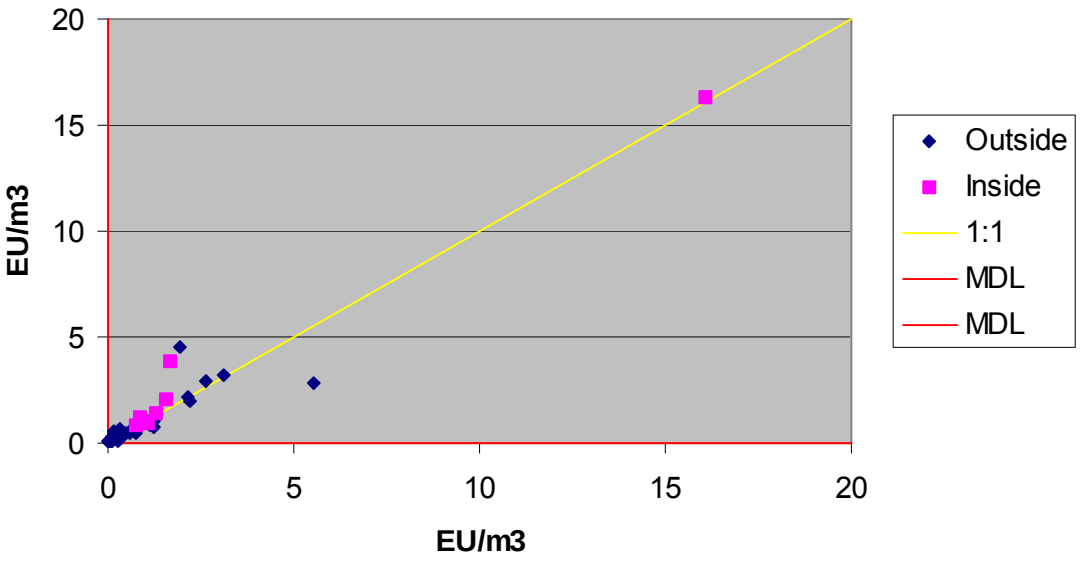


Figure 3.4.5-18. Scatter plot of MEMS duplicate endotoxin samples. All points shown were used in precision estimate.

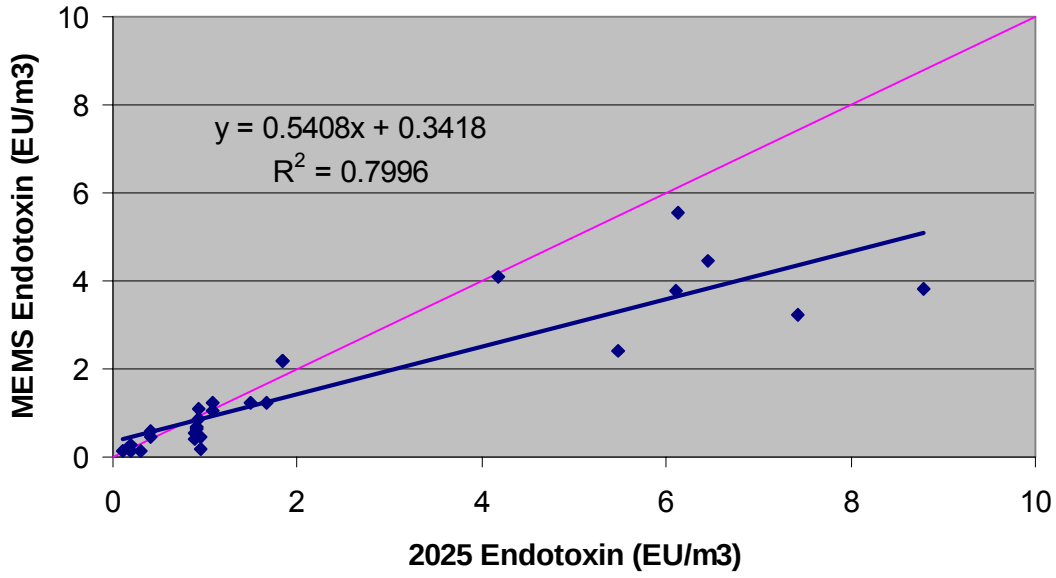


Figure 3.4.5-19. Scatter plot of MEMS versus RP 2025 duplicate endotoxin samples. All of the 2025 values greater than 4 EU/m^3 were in July, August, and September 2002. Corresponding PM_{10} values do not exhibit this trend, suggesting a problem in endotoxin analysis.

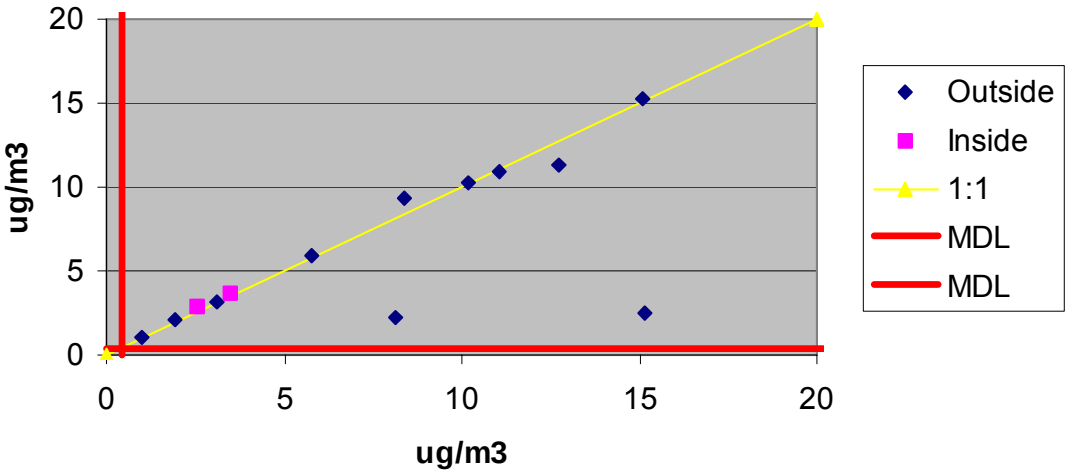


Figure 3.4.5-20. Scatter plot of MEMS duplicate total nitrate (front filter plus back filter) samples. Table 3.4.5-8 gives statistics for the data as shown and for data without the two outliers.

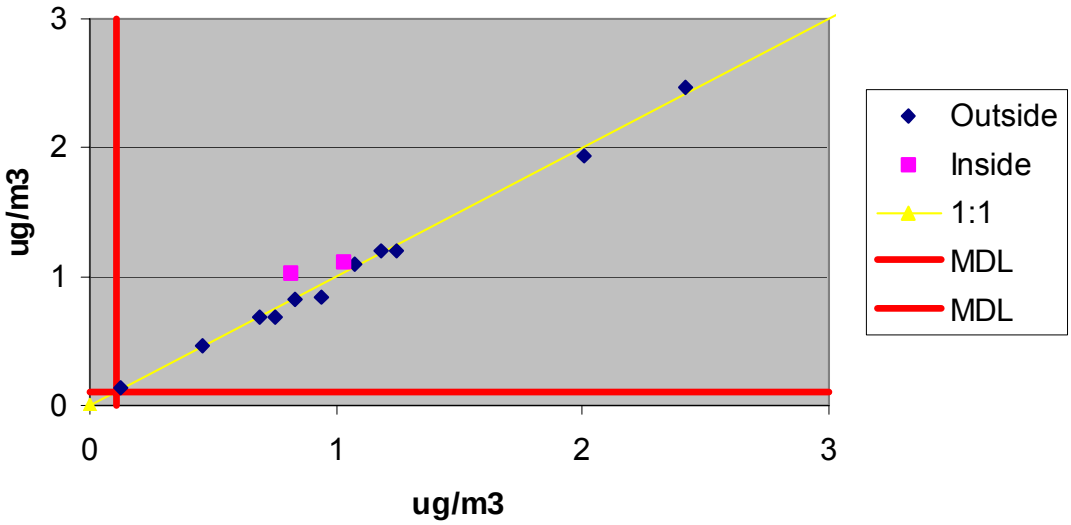


Figure 3.4.5-21. Scatter plot of MEMS duplicate sulfate samples. Note that this is sulfate, not $(NH_4)_2SO_4$.

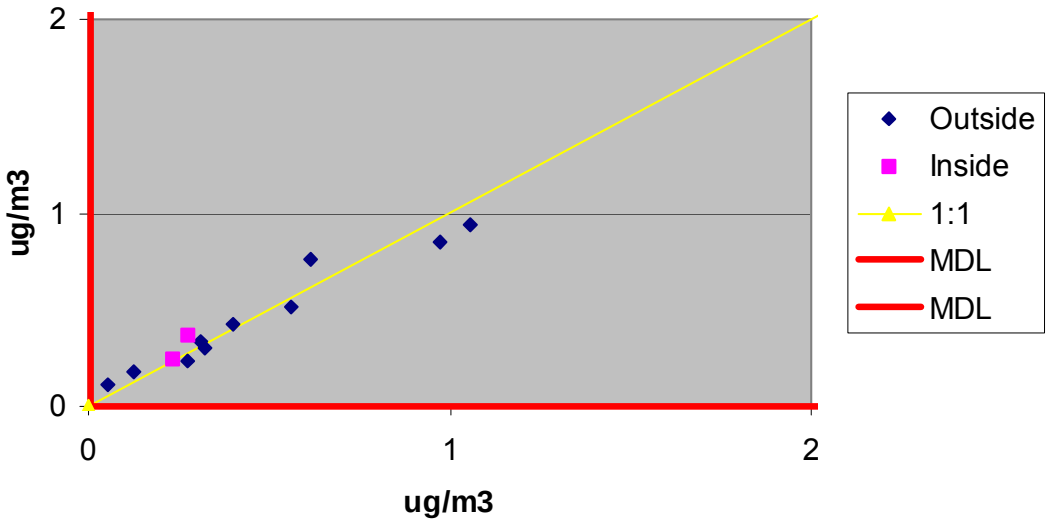


Figure 3.4.5-22. Scatter plot of MEMS duplicate aluminum samples.

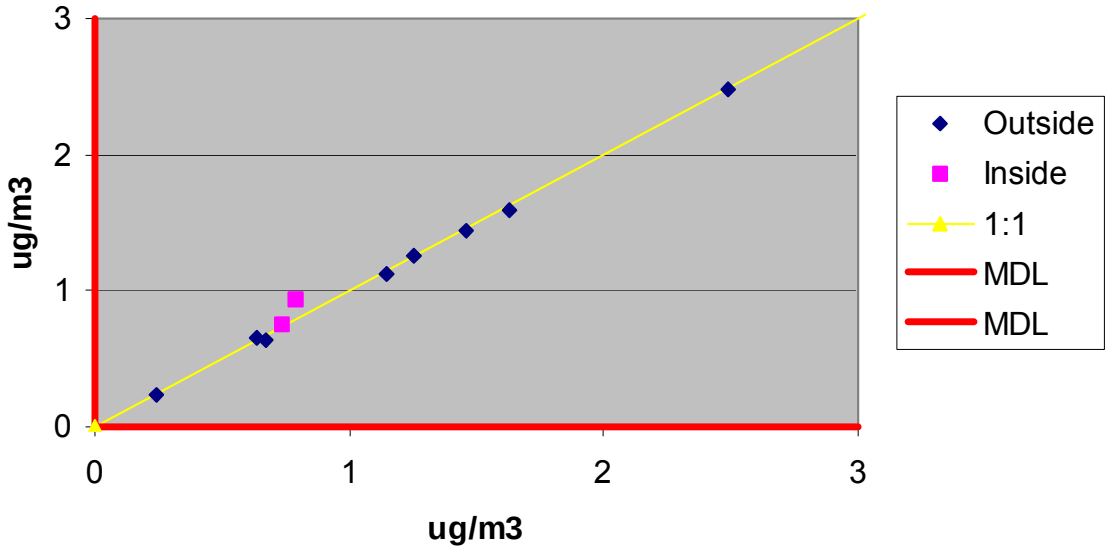


Figure 3.4.5-23. Scatter plot of MEMS duplicate silicon samples.

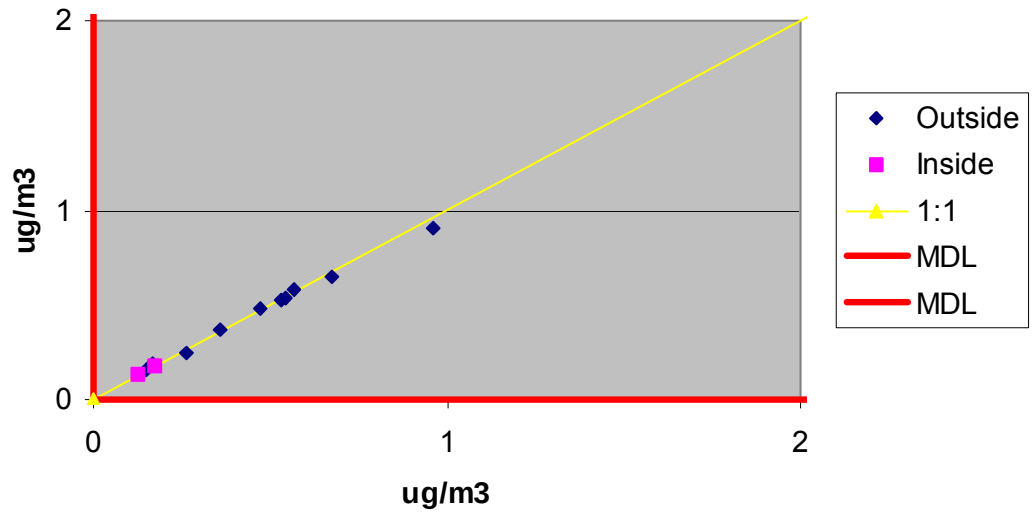


Figure 3.4.5-24. Scatter plot of MEMS duplicate iron samples.

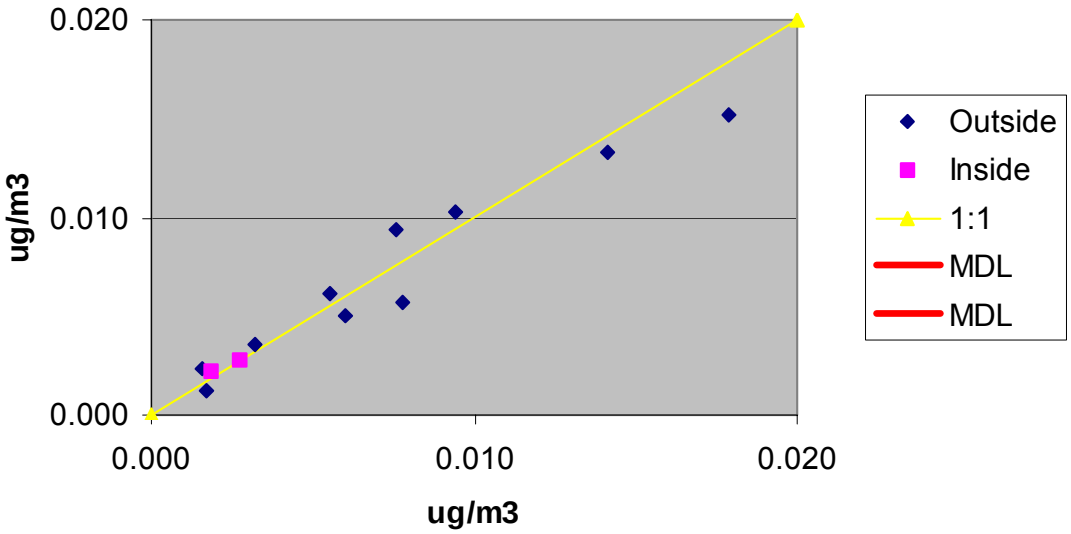


Figure 3.4.5-25. Scatter plot of MEMS duplicate manganese samples.

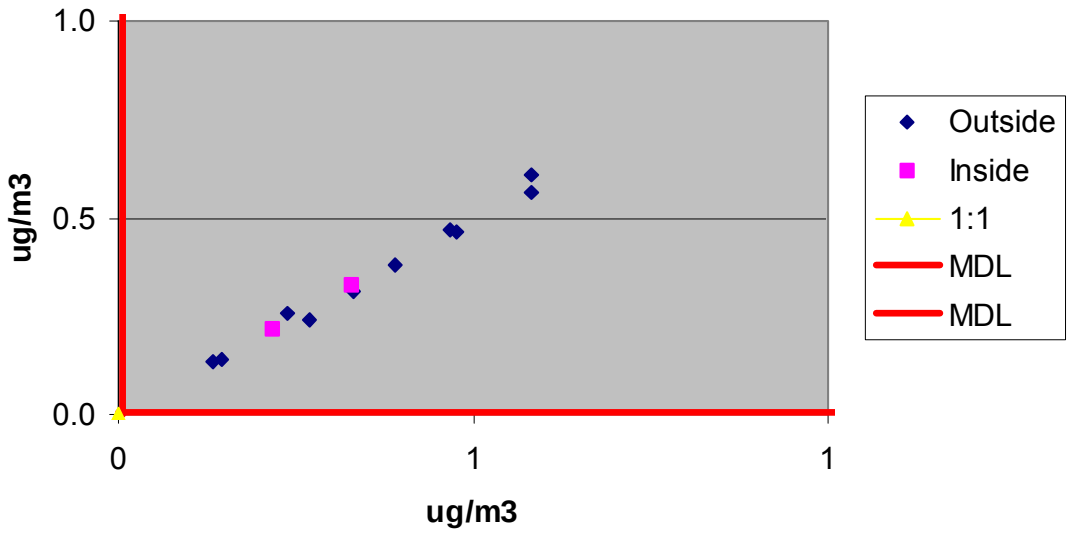


Figure 3.4.5-26. Scatter plot of MEMS duplicate potassium samples.

3.4.6 Residence Geocoding and Traffic Assignments

3.4.6.1 Residence Geocoding

Accurate locations of subjects are required for assigning traffic indicator variables used in estimating exposures. Since children generally spend the majority of time at their residence, we chose to estimate exposure based on traffic near their residences. The residence locations were determined by geocoding the residence addresses. The addresses were first standardized to correct for typographical errors, mis-reported address numbers, zip-codes, and street names. Next, the Eagle Geocoding Technology system was used to locate addresses based on the TeleAtlas MultiNet™ USA (TAMN) street-level database, the most accurate database of its kind in the world (196). The Eagle standardization software translates each street address to a known format, corrects spelling of street and city names, corrects and adds zipcodes, and substitutues standard abbreviations for address components. The standardized addresses are then geocoded to the TAMN using proprietary "fuzzy logic" address matching technology designed to return the most accurate match possible. It first searches for an exact street-level match. If an exact match is not found, successively larger areas are searched - from approximate street-level matches to a series of widening zip code vicinities until a match is found (196). Finally, the estimated accuracy, or match type, is reported for each geocoded address.

Geocoded records with match type 1 indicate an exact house number match to the correct side of the street or unique intersection. Match type 2 addresses are located to the correct block, but position along the block is unknown. More than 97% of the FACES residences were match type 1 on the second iteration. The remaining match type 2 addresses, which are less accurate than the match type 1 addresses, were investigated and manually corrected using GPS coordinates, when available from home visits, or online mapping services, such as MapQuest and

Yahoo. All GIS processing and analyses were performed using the Environmental Systems Research Institute (ESRI) ArcGIS software.

3.4.6.2 Traffic Assignments

Vehicle activity data for Fresno County in 2000 were obtained from the California Department of Transportation (Caltrans). The data were GIS-based and contained estimates of total annual average daily traffic (AADT) volumes traveling both ways on road segments with modest activity. Caltrans records traffic count data for freeways continuously and collects data for other major road types (i.e., arterial and collector roadways) every three years. The basis of the Caltrans roadway network was the USGS Digital Line Graph (DLG) data with modifications and additions made by Caltrans.

Heavy-duty vehicle (HDV) fractions of total traffic volume in Fresno/Clovis were derived from the 2002 Caltrans statewide truck-traffic-volume database for freeways and state highways. This database is linked to the state post-mile roadway system and relies on data from the weigh-in-motion (WIM) sensors for Highways 99 and 41, and estimated HDV fractions for other locations in Fresno/Clovis.

Comparison of the DLG/Caltrans and TeleAtlas roadway locations in southern California showed discrepancies of up to 250 m in roadway locations (197); aerial photography confirmed that the TeleAtlas roadways locations were more accurate than the DLG/Caltrans roadway locations. Although we did not evaluate the DLG/Caltrans roadway location accuracy in Fresno, we elected to transfer the traffic volume data and HDV fractions to the TeleAtlas roadway network to have the traffic volumes on the same roadway network that was used to geocode the residences. The AADT and HDV fractions were transferred using the software and methods developed by Wu et al(198).

We wanted to examine the relationship between FACES participant health status and simple traffic indicators that could be surrogates for participants' exposure to motor vehicle emissions. The simple traffic metrics were (1) the distance from residences to nearest roadways of various types, (2) inverse-distance squared traffic volume on nearest road, and (3) GIS-mapped traffic density assignments at residences.

The first two sets of traffic metrics consisted of the distances from residences to the nearest roadways of different types and the associated LDV and HDV traffic volumes on those roads. GIS tools were used to calculate the distance to the nearest (1) interstate freeway, U.S. highway, or limited access highway; (2) other highways; (3) arterial roads; (4) collector roads; and (5) local roads. An advantage of this metric is that the calculations were carried out for all roads, not just the roads for which traffic volumes were available. Traffic volumes were not available on most local roads and LDV/HDV traffic volume splits were not known with certainty on most arterial, collector, and local roads. The database of distance and volume metrics were compiled and used to obtain an understanding of which subjects were living within the zone of influence (e.g., 50 m, 100 m, 150 m, 200 m, etc.) of busy roads. Figure 3.4.6-1 shows the distribution of distances to roadways from the FACES residences. For the subset of nearest

roads with Caltrans traffic volume data, Figure 3.4.6-2 show the distribution of inverse-distance squared weighted traffic volume at FACES residences.

The third approach for characterization of traffic exposures was to calculate traffic densities, which vary more smoothly in space than the distances to nearest roads. They also capture the effects of intersection and multiple roadway influences that are missed with only distance to the nearest roadways. The link-based traffic volumes are used to generate maps of traffic density using the ARCInfo Spatial Analyst software. Figure 3.4.6-3 show one traffic density map created with a Gaussian decay function that has traffic densities decreasing by ~90% between the roadway and 150 m away (perpendicular) from the roadways, which is consistent with the characteristics observed by Zhu et al. (199). Figure 3.4.6-3 also shows a traffic density map created with more gradual pollutant dispersion parameters (90% falloff in 300m). These densities reflect proximity to traffic without consideration of differential exposures caused by meteorology. The traffic densities are mapped as though wind speeds and directions were uniformly distributed across all quadrants. The traffic density map for Fresno clearly shows high densities in narrow bands along the freeways, moderate densities along major arterials, and lower densities in the suburban neighborhoods. A database of densities at all of the FACES residences was compiled for use in the health analysis. The distribution of estimated traffic density at FACES residences based on the 150-meter decay parameterization is shown in Figure 3.4.5-4.

Figure 3.4.6-1: The distribution of distances from FACES residences to nearest freeways, arterial roadways, and collector roadways.

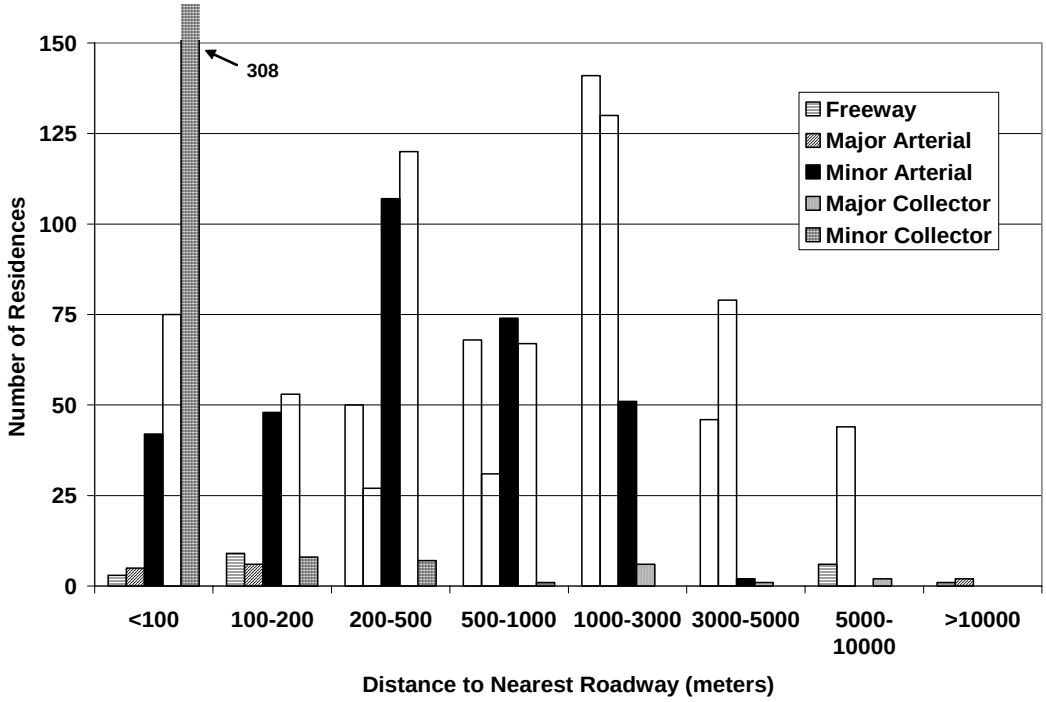


Figure 3.4.6-2: The distribution of inverse-distance squared weighted traffic at FACES residences.

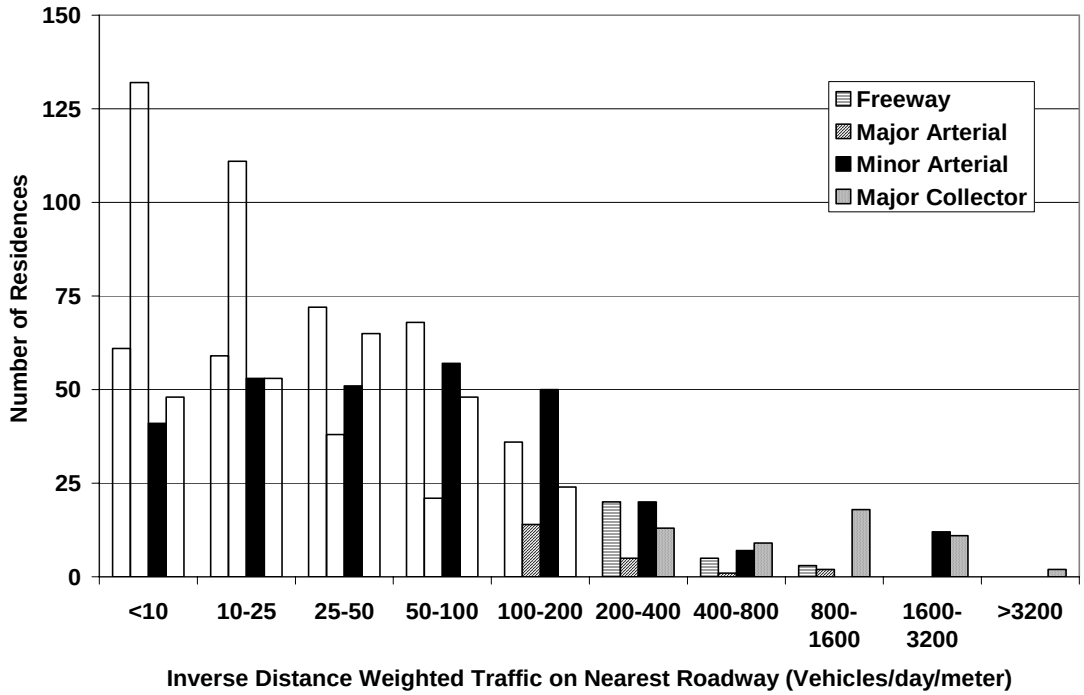


Figure 3.4.6-3: Spatial maps of traffic density in Fresno near the central site based on the 150-meter (left) and 300-meter decay parameterization.

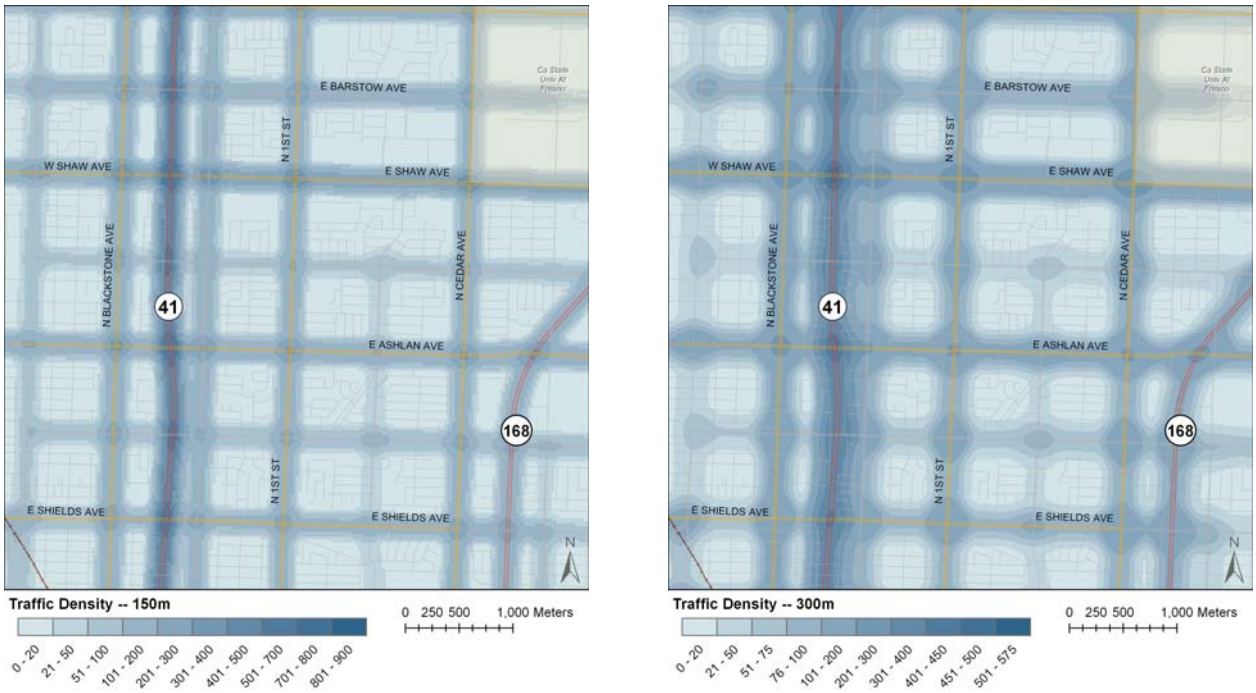
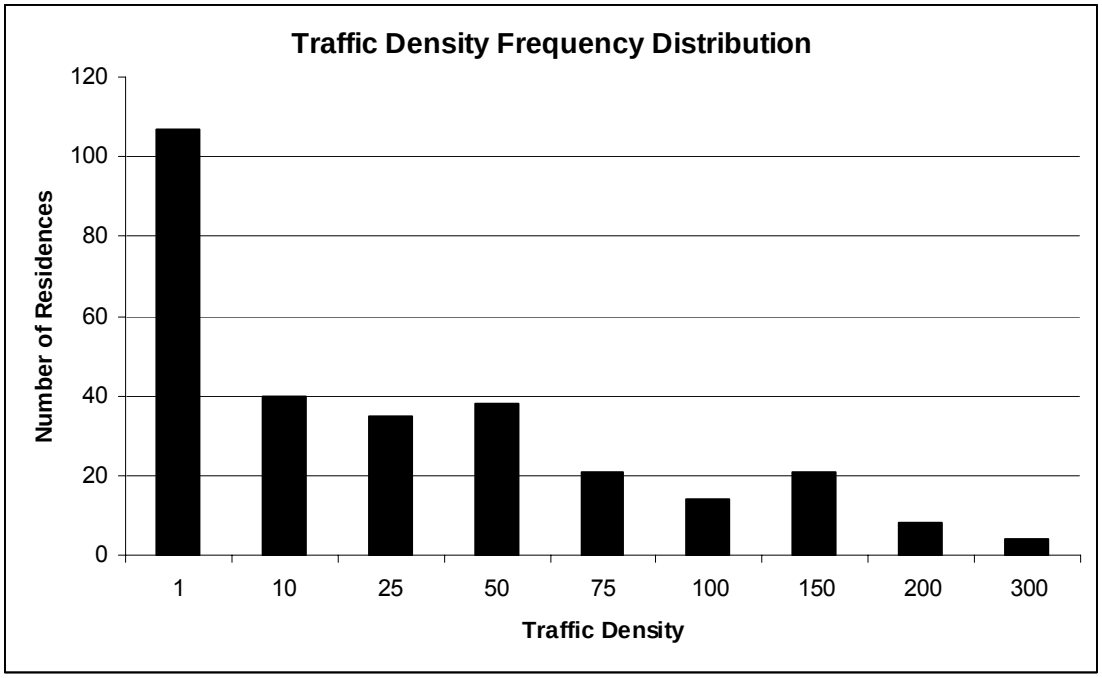


Figure 3.4.6-4: The distribution of estimated traffic density at FACES residences based on the 150-meter decay parameterization



3.4.7 Exposure Modeling

3.4.7.1 Background

Most panel studies of air pollution health effects use either personal monitoring data or central site air monitoring data to assign exposures. The cost of collection of individual exposure monitoring data for the numerous agents of interest in FACES was prohibitive (millions of dollars) for the large number of subjects and repeated panels in the study. Personal sampling on all of the subjects for even one panel (as recommended by the investigators for model validation purposes) was not feasible within the project resource limits (set by ARB). Assignment of exposures based on central air monitoring data alone is straightforward but suffers from potentially large exposure assignment errors. To address this dilemma, data were collected during the one-year sub-study in FACES to support an alternate approach in which individual exposures of each subject for each panel day were estimated (modeled) in a manner that accounts for spatial variability within the community and indoor/outdoor pollutant differences at residences. The sub-study data for homes and schools were used to develop and apply individual exposure models in the FACES study.

When personal measurements are not available, individual exposures are estimated with microenvironmental exposure models that use housing characteristics and time-activity data in combination with fixed site air monitoring data. The models incorporate sub-models and data to estimate concentrations in each microenvironment occupied by the subject. Exposure models combine the microenvironmental concentrations with human time-activity data. The models assume a subject travels through a finite number of microenvironments during a day, and they estimate individual exposures (E) as the time-weighted average of the concentrations in the microenvironments (C) that the subject occupies on that day.

$$E_{i,k} = \left[\frac{1}{\sum_j \Delta t_{i,j,k}} \right] \sum_j \left(C_{i,j,k} \ \Delta t_{i,j,k} \right) \qquad (3.4.7\text{-}1)$$

Where $\Delta t_{i,j,k}$ is the time spent in the the jth microenvironment by the ith subject on the kth day. The models commonly estimate the 24-hr average and daily 8-hr maximum exposures for a subject.

Population exposure models use a probabilistic approach to sample randomly from distributions of data for exposure factors and predict distributions of individual exposure for the population of interest (200-204). Recently, exposure models have been adapted to cohort studies where they predict distributions of exposures for individual subjects. For example, the Individual Exposure Model (IEM) (205) was developed to estimate individual exposures of subjects who participate in the Southern California Children's Health Study (115, 197) and similar long-term studies of air pollution health effects. The IEM model uses central site air monitoring data and incorporates subject-specific time-activity, residence and school locations, proximity to traffic, and housing characteristics in exposure estimates for each subject. A similar approach was adopted for FACES.

3.4.7.2 FACES Individual exposure Model

The FACES individual exposure model is a microenvironmental model that is intended to characterize exposure of subjects to air pollution of outdoor origin. The microenvironments considered in the model are indoors and outdoors at residences, indoors and outdoors at schools, and in vehicles. This limited set of microenvironments was selected, because the majority of children's time is spent in these locations and concentrations for these microenvironments can be estimated from the FACES Home Intensive sub-study or similar studies (for vehicles and inside classrooms). There are three components of the model: (1) the time-activity module, (2) outdoor concentration modules, and (3) indoor concentration module. These are described below.

3.4.7.2.1 Time-activity

The FACES subjects filled out daily diaries during panel studies. The initial diary form (questionnaire) requested information on the children's activity and locations during 5 time periods each day. The diary was designed to provide the amount of time spent in the specific microenevironments considered in the exposure model. Unfortunately, very few children (<5%) provided reliable time-resolved time-activity data. Telephone follow-up was not effective, because too much time elapsed between the panel days and the time the diaries were submitted and reviewed. The initial time-activity data were unusable. In response to this problem, the daily diaries were modified to collect specific activity data during the morning and afternoon time periods. The modified questionnaire asked whether children were engaged in outdoor sports, indoor sports, travel by car, and/or travel by bus. Data collection with the modified diaries was good; more than 90% of the subjected provided data on 12 of 14 panel days. The original and modified diary also collected data to determine if a subject was sick and did not attend school on a particular day, and whether the subject traveled away from Fresno on that day. Individual exposures were not estimated for subjects that traveled more than 20 miles from Fresno on a panel day.

The approach used for estimating time spent in microenvironments relies on the average time-use observed for children ages 6-11 years in California by Wiley (167). Wiley surveyed ~1200 children and found that, on average, children ages 6- 11 years spent 71% time indoors at home, 12% time indoors in other locations, which included school, 13% time outdoors, and 4% time in transit. We have decomposed Wiley's average time-use data (with numerous assumptions) into the categories shown in Table 3.4.7-1. Time spent in five microenvironments is divided into the four time periods used in the model (8 am to noon, noon to 8 pm. 8 pm to 6 am, and 6 am to 8 am) and is distinguished by the type of day (non-summer weekday, non-summer weekend day, summer day, holiday, and sick day).

The day-specific activity data for each child is used to modify the average time use profiles. We assume the children are normally engaged in the specific activities identified on the questionnaire. If they responded negatively,then they were not in the specific activity and the average time-use profile is modified as shown in Table 3.4.7-2. For example, if a child indicates that s/he did not ride in a car or bus in the morning of a non-summer weekday (i.e., school day), the time normally assigned to in-transit between 6 am and 8 am is reassigned to outdoors at school. Similarly, if a child indicates that s/he did not engage in outdoor sports in the afternoon,

the time normally assigned to outdoors at school and residence is reduced by 2/3, while time spend indoors at residence and schools is increased accordingly. For children this age, we interpret outdoor sports as time outdoors. Time-use profiles are not adjusted based on responses that indicate indoor sports. Also, if the specific activity data are missing, the child's most frequent response to the specific activity questions for that type of day was used to fill in the missing information.

The school schedule and each child's daily diaries determined the day type. The majority of children attend schools in the Fresno Unified School District (FUSD), consequently, this school's schedule was adopted for all FACES subjects. The school schedule for each year was used to determine which days are non-summer weekdays, non-summer weekend days, summer days, and holidays. The diary data were used to determine whether a child was sick on any type of day.

The time periods for the exposure model were determined by the FACES integrated pollutant averaging times (see Table 3.4.8-1). For many pollutants simulated in the exposure model, the daily daytime (8 AM – 8 PM) and nighttime (8 PM - 8 AM) average concentrations were available; however, for pollens and spores, the data were provided for morning (6 AM - noon), afternoon (noon - 8 PM), and evening (8 PM to 6 AM) time periods. The four time periods for the exposure model were selected to make reasonable use of the time-resolved exposure data, with the recognition that we don't have hourly time resolution for either time activity or concentrations of many constituents.

3.4.7.2.2 Outdoor Concentrations

One goal of the exposure component of FACES was to investigate spatial gradients in outdoor or ambient pollutants and to incorporate the findings into the exposure assignments for subjects. The exposure model was designed to use outdoor concentrations resolved to the appropriate spatial scales as inputs. Specifically, the model uses estimates of the outdoor concentrations at each subject's residence and school. In addition to the central site data, measurements were available from other routine SJVAQMD air quality monitoring stations and from selected residences and schools on an intermittent basis.

Local outdoor concentrations were estimated based on the daily ambient data and spatial mapping techniques. Several methods were used for spatial mapping and outdoor exposure assignments, because the temporal and spatial coverage varied considerably by day and by pollutant. The methods included nearest station assignments, inverse distance squared weighted assignments, and adjusted central site assignments. The outdoor concentration assignments were made based on the following methods.

Method 1: If measurement data were available on the day of interest at one or more locations within 1 km of the target location, the exposure assignment was based on the concentration data from the nearest location. The nearest location may be the Central Site, a SJVAQMD site, an ARB Trailer, or a FACES residence.

Method 2: If measurement data were available on the day of interest at 3 or more locations between 1 km and 50 km of the target location, the exposure assignment was based on an estimate made by inverse distance-squared weighted (IDSW) interpolation of measurements from the 3 nearest locations.

Method 3: If measurement data were available on the day of interest at fewer than 3 locations between 1 km and 50 km of the target location and one of those locations was the central site, the exposure assignment was based on the Central Site measurement adjusted according to the average spatial gradient map for specific pollutants in Fresno (see spatial gradient map development discussion below).

The outdoor concentration estimation methodology applied these methods in hierarchal order. This approach gave the highest priority to use of day-specific data from a nearby monitor (Method 1), the second highest priority to a day-specific surface of interpolated values (Method 2), and the third priority to the daily central site values adjusted for average spatial gradients (Method 3). For the November 1, 2000 to March 31, 2003 exposure model application period, the concentrations of NO_2 and ozone were most frequently assigned based on Method 2; because they were measured hourly at 3 or 4 stations in the community. Concentrations of $PM_{2.5}$ mass, $PM_{2.5}$ EC, $PM_{2.5}$ OC, $PM_{2.5-10}$ mass, PM_{10} mass, endotoxin, agricultural fungi, *Cladosporium*, *Alternaria*, total fungal spores, and total pollens were assigned most frequently based on Method 3. On panel days during the Home Intensity period (March 2002 to February 2003), the outdoor concentrations of latter group of species were assigned frequently based on Methods 1 and 2.

Average spatial gradient maps were developed for use in Method 3 estimates. The time-averaged ratio (R_{cs}) of concentrations at measurement locations in the community to those at the central air monitoring site were compiled and mapped for $PM_{2.5}$ mass, $PM_{2.5}$ EC, $PM_{2.5}$ OC, $PM_{2.5-10}$ mass, PM_{10} mass, endotoxin, agricultural fungi, *Cladosporium*, *Alternaria*, total fungal spores, and total pollens during the Home Intensity study period. Since the spatial measurements were obtained intermittently over a 13-month period, the ratio to the Central Site concentration was used instead of the absolute concentration to minimize temporal confounding caused by variation in meteorological conditions on the measurement days. Spatial measurements were available for ~90 locations in Fresno and Clovis; however, measurements were available at no more than 8 locations on any given day. The spatial maps of average ratios to the central site concentrations are shown in Figures 3.4.7-1 and 3.4.7-2. These maps were created by Kriging the average ratios (from all seasons of the year), which produces relatively smooth spatial maps of relative concentration gradients across the community. Kriging was used because it produces the best linear unbiased estimates and it has been used successfully in numerous epidemiologic studies (206, 207). These maps cover the area where 97% of the residences are located; most of the subjects lived within 10 km of the central site. The outer portions of these maps are less accurate than the inner portions due to sparse data (and residences) along the boundaries. The summary statistics of the estimated ratios for FACES residence concentrations to central site concentrations, listed in Table 3.4.7-3, indicate that the average ratios are slightly less than one (0.95-0.99) for $PM_{2.5}$, $PM_{2.5-10}$, and PM_{10},; below one (0.74 – 0.77) for $PM_{2.5}$ EC and OC; and above one (1.17 to 4.13) for the biological agents. The spatial variability in the estimated ratios is low for $PM_{2.5}$ and PM_{10}, and high for agricultural fungi, alternaria, endotoxin, and total pollens. The spatial variability in the estimated ratios is greater for $PM_{2.5}$ EC and OC than for $PM_{2.5}$ and PM_{10} mass.

3.4.7.2.3 Indoor Concentrations

Indoor concentrations (Cin) in most modern microenvironmental exposure models are calculated with the single-compartment, steady-state mass balance equation (205, 208[Ozkaynak, 1996 #158, 209[Burke, 2001 #149):

$$C_{in} = \frac{p\,a\,C_{out}}{a+k} + \frac{Q_{is}}{(a+k)V} \qquad (3.4.7\text{-}2)$$

where p is the penetration coefficient, a is the air exchange rate (h^{-1}), C_{out} is the concentration outside of the building, k is the indoor decay rate (h^{-1}) which represents both deposition and chemical reaction losses, Q_{is} is the indoor source emission rate ($\mu g\ h^{-1}$),) or chemical production rate, and V is the building volume (m^3). The first term in the equation represents the contribution of outdoor air infiltration to the indoor concentration, while the second term represents the contribution of indoor sources. Note in the absence of indoor pollution sources, the equation reduces to:

$$C_{in} = \frac{pa}{(a+k)}\,C_{out} \qquad (3.4.7\text{-}3)$$

where $pa/(a+k)$ is the indoor-outdoor concentration ratio. This simplification is particularly relevant for the FACES individual exposure model, because we limited the scope of the individual exposure simulations to exposure pollutants of outdoor origin. Several studies have found a stronger relation between particulate matter pollution and adverse health effects for ambient-origin particles than non-ambient particles (e.g. (203, 210, 211); however, we, by no means assume this will be case with FACES analyses. The importance of indoor sources to total individual exposure is likely to vary considerably by pollutants. We chose to omit the contributions of indoor sources to individual exposure in the simulations, but factors related to the presence of indoor sources were reserved as potential covariates in the epidemiologic analyses.

The penetration coefficient p and the deposition rate k vary by particle size, season, and air exchange rate. Table 3.4.7-4 lists the penetration factors and decay rates used in the simulations. For all gaseous pollutants, a unit penetration coefficient was assumed. In the case of particles, several studies indicate that p is close to one (212-214) for a wide range of diameters, while several other studies indicate the penetration factor may be significantly less than one (208, 215). Other studies suggest particle penetration factors are closely associated with air exchange rates (Suh et al., 2004). A penetration coefficient of 0.95 was used for $PM_{2.5}$ mass, $PM_{2.5}$ EC, PM $_{2.5}$ OC, and PM_{10} mass (209). This is reasonable since homes in California typically have higher air exchange rates than the national average (216), and penetration factors increase to around one at approximately two or more air exchanges per hour (217). A slightly lower penetration factor (0.90) was used for $PM_{2.5\text{-}10}$ mass, endotoxin, agricultural fungi, Cladosporium, and total fungal spores to reflect a higher probability of impaction during penetration. A much lower penetration factor (0.20) was used for Alternaria and total pollens based on their large particle diameters and the low indoor/outdoor ratios of these species in the FACES residences.

An indoor decay rate of 1.0 h_1-1 was used for NO_2 ,(218), which was within the range of 0.2-1.3 h-1 found by (219). A considerably higher rate (2.8 h-1) was used for ozone, based on the studies of Reiss and coworkers that showed rapid ozone absorption to common indoor surfaces (220-222). Lower indoor loss rates of 0.39 and 0.65 h-1 were used for $PM_{2.5}$ and PM_{10} mass, respectively, based on PTEAM data analysis. (223, 224). These parameters imply that the average loss rate for $PM_{2.5-10}$ is 1.04 h-1 for the average air exchange rate (see discussion below) and outdoor $PM_{2.5}/PM_{10}$ ratio in Fresno (0.5). Under the assumption that indoor particle losses are due predominately to deposition, rather than evaporation, we used the same indoor loss rates for $PM_{2.5}$ OC and $PM_{2.5}$ EC as for $PM_{2.5}$ mass. It is recognized that evaporation of ammonium nitrate and volatile organics in the indoor environment can also be a significant loss process for $PM_{2.5}$. Ammonium nitrate particles were not modeled explicitly in the analysis (rather it was included as a portion of $PM_{2.5}$ mass), and no attempt was made to account for OC evaporation; because the processes are not well characterized. It should be noted that parameterizing indoor loss processes that include deposition on different indoor surfaces, chemical reactions, and evaportation, using a constant rate for each pollutant is highly simplified and uncertain.

The loss rates for the biological agents are not reported in the literature. The indoor loss rate for endotoxin was assumed to be the same as for coarse particles (1.04 h-1), because ambient endotoxin concentrations are highly correlated with $PM_{2.5-10}$ in Fresno and endotoxin particles are suspected of being predominantly in the 2.5-10 μm size range. The loss rates for fungal spores and pollens were estimated from the mass balance equation based on the mean indoor/outdoor concentration ratios observed in FACES residences and in the estimated mean air exchange rate. After exclusion of I/O ratios above 1, the mean I/O ratio was ~0.2 for Cladosporium, agricultural fungi, and total fungi and ~0.03 for Alternaria and total pollens. These low I/O ratios, in combination with the assumed penetration factors, imply indoor loss rates of 3 h-1 and 4.8 h-1. Based on deposition theory, these loss rates are plausible for particles with mean diameters above 10 μm.

Air exchange rates (a) characterize ventilation conditions in residences. The air exchange rate is known to depend on a large number of factors that include building type, building construction or age, building volume, HVAC system (type and operating mode), window positions, season, ambient conditions, and resident activities (216, 225, 226). The FACES measurements did not include air exchange rate data for residences. Several studies suggest ventilation conditions and air exchange rates can be estimated from simultaneously collected indoor and outdoor concentration data for residences and pollutants with little evidence of indoor source contributions. For example, (227) successfully derived air exchange rates from sulfate indoor/outdoor ratios and (228) derived ventilation rates from light-scattering by particle (Bscat) indoor/outdoor ratios. We investigated the extent to which 13 factors available from the daily Home Intensive questionnaire (listed in Table 3.4.7-5) could explain variations in sulfate, EC, and Bscat I/O ratios in FACES residences. Most of these factors were selected originally to identify indoor sources. We found that questionnaire data related to whether the HVAC system was in use and whether window/door positions were open for more than 30 minutes explained 70% of the variance in daily sulfate I/O ratios. Questionnaires were not able to explain as much of the variance in EC and Bscat I/O ratios as the sulfate I/O ratios, but this result is probably due to the greater difficulty in the identification of residences with little evidence of indoor sources of EC and Bscat compared to residences without indoor sources of sulfate (for which there are no known indoor sources). Window/door position and HVAC use also explained more of the

variance in EC and Bscat than any other factors. Also, it should be noted that almost all FACES residences used gas heaters as the primary heating method and had some type of air conditioning system.

Since the FACES daily panel questionnaire contained data for window/door position and HVAC use for virtually all residences and subjects, we chose to estimate daily air exchange rates from those responses and average air exchange rates implied by the sulfate I/O ratios from the FACES Home Intensive sub-study. Table 3.4.7-6 shows the mean observed sulfate I/O ratios and air exchange rates determined from the mass balance equation with p=0.95, k=0.39, and Q=0 (i.e., for sulfate), for the warm and cool seasons, with windows/door open and closed, and with air conditioning or heating on or off. The results are consistent with physical expectations: higher air exchange rates are estimated for conditions when windows and doors are open and air conditioning units are not in use. The means exchange rate estimates ranges from 0.41 h-1 in the cool season with windows closed and no heating to 1.25 h-1 in the warm season with windows open and air conditioning off. These rates are consistent with measurements from other California residences (226).

In modeling subjects' individual exposures on panel days, the air exchange rates were estimated for daytime and nighttime, based on the daily questionnaire data and the mean rates shown in Table 3.4.7-6. For panel days where questionnaire data were missing and for all non-panel days we assumed: (1) air conditioning was used with closed windows in the warm season, if the maximum daily temperature was 26^{o}C or greater and the other questionnaire data indicated air conditioner use on 20% or more of panel days of this day type; and (2) gas heater was used with closed windows in the cool season, if the minimum daily temperature was 10^{o}C or lower and the other questionnaire data indicated heater use on 5% or more of panel days of this day type. Otherwise, the missing data defaults were no air conditioner use with windows/doors open in the warm season, and no heater use with windows/doors open in the cool season.

3.4.7.2.4 Non-Residential Locations

Estimates of indoor and outdoor concentrations for subjects at locations other than their residences were less refined than those above. For example, the outdoor concentrations at schools were assumed to be the same as at residences. This assumption needs to be verified in future evaluations. The concentrations inside school buildings were estimated under the assumption of an air exchange of 1. h^{-1}. Classrooms may have a wide range of air exchanges rates (Daisey et al 1998; Shendell et al., 2003) and we chose a moderately low air exchange rate to reflect the extensive use of sir conditioning in Fresno schools. The in-transit microenvironment was distinguished because children may be exposed to significantly higher pollutant concentrations during their travel between home and school and during other times spent in vehicles. Measurement data collected in California were used to obtain the in-vehicle pollutant concentrations appropriate for California vehicle mix and roadways (229-231) (232). In-vehicle concentrations typical of urban conditions (e.g., Los Angeles), shown in Table 3.4.7-7, were used for NO_2, $PM_{2.5}$ mass, $PM_{2.5}$ EC, and $PM_{2.5}$ OC, $PM_{2.5\text{-}10}$ mass, and PM_{10} mass. The in-transit vehicle concentrations of other constituents were assumed to be proportional to ambient concentrations at their homes (ozone at 30% and biological agents at 100%).

3.4.7.3 Exposure Model Design, Construction and Use

The FACES exposure model consists of two computer programs and associated data files. The first program estimates local ambient concentrations at receptor locations of interest (residences or schools) on a daily basis using ambient concentration data from the routine air monitoring stations, ARB trailers, and FACES residences. It assesses the availability of measurement data for each pollutant on each day and selects the optimum method to estimate local daily concentrations for each receptor of interest. The hierarchy of estimation methods is (1) to use locally measured (within 1 km of receptor) day-specific concentrations, (2) to spatially interpolate day-specific concentrations from three or more nearby measurement locations to the receptor location (i.e., a day-specific map), or (3) to use central-site measured day-specific concentrations adjusted according to the average spatial gradient map for specific pollutants in Fresno for the estimate. The program outputs the local concentration estimates for various averaging time for all receptors on all days of the year.

The second program is the microenvironmental personal exposure model. It estimates personal exposures based on estimates of time-spent in five microenvironments and concentrations of ambient origin in those microenvironments. The time each subject spends indoors and outdoors at home, indoors and outdoors at school, and in vehicles on each day is assessed from their daily diaries and average time-use data for children. A mass balance model is incorporated for estimation of indoor concentrations from air exchange rates determined using daily diary information on housing HVAC operations, pollutant penetration and deposition rates obtained from the literature, and the local ambient concentrations estimates output from the first program. Typical concentrations measured in vehicles are used for the in-vehicle microenvironment. The microenvironmental exposure model is applied to generate personal exposure concentration estimates for the FACES subjects on all days of the year for ozone, NO_2, $PM_{2.5}$ mass, PM_{10} mass, EC, OC, endotoxin, agricultural fungi, *Cladosporium*, *Altenaria*, total fungal spores, and total pollens. The model estimates are used in the health analyses on days with daily diaries and health outcomes.

Table 3.4.7-1: Average Time-Use for Children by Day Type and Time Period.

Day Type	Time Period	*Time Spent in Microenvironment (minutes per day)*					
		Indoors Residence	**INDOORS SCHOOL/ OTHER**	**Outdoors Residence**	**Outdoors School**	**In-Transit**	**Total**
Non-summer Weekday	8 am – Noon	0	202	0	38	0	240
	Noon - 8 pm	243	98	60	37	42	480
	8 pm – am	600	0	0	0	0	600
	6 am - 8 am	92	0	0	0	28	120
Non-summer Weekend Day	8 am – Noon	141	13	69	0	17	240
	Noon - 8 pm	279	27	141	0	33	480
	8 pm - 6am	600	0	0	0	0	600
	6am - 8 am	120	0	0	0	0	120
Summer Day	8 am – Noon	121	17	89	0	13	240
	Noon - 8 pm	239	33	181	0	27	480
	8 pm - 6am	600	0	0	0	0	600
	6am - 8 am	120	0	0	0	0	120
Holiday	8 am – Noon	131	17	79	0	13	240
	Noon - 8 pm	259	33	161	0	27	480
	8 pm - 6am	600	0	0	0	0	600
	6am - 8 am	120	0	0	0	0	120
Sick Day	8 am – Noon	240	0	0	0	0	240
	Noon - 8 pm	480	0	0	0	0	480
	8 pm - 6am	600	0	0	0	0	600
	6am - 8 am	120	0	0	0	0	120

Table 3.4.7-2: Alternate Time-Use for Various Diary Activity Responses								
				Alternate Time Use (minutes per day)				
Diary Activity Response	**Assumption**	**Day Type[1]**	**Time Period**	**Indoors Residence**	**Indoors School / Other**	**Outdoors Residence**	**Outdoors School**	**In-Transit**
No Morning Car/Bus Travel	Time is spent outdoors instead of in transit	NS WD	6am - 8 am	92	0	0	28	0
No Morning Outdoor Sports	2/3 of time outdoors is instead spent indoors	NS WD	8 am - Noon	0	227	0	13	0
		NS WE	8 am - Noon	187	13	23	0	17
		Summer	8 am - Noon	180	17	30	0	13
		Holiday	8 am - Noon	184	17	26	0	13
No Morning Car/Bus or Outdoor Sports	2/3 of time outdoors is instead spent indoors	NS WD	8 am - Noon	0	227	0	13	0
	Time is spent outdoors instead of in transit	NSWD	6am - 8 am	92	0	0	28	0
	2/3 of time outdoors is instead spent indoors	NS WE	8 am - Noon	187	13	23	0	17
		Summer	8 am - Noon	180	17	30	0	13
		Holiday	8 am - Noon	184	17	26	0	13
No Afternoon Car/Bus	Time is spent outdoors instead of in transit	NS WD	Noon - 8 pm	243	98	60	79	0
		NS WE	Noon - 8 pm	279	27	141	33	0
		Summer	Noon - 8 pm	239	33	181	27	0
		Holiday	Noon - 8 pm	259	33	161	27	0
No Afternoon Outdoor Sports	2/3 of time outdoors is instead spent indoors	NS WD	Noon - 8 pm	283	123	20	12	42
		NS WE	Noon - 8 pm	373	27	47	0	33
		Summer	Noon - 8 pm	360	33	60	0	27
		Holiday	Noon - 8 pm	366	33	54	0	27
No Afternoon Car/Bus or Outdoor Sports	2/3 of time outdoors is instead spent indoors and transit time is instead spent outdoor	NS WD	Noon - 8 pm	283	123	20	54	0
		NS WE	Noon - 8 pm	373	27	80	0	0
		Summer	Noon - 8 pm	360	33	87	0	0
		Holiday	Noon - 8 pm	366	33	81	0	0

[1] NS WD = Non-summer Weekday; NS WE = Non-summer Weekend day

Table 3.4.7-3: Summary Statistics of Ratios of Estimated Concentrations at FACES Residences to Central Site Concentrations					
Species	**Mean**	**Standard Deviation**	**Coefficient of Variability (%)**	**Minimum**	**Maximum**
$PM_{2.5}$ Mass	0.98	0.10	10	0.63	1.33
PM Coarse Mass	0.99	0.18	18	0.58	1.96
PM_{10} Mass	0.95	0.12	12	0.60	1.31
$PM_{2.5}$ EC	0.74	0.17	23	0.17	1.44
$PM_{2.5}$ OC	0.77	0.11	17	0.55	1.22
Total Fungal Spores	1.31	0.21	16	0.31	2.79
Cladosporium	1.20	0.19	16	0.31	2.52
Agricultural Fungi	1.98	0.59	30	0.34	4.92
Alternaria	4.13	1.44	35	0.80	11.72
Endotoxin	1.53	0.46	30	0.62	3.11
Total Pollens	1.17	0.43	36	0.12	4.00

Table 3.4.7-4. Penetration factors and indoor loss rates for selected pollutants		
Species	**Penetration Factor**	**Indoor Loss Rate (per hour)**
Ozone	1.00	2.80
NO_2	1.00	1.00
$PM_{2.5}$ mass	0.95	0.39
$PM_{2.5}$ EC	0.95	0.39
$PM_{2.5}$ OC	0.95	0.39
PM_{10} mass	0.95	0.65
$PM_{2.5\text{-}10\ 5}$ mass	0.90	1.04
Endotoxin	0.90	1.04
Agricultural Fungi	0.90	3.00
Cladosporium	0.90	3.00
Total Fungal Spores	0.90	3.00
Alternaria	0.20	4.80
Total Pollen	0.20	4.80

Table 3.4.7-5: Daily Housing and Activity Related Parameters	
Number	**Variable**
1	Air conditioner use
2	Gas heater use
3	Windows /door position in daytime
4	Windows /doors position in nighttime
5	Vacuuming
6	Kerosene heater use
7	Wood stove use
8	Fireplace use
9	Candles, incense, oil lamp use
10	Stove use for frying or charring food
11	Automatic oven cleaning
12	Gas stovetop use
13	Gas oven use

Table 3.4.7-6: $PM_{2.5}$ Sulfate I/O Ratios in FACES Residences in Different Seasons with Different Windows/Doors Positions and HVAC Operating Modes

Season	Windows and Doors Position[3]	Heating, Ventilating and Air Conditioning[3]	Mean and Standard Deviation of I/O Ratio for $PM_{2.5}$ Sulfate[1]	Mean and Standard Deviation of Estimated Air Exchange Rate (/hr)[2]
Warm	Open	AC=Off	0.72 ±0.16	1.25 ±0.08
		AC=On	0.63 ±0.19	0.75 ±0.09
	Closed	AC=Off	0.55 ±0.22	0.53 ±0.12
		AC=On	0.52 ±0.18	0.47 ±0.09
Cool	Open	Gas Heating=Off	0.70 ±0.18	1.09 ±0.09
		Gas Heating=On	0.63 ±0.15	0.78 ±0.08
	Closed	Gas Heating=Off	0.48 ±0.21	0.41 ±0.11
		Gas Heating=On	0.59 ±0.15	0.63 ±0.07

[1] Determined from Home Intensive measurements and daily time-activity surveys
[2] Estimated from the mass balance equation assuming p=0.95, k=0.39, and Q=0
[3] Window/door position and HVAC use determine more than 70% of variance in SO4 I/O ratio in each season

Table 3.4.7-7: In-transit Pollutant Concentrations	
Species	**In Transit Concentration**
O_3-8hmx	0.30 xC_{out}
O_3	0.30 x C_{out}
NO_2	3.00 x C_{out}
$PM_{2.5}$ mass	49. $\mu g/m^3$
$PM_{2.5}$ EC	7.0 $\mu g/m^3$
$PM_{2.5}$ OC	21.0 $\mu g/m^3$
$PM_{2.5-10}$	11.0 $\mu g/m^3$
PM_{10} mass	60.0 $\mu g/m^3$
Endotoxin	1.00 x C_{out}
Agricultural Fungi	1.00 x C_{out}
Cladosporium	1.00 x C_{out}
Total Fungal Spores	1.00 x C_{out}
Alternaria	1.00 x C_{out}
Total Pollen	1.00 x C_{out}

Figure 3.4.7-1: Average spatial concentration gradients in Fresno and Clovis for $PM_{2.5}$ mass, light scattering, $PM_{2.5}$ OC, $PM_{2.5}$ EC, PM_{10} mass, and $PM_{2.5-10}$ mass expressed as ratios of ambient concentration to central site concentrations

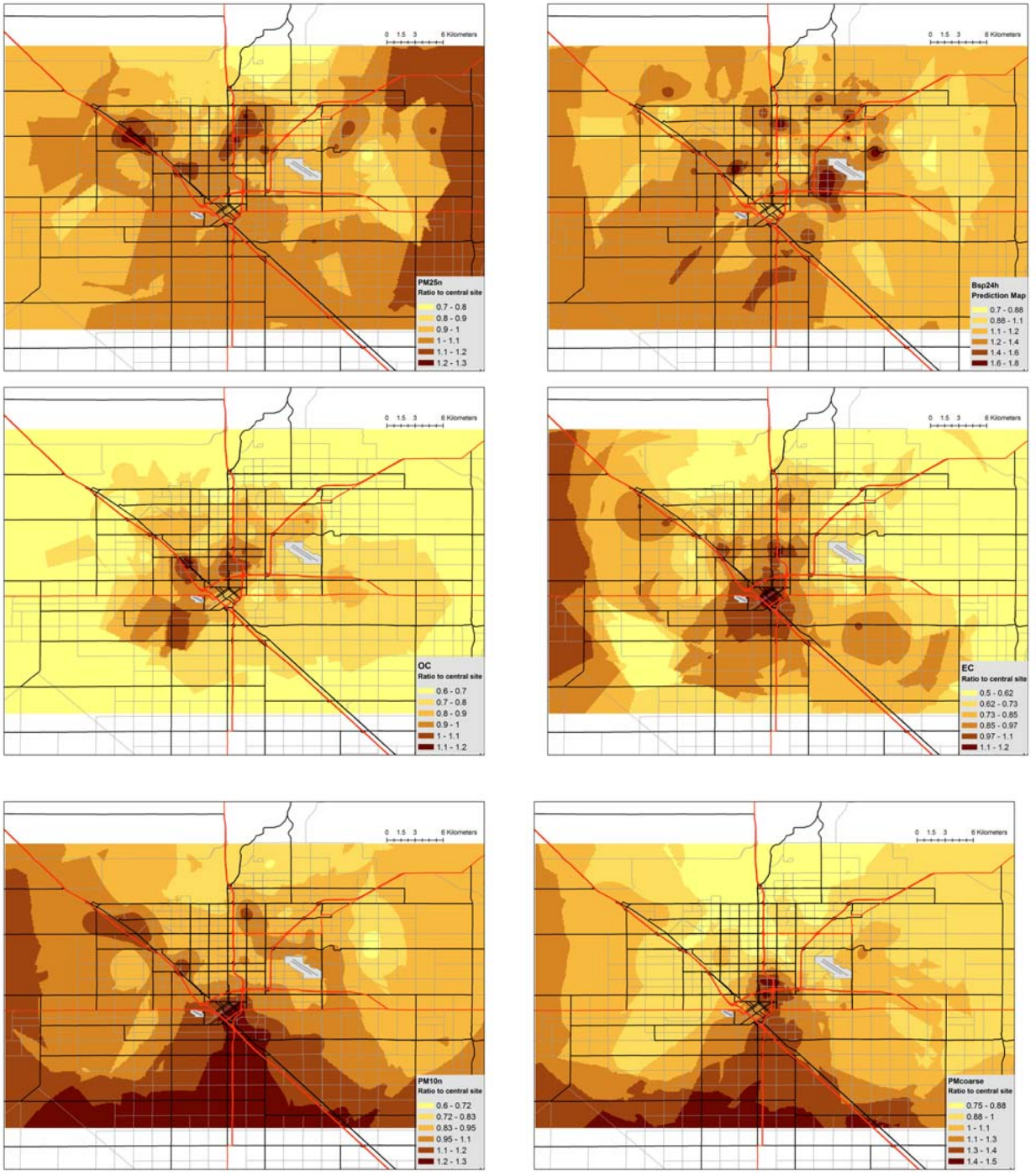
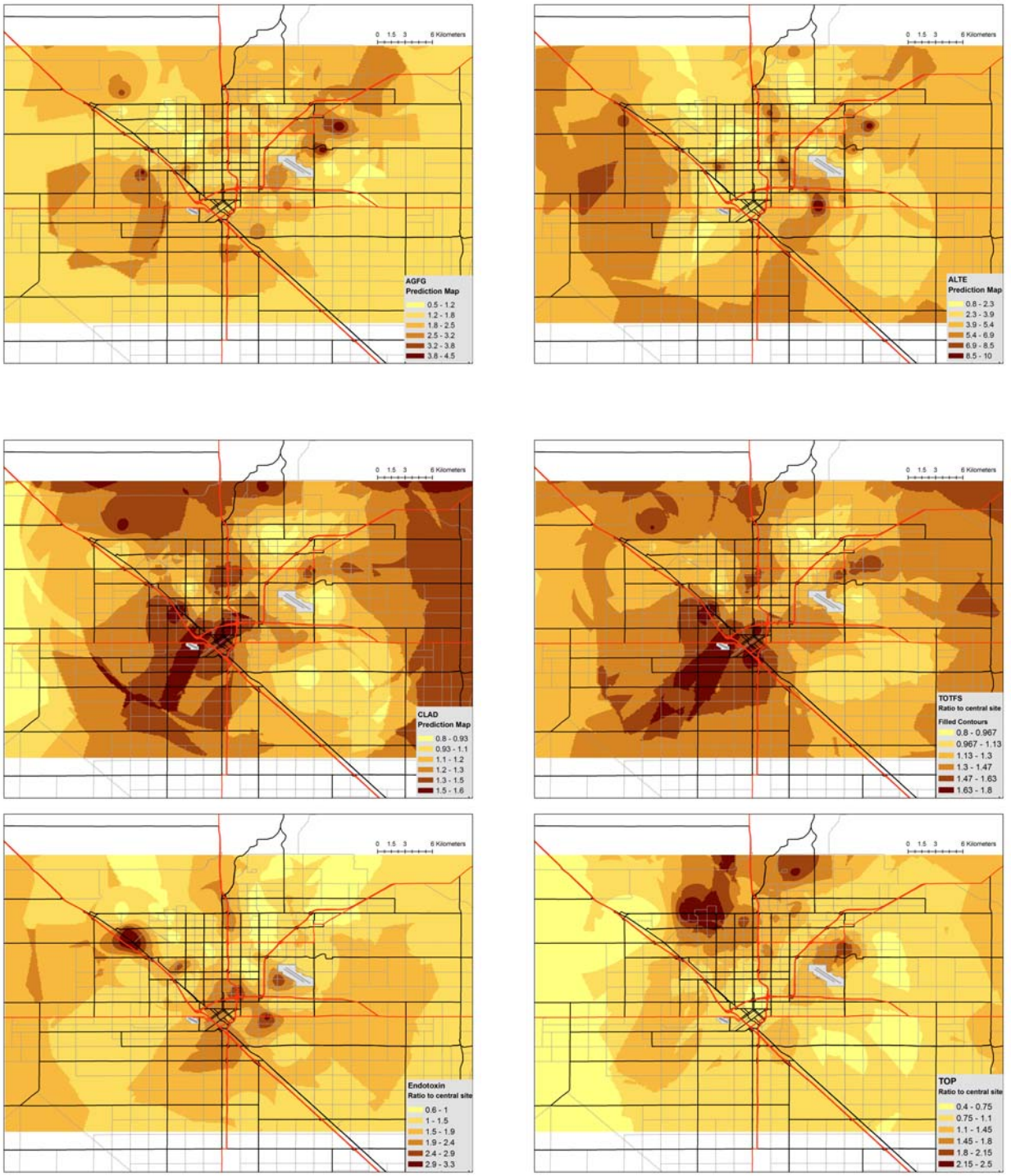


Figure 3.4.7-2: Average spatial concentration gradients in Fresno and Clovis for agricultural fungi, alternaria, cladosporium, total fungal spores, endotoxin, and total pollens expressed as ratios of ambient concentration to central site concentrations



3.4.8 Exposure Metrics

A relational database of exposure metrics has been compiled for use in current and future epidemiologic analyses of FACES data. These data are primarily metrics of daily exposure but also include 14-day average exposures for a subset of agents routinely measured in homes. The time-averaging periods used for the different metrics depend on the type of parameter. Table 3.4.8-1 lists the seven groups of time-averaging periods used for the various metrics. All of the daily exposure metric groups include the 24-hr average. However, since there is potential interest in epidemiologic analyses for days to start at both 8 AM and 8 PM, the data contains daily metrics for averaging periods beginning at both times for most continuously measured parameters.

Table 3.4.8-2 provides a list of the 121 airborne pollutants, biological agents, and meteorological parameters contained in the database. Five to eight daily metrics are provided for many of these parameters. The parameters are grouped into seven types of data: gases, continuous PM, integrated PM, integrated PAH, pollen and spores, meteorological, and panel. Note that the house dust sample chemical composition data are included in a separate database to avoid confusion with the airborne concentration data. The types of locations for which the exposure metrics are available are also listed (central site, ARB trailer (school), SJVAQMD site, FACES residence, etc.). The database for these metrics includes the quality assured and chemically analyzed data collected between 11/1/2000 and 3/31/2003.

Another relational database of modeled individual exposure to pollutants of outdoor origin was compiled for the FACES participants. In addition to panel days, the database includes daily estimates for all FACES subjects on all days between 11/1/2000 and 3/31/2003. The contents of the database are described in Table 3.4.8-3 and include ozone, NO_2, $PM_{2.5}$, EC, OC, $PM_{2.5-10}$, PM_{10}, endotoxin, agricultural fungi, *Cladosporium*, total fungi, *Alternaria*, and total pollens. Estimates were made for 24-hour periods beginning at 8 AM each day for all of the parameters except ozone where both 24-hr average and 8-hour daily maximum individual exposures were estimated. Estimates were not always feasible -99 indicates missing values. For reference purposes, the Central Site ambient concentrations (actual or spatially mapped estimates in place of missing values) are included in this dataset as ID number 9999. In addition, a method code is included for how outdoor concentration values were determined for each individual exposure estimate.

Table 3.4.8-1: FACES Daily Exposure Metric Averaging Times by Group	
Exposure Metric Group	**Time Averaging Periods**
1	24-hr average concentration (8 PM - 8 PM)
2	24-hr average (8 AM - 8 AM) 24-hr average (8 PM - 8 PM) 12-hr average daytime (8 AM - 8 PM) 12-hr average nighttime (8 PM - 8 AM) 8-hr daily maximum (8 AM - 8 AM) 8-hr daily maximum (8 PM - 8 PM) 1-hr daily maximum (8 AM - 8 AM) 1-hr daily maximum (8 PM - 8 PM)
3	24-hr average (8 AM - 8 AM) 24-hr average (8 PM - 8 PM) 6-hr average morning (6 AM - 12 PM) 8-hr average afternoon (12 PM - 8 PM) 10-hr average nighttime (8 PM - 6 AM) 2-hr daily maximum (8 PM - 8 PM)
4	24-hr average (8 AM - 8 AM) 24-hr average (8 PM - 8 PM) 1-hr daily minimum (8 AM - 8 AM) 1-hr daily minimum (8 PM - 8 PM) 1-hr daily maximum (8 AM - 8 AM) 1-hr daily maximum (8 PM - 8 PM)
5	1-hr average at 10 AM, 2 PM, and 8 PM
6	1-hr average at 10 AM, 2 PM, and 8 PM 24-hr average (8 AM - 8 AM) 24-hr average (8 PM - 8 PM) 1-hr daily maximum (8 AM - 8 AM) 1-hr daily maximum (8 PM - 8 PM)
7	Panel duration, typically 14 days

Table 3.4.8-2: Parameters Contained in the FACES Exposure Metrics Database					
Pollutant or Parameter	**Description**	**Units**	**Group**	**Exposure Metric Group[1]**	**Locations[2]**
CO	Carbon monoxide concentration	ppm	Gases	2	CS, SJV
EC	$PM_{2.5}$ elemental carbon concentration from Aethalometer BC	µg/m^3	Continuous PM	2	CS, T
EC	$PM_{2.5}$ elemental carbon concentration by TOR	ug/m^3	Integrated PM	1	CS, HI
Endotoxin	Endotoxin concentration	EU/m^3	Integrated PM	1	CS, T, HI
ETS	Environmental Tobacco Smoke concentration (also known as SHS)	ug/m^3	Integrated PM	1	HI
ETS	Environmental Tobacco Smoke concentration (also known as SHS)	ug/m^3	Panel	7	HR
NO	Nitric oxide concentration by chemiluminescence	ppb	Gases	2	CS, T, SJV
NO_2	Nitrogen dioxide concentration by chemiluminescence	ppb	Gases	2	CS, T, SJV
NO_2	Nitrogen dioxide concentration by Palmes Tubes	ppb	Panel	7	HI, HR
NO_3	$PM_{2.5}$ nitrate concentration by R&P (adjusted)	µg/m^3	Continuous PM	2	CS, T
NO_3tot	$PM_{2.5}$ NO_3 concentration, volatilized N losses corrected, by IC	ug/m^3	Integrated PM	1	HI
NH_4NO_3tot	$PM_{2.5}$ NH_4NO_3 concentration, volatilized N losses corrected, by IC	ug/m^3	Integrated PM	1	HI
NOx	Nitrogen oxides concentration by chemiluminescence	ppb	Gases	2	CS, T, SJV
O_3	Ozone concentration by UV	ppb	Gases	2	CS, T, SJV
O_3	Ozone concentration by IC	ppb	Panel	7	HI, HR
OC	$PM_{2.5}$ organic carbon concentration by R&P	µg/m^3	Continuous PM	2	CS, T
OC	$PM_{2.5}$ organic carbon concentration by TOR	ug/m^3	Integrated PM	1	HI
PH	Aggregated particle PAH concentration by EcoChem	µg/m^3	Continuous PM	2	CS, T
PM_{10}	PM_{10} mass concentration by BAM	µg/m^3	Continuous PM	2	CS, T
PM10n	PM_{10} mass concentration, volatilized N losses corrected	ug/m^3	Integrated PM	1	HI
$PM_{2.5}$	$PM_{2.5}$ mass concentration by BAM	µg/m^3	Continuous PM	2	CS, T
$PM_{2.5n}$	$PM_{2.5}$ mass concentration, volatilized N losses corrected	ug/m^3	Integrated PM	1	HI
$PM_{2.5-10}$	PM coarse mass (2.5-10 µm) concentration by BAM	µg/m^3	Continuous PM	2	CS, T, HI
PN	Particle number concentration	1000/cm^3	Continuous PM	2	CS, T
SO_4	$PM_{2.5}$ sulfate concentration by R&P	µg/m^3	Continuous PM	2	CS, T
SO_4	$PM_{2.5}$ sulfate concentration by IC	ug/m^3	Integrated PM	1	HI
NH_42SO_4	$PM_{2.5}$ NH_42SO_4 concentration by IC	ug/m^3	Integrated PM	1	HI
SP	Light extinction by particle scattering	1/Mm	Continuous PM	2	CS, T, HI
TC	$PM_{2.5}$ total carbon concentration by R&P	µg/m^3	Continuous PM	2	CS, T, HI
TC	$PM_{2.5}$ total carbon concentration by TOR	µg/m^3	Integrated PM	1	HI
RH	Relative humidity	%	Meteorological	4	CS, T, SJV

Table 3.4.8-2: Parameters Contained in the FACES Exposure Metrics Database					
Pollutant or Parameter	**Description**	**Units**	**Group**	**Exposure Metric Group[1]**	**Locations[2]**
T	Temperature	degrees C	Meteorological	4	CS, T, SJV
WD	Wind direction	degrees C	Meteorological	5	CS, T, SJV
WS	Wind speed	knots	Meteorological	6	CS, T, SJV
AG	Silver concentration (in PM_{10})	ug/m^3	Integrated PM	1	CS, T, HI
AL	Aluminum concentration (in PM_{10})	ug/m^3	Integrated PM	1	CS, T, HI
AS	Arsenic concentration (in PM_{10})	ug/m^3	Integrated PM	1	CS, T, HI
AU	Gold concentration (in PM_{10})	ug/m^3	Integrated PM	1	CS, T, HI
BA	Barium concentration (in PM_{10})	ug/m^3	Integrated PM	1	CS, T, HI
BR	Bromine concentration (in PM_{10})	ug/m^3	Integrated PM	1	CS, T, HI
CA	Calcium concentration (in PM_{10})	ug/m^3	Integrated PM	1	CS, T, HI
CD	Cadmium concentration (in PM_{10})	ug/m^3	Integrated PM	1	CS, T, HI
CL	Chlorine concentration (in PM_{10})	ug/m^3	Integrated PM	1	CS, T, HI
CO	Cobalt concentration (in PM_{10})	ug/m^3	Integrated PM	1	CS, T, HI
CR	Chromium concentration (in PM_{10})	ug/m^3	Integrated PM	1	CS, T, HI
CU	Copper concentration (in PM_{10})	ug/m^3	Integrated PM	1	CS, T, HI
FE	Iron concentration (in PM_{10})	ug/m^3	Integrated PM	1	CS, T, HI
GA	Gallium concentration (in PM_{10})	ug/m^3	Integrated PM	1	CS, T, HI
HG	Mercury concentration (in PM_{10})	ug/m^3	Integrated PM	1	CS, T, HI
IN	Indium concentration (in PM_{10})	ug/m^3	Integrated PM	1	CS, T, HI
KP	Potassium concentration (in PM_{10})	ug/m^3	Integrated PM	1	CS, T, HI
LA	Lanthanum concentration (in PM_{10})	ug/m^3	Integrated PM	1	CS, T, HI
MG	Magnesium concentration (in PM_{10}) (qualitative only)	ug/m^3	Integrated PM	1	CS, T, HI
MN	Manganese concentration (in PM_{10})	ug/m^3	Integrated PM	1	CS, T, HI
MO	Molybdenum concentration (in PM_{10})	ug/m^3	Integrated PM	1	CS, T, HI
NA	Sodium concentration (in PM_{10}) (qualitative only)	ug/m^3	Integrated PM	1	CS, T, HI
NI	Nickel concentration (in PM_{10})	ug/m^3	Integrated PM	1	CS, T, HI
PB	Lead concentration (in PM_{10})	ug/m^3	Integrated PM	1	CS, T, HI
PD	Palladium concentration (in PM_{10})	ug/m^3	Integrated PM	1	CS, T, HI
PH	Phosphorous concentration (in PM_{10})	ug/m^3	Integrated PM	1	CS, T, HI
RB	Rubidium concentration (in PM_{10})	ug/m^3	Integrated PM	1	CS, T, HI
SB	Antimony concentration (in PM_{10})	ug/m^3	Integrated PM	1	CS, T, HI

Table 3.4.8-2: Parameters Contained in the FACES Exposure Metrics Database					
Pollutant or Parameter	**Description**	**Units**	**Group**	**Exposure Metric Group[1]**	**Locations[2]**
SE	Selenium concentration (in PM_{10})	ug/m^3	Integrated PM	1	CS, T, HI
SI	Silicon concentration (in PM_{10})	ug/m^3	Integrated PM	1	CS, T, HI
SN	Tin concentration (in PM_{10})	ug/m^3	Integrated PM	1	CS, T, HI
SR	Strontium concentration (in PM_{10})	ug/m^3	Integrated PM	1	CS, T, HI
SU	Sulfur concentration (in PM_{10})	ug/m^3	Integrated PM	1	CS, T, HI
TI	Titanium concentration (in PM_{10})	ug/m^3	Integrated PM	1	CS, T, HI
TL	Thallium concentration (in PM_{10})	ug/m^3	Integrated PM	1	CS, T, HI
UR	Uranium concentration (in PM_{10})	ug/m^3	Integrated PM	1	CS, T, HI
VA	Vanadium concentration (in PM_{10})	ug/m^3	Integrated PM	1	CS, T, HI
YT	Yttrium concentration (in PM_{10})	ug/m^3	Integrated PM	1	CS, T, HI
ZN	Zinc concentration (in PM_{10})	ug/m^3	Integrated PM	1	CS, T, HI
ZR	Zirconium concentration (in PM_{10})	ug/m^3	Integrated PM	1	CS, T, HI
ACE	Acenaphthene concentration (Gas+PM_{10})	ng/m^3	Integrated PAH	1	CS, T, HI
ACY	Acenaphthylene concentration (Gas+PM_{10})	ng/m^3	Integrated PAH	1	CS, T, HI
ANT	Anthracene concentration (Gas+PM_{10})	ng/m^3	Integrated PAH	1	CS, T, HI
BAA	Benz(a)anthracene concentration (Gas+PM_{10})	ng/m^3	Integrated PAH	1	CS, T, HI
BAP	Benzo(a)pyrene concentration (Gas+PM_{10})	ng/m^3	Integrated PAH	1	CS, T, HI
BBF	Benzo(b)flouranthene concentration (Gas+PM_{10})	ng/m^3	Integrated PAH	1	CS, T, HI
BGP	Benzo(ghi)perylene concentration (Gas+PM_{10})	ng/m^3	Integrated PAH	1	CS, T, HI
BKF	Benzo(k)flouranthene concentration (Gas+PM_{10})	ng/m^3	Integrated PAH	1	CS, T, HI
CRY	Chrysene concentration (Gas+PM_{10})	ng/m^3	Integrated PAH	1	CS, T, HI
DBA	Dibenz(a,h)anthracene concentration (Gas+PM_{10})	ng/m^3	Integrated PAH	1	CS, T, HI
FLT	Flouranthene concentration (Gas+PM_{10})	ng/m^3	Integrated PAH	1	CS, T, HI
FLU	Flourene concentration (Gas+PM_{10})	ng/m^3	Integrated PAH	1	CS, T, HI
ICP	Indeno(1,2,3-cd)pyrene concentration (Gas+PM_{10})	ng/m^3	Integrated PAH	1	CS, T, HI
NAPCC	Napthalene concentration (Gas+PM_{10}) from Chemcombs	ng/m^3	Integrated PAH	1	CS, T, HI
NAPST	Napthalene concentration from Sorbent Tubes	ng/m^3	Integrated PAH	1	CS, T, HI
PHE	Phenathrene concentration (Gas+PM_{10})	ng/m^3	Integrated PAH	1	CS, T, HI
PYR	Pyrene concentration (Gas+PM_{10})	ng/m^3	Integrated PAH	1	CS, T, HI
AGFG	Agricultural fungi concentration (see note 3)	$spores/m^3$	Pollen & Spores	3	CS, T, HI
ALTE	Alternaria concentration	$spores/m^3$	Pollen & Spores	3	CS, T, HI

Table 3.4.8-2: Parameters Contained in the FACES Exposure Metrics Database					
Pollutant or Parameter	**Description**	**Units**	**Group**	**Exposure Metric Group[1]**	**Locations[2]**
ASP	Aspergillus/Penicillium concentration	spores/m^3	Pollen & Spores	3	CS, T, HI
CLAD	Cladosporium concentration	spores/m^3	Pollen & Spores	3	CS, T, HI
TOTFS	Total fungal spores (see Note 3)	spores/m^3	Pollen & Spores	3	CS, T, HI
AMB	Ambrosia concentration	pollen/m^3	Pollen & Spores	3	CS, T, HI
ART	Artemesia concentration	pollen/m^3	Pollen & Spores	3	CS, T, HI
BET	Betulaceae concentration	pollen/m^3	Pollen & Spores	3	CS, T, HI
CEL	Celtis concentration	pollen/m^3	Pollen & Spores	3	CS, T, HI
CHA	Chenopodiaceae/Amaranth concentration	pollen/m^3	Pollen & Spores	3	CS, T, HI
CUT	Cupressaceae and Sequoia concentration	pollen/m^3	Pollen & Spores	3	CS, T, HI
JUG	Average Carya and Juglans concentration	pollen/m^3	Pollen & Spores	3	CS, T, HI
LIQ	Liquidambar concentration	pollen/m^3	Pollen & Spores	3	CS, T, HI
MOR	Morus concentration	pollen/m^3	Pollen & Spores	3	CS, T, HI
OLE	Olea, Fraxinus, and Ligustrum concentration	pollen/m^3	Pollen & Spores	3	CS, T, HI
PIS	Pistacea concentration	pollen/m^3	Pollen & Spores	3	CS, T, HI
PLA	Platanus concentration	pollen/m^3	Pollen & Spores	3	CS, T, HI
POA	Poaceae (including Cerealea) concentration	pollen/m^3	Pollen & Spores	3	CS, T, HI
QUE	Quercus concentration	pollen/m^3	Pollen & Spores	3	CS, T, HI
ULZ	Ulmus/Zelkova concentration	pollen/m^3	Pollen & Spores	3	CS, T, HI
TOP	Total Pollen Grain concentration (see note 3)	pollen/m^3	Pollen & Spores	3	CS, T, HI

[1] See Table 3.4.8-1 for definition of the exposure metrics averaging times.

[2] The location codes are defined as:

CS = Central site, ARB's First Street Ambient Air Monitoring Station
T = ARB Trailers located at FACES participants schools
SJV = SJVAQMD Ambient Air Monitoring Stations
HI = Inside and outside FACES residences during the Home Intensive Study
HR = Primarily inside FACES residences during routine panels

Table 3.4.8-3: Exposure Modeling Database Contents	
Parameter	**Description**
peR	Record number
ID	FACES Subject ID
Year	Start Year
Month	Start Month
Day	Start Date
peO_3-8hrmx	Individual exposure to Pollution of Outdoor Origin Ozone 8-hr maximum for 8 AM Start Date to 8 AM Next Day (ppb)
peO_3	Individual exposure to Pollution of Outdoor Origin Ozone 24-hr for 8 AM Start Date to 8 AM Next Day (ppb)
peNO2	Individual exposure to Pollution of Outdoor Origin NO_2 24-hr for 8 AM Start Date to 8 AM Next Day (ppb)
$pePM_{2.5}$	Individual exposure to Pollution of Outdoor Origin $PM_{2.5}$ Mass for 8 AM Start Date to 8 AM Next Day (µg/m3)
peEC	Individual exposure to Pollution of Outdoor Origin $PM_{2.5}$ EC for 8 AM Start Date to 8 AM Next Day (µg/m3)
peOC	Individual exposure to Pollution of Outdoor Origin $PM_{2.5}$ OC for 8 AM Start Date to 8 AM Next Day (µg/m3)
$pePM_{2.5-10}$	Individual exposure to Pollution of Outdoor Origin $PM_{2.5-10}$ Mass for 8 AM Start Date to 8 AM Next Day (µg/m3)
$pePM_{10}$	Individual exposure to Pollution of Outdoor Origin PM_{10} Mass for 8 AM Start Date to 8 AM Next Day (µg/m3)
peENDO	Individual exposure to Pollution of Outdoor Origin Endotoxin for 8 AM Start Date to 8 AM Next Day (EU/m3)
peAGFG	Individual exposure to Pollution of Outdoor Origin Agricultural Fungal Spores for 8 AM Start Date to 8 AM Next Day (spores/m3)
peCLAD	Individual exposure to Pollution of Outdoor Origin Cladosporium Spores for 8 AM Start Date to 8 AM Next Day (spores/m3)
peTOTFS	Individual exposure to Pollution of Outdoor Origin Total Fungal Spores for 8 AM Start Date to 8 AM Next Day (spores/m3)
peALTE	Individual exposure to Pollution of Outdoor Origin Alternaria Spores for 8 AM Start Date to 8 AM Next Day (spores/m3)
peTOP	Individual exposure to Pollution of Outdoor Origin Total Pollen for 8 AM Start Date to 8 AM Next Day (grains/m3)
m(i)	Method codes for how the outdoor concentration is used for each individual exposure estimate listed above

3.5 HEALTH OUTCOMES/ENDPOINTS METHODOLOGY

3.5.1 Development of Health Outcomes and other Endpoints of Interest

3.5.1.1 Spirometry

The application of spirometry to a group of children with asthma posed some problems for quality control. Asthma itself has the potential to increase the variability of lung function measures at a given test session (e.g., post-inhalation bronchoconstriction). In addition, during exacerbations, function can deteriorate and present itself not only as decreased levels of various measures but with further increases in within-subject, within-test session variance (IBT personal observations). Finally, it is well know that young children cannot maintain a forced vital capacity maneuver for 6-seconds, the minimum duration criterion for adult testing (233). Based on the experience of IBT in large-scale epidemiological studies of children and the clinical experience of AF as a pediatric pulmonologist, we set the acceptable duration time to be at least two-sections, provided that all other end of test criteria were met and the curve passed visual quality control. Finally, a decision was made to use a "time to peak flow criterion" of 120 msec, which is based on the adult criteria. However, based on published data (234) and our personal observations, this criterion was too strict to be achieved by children when they were performing the test in an unsupervised environment, as would be the case during the panel studies. Therefore, we extended the acceptability criterion to less than 200 msec for an otherwise acceptable tracing in the panel study data. We retained the 120 msec criterion for the 6-monthly sessions, since these were supervised by a trained technician. Reproducibility was not a criterion for retention of tracings, since changes in variability was an endpoint of interest and, in the face of post-inhalation bronchoconstriction would have lead to the exclusion of tracings that reflect the actual physiology at the time.

To add an additional layer of quality control, it was decided that the tracings from all testing sessions (6-monthly and panel studies) would be reviewed by two of the investigators (IBT, JB) who would ultimately make the final decision for which curves to accept, independent of the machine based criteria . This decision was prompted by the observation that machine decisions often did not agree with visual inspection. IBT and JB regularly "calibrated" each other by comparing results from independently graded tracings. Differences in reading were very rare. After 3-years of following this procedure, a staff member with extensive experience in the administration and interpration of spirometry took over this responsibility(LC). His work was calibrated against JB to ensure quality control. In addition, any tracings where LC was unsure of the classification were referred to IBT for a decision.

3.5.1.1.1 Spirometry for Field Office Visits

A standard rolling seal spirometer (Patrick Morgan Co., Haverhill, MA) was chosen for use in the field office sincethis instrument was used extensively in the University of Southern

California Children's Health Study. The details of this instrument are described in Mortimer et al, 2003.

3.5.1.1.2 Spirometry for 14-Day Panel Studies

This study was originally designed when most published panel studies had relied on self-tracking data such as peak flow meters and hand-written diaries to assess asthma morbidity. Although these studies have been extremely useful in the identification and documentation of variations in pulmonary function and symptoms, this method of data collection has important limitations that we hoped to overcome in our study. In both studies and in clinical practice, peak flow monitoring compliance has been poor. Traditional peak flow and symptom diaries limit the investigators ability to identify falsified readings or to assess the technique of the recorded maneuver. Completion of diaries can often be tedious and confusing, particularly for children, or those individuals from low-literacy or non-English speaking populations. Peak expiratory flow (PEFR) is an effort–dependent measurement that requires frequent re-training and is subject to transcription errors,decreased data quality, and compliance over time (235). It is mainly a measure of large airway caliber and does not fully capture all aspects of pulmonary function—in particular, PEFR does not reflect changes in small airways that occur over time from O_3 (236-239) and NO_2 (240) exposure -pollutants known to have their greatest effects on the respiratory bronchiole portion of the lung.

We tested an array of hand-held, electronic spirometers and collected measures including PEFR, FEV_1, FVC, FEF_{25-75} and FEF_{75}. FEF_{75} is particularly important since it is a measure indicating respiratory bronchiole function , thesite of maximum deposition of ozone and NO_2 in the lung. For all devices each entry is marked with the date and time that each measure was collected. Many of the devices included quality control software to ensure proper technique was used before a measure is recorded. The instruments had been developed for clinical, rather than epidemiological use, consequently most devices have visual indicators, which provide feedback to the participants, indicating whether they were in the "Red/ Yellow/ or Green" zones (53). Some instruments also included an option for asking questions, such as 'Did you take any medications today?" We evaluated several devices:the Asthma Monitor 1 (Ferraris Medical, Holland NY), Airwatch (ENACT, Mountain View, CA), Simplicity (Mallinckrodt, St. Louis MO) AccuTrax (Korr Medical Technologies, Inc. Salt Lake City, Utah) and the *EasyOne*® (ndd, Chelmford, MA}. We selected the *EasyOne*® for several reasons: 1) the company was able to modify the software to meet our specific needs; 2) it met all of the performance requirements specified by the American Thoracic Society (233); 3) the Access database where the data is downloaded made it very easy for electronic transfer to to analysis-ready SAS data sets; 4) the paper reports provided easy to read flow and time-volume curves for quality control; 5) the company provided quality control measures on the paper reports in addition to the spirometric measures of interest; 6) questions could be programmed into the spirometers for completion after the morning and evening test sessions.

To determine if the *EasyOne*® would give comparable results to those obtained with the rolling seal spirometers, we designed a tandem system in the field office such that the *EasyOne*® became the mouthpiece for the rolling seal spirometers. The details of this testing and the setup have been published (1) (see Appendix C). Results confirmed that the two instruments gave

completely interchangeable results with the exception of FEF_{25-75}. Differences in the results can be explained by different end-of-test criteria for the two instruments -zero flow for the rolling seal and ≤20 ml/sec averaged over the last 2 seconds.

3.5.1.2 Asthma Symptoms

We asked the adult caregiver of each participant questions about their child's asthma symptoms every 3-months (every 6 months at the FO and every 3 months for the telephone questionnaire) (see Appendix A). The questions asked were based primarily on the International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire, but also included questions from the Children's Health Study and the International Union Against Tuberculosis and Lung Disease (IUATLD) questionnaires. For the analyses reported in the results section , we focus on wheeze and cough, two symptoms of asthma. We selected these two symptoms for the initial analyses of potential associations between air pollutants and asthma, because most children wheeze when their asthma is active; those that do not wheeze when their condition worsens often experience increased cough instead (cough-variant asthma). During the 3-monthly telephone contacts, we asked whether, and if "yes" how frequently, the study children had experienced wheeze (or cough if cough-variant asthma had been previously identified) in both the past 3 months and past 2 weeks. In addition, during the 2-week panel studies, each child answered symptom and rescue medication questions that were programmed into the *EasyOne*® spirometer two times per day (morning and evening) after s/he performed spirometry (See Appendix C). Again, wheeze and cough were the two symptoms that questions were asked about.

3.5.1.3 Classification of Asthma Severity

Asthma severity is one of the main study outcomes. Disentangling control of asthma with medications from the underlying severity of disease presents a difficult but essential challenge for the longitudinal portion of the study, since treatment with medications can modify the short-term responses to such exposures (41). The updated GINA classification scheme for asthma severity includes symptoms and lung function components and recognizes that treatment with medication can modify these components (241). Each of these components can be affected by changes in ambient pollutants, and can influence the other. We needed to develop a quantifiable approach to classify asthma severity , that captures variability among the population, and can be used to rate children repeatedly over time.

No single severity classification scheme, which includes the original GINA approach, was satisfactory. Therefore, we developed and prospectively evaluated a multi-component approach (see Appendix H). Four different schemes were evaluated: 1) an integrated scoring scheme, previously evaluated in adults, that was modified for children and includes symptoms, medication use and health utilization history (pediatric Blanc score) (242); 2) a newly developed medication step scheme based on GINA treatment recommendations; 3) the symptom/disability component of the GINA step scheme; and 4) the pulmonary function component of the GINA step scheme. These four schemes were applied to baseline questionnaire and spirometry data for the 302 children, who were enrolled at the time of the analysis, to assess the distributions across severity categories for each scheme. Regression models were developed to evaluate how well

each scheme predicted subsequent asthma symptoms, health care utilization, and disease-specific disability reported at 3-month intervals. Receiver operator curves (ROC) were derived from these models.

The GINA symptoms step, the medication step, and the pediatric Blanc scoring schemes provided reasonable distributions of severity, but the GINA pulmonary function step scheme did not classify many children (n=5) as having moderate or severe asthma. The range of C statistics are presented in Table 3.1.1-1. The predictive power of each of the schemes for subsequent asthma outcomes was generally low. The GINA symptoms step scheme showed the best overall performance. The pediatric Blanc score was most likely to predict subsequent physician visits for asthma care. The GINA pulmonary function scheme had the worst predictive power in nearly every case. Addition of demographic covariates to the regression models somewhat improved the predictive power of the GINA symptom scheme (area under ROC range, 0.65-0.70). These results support other studies (243) that suggest lung function should not be used as the sole criterion for classifying asthma severity in children but that assessing symptoms, disability, health care utilization, and medication use should also be considered. Based on these results, we plan to use the GINA symptom scheme and pediatric Blanc scores to assess asthma severity over time.

3.5.1.4 Skin-prick Tests and Designation of Atopic Status

Subjects were asked to abstain from using long-acting antihistamines for the 24 hours prior to testing, if possible. However, testing was performed even if subjects were taking antihistamines and this medication use was recorded.

Skin-prick allergen sensitivity tests were performed using the MultiTest device (donated by Lincoln Laboratory, Decateur, IL). Saline and histamine controls, and 14 antigens (Hollister-Stier, Spokane, WA) relevant to the Fresno environment were evaluated. The antigens included Bermuda grass, standardized cat pelt, standardized mite mix (D *pteronissinus, D. ferinae*), Olive, Standardized grass pollen (perennial Ryegrass), Chinese Juniper, Oak mix, Mugwort Sagebrush, *Alternaria tenuis*, dog hair and dander, *Cladosporium*, cockroach mix, Common Privet, and Mountain Cedar. Wheal size was measured as the average of two perpendicular lines, one of which marked the longest dimension of the wheal.

A positive test was defined as a wheal ≥3 mm larger than the saline control in the presence of a positive histamine control. If all antigen responses were negative in the presence of a negative histamine reaction, testing was considered indeterminate. A positive response to antigen in the presence of negative saline and histamine controls was considered positive.

Atopy was defined as one or more positive skin tests. A test was classified as negative for the purpose of this analysis if a subject completed the entire test, failed to respond to any antigen and the histamine control was positive. Not all children were skin-tested; therefore an additional measure of atopy was defined based on the child *ever* having been diagnosed by a physician as having hay fever or allergic rhinitis. The alternative definition has only been used in the traffic analysis where the two variables for atopy were evaluated independently.

Table 3.5.1-1: Range of Area Under the Receiver-Operator Curves (C-Statistic) for Various Asthma Severity Classification Algorithms	
Outcomes	**Range**
MD visit, past 3mo	0.51-0.63
Wheeze, past 3mo	0.55-0.61
Wheeze, past 2wk	0.55-0.60
Missed school, past 3mo	0.55-0.63
Missed school, past2wk	0.51-0.62
Missed sports, past 3mo	0.54-0.64
Missed sports, past 2wk	0.54-0.63
Missed sleep, past 3mo	0.54-0.63
Missed sleep, past 2wk	0.55-0.65

3.5.2 Health Outcomes Included in the Analyses in the Final Report

3.5.2.1 Acute Effects

The principal aim of analyzing various lung function metrics is to obtain individual level estimates on the causal relation that acute changes in ambient pollutants may have on these measures. In other words, we are creating a set of regression parameters that characterize acute functional responses to acute changes in various ambient pollutants.. Ultimately, we will analyze the various function measures that were obtained, with our principal interest on measures related to small airways (primarily FEF_{75} and, secondarily FEF_{25-75}). We are also interested in the modifying effect of the FEF_{25-75}/FVC ratio, which is an estimate of intrinsic small airway size (244), has been shown to be a sensitive measure in asthma (245), and has been shown to modify the functional response of small airways to long-term ozone exposure (239). However, due to time constraints we limit the analysis in this report to FEV_1 and to single pollutants (e.g. $PM_{2.5}$), with other pollutants treated as confounders. We began the analysis with FEV_1, due to its long history of use in respiratory epidemiology and its predictive capacity for future adverse cardiopulmonary outcomes (246).

The choice of other asthma outcomes is complex. There is no generally accepted definition for an exacerbation of asthma (247), and although we have developed a working definition (see section 3.5.1), we will focus mainly on simpler outcomes that can be measured easily on a daily basis (almost all definitions of an exacerbation require more than a single day's observation). The principal outcomes are acute medication use, wheeze, and cough as reported on the questions completed at each home lung function session. For this report, we report only on acute medication use for some analyses. We focus on medication use, since it can modify the lung function or symptom response to acute exposures to ambient pollutants and/or be modified by such exposure and it has been an area of interest for a number of investigative teams.

3.5.2.2 Chronic Effects

The two endpoints for this set of analyses are growth of various measures of lung function and asthma severity in relation to time-dependent responses to acute changes in air pollution, i.e., the regression coefficients that describe each individual child's response to acute changes in daily ambient concentrations of pollutants are the "exposure" for these analyses. For this report, we focus only on changes in pulmonary function growth (FEV1) relative to acute response to NO_2.

3.6 STATISTICAL ANALYTIC METHODS

3.6.1 Overview of Health Analyses in Final Report

As mentioned above, the overall FACES study has two classes of endpoints that can be related to the two components of the study: lung function measures and asthma symptoms and severity. They are addressed in this section from the point of view of the statistical analyses that we are undertaking.

3.6.2 Motivation for Use of Marginal Structural Models (MSM)

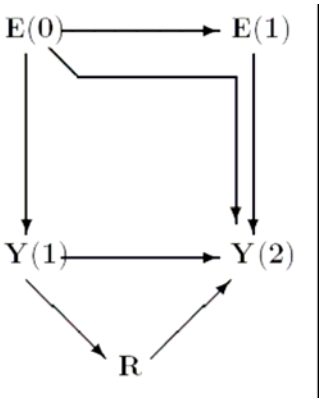


Figure 3.6.2_1: Directed acyclic graph of simple data structure

(**NB:** This section briefly summarizes the more technical presentation in Appendix I, which should be read for a full explanation of the theory and application of this method. Some of the material in this section is found verbatim in Appendix I for continuity of reading.) We have chosen to base our primary inferences on analyses carried out with MSMs. The major motivation for the use of MSMs is to investigate the short-term effects of air pollution on asthma responses in the presence of time-dependent confounders that also are on one of the causal pathways defining the effects of interest. It is now well known (2), traditional analyses based on association models typically lead to a biased estimation of causal effects in the presence of time-dependent confounders.

To illustrate this issue and emphasize the importance of MSMs , we consider the following question of interest: "What is the short-term causal effect of a two-day exposure to ambient concentrations of $PM_{2.5}$ on morning FEV_1 measurements in the cohort?". A simplifed version of the panel data that could be used to answer this question contains the following variables: (1) the exposure variables: $PM_{2.5}$ levels on 2 consecutive days denoted with $E(0)$ and $E(1)$; (2) the outcome variable: morning FEV_1 after exposure to $PM_{2.5}$ over 2 days, denoted with $Y(2)$; (3) 2 time-dependent covariates: FEV_1 measured in the evening prior to outcome report denoted with $Y(1)$ and rescue medication use during the night prior to outcome report denoted with R. The directed acyclic graph (DAG) (Figure 3.6.2-1) represents the assumed relationships between these variables. It is important to note that for any given question, more than one DAG could be drawn and tested. Note, however, that the general MSM

methodology and, thus, the inferences made in this study are not based on the assumption of a DAG. Instead, they rely on a weaker time-ordering assumption that is a consequential tothe data collection protocol. We only use a DAG here for illustration and clarity. Indeed, the DAG just makes explicit the causal (in contrast to associational) relations that are being considered in the data.

Note that the effect of rescue medication on morning FEV_1 is confounded by the level of FEV_1 in the evening prior to the outcome report. This hypothesis has been verified in analyses of our data. In this example, the question of interest, *a priori,* could be answered by regression of the outcome on the 2-day history of exposure with association models. Indeed in this simplified data, the level of $PM_{2.5}$ is randomized, i.e. its effect on FEV_1 is not confounded by any variables. Therefore, an association analysis could provide an estimate of the causal effect of $PM_{2.5}$ on FEV_1. However, this approach does not allow investigation of the true $PM_{2.5}$ effect of interest i.e., the effect of $PM_{2.5}$ on FEV_1 *if no subject were to use their rescue medication*, which provides the population-level estimate of the effect of $PM_{2.5}$ itself on FEV_1 in children with asthma. Failure to account for rescue medication use may lead to underestimation of the true causal effect of interest. A naive, alternative approach which considers the joint effect of $PM_{2.5}$ and rescue medication use would consist of regressing the outcome on the 2-day history of exposure and rescue medication, with adjustment for any confounders of the effects of both the exposure and rescue medication variables. Such an approach would include the measurements of evening FEV_1 as a covariate and, thus, adjust for a variable that is on one of the causal pathways of interest. This approach leads to a biased estimation of the effect of interest (2). An MSM approach can be used to overcome this problem. In addition to the compelling argument described above in favor of an MSM approach, one should also note that MSMs provide a more appropriate investigation of the effects of interest, since in MSM analyses the causal parameter of interest can be defined as a causal effect adjusted only for the variables that define subgroups of interest. An association model analysis does not necessarily allow investigation of such effects, since one has to adjust for all confounding variables and the effect estimate is conditional on the values of the covariates in the model. The estimated effect then, at best (i.e. if there is no time-dependent confounders on a causal pathway of interest) can be investigated for population subgroups as defined by all the confounding variables. Such subgroups are typically not of interest from epidemiological and policy making viewpoints. In contrast, the MSM estimates the causal effect of the pollutant, with no other covariates in the model since these covariates are included only in the treatment model, as described in Appendix I.

To understand the concepts behind MSMs, the concept of counterfactuals has to be introduced. The idea of counterfactuals is not new and can be traced back to Hume and Neyman, (248) and to R.A Fisher in more modern times (249). Simply put, the data that we observe for each subject in a given study represents only one exposure possibility and only one possible outcome that the subject could have experienced. However, the subject could have experienced a different exposure that potentially resulted in a different outcome. These counterfactual outcomes (or exposure-specific outcomes) represent missing data for that subject, and the MSM analyses can be seen as a missing data problem ((2)--again, not a new idea (e.g. see (250). Three basic assumptions are required for the estimation of MSM parameters: 1) the observed data are a censored representation of all the possible counterfactuals for a given subject, also known as "consistency assumption"; 2) the exposure precedes the response, also known as "time-ordering assumption"; and 3) there are no unmeasured confounding variables, also known as "sequential

randomization assumption" (at each time point, exposure is randomized with respect to the counterfactual outcome, given past exposure and past covariates) (2). In addition, the experimental treatment assignment assumption insures that inferences about MSM parameters do not rely on guessed models or model extensions. The importance of this assumption (for a given past exposure regimen, the set of all possible exposure regimens at time *t* is not affected by the pattern of covariates—i.e., all possible exposure patterns are present in the observed data) was underlined during the course of this study. This later requirement is a *sine qua non*, in practice and theory for consistent estimation of MSM parameters with the inverse probability of treatment weight estimator—so called-IPTW (251, 252).

For readers who are not familiar with the MSM terminology, we have provided a simplified, non-technical explanation of the ETA and SRA assumptions which are so essential to these methods. The term SRA (sequential randomization data) is used for longitudinal data and the term "no unmeasured confounder (NUC) is reflects the parallel concept used for point-treatment studies. Both assume that there are no unmeasured factors that are related to the probability of exposure (or what the MSM literature calls *treatment*). Before describing how this fits in the MSM analysis, it is important to say that this assumption is not unique to MSMs and *always* is needed for traditional modeling techniques as well. We always assume (but often fail to state explicitly) that the estimates we obtain in a study are valid only if there is not some unmeasured factor that is related to the exposure and outcome that is not considered.

Consider a simple point-treatment study that examines the impact of one exposure variable (e.g. yesterday's $PM_{2.5}$) on an outcome (today's FEV_1). Proper estimate of the $PM_{2.5}$ effect requires that there are NUC, i.e.. other variables that influence both FEV_1 and $PM_{2.5}$ but are not measured and, therefore, cannot be included in a model for this effect. Note that, in a point treatment study, one can consider the effect of multiple treatments (exposures) (e.g. yesterday's ozone and yesterday's $PM_{2.5}$) on an outcome (today's FEV_1); but the treatments must occur at the same time.

The sequential randomization assignment assumption is a generalized version for of the 'no unmeasured confounder' assignment that applies to point-treatment data. Consider a more complicated model where we are interested in the effect of several treatments that do not happen at the same time in relation to some outcome. Suppose a clinic trial is conducted and people are randomized to drug A or B at time 1 and then, 6 months later, an outcome is measured. Then suppose that the drug is randomly assigned again and, 6 months later, another outcome measure is obtained. If the randomization at each time point really worked, there should be no covariates which are related to the probability of receiving a treatment at each time point; therefore, the treatment cannot be confounded. If the treatment was not randomized but was based on a measured covariate (such as sex), then one can adjust for sex in the model to obtain an unconfounded estimate. The problem arises if, for example, the person just gets to chose what drug they take next and bases the choice on how the drug affect him/her. In this case, we do not have data on the covariate that determined the probability of treatment; and, thus, the SRA assumption is violated. In this case treatment was not randomized at each time point, and there are unmeasured factors (those that influenced the subject's choice) that influence which treatment was assigned. This is an example of time-dependent confounding. An analogous situation may occur in a longitudinal analysis of the effect of estimated individual-exposure to air pollutantson pulmonary function data If exposure to high concentrations of a pollutant, e.g.,

$PM_{2.5}$--causes a child to have symptoms, the child may choose to stay indoors on subsequent high pollutant days, thereby modifying his/her estimated individual-exposure level of $PM_{2.5}$ (NOTE: These estimated individual exposures are adjusted for the amount of time spent outdoors while the central-site exposure measures do not take individual-levels behaviors into account.).

Experimental Treatment Assignment Assumption (ETA)

This assumption is needed for the IPTW estimator to be consistent but is not necessary for the G-computation or double-robust estimators to be consistent. Much of the MSM literature was developed with randomized studies in mind; and, therefore, refers to "exposures" as "treatments." Hence the "T" in ETA refers to exposures. The assumption requires that the assignment of treatment be considered under different "experiments". In other words, for each combination of possible confounders, the treatment should not be assigned deterministically to each subject, with a probability of treatment equal to 0 or 1. For example, we are interested in the effect of medication use (our treatment) on FEV_1 (our outcome); and we think this could be confounded by morning wheeze (our covariate). Assume everyone who wheezed in the morning took rescue medication. Then, the probability of treatment (medication use) is equal to1, if wheeze occurred. Therefore, it would be impossible to disentangle the effect of medication use on FEV_1 from the effect of wheeze on FEV_1, because of this 1-to-1 relation between medication and wheeze. Before undertaking an IPTW analysis, one must evaluate whether the treatment of interest was assigned deterministically – i.e.; are there characteristics of the population that determined that treatment was always or never assigned. Similarly for observational data, are there characteristics that define who could never be exposed or who would always be exposed. This is common in occupational studies, where certain job classifications assign exposure deterministically by definition. IPTW could not be used in these settings. After the final model for the IPTW weights has been identified (through cross-validation or some model selection process), one should confirm that the ETA holds in practice as well as in theory.

Readers who are more familiar with the IPTW methods will note that the goal is to re-weight the population to remove confounding. If these certain outcomes *never* occurred for a subgroup defined by certain characteristics, there are insufficient data to estimate the effect, even in a reweighted population (i.e. reweighting a number by zero results in zero). Indeed, if the ETA assumption is violated in theory; then, the IPTW estimator will not be consistent. If the ETA assumption is violated practically; then, the finite sample performance of the IPTW estimator will not be very good either.

At its core, the ETA assumption is an assumption about the information contained in the data. If the ETA assumption is violated, then this means that there is insufficient information in the data to disentangle the effect of the treatment from the confounders' effects. This will be true for any statistical method that aims at estimation of an MSM parameter.

In theory, the G-computation or Double Robust (D-R) estimators can properly estimate the MSM coefficients even when the ETA assumption is violated. However, it is important to realize that the practical results produced by these estimators will then heavily depend on model assumptions instead of real information in the data. Both estimators will use model extrapolations to disentangle the effect of the treatment from the effects of confounders, since there is insufficient information in the data to do so.

In summary, if the ETA is violated; then, the only avenue to achieve a consistent estimator is to use the G-computation or double robust estimators. Since these estimators will rely on model assumptions (which are not testable), we still might get a biased estimate if the models used are mis-specified (likely scenario). In this case, it is difficult to determine which is the best estimator to use (although, in theory, the D-R has the greatest chance of being consistent) and inference on causal estimates of effect will be compromised.

As discussed in future sections, the MSM analyses presented in this final report were obtained with G-computation estimation, not with IPTW estimation. For both methods, the SRA assumption must be met. The ETA assumption is not necessary for G-computation to be consistent. We had subject-matter knowledge that led us to believe that the ETA would be violated in our data; therefore we devoted our resources to the implementation of G-computation. Further evaluation of the $PM_{2.5}$ suggests by and large, the ETA is met and we will be able to implement IPTW in future analyses.

3.6.3 Summary of Three MSM Estimators

Inference about MSM parameters (in our case, the unit effect of a given pollutant on the outcome) can be based on three estimators: (1) the Inverse Probability of Treatment Weighted (IPTW) ((251, 253)); (2) G-computation (G-comp) ((254, 255)), and (3)Double Robust (DR) estimators ((251, 256)). The differences between these three estimators are explained in Appendix I. Basically, the consistency property of each estimator relies on different model assumptions. For the analyses presented in this report, the G-computation estimator was preferred due to a potential violation of the ETA assumption but all estimators will be considered in subsequent analyses.

3.6.4 Non-Parametric MSM Causal Effects and History-Restricted MSM

In the course of carrying out the analyses for FACES, two drawbacks of the current MSM methodology became apparent. To address this issue, two of the investigators (MvdL, RN) developed nonparametric MSM causal effects and *history restricted MSM*s (HRMSM) to address both issues. Nonparametric MSM causal effects were developed as an alternative to the current parametric MSM approach for which the investigation o*f causal effec*ts relies on the assumption of a correctly specified parametric MSM. Non-parametric MSM causal effects generalize the concept of causal effects as introduced originally by the parametric MSM approach. Causal inference with non-parametric MSM does not rely on the assumed correct specification of a parametric MSM but, instead, defines causal effects based on a user-specified working causal model (255).

HRMSM were introduced as a new class of MSMs that allows investigators to analyze the causal effect of a treatment on an outcome based on a fixed, shorter and user-specified history of exposure compared to previous MSM approaches, which used all past time for capturing the exposure history—i.e., the latter represents the treatment causal effect of interest based on a treatment history defined by the treatments assigned between the study's start and outcome collection. Beyond allowing a more flexible causal analysis, the proposed HRMSMs also mitigate computing issues related to MSMs (255) as well as statistical power concerns when

designing longitudinal studies. This new class of MSMs can be viewed as an alternative causal inference tool to MSMs. We argued based on practical considerations that an HRMSM-based causal inference strategy often may be more suitable than an MSM-based causal inference strategy for Public Health research. We believe these considerations should motivate the use of this methodology in many practical applications and in particular in this project. Indeed HRMSMs, when coupled with the recently developed data-adaptive method for model fitting (see below) provide greater flexibility in the evaluation of air pollution lag effects. Once the investigator specifies a specific time frame over which the effect of the pollutant exposure is of interest, the data-adaptive model selection procedure for MSM can provide guidance on how each level of the pollutant during the specified time frame should enter the model of the causal relationship between the pollutant and asthma outcome.

3.6.5 Data-Adaptive Estimation/Model Selection and Application of the Deletion/Substitution/Addition (DSA) Algorithm

A general cross-validated data-adaptive estimation/model selection procedure recently developed by one of the investigators (257) can be used to select models for the g and FX part of the likelihood on which the IPTW, G-computation and DR estimators rely (see Appendix I). The same methodology can be used to perform a causal model selection procedure to better characterize causal effects. This procedure is preferred over more conventional methods to optimize a model fit because of 1) the limitations of a more traditional model selection procedure with missing data; 2) recent promising theoretical and practical results associated with this methodology (257); and 3) a recent real-data comparison between this approach and more traditional approaches in the literature based on the Akaike Information Criterion (AIC). One compelling argument for a model selection procedure based on cross-validation is the presence of missing data in observational studies. Model selection criteria like AIC or the Bayesian Information criteria (BIC) only allow comparison of models fitted on the same number of observations. This typically leads to an important loss of information. Cross-validation procedure allows comparisons of a model fitted with different number of observation and, thus, can be used in this context to better compare models without loss of information. In addition, it should be noted that model selection procedures for causal models have not been treated in the literature until the recent development of this general cross-validated data-adaptive model selection procedure. One important new theoretical result establishes that data, even finite samples, contain enough information to engage in an intensive data adaptive search among all candidate estimators if employing cross-validation to select the models that is used to answer the question of interest in practice. Thus a model selection procedure based on cross-validation methods can be combined with the recently developed Deletion/Substitution/Addition (D/S/A) algorithm that. The D/S/A algorithm generates candidate estimators to perform an intensive and thorough search among the space of possible models; was developed, implemented and tested (258) as part of this new model selection procedure.

3.6.6 Strategies for Handling Missing Data

Causal inference can be viewed as a missing data problem and it should not surprise the reader that this approach is based on the same general methodology used for MSM estimation.

We can divide the type of missing data in two categories: 1) missing data for the variables which do not appear in the MSM but which are used in models for the nuisance parameters; and 2) missing data for the variables in the MSM (i.e. the outcome, (Y), treatment, (A) and, baseline covariates, (V)).

Both types of missing data could be ignored without loss of consistency if the censoring mechanism is believed to be uninformative (at random), i.e. one can simply drop the observations for which data are missing (e.g. if air pollutants are not measured due to material failure). However even for such uninformative missing data, one of the approaches described in appendix I may result in increased estimation efficiency by capturing potential empirical confounding. Informative censoring for both types of missing data can be handled as described in Appendix I.

3.6.7 Repeated Measures

The panel study component involves repeated measures within a panel and repeated panels. The discussion of how we propose to address this feature of the data is technical and is best read in Appendix I, which presents a clear strategy.

3.6.8 Methods for the Conventional Analysis of Short-term Effects

This section provides a detailed description of the model development for an examination of the effect of estimated individual exposure to $PM_{2.5}$ on A.M. FEV_1. Similar steps were used for estimates of individual exposure to NO_2 and for Central Site measurements for $PM_{2.5}$, NO_2 and NO, which are described in Sections 3.4.7 and 3.4.2 (also see Appendix I).

For the personal estimates of $PM_{2.5}$, we restricted our analyses to the months of October through February since $PM_{2.5}$ levels are highest and most variable during these months in Fresno. In contrast, $PM_{2.5}$ levels are low for the remainder of the year and little variation is seen. Despite this restriction, the range of $PM_{2.5}$ levels included the low levels seen during the remainder of each year. Ozone levels are very low during these months and are not considered as a possible confounder. The estimated individual exposures to $PM_{2.5}$ were derived from the models discussed in section 3.4.6.

We used the data-adaptive estimation/model selection procedure with the DSA algorithm (see section 3.6.5 for explanation) to select the best mean regression models, i.e., best in the sense that it predicts FEV_1 measurements best. The data-adaptive model selection procedure chooses the best model based on V-fold cross-validation, i.e., it selects the model with the smallest cross-validated risk (residuals). We used 5-fold cross-validation and constrained the model search. Specific constraints are discussed in the appropriate sections that present results of this approach.

For each pulmonary function testing session, the outcome measure was defined as the mean of two (or three) FEV_1 values that were graded as "acceptable" by our reviewers (See Section 3.5.1.1). If fewer than two acceptable efforts were available from that session, the FEV_1 value was set to missing. This missing value occurred for 7% of the completed panel-days.

Additional panel-days were missing because a child did not complete the efforts for a given session due to illness or because s/he was unable or unwilling to perform the test on that day. This censoring is not addressed in the conventional model analysis, but is discussed in detail in the MSM analysis section (Section 3.6.5). We limited the analysis to morning measures only for several reasons. First, morning values are better indicators of asthmatics who are susceptible to airway narrowing (259) asthma exacerbations. Therefore, use of morning measures may identify children at greater risk for adverse health outcomes. The most severe bronchoconstriction occurs in the morning when measurable differences between and within individuals may be greatest. Second, evening measures are more likely to be influenced by recent use of rescue or controller medication during the day, which may attenuate the association between air pollution and lung function. Third, we presently have incomplete individual-level information to adjust for time the child spent outdoors or exercising, both of which affect respiratory dose(260) . Finally, if we were to include both a morning and evening measure, the lag structures are not comparable and would be difficult to interpret. For example, lag 0 represents the exposures that occurred in the 24 hours prior to the morning measurement, whereas for the evening measures, that same lag 0 value would represent the exposures that occurred 12 to 36 hours earlier.

For the $PM_{2.5}$ season (October to February of each year), a total of 4032 morning panel sessions were collected from November 2000 – March 2003. Of these, 3111 had at least 2 acceptable FEV_1 tracings. A session was not completed on 696 panel days and fewer than two of the FEV_1 tracings were acceptable for the remaining 225 days. There were 484 panel days where $PM_{2.5}$ data were not available from the Central Site due to maintenance or instrument problems, electrical power outages, and data system issues that occurred mostly during the second winter (2001). These missing data were imputed based on light scattering data from the Radiance Research nephelometer (with an RH-controlled heater) along with trailer data. These data were highly corrected (r^2>0.88) with $PM_{2.5}$ mass at Fresno First St during the cool season. Missing 12-hour daytime $PM_{2.5}$ mass was estimated from 0.262*[Neph - 12hr daytime] (r^2=0.902). Missing 12-hour nighttime $PM_{2.5}$ mass was estimated from 0.230*[Neph - 12hr nighttime] (r^2=0.886). After imputation there were no missing values for ambient $PM_{2.5}$, and only 14 panel days for which estimated individual exposure to $PM_{2.5}$ were not available, all from one child.

In order to facilitate ease in reading, specific details of the modeling are presented in the Results section.

3.6.9 Chronic Analysis of Acute Pollutant Effects

As noted above, one of the primary hypotheses of FACES is that the acute effect of air pollution exposures influences the longer-term respiratory health of asthmatic children. This analysis will be referred to as the "chronic" analysis throughout this document. To address this question, we evaluated the effect of acute exposure to NO_2 based on pulmonary function obtained over a 2-week period. We then evaluated how this acute effect impacted pulmonary function growth between field office visits. To assist the reader in the interpretation of these chronic analysis results, we have presented the methods and results together in Section 4.2.4.

3.6.10 Methods used for Analysis of Altered Pulmonary Function and Highway Traffic Near the Residence (See Appendix J for additional details)

3.6.10.1 Pulmonary Function

Pre-bronchodilator pulmonary function measures were used in this analysis to reflect the usual state of the child's functional status: measures included FVC, FEV_1, the ratio of FEV1 to FVC (FEV_1/FVC%), PEFR, forced expiratory flow between 25 and 75% of vital capacity (FEF_{25-75}), and the ratio of FEF_{25-75} to FVC (FEF_{25-7}5/FVC). The FEF_{25-75}/FVC ratio has the interpretation of the reciprocal of the time constant of the lung (Tager et al., 1986), similar to Meade's $Vmax_{50}$ /(VC*Pst$(L)_{50}$) (i.e., instantaneous flow at 50% divided by vital capacity times elastic recoil pressure at 50% of vital capacity) and is reflective of intrinsic airway size (Mead et al., 1980).

For each of the measures (FVC, FEV_1, PEFR, FEF_{25-75}), the mean of the first three (but not less than two) acceptable tracings was calculated. Sex and race/ethnicity-specific percent-of-predicted (%predicted) values were computed based on equations for African American, Mexican-American or Caucasian persons <20 years of age from the third National Health and Nutrition Examination Survey (NHANES III) data (4). A reference equation for FEF_{25-75}/FVC was not available; therefore, the raw data for FEF_{25-75}/FVC were used in all analyses.

3.6.10.2 Potential Effect Modifiers (Severity and Atopy)

The symptom/disability-based criteria of the Global Initiative for Asthma (GINA) asthma severity classification scheme and parental report of symptom frequency were both used to designate asthma severity status for each child at baseline (see section 3.5.1). Skin-prick allergen sensitivity tests were performed with the MultiTest device (donated by Lincoln Laboratory, Decateur, IL). Saline and histamine controls, and fourteen antigens (Hollister-Stier, Spokane, WA) relevant to the Fresno environment were evaluated. Atopy was defined as one or more positive skin tests. A test was classified as negative for the purpose of this analysis if a subject failed to respond to any antigen and the histamine control was positive. Not all children completed skin tests; therefore an additional measure of atopy was defined based on ever having been diagnosed by a physician as having hay fever or allergic rhinitis. The two variables for atopy were evaluated independently. Both definitions of atopy were considered in the analysis (see Section 3.5.1). Each of the atopy variables was evaluated independently.

3.6.10.3 Traffic

This analysis focuses on the impact of highway traffic near homes. The location of each child's primary residence relative to the closest highway (Functional Roadway Class 1) and the motor vehicle activity on that road were used as markers of their potential exposures to vehicle emissions. The roadway locations were based on the TeleAtlas MultiNet™ USA (TAMN) roadway database. This database contains detailed roadway and address information, with high positional accuracy (see Section 3.4.6.1). The locations of the subjects' residences on the TAMN were determined by submitting their standardized baseline addresses to the TeleAtlas Eagle

Geocoding Technology Service. Traffic volumes for the year 2000 were obtained from the California Department of Transportation (CALTRANS). The data included annualized average daily traffic (AADT) count and the fraction of that count made up of heavy-duty vehicles (HDV, vehicles with six or more axles). Most HDV are diesel-powered. ArcInfo (Environmental Systems Research Institute, Inc. (ESRI)) was used to preprocess the roadway segment and traffic count data. Each direction-of-travel was represented as a separate roadway segment with half of the total AADT for the highway segment. ArcGIS software (ESRI, Inc.) was used to calculate the distance from each child's primary residence to the nearest highway segment in the TAMN. The inverse-distance-weighted annual average daily traffic count (IDWT) was computed (AADT/distance). A surrogate measure of potential diesel exhaust exposure was computed by multiplying the IDWT by the HDV fraction (IDWTH). A variable (comprised of 3 dummy variables) was created based on self-report of residence proximity to "the nearest freeway, major highway, major intersection, or street with heavy traffic." Response options included: immediately in front, behind, or beside residence; one block away; >1-to-3 blocks away; >4 blocks away. The reference group was set as those >4 blocks way.

3.6.10.4 Ambient Air Quality and Meteorological Data:

To account for variation in pulmonary function measurements related to short-term pollutant levels and weather conditions on the day of/prior to lung function testing, the current and prior-day average 24-hour average O_3, NO_2, $PM_{2.5}$, and particulates between 2.5 and 10 microns ($PM_{2.5-10}$), or day-of-test 24-hour average temperature and relative humidity were evaluated in candidate models. Daily pollutant and meteorological data collected at the Fresno "Supersite" were used. Based on an evaluation of meteorological and air pollution patterns in the Fresno region, three distinct seasons were defined: Spring (February-May), summer (June-September), winter (October-January).

3.6.10.5 Questionnaire-Based Exposure Information

Current exposure to second hand smoke (SHS) was defined in two ways: 1) if either parent stated that they currently smoked, and 2) the number of microenvironments (e.g., different rooms in home, vehicle) in which anyone smoked and the child spent time. We also considered presence of pets (any fur-bearing pet, pet birds), pests (rodents, insects), natural gas appliances, mold or mildew on interior surfaces, water damage, presence of an attached garage, the presence/use of air conditioning or fan for cooling, and markers of home ventilation that included whether the home was completely closed during the month prior to and/or the month in which the lung function test was conducted.

3.6.10.6 Statistical Analyses

Multiple linear regression was used to evaluate the associations between prebronchodilator pulmonary function and surrogate measures of traffic-related exposures at the primary residence. The analyses were restricted to 214 Hispanic, African-American, and Caucasian children for whom spirometry data, as well as traffic and daily central-site ambient air quality data were available at the time of the analysis. For each pulmonary function measure, a

series of linear regressions were implemented to identify an appropriate model. Initially, backwards and forwards stepwise linear regressions were used to evaluate a priori potential confounders or effect-modifiers of associations between traffic exposure and pulmonary function. Sex, race/ethnicity, age, and height were considered because predicted values were not generated from the study population. Time-dependent variables (e.g., an acute respiratory illness, asthma related symptoms, or rescue medication use within the two weeks prior to the date of examination, or season in which examination occurred) were considered because participants were recruited over several years.

A best subsets selection method was then used to identify the optimum subset of candidate covariates; model selection was based on minimization of the Akaike's Information Criterion (AIC). This step was repeated with the time-dependent daily pollutant (O_3, NO_2, $PM_{2.5}$, $PM_{2.5-10}$) and meteorological (temperature, humidity) variables added one at a time; these variables were not included in the stepwise selection step due to their relatively high collinearity. Candidate covariates with partial R^2 of < 0.01 (and $p>0.05$), or with a large numbers of missing observations, were removed from the model if it did not result in a >15% change in the IDWT effect estimate and the standard error of that estimate was unaltered.

The residuals from the final model for each pulmonary function measure were checked to verify that model assumptions were met. For mean FEF_{25-75}/FVC, a natural log transformation was required to meet those assumptions. Possible effect modifiers considered were years-in-residence, asthma severity, atopic status and FEF_{25-75}/FVC ratio. All continuous, independent variables (except traffic measures) were centered on their population means. Statistical Analysis System (SAS) software (version 8.2; SAS Institute, Cary, NC) was used for all analyses.

4. RESULTS

4.1 EXPOSURE ASSESSMENT

4.1.1 Air Quality Conditions at the Central Site, Schools, and other Fixed Sites

This section summarizes results for the continuous and integrated measurements at the central site (Fresno First Street), schools, and other fixed sites in the study area. These tables and figures illustrate the types of variations found in outdoor exposures over a range of temporal scales for the base period, April 1, 2001, through March 31, 2003. In a few cases, data were collected as early as November 1, 2000, and are illustrated; in some cases, data are available for a shorter period only. The data used in this section are the measured values from the daily exposure database for 8 p.m. to 8 p.m.; diurnal plots were prepared if hourly data were available. Elemental carbon (EC) concentrations were calculated using black carbon (BC) concentrations measured by the Aethalometer™ and a correlation between BC and EC measured by the Federal Reference Method (FRM) at the central site; organic carbon (OC) concentrations were calculated by subtracting calculated EC from measured total carbon (TC). All other concentrations were measured. Abbreviations and units are defined in Table 3.4.8-2; definitions of the various time averages for parameters are shown in Table 3.4.8-1.

The following subsections describe summary statistics, seasonal characteristics as described by box whisker plots by month, day-to-day characteristics as described by time-series for pollutant daily averages, diurnal characteristics for hourly pollutant concentrations, and relationships among selected measured concentrations. In general, each table and group of figures are organized by pollutant group, including particulate matter (PM); gaseous, biological, and polycyclic aromatic hydrocarbon (PAH) species; and trace elements. In a few cases, information on meteorological parameters such as relative humidity (RH), temperature, and wind speed and direction are also included.

4.1.1.1 Summary Statistics

Summary statistics for daily pollutant concentrations measured at the central site, schools, and other fixed sites are shown in Tables 4.1.1-1 through 4.1.1-11; these data illustrate the distribution characteristics of the daily, 24-hr, 8 p.m.-to-8 p.m., pollutant concentrations. For ozone and NO_2, we used the daily 8-hr maximum concentrations. The number of daily averages for each pollutant is also shown in the tables. For some pollutants at a few sites, the number of daily averages is limited, due to problems with the monitor (particle scattering at Fremont School, for example) or to a new sampling and analysis method starting later (naphthalene at Bullard and Viking Schools, for example).

4.1.1.2 Seasonal Characteristics

Box whisker plots are commonly used to display a large amount of data and are particularly useful in assessing differences among data. Box whisker plots are drawn in different

ways by different software programs. However, most box whisker plots show an interquartile range (i.e., 25th to 75th percentile) and some way to illustrate data outside this range. Figure 4.1.1-1 shows an illustrated box whisker plot of the type we have used in this section. The box shows the 25th, 50th (median), and 75th percentiles. The whiskers always end on a data point; when the plots show no data beyond the end of a whisker, the whisker shows the value of the highest or lowest data point. The whiskers have a maximum length equal to 1.5 times the length of the box (the interquartile range). If data are outside this range, the points are shown on the plot and the whisker ends on the highest or lowest data point within the range of the whisker. The "outliers" are further identified by asterisks representing the points that fall within 3 times the interquartile range from the end of the box and circles representing points beyond.

The box whisker plots in Figures 4.1.1-2 through 4.1.1-19 show the distributions of concentrations by month at the central site for PM parameters ($PM_{2.5}$; PM_{10}; $PM_{2.5-10}$; $PM_{2.5}$ number; b_{sp}; $PM_{2.5}$ EC, OC, nitrate, and sulfate; PMPAH), gaseous species (ozone, CO, NO, NO_2), and meteorological parameters (RH, temperature, wind speed, and wind direction). The box whisker plots are shown for the 24-hr average concentration; however, the daily maximum 8-hr average concentration is used for ozone. These plots show the seasonal patterns of the various parameters; the concentrations of some parameters are highest during the summer months, while the concentrations of others are highest during the winter months.

The monthly distributions of $PM_{2.5}$ (see Figure 4.1.1-2) show a seasonal pattern: $PM_{2.5}$ concentrations are lowest during the March through October period and highest from November through February. The range of $PM_{2.5}$ concentrations within a given month are very high when concentrations are high (November through February) and generally lower the rest of the year. Note, however, that there are four or five days with outlier $PM_{2.5}$ concentrations in July and August (individual points above the whisker).

The monthly distributions of PM_{10} (see Figure 4.1.1-3) show less of a seasonal pattern than the monthly distributions of $PM_{2.5}$. PM_{10} concentrations are somewhat higher during the winter months than other months, but the boxes for all months overlap. Note that there are some outlier concentrations during many months.

The monthly distributions of $PM_{2.5-10}$ (see Figure 4.1.1-4) show a gradual increase from January through October and then a sharp drop in concentrations when the rainy season begins. Note that there are some outlier concentrations during most months.

The monthly distributions of particle number ($PM_{2.5}$ number) (see Figure 4.1.1-5) show less of a seasonal pattern than the monthly distributions of $PM_{2.5}$. $PM_{2.5}$ number concentrations are somewhat higher during the winter months, but the boxes for all months overlap. Note that both high and low outlier concentrations occur during many months.

The monthly distributions of particle scattering (b_{sp}) (see Figure 4.1.1-6) are shaped like the $PM_{2.5}$, EC and PMPAH distributions. Low values occur months March through September while the high values occur months November through February. The range of the monthly b_{sp} distributions is very large: the medians cover a range of about 8 between the low and high months. The whiskers of the monthly boxes indicate a very wide range of b_{sp} within the months

of November through February and a fairly narrow range during other months, especially April through August.

The monthly distributions of EC concentrations (see Figure 4.1.1-7) are lowest from March through October and highest from November through February. The range of the monthly EC concentration distributions is large: the medians cover a range of about a factor of 8 between the low and high months. The whiskers of the monthly boxes indicate a fairly wide range of EC concentrations within the months of November through February and a narrower range of concentrations during the other months. EC concentrations were calculated using BC concentrations measured by the Aethalometer™ and a correlation between BC and EC measured by the FRM at the central site.

The monthly distributions of OC concentrations (see Figure 4.1.1-8) are incomplete; however, OC concentrations are lowest during the spring and summer and highest during the winter. OC was calculated by subtracting calculated EC from measured TC. The whiskers of the monthly boxes indicate a fairly wide range of OC concentrations within the winter months and a narrower range of concentrations during the spring and summer months. The continuous carbon monitor operated poorly, and there are many large gaps in the data record.

The monthly distributions of PM nitrate (see Figure 4.1.1-9) show a seasonal pattern similar to that for EC: PM nitrate concentrations are lowest during the April through October period and highest from October through February. The range of PM nitrate concentrations within a given month is quite low during most months, but very high when concentrations are the highest (December and January).

The monthly distributions of PM sulfate (see Figure 4.1.1-10) show a seasonal pattern with higher concentrations in both the summer and the winter, due to photochemical conversion in the summer and wet-chemical conversion in the winter. The range of PM sulfate concentrations within a given month is modest during most months, but very high when concentrations are the highest (November and February).

The monthly distributions of PMPAH (see Figure 4.1.1-11) show that concentrations are low April through September and high November through February. The range of the monthly PMPAH concentration distributions is very large: the medians range from factor 9 to 13 between the low and high months. The whiskers of the monthly boxes indicate a fairly wide range of PMPAH concentrations within the months of November through February and a narrower range of concentrations during other months, especially April through August.

The monthly distributions of 8-hr daily maximum ozone concentrations (see Figure 4.1.1-12) show that ozone concentrations increase each month from January through June, are highest during May through September, and then decrease from October through December. Note that the central boxes (showing the 25^{th} to 50^{th} percentiles) of May through September overlap with the central boxes for the other months only slightly or not at all; this shows that ozone concentrations during these months are statistically significantly different from concentrations during the other months. Also notice that the monthly ozone concentration distributions cover a range from the lowest to the highest of about a factor of 4. The whiskers of the monthly boxes indicate a fairly wide range of ozone concentrations during each month.

The monthly distributions of CO concentrations (see Figure 4.1.1-13) are shaped like the EC and PMPAH distributions. The low months are April through September while the high concentration months are October through February. The range of the monthly CO concentration distributions is large: the medians range from factor 4 to 8 between the low and high months. The whiskers of the monthly boxes indicate a fairly wide range of CO concentrations within the months of October through February and a narrower range of concentrations during the other months.

The monthly distributions of NO concentrations (see Figure 4.1.1-14) are shaped like the CO, EC, and PMPAH distributions. The monthly pattern of NO concentrations is the inverse of that for ozone concentrations. NO concentrations are lowest during the middle of the year, April through September, and highest during October through February. The NO distributions during October through February are statistically significantly different from the April through September distributions. The range of the monthly NO concentration distributions is very large: the medians cover a range of about a factor of 6 to greater than 10 between the low and high months. The whiskers of the monthly boxes indicate a fairly wide range of NO concentrations within the months of October through March, but a very narrow range of concentrations during the months of May through August.

The monthly distributions of NO_2 concentrations are shaped like the NO distributions, but with a very narrow range (see Figure 4.1.1-15). The monthly NO_2 concentrations are lowest during April through August and highest during October, but the monthly distributions overlap significantly. The range of the monthly median NO_2 concentration distributions is only a factor of 2 to 3.

The monthly distributions of RH and temperature (shown in Figures 4.1.1-16 and 4.1.1-17) are as expected: relative humidity is lowest during the summer and highest during the winter months. The range in values is fairly consistent across the complete year with only a few outliers in a few months.

The monthly distributions for wind speed and wind direction at 2 p.m. are illustrated in Figures 4.1.1-18 and 4.1.1-19. Median wind speeds are slightly higher during the summer months than during the rest of the year with slightly narrower distributions in July and August than during other months. Wind directions from the north, east, south, and west are 0, 90, 180, and 270 degrees. Median wind direction is from the west-northwest for most months of the year (March through November), but notice that the distributions are very narrow (wind direction is very consistent) during the May through October period; this illustrates the very consistent daily pattern of afternoon flow along the SJV from west-northwest toward the east-southeast. The very wide distributions during November through March illustrate that the timing of this afternoon flow is not as consistent during these months.

There are both similarities and differences in the seasonal distributions. The highest concentrations and high variability of several species ($PM_{2.5}$, b_{sp}, EC, PMPAH, PM nitrate, and NO) occur in the winter while PM_{10} and particle number have the same general seasonal pattern with less month-to-month and within-month variation. The $PM_{2.5-10}$ seasonal distribution shows a completely different pattern: a gradual increase from January through October and then a sharp drop in concentrations when the rainy season begins. PM sulfate shows summer and winter

peaks. Ozone concentrations are highest in the summer. Many species exhibit monthly distributions, which vary by a factor of 5-15 between the low and high months.

4.1.1.3 Day-to-day Characteristics

The time series plots in Figures 4.1.1-20 through 4.1.1-69 show the daily 24-hr average concentrations at the central site for PM parameters ($PM_{2.5}$; PM_{10}; $PM_{2.5-10}$; $PM_{2.5}$ number; b_{sp} ; $PM_{2.5}$ EC, OC, nitrate, and sulfate; PMPAH), gaseous species (8-hr daily maximum ozone, CO, NO, NO_2); meteorological parameters (RH, temperature, wind speed, and wind direction); biological agents (fungal spores, endotoxin, and pollen grains); PAH species; and selected PM_{10} trace elements. These plots cover the period from November 1, 2000, through March 31, 2003. These plots show the seasonal patterns of the various parameters; the concentrations of some parameters are highest during the summer months, while concentrations of others are highest during the winter months. These plots also illustrate the day-to-day variations in these parameters.

Daily average $PM_{2.5}$ concentration patterns (see Figure 4.1.1-20) show low concentrations with low day-to-day variation during the April through September period and higher concentrations and higher variability during the rest of the year. The range of daily average $PM_{2.5}$ concentrations between summer and winter is wide, typically about a factor of 6.

Daily average PM_{10} concentration patterns (see Figure 4.1.1-21) also show differences across the seasons, although summer-to-winter differences in PM_{10} concentrations are not as great as with $PM_{2.5}$. PM_{10} concentrations during the February through August period are slightly lower with less day-to-day variability than during the rest of the year. The range of daily average PM_{10} concentrations between summer and winter is wide, typically a factor of 6 to 10.

Daily average $PM_{2.5-10}$ concentration patterns (see Figure 4.1.1-22) show low concentrations from about November through February, with concentrations gradually increasing throughout the rest of the year until the following November. It is likely that the significant drop in $PM_{2.5-10}$ concentrations occurs when the rains start in the fall. The day-to-day variability is similar much of the year, but increases as concentrations increase. The range of daily average $PM_{2.5-10}$ concentrations between low concentrations in the winter and the highest concentrations in the late summer and early fall is wide, up to about a factor of 6.

Daily average $PM_{2.5}$ number concentration patterns (see Figure 4.1.1-23) show similar typical and minimum concentrations throughout the year, but higher maximum concentrations and much higher variability in the winter (November through February) than during the rest of the year. The range of maximum daily average $PM_{2.5}$ number concentrations between summer and winter is about a factor of 2.

Daily average b_{sp} patterns (see Figure 4.1.1-24) are very similar to the pattern for $PM_{2.5}$, with low values and low day-to-day variation during the period from April through September and with higher values and much larger variations during the rest of the year. The range of daily average b_{sp} between summer and winter is very wide, typically a factor of 10 to 20.

Daily average EC concentration patterns (see Figure 4.1.1-25) are very similar to those of PMPAHs, CO, and NO, as might be expected for these primary pollutants. Daily average EC concentrations are low with low or modest day-to-day variation during the period from March through September and higher with much larger variation during the rest of the year. Daily average EC concentrations reach highs of about 8-15 $\mu g/m^3$ during the winter months. The range of daily average EC concentrations between summer and winter is wide, typically a factor of 8 to 10.

Daily average OC concentration data is limited during this period (see Figure 4.1.1-26); therefore, the OC seasonal pattern information is incomplete. However, winter concentrations and variability appear to be higher than concentrations and variability during February through July. The range of daily average OC concentrations between winter and spring-early-summer appears to be a factor of 2 to 5.

Daily average $PM_{2.5}$ nitrate concentration patterns (see Figure 4.1.1-27) are low with low day-to-day variation during the period from March through September and are higher with much larger variation during the rest of the year. The range of daily average $PM_{2.5}$ nitrate concentrations between summer and winter is wide, typically a factor of 5 up to 20.

Daily average $PM_{2.5}$ sulfate concentration data is limited during this period (see Figure 4.1.1-28); therefore, the $PM_{2.5}$ sulfate seasonal pattern information is incomplete. There appear to be similar concentrations with a wide day-to-day variability throughout the February to December period.

Daily average PMPAH concentration patterns (see Figure 4.1.1-29) are very similar to those of EC, CO, and NO, as might be expected for these primary pollutants. Daily average PMPAH concentrations are low with low day-to-day variation during the period from March through September and higher with much larger variation during the rest of the year. The range of daily average particulate PAH concentrations between summer and winter is very wide, typically a factor of 15 to 25.

Daily average ozone concentrations (see Figure 4.1.1-30) increase each month from January through April, are highest during May through early October, and then decrease during October through December. Note that daily average ozone concentrations are typically below 20 ppb during November, December, and January; these concentrations are below the natural background of about 40 ppb, indicating that titration of ozone by fresh NO emissions is likely a major phenomena during this period. Average daily ozone concentrations reach highs of 50-65 ppb during the summer months. The range of daily average ozone concentrations is about a factor of 5.

Daily average CO concentration patterns are very similar to those of EC, PMPAH, and NO, as might be expected for these primary pollutants (see Figure 4.1.1-31). Daily average CO concentrations are low with only modest day-to-day variation during the period from March into September and are higher with larger variations during the rest of the year. Daily average CO concentrations reach highs of 1.5 to 2.5 ppm during the winter months. The range of daily average CO concentrations between summer and winter is wide, typically about a factor of 8.

Daily average NO concentration patterns (see Figure 4.1.1-32) are very similar to those of EC, PMPAH, and CO: very low concentrations with little day-to-day variation during the months of March through July and higher concentrations and very large variations during the months of October through January. Daily average NO concentrations reach highs of 60 to 120 ppb during the winter months. The range of daily average NO concentrations between summer and winter is very wide, up to a factor of 50.

Daily average NO_2 concentrations (see Figure 4.1.1-33) show only a modest seasonal pattern with slightly lower concentrations during the months of March through August than in other months. Day-to-day variation in NO_2 concentrations is similar throughout the year. Daily average NO_2 concentrations typically range from 10 ppb to 35 ppb, with the full range from lowest to highest from 8 ppb to 50 ppb. Note that the daily pattern is slightly different during the two winter seasons shown: daily concentrations in November and December 2001 are lower than those during November and December 2000. Also note that there are occasional multi-day periods of high concentrations (see the late-December 2000 period, for example).

Daily average RH and temperature patterns (see Figures 4.1.1-34 and 4.1.1-35) are opposite and show similar variability throughout the year, as expected. RH is highest during the winter and lowest during the summer while temperatures are highest during the summer and lowest during the winter. The range of daily RH is about a factor of 2 between the high and low season, while the range for temperature is a factor of 3 to 4.

Figures 4.1.1-36 and 4.1.1-37 show the hourly wind speed and wind direction at 2 p.m. Wind speeds at 2 p.m. are slightly higher during the summer than the winter, but the range in the day-to-day variations are similar throughout the year. Hourly wind direction at 2 p.m. is typically 270 to 315 degrees during most of the year, but varies significantly more during the winter and spring than during the summer.

Figures 4.1.1-38 through 4.1.1-44 show the daily average concentration patterns for the biological agents (fungal spores, endotoxin, and pollen grains). The patterns for *Alternaria*, agricultural fungi, and total pollen grains (Figures 4.1.1-38, 4.1.1-39, and 4.1.1-44) are similar: low concentrations and low variability during much of the year with a few periods during the spring (March and April) of higher concentrations. There are also a few individual days in the winter with high concentrations. Note also that concentrations for *Alternaria* and agricultural fungi in spring 2001 are much higher than concentrations in the springs of 2002 and 2003.

The daily average concentration patterns for *Cladosporium* and total fungal spores (Figures 4.1.1-40 and 4.1.1-42) are similar: high concentrations and high variability for November 2000 through April 2001 and for November-December 2002 (but not continuing into 2003). Note that the data for winter 2001-2002 are missing, but the concentrations for January-April 2002 are also low.

The daily average concentrations for *Aspergillus/Penicillium* (Figure 4.1.1-41) show a modest seasonal pattern with generally lower concentrations in the spring and early summer and higher concentrations in the fall and winter. However, day-to-day variability is quite high and the seasonal pattern seems to vary some from year to year.

The daily average concentration pattern for endotoxin (Figure 4.1.1-43) shows higher concentrations with higher day-to-day variability (up to a factor of 3-4) in the warmer season (June-October) and lower concentrations with lower day-to-day variability in the November-May period. The range of concentrations between the high and low seasons is a factor of 5 to 10.

Figures 4.1.1-45 through 4.1.1-60 show the daily average concentration patterns for individual PAH species; note that the number of days with data is much more limited than that of other parameters (14 days for naphthalene, 27 days for the other species). The concentrations for all these species (except naphthalene) are low with either low or modest day-to-day variability for the period June-October 2002 and higher with high day-to-day variability for the period November 2002-February 2003. Naphthalene data are not available until about October 2002, so lower concentrations through October are not evident in the data.

Figures 4.1.1-61 through 4.1.1-69 show the daily average concentration patterns for selected trace elements. In general, the concentration patterns for aluminum, cobalt, iron, manganese, nickel (to a lesser extent), and silicon show low concentrations from about November through February, with concentrations gradually increasing throughout the rest of the year until the following November. As with $PM_{2.5-10}$ concentrations, it is likely that the significant drop in concentrations of these crustal (soil dust) species occurs when the rains start in the fall. The day-to-day variability is similar much of the year, but increases when the concentrations are highest. The range of daily average concentrations of these species between low concentrations in the winter and the highest concentrations in the late summer and early fall is up to about a factor of 5. The daily average concentration pattern for copper (see Figure 4.1.1-63) shows low concentrations much of the year and a few days with higher concentrations in summer and early fall. The daily average concentrations of potassium (see Figure 4.1.1-65) are low with low day-to-day variability during most of the year with only a few days with high concentrations, likely due to fireworks on the Fourth of July. There is little change (less than a factor of 2) in potassium concentrations during the fall agricultural burn or winter home-heating seasons, illustrating that potassium is only a modest tracer for these sources.

In summary, these daily-average time series plots indicate wide variations in seasonal patterns of the various parameters; the concentrations of some parameters are highest during the summer months, while the concentrations of others are highest during the winter months. These plots also illustrate the considerable day-to-day variation of many of these parameters, especially within the months of highest concentrations.

4.1.1.4 Diurnal Characteristics

The diurnal plots in Figures 4.1.1-70 through 4.1.1-87 show hourly average concentrations at the central site for PM parameters ($PM_{2.5}$; PM_{10}; $PM_{2.5-10}$; $PM_{2.5}$ number; b_{sp}; $PM_{2.5}$ EC, OC, nitrate, and sulfate; and PMPAHs), gaseous species (ozone, CO, NO, and NO_2), and meteorological parameters (RH, temperature, wind speed, and wind direction). These plots show the average diurnal concentration profiles and, thus, illustrate the typical concentration pattern that occurs each day.

Figures 4.1.1-70 through 4.1.1-72 show the average diurnal concentration patterns for $PM_{2.5}$, PM_{10}, and $PM_{2.5-10}$. These patterns are similar to each other with minimums in the early morning and late afternoon and peaks in the late morning and at night. As expected, average hourly PM_{10} concentrations are higher than those for $PM_{2.5}$.

The diurnal distribution of $PM_{2.5}$ number concentrations for the central site (see Figure 4.1.1-73) shows a minimum in the early morning and another in the late afternoon, with peaks in the morning rush hour and in the late evening. This pattern is repeated for other primary pollutants: EC (see Figure 4.1.1-75), PMPAH (see Figure 4.1.1-79), CO (see Figure 41.1-81), and NO (see Figure 4.1.1-82). These patterns are expected because concentrations of these pollutants are likely dominated by fresh motor vehicle emissions (although wintertime fireplace emissions and some other sources likely also contribute) and because low mixing heights at night result in high concentrations.

Figure 4.1.1-74 shows the diurnal pattern of b_{sp} values for the central site. The characteristics of the b_{sp} values are fairly flat with a general minimum in the afternoon and the highest values late in the evening. The average diurnal pattern for OC (see Figure 4.1.1-76) is also fairly flat with a general minimum most of the day and the highest concentrations at night. The average diurnal pattern for $PM_{2.5}$ nitrate and sulfate (see Figures 4.1.1-77 and 4.1.1-78) are also very flat with a general maximum late in the morning.

Figures 4.1.1-80 and 4.1.1-82 show the average diurnal concentration pattern for ozone and NO. These patterns illustrate the typical daily emissions/photochemical pattern: high NO concentrations during the morning and evening periods indicating fresh emissions and low mixing heights, and ozone concentrations steadily increasing in the morning daylight hours to a maximum at 1400-1500 PST in the afternoon. This pattern also illustrates the potential of high ozone exposures during afternoon outdoor activities.

The average diurnal patterns for RH and temperature (shown in Figures 4.1.1-84 and 4.1.1-85) are expected: RH is highest during the night and lowest during the day while temperature is lowest at night and slowly increasing during the daytime.

The average diurnal pattern for wind speed (see Figure 4.1.1-86) shows minimum average speeds in the early morning gradually increasing until later in the afternoon and then slightly decreasing in the evening. The average diurnal pattern for wind direction (see Figures 4.1.1-87) shows southwest to southerly flow in the morning turning to easterly by late afternoon. However, care must be taken in interpreting these patterns because wind conditions on any given day will not be represented by average conditions.

The wide variations in individual parameter concentrations and the lack of correlation for certain species are a tremendous asset to the study because they enhance the likelihood of identifying the agents associated with exacerbation of asthma symptoms.

4.1.1.5 Relationships among Continuously Measured Parameters

The scatter plot matrices in Figures 4.1.1-88 through 4.1.1-91 show two-parameter relative scatter plots between PM parameters ($PM_{2.5}$; PM_{10}; $PM_{2.5-10}$; $PM_{2.5}$ number; b_{sp}; $PM_{2.5}$ EC, OC, nitrate, and sulfate; PMPAHs), gaseous species (ozone, CO, NO, and NO_2), biological agents (fungal spores, endotoxin, and pollen grains), PAH species, and selected PM_{10} trace elements measured at the central site. Note that the relative distribution for each parameter is also shown as a bar chart. These plots illustrate the relationships between the various parameters; some are related in a linear fashion, some in a non-linear fashion, and others appear to be unrelated.

Figure 4.1.1-88 shows the scatter plot matrix for 24-hr averaged concentrations of the PM parameters ($PM_{2.5}$; PM_{10}; $PM_{2.5-10}$; $PM_{2.5}$ number; b_{sp}; $PM_{2.5}$ EC, OC, nitrate, and sulfate; PMPAHs) and gaseous species (ozone, CO, NO, and NO_2). There is a very tight linear relationship, with $r \geq 0.9$, between pairs of the primary species: CO, NO, and PMPAH, as expected. There is also a very tight linear relationship, with $r \geq 0.9$, between $PM_{2.5}$ mass and b_{sp} and $PM_{2.5}$ OC and $PM_{2.5}$ nitrate. Note also that several pairs ($PM_{2.5}$ and PM_{10}, PM_{10} and $PM_{2.5-10}$, $PM_{2.5}$ mass and b_{sp}, PM_{10} mass and b_{sp}, and PMPAH and $PM_{2.5}$ EC, for example) show an "alligator shape" in their relationship; the two branches may indicate different relationships during warm and cool seasons. There is fairly large scatter of most pollutants with ozone.

Figure 4.1.1-89 shows the scatter plot matrix for 24-hr averaged concentrations of the biological agents (fungal spores, endotoxin, and pollen grains), selected gaseous species (NO and NO_2) and selected PM parameters ($PM_{2.5}$ and PM_{10} mass; and $PM_{2.5}$ EC, OC, and sulfate). Besides the excellent correlation ($r = 0.98$) for *Cladosporium* (CLAD) and total fungal spores (TOTFS), there is very poor correlation and significant scatter among the biological agents and these selected gaseous and PM species. This illustrates the benefits of including these independent biological agents in the FACES study.

Figure 4.1.1-90 shows the scatter plot matrix for 24-hr averaged concentrations of the continuous PMPAH measurement and 24-hr averaged concentrations of individual PMPAH species. Although the number of pairs is limited (16-17 for naphthalene and 28 for the rest of the PAH species), there are modest correlations (r of 0.64 to 0.87) for PMPAH and the individual PAH species. Naphthalene correlations are modest, at best (r of 0.45 to 0.78). Among the rest of the PAH species, the correlations are good to excellent with many pairs showing correlation coefficients (r) over 0.9.

Figure 4.1.1-91 shows the scatter plot matrix for 24-hr averaged concentrations of selected PM parameters ($PM_{2.5}$, PM_{10}, and $PM_{2.5-10}$ mass) and selected trace elements. There is a very tight linear relationship ($r \geq 0.9$) among aluminum, iron, manganese, and silicon, as expected for these soil elements. These elements are also well correlated (r of 0.71 to 0.89) with $PM_{2.5-10}$. There is a fair amount of scatter, or no relationship at all, for most of the remaining pairs with trace elements.

The variations and relationships in Figures 4.1.1-88 through 4.1.1-91 illustrate a wide variety of patterns among the pollutants. These patterns depend on numerous factors, including source strength and location, seasonal sources (e.g., wood smoke in the winter), weather patterns

and meteorology, and photochemistry. During some seasons, for example, some pollutants might be expected to be related to each other, while other pollutants may not be related at all.

Table 4.1.1-1 Summary statistics for pollutant concentrations at Fresno Central site based on 24-hr averages for 4/1/2001 to 3/31/2003.

Pollutant	No. of Samples	Minimum	10th Percentile	25th Percentile	Median	Mean	75th Percentile	90th Percentile	Maximum	Units
Particulate Matter										
$PM_{2.5}$ Mass[1]	711	1.85	7.13	11.31	18.46	25.28	32.52	54.40	108.92	$\mu g/m^3$
PM_{10} Mass	705	8.08	21.96	32.82	45.21	49.16	62.22	81.41	127.35	$\mu g/m^3$
PM Coarse Mass[1]	686	0	5.96	10.66	21.60	23.88	34.17	46.63	113.13	$\mu g/m^3$
$PM_{2.5}$ Number	670	1.93	8.80	11.07	13.51	14.27	16.40	20.96	33.31	$1000/cm^3$
B_{scat}	681	8.83	17.67	25.82	46.90	79.21	99.10	195.77	501.24	Mm-1
$PM_{2.5}$ EC	617	0.19	0.48	0.79	1.49	2.46	3.17	5.68	16.31	$\mu g/m^3$
$PM_{2.5}$ OC	151	2.94	4.13	4.83	6.07	7.60	8.58	12.55	25.10	$\mu g/m^3$
$PM_{2.5}$ NO_3	695	0.25	0.71	1.24	2.55	4.23	6.08	10.32	22.31	$\mu g/m^3$
$PM_{2.5}$ SO_4	304	0.15	0.62	0.86	1.19	1.30	1.66	2.20	3.14	$\mu g/m^3$
$PM_{2.5}$ PAH	729	1.01	1.62	2.32	4.34	8.92	11.74	24.57	50.04	$\mu g/m^3$
Gases[2]										
O_3	720	3.33	8.68	14.53	30.31	30.42	44.09	52.84	76.10	ppb
O_3 8-hr max	720	3.50	15.94	27.91	50.38	50.79	70.13	86.69	119.50	ppb
CO	722	0.004	0.11	0.17	0.34	0.50	0.70	1.24	2.06	ppm
NO	724	0.11	1.08	2.08	6.65	16.71	23.26	53.25	99.92	ppb
NO_2	724	4.81	9.54	13.58	19.02	20.18	25.36	31.86	52.77	ppb
NO_2 8-hr max	724	7.00	12.33	17.81	25.13	26.43	33.71	41.84	66.00	ppb
NO_x	724	6.10	11.22	16.14	26.04	36.69	50.71	82.90	140.96	ppb

[1] $PM_{2.5}$ Mass estimated for 61 days

[2] Carbon monoxide data were missing for this period.

Table 4.1.1-1 Summary statistics for pollutant concentrations at Fresno Central site based on 24-hr averages for 4/1/2001 to 3/31/2003.

Pollutant	No. of Samples	Minimum	10th Percentile	25th Percentile	Median	Mean	75th Percentile	90th Percentile	Maximum	Units
Biological Agents										
ALTE	564	13.5	13.5	27	54	84.3	94.5	148.5	1039.5	spores/m^3
AGFG	599	13.5	40.5	124.9	405	591.2	715.5	1066.5	14310	spores/m^3
CLAD	618	351	1128.6	1795.5	3429	4918.7	6088.5	9135.5	45306	spores/m^3
ASP	605	13.5	81	148.5	310.5	411.1	567	850.5	2430	spores/m^3
TOTFS	618	405	1821.2	2578.5	4340.3	5971.2	7222.5	10904.0	47236.5	spores/m^3
Endotoxin	558	0	0.24	0.54	1.33	2.0	3.12	4.99	9.43	EU/m^3
TOP	420	0	4.4	11.0	26.4	128.0	88.6	293.2	2588.3	grains/m^3
Polycyclic Aromatic Hydrocarbons										
ACE	28	0.10	0.16	0.32	1.03	1.54	2.62	3.21	6.46	ng/m^3
ACY	28	0	0.05	0.09	0.37	2.34	1.85	7.32	18.60	ng/m^3
ANT	28	0	0	0	0.02	0.40	0.51	1.19	3.27	ng/m^3
BAA	28	0.01	0.02	0.06	0.20	0.49	0.65	1.58	2.31	ng/m^3
BAP	28	0	0.01	0.03	0.32	0.53	0.74	1.58	2.03	ng/m^3
BBF	28	0	0.02	0.16	0.48	0.65	0.94	1.89	2.22	ng/m^3
BGP	28	0	0.04	0.16	0.59	0.68	1.12	1.43	1.96	ng/m^3
BKF	28	0	0.02	0.04	0.25	0.30	0.47	0.71	1.07	ng/m^3
CRY	28	0.01	0.07	0.20	0.49	0.82	1.16	2.30	3.46	ng/m^3
DBA	28	0	0	0.02	0.07	0.18	0.31	0.51	0.58	ng/m^3
FLT	28	0.10	0.23	0.52	0.92	1.56	2.39	3.34	7.24	ng/m^3
FLU	28	0.18	1.14	1.53	2.85	3.75	5.80	7.57	11.35	ng/m^3
ICP	28	0	0	0.13	0.57	0.74	1.09	1.83	2.19	ng/m^3
NAPST	17	0	0	148.6	228.4	302.8	594.6	663.5	702.9	ng/m^3
PHE	28	1.79	2.12	3.73	5.67	8.66	12.97	18.08	31.64	ng/m^3
PYR	28	0.12	0.28	0.59	0.96	1.62	2.35	3.38	7.45	ng/m^3

[1] $PM_{2.5}$ Mass estimated for 61 days.

Table 4.1.1-1 Summary statistics for pollutant concentrations at Fresno Central site based on 24-hr averages for 4/1/2001 to 3/31/2003.

Pollutant	No. of Samples	Minimum	10th Percentile	25th Percentile	Median	Mean	75th Percentile	90th Percentile	Maximum	Units
PM_{10} Trace Elements										
AL	533	0	0.06	0.38	0.95	1.24	1.76	2.91	5.68	ng/m^3
AS	533	0	0	0	0.001	0.002	0.002	0.004	0.010	ng/m^3
AU	533	0	0	0	0	0.001	0.001	0.003	0.007	ng/m^3
BA	533	0	0	0.009	0.036	0.042	0.060	0.084	1.089	ng/m^3
BR	533	0	0.002	0.003	0.005	0.005	0.007	0.009	0.019	ng/m^3
CA	533	0	0.138	0.249	0.495	0.570	0.765	1.136	2.110	ng/m^3
CD	533	0	0	0	0	0.001	0.001	0.003	0.009	ng/m^3
CL	533	0	0.013	0.032	0.093	0.291	0.324	0.790	3.841	ng/m^3
CO	533	0	0.001	0.002	0.004	0.006	0.008	0.014	0.031	ng/m^3
CR	533	0	0	0.001	0.002	0.002	0.004	0.005	0.023	ng/m^3
CU	533	0	0.004	0.007	0.011	0.016	0.019	0.030	0.224	ng/m^3
FE	533	0	0.227	0.443	0.759	0.907	1.158	1.921	3.213	ng/m^3
GA	533	0	0	0	0	0.0005	0.0003	0.002	0.005	ng/m^3
KP	533	0	0.201	0.343	0.523	0.622	0.772	1.095	12.430	ng/m^3
LA	533	0	0	0	0	0.014	0.025	0.045	0.154	ng/m^3
MG	533	0	0	0	0.0275	0.058	0.096	0.162	0.505	ng/m^3
MN	533	0	0.003	0.007	0.015	0.018	0.023	0.039	0.069	ng/m^3
MO	533	0	0	0	0	0.001	0.002	0.004	0.009	ng/m^3
NA	533	0	0	0	0.09	0.21	0.36	0.59	1.43	ng/m^3
NI	533	0	0.0001	0.001	0.001	0.001	0.002	0.002	0.007	ng/m^3
PB	533	0	0	0.00107	0.0042	0.005	0.007	0.010	0.122	ng/m^3
PD	533	0	0	0	0	0.001	0.001	0.003	0.006	ng/m^3
PH	533	0	0	0	0	0.002	0	0.004	0.075	ng/m^3

[1] $PM_{2.5}$ Mass estimated for 61 days.

Table 4.1.1-1 Summary statistics for pollutant concentrations at Fresno Central site based on 24-hr averages for 4/1/2001 to 3/31/2003.

Pollutant	No. of Samples	Minimum	10th Percentile	25th Percentile	Median	Mean	75th Percentile	90th Percentile	Maximum	Units
PM_{10} Trace Elements (continued)										
RB	533	0	0	0.0005	0.0016	0.002	0.003	0.004	0.007	ng/m^3
SB	533	0	0	0	0	0.003	0.005	0.011	0.059	ng/m^3
SE	533	0	0.0002	0.001	0.002	0.002	0.003	0.005	0.010	ng/m^3
SI	533	0.005	0.63	1.40	3.30	4.20	5.85	9.67	17.23	ng/m^3
SN	533	0	0	0	0.004	0.005	0.008	0.012	0.027	ng/m^3
SR	533	0	0.001	0.003	0.005	0.006	0.008	0.012	0.190	ng/m^3
SU	533	0.01	0.33	0.45	0.67	0.71	0.91	1.14	2.86	ng/m^3
TI	533	0	0	0.018	0.050	0.064	0.095	0.153	0.306	ng/m^3
TL	533	0	0	0	0	0.0003	0.0003	0.001	0.005	ng/m^3
UR	533	0	0	0	0	0.001	0.001	0.002	0.006	ng/m^3
VA	533	0	0	0	0.0001	0.003	0.005	0.008	0.017	ng/m^3
YT	533	0	0	0	0.0004	0.001	0.001	0.002	0.005	ng/m^3
ZN	533	0.001	0.010	0.015	0.024	0.029	0.037	0.055	0.145	ng/m^3
ZR	533	0	0.000	0.001	0.002	0.003	0.004	0.005	0.010	ng/m^3

[1] $PM_{2.5}$ Mass estimated for 61 days.

Table 4.1.1-2 Summary statistics for pollutant concentrations at Fremont site based on 24-hr averages for 6/10/2002 to 3/31/2003.

Pollutant	No. of Samples	Minimum	10th Percentile	25th Percentile	Median	Mean	75th Percentile	90th Percentile	Maximum	Units
Particulate Matter										
$PM_{2.5}$ Mass	287	4.53	10.12	14.79	25.70	31.39	43.22	59.14	119.30	$\mu g/m^3$
PM_{10} Mass	280	12.18	23.89	31.16	48.22	50.81	64.13	82.46	133.21	$\mu g/m^3$
PM Coarse Mass	273	1.83	6.48	9.81	16.89	18.77	25.14	32.91	86.38	$\mu g/m^3$
$PM_{2.5}$ Number	277	9.46	18.41	22.96	27.35	28.88	34.05	42.13	54.82	$1000/cm^3$
B_{scat}	120	9.54	15.79	23.31	39.59	64.08	97.05	142.55	298.22	Mm-1
$PM_{2.5}$ EC	291	0.20	0.63	0.99	1.78	2.20	2.90	4.32	8.43	$\mu g/m^3$
$PM_{2.5}$ OC	272	3.86	5.59	6.76	9.00	10.73	12.47	18.45	48.84	$\mu g/m^3$
$PM_{2.5}$ NO_3	283	0.35	0.94	1.88	3.54	4.65	6.50	9.80	20.74	$\mu g/m^3$
$PM_{2.5}$ PAH	290	1.59	3.82	5.90	10.05	15.73	20.69	35.34	77.64	v
Gases										
O_3	288	1.52	6.11	11.30	23.64	25.88	40.26	48.98	71.22	ppb
O3 8-hr max	288	1.84	11.76	23.36	44.49	49.16	72.97	89.91	124.40	ppb
CO	269	0.12	0.24	0.39	0.64	0.80	1.07	1.62	2.64	ppm
NO	288	1.62	3.66	5.32	12.33	25.75	38.14	68.65	133.46	ppb
NO_2	288	6.99	13.17	16.86	20.82	21.59	25.79	30.87	43.72	ppb
NO_2 8-hr max	288	9.23	17.87	21.57	26.35	27.76	33.29	41.04	55.99	ppb
NO_x	288	8.71	18.28	23.53	36.44	50.49	67.70	103.65	179.69	ppb
Biological Agents										
ALTE	270	13.5	27	40.5	87.75	139.35	202.5	317.25	918	$spores/m^3$
AGFG	276	13.5	27	94.5	324	347.7	513	729	1323	$spores/m^3$
CLAD	287	810	1528.2	2180.3	3847.5	5638.2	6277.5	10683.9	44955	$spores/m^3$
ASP	284	13.5	67.5	162	351	453.1	654.75	973.35	2254.5	$spores/m^3$
TOTFS	287	918	2027.7	2808	4819.5	6552	7749	11261.7	46170	$spores/m^3$
Endotoxin	263	0.06	0.29	0.65	2.19	3.05	4.91	6.92	12.39	EU/m^3
TOP	291	0	5.5	15.4	29.7	196.9	75.9	439.12	3175.7	$grains/m^3$

Table 4.1.1-2 Summary statistics for pollutant concentrations at Fremont site based on 24-hr averages for 6/10/2002 to 3/31/2003.

Pollutant	No. of Samples	Minimum	10th Percentile	25th Percentile	Median	Mean	75th Percentile	90th Percentile	Maximum	Units
Polycyclic Aromatic Hydrocarbons										
ACE	27	0.25	0.40	0.65	1.91	1.97	2.63	4.51	5.32	ng/m^3
ACY	27	0	0.01	0.11	0.20	1.73	2.91	4.90	11.87	ng/m^3
ANT	27	0	0	0	0.03	0.27	0.24	1.09	2.18	ng/m^3
BAA	27	0	0.01	0.04	0.10	0.42	0.53	1.52	2.26	ng/m^3
BAP	27	0	0.002	0.02	0.19	0.52	0.67	1.26	3.07	ng/m^3
BBF	27	0	0.003	0.05	0.36	0.63	0.80	2.07	3.04	ng/m^3
BGP	27	0	0.01	0.07	0.52	0.58	0.99	1.45	2.61	ng/m^3
BKF	27	0	0	0.02	0.12	0.27	0.44	0.62	1.60	ng/m^3
CRY	27	0	0.03	0.17	0.34	0.73	1.00	2.18	3.68	ng/m^3
DBA	27	0	0	0.00	0.04	0.13	0.23	0.41	0.52	ng/m^3
FLT	27	0.06	0.20	0.53	0.79	1.38	2.03	3.57	3.98	ng/m^3
FLU	27	0.04	1.46	2.52	3.74	4.04	5.47	8.05	8.76	ng/m^3
ICP	27	0	0	0.06	0.27	0.70	1.09	1.73	3.21	ng/m^3
NAPST	14	0	0	0	239.2	340.2	602.5	880.5	910.2	ng/m^3
PHE	27	0.42	2.65	3.94	5.90	8.48	12.11	20.51	22.40	ng/m^3
PYR	27	0.001	0.13	0.44	1.02	1.50	2.09	4.09	4.79	ng/m^3

Table 4.1.1-2 Summary statistics for pollutant concentrations at Fremont site based on 24-hr averages for 6/10/2002 to 3/31/2003.

Pollutant	No. of Samples	Minimum	10th Percentile	25th Percentile	Median	Mean	75th Percentile	90th Percentile	Maximum	Units
PM_{10} Trace Elements										
AL	260	0	0.08	0.39	1.19	1.54	2.50	3.67	5.80	ng/m^3
AS	260	0	0	0	0.0008	0.001	0.002	0.004	0.008	ng/m^3
AU	260	0	0	0	0	0.001	0.001	0.002	0.007	ng/m^3
BA	260	0	0	0	0.025	0.031	0.051	0.070	0.127	ng/m^3
BR	260	0	0.002	0.004	0.005	0.006	0.009	0.011	0.019	ng/m^3
CA	260	0.0591	0.141	0.302	0.568	0.694	1.039	1.429	2.175	ng/m^3
CD	260	0	0	0	0	0.001	0.001	0.003	0.008	ng/m^3
CL	260	0	0.020	0.037	0.112	0.396	0.516	1.081	3.818	ng/m^3
CO	260	0	0.001	0.003	0.007	0.010	0.015	0.023	0.047	ng/m^3
CR	260	0	0	0.001	0.003	0.003	0.005	0.007	0.012	ng/m^3
CU	260	0.0003	0.004	0.006	0.011	0.019	0.019	0.033	0.370	ng/m^3
FE	260	0.0821	0.224	0.467	0.896	1.083	1.608	2.271	3.554	ng/m^3
GA	260	0	0	0	0	0.0006	0.0011	0.002	0.006	ng/m^3
KP	260	0.0766	0.200	0.382	0.604	0.690	1.004	1.283	1.933	ng/m^3
LA	260	0	0	0	0	0.015	0.023	0.050	0.107	ng/m^3
MG	260	0	0	0	0.0239333	0.060	0.107	0.167	0.395	ng/m^3
MN	260	0	0.004	0.008	0.017	0.022	0.033	0.049	0.073	ng/m^3
MO	260	0	0	0	0.0005853	0.001	0.003	0.004	0.009	ng/m^3
NA	260	0	0	0	0.01	0.15	0.21	0.46	1.66	ng/m^3
NI	260	0	0.0004	0.001	0.001	0.001	0.002	0.003	0.008	ng/m^3
PB	260	0	0	0.0028465	0.00715	0.008	0.011	0.016	0.055	ng/m^3
PD	260	0	0	0	0	0.001	0.001	0.003	0.009	ng/m^3
PH	260	0	0	0	0	0.004	0	0.0165	0.1284	ng/m^3

Table 4.1.1-2 Summary statistics for pollutant concentrations at Fremont site based on 24-hr averages for 6/10/2002 to 3/31/2003.

Pollutant	No. of Samples	Minimum	10th Percentile	25th Percentile	Median	Mean	75th Percentile	90th Percentile	Maximum	Units
PM_{10} Trace Elements (continued)										
RB	260	0	0	0	0.0016	0.002	0.003	0.005	0.009	ng/m^3
SB	260	0	0	0	0.00045	0.004	0.008	0.014	0.029	ng/m^3
SE	260	0	0.0001	0.001	0.002	0.003	0.004	0.005	0.010	ng/m^3
SI	260	0.238	0.59	1.53	3.82	5.23	8.35	12.07	18.88	ng/m^3
SN	260	0	0	0	0.004	0.005	0.008	0.014	0.020	ng/m^3
SR	260	0	0.001	0.003	0.006	0.007	0.010	0.014	0.085	ng/m^3
SU	260	0.15	0.33	0.50	0.72	0.77	0.98	1.26	2.36	ng/m^3
TI	260	0	0.0061	0.026	0.061	0.082	0.139	0.183	0.347	ng/m^3
TL	260	0	0	0	0	0.0003	0.0004	0.001	0.003	ng/m^3
UR	260	0	0	0	0	0.001	0.001	0.002	0.005	ng/m^3
VA	260	0	0	0	0.001	0.004	0.006	0.011	0.021	ng/m^3
YT	260	0	0	0	0.0004	0.001	0.001	0.002	0.005	ng/m^3
ZN	260	0.004	0.011	0.017	0.029	0.034	0.043	0.061	0.171	ng/m^3
ZR	260	0	0.0003	0.001	0.003	0.003	0.004	0.005	0.009	ng/m^3

Table 4.1.1-3 Summary statistics for pollutant concentrations at Bullard site based on 24-hr averages for 6/10/2002 to 7/25/2002.

Pollutant	No. of Samples	Minimum	10th Percentile	25th Percentile	Median	Mean	75th Percentile	90th Percentile	Maximum	Units
Particulate Matter										
$PM_{2.5}$ Mass	43	4.46	5.16	7.23	9.90	10.39	12.48	15.98	21.66	$\mu g/m^3$
PM_{10} Mass	44	24.30	27.33	31.27	36.99	37.80	42.65	49.50	60.67	$\mu g/m^3$
PM Coarse Mass	43	18.79	21.14	24.00	26.69	27.77	31.81	35.18	42.57	$\mu g/m^3$
$PM_{2.5}$ Number	45	11.61	15.45	17.13	22.47	22.79	28.45	29.80	33.96	$1000/cm^3$
B_{scat}	45	8.84	10.57	18.85	24.18	23.89	29.09	33.90	42.97	Mm-1
$PM_{2.5}$ EC	42	0.15	0.31	0.40	0.63	0.71	0.91	1.24	1.83	$\mu g/m^3$
$PM_{2.5}$ OC	41	3.74	4.04	4.49	5.08	5.19	5.54	6.27	8.56	$\mu g/m^3$
$PM_{2.5}$ NO_3	44	0.12	0.24	0.55	1.03	1.17	1.57	2.35	3.77	$\mu g/m^3$
$PM_{2.5}$ PAH	45	1.53	1.72	1.95	2.29	2.60	3.02	4.06	4.61	$\mu g/m^3$
Gases										
O_3	44	28.86	38.10	42.78	46.83	47.84	54.02	58.53	69.29	ppb
O_3 8-hr max	44	42.16	60.86	68.53	71.75	77.14	83.77	96.88	122.75	ppb
CO	45	0.10	0.15	0.18	0.21	0.22	0.25	0.30	0.43	ppm
NO	44	0.16	0.61	1.07	1.52	1.95	2.57	3.92	5.77	ppb
NO_2	44	4.97	6.86	8.05	9.46	10.68	13.54	14.66	18.39	ppb
NO_2 8-hr max	44	7.55	9.23	11.23	13.77	15.51	19.10	23.69	28.89	ppb
NO_x	44	5.79	7.92	8.75	10.70	12.31	15.54	19.41	21.43	ppb
Biological Agents										
ALTE	41	13.5	27	40.5	54	61.90	81	94.5	216	$spores/m^3$
AGFG	42	175.5	306.5	351	465.8	461.9	526.5	621	877.5	$spores/m^3$
CLAD	42	1080	1424.3	1701	2099.3	2103.1	2457	2787.8	3537	$spores/m^3$
ASP	41	27	67.5	121.5	216	246.95	310.5	432	904.5	$spores/m^3$
TOTFS	42	1620	2200.5	2389.5	2821.5	2866.5	3294	3595.1	4657.5	$spores/m^3$
Endotoxin	40	0.57	1.16	2.05	3.02	3.17	4.14	5.18	6.65	EU/m^3
TOP	42	13.2	25.4	33.0	41.8	49.4	58.3	76.8	130.9	$grains/m^3$

Table 4.1.1-3 Summary statistics for pollutant concentrations at Bullard site based on 24-hr averages for 6/10/2002 to 7/25/2002.

Pollutant	No. of Samples	Minimum	10th Percentile	25th Percentile	Median	Mean	75th Percentile	90th Percentile	Maximum	Units
Polycyclic Aromatic Hydrocarbons										
ACE	2	0.15	0.15	0.15	0.65	0.65	1.16	1.16	1.16	ng/m^3
ACY	2	0	0.07	0.07	0.07	0.07	0.08	0.08	0.08	ng/m^3
ANT	2	0	0	0	0	0	0	0	0	ng/m^3
BAA	2	0	0	0	0.03	0.03	0.05	0.05	0.05	ng/m^3
BAP	2	0	0	0	0.01	0.01	0.02	0.02	0.02	ng/m^3
BBF	2	0	0	0	0.04	0.04	0.08	0.08	0.08	ng/m^3
BGP	2	0	0	0	0.04	0.04	0.07	0.07	0.07	ng/m^3
BKF	2	0	0	0	0.02	0.02	0.04	0.04	0.04	ng/m^3
CRY	2	0	0	0	0.09	0.09	0.18	0.18	0.18	ng/m^3
DBA	2	0	0	0	0	0	0	0	0	ng/m^3
FLT	2	0.20	0.20	0.20	0.64	0.64	1.07	1.07	1.07	ng/m^3
FLU	2	1.14	1.14	1.14	3.13	3.13	5.11	5.11	5.11	ng/m^3
ICP	2	0	0	0	0	0	0	0	0	ng/m^3
PHE	2	3.77	3.77	3.77	5.45	5.45	7.13	7.13	7.13	ng/m^3
PYR	2	0.66	0.66	0.66	0.68	0.68	0.71	0.71	0.71	ng/m^3

Table 4.1.1-3 Summary statistics for pollutant concentrations at Bullard site based on 24-hr averages for 6/10/2002 to 7/25/2002.

Pollutant	No. of Samples	Minimum	10th Percentile	25th Percentile	Median	Mean	75th Percentile	90th Percentile	Maximum	Units
PM_{10} Trace Elements										
AL	33	0.69	0.92	1.13	1.38	1.35	1.50	1.75	2.53	ng/m^3
AS	33	0	0	0	0	0.001	0.001	0.002	0.004	ng/m^3
AU	33	0	0	0	0	0.001	0.000	0.002	0.004	ng/m^3
BA	33	0	0	0.005	0.031	0.043	0.066	0.083	0.344	ng/m^3
BR	33	0.001	0.002	0.002	0.004	0.004	0.005	0.006	0.008	ng/m^3
CA	33	0.339	0.391	0.473	0.558	0.581	0.644	0.826	0.888	ng/m^3
CD	33	0	0	0	0	0.001	0.001	0.004	0.010	ng/m^3
CL	33	0	0.003	0.009	0.020	0.177	0.064	0.539	2.357	ng/m^3
CO	33	0.0004	0.002	0.004	0.005	0.005	0.007	0.008	0.010	ng/m^3
CR	33	0	0.0002	0.001	0.002	0.002	0.003	0.003	0.005	ng/m^3
CU	33	0.0037	0.005	0.007	0.008	0.017	0.017	0.030	0.149	ng/m^3
FE	33	0.485	0.553	0.703	0.806	0.840	0.979	1.167	1.291	ng/m^3
GA	33	0	0	0	0	0.0006	0.0005	0.003	0.004	ng/m^3
KP	33	0.324	0.355	0.477	0.541	0.690	0.617	0.724	5.754	ng/m^3
LA	33	0	0	0	0	0.009	0.012	0.031	0.088	ng/m^3
MG	33	0	0	0.00925	0.0511	0.071	0.110	0.155	0.338	ng/m^3
MN	33	0.0093	0.012	0.016	0.018	0.018	0.021	0.023	0.029	ng/m^3
MO	33	0	0	0	0.002	0.002	0.004	0.005	0.006	ng/m^3
NA	33	0	0	0	0.15	0.22	0.35	0.70	0.84	ng/m^3
NI	33	0	0.0003	0.001	0.001	0.001	0.001	0.002	0.002	ng/m^3
PB	33	0	0	0.003	0.005	0.007	0.006	0.008	0.069	ng/m^3
PD	33	0	0	0	0	0.0005	0.0004	0.002	0.004	ng/m^3
PH	33	0	0	0	0	0.0002	0	0	0.0062	ng/m^3

Table 4.1.1-3 Summary statistics for pollutant concentrations at Bullard site based on 24-hr averages for 6/10/2002 to 7/25/2002.

Pollutant	No. of Samples	Minimum	10th Percentile	25th Percentile	Median	Mean	75th Percentile	90th Percentile	Maximum	Units
PM_{10} Trace Elements (continued)										
RB	33	0.0003	0.0010	0.0014	0.0019	0.002	0.002	0.003	0.004	ng/m^3
SB	33	0	0	0	0	0.003	0.002	0.011	0.025	ng/m^3
SE	33	0.0005	0.0012	0.002	0.004	0.004	0.005	0.006	0.013	ng/m^3
SI	33	2.467	2.79	3.68	4.21	4.32	5.01	5.84	6.83	ng/m^3
SN	33	0	0	0	0.001	0.005	0.009	0.014	0.019	ng/m^3
SR	33	0.003	0.003	0.005	0.006	0.008	0.007	0.008	0.076	ng/m^3
SU	33	0.29	0.49	0.65	0.83	0.79	0.89	1.00	1.69	ng/m^3
TI	33	0.001	0.023	0.051	0.072	0.064	0.082	0.094	0.104	ng/m^3
TL	33	0	0	0	0	0	0	0	0.000	ng/m^3
UR	33	0	0	0	0	0.0003	0.0003	0.0011	0.003	ng/m^3
VA	33	0	0	0	0	0.003	0.006	0.007	0.012	ng/m^3
YT	33	0	0	0	0.0003	0.001	0.001	0.002	0.003	ng/m^3
ZN	33	0.007	0.008	0.009	0.012	0.013	0.015	0.018	0.037	ng/m^3
ZR	33	0	0.001	0.001	0.002	0.002	0.003	0.004	0.005	ng/m^3

Table 4.1.1-4 Summary statistics for pollutant concentrations at Viking based on 24-hr averages for 7/26/2002 to 9/27/2002.

Pollutant	No. of Samples	Minimum	10th Percentile	25th Percentile	Median	Mean	75th Percentile	90th Percentile	Maximum	Units
Particulate Matter										
$PM_{2.5}$ Mass	62	5.37	10.30	15.27	18.81	20.54	22.92	31.88	56.23	$\mu g/m^3$
PM_{10} Mass	59	28.90	39.45	47.08	63.78	62.83	74.58	84.15	105.37	$\mu g/m^3$
PM Coarse Mass	59	20.84	25.55	32.55	43.86	43.24	54.30	60.11	81.95	$\mu g/m^3$
$PM_{2.5}$ Number	42	9.30	11.59	13.00	14.66	14.94	17.28	18.51	19.76	$1000/cm^3$
$PM_{2.5}$ EC	62	0.30	0.62	0.88	1.27	1.31	1.60	2.02	2.75	$\mu g/m^3$
$PM_{2.5}$ OC	57	3.97	4.77	5.75	6.70	7.15	7.74	11.24	14.16	$\mu g/m^3$
$PM_{2.5}$ NO_3	62	0.66	1.09	1.67	2.74	3.04	4.11	5.43	6.47	$\mu g/m^3$
$PM_{2.5}$ PAH	62	1.84	2.42	2.99	4.29	4.39	5.57	6.56	8.47	$\mu g/m^3$
Gases										
O_3	62	29.21	34.45	41.64	48.74	48.46	55.57	60.15	68.99	ppb
O_3 8-hr max	62	47.62	60.06	69.40	82.02	82.47	97.39	106.68	114.51	ppb
CO	61	0	0.20	0.24	0.34	0.35	0.43	0.53	0.69	ppm
NO	62	-0.21	0.81	1.37	2.42	2.86	3.76	5.41	10.31	ppb
NO_2	62	7.93	9.97	13.22	17.00	16.81	20.14	23.86	29.04	ppb
NO_2 8-hr max	62	10.63	12.73	17.84	24.11	23.66	28.19	31.90	44.90	ppb
NO_x	62	7.75	10.77	14.52	18.83	19.31	23.53	27.69	33.27	ppb
Biological Agents										
ALTE	57	13.5	43.2	67.5	94.5	99.95	124.875	162	216	$spores/m^3$
AGFG	57	148.5	364.5	391.5	472.5	517.26	637.875	712.8	918	$spores/m^3$
CLAD	57	2187	3774.6	4887	6966	6764.2	8494.9	9328.5	11772	$spores/m^3$
ASP	57	54	326.7	563.6	796.5	815.4	1056.4	1306.8	1606.5	$spores/m^3$
TOTFS	57	2929.5	4676.4	5950.1	8572.5	8196.9	9986.6	11110.5	13648.5	$spores/m^3$
Endotoxin	62	1.33	1.96	2.64	4.48	4.53	6.15	6.91	9.61	EU/m^3
TOP	56	3.3	16.7	23.1	36.3	102.9	50.1	138.7	1328.8	$grains/m^3$

Table 4.1.1-4 Summary statistics for pollutant concentrations at Viking based on 24-hr averages for 7/26/2002 to 9/27/2002.

Pollutant	No. of Samples	Minimum	10th Percentile	25th Percentile	Median	Mean	75th Percentile	90th Percentile	Maximum	Units
Polycyclic Aromatic Hydrocarbons										
ACE	7	0.08	0.14	0.37	0.42	0.49	0.63	0.91	0.98	ng/m^3
ACY	7	0	0.004	0.03	0.10	0.09	0.16	0.18	0.18	ng/m^3
ANT	7	0	0	0	0	0	0	0	0	ng/m^3
BAA	7	0	0.002	0.01	0.03	0.03	0.06	0.07	0.07	ng/m^3
BAP	7	0	0	0	0.01	0.02	0.03	0.06	0.06	ng/m^3
BBF	7	0	0	0	0.004	0.05	0.09	0.18	0.20	ng/m^3
BGP	7	0	0.029	0.03	0.04	0.09	0.13	0.19	0.20	ng/m^3
BKF	7	0	0	0	0.01	0.02	0.03	0.10	0.11	ng/m^3
CRY	7	0.05	0.05	0.06	0.07	0.15	0.16	0.48	0.55	ng/m^3
DBA	7	0	0	0	0.001	0.01	0.02	0.06	0.07	ng/m^3
FLT	7	0.05	0.06	0.11	0.28	0.36	0.68	0.79	0.79	ng/m^3
FLU	7	0.09	0.18	0.67	1.22	1.23	1.88	2.06	2.08	ng/m^3
ICP	7	0	0	0.01	0.07	0.09	0.16	0.18	0.18	ng/m^3
PHE	7	1.24	1.27	1.45	3.13	3.19	4.26	6.40	6.88	ng/m^3
PYR	7	0	0.002	0.02	0.11	0.29	0.52	0.91	0.99	ng/m^3

Table 4.1.1-4 Summary statistics for pollutant concentrations at Viking based on 24-hr averages for 7/26/2002 to 9/27/2002.

Pollutant	No. of Samples	Minimum	10th Percentile	25th Percentile	Median	Mean	75th Percentile	90th Percentile	Maximum	Units
PM_{10} Trace Elements										
AL	61	0.73	1.31	1.75	2.31	2.43	3.04	3.75	4.98	ng/m^3
AS	61	0	0	0	0	0.0005	0.001	0.002	0.005	ng/m^3
AU	61	0	0	0	0.0004	0.001	0.002	0.003	0.004	ng/m^3
BA	61	0	0	0.000	0.028	0.030	0.050	0.069	0.108	ng/m^3
BR	61	0.0019	0.003	0.006	0.008	0.008	0.010	0.012	0.015	ng/m^3
CA	61	0.348	0.562	0.706	0.889	0.941	1.203	1.341	1.826	ng/m^3
CD	61	0	0	0	0	0.001	0.001	0.003	0.007	ng/m^3
CL	61	0	0.012	0.016	0.026	0.052	0.047	0.085	0.772	ng/m^3
CO	61	0.0029	0.006	0.009	0.011	0.011	0.014	0.017	0.027	ng/m^3
CR	61	0	0.00102	0.002	0.003	0.003	0.005	0.006	0.009	ng/m^3
CU	61	0.0037	0.009	0.012	0.016	0.023	0.025	0.046	0.097	ng/m^3
FE	61	0.5163	0.830	1.015	1.408	1.450	1.880	2.119	2.829	ng/m^3
GA	61	0	0	0	0	0.0006	0.0013	0.002	0.003	ng/m^3
KP	61	0.3302	0.534	0.627	0.852	0.853	1.048	1.185	1.543	ng/m^3
LA	61	0	0	0	0	0.008	0.004	0.036	0.072	ng/m^3
MG	61	0	0	0.01945	0.0936	0.098	0.134	0.221	0.419	ng/m^3
MN	61	0.0128	0.017	0.021	0.031	0.031	0.039	0.046	0.062	ng/m^3
MO	61	0	0	0.0008	0.0026	0.003	0.004	0.005	0.007	ng/m^3
NA	61	0	0	0	0	0.13	0.21	0.46	0.62	ng/m^3
NI	61	0.0003	0.0009	0.001	0.002	0.002	0.002	0.002	0.007	ng/m^3
PB	61	0.0025	0.00398	0.005625	0.0071	0.008	0.009	0.010	0.025	ng/m^3
PD	61	0	0	0	0	0.0004	0.0003	0.002	0.004	ng/m^3
PH	61	0	0	0	0	0.003	0	0.00212	0.0602	ng/m^3

Table 4.1.1-4 Summary statistics for pollutant concentrations at Viking based on 24-hr averages for 7/26/2002 to 9/27/2002.

Pollutant	No. of Samples	Minimum	10th Percentile	25th Percentile	Median	Mean	75th Percentile	90th Percentile	Maximum	Units
PM_{10} Trace Elements (continued)										
RB	61	0.0004	0.001	0.002	0.003	0.003	0.004	0.005	0.007	ng/m^3
SB	61	0	0	0	0	0.0005	0	0.002	0.008	ng/m^3
SE	61	0	0.0004	0.001	0.002	0.002	0.003	0.004	0.007	ng/m^3
SI	61	2.80	4.14	5.30	7.46	7.57	9.96	11.03	15.28	ng/m^3
SN	61	0	0	0	0.001	0.003	0.004	0.011	0.027	ng/m^3
SR	61	0.004	0.005	0.007	0.009	0.009	0.012	0.013	0.017	ng/m^3
SU	61	0.36	0.47	0.58	0.71	0.73	0.87	1.04	1.11	ng/m^3
TI	61	0.033	0.062	0.084	0.125	0.125	0.158	0.198	0.230	ng/m^3
TL	61	0	0	0	0	0.0001	0	0	0.002	ng/m^3
UR	61	0	0	0	0	0.001	0.001	0.002	0.004	ng/m^3
VA	61	0	0	0.0002	0.004	0.005	0.009	0.011	0.015	ng/m^3
YT	61	0	0	0	0.000	0.001	0.001	0.002	0.003	ng/m^3
ZN	61	0.007	0.013	0.016	0.023	0.023	0.027	0.032	0.058	ng/m^3
ZR	61	0	0.000	0.002	0.003	0.003	0.004	0.005	0.011	ng/m^3

Table 4.1.1-5 Summary statistics for pollutant concentrations at Burroughs site based on 24-hr averages for 10/1/2002 to 11/19/2002.

Pollutant	No. of Samples	Minimum	10th Percentile	25th Percentile	Median	Mean	75th Percentile	90th Percentile	Maximum	Units
Particulate Matter										
$PM_{2.5}$ Mass	43	7.19	14.55	21.88	30.90	32.98	42.65	60.13	65.07	$\mu g/m^3$
PM_{10} Mass	42	11.43	36.87	71.19	80.56	78.13	90.12	111.58	135.59	$\mu g/m^3$
PM Coarse Mass	42	4.48	12.03	35.83	49.67	44.90	58.10	66.36	82.79	$\mu\mu g/m^3$
$PM_{2.5}$ Number	43	14.38	15.82	18.60	22.37	23.22	27.56	30.02	37.18	$1000/cm^3$
$PM_{2.5}$ EC	46	0.37	1.12	1.92	2.59	2.57	3.07	4.04	5.14	$\mu g/m^3$
$PM_{2.5}$ OC	36	4.77	5.31	6.54	7.69	7.86	9.08	10.31	12.44	$\mu g/m^3$
$PM_{2.5}$ NO_3	42	1.48	1.81	5.46	9.46	10.87	16.08	22.31	24.11	$\mu g/m^3$
$PM_{2.5}$ PAH	43	5.46	9.37	14.12	20.80	23.12	28.71	39.86	57.65	$\mu g/m^3$
Gases										
O_3	43	4.30	10.52	15.36	21.05	20.83	25.99	30.21	34.90	ppb
O_3 8-hr max	43	9.25	18.98	35.34	49.91	47.97	61.04	73.30	82.33	ppb
CO	43	0	0.43	0.58	0.93	1.00	1.31	1.65	2.18	ppm
NO	43	3.34	6.76	13.00	30.98	32.21	42.69	65.09	81.56	ppb
NO_2	43	11.85	18.91	22.29	31.77	29.11	34.35	38.55	43.44	ppb
NO_2 8-hr max	43	14.34	23.85	27.94	36.97	35.88	44.22	49.27	51.05	ppb
NO_x	43	15.54	26.12	38.90	61.83	60.96	77.95	103.05	120.24	ppb
Biological Agents										
ALTE	43	13.5	24.3	40.5	67.5	72.21	94.5	151.2	175.5	$spores/m^3$
AGFG	45	13.5	67.5	195.75	378	348.6	486	594	810	$spores/m^3$
CLAD	45	3807	5008.5	5518.1	6493.5	10232.1	8991	24016.5	49396.5	$spores/m^3$
ASP	45	13.5	216	448.9	621	650.10	803.3	1134	1498.5	$spores/m^3$
TOTFS	45	4131	6007.5	6669	7857	11299.8	10199.3	24435	50328	$spores/m^3$
Endotoxin	44	0.20	0.49	1.38	3.22	3.41	4.78	5.98	9.02	EU/m^3
TOP	46	1.1	2.2	4.4	7.2	11.5	13.2	31.0	47.3	$grains/m^3$

Table 4.1.1-5 Summary statistics for pollutant concentrations at Burroughs site based on 24-hr averages for 10/1/2002 to 11/19/2002.

Pollutant	No. of Samples	Minimum	10th Percentile	25th Percentile	Median	Mean	75th Percentile	90th Percentile	Maximum	Units
Polycyclic Aromatic Hydrocarbons										
ACE	6	0.19	0.19	0.22	0.22	0.84	0.67	3.26	3.55	ng/m^3
ACY	6	0	0.01	0.06	0.21	0.41	0.53	1.33	1.42	ng/m^3
ANT	6	0	0	0	0.02	0.04	0.03	0.14	0.15	ng/m^3
BAA	6	0.00	0.00	0.00	0.05	0.15	0.33	0.44	0.46	ng/m^3
BAP	6	0	0.02	0.05	0.14	0.22	0.49	0.50	0.50	ng/m^3
BBF	6	0	0.07	0.26	0.43	0.44	0.70	0.76	0.77	ng/m^3
BGP	6	0	0.13	0.52	0.77	0.77	1.19	1.25	1.25	ng/m^3
BKF	6	0	0.01	0.06	0.13	0.21	0.27	0.61	0.65	ng/m^3
CRY	6	0.01	0.02	0.13	0.15	0.27	0.53	0.63	0.64	ng/m^3
DBA	6	0	0	0.00	0.04	0.05	0.07	0.12	0.12	ng/m^3
FLT	6	0.24	0.25	0.31	0.53	0.57	0.87	0.94	0.95	ng/m^3
FLU	6	1.56	1.56	1.57	3.00	2.79	3.67	3.90	3.92	ng/m^3
ICP	6	0	0	0.08	0.26	0.40	0.86	0.97	0.98	ng/m^3
NAPST	6	0	0	0.00	197.39	162.06	278.59	296.94	298.98	ng/m^3
PHE	6	1.99	2.00	2.08	3.47	3.53	4.36	5.65	5.80	ng/m^3
PYR	6	0.42	0.43	0.53	0.60	0.82	1.30	1.47	1.49	ng/m^3

Table 4.1.1-5 Summary statistics for pollutant concentrations at Burroughs site based on 24-hr averages for 10/1/2002 to 11/19/2002.

Pollutant	No. of Samples	Minimum	10th Percentile	25th Percentile	Median	Mean	75th Percentile	90th Percentile	Maximum	Units
PM_{10} Trace Elements										
AL	46	0.09	0.22	0.57	2.62	2.33	3.33	3.95	4.61	ng/m^3
AS	46	0	0	0.0001	0.001	0.002	0.003	0.004	0.005	ng/m^3
AU	46	0	0	0	0	0	0	0.001	0.005	ng/m^3
BA	46	0	0	0	0.025	0.035	0.062	0.093	0.120	ng/m^3
BR	46	0.0019	0.004	0.007	0.008	0.009	0.010	0.013	0.035	ng/m^3
CA	46	0.0678	0.186	0.345	1.063	0.933	1.306	1.460	1.655	ng/m^3
CD	46	0	0	0	0	0.001	0.002	0.003	0.006	ng/m^3
CL	46	0.0374	0.042	0.065	0.156	0.314	0.304	0.668	3.689	ng/m^3
CO	46	0.0009	0.004	0.009	0.024	0.020	0.029	0.033	0.041	ng/m^3
CR	46	0	0.001	0.003	0.006	0.005	0.008	0.009	0.010	ng/m^3
CU	46	0.0016	0.007	0.009	0.014	0.014	0.019	0.024	0.030	ng/m^3
FE	46	0.1302	0.352	0.618	1.878	1.673	2.427	2.631	3.006	ng/m^3
GA	46	0	0	0	0	0.0005	0.0001	0.002	0.004	ng/m^3
KP	46	0.1088	0.296	0.435	1.066	0.927	1.240	1.412	1.569	ng/m^3
LA	46	0	0	0	0	0.013	0.014	0.052	0.073	ng/m^3
MG	46	0	0	0	0.0263	0.057	0.075	0.174	0.373	ng/m^3
MN	46	0.0018	0.006	0.010	0.038	0.033	0.049	0.053	0.058	ng/m^3
MO	46	0	0	0	0.00045	0.001	0.003	0.004	0.006	ng/m^3
NA	46	0	0	0	0	0.16	0.26	0.50	1.10	ng/m^3
NI	46	0	0.0003	0.001	0.003	0.002	0.003	0.004	0.004	ng/m^3
PB	46	0	0.0022	0.0061	0.0097	0.009	0.012	0.015	0.017	ng/m^3
PD	46	0	0	0	0.0001	0.001	0.002	0.003	0.004	ng/m^3
PH	46	0	0	0	0	0.002	0	0.009	0.028	ng/m^3

Table 4.1.1-5 Summary statistics for pollutant concentrations at Burroughs site based on 24-hr averages for 10/1/2002 to 11/19/2002.

Pollutant	No. of Samples	Minimum	10th Percentile	25th Percentile	Median	Mean	75th Percentile	90th Percentile	Maximum	Units
PM_{10} Trace Elements (continued)										
RB	46	0	0.0004	0.0018	0.0036	0.003	0.005	0.005	0.007	ng/m^3
SB	46	0	0	0	0.0025	0.004	0.007	0.010	0.024	ng/m^3
SE	46	0	0.0004	0.001	0.002	0.002	0.002	0.003	0.005	ng/m^3
SI	46	0.321	1.20	2.20	9.46	8.16	11.59	13.12	14.37	ng/m^3
SN	46	0	0	0.003	0.006	0.007	0.012	0.015	0.021	ng/m^3
SR	46	0	0.002	0.004	0.010	0.010	0.015	0.016	0.019	ng/m^3
SU	46	0.15	0.41	0.65	0.94	0.92	1.15	1.47	1.81	ng/m^3
TI	46	0	0.027	0.054	0.138	0.130	0.191	0.214	0.264	ng/m^3
TL	46	0	0	0	0	0.0002	0	0.001	0.003	ng/m^3
UR	46	0	0	0	0	0	0.001	0.002	0.005	ng/m^3
VA	46	0	0	0.0013	0.005	0.006	0.009	0.017	0.022	ng/m^3
YT	46	0	0	0	0.001	0.001	0.002	0.003	0.004	ng/m^3
ZN	46	0.007	0.022	0.033	0.045	0.045	0.057	0.071	0.125	ng/m^3
ZR	46	0	0	0.002	0.004	0.004	0.005	0.007	0.020	ng/m^3

Table 4.1.1-6 Summary statistics for pollutant concentrations at Copper Hills site based on 24-hr averages for 11/24/2002 to 1/8/2003.

Pollutant	No. of Samples	Minimum	10th Percentile	25th Percentile	Median	Mean	75th Percentile	90th Percentile	Maximum	Units
Particulate Matter										
$PM_{2.5}$ Mass	42	5.70	8.55	12.24	28.06	30.33	44.78	59.24	66.68	$\mu g/m^3$
PM_{10} Mass	42	11.40	14.02	23.56	40.43	41.91	56.43	74.51	83.00	$\mu g/m^3$
PM Coarse Mass	39	2.14	3.89	5.29	8.50	10.01	13.85	19.08	29.59	$\mu g/m^3$
$PM_{2.5}$ Number	44	5.96	7.20	11.19	13.76	13.76	17.27	18.54	19.84	$1000/cm^3$
$PM_{2.5}$ EC	45	0.18	0.39	0.78	1.51	1.52	2.07	2.41	3.43	$\mu g/m^3$
$PM_{2.5}$ OC	42	3.99	4.32	5.30	6.94	7.04	8.34	9.65	12.54	$\mu g/m^3$
$PM_{2.5}$ NO_3	40	0.77	1.34	3.60	8.43	9.33	13.87	19.44	25.43	$\mu g/m^3$
$PM_{2.5}$ PAH	44	2.16	2.94	4.40	8.18	8.85	11.64	15.50	23.36	$\mu g/m^3$
Gases										
O_3	44	5.31	6.12	10.88	14.83	15.41	18.59	25.98	32.32	ppb
O_3 8-hr max	44	8.82	11.51	19.95	26.64	25.35	31.72	36.94	40.16	ppb
CO	41	0	0.24	0.29	0.40	0.41	0.52	0.57	0.64	ppm
NO	44	0.81	1.37	2.37	8.09	8.78	12.76	18.11	29.74	ppb
NO_2	44	5.95	8.04	11.69	14.75	14.40	17.51	19.86	23.06	ppb
NO_2 8-hr max	44	6.92	11.25	14.28	18.12	18.00	21.39	24.78	32.57	ppb
NO_x	44	7.41	9.04	13.76	23.24	22.88	29.72	36.21	47.35	ppb
Biological Agents										
ALTE	29	13.5	13.5	13.5	27	45.16	57.375	102.6	148.5	$spores/m^3$
AGFG	37	13.5	13.5	27	67.5	97.05	135	199.8	418.5	$spores/m^3$
CLAD	43	567	823.5	1458	3685.5	7186.4	13142.3	16748.1	25528.5	$spores/m^3$
ASP	43	13.5	51.3	94.5	243	316.2	469.1	693.9	1228.5	$spores/m^3$
TOTFS	43	810	988.2	1566	3793.5	7616.5	14127.8	17447.4	26865	$spores/m^3$
Endotoxin	39	0.028	0.08	0.11	0.29	0.52	0.82	1.27	1.83	EU/m^3
TOP	44	0	2.1	3.3	12.1	37.4	27.5	82.0	601.7	$grains/m^3$

Table 4.1.1-6 Summary statistics for pollutant concentrations at Copper Hills site based on 24-hr averages for 11/24/2002 to 1/8/2003.

Pollutant	No. of Samples	Minimum	10th Percentile	25th Percentile	Median	Mean	75th Percentile	90th Percentile	Maximum	Units
Polycyclic Aromatic Hydrocarbons										
ACE	6	0.78	0.84	1.45	3.06	2.67	3.33	4.23	4.33	ng/m^3
ACY	6	0	0.02	0.04	0.11	1.22	0.80	5.69	6.23	ng/m^3
ANT	6	0	0	0	0.09	0.19	0.17	0.70	0.76	ng/m^3
BAA	6	0.12	0.13	0.22	0.22	0.31	0.34	0.71	0.75	ng/m^3
BAP	6	0	0.17	0.23	0.30	0.37	0.39	0.75	0.79	ng/m^3
BBF	6	0	0.21	0.27	0.34	0.41	0.48	0.76	0.79	ng/m^3
BGP	6	0	0.23	0.25	0.36	0.40	0.45	0.73	0.76	ng/m^3
BKF	6	0	0.11	0.13	0.21	0.22	0.27	0.38	0.39	ng/m^3
CRY	6	0.19	0.20	0.31	0.38	0.52	0.56	1.24	1.32	ng/m^3
DBA	6	0	0	0.05	0.06	0.07	0.10	0.14	0.14	ng/m^3
FLT	6	0.40	0.41	0.51	0.88	0.95	1.17	1.81	1.88	ng/m^3
FLU	6	0.47	0.57	1.47	2.17	2.31	3.30	4.17	4.26	ng/m^3
ICP	6	0	0	0.48	0.80	0.72	0.93	0.94	0.94	ng/m^3
NAPST	5	77	77	111.75	166.56	177.81	235.45	312.31	312.31	ng/m^3
PHE	6	1.82	1.94	2.98	5.67	5.70	7.49	10.25	10.56	ng/m^3
PYR	6	0.29	0.32	0.59	0.93	0.98	1.11	1.92	2.01	ng/m^3

Table 4.1.1-6 Summary statistics for pollutant concentrations at Copper Hills site based on 24-hr averages for 11/24/2002 to 1/8/2003.

Pollutant	No. of Samples	Minimum	10th Percentile	25th Percentile	Median	Mean	75th Percentile	90th Percentile	Maximum	Units
PM_{10} Trace Elements										
AL	39	0	0	0	0.15	0.32	0.50	0.95	1.68	ng/m^3
AS	39	0	0	0.00003	0.001	0.001	0.002	0.004	0.005	ng/m^3
AU	39	0	0	0	0	0.001	0.000	0.003	0.004	ng/m^3
BA	39	0	0	0	0	0.011	0.019	0.038	0.053	ng/m^3
BR	39	0	0.001	0.002	0.003	0.004	0.005	0.007	0.014	ng/m^3
CA	39	0.031	0.053	0.081	0.160	0.212	0.332	0.430	0.683	ng/m^3
CD	39	0	0	0	0	0.001	0.001	0.003	0.005	ng/m^3
CL	39	0.007	0.043	0.142	0.216	0.485	0.615	1.004	2.958	ng/m^3
CO	39	0	0.001	0.001	0.003	0.003	0.005	0.008	0.013	ng/m^3
CR	39	0	0	0.0001	0.001	0.001	0.002	0.003	0.003	ng/m^3
CU	39	0.0006	0.001	0.004	0.007	0.007	0.010	0.013	0.014	ng/m^3
FE	39	0.033	0.059	0.135	0.229	0.294	0.424	0.663	0.876	ng/m^3
GA	39	0	0	0	0	0.0006	0.001	0.002	0.003	ng/m^3
KP	39	0.063	0.118	0.173	0.286	0.333	0.478	0.587	0.815	ng/m^3
LA	39	0	0	0	0	0.014	0.023	0.042	0.069	ng/m^3
MG	39	0	0	0	0	0.021	0.031	0.079	0.126	ng/m^3
MN	39	0.0001	0.001	0.002	0.004	0.005	0.008	0.012	0.017	ng/m^3
MO	39	0	0	0	0.0005	0.002	0.003	0.004	0.017	ng/m^3
NA	39	0	0	0	0.02	0.14	0.20	0.47	0.84	ng/m^3
NI	39	0	0	0.0003	0.001	0.001	0.001	0.001	0.002	ng/m^3
PB	39	0	0	0.0004	0.0029	0.003	0.005	0.009	0.013	ng/m^3
PD	39	0	0	0	0	0.001	0.001	0.003	0.004	ng/m^3
PH	39	0	0	0	0	0.002	0	0.00712	0.0246	ng/m^3

Table 4.1.1-6 Summary statistics for pollutant concentrations at Copper Hills site based on 24-hr averages for 11/24/2002 to 1/8/2003.

Pollutant	No. of Samples	Minimum	10th Percentile	25th Percentile	Median	Mean	75th Percentile	90th Percentile	Maximum	Units
PM_{10} Trace Elements (continued)										
RB	39	0	0	0	0.0004	0.001	0.001	0.002	0.003	ng/m^3
SB	39	0	0	0	0.0036	0.005	0.006	0.014	0.026	ng/m^3
SE	39	0	0	0.0002	0.001	0.001	0.001	0.002	0.005	ng/m^3
SI	39	0.096	0.19	0.53	0.90	1.40	1.96	3.13	7.71	ng/m^3
SN	39	0	0	0.0004	0.005	0.005	0.007	0.009	0.023	ng/m^3
SR	39	0	0.00016	0.001	0.002	0.002	0.003	0.004	0.008	ng/m^3
SU	39	0.08	0.09	0.23	0.51	0.53	0.82	1.04	1.44	ng/m^3
TI	39	0	0	0.001	0.016	0.022	0.037	0.060	0.085	ng/m^3
TL	39	0	0	0	0	0.0003	0.0006	0.001	0.002	ng/m^3
UR	39	0	0	0	0	0.0005	0.001	0.002	0.002	ng/m^3
VA	39	0	0	0	0.001	0.002	0.003	0.006	0.008	ng/m^3
YT	39	0	0	0	0	0	0	0.001	0.002	ng/m^3
ZN	39	0.002	0.005	0.012	0.019	0.026	0.030	0.063	0.100	ng/m^3
ZR	39	0	0	0.0001	0.001	0.001	0.002	0.003	0.004	ng/m^3

Table 4.1.1-7 Summary statistics for pollutant concentrations at Forkner site based on 24-hr averages for 1/9/2003 to 2/19/2003.

Pollutant	No. of Samples	Minimum	10th Percentile	25th Percentile	Median	Mean	75th Percentile	90th Percentile	Maximum	Units
Particulate Matter										
$PM_{2.5}$ Mass	39	9.75	14.51	20.54	29.29	28.52	38.50	39.25	49.21	$\mu g/m^3$
PM_{10} Mass	40	15.67	22.27	30.54	39.50	38.43	46.88	50.93	59.54	$\mu g/m^3$
PM Coarse Mass	39	4.42	6.00	7.35	9.04	9.71	12.38	13.20	15.36	$\mu g/m^3$
$PM_{2.5}$ Number	40	4.04	5.50	8.13	13.93	13.26	17.71	19.98	24.19	$1000/cm^3$
B_{scat}	35	28.46	40.63	62.92	107.66	100.62	130.29	149.88	164.43	Mm-1
$PM_{2.5}$ EC	40	0.19	0.83	1.03	1.40	1.49	1.91	2.35	2.83	$\mu g/m^3$
$PM_{2.5}$ OC	12	5.92	5.94	6.03	6.65	7.42	8.16	10.99	11.48	$\mu g/m^3$
$PM_{2.5}$ NO_3	36	1.76	2.29	3.39	4.45	4.31	5.27	5.94	6.91	$\mu g/m^3$
$PM_{2.5}$ PAH	40	1.71	3.98	6.44	8.02	9.38	11.38	17.58	20.79	$\mu g/m^3$
Gases										
O_3	40	3.56	4.19	5.73	9.38	10.27	12.90	17.79	30.21	ppb
O_3 8-hr max	40	6.00	6.75	8.69	19.50	19.57	25.38	34.00	39.63	ppb
NO	40	1.58	4.40	8.81	14.22	16.73	22.08	35.49	44.94	ppb
NO_2	40	6.00	9.21	12.72	16.06	15.43	17.95	20.99	24.02	ppb
NO_2 8-hr max	40	8.00	10.69	14.63	19.06	19.12	22.75	26.75	34.38	ppb
NO_x	40	7.58	13.92	23.84	32.07	32.16	39.50	53.28	61.46	ppb
Biological Agents										
ALTE	28	13.5	13.5	13.5	27	38.09	54	81	135	$spores/m^3$
AGFG	33	13.5	13.5	13.5	54	60.14	84.375	124.2	216	$spores/m^3$
CLAD	36	445.5	1821.15	3321	5244.75	5515.88	7101	10316.7	16024.5	$spores/m^3$
ASP	36	54	83.7	168.75	270	418.88	621	990.9	1336.5	$spores/m^3$
TOTFS	36	661.5	2025	3523.5	5845.5	6019.50	7499.25	11342.7	16348.5	$spores/m^3$
Endotoxin	37	0.047	0.13	0.20	0.30	0.45	0.51	1.15	1.72	EU/m^3
TOP	36	6.6	39.1	62.7	149.1	237.7	340.5	547.9	973.5	$grains/m^3$

Table 4.1.1-7 Summary statistics for pollutant concentrations at Forkner site based on 24-hr averages for 1/9/2003 to 2/19/2003.

Pollutant	No. of Samples	Minimum	10th Percentile	25th Percentile	Median	Mean	75th Percentile	90th Percentile	Maximum	Units
Polycyclic Aromatic Hydrocarbons										
ACE	5	0.66	0.66	0.89	1.74	1.57	2.25	2.26	2.26	ng/m^3
ACY	5	0	0	0.01	0.06	0.55	1.12	1.78	1.78	ng/m^3
ANT	5	0	0	0	0.07	0.11	0.18	0.38	0.38	ng/m^3
BAA	5	0.07	0.07	0.15	0.18	0.27	0.41	0.59	0.59	ng/m^3
BAP	5	0	0.18	0.20	0.24	0.41	0.64	0.84	0.84	ng/m^3
BBF	5	0	0.27	0.32	0.59	0.61	0.76	1.20	1.20	ng/m^3
BGP	5	0	0.30	0.31	0.38	0.49	0.70	0.78	0.78	ng/m^3
BKF	5	0	0.09	0.11	0.15	0.21	0.33	0.35	0.35	ng/m^3
CRY	5	0.16	0.16	0.24	0.40	0.48	0.69	1.01	1.01	ng/m^3
DBA	5	0	0	0.08	0.10	0.13	0.17	0.28	0.28	ng/m^3
FLT	5	0.74	0.74	0.75	0.85	1.06	1.17	2.08	2.08	ng/m^3
FLU	5	1.75	1.75	2.51	2.81	3.23	3.96	5.33	5.33	ng/m^3
ICP	5	0	0	0.30	0.46	0.63	1.14	1.18	1.18	ng/m^3
NAPST	3	112	112	124.25	160.89	173.07	224.94	246.28	246.28	ng/m^3
PHE	5	4.31	4.31	4.38	5.46	6.72	8.54	12.06	12.06	ng/m^3
PYR	5	0.59	0.59	0.61	0.74	0.97	1.23	1.92	1.92	ng/m^3

Table 4.1.1-7 Summary statistics for pollutant concentrations at Forkner site based on 24-hr averages for 1/9/2003 to 2/19/2003.

Pollutant	No. of Samples	Minimum	10th Percentile	25th Percentile	Median	Mean	75th Percentile	90th Percentile	Maximum	Units
PM_{10} Trace Elements										
AL	37	0	0	0	0.14	0.20	0.26	0.51	0.95	ng/m^3
AS	37	0	0	0.0007	0.0016	0.002	0.003	0.005	0.007	ng/m^3
AU	37	0	0	0	0	0	0	0	0.004	ng/m^3
BA	37	0	0	0	0.014	0.020	0.040	0.053	0.066	ng/m^3
BR	37	0	0	0.001	0.004	0.003	0.004	0.006	0.007	ng/m^3
CA	37	0	0.038	0.084	0.124	0.181	0.289	0.408	0.493	ng/m^3
CD	37	0	0	0	0	0	0	0.002	0.004	ng/m^3
CL	37	0	0.045	0.065	0.153	0.243	0.380	0.609	0.791	ng/m^3
CO	37	0	0	0	0.002	0.002	0.003	0.005	0.006	ng/m^3
CR	37	0	0	0	0.001	0.001	0.002	0.003	0.006	ng/m^3
CU	37	0	0.001	0.004	0.006	0.008	0.010	0.017	0.020	ng/m^3
FE	37	0	0.068	0.156	0.243	0.288	0.371	0.581	0.889	ng/m^3
GA	37	0	0	0	0	0.0005	0.0007	0.002	0.003	ng/m^3
KP	37	0	0.082	0.136	0.212	0.246	0.329	0.450	0.668	ng/m^3
LA	37	0	0	0	0.0088	0.015	0.020	0.045	0.068	ng/m^3
MG	37	0	0	0	0	0.034	0.046	0.101	0.198	ng/m^3
MN	37	0	0.001	0.002	0.004	0.005	0.007	0.010	0.013	ng/m^3
MO	37	0	0	0	0	0	0	0.002	0.005	ng/m^3
NA	37	0	0	0	0.10	0.18	0.28	0.58	0.61	ng/m^3
NI	37	0	0	0.0002	0.001	0.001	0.001	0.002	0.002	ng/m^3
PB	37	0	0	0	0.0016	0.003	0.004	0.009	0.016	ng/m^3
PD	37	0	0	0	0	0.001	0.002	0.002	0.004	ng/m^3
PH	37	0	0	0	0	0.005	0.0063	0.01708	0.0357	ng/m^3

Table 4.1.1-7 Summary statistics for pollutant concentrations at Forkner site based on 24-hr averages for 1/9/2003 to 2/19/2003.

Pollutant	No. of Samples	Minimum	10th Percentile	25th Percentile	Median	Mean	75th Percentile	90th Percentile	Maximum	Units
PM_{10} Trace Elements (continued)										
RB	37	0	0	0	0	0	0	0	0.002	ng/m^3
SB	37	0	0	0.0032	0.0076	0.008	0.013	0.017	0.024	ng/m^3
SE	37	0	0	0.0001	0.001	0.001	0.002	0.003	0.005	ng/m^3
SI	37	0.003	0.23	0.34	0.64	0.99	1.37	2.47	3.68	ng/m^3
SN	37	0	0	0	0.003	0.005	0.006	0.014	0.023	ng/m^3
SR	37	0	0	0	0.001	0.001	0.002	0.004	0.008	ng/m^3
SU	37	0.01	0.22	0.28	0.53	0.63	0.83	1.30	2.07	ng/m^3
TI	37	0	0	0.002	0.012	0.015	0.025	0.034	0.048	ng/m^3
TL	37	0	0	0	0.0003	0.0005	0.0008	0.001	0.002	ng/m^3
UR	37	0	0	0	0	0.001	0.001	0.002	0.006	ng/m^3
VA	37	0	0	0	0	0.001	0.002	0.003	0.005	ng/m^3
YT	37	0	0	0	0	0	0	0.001	0.001	ng/m^3
ZN	37	0	0.004	0.012	0.021	0.026	0.029	0.046	0.140	ng/m^3
ZR	37	0	0	0.0005	0.001	0.001	0.002	0.003	0.004	ng/m^3

Table 4.1.1-8 Summary statistics for pollutant concentrations at Holland site based on 24-hr averages for 2/20/2003 to 3/31/2003.

Pollutant	No. of Samples	Minimum	10th Percentile	25th Percentile	Median	Mean	75th Percentile	90th Percentile	Maximum	Units
Particulate Matter										
$PM_{2.5}$ Mass	40	5.20	8.76	11.90	16.55	19.63	26.95	31.44	48.18	$\mu g/m^3$
PM_{10} Mass	40	9.70	19.30	22.69	30.73	33.46	43.67	49.49	66.23	$\mu g/m^3$
PM Coarse Mass	39	6.15	7.97	10.83	14.00	14.13	17.86	20.15	22.25	$\mu g/m^3$
$PM_{2.5}$ Number	40	13.54	19.46	20.52	23.21	23.98	27.25	29.75	37.17	$1000/cm^3$
B_{scat}	40	7.36	14.51	22.38	31.19	49.99	74.02	88.96	166.07	Mm-1
$PM_{2.5}$ EC	40	0.18	0.41	0.72	1.05	1.27	1.96	2.30	2.79	$\mu g/m^3$
$PM_{2.5}$ OC	27	2.04	2.80	3.74	5.06	5.48	7.15	8.06	10.40	$\mu g/m^3$
$PM_{2.5}$ NO_3	40	0.19	0.83	1.26	2.07	2.61	4.22	5.00	6.47	$\mu g/m^3$
$PM_{2.5}$ PAH	40	2.79	4.02	4.54	7.73	9.46	13.96	17.35	21.08	$\mu g/m^3$
Gases[1]										
O_3	40	11.48	14.08	15.13	18.90	19.73	23.28	28.07	31.21	ppb
O_3 8-hr max	40	21.50	27.94	30.38	35.00	35.94	39.63	45.81	61.00	ppb
NO	39	2.88	5.46	8.96	12.58	22.38	37.97	54.30	63.29	ppb
NO_2	39	7.60	10.39	14.46	19.27	17.96	22.10	23.57	24.38	ppb
NO_2 8-hr max	39	11.88	13.00	17.61	25.88	23.16	28.44	30.13	36.75	ppb
NO_x	39	11.60	16.23	23.33	33.92	40.32	59.04	76.35	85.50	ppb
Biological Agents										
ALTE	36	13.5	27	40.5	54	74.6	87.8	148.5	297	$spores/m^3$
AGFG	40	13.5	13.5	40.5	67.5	85.73	108	195.75	297	$spores/m^3$
CLAD	40	1539	2112.8	2713.5	3699	4099.3	5055.8	7249.5	8194.5	$spores/m^3$
ASP	37	27	70.2	124.875	256.5	273.28	381.375	545.4	715.5	$spores/m^3$
TOTFS	40	1579.5	2450.25	3091.5	4158	4504.95	5595.75	7620.75	8761.5	$spores/m^3$
Endotoxin	38	0.19	0.32	0.47	0.70	0.85	1.06	1.69	2.52	EU/m^3
TOP	40	39.6	88.6	189.2	1264.5	1607.8	2610.3	3943.5	4439.6	$grains/m^3$

[1] Carbon monoxide data were missing for this period.

Table 4.1.1-8 Summary statistics for pollutant concentrations at Holland site based on 24-hr averages for 2/20/2003 to 3/31/2003.

Pollutant	No. of Samples	Minimum	10th Percentile	25th Percentile	Median	Mean	75th Percentile	90th Percentile	Maximum	Units
PM_{10} Trace Elements										
AL	39	0	0.02	0.16	0.41	0.48	0.82	0.97	1.22	ng/m^3
AS	39	0	0	0	0.0012	0.001	0.003	0.004	0.005	ng/m^3
AU	39	0	0	0	0	0	0	0.001	0.003	ng/m^3
BA	39	0	0	0.016	0.042	0.041	0.059	0.080	0.107	ng/m^3
BR	39	0	0.0004	0.001	0.003	0.003	0.005	0.005	0.006	ng/m^3
CA	39	0.1092	0.136	0.222	0.275	0.306	0.382	0.474	0.674	ng/m^3
CD	39	0	0	0	0	0.001	0.000	0.003	0.006	ng/m^3
CL	39	0.0102	0.022	0.034	0.105	0.295	0.352	0.925	2.097	ng/m^3
CO	39	0.0001	0.001	0.002	0.003	0.004	0.005	0.007	0.010	ng/m^3
CR	39	0	0	0.000	0.001	0.001	0.002	0.003	0.005	ng/m^3
CU	39	0.0022	0.004	0.006	0.009	0.010	0.014	0.018	0.020	ng/m^3
FE	39	0.160	0.217	0.327	0.525	0.534	0.705	0.818	0.995	ng/m^3
GA	39	0	0	0	0	0.0009	0.0023	0.003	0.004	ng/m^3
KP	39	0.105	0.165	0.212	0.315	0.299	0.374	0.421	0.533	ng/m^3
LA	39	0	0	0	0.0025	0.016	0.023	0.057	0.080	ng/m^3
MG	39	0	0	0	0.0307	0.043	0.078	0.120	0.186	ng/m^3
MN	39	0	0.003	0.005	0.008	0.008	0.010	0.013	0.017	ng/m^3
MO	39	0	0	0	0	0.001	0.001	0.003	0.003	ng/m^3
NA	39	0	0	0	0.08	0.16	0.22	0.59	0.68	ng/m^3
NI	39	0	0.0002	0.001	0.001	0.001	0.001	0.002	0.002	ng/m^3
PB	39	0	0	0	0	0.001	0.002	0.006	0.009	ng/m^3
PD	39	0	0	0	0	0.001	0.001	0.002	0.005	ng/m^3
PH	39	0	0	0	0	0.003	0	0.00848	0.0331	ng/m^3

Table 4.1.1-8 Summary statistics for pollutant concentrations at Holland site based on 24-hr averages for 2/20/2003 to 3/31/2003.

Pollutant	No. of Samples	Minimum	10th Percentile	25th Percentile	Median	Mean	75th Percentile	90th Percentile	Maximum	Units
PM_{10} Trace Elements (continued)										
RB	39	0	0	0	0	0.0003	0	0.001	0.002	ng/m^3
SB	39	0	0	0	0.0089	0.009	0.017	0.020	0.027	ng/m^3
SE	39	0	0	0.0001	0.001	0.001	0.001	0.002	0.004	ng/m^3
SI	39	0.380	0.73	1.24	1.75	1.94	2.46	3.31	4.55	ng/m^3
SN	39	0	0	0	0.002	0.003	0.004	0.008	0.012	ng/m^3
SR	39	0.0004	0.001	0.002	0.003	0.003	0.004	0.005	0.009	ng/m^3
SU	39	0.18	0.23	0.32	0.46	0.53	0.68	0.96	1.22	ng/m^3
TI	39	0	0	0.001	0.019	0.023	0.037	0.055	0.074	ng/m^3
TL	39	0	0	0	0	0.0002	0.0001	0.001	0.002	ng/m^3
UR	39	0	0	0	0.0001	0.001	0.002	0.002	0.005	ng/m^3
VA	39	0	0	0	0	0.001	0.002	0.006	0.010	ng/m^3
YT	39	0	0	0	0	0	0.001	0.001	0.003	ng/m^3
ZN	39	0.008	0.010	0.016	0.021	0.024	0.033	0.039	0.045	ng/m^3
ZR	39	0	0	0.0005	0.002	0.002	0.003	0.004	0.006	ng/m^3

Table 4.1.1-9 Summary statistics for pollutant concentrations at Clovis site based on 24-hr averages for 4/1/2001 to 3/31/2003.

Pollutant	No. of Samples	Minimum	10th Percentile	25th Percentile	Median	Mean	75th Percentile	90th Percentile	Maximum	Units
Gases										
O_3	714	1.93	9.96	17.88	33.86	32.67	46.19	54.59	73.58	ppb
O_3 8-hr max	714	4.50	19.83	32.06	52.06	53.07	72.17	89.38	118.63	ppb
CO	723	0	0.26	0.31	0.41	0.49	0.60	0.86	1.38	ppm
NO	709	0	0.96	1.73	3.83	8.86	11.86	26.97	49.79	ppb
NO_2	708	2.79	7.51	10.09	14.64	15.44	19.82	24.36	41.23	ppb
NO_2 8-hr max	708	4.63	10.08	13.75	19.56	20.33	25.69	31.04	51.67	ppb
NO_x	709	2.79	8.59	12.21	18.77	24.15	32.52	49.45	77.27	ppb

Table 4.1.1-10 Summary statistics for pollutant concentrations at Drummond site based on 24-hr averages for 4/1/2001 to 3/31/2003.

Pollutant	No. of Samples	Minimum	10th Percentile	25th Percentile	Median	Mean	75th Percentile	90th Percentile	Maximum	Units
Gases										
O_3	727	7.33	13.07	18.85	31.70	31.63	42.38	49.63	69.29	ppb
O_3 8-hr max	727	7.63	19.88	30.54	51.47	51.13	69.72	83.65	113.38	ppb
CO	724	0	0.31	0.38	0.57	0.51	0.70	0.94	1.75	ppm
NO	663	0.25	1.77	3.46	15.46	7.91	22.16	41.39	97.73	ppb
NO_2	663	6.73	11.33	14.77	20.04	19.29	24.18	29.94	44.40	ppb
NO_2 8-hr max	663	8.88	14.75	19.27	26.08	25.33	31.75	38.95	55.00	ppb
NO_x	664	7.50	13.96	19.29	35.39	28.19	46.78	66.78	127.15	ppb

Table 4.1.1-11 Summary statistics for pollutant concentrations at Sierra Sky Park site based on 24-hr averages for 4/1/2001 to 3/31/2003.

Pollutant	No. of Samples	Minimum	10th Percentile	25th Percentile	Median	Mean	75th Percentile	90th Percentile	Maximum	Units
Gases										
O_3	724	12.71	24.06	32.14	45.68	44.40	55.98	62.89	87.09	ppb
O_3 8-hr max	724	13.75	32.49	45.88	65.88	65.03	82.50	98.04	132.50	ppb
CO	720	0	0.25	0.29	0.36	0.42	0.50	0.68	1.20	ppm
NO	700	0.17	0.79	1.40	2.75	5.91	7.50	16.23	44.75	ppb
NO_2	700	4.50	8.44	11.04	14.43	15.05	18.79	22.45	40.27	ppb
NO_2 8-hr max	700	4.88	11.94	15.09	20.00	20.28	24.53	29.18	49.50	ppb
NO_x	700	4.75	9.46	12.46	17.21	20.83	27.13	37.86	73.19	ppb

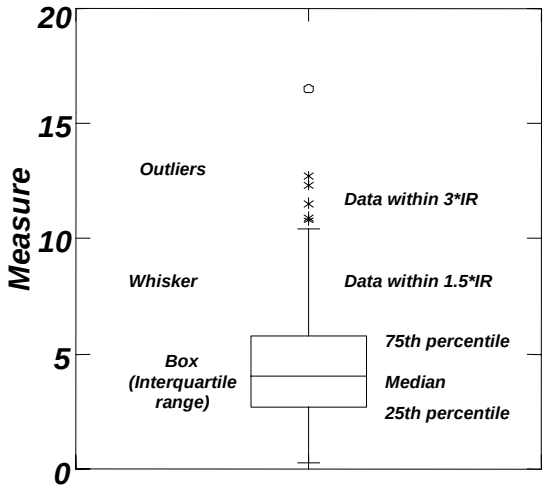


Figure 4.1.1-1. Illustration of a box whisker plot as defined by SYSTAT statistical software.

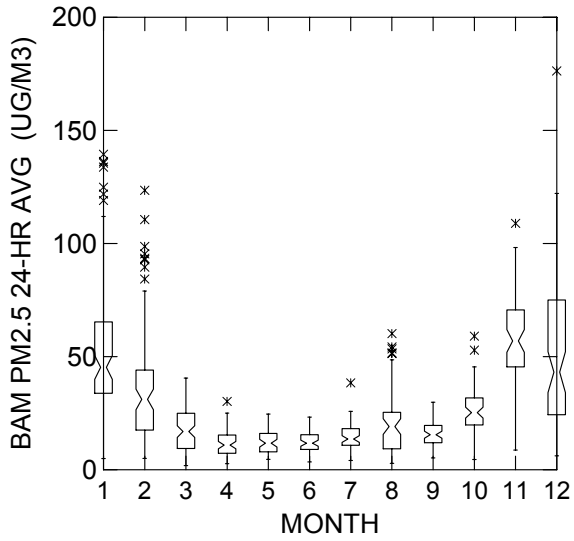


Figure 4.1.1-2. Monthly box whisker plots of 24-hr average $PM_{2.5}$ mass at the Central Site (Fresno First Street) for April 1, 2001, through March 31, 2003; concentrations are in $\mu g/m^3$. Numbers 1-12 along the x-axis refer to months, January-December.

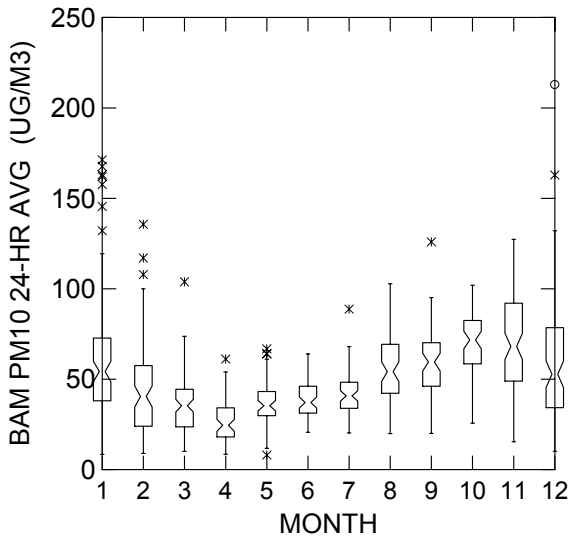


Figure 4.1.1-3. Monthly box whisker plots of 24-hr average PM_{10} mass at the Central Site (Fresno First Street) for April 1, 2001, through March 31, 2003; concentrations are in $\mu g/m^3$. Numbers 1-12 along the x-axis refer to months, January-December.

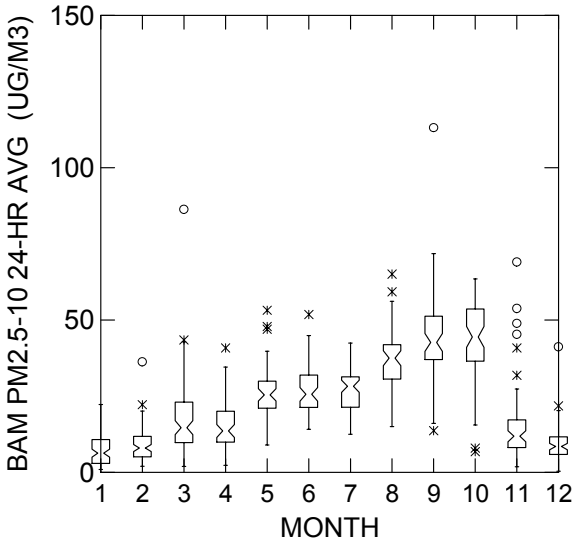


Figure 4.1.1-4. Monthly box whisker plots of 24-hr average $PM_{2.5-10}$ (PM coarse) mass at the Central Site (Fresno First Street) for April 1, 2001, through March 31, 2003; concentrations are in $\mu g/m^3$. Numbers 1-12 along the x-axis refer to months, January-December.

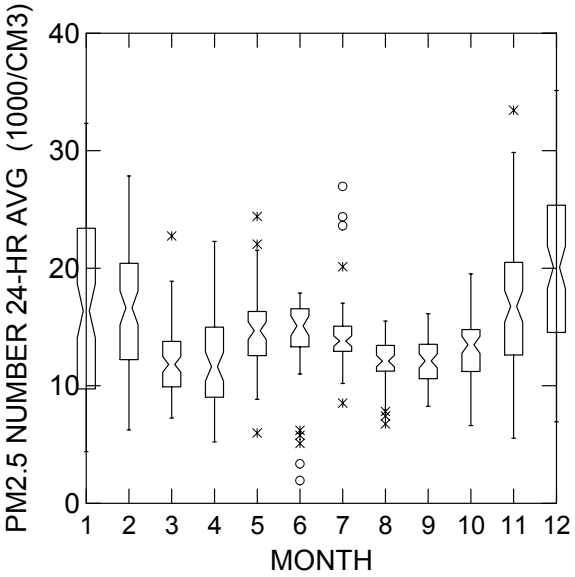


Figure 4.1.1-5. Monthly box whisker plots of 24-hr average $PM_{2.5}$ number at the Central Site (Fresno First Street) for April 1, 2001, through March 31, 2003; concentrations are in $1000/cm^3$. Numbers 1-12 along the x-axis refer to months, January-December.

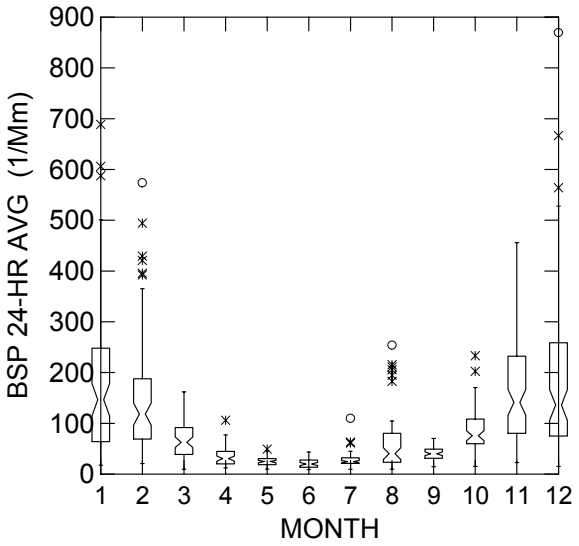


Figure 4.1.1-6. Monthly box whisker plots of 24-hr average particle scattering (b_{sp}) at the Central Site (Fresno First Street) for April 1, 2001, through March 31, 2003; concentrations are in Mm^{-1}. Numbers 1-12 along the x-axis refer to months, January-December.

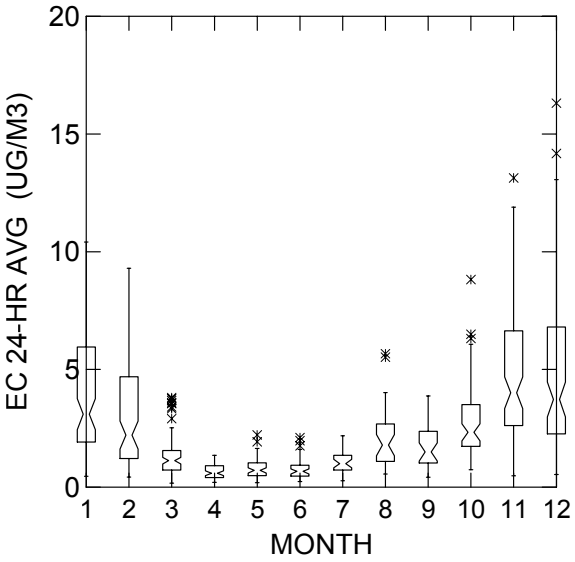


Figure 4.1.1-7. Monthly box whisker plots of 24-hr average $PM_{2.5}$ EC at the Central Site (Fresno First Street) for April 1, 2001, through March 31, 2003; concentrations are in $\mu g/m^3$. Numbers 1-12 along the x-axis refer to months, January-December.

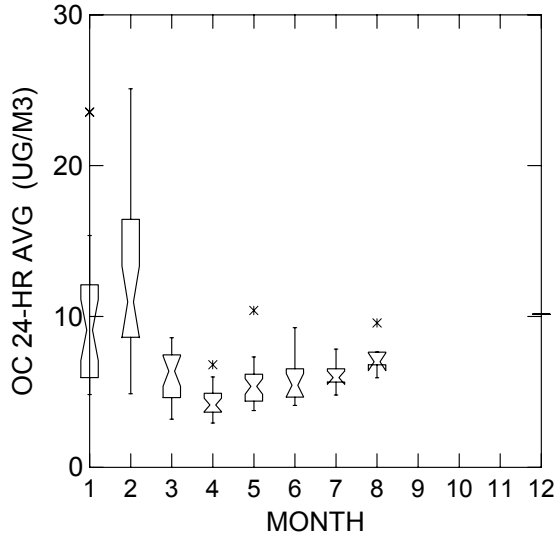


Figure 4.1.1-8. Monthly box whisker plots of 24-hr average $PM_{2.5}$ OC at the Central Site (Fresno First Street) for April 1, 2001, through March 31, 2003; concentrations are in $\mu g/m^3$. Numbers 1-12 along the x-axis refer to months, January-December.

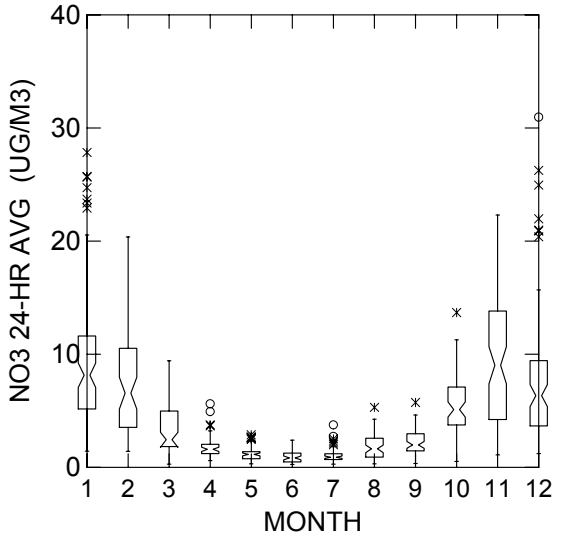


Figure 4.1.1-9. Monthly box whisker plots of 24-hr average $PM_{2.5}$ nitrate (NO_3) at the Central Site (Fresno First Street) for April 1, 2001, through March 31, 2003; concentrations are in $\mu g/m^3$. Numbers 1-12 along the x-axis refer to months, January-December.

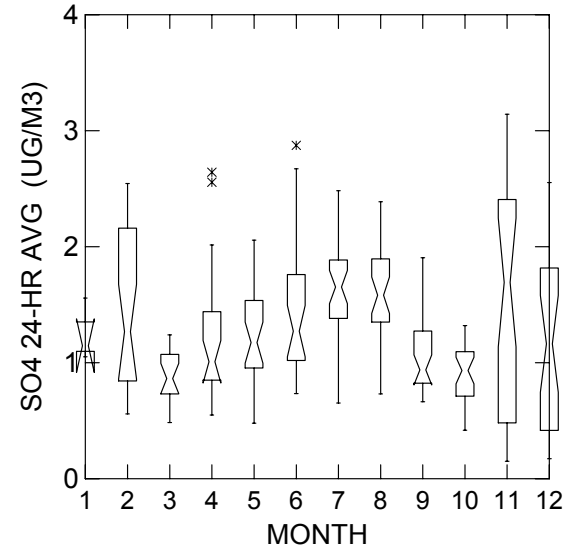


Figure 4.1.1-10. Monthly box whisker plots of 24-hr average $PM_{2.5}$ sulfate (SO_4) at the Central Site (Fresno First Street) for April 1, 2001, through March 31, 2003; concentrations are in $\mu g/m^3$. Numbers 1-12 along the x-axis refer to months, January-December.

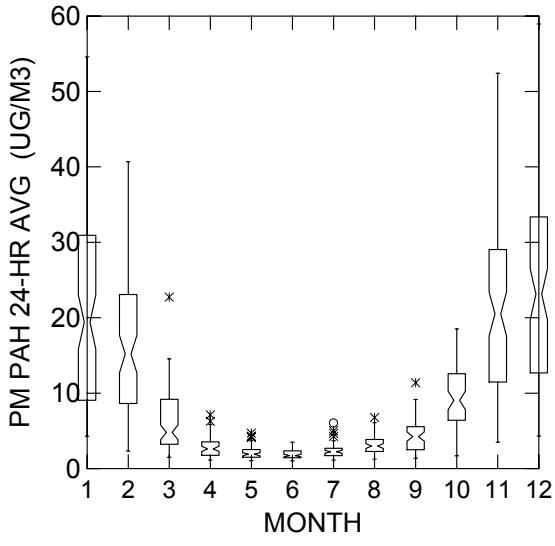


Figure 4.1.1-11. Monthly box whisker plots of 24-hr average particulate polycyclic aromatic hydrocarbons (PMPAH) at the Central Site (Fresno First Street) for April 1, 2001, through March 31, 2003; concentrations are in ng/m^3. Numbers 1-12 along the x-axis refer to months, January-December.

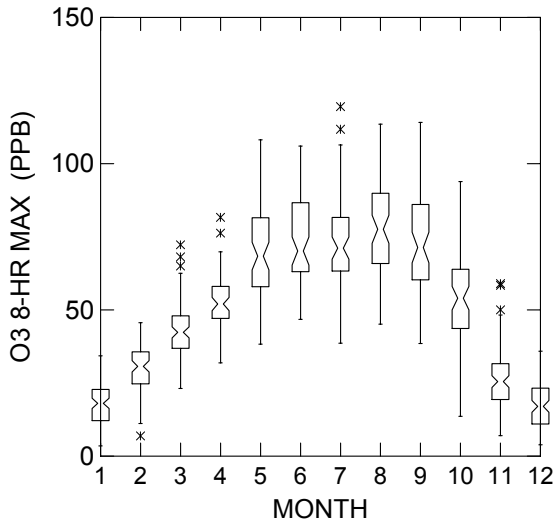


Figure 4.1.1-12. Monthly box whisker plots of 8-hr daily maximum ozone (O_3) at the Central Site (Fresno First Street) for April 1, 2001, through March 31, 2003; concentrations are in ppb. Numbers 1-12 along the x-axis refer to months, January-December.

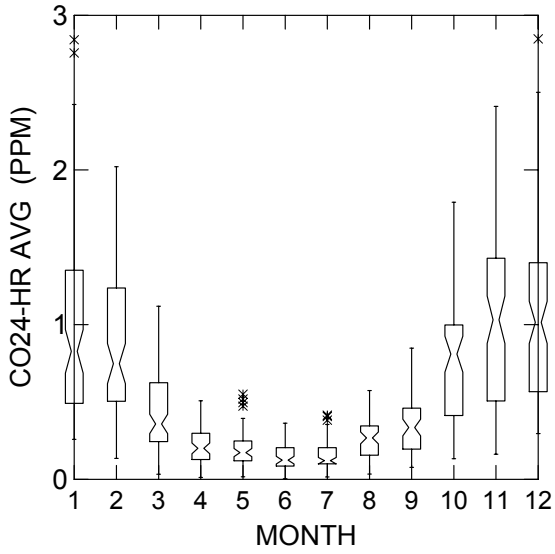


Figure 4.1.1-13. Monthly box whisker plots of 24-hr average carbon monoxide (CO) at the Central Site (Fresno First Street) for April 1, 2001, through March 31, 2003; concentrations are in ppm. Numbers 1-12 along the x-axis refer to months, January-December.

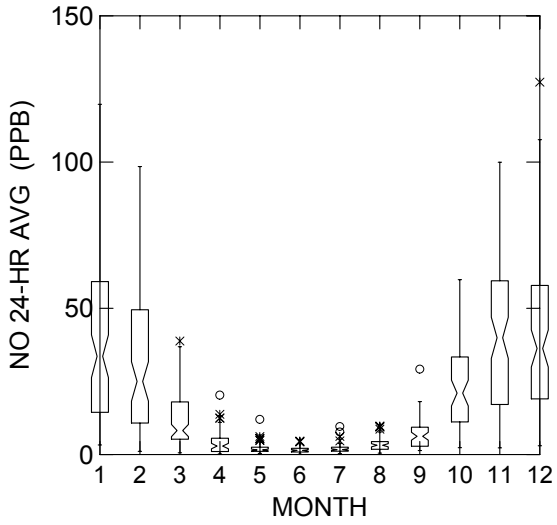


Figure 4.1.1-14. Monthly box whisker plots of 24-hr average nitric oxide (NO) at the Central Site (Fresno First Street) for April 1, 2001, through March 31, 2003; concentrations are in ppb. Numbers 1-12 along the x-axis refer to months, January-December.

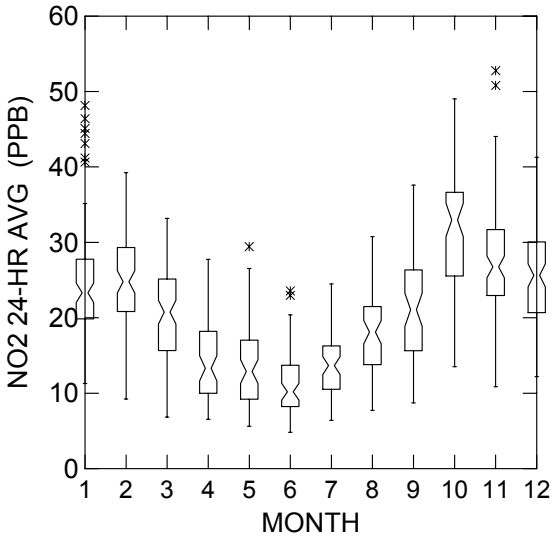


Figure 4.1.1-15. Monthly box whisker plots of 24-hr average nitrogen dioxide (NO_2) at the Central Site (Fresno First Street) for April 1, 2001, through March 31, 2003; concentrations are in ppb. Numbers 1-12 along the x-axis refer to months, January-December.

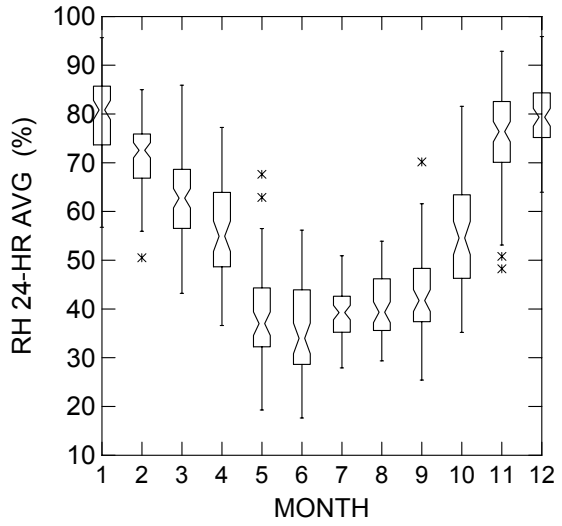


Figure 4.1.1-16. Monthly box whisker plots of 24-hr average relative humidity (RH) at the Central Site (Fresno First Street) for April 1, 2001, through March 31, 2003; units are percent. Numbers 1-12 along the x-axis refer to months, January-December.

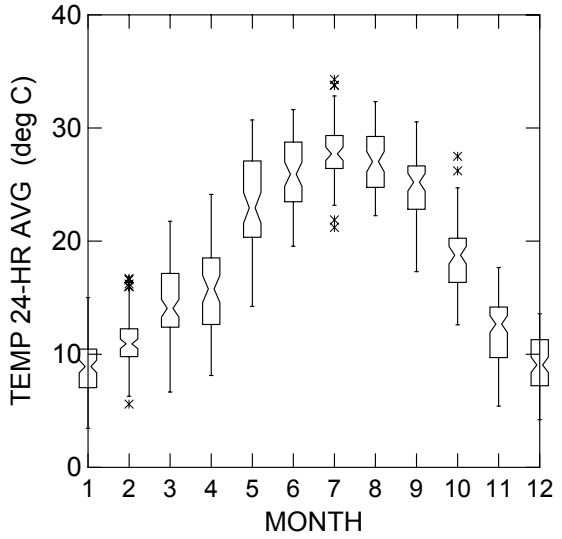


Figure 4.1.1-17. Monthly box whisker plots of 24-hr average temperature (Temp) at the Central Site (Fresno First Street) for April 1, 2001, through March 31, 2003; units degrees centigrade. Numbers 1-12 along the x-axis refer to months, January-December.

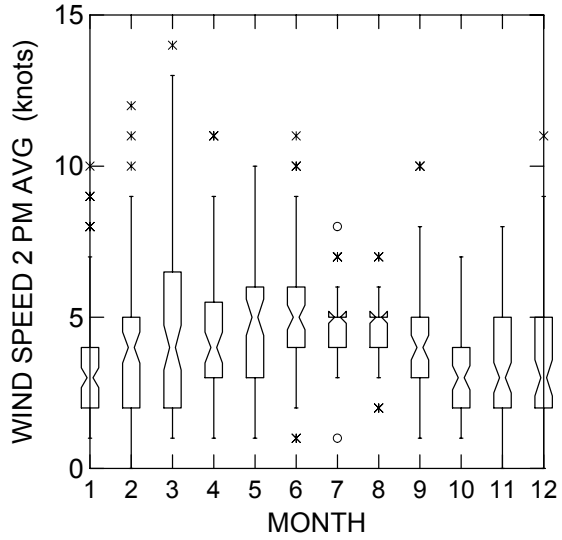


Figure 4.1.1-18. Monthly box whisker plots of 2 p.m. wind speed at the Central Site (Fresno First Street) for April 1, 2001, through March 31, 2003; units are knots. Numbers 1-12 along the x-axis refer to months, January-December.

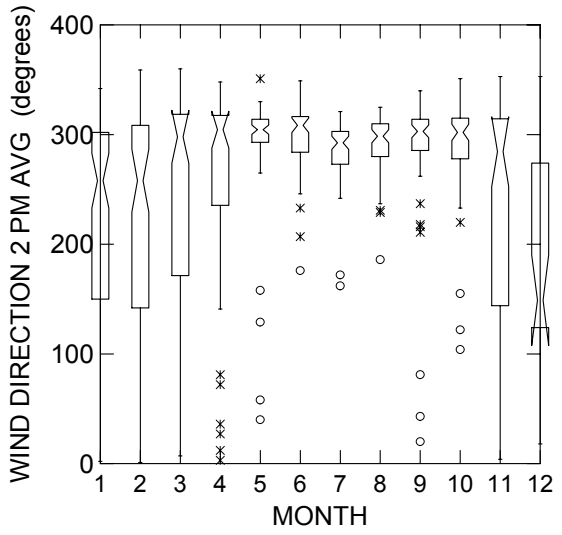


Figure 4.1.1-19. Monthly box whisker plots of 2 p.m. wind direction at the Central Site (Fresno First Street) for April 1, 2001, through March 31, 2003; units are degrees. Numbers 1-12 along the x-axis refer to months, January-December.

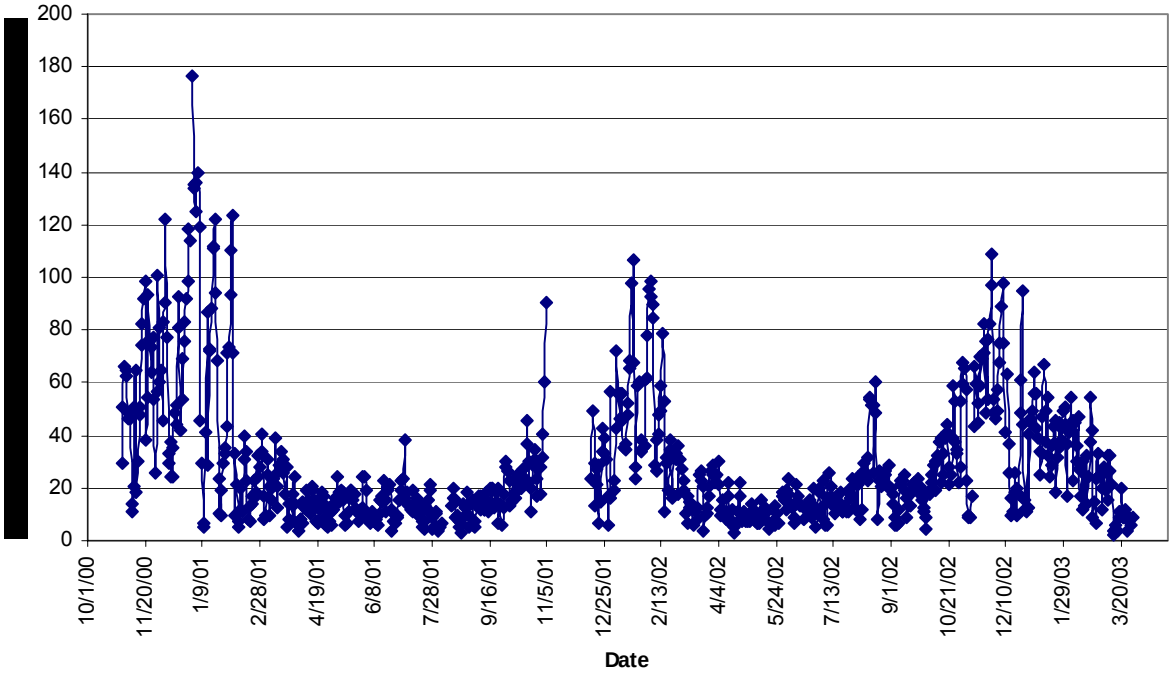


Figure 4.1.1-20. Daily (24-hr average) time series plot of $PM_{2.5}$ mass ($BAM_{2.5}$) at the Central Site (Fresno First Street) for November 1, 2000, through March 31, 2003; concentrations are in $\mu g/m^3$.

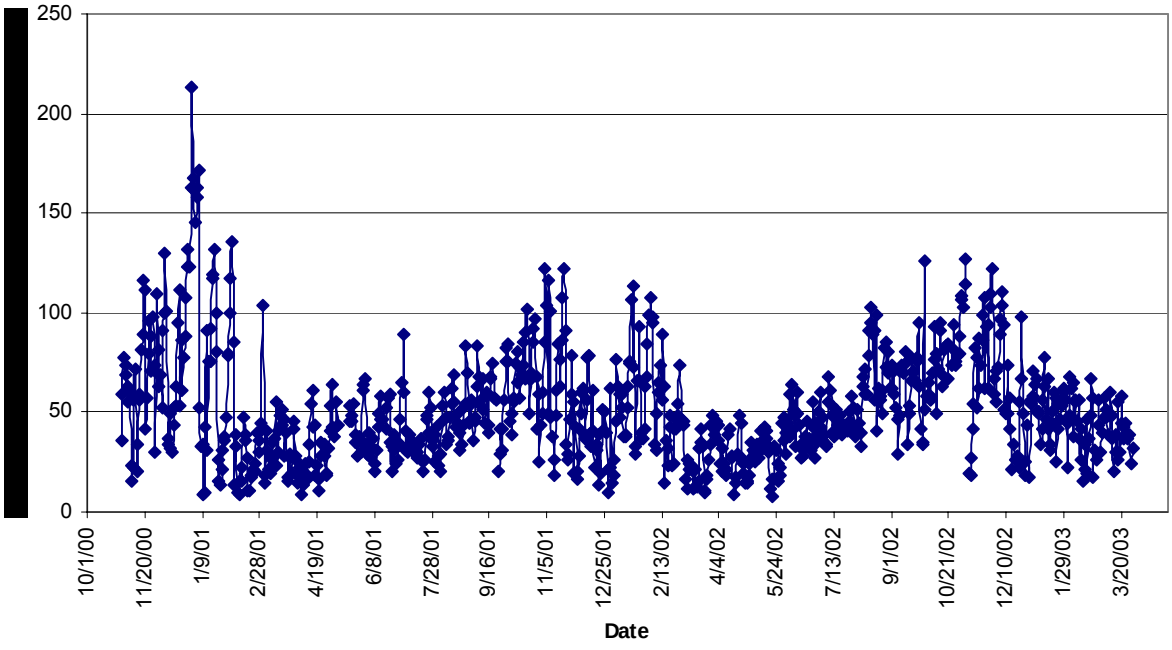


Figure 4.1.1-21. Daily (24-hr average) time series plot of PM_{10} mass (BAM_{10}) at the Central Site (Fresno First Street) for November 1, 2000, through March 31, 2003; concentrations are in $\mu g/m^3$.

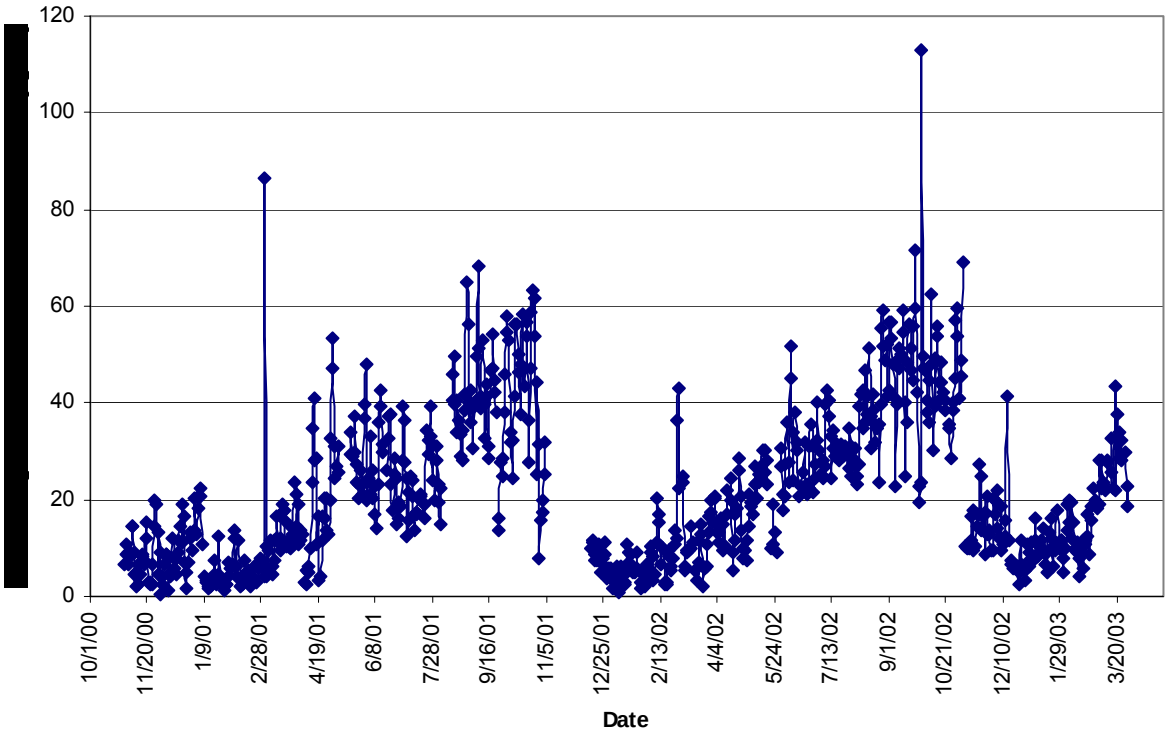


Figure 4.1.1-22. Daily (24-hr average) time series plot of $PM_{2.5-10}$ mass (coarse, $BAM_{2.5-10}$) at the Central Site (Fresno First Street) for November 1, 2000, through March 31, 2003; concentrations are in $\mu g/m^3$.

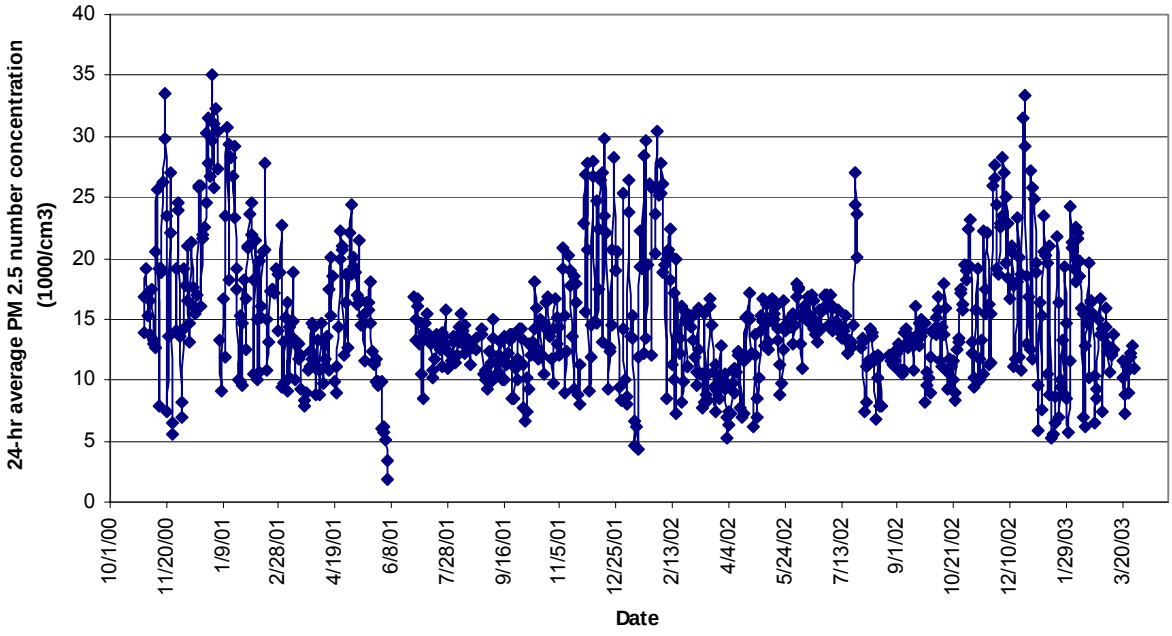


Figure 4.1.1-23. Daily (24-hr average) time series plot of $PM_{2.5}$ number at the Central Site (Fresno First Street) for November 1, 2000, through March 31, 2003; concentrations are in $1000/cm^3$.

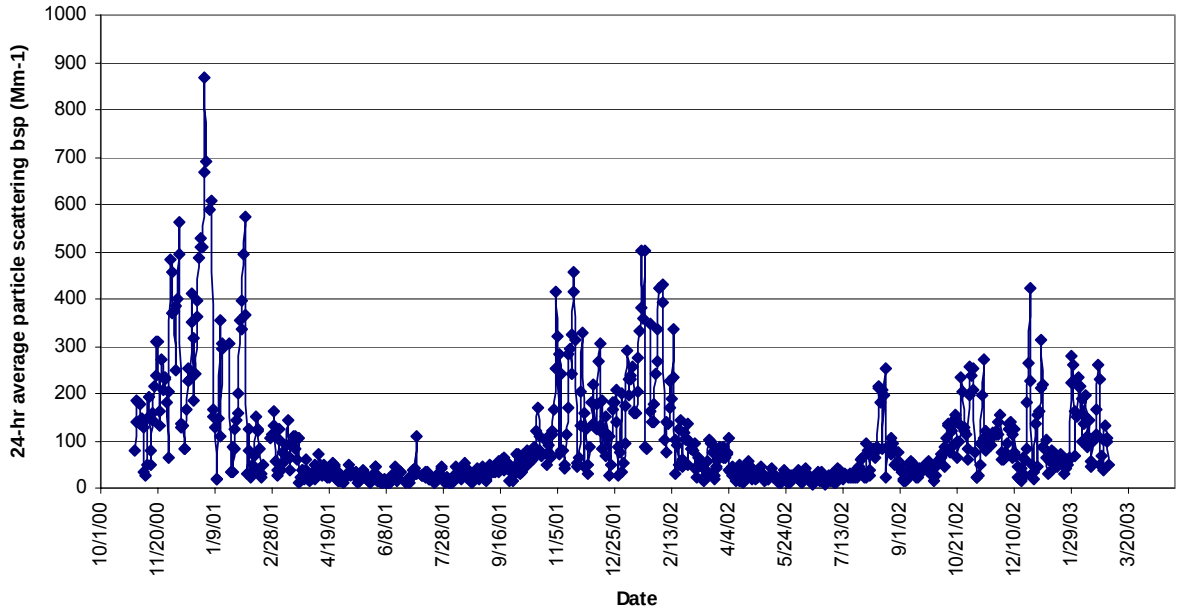


Figure 4.1.1-24. Daily (24-hr average) time series plot of particle scattering (b_{sp}) at the Central Site (Fresno First Street) for November 1, 2000, through March 31, 2003; concentrations are in Mm^{-1}.

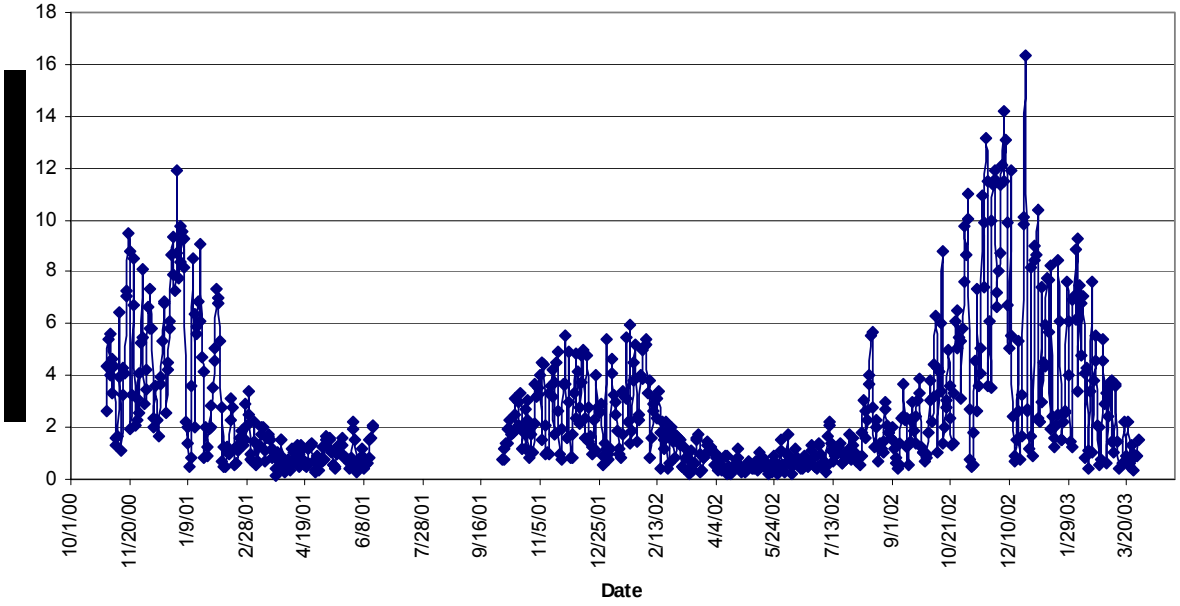


Figure 4.1.1-25. Daily (24-hr average) time series plot of elemental carbon (EC) at the Central Site (Fresno First Street) for November 1, 2000, through March 31, 2003; concentrations are in $\mu g/m^3$.

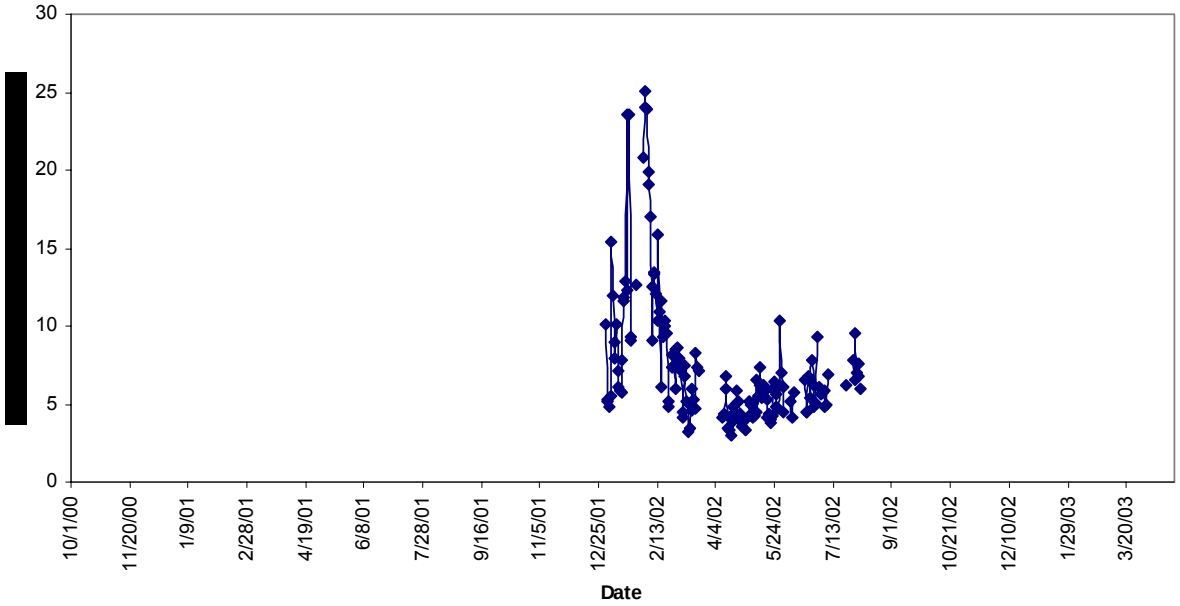


Figure 4.1.1-26. Daily (24-hr average) time series plot of organic carbon (OC) at the Central Site (Fresno First Street) for November 1, 2000, through March 31, 2003; concentrations are in $\mu g/m^3$.

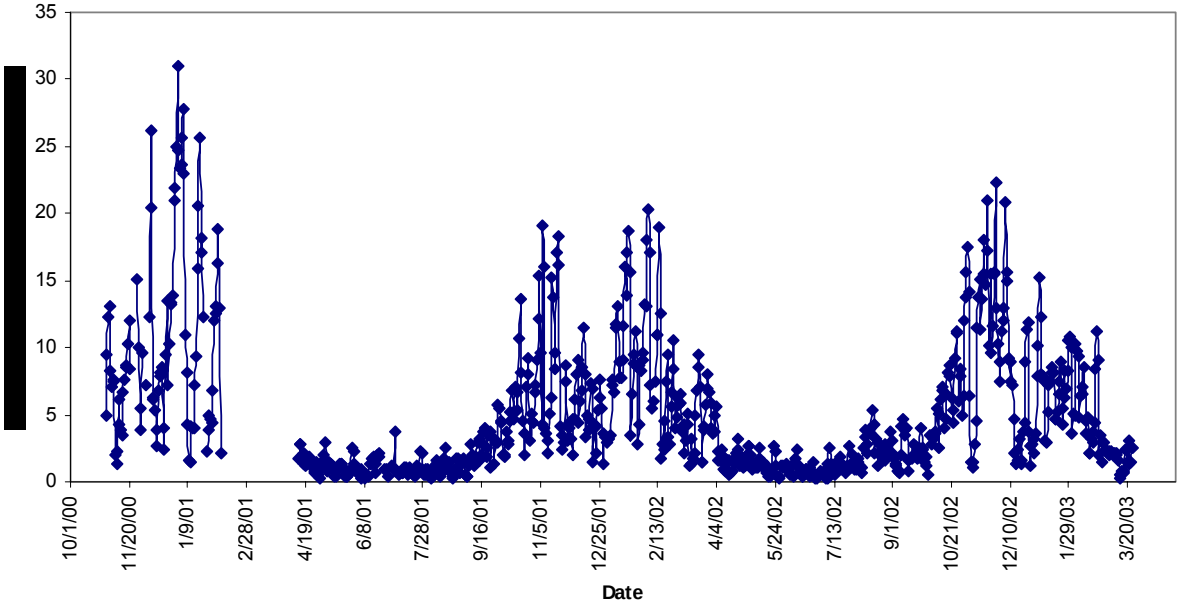


Figure 4.1.1-27. Daily (24-hr average) time series plot of $PM_{2.5}$ nitrate (NO_3) at the Central Site (Fresno First Street) for November 1, 2000, through March 31, 2003; concentrations are in $\mu g/m^3$.

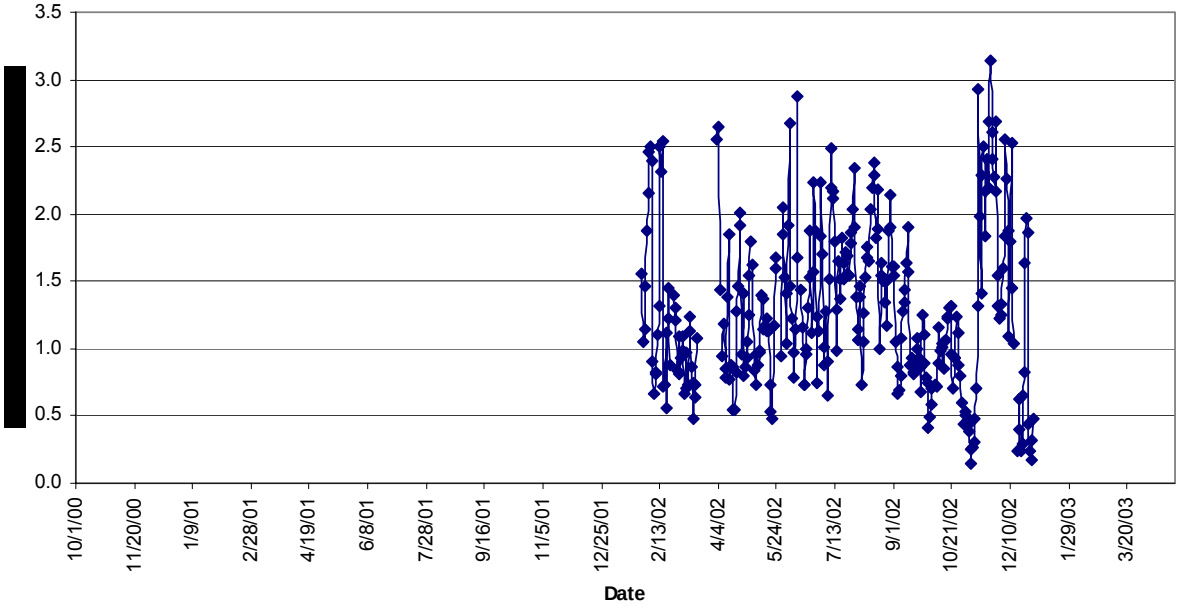


Figure 4.1.1-28. Daily (24-hr average) time series plot of $PM_{2.5}$ sulfate (SO_4) at the Central Site (Fresno First Street) for November 1, 2000, through March 31, 2003; concentrations are in $\mu g/m^3$.

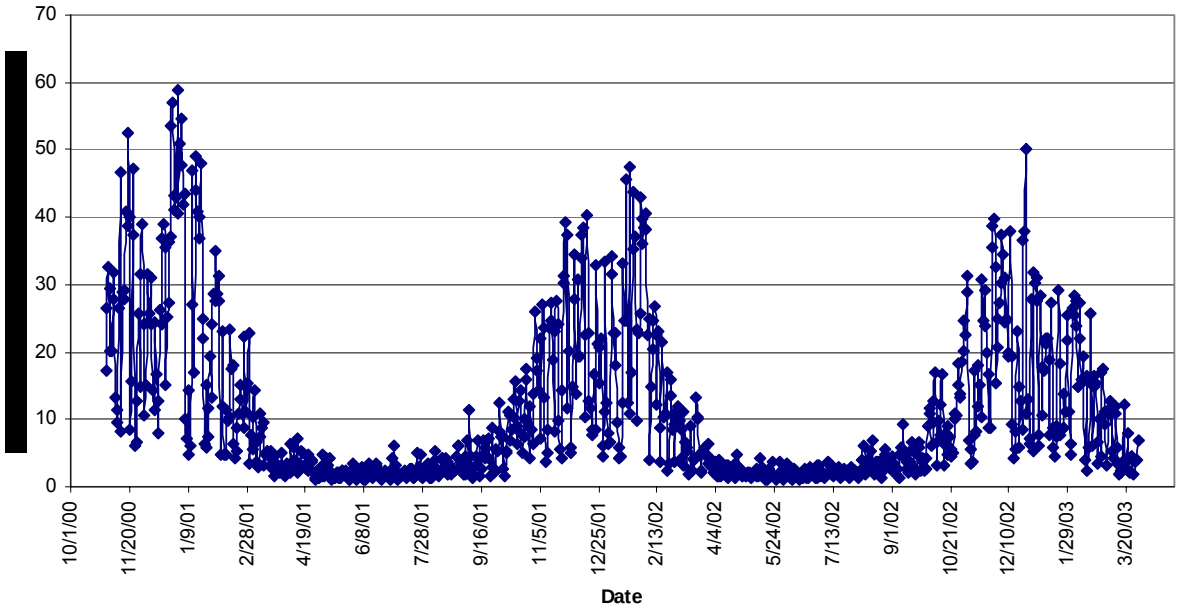


Figure 4.1.1-29. Daily (24-hr average) time series plot of particulate polycyclic aromatic hydrocarbons (PMPAH) at the Central Site (Fresno First Street) for November 1, 2000, through March 31, 2003; concentrations are in ng/m^3.

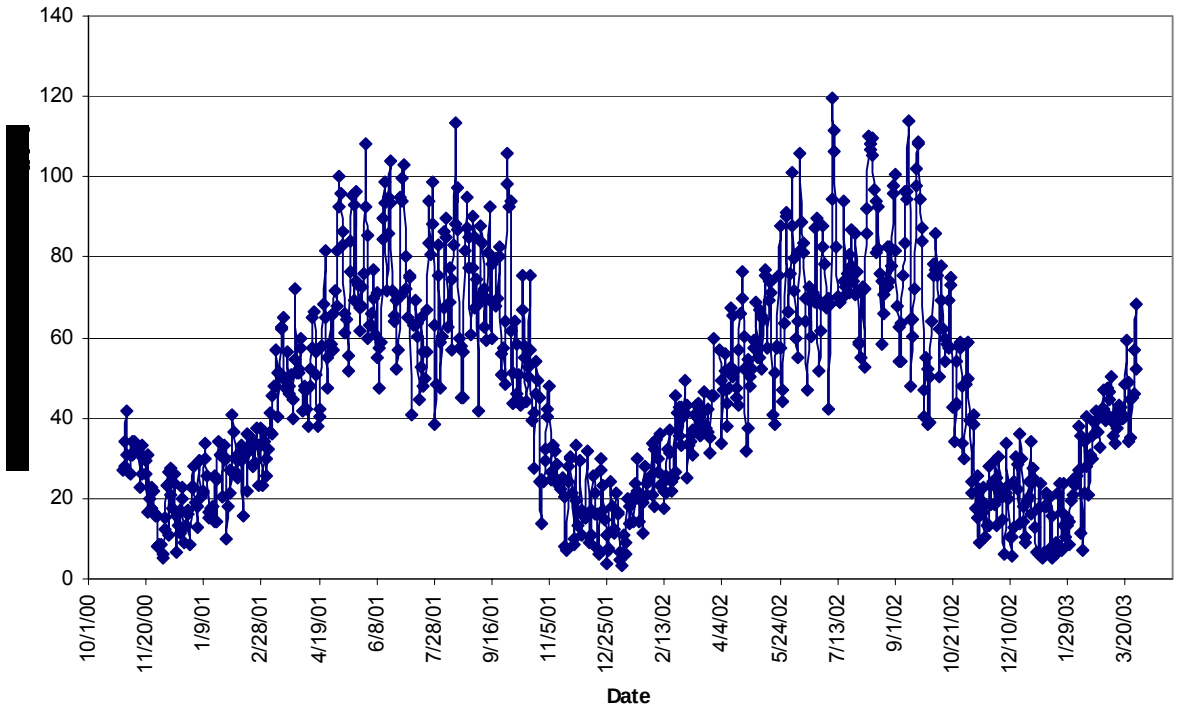


Figure 4.1.1-30. Daily (8-hr daily maximum) time series plot of ozone (O_3) at the Central Site (Fresno First Street) for November 1, 2000, through April 30, 2002; concentrations are in ppb.

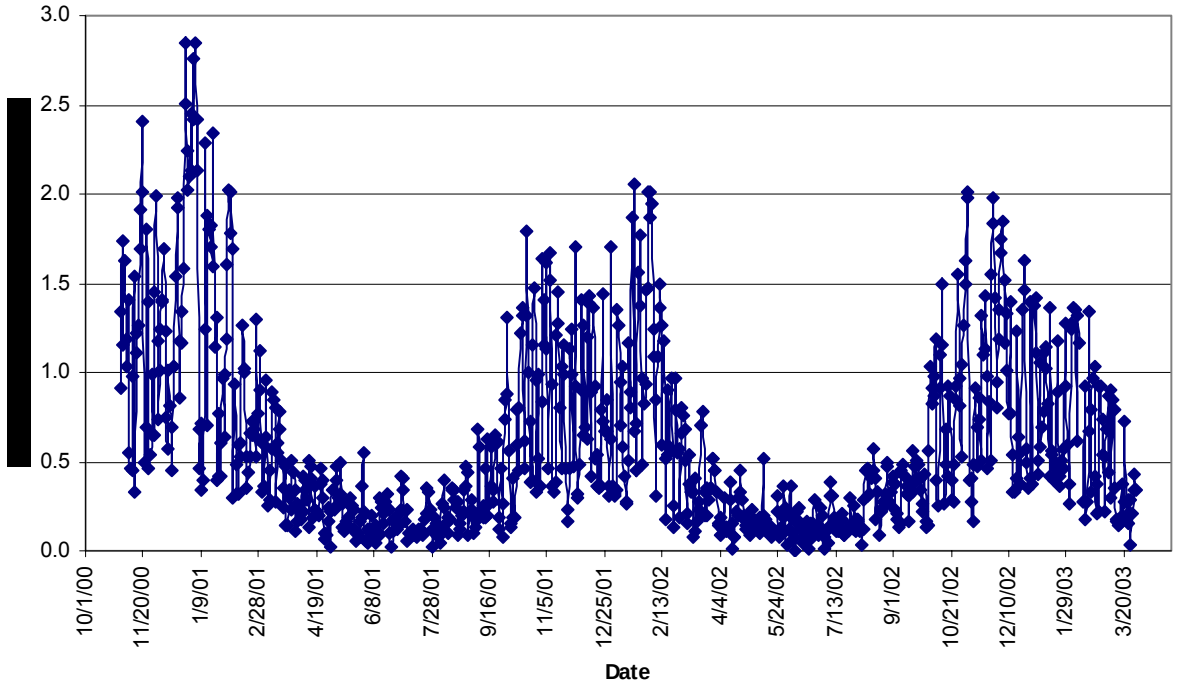


Figure 4.1.1-31. Daily (24-hr average) time series plot of carbon monoxide (CO) at the Central Site (Fresno First Street) for November 1, 2000, through April 30, 2002; concentrations are in ppm.

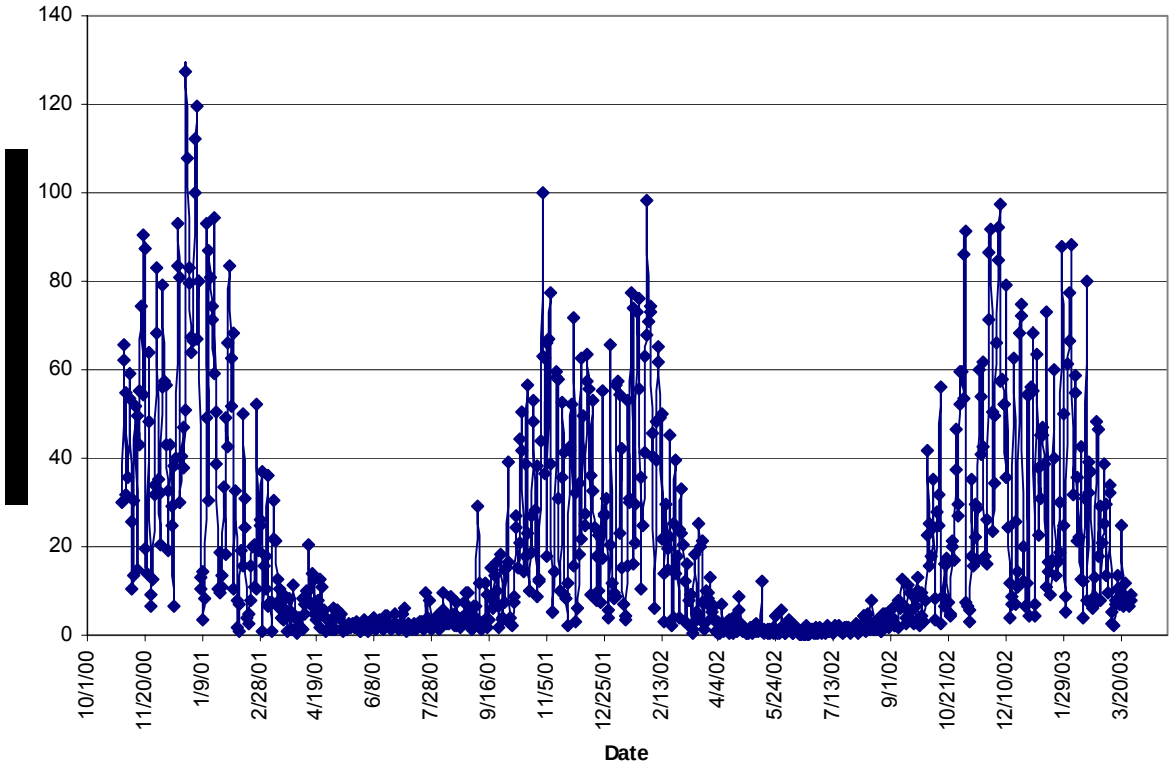


Figure 4.1.1-32. Daily (24-hr average) time series plot of nitric oxide (NO) at the Central Site (Fresno First Street) for November 1, 2000, through April 30, 2002; concentrations are in ppb.

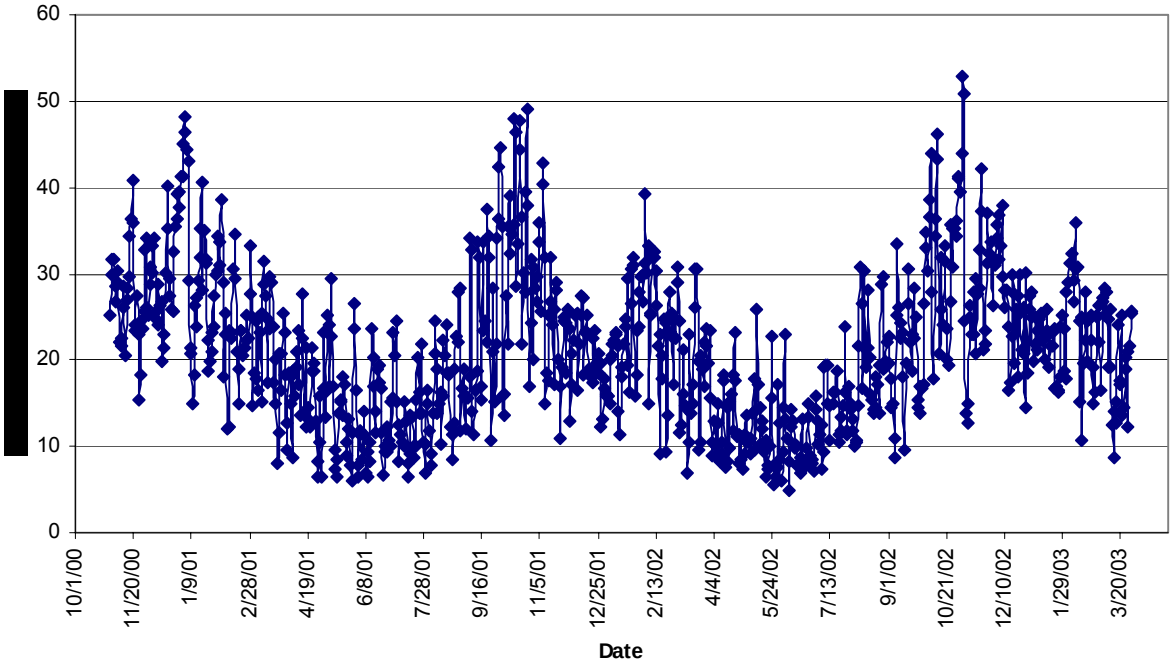


Figure 4.1.1-33. Daily (24-hr average) time series plot of nitrogen dioxide (NO_2) at the Central Site (Fresno First Street) for November 1, 2000, through April 30, 2002; concentrations are in ppb.

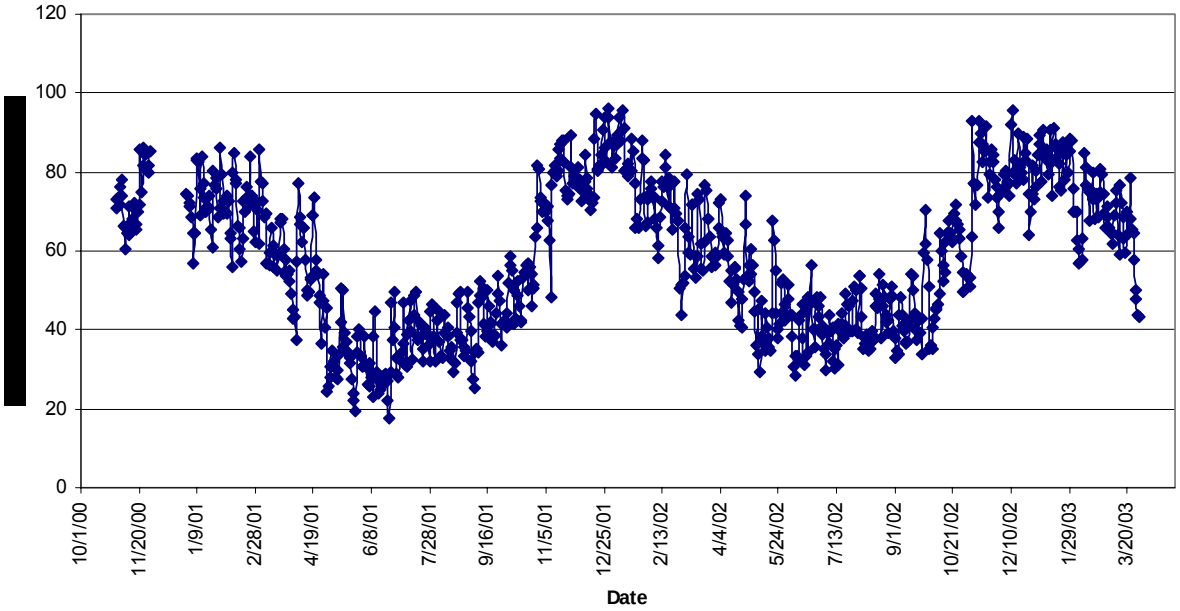


Figure 4.1.1-34. Daily (24-hr average) time series plot of relative humidity at the Central Site (Fresno First Street) for November 1, 2000, through April 30, 2002; units are percent.

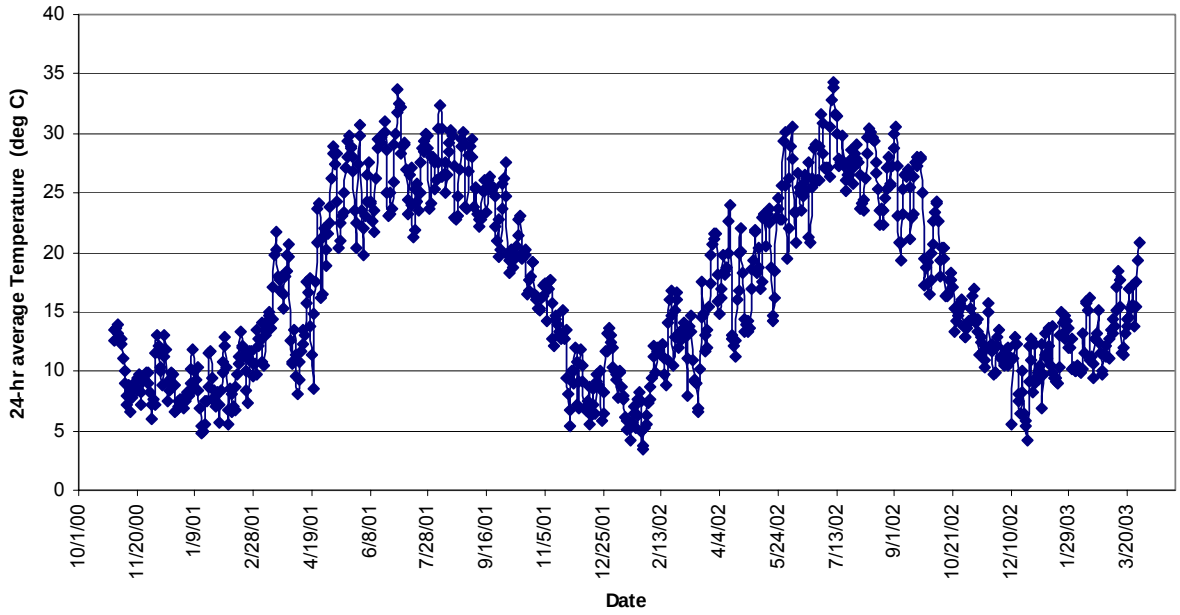


Figure 4.1.1-35. Daily (24-hr average) time series plot of temperature at the Central Site (Fresno First Street) for November 1, 2000, through April 30, 2002; units are degrees Centigrade.

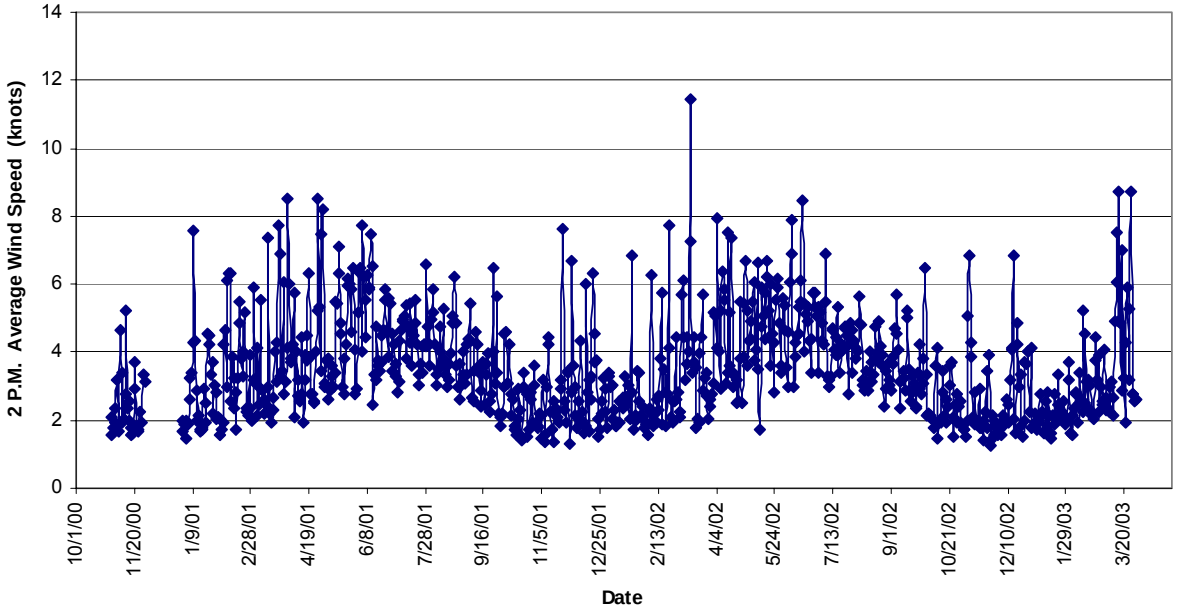


Figure 4.1.1-36. Daily time series plot of 2 p.m. wind speed at the Central Site (Fresno First Street) for November 1, 2000, through April 30, 2002; units are knots.

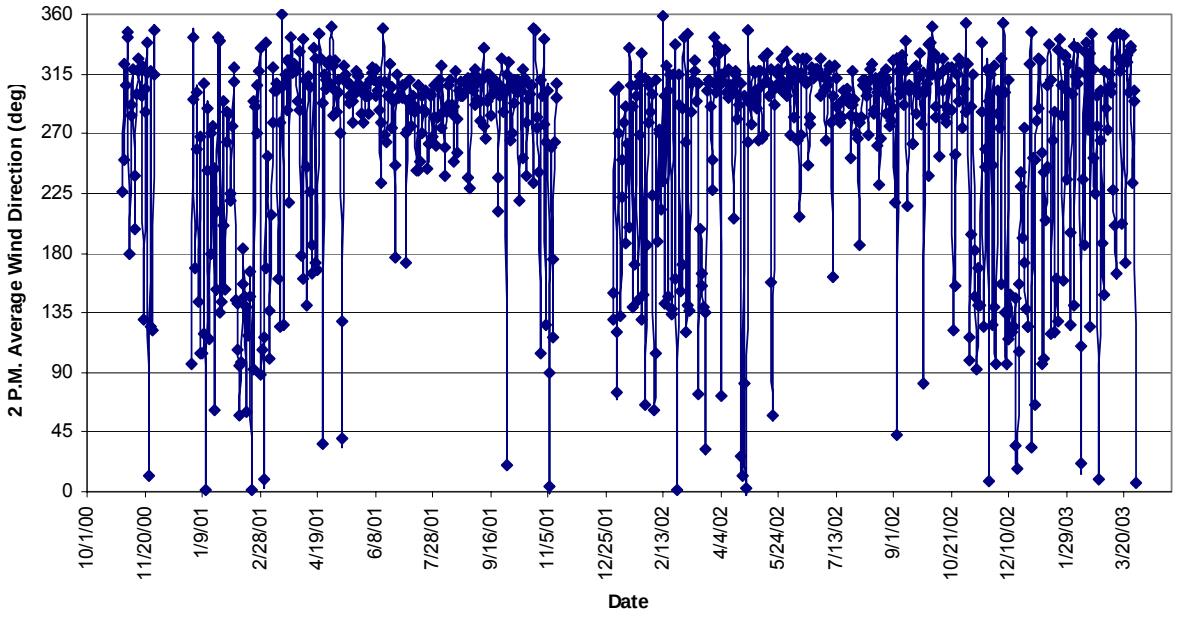


Figure 4.1.1-37. Daily time series plot of 2 p.m. wind direction at the Central Site (Fresno First Street) for November 1, 2000, through April 30, 2002; units are degrees.

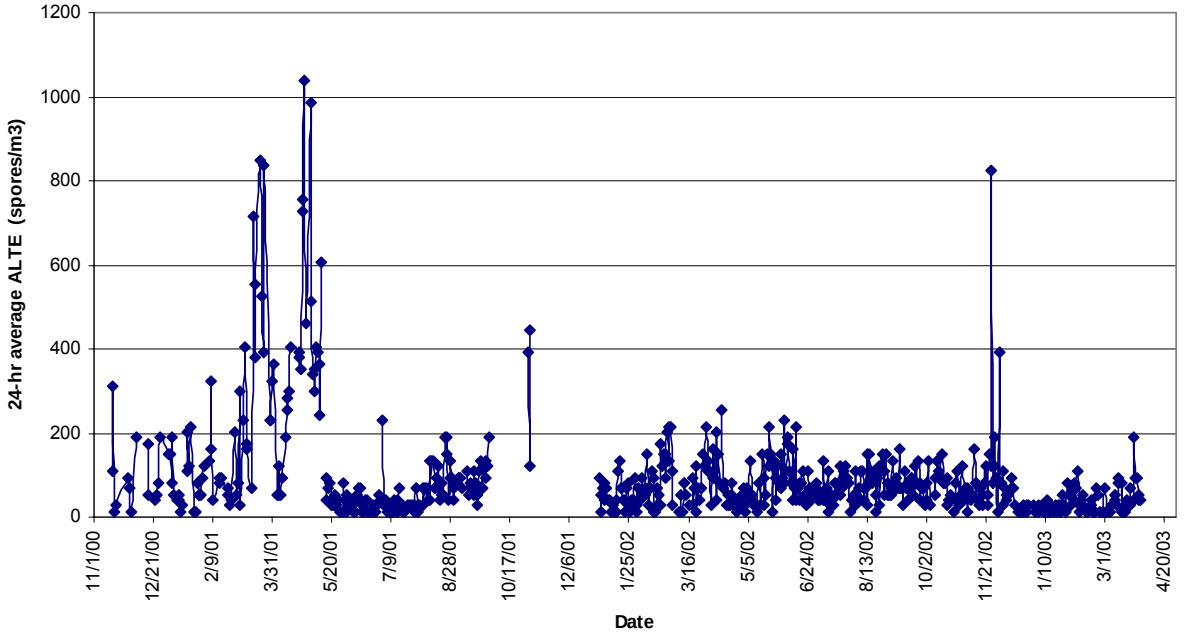


Figure 4.1.1-38. Daily (24-hr average) time series plot of *Alternaria* (ALTE) at the Central Site (Fresno First Street) for November 15, 2000, through March 31, 2003; concentrations are in spores/m^3.

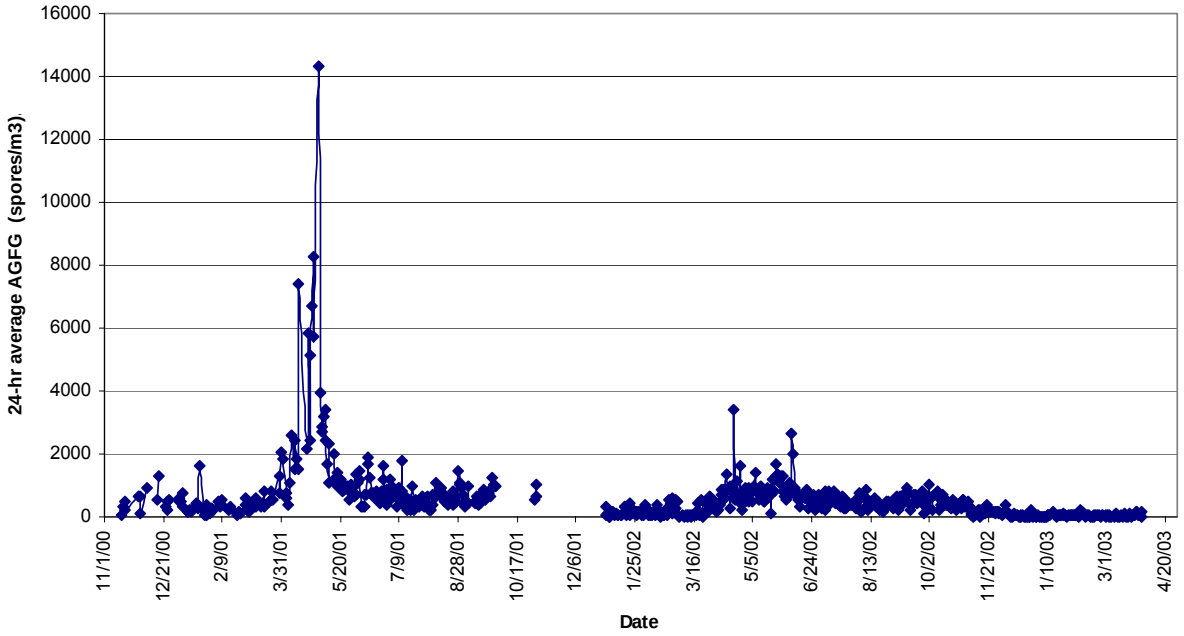


Figure 4.1.1-39. Daily (24-hr average) time series plot of agricultural fungi (AGFG) at the Central Site (Fresno First Street) for November 1, 2000, through March 31, 2003; concentrations are in spores/m^3.

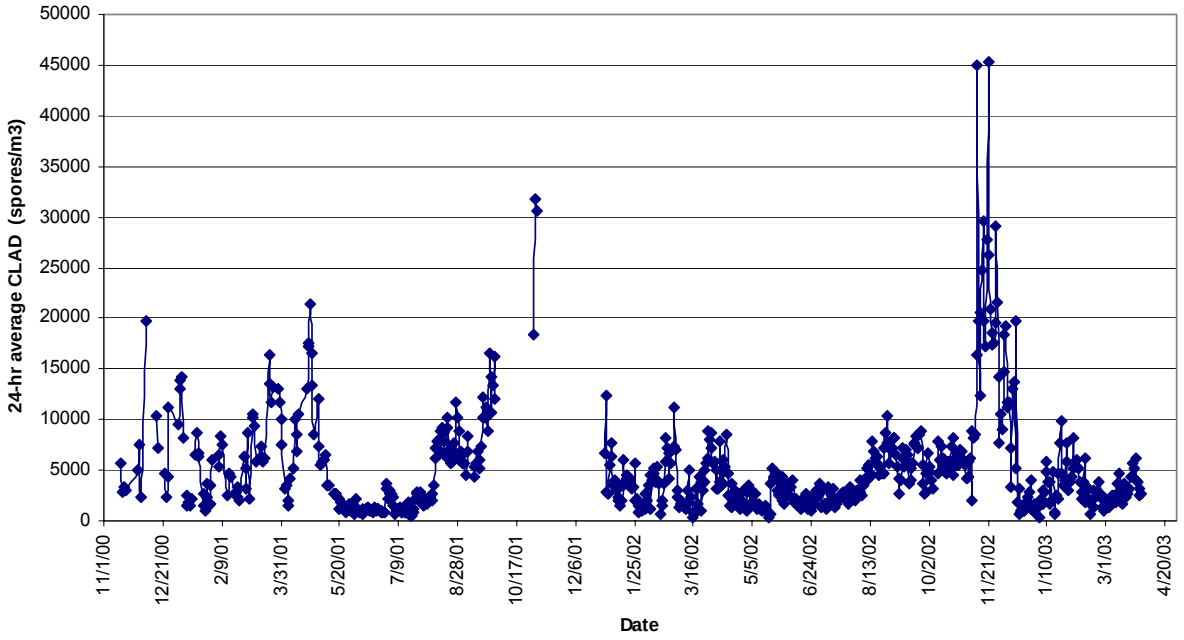


Figure 4.1.1-40. Daily (24-hr average) time series plot of *Cladosporium* (CLAD) at the Central Site (Fresno First Street) for November 15, 2000, through March 31, 2003; concentrations are in spores/m^3.

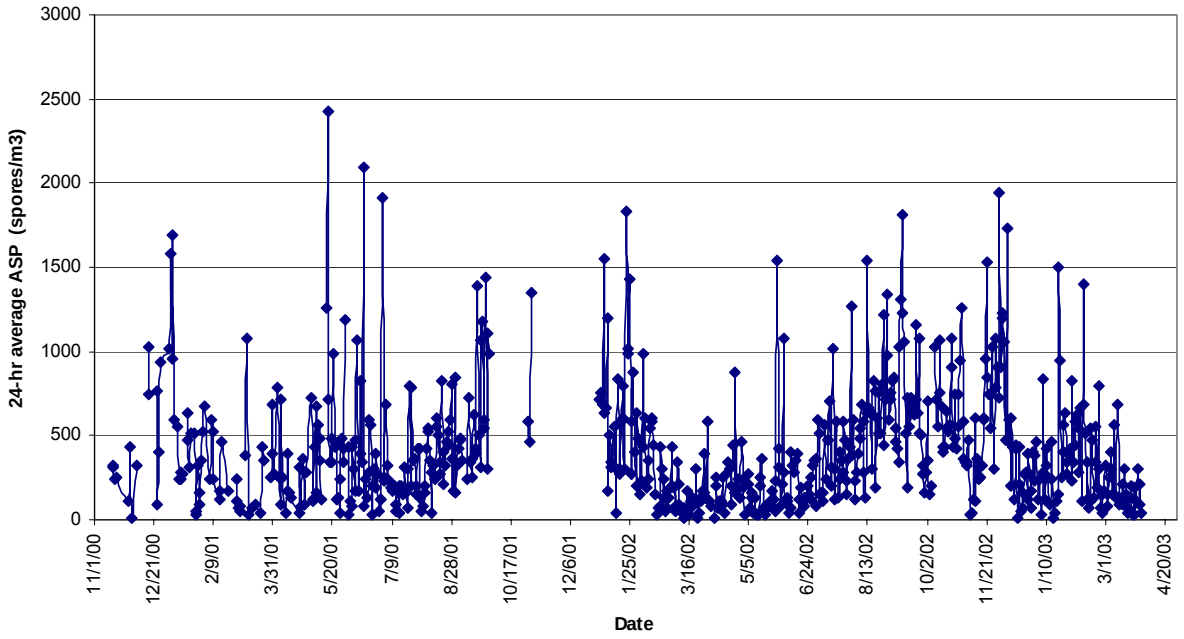


Figure 4.1.1-41. Daily (24-hr average) time series plot of *Aspergillus/Penicillium* (ASP) at the Central Site (Fresno First Street) for November 15, 2000, through March 31, 2003; concentrations are in spores/m^3.

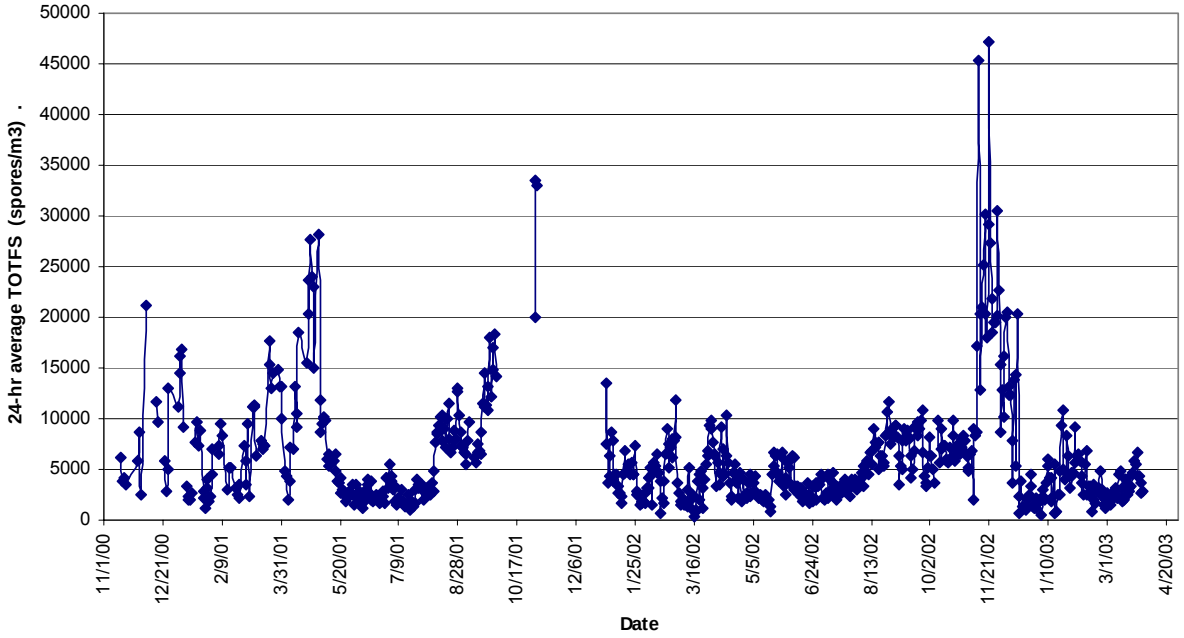


Figure 4.1.1-42. Daily (24-hr average) time series plot of total fungal spores (TOTFS) at the Central Site (Fresno First Street) for November 15, 2000, through March 31, 2003; concentrations are in spores/m^3.

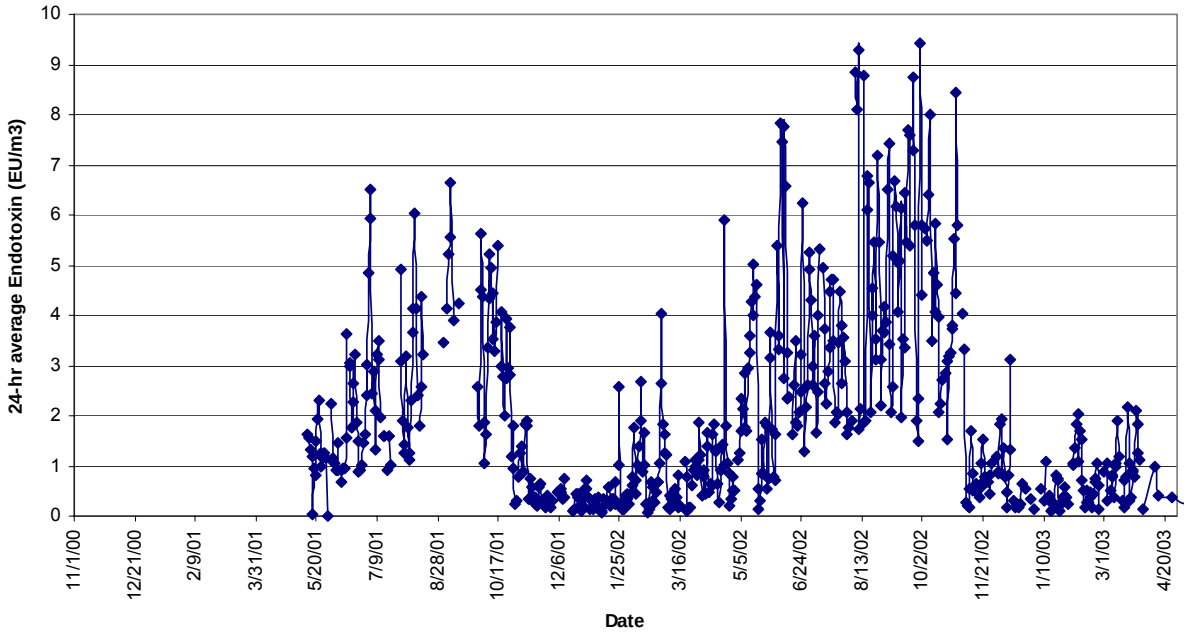


Figure 4.1.1-43. Daily (24-hr average) time series plot of endotoxin at the Central Site (Fresno First Street) for November 15, 2000, through March 31, 2003; concentrations are in EU/m^3.

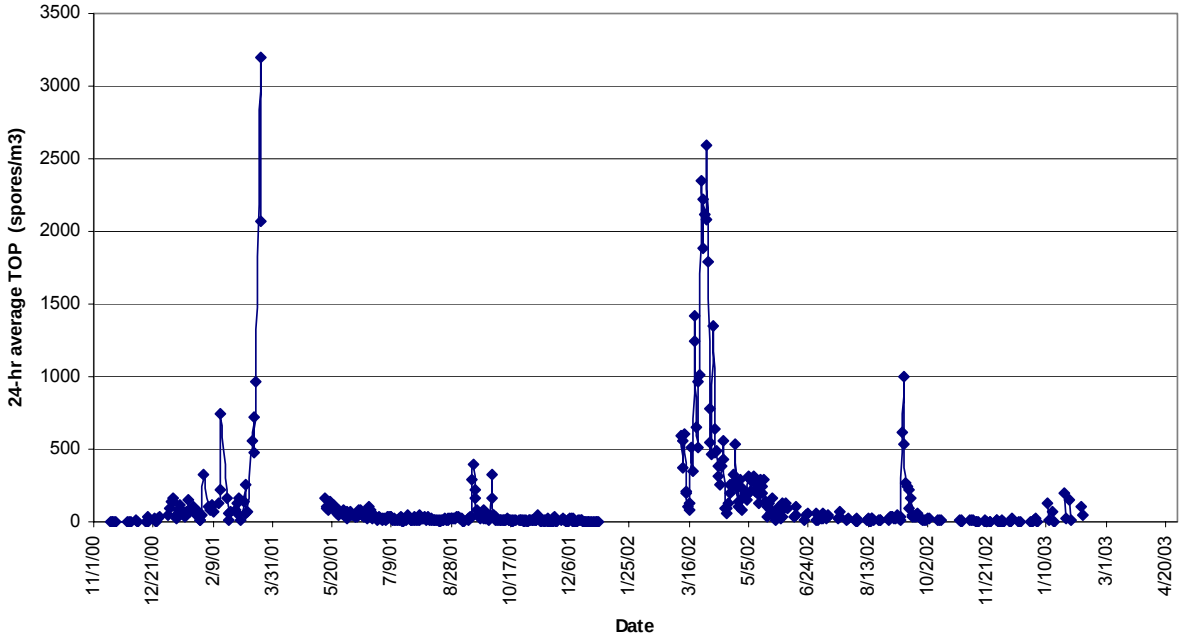


Figure 4.1.1-44. Daily (24-hr average) time series plot of total pollen grains (TOP) at the Central Site (Fresno First Street) for November 15, 2000, through March 31, 2003; concentrations are in spores/m^3.

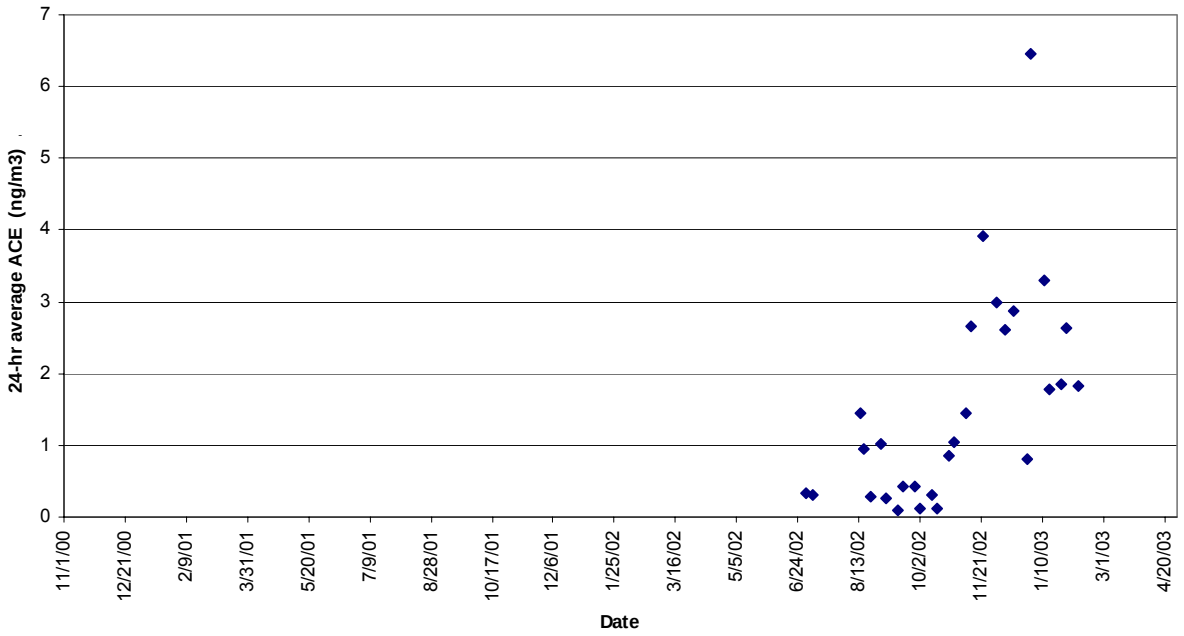


Figure 4.1.1-45. Daily (24-hr average) time series plot of PAH species acenaphthene (ACE) at the Central Site (Fresno First Street) for June 2002 through February 2003; concentrations are in ng/m^3.

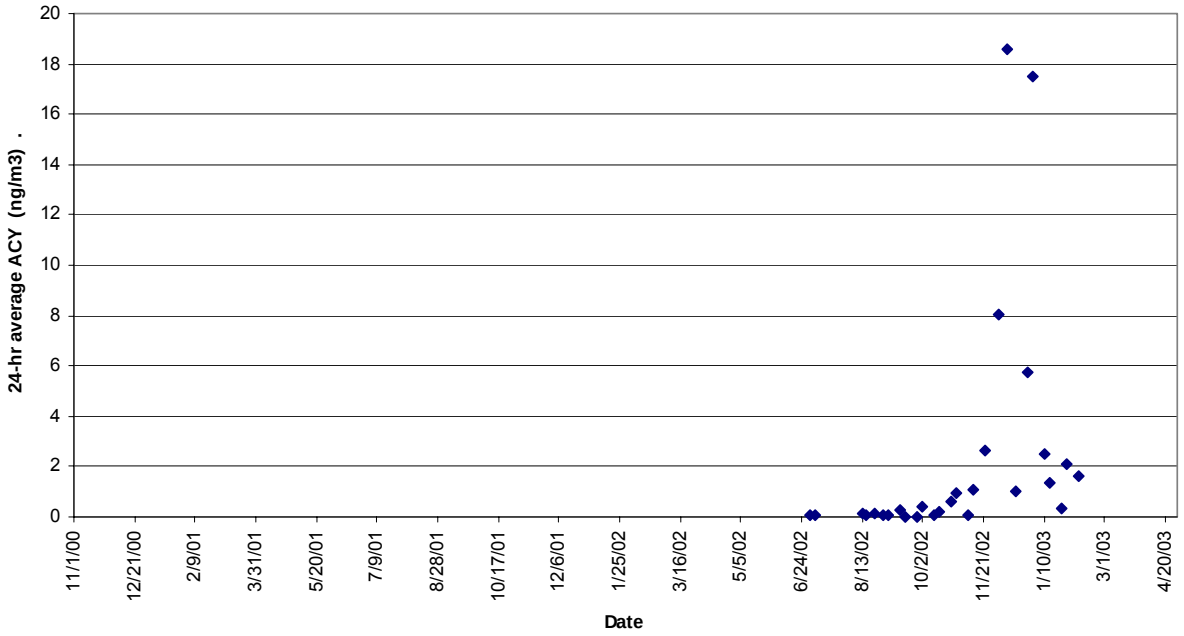


Figure 4.1.1-46. Daily (24-hr average) time series plot of PAH species acenaphthylene (ACY) at the Central Site (Fresno First Street) for June 2002 through February 2003; concentrations are in ng/m^3.

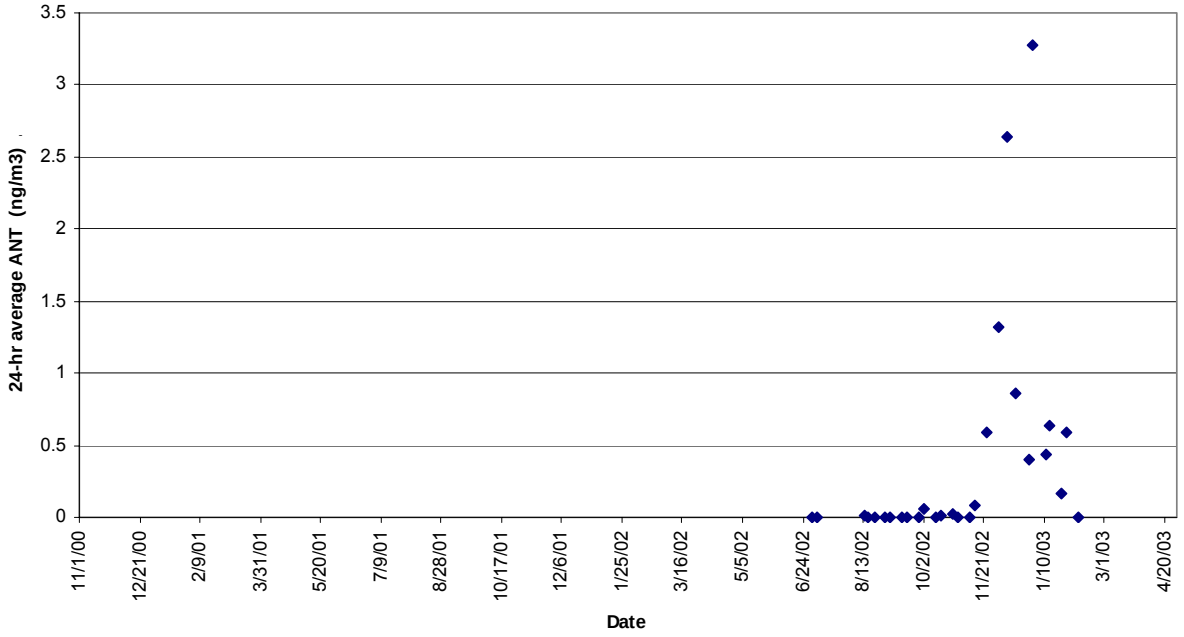


Figure 4.1.1-47. Daily (24-hr average) time series plot of PAH species anthracene (ANT) at the Central Site (Fresno First Street) for June 2002 through February 2003; concentrations are in ng/m^3.

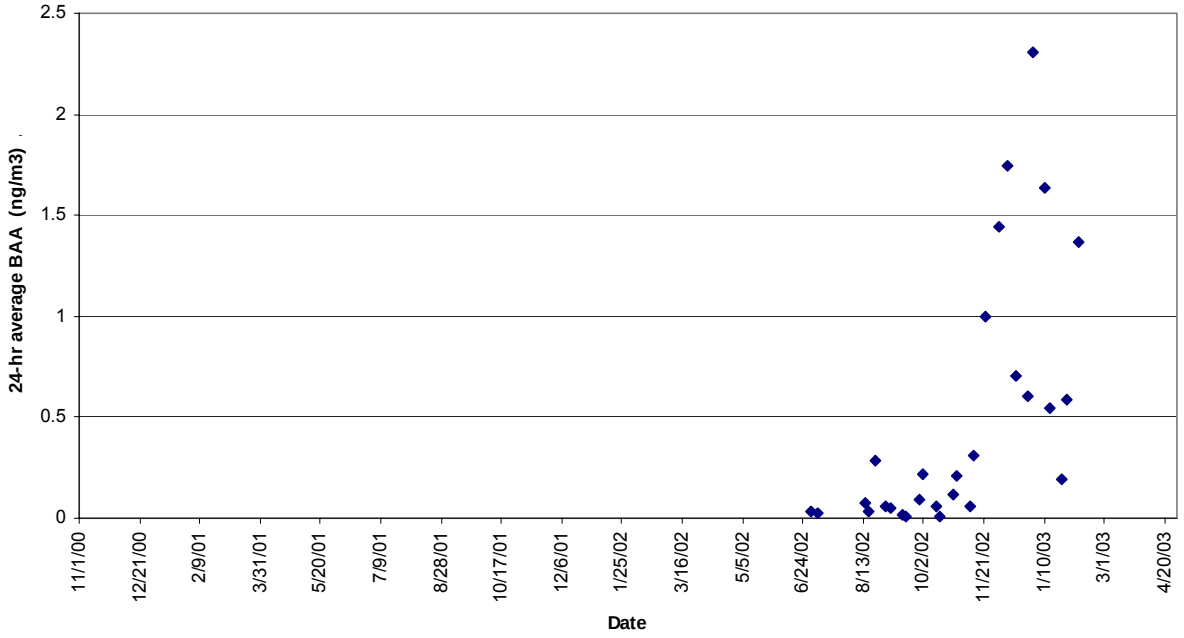


Figure 4.1.1-48. Daily (24-hr average) time series plot of PAH species benz[a]anthracene (BAA) at the Central Site (Fresno First Street) for June 2002 through February 2003; concentrations are in ng/m^3.

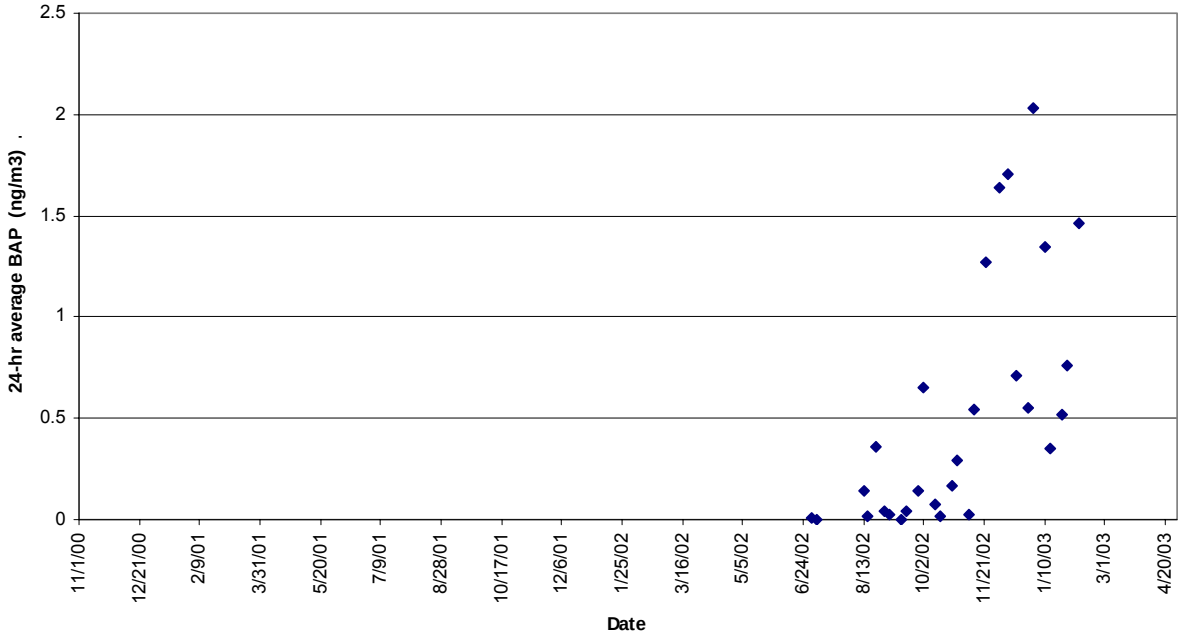


Figure 4.1.1-49. Daily (24-hr average) time series plot of PAH species benzo[a]pyrene (BAP) at the Central Site (Fresno First Street) for June 2002 through February 2003; concentrations are in ng/m^3.

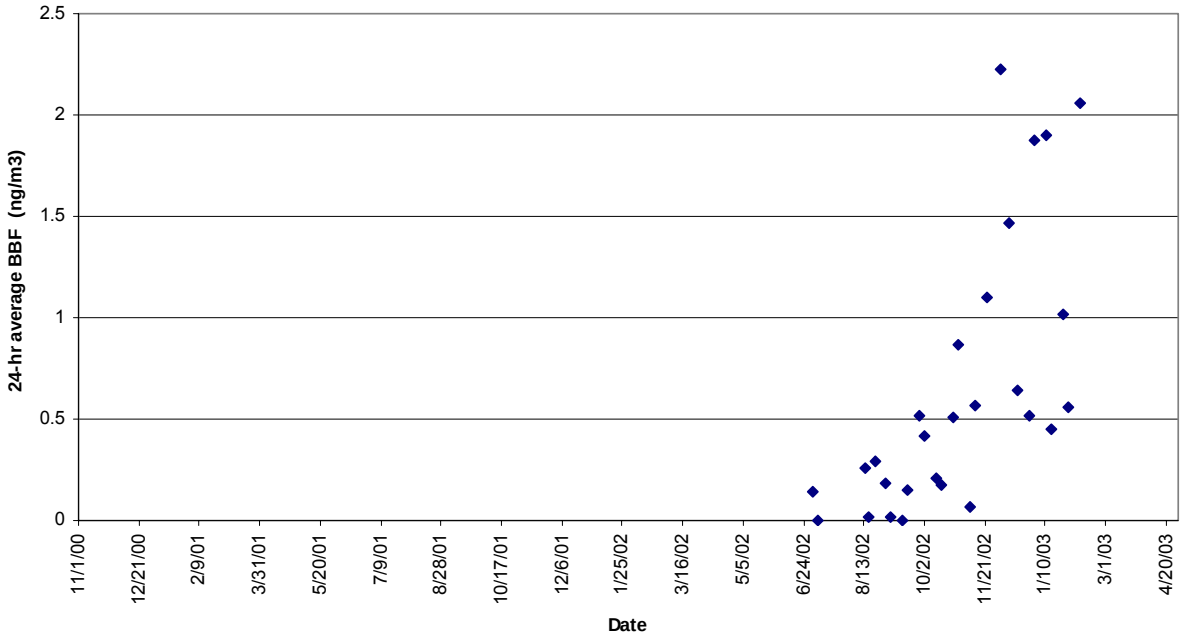


Figure 4.1.1-50. Daily (24-hr average) time series plot of PAH species benzo[b]flouranthene (BBF) at the Central Site (Fresno First Street) for June 2002 through February 2003; concentrations are in ng/m^3.

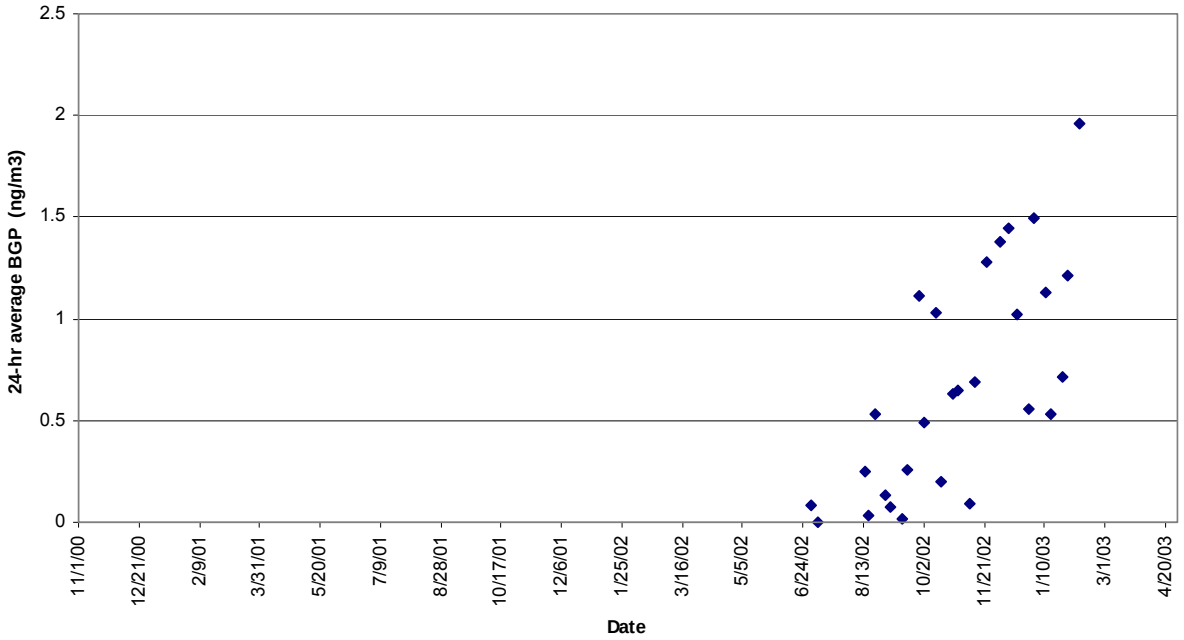


Figure 4.1.1-51. Daily (24-hr average) time series plot of PAH species benzo[ghi]perylene (BGP) at the Central Site (Fresno First Street) for June 2002 through February 2003; concentrations are in ng/m^3.

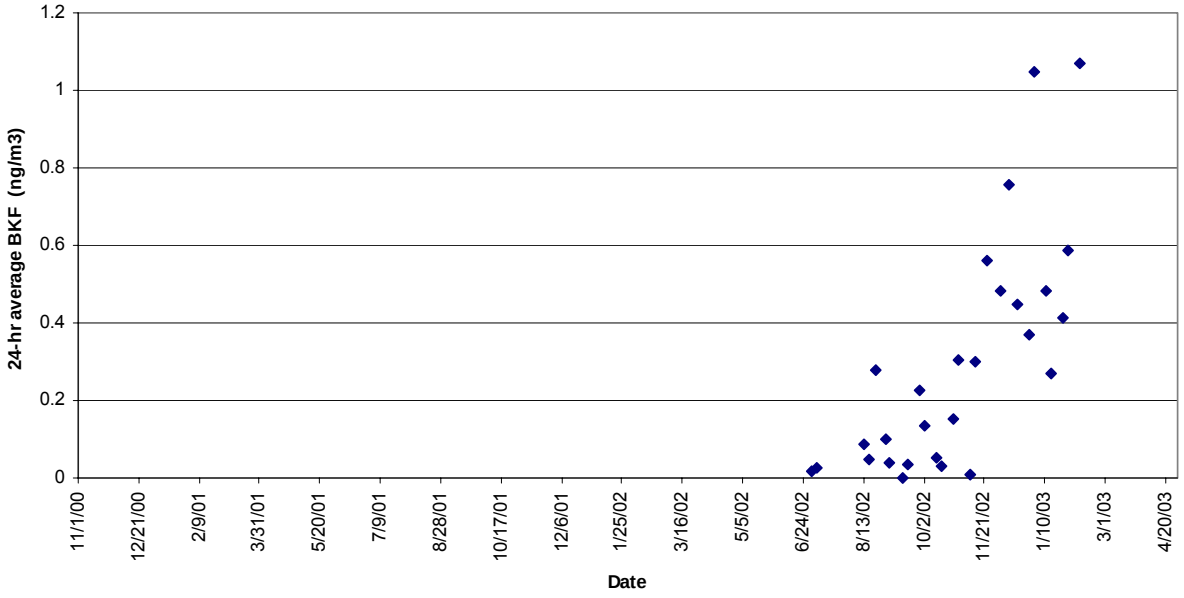


Figure 4.1.1-52. Daily (24-hr average) time series plot of PAH species benzo[k]flouranthene (BKF) at the Central Site (Fresno First Street) for June 2002 through February 2003; concentrations are in ng/m^3.

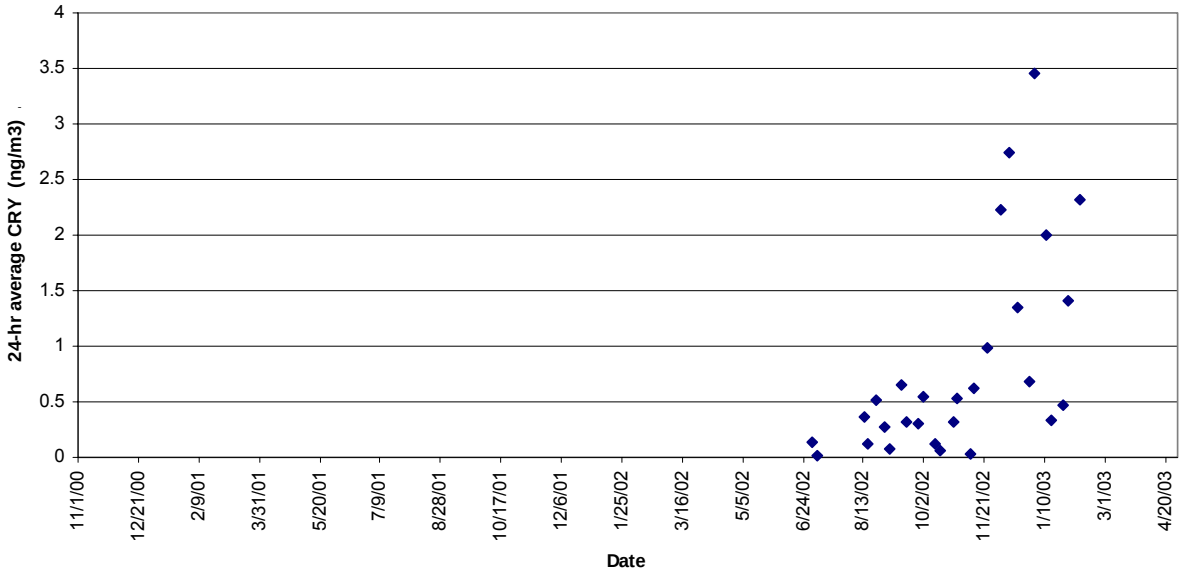


Figure 4.1.1-53. Daily (24-hr average) time series plot of PAH species chrysene (CRY) at the Central Site (Fresno First Street) for June 2002 through February 2003; concentrations are in ng/m^3.

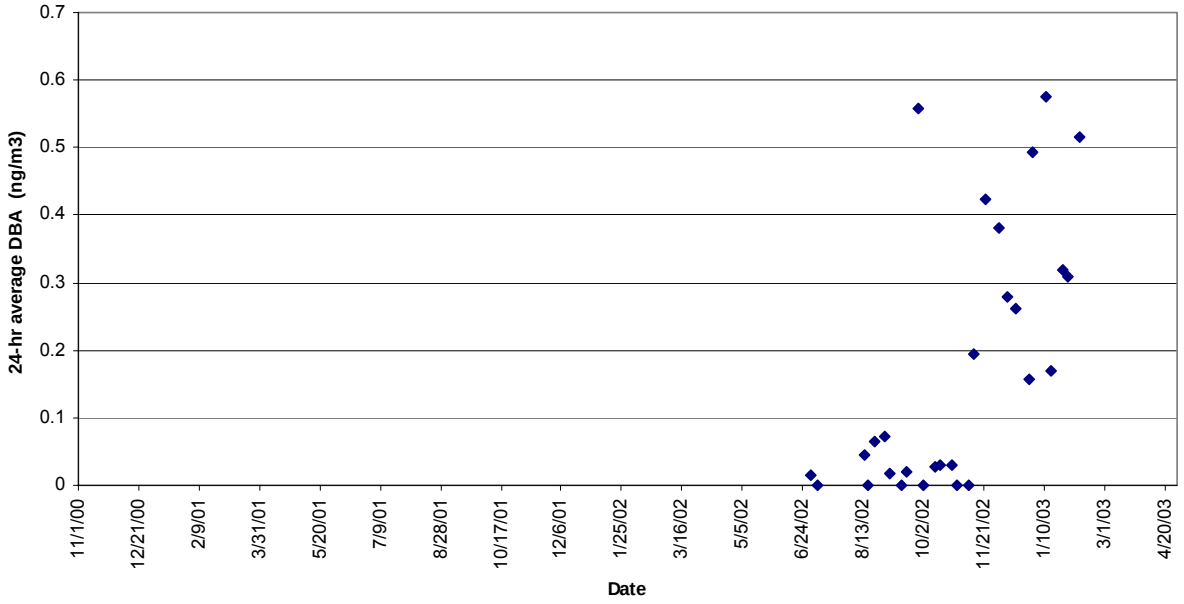


Figure 4.1.1-54. Daily (24-hr average) time series plot of PAH species dibenz[a,h]anthracene (DBA) at the Central Site (Fresno First Street) for June 2002 through February 2003; concentrations are in ng/m^3.

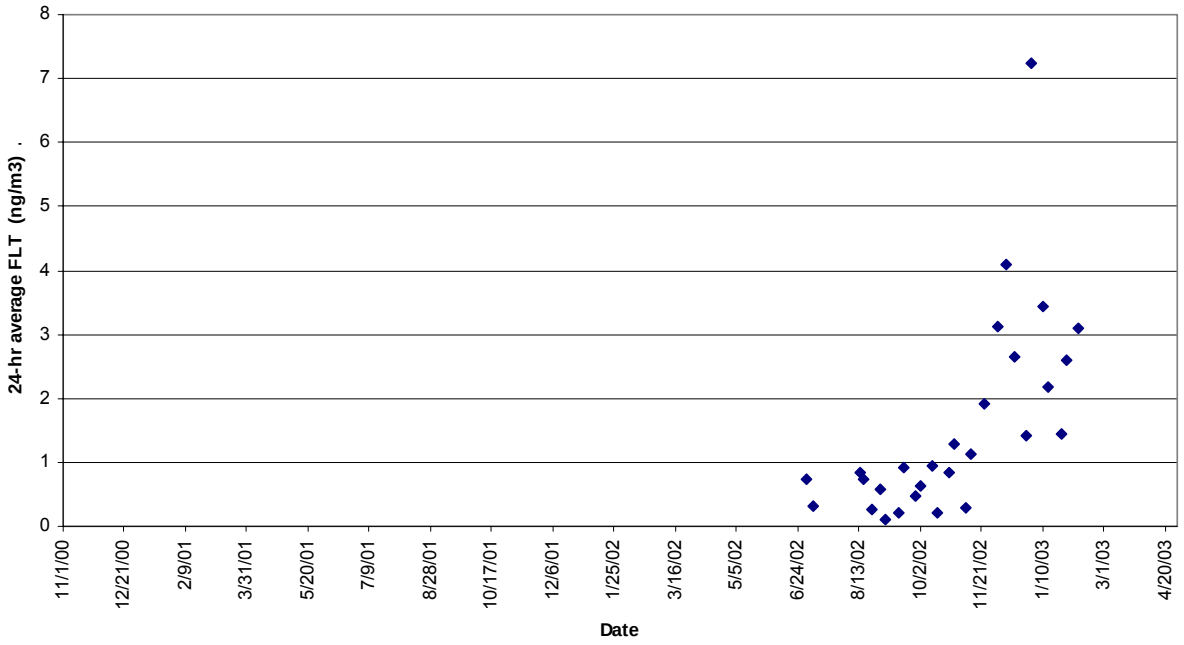


Figure 4.1.1-55. Daily (24-hr average) time series plot of PAH species flouranthene (FLT) at the Central Site (Fresno First Street) for June 2002 through February 2003; concentrations are in ng/m^3.

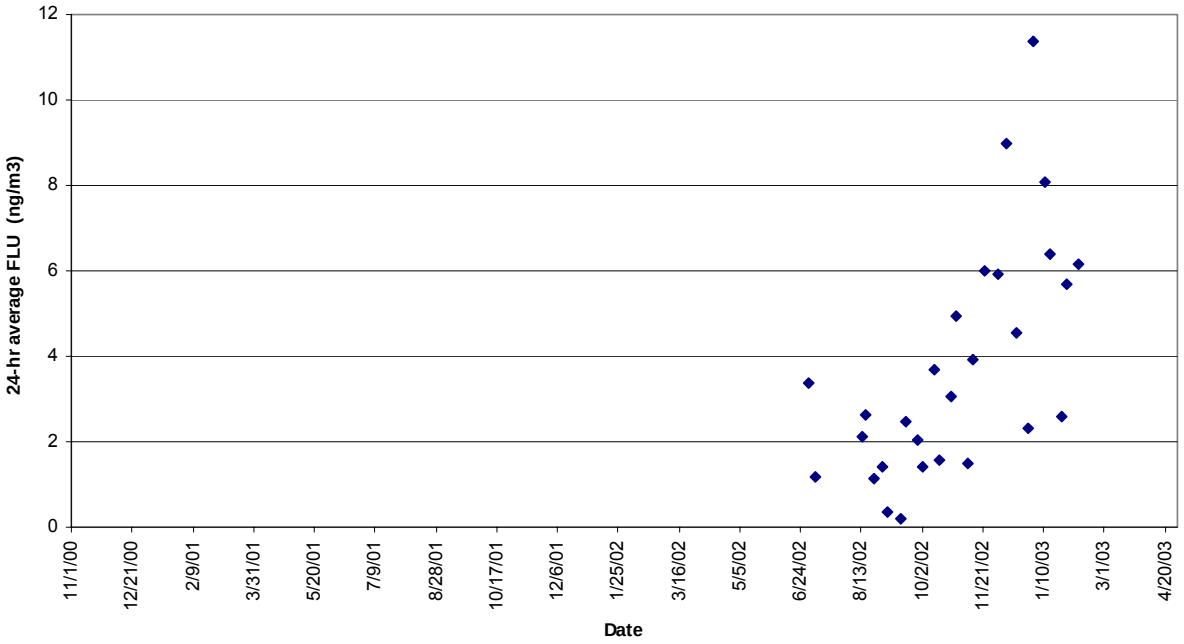


Figure 4.1.1-56. Daily (24-hr average) time series plot of PAH species flourene (FLU) at the Central Site (Fresno First Street) for June 2002 through February 2003; concentrations are in ng/m^3.

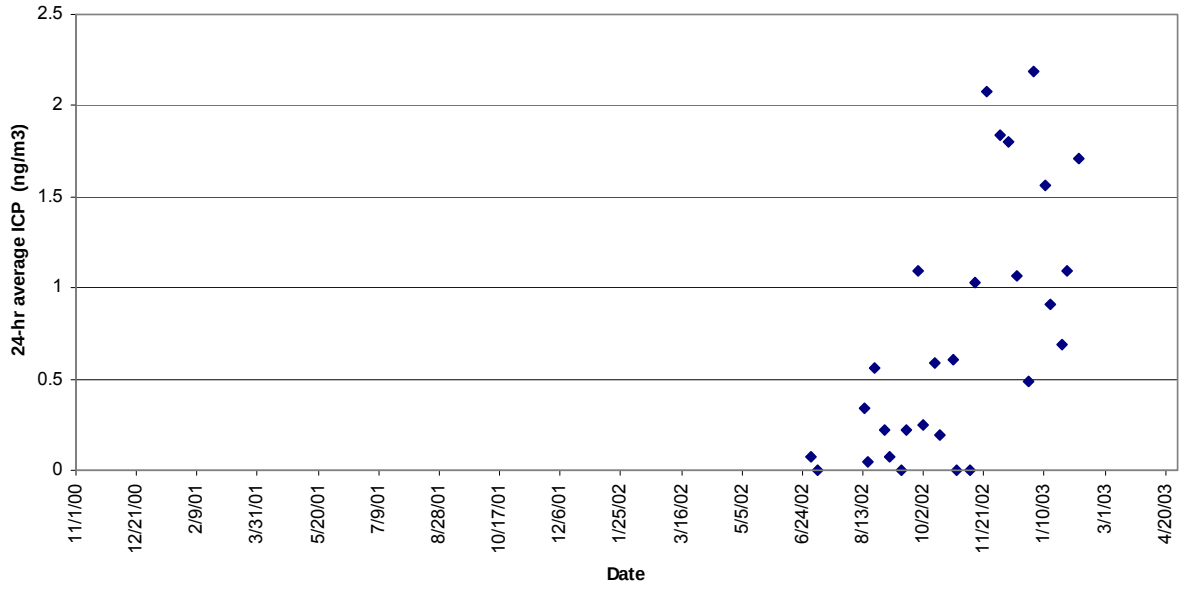


Figure 4.1.1-57. Daily (24-hr average) time series plot of PAH species indeno[1,2,3-cd]pyrene (ICP) at the Central Site (Fresno First Street) for June 2002 through February 2003; concentrations are in ng/m^3.

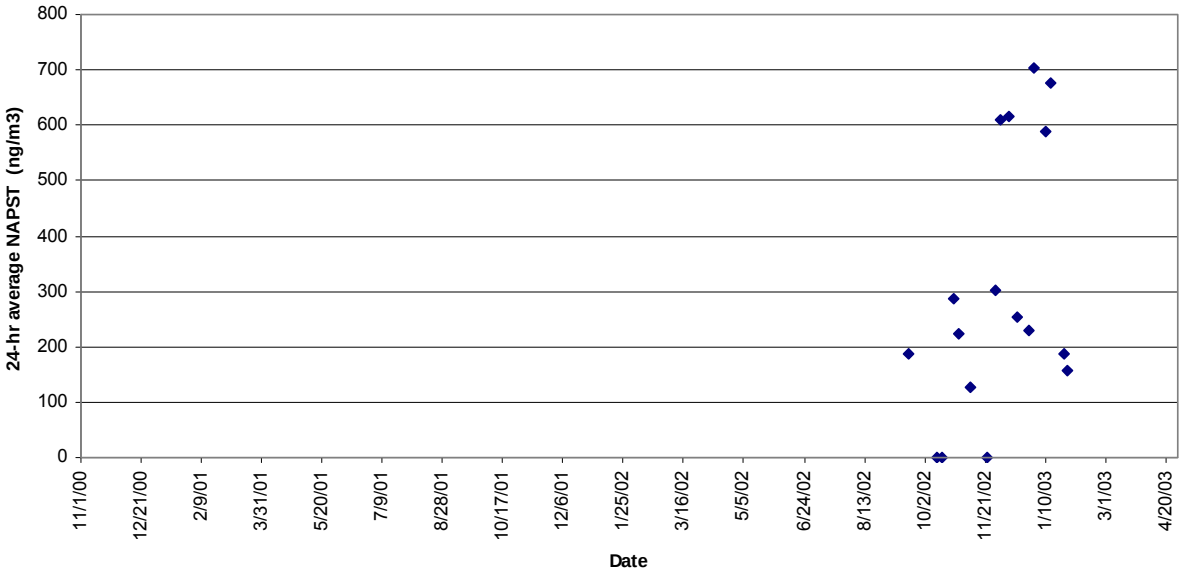


Figure 4.1.1-58. Daily (24-hr average) time series plot of PAH species napthalene (NAPST) at the Central Site (Fresno First Street) for June 2002 through February 2003; concentrations are in ng/m^3.

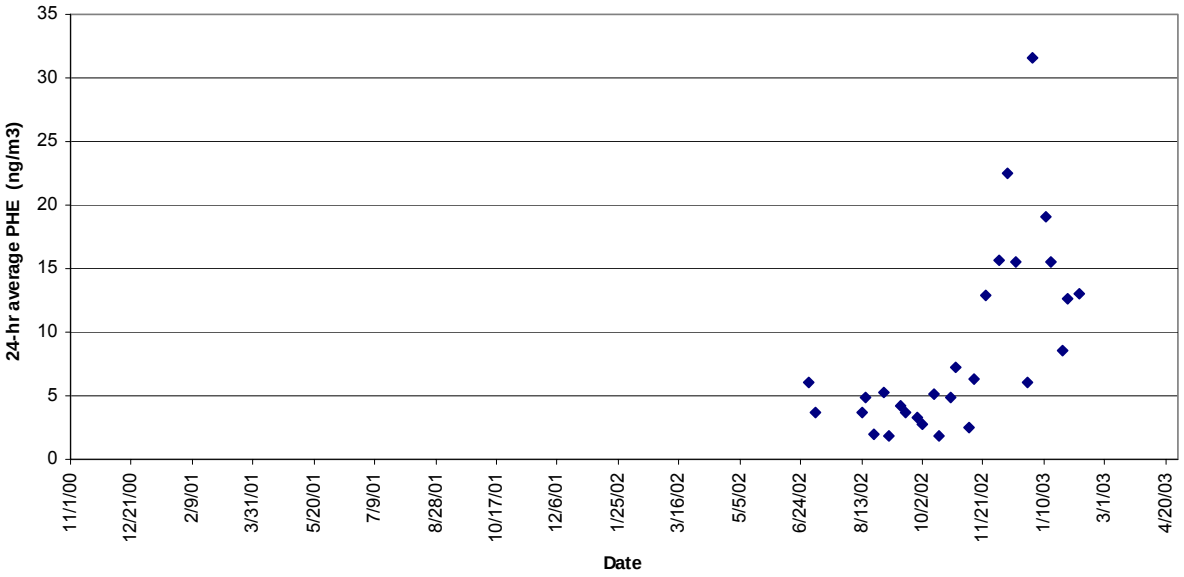


Figure 4.1.1-59. Daily (24-hr average) time series plot of PAH species phenathrene (PHE) at the Central Site (Fresno First Street) for June 2002 through February 2003; concentrations are in ng/m^3.

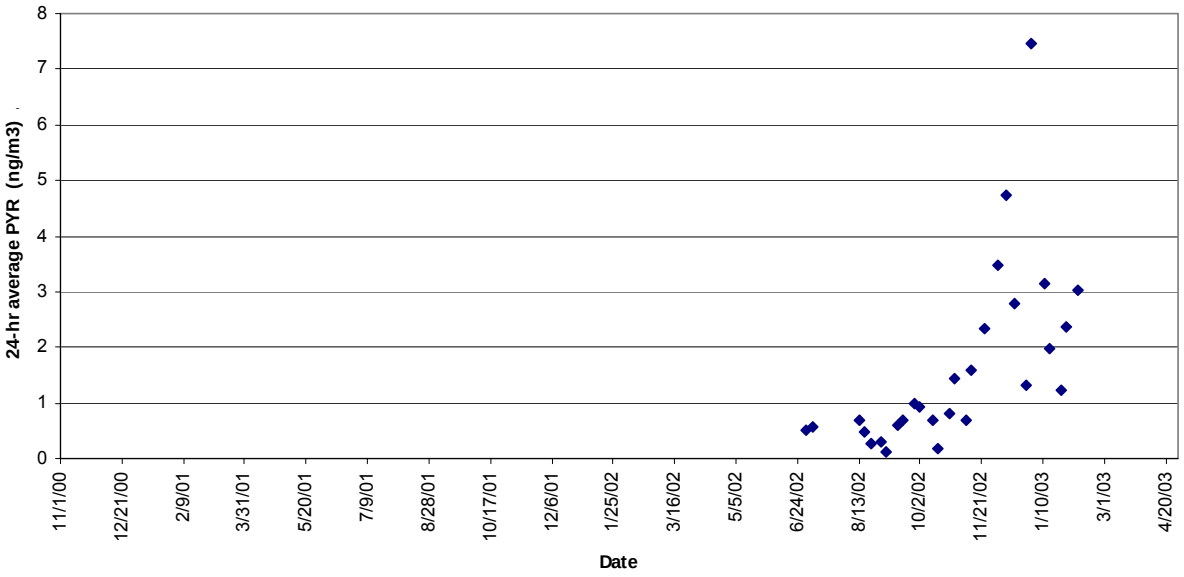


Figure 4.1.1-60. Daily (24-hr average) time series plot of PAH species pyrene (PYR) at the Central Site (Fresno First Street) for June 2002 through February 2003; concentrations are in ng/m^3.

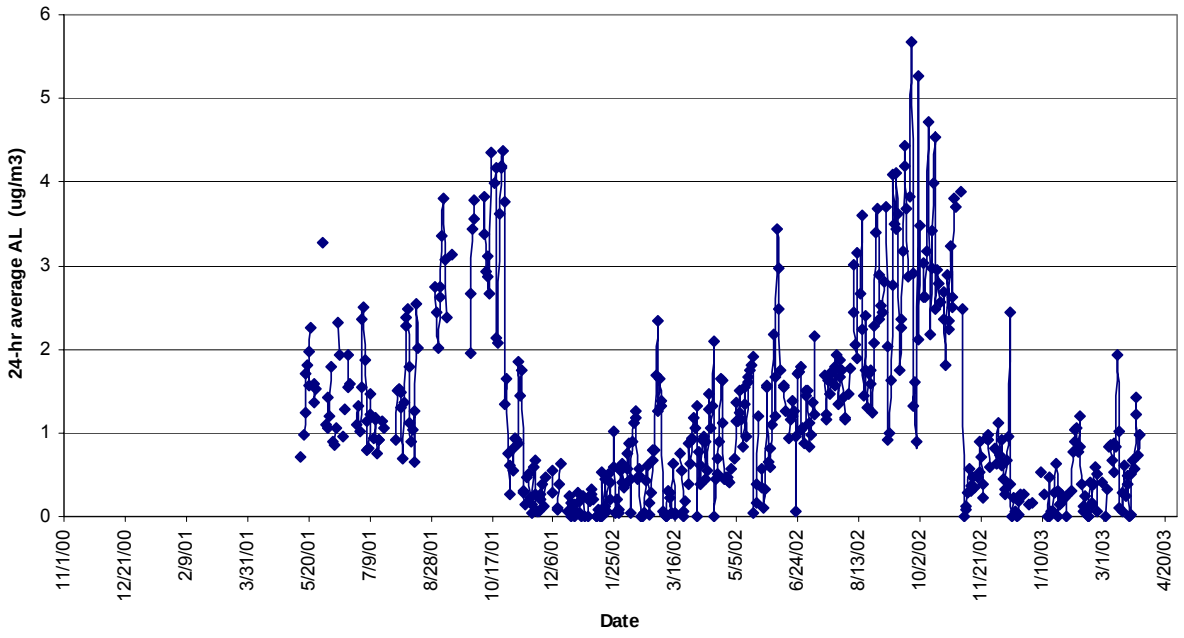


Figure 4.1.1-61. Daily (24-hr average) time series plot of PM_{10} aluminum (AL) at the Central Site (Fresno First Street) for May 2001 through April 2003; concentrations are in $\mu g/m^3$.

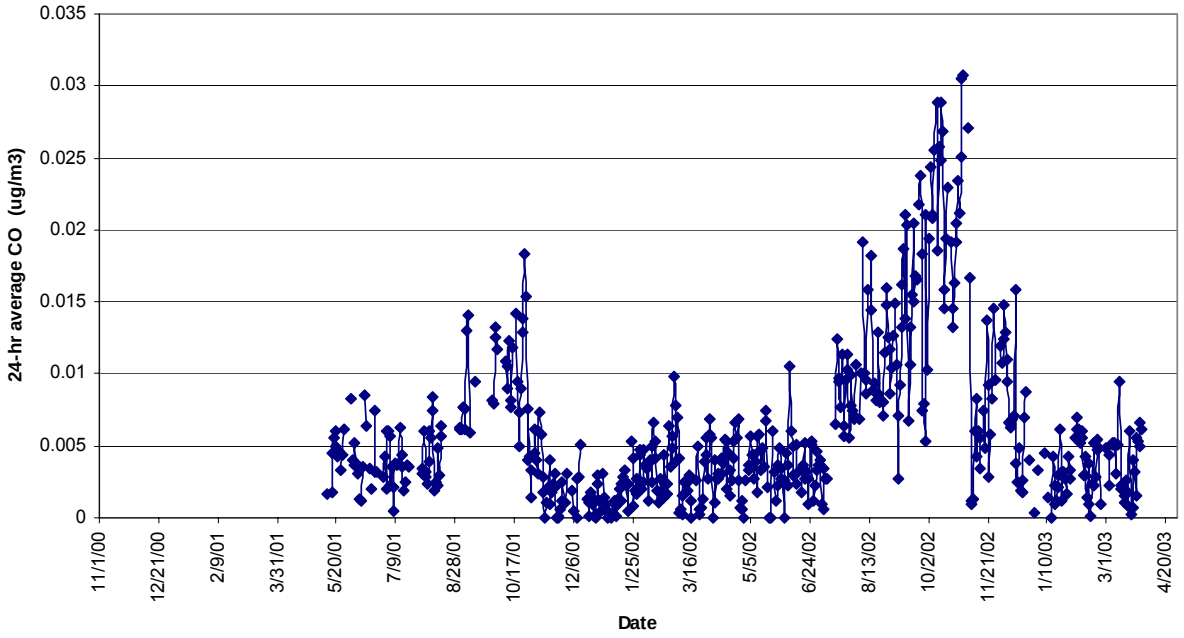


Figure 4.1.1-62. Daily (24-hr average) time series plot of PM_{10} cobalt (CO) at the Central Site (Fresno First Street) for May 2001 through April 2003; concentrations are in $\mu g/m^3$.

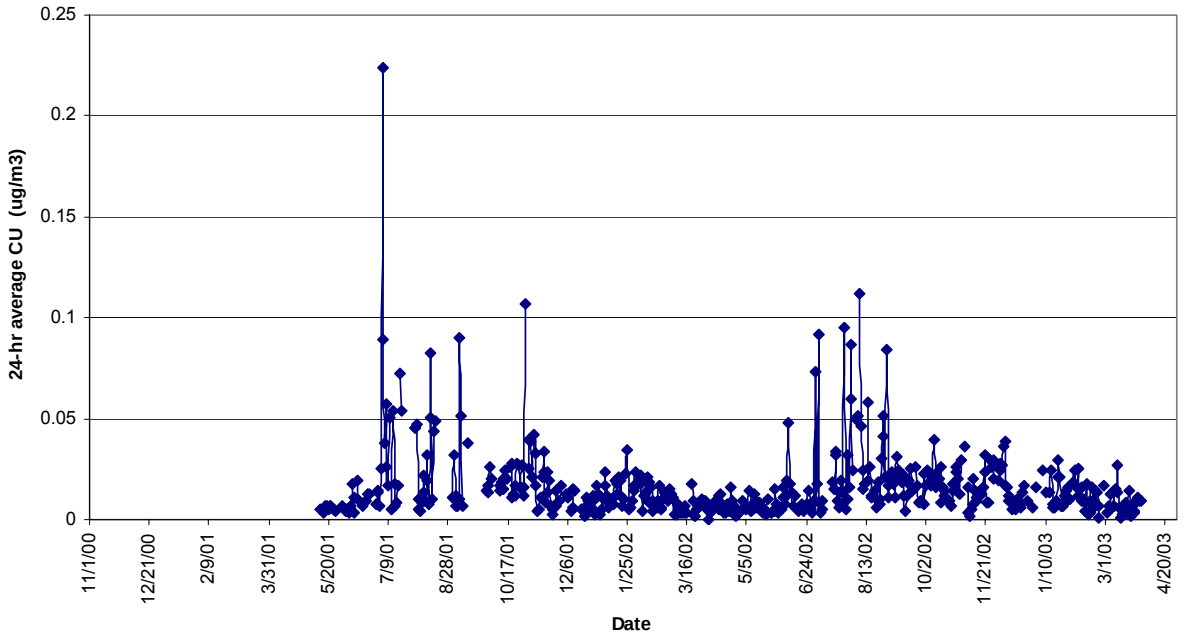


Figure 4.1.1-63. Daily (24-hr average) time series plot of PM_{10} copper (CU) at the Central Site (Fresno First Street) for May 2001 through April 2003; concentrations are in $\mu g/m^3$.

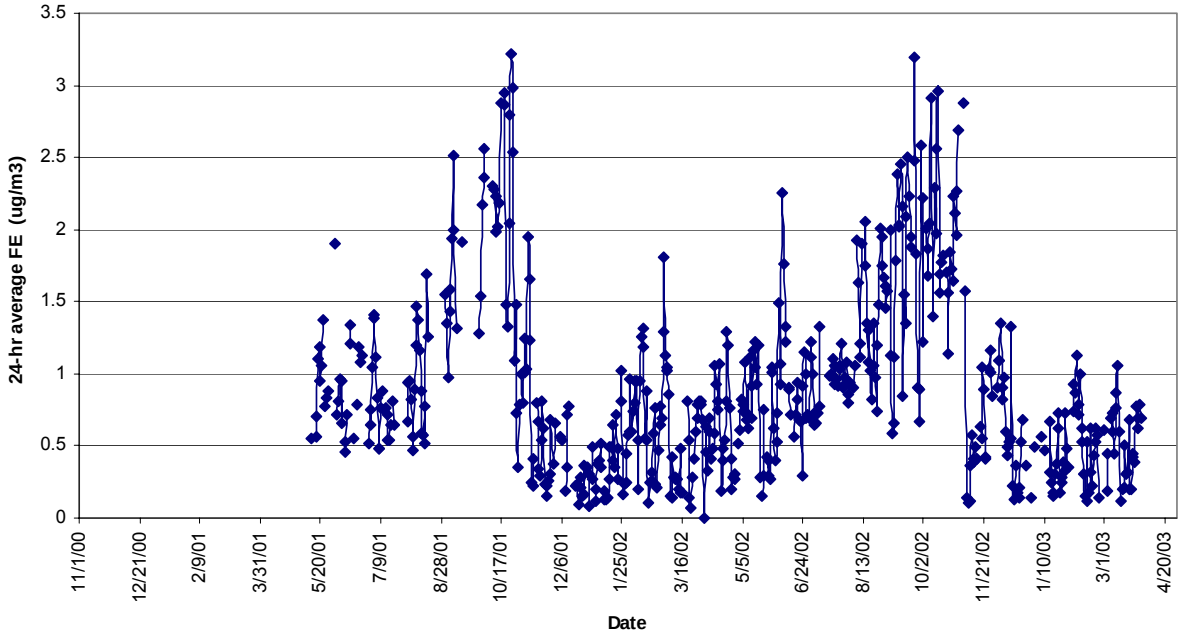


Figure 4.1.1-64. Daily (24-hr average) time series plot of PM_{10} iron (FE) at the Central Site (Fresno First Street) for May 2001 through April 2003; concentrations are in $\mu g/m^3$.

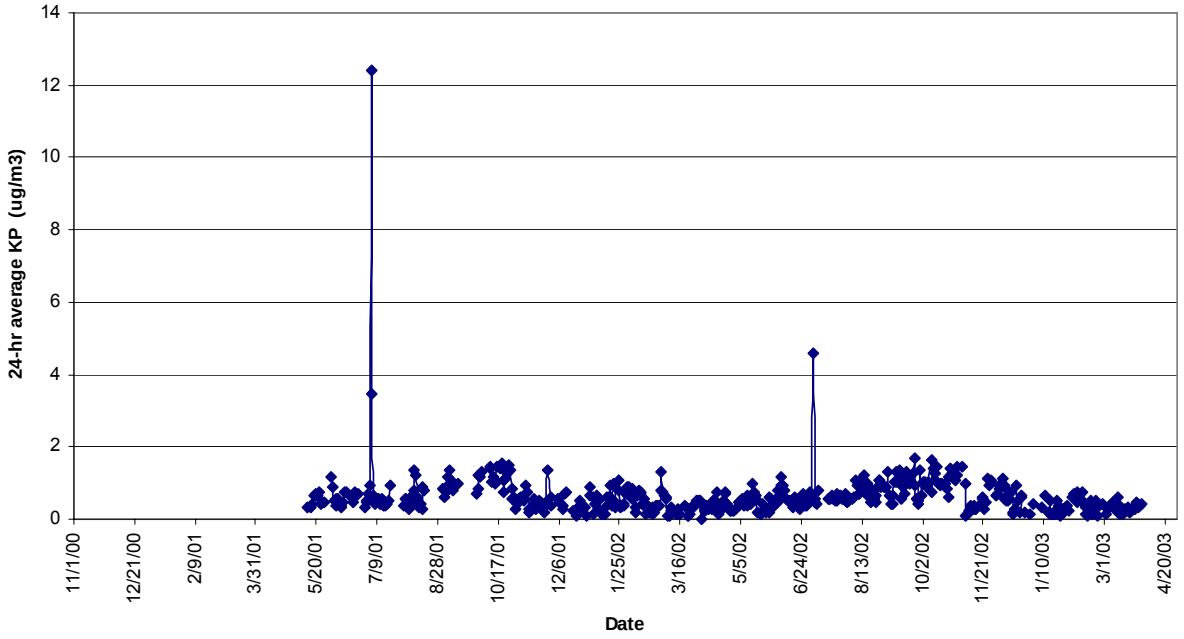


Figure 4.1.1-65. Daily (24-hr average) time series plot of PM_{10} potassium (KP) at the Central Site (Fresno First Street) for May 2001 through April 2003; concentrations are in $\mu g/m^3$.

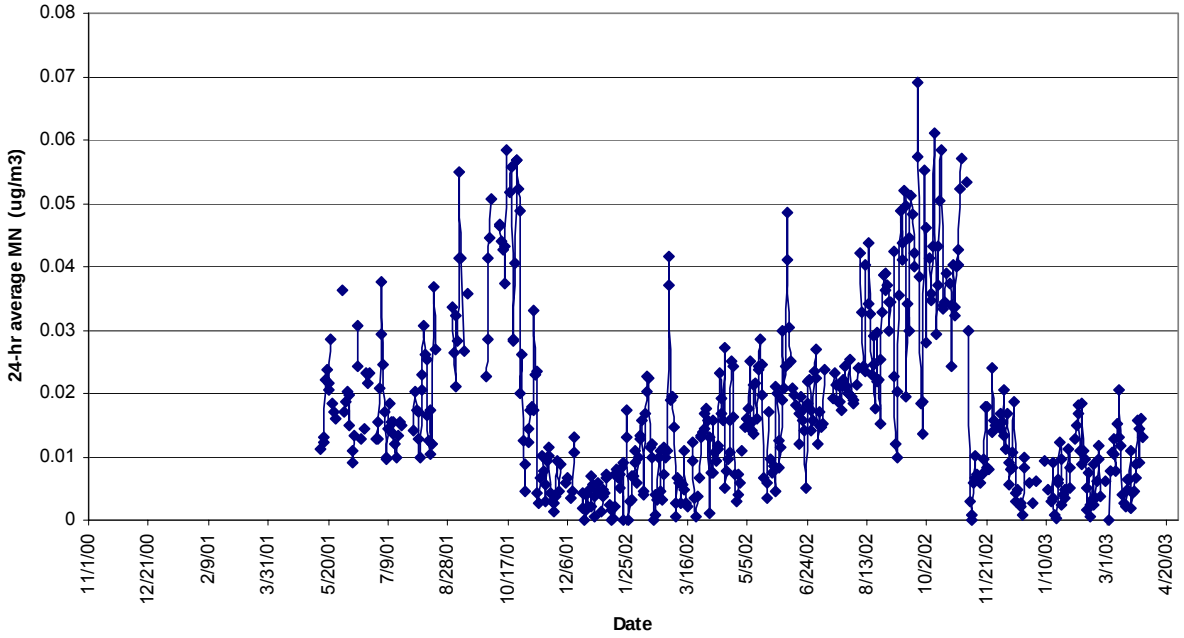


Figure 4.1.1-66. Daily (24-hr average) time series plot of PM_{10} manganese (MN) at the Central Site (Fresno First Street) for May 2001 through April 2003; concentrations are in $\mu g/m^3$.

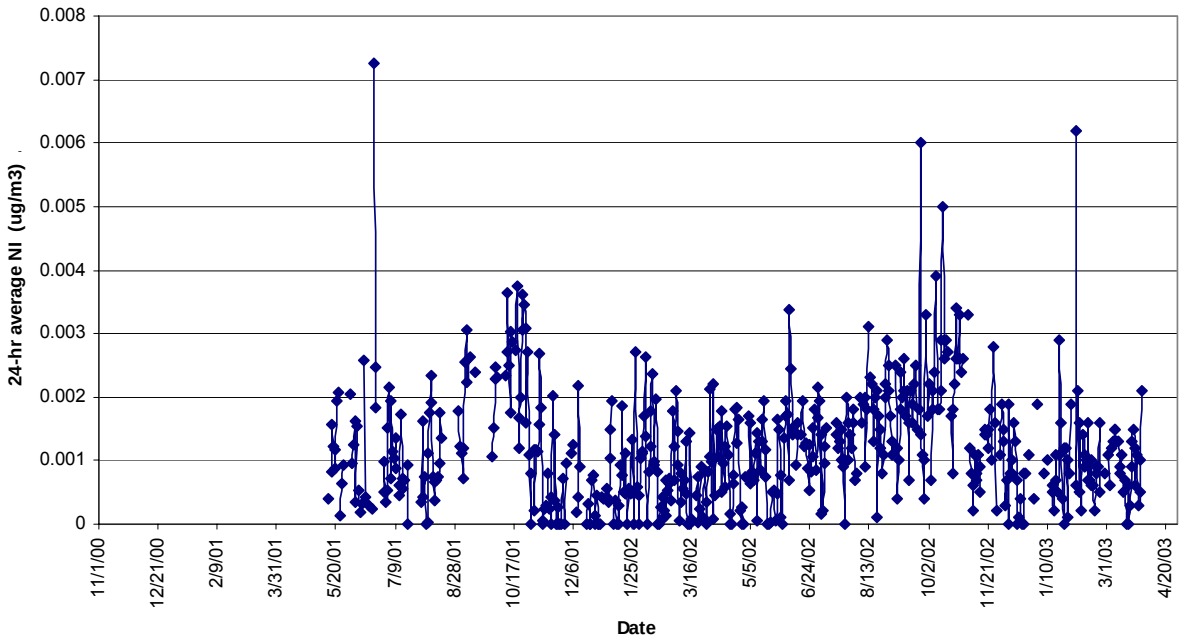


Figure 4.1.1-67. Daily (24-hr average) time series plot of PM_{10} nickle (NI) at the Central Site (Fresno First Street) for May 2001 through April 2003; concentrations are in $\mu g/m^3$.

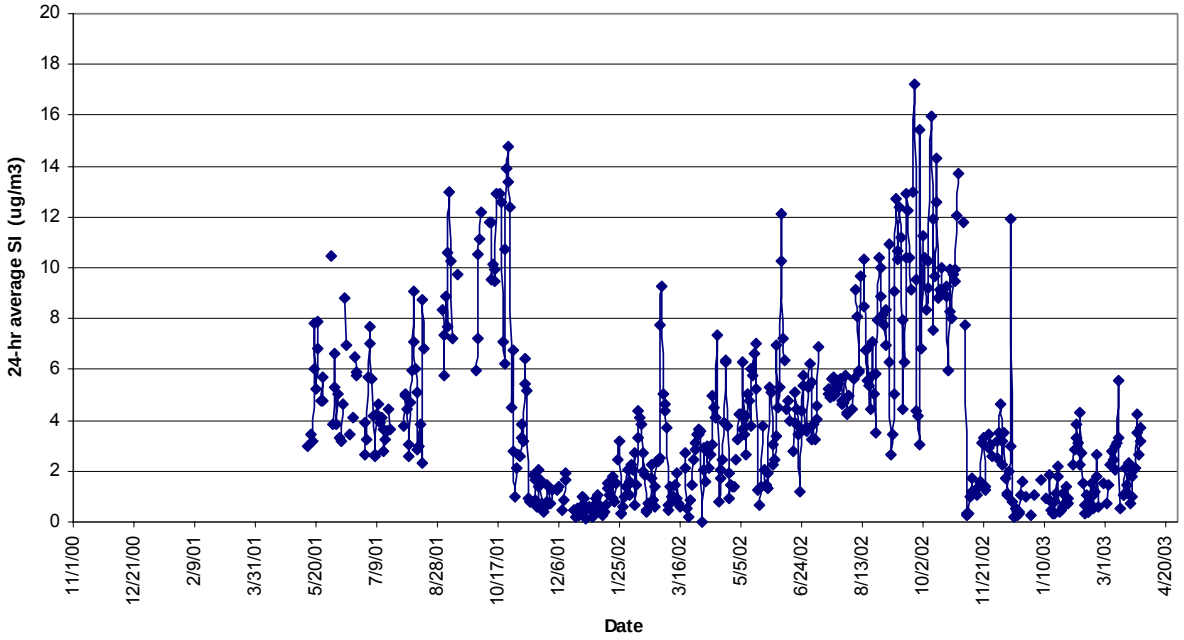


Figure 4.1.1-68. Daily (24-hr average) time series plot of PM_{10} silicon (SI) at the Central Site (Fresno First Street) for May 2001 through April 2003; concentrations are in $\mu g/m^3$.

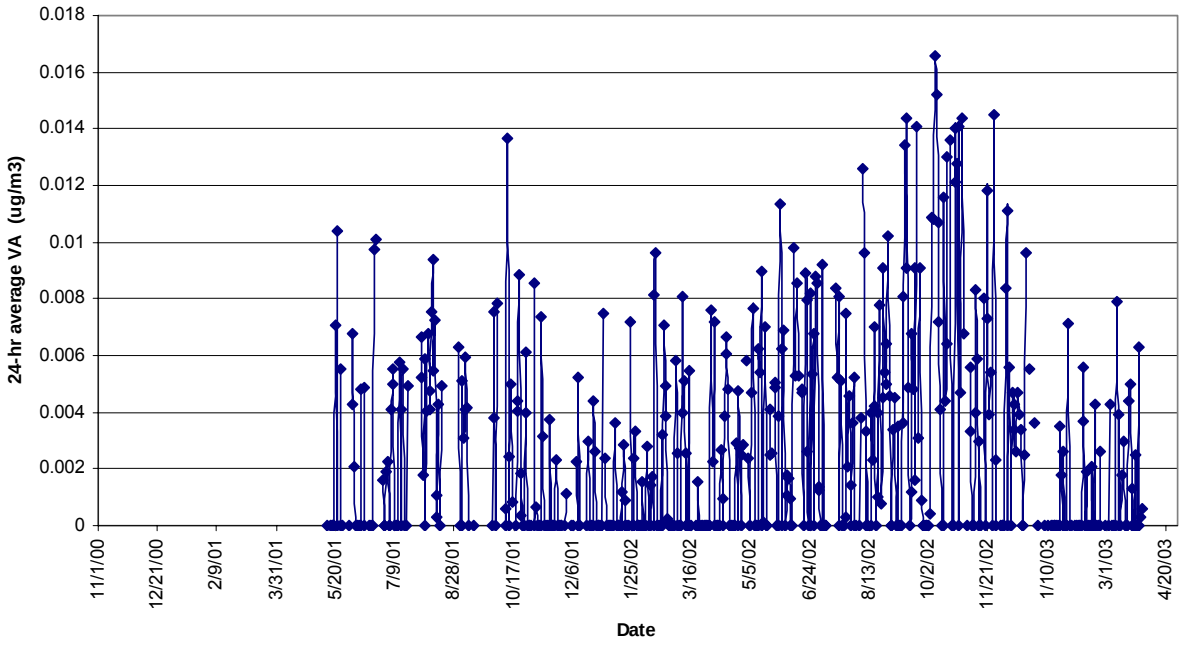


Figure 4.1.1-69. Daily (24-hr average) time series plot of PM_{10} vanadium (VA) at the Central Site (Fresno First Street) for May 2001 through April 2003; concentrations are in $\mu g/m^3$.

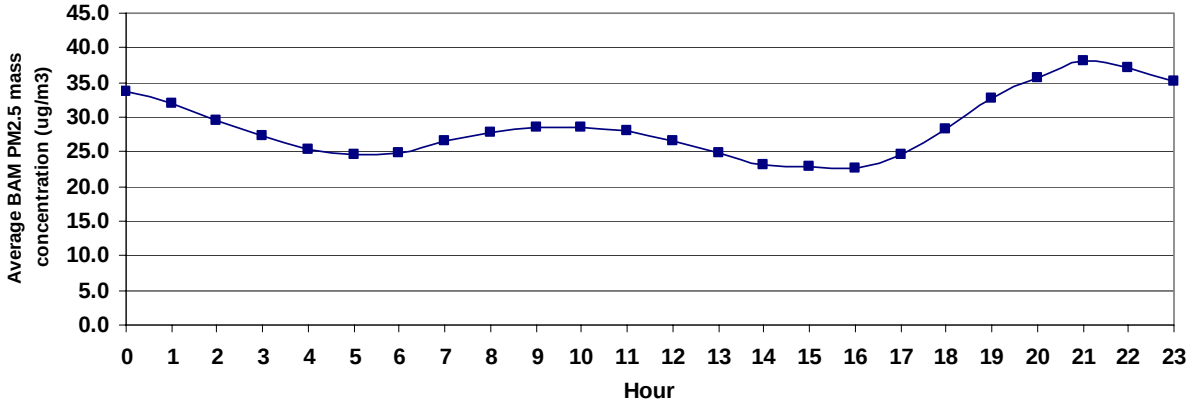


Figure 4.1.1-70. Average diurnal profile of $PM_{2.5}$ mass (BAM $PM_{2.5}$) at the Central Site (Fresno First Street) for April 1, 2001, through March 31, 2003; concentrations are in $\mu g/m^3$.

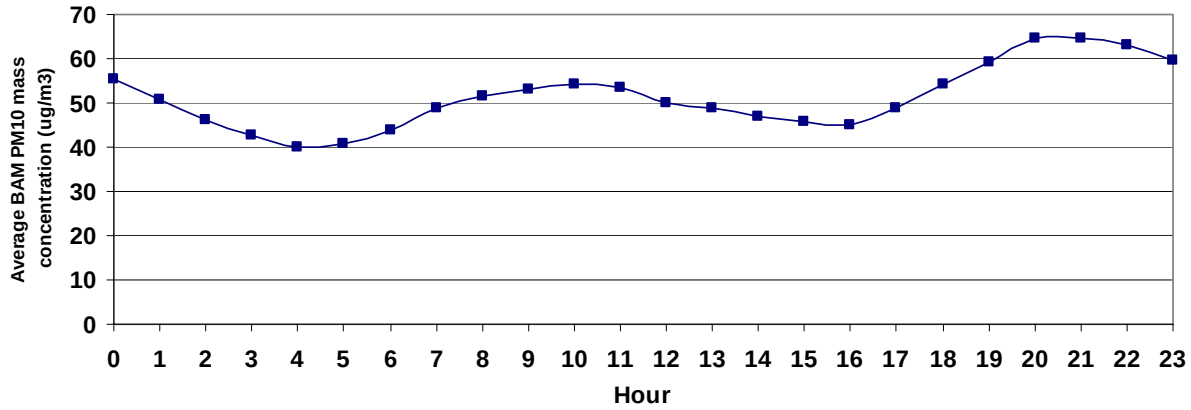


Figure 4.1.1-71. Average diurnal profile of PM_{10} mass (BAM PM_{10}) at the Central Site (Fresno First Street) for April 1, 2001, through March 31, 2003; concentrations are in $\mu g/m^3$.

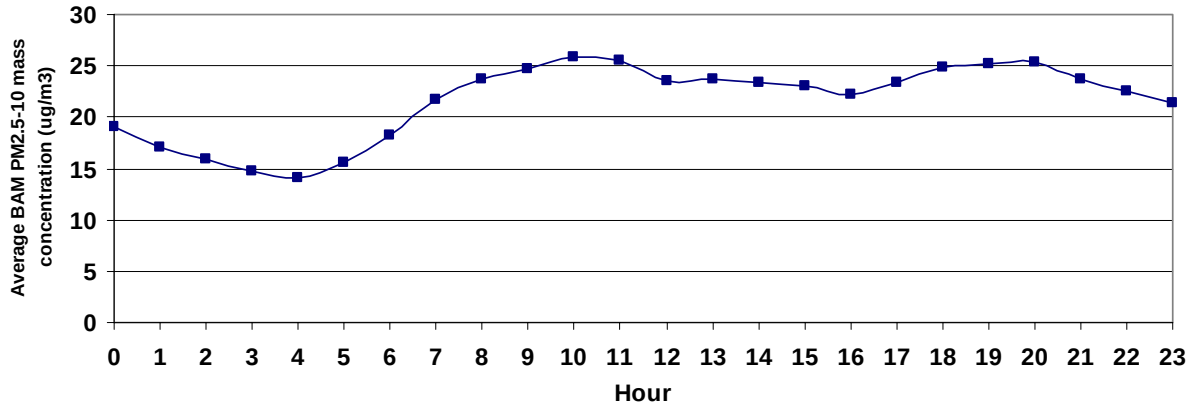


Figure 4.1.1-72. Average diurnal profile of $PM_{2.5-10}$ mass (coarse, BAM $PM_{2.5-10}$) at the Central Site (Fresno First Street) for April 1, 2001, through March 31, 2003; concentrations are in $\mu g/m^3$.

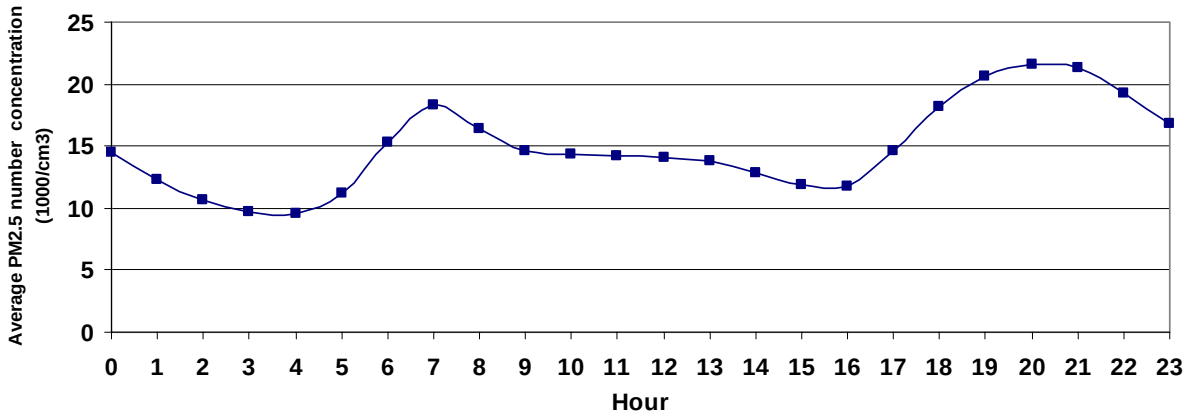


Figure 4.1.1-73. Average diurnal profile of $PM_{2.5}$ number at the Central Site (Fresno First Street) for April 1, 2001, through March 31, 2003; concentrations are in $1000/cm^3$.

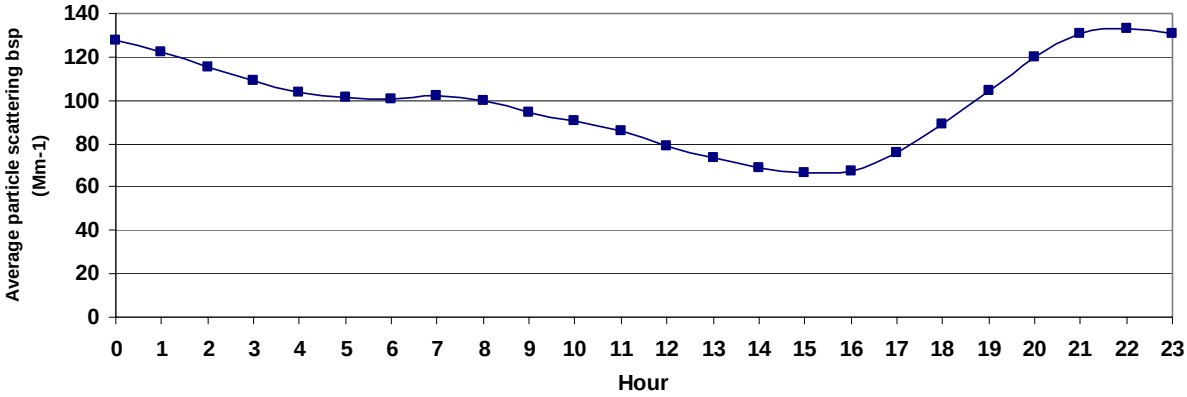


Figure 4.1.1-74. Average diurnal profile of particle scattering (b_{sp}) at the Central Site (Fresno First Street) for April 1, 2001, through March 31, 2003; concentrations are in Mm^{-1}.

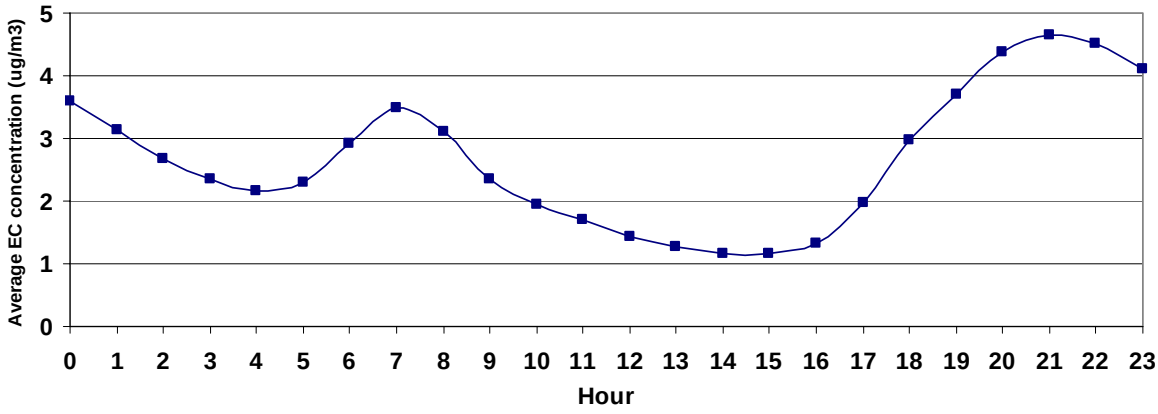


Figure 4.1.1-75. Average diurnal profile of $PM_{2.5}$ elemental carbon (EC) at the Central Site (Fresno First Street) for April 1, 2001, through March 31, 2003; concentrations are in $\mu g/m^3$.

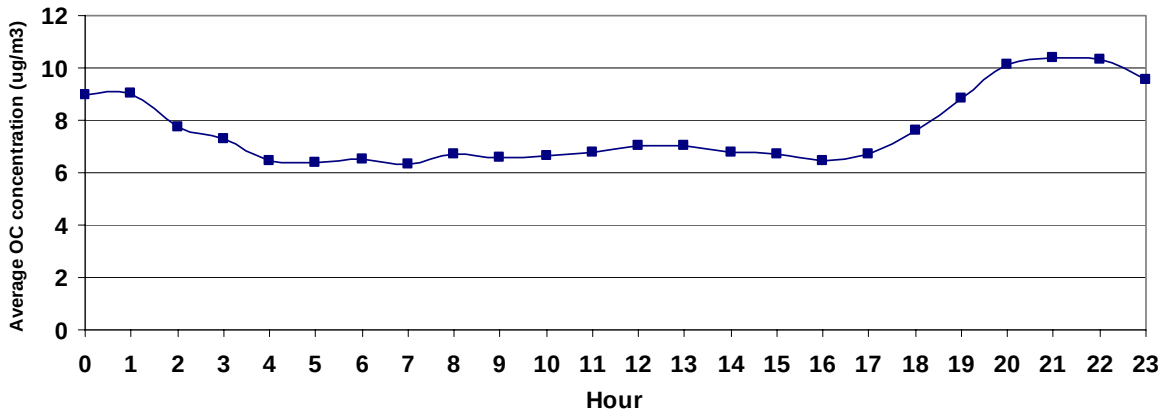


Figure 4.1.1-76. Average diurnal profile of $PM_{2.5}$ organic carbon (OC) at the Central Site (Fresno First Street) for April 1, 2001, through March 31, 2003; concentrations are in $\mu g/m^3$.

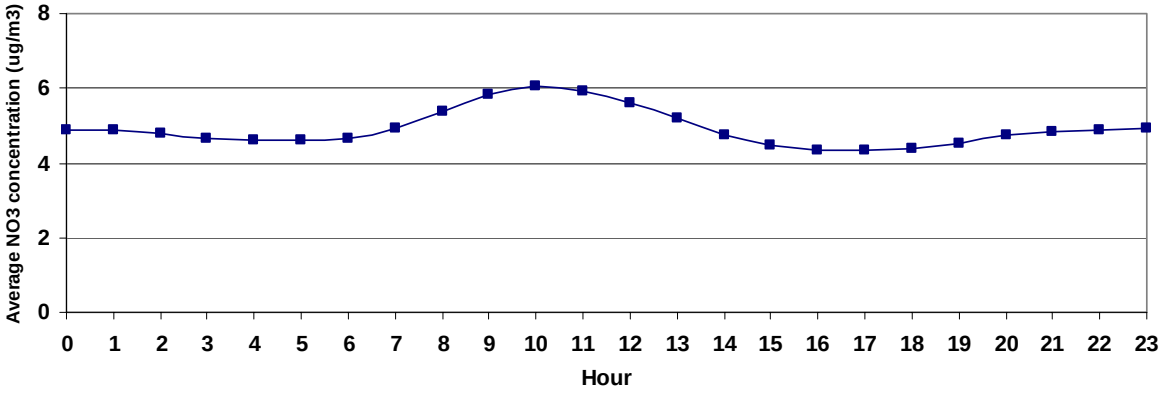


Figure 4.1.1-77. Average diurnal profile of $PM_{2.5}$ nitrate (NO_3) at the Central Site (Fresno First Street) for April 1, 2001, through March 31, 2003; concentrations are in $\mu g/m^3$.

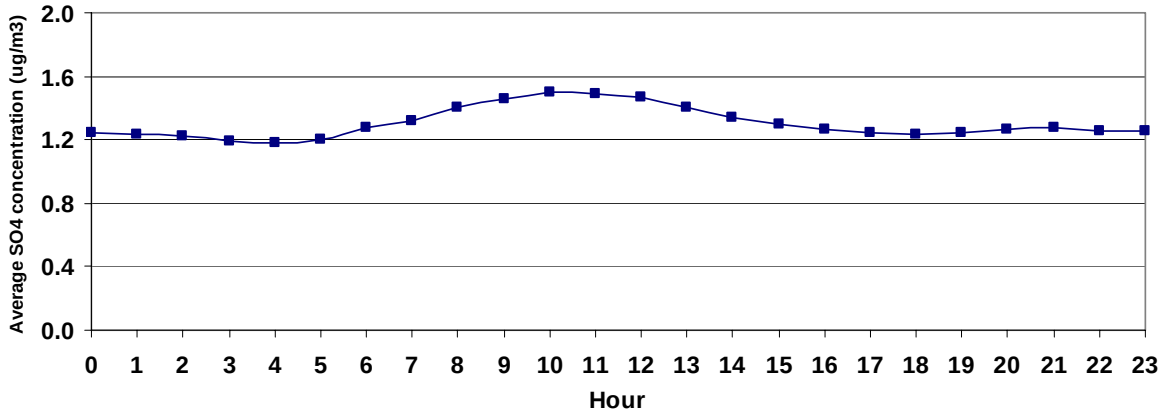


Figure 4.1.1-78. Average diurnal profile of $PM_{2.5}$ sulfate (SO_4) at the Central Site (Fresno First Street) for April 1, 2001, through March 31, 2003; concentrations are in $\mu g/m^3$.

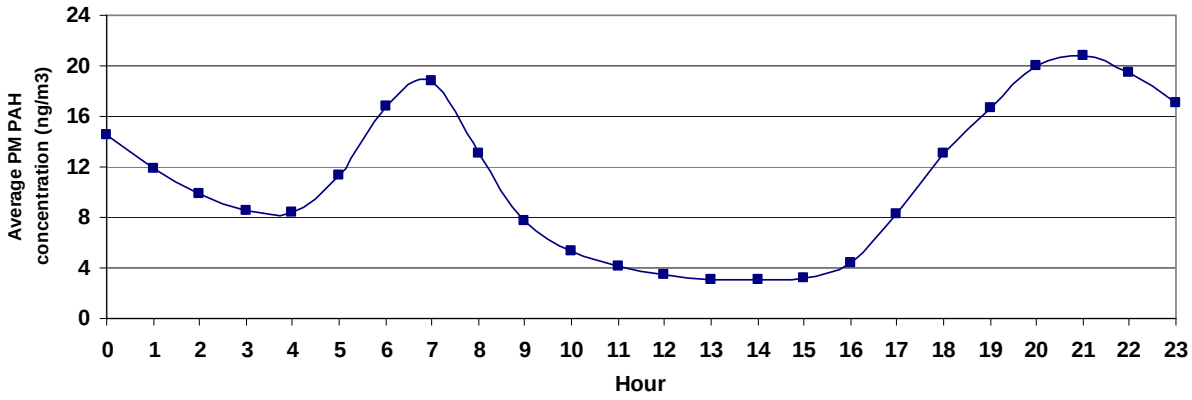


Figure 4.1.1-79. Average diurnal profile of particulate polycyclic aromatic hydrocarbons (PMPAH) at the Central Site (Fresno First Street) for April 1, 2001, through March 31, 2003; concentrations are in ng/m^3.

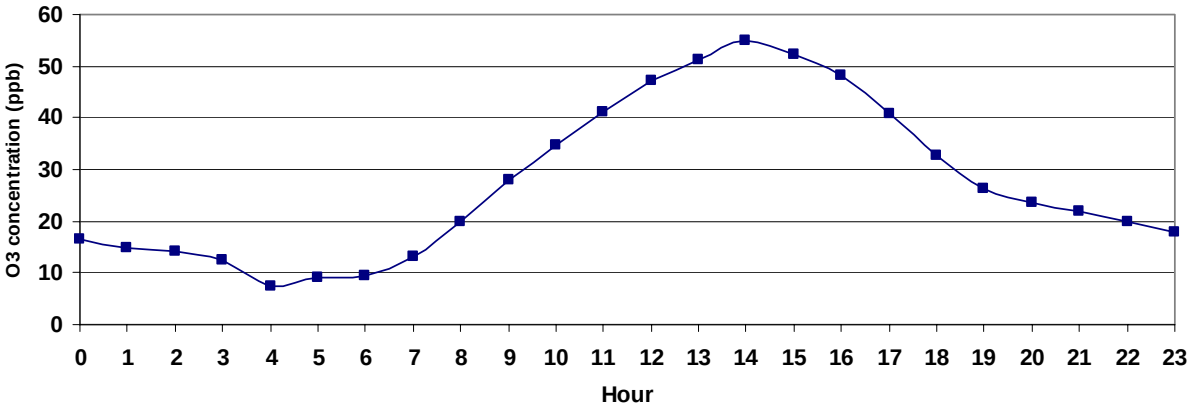


Figure 4.1.1-80. Average diurnal profile of ozone (O_3) at the Central Site (Fresno First Street) for April 1, 2001, through March 31, 2003; concentrations are in ppb.

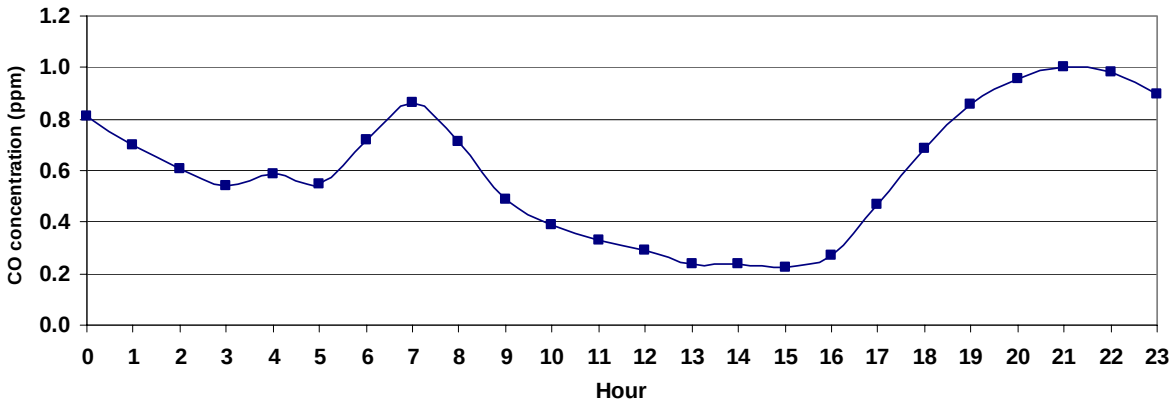


Figure 4.1.1-81. Average diurnal profile of carbon monoxide (CO) at the Central Site (Fresno First Street) for April 1, 2001, through March 31, 2003; concentrations are in ppm.

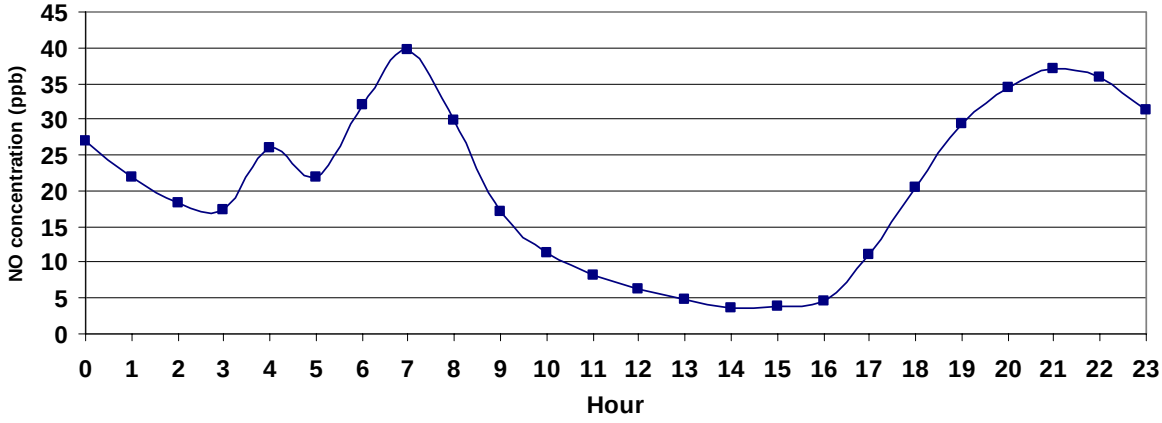


Figure 4.1.1-82. Average diurnal profile of nitric oxide (NO) at the Central Site (Fresno First Street) for April 1, 2001, through March 31, 2003; concentrations are in ppb.

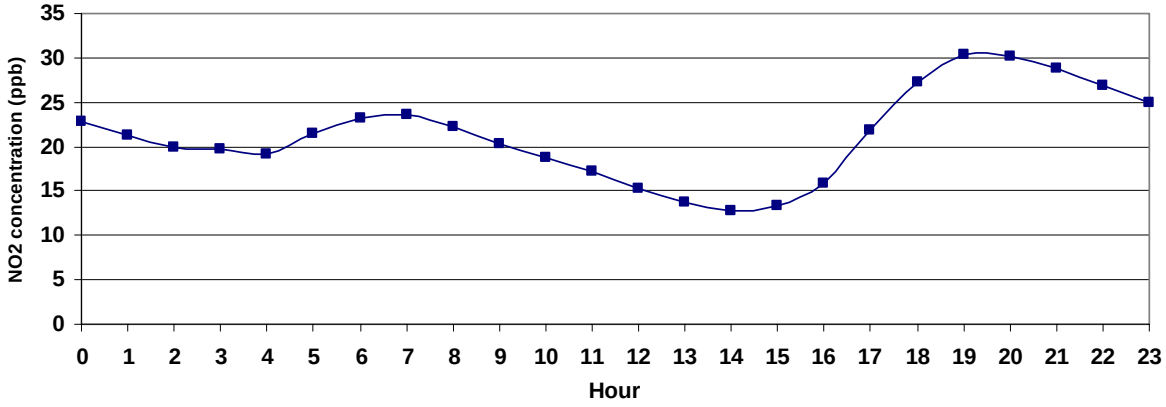


Figure 4.1.1-83. Average diurnal profile of nitrogen dioxide (NO_2) at the Central Site (Fresno First Street) for April 1, 2001, through March 31, 2003; concentrations are in ppb.

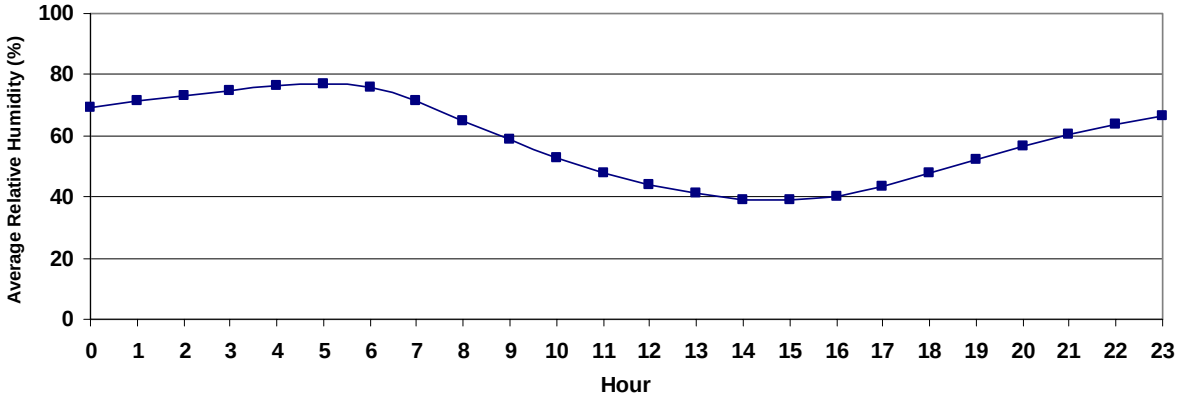


Figure 4.1.1-84. Average diurnal profile of relative humidity at the Central Site (Fresno First Street) for April 1, 2001, through March 31, 2003; units are percent.

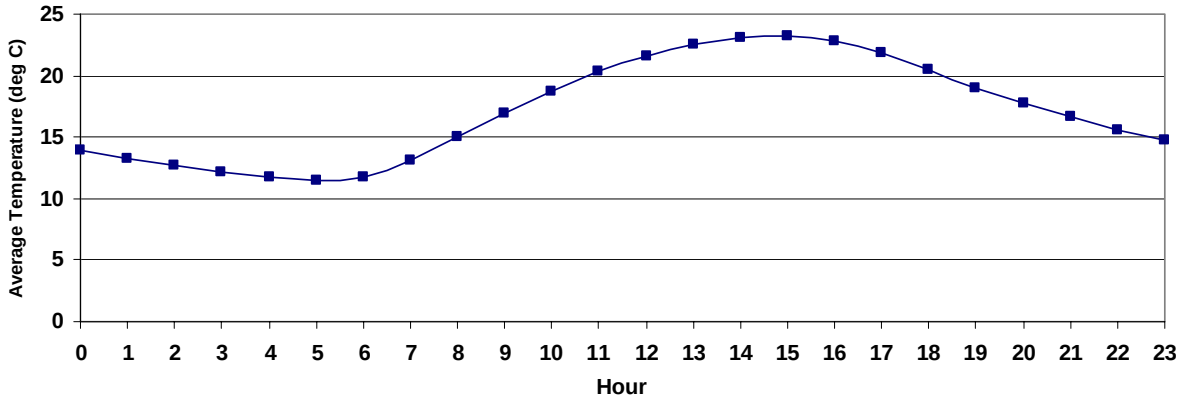


Figure 4.1.1-85. Average diurnal profile of temperature at the Central Site (Fresno First Street) for April 1, 2001, through March 31, 2003; units degrees Centigrade.

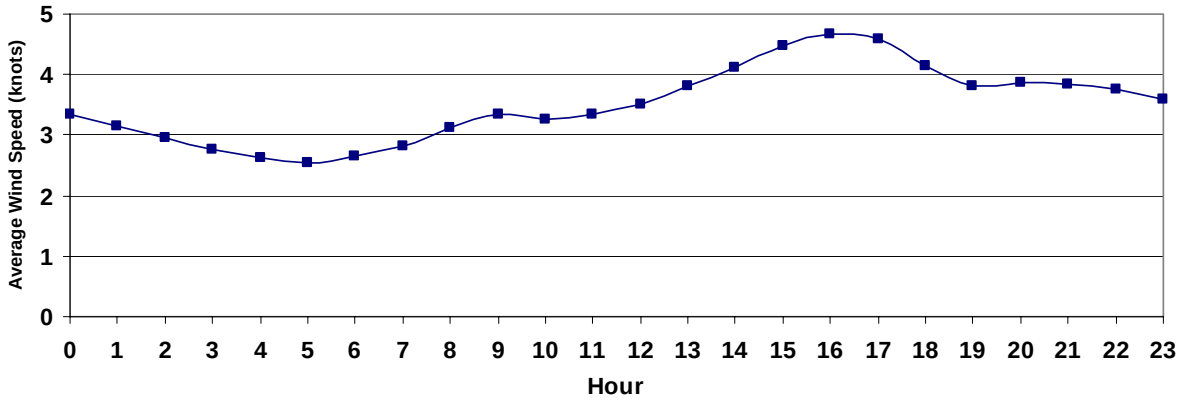


Figure 4.1.1-86. Average diurnal profile of wind speed at the Central Site (Fresno First Street) for April 1, 2001, through March 31, 2003; units are knots.

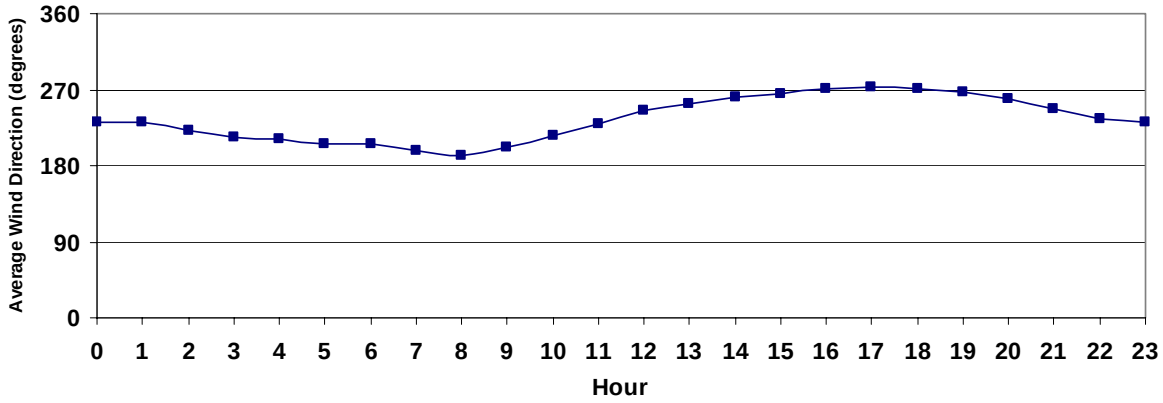


Figure 4.1.1-87. Average diurnal profile of wind direction at the Central Site (Fresno First Street) for April 1, 2001, through March 31, 2003; units are degrees.

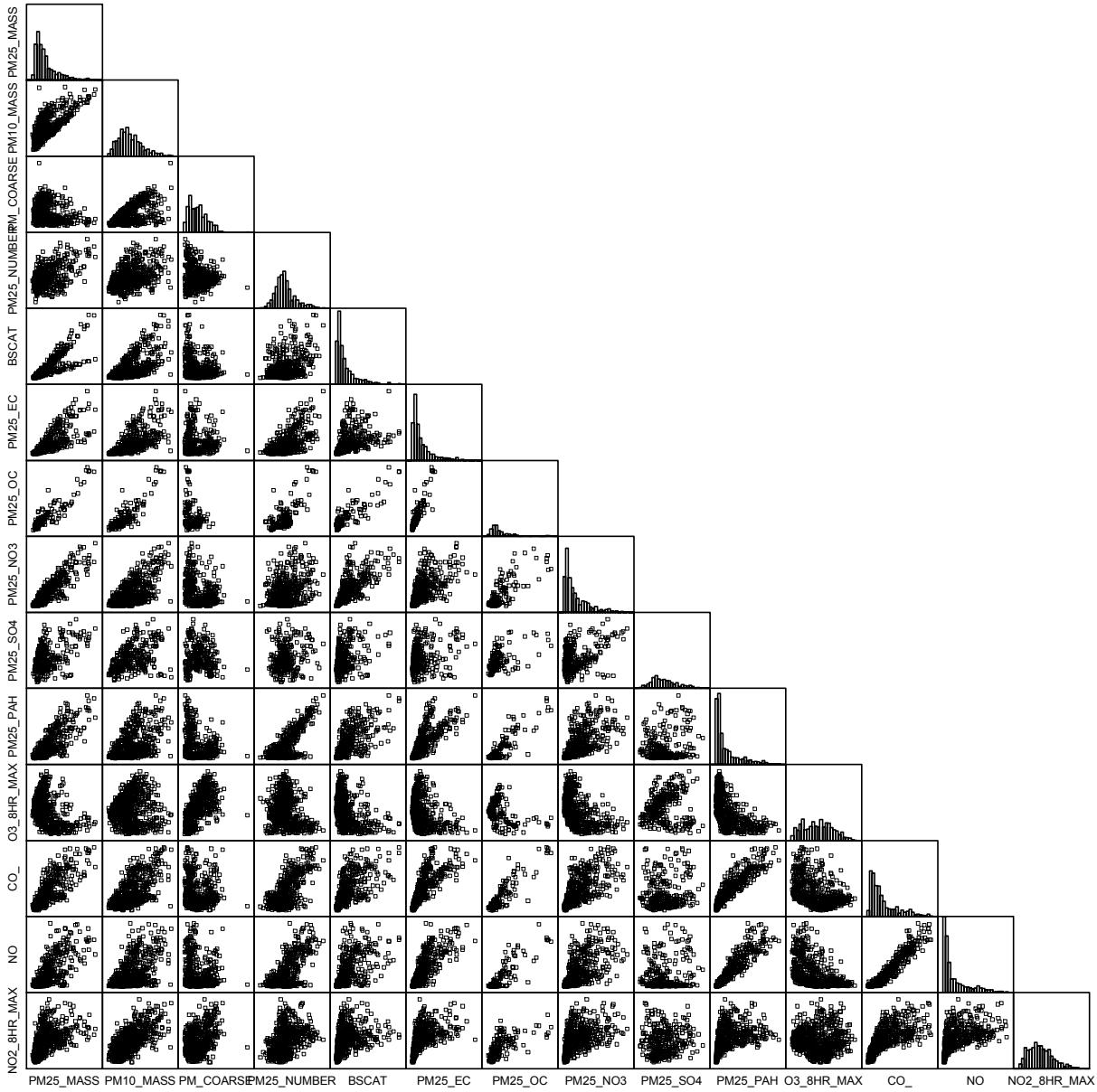


Figure 4.1.1-88. Scatter-plot matrix of 24-hr average concentrations at the Central Site (Fresno First Street) for April 1, 2001, through March 31, 2003. Shown are results for the following parameters: $PM_{2.5}$ mass (PM25_MASS), PM_{10} mass (PM10_MASS), $PM_{2.5\text{-}10}$ mass (PM_COARSE), $PM_{2.5}$ number (PM25_NUMBER), particle scattering (BSCAT), $PM_{2.5}$ elemental carbon (PM25_EC), $PM_{2.5}$ organic carbon (PM25_OC), $PM_{2.5}$ nitrate (PM25_NO3), $PM_{2.5}$ sulfate (PM25_SO4), $PM_{2.5}$ polycyclic aromatic hydrocarbons (PM25_PAH), 8-hr maximum ozone (O_3_8HR_MAX), carbon monoxide (CO_), nitric oxide (NO), and 8-hr maximum nitrogen dioxide (NO_2_8HR_max).

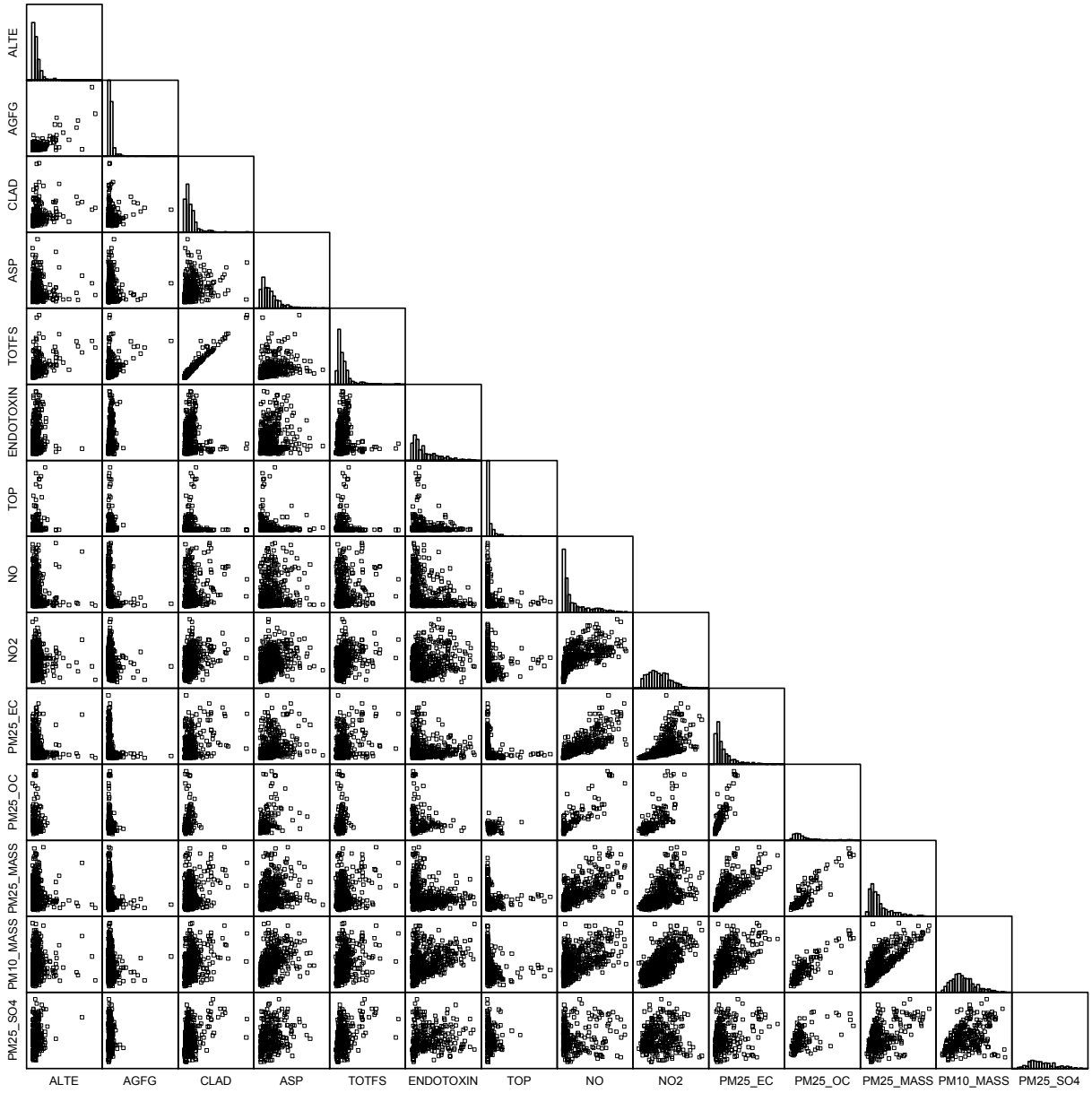


Figure 4.1.1-89. Scatter-plot matrix of 24-hr average concentrations at the Central Site (Fresno First Street) for April 1, 2001, through March 31, 2003. Shown are results for the following parameters: biological agents ALTE, AGFG, CLAD, ASP, TOTFS, ENDOTOXIN, AND TOP; gases NO and NO_2; and $PM_{2.5}$ elemental carbon (PM25_EC), $PM_{2.5}$ organic carbon (PM25_OC), $PM_{2.5}$ mass (PM25_MASS), PM_{10} mass (PM10_MASS), and $PM_{2.5}$ sulfate (PM25_SO4).

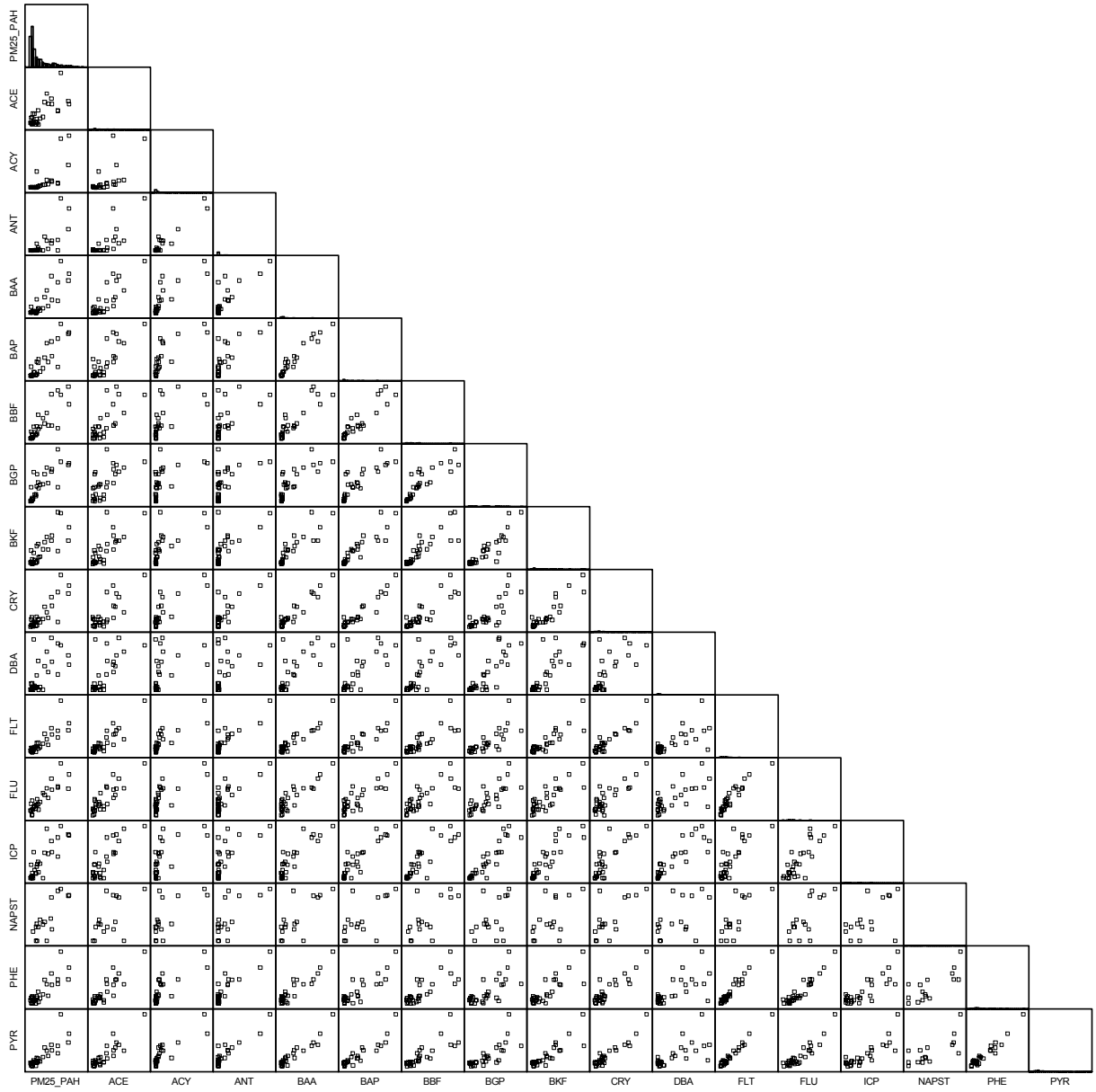


Figure 4.1.1-90. Scatter-plot matrix of 24-hr average concentrations at the Central Site (Fresno First Street) for April 1, 2001, through April 30, 2002. Shown are results for the following parameters: $PM_{2.5}$ polycyclic aromatic hydrocarbons (PM25_PAH) and PAH species ACE, ACY, ANT, BAA, BAP, BBF, BGP, BKF, CRY, DBA, FLT, FLU, ICP, NAPST, PHE, and PHY.

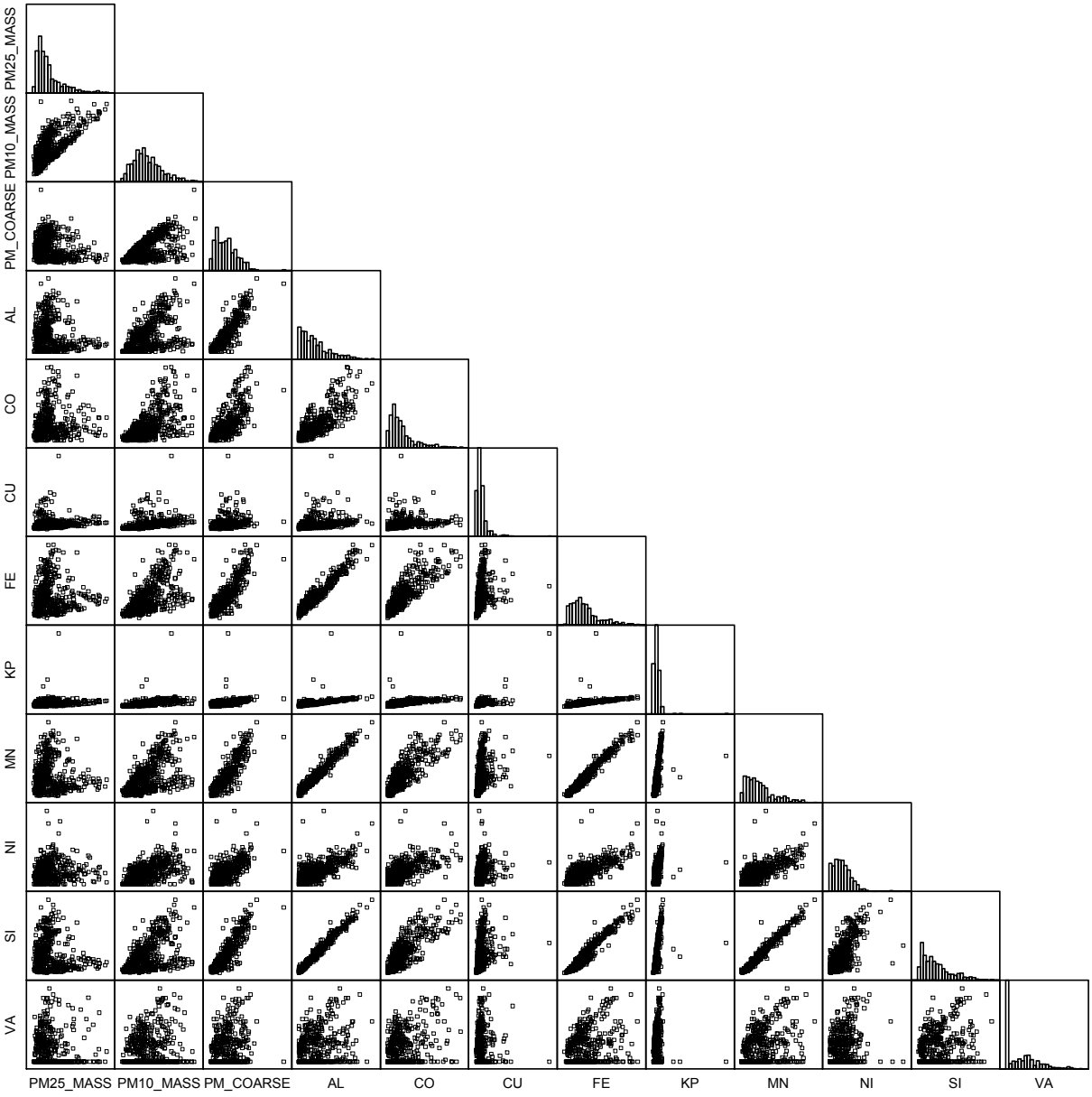


Figure 4.1.1-91. Scatter-plot matrix of 24-hr average concentrations at the Central Site (Fresno First Street) for April 1, 2001, through March 31, 2003. Shown are results for the following parameters: $PM_{2.5}$ mass (PM25_MASS), PM_{10} mass (PM10_MASS), $PM_{2.5-10}$ mass (PM_COARSE), and trace elements AL, CO, CU, FE, KP, MN, NI, SI, and VA.

4.1.2 Housing Characteristics and Exposures Reported at Baseline

Questions about housing characteristics and exposures near or in the residence were asked as part of the baseline questionnaire, as part of the self-administered daily diary from the panel visit, as part of a home survey that was interviewer-administered at the beginning or end of each two-week panel in which environmental samples were taken and at follow-up clinic visits where the child had moved to a new residence since the previous visit. To characterize housing, at baseline, this section will first review the information from the baseline questionnaire.

4.1.2.1 Housing Characteristics

At baseline, the adult answered a series of questions about potential sources of indoor air pollution and allergens. These questions were asked again if the child moved homes. Characteristics reported at baseline are used here to describe the distribution of characteristics in child's homes. In two cases, other sources were used. Proximity to agricultural fields was asked as part of a home survey done during the panel visit. Smoking policy was asked as part of each follow-up visit, but not at baseline.

4.1.2.1.1 Heating

Table 4.1.2-1 shows the types of heating in children's homes and the main types of fuel used. Forced air was the main heating system in 79.1% of homes. Portable space heaters were the main source of heat in only 3.0% of homes. Natural gas and electricity were the two most common forms of fuel used. Natual gas was used in 56.8% of homes, while electric heat was the main fuel used in 38.4% of homes.

4.1.2.1.2 Cooling

As of March 31, 2003, 94.5% of study homes had air conditioning. Air conditioning was frequenty used during Fresno's hot summers in 172 homes either "almost always" (53.7%) or "more than half of the time" (21.4%). It was infrequently used in 32 homes either on fewer than 10 days (6.6%) or never (7.4%). Fans, although present in 24.7% of homes, were not used as frequnetly as air conditioning. In fact, in the summer, fans were used on fewer than 10 days or never in 1.3% and 76.2% of homes respectively.

4.1.2.1.3 Gas Appliances

Forty-one percent of homes had a gas cooking appliance. Of these, 12.4% had been used to heat the home in winter. However, this behavior was not common in the cohort as a whole (5.1%). Gas water heaters and dryers were less common than gas cooking appliances; 23.0% of homes had gas water heaters and 12.4% had gas dryers. Gas appliances were used for an hour or more each day in 24.2% of homes.

4.1.2.1.4 Air Cleaners and Dehumidifiers

Air cleaners or dehumidifiers were used by 16.7% of homes. Of those using air cleaners, particle filters were the type used most frequently.

4.1.2.1.5 Pets

Furry pets (dogs, cats or rodents) were present in 40.9% of children's homes. Furry pets were allowed in the child's bedrooms in 28.1% of homes. About one-fifth of the participants had a cat (22.1%). Cats were allowed in children's bedrooms in 13.6% of homes. A furry pet was allowed in the asthmatic child's bedroom for 28.1% of the cohort.

4.1.2.1.6 Other sources of indoor air pollution and allergen exposure

Table 4.1.2-6 lists other potential sources of indoor air pollution and allergen exposure reported during the baseline interview. Almost ¼ of homes reported problems with mice or rats (23.7%). Cockroaches were reported in 19.9% of homes. Problems with mold or mildew "ever: in the child's home were prevalent (56.5%) and occurred in the past year in 40.4% of homes (n=93).

Water damage or flooding, a potential source for fungal spores and dust mites was reported in 26.0% of cohort homes, and in 16.2% of homes, this had happened in the past 12 months. Water damage or flooding in the child's room was reported for only 8 children (3.4%). Carpet, a potential source of dust mites, was very commonly used in the cohort both in living rooms (90.3%) and in the study participant's bedroom (93.2%). Many children had stuffed animals in their rooms (80.1%), also a potential source of dust mites.

An attached garage is a potential source of indoor CO. Many homes had attached garages (59.3%), but few adults would warm up their cars for more than 2 to 3 minutes in the garages (5.5%).

4.1.2.1.7 Second Hand Smoke Exposures

At baseline, each adult participant was asked a series of questions about the child's smoke exposures both in the home and outside of it. Smokers either lived in or regularly visited the child's home for 21.9% of the cohort (Table 4.2.1-7)), however smoking was not allowed in the home at any time in 94.3% of households (Table 4.2.1-8).

4.1.2.1.8 Potential sources of outdoor air pollution near the home

Adults were asked the approximate distance to traffic (defined as the nearest freeway, major highway, major intersection or street with heavy traffic). There was a road with traffic adjacent to the home for 24.6% of the cohort, a block away for 28.8%, up to 3 blocks away for 25.0% and more than 4 blocks away for 21.6%.

As part of a home survey that was done at each home visit where environmental samples were taken, the interviewers observed distance to agricultural fields. Table 4.1.2-9 shows the distribution of responses at the first home visit. By the end of March 2003, 172 participants (72.9%) had at least one home visit. Most homes were not located near agricultural fields or fields were more than 4 blocks away (79.1%). Only nine homes (5.2%) were adjacent to agricultural fields.

4.1.2.2 Exposures Reported on the Daily Diary

On each day of the panel visit, the child and/or an adult was asked to fill out a daily diary. There were several questions that were asked about exposures in the home on that day. These were used for individual exposure models. A revised diary began being used on October 28, 2002, however, for the most part, these questions were similar on both versions.

4.1.2.2.1 Heating, Cooling and Ventilation

Woodstoves and fireplaces were used on very few panel-days, 3.0% and 6.5% respectively. Kerosene heaters were used on 40 of 6,435 panel-days. Air conditioners were used often, 27.3% of the time. Windows were left open for at least 30 minutes 42.7% of the time, and overnight on 13.6% of panel-days (see Table 4.1.2-10).

4.1.2.2.2 Other Daily Indoor Exposures

At baseline, 41.1% of participants reported that they used either a gas cooktop or range in their home. A gas oven, which could elevate NO_2 concentrations, was used on 14.1% of panel-days. A child was in the home while it was vacuumed on 27.3% of panel-days. Smoking was infrequent, occurring on only 164 panel-days (see Table 4.1.2-10).

Table 4.1.2-1. Home Heating in Child's Home to March 31, 2003		
MAIN HEATING SYSTEM IN CHILD'S HOME (N=234)		
Forced air	185	79.1
Built-in electric units	5	2.1
Wall heater	27	11.5
Floor heater	4	1.7
Stove or range	4	1.7
Portable space heaters	7	3.0
Wood stove	2	0.85
MAIN TYPE OF FUEL USED TO HEAT CHILD'S HOME (N=229)	#	%
Gas from utility company	130	56.8
Electricity	88	38.4
Bottles, Tanks, or LP gas	5	2.2
Wood	5	2.2
Solar	1	0.44

Table 4.1.2-2 Sources of Cooling reported at baseline		
	#	%
CHILD'S HOME HAS AIR CONDITIONING (N=236)	223	94.5
FREQUENCY OF AIR CONDITIONING USE DURING SUMMER (N=229)		
Never	17	7.4
Hardly ever (less than 10 days)	15	6.6
Less than one quarter of the time	8	3.5
Less than one half of the time	17	7.4
More than half of the time	49	21.4
Almost always	123	53.7
FAN IS USED TO COOL CHILD'S HOME DURING THE SUMMER (N=235)	58	24.7
FREQUENCY OF FAN USE WHEN CHILD IS HOME DURING SUMMER (N=235)		
Never	179	76.2
Hardly ever (less than 10 days)	3	1.3
Less than one quarter of the time	6	2.6
Less than one half of the time	1	0.43
More than half of the time	10	4.3
Almost always	36	15.3

Table 4.1.2-3Gas appliances in child's home to March 31, 2003		
GAS APPLIANCES		
Gas cooking appliance in child's home (N=236)	97	41.1
If have a gas appliance, use it to heat home in winter (N=97)	12	12.4
Gas appliance ever used to heat home (N=236)	12	5.1
Gas water heater in the living quarters (N=235)	54	23.0
Gas dryer in child's home (N=234)	29	12.4
HOURS PER DAY A GAS APPLIANCE IS USED IN THE HOME (N=236)		
None (includes those w/o a gas appliance)	143	60.6
Less than 1 hour	36	15.3
1 to 3 hours	49	20.8
More than 3 hours	8	3.4

Table 4.1.2-4. Air cleaners/Dehumidifier use at baseline, to March 31, 2003		
	#	%
Ever use particle filter	22	9.4
Ever use ion generator	5	2.2
Ever use dehumidifier	9	3.9
Use air cleaners / dehumidifiers	39	16.7

N=233. Three baselined adults gave answers of "Don't Know" for these questions.

Table 4.1.2-5 Pets reported in child's home at baseline (N=235)		
	#	%
Pet dog, cat or rodent in child's home	96	40.9
Pet dog, cat or rodent allowed in child's bedroom	66	28.1
Pet Cats	52	22.1
Pet Dogs	53	22.6
Pet Rodents	15	6.4
Birds	19	8.1
Cats go into child's room	37	15.7
Dogs go into child's room	32	13.6
Pet rodents in child's room	8	3.4

Table 4.1.2-6. Other potential sources of indoor air problems			
	N	#	%
Problems with Mice or rats	236	56	23.7
Problems with Cockroaches	236	47	19.9
Mold or mildew inside child's home	230	130	56.5
Mold or mildew in the home in the 12 months	308	93	40.4
Flooding or water damage has occurred in child's home	235	61	26.0
Child's bedroom has flooded	235	8	3.4
Flooding or water damage within the past year	235	38	16.2
Carpet in child's bedroom	236	220	93.2
Carpet in the living room	236	213	90.3
Stuffed animals in child's room	236	189	80.1
Garage attached to child's home	236	140	59.3
Cars left to warm up in a garage for more than 2-3 min	236	13	5.5

Table 4.1.2-7 Self-reported Exposures in the Home at Baseline (N=315)		
	#	%
Respondent is a current smoker	32	10.2
Any smokers live in or regularly visit the home	69	21.9

Table 4.1.2-8 Smoking Policy or Rules in the Home (N=167)*		
	#	%
Smokers can smoke in any room	1	0.5
Smoking allowed in certain rooms	5	2.4
No smoking allowed in the home when the child is at home	1	0.5
No smoking allowed in the home at any time	200	94.3
No smoking policy	5	2.4

*This question was asked at each follow-up visit. There were 212 households who had a follow-up visit by March 31, 2003. The answer to the earliest follow-up visit completed was used here.

Table 4.1.2-9 Potential sources of outdoor air pollution near the home		
	#	**%**
Distance to nearest freeway (N=236)		
Immediately in front, behind or beside home	58	24.6
One block away	68	28.8
One to 3 blocks away	59	25.0
More than 4 blocks away	51	21.6
Distance to agricultural fields (N=172)*		
Immediately in front, behind or beside home	9	5.2
One block away	8	4.7
1 to 3 blocks away	19	11.0
More than 4 blocks away/none nearby	136	79.1

*Reported at the first home visit in which a home survey was done.

Table 4.1.2.-10 Daily Exposures in the Home as Reported in the Daily Diary (November 30, 2000 to March 31, 2003)			
	N*	**#**	**%**
HOME EXPOSURES			
Wood stove used today in child's home	6435	195	3.0
Fireplace used today in child's home	6435	417	6.5
Kerosene heater used today in child's home	6435	40	0.6
Air conditioner on today in child's home	7127	1943	27.3
Windows open more than 30 minutes	6458	2760	42.7
Windows open overnight	6143	833	13.6
Stove burners on for 10 minutes or more	5996	2883	48.1
*Gas oven on for 10 minutes or more**	6147	869	14.1
Someone vacuumed today while child home	6173	1682	27.3
Someone smoked today while child was in home	6373	164	2.6

* The diary is self-administered. The N is the number of non-missing values for that question except where otherwise specified.;the unit of observation is child-day. *Denominator is total number of people answering the question, some of whom do not have gas stoves. In the revised version (version 5.0) , the diary allows the respondent to specify whether there is a gas stove in the house; the earlier version does not.

4.1.3 Time-Location-Activity during Panel Visits

The individual exposure models relied on estimates of time/location and activity. The daily diary included several questions related to the time location and activity of the child. Questions related to location, transportation use and physical activity level were asked in much more detail (in time scale, in type of activities specified and in geographic resolution) in the first version of the diary (see Section 3.2.3.6) but because of the high level of missingness these questions were revised. The revised questions had much higher completion rates in the revised diary. The results below are reported for the revised version. The number of observations for diary questions about transportation and physical activity level is about 1/3 that of other diary questions with air pollution data to March 31, 2003.

Each diary can be used to determine whether the child went to school that day. Since the location of each child's school is determined every 3 months, air pollution exposures during that time can be assigned based on the distance of the air pollution monitor to the school. Children went to school on 54.2% of panel-days. Children spent time away from the Fresno/Clovis area on 7.0% of panel-days.

There are only two time periods in the revised diary: "AM" (before 12 noon) and "PM" (after 12 noon until bedtime). Transportation use and physical activity levels (indoors and outdoors) were asked for these two time periods. Children rode in cars frequently, both in mornings (70.8%) and afternoons and evenings (75.3%), but rode in buses less often (10.5% and 11.8% in AM and PM hours, respectively). Children more often reported activities outdoors (51.8% in AM hours, 50.7% in PM hours) than indoor activities (20.9% before 12 noon and 26.5% after 12 noon). To assess the intensity of activity, children were asked if they breathed hard because of it. For each time period, about 20% of children reported an outdoor activity that made them breathe hard. Children breathed hard in response to indoor activities during 8.2% of AM hours and 11.8% of PM hours (Table 4.1.3-1).

Table 4.1.3-1 Responses to Time/Location/Activity Questions on Daily Diary			
LOCATION	N*	#	%
Went to school Today	6455	3496	54.2
Spent time more than 20 miles away from Fresno/Clovis today	6231	434	7.0
TRANSPORTATION**			
Ride in a car or van AM	2030	1437	70.8
Ride in a car or van PM	2020	1520	75.3
Ride in a bus AM	2012	211	10.5
Ride in a bus PM	2018	239	11.8
PHYSICAL ACTIVITY LEVEL**			
Indoor physical activity AM	2012	421	20.9
Indoor physical activity PM	2016	535	26.5
Breathe hard due to indoor activity AM	1996	163	8.2
Breathe hard due to indoor activity PM	1985	195	9.8
Outdoor physical activity AM	2002	1036	51.8
Outdoor physical activity PM	2000	1013	50.7
Breathe hard due to outdoor activity AM	1953	392	20.1
Breathe hard due to outdoor activity PM	1961	416	21.2

* The diary is self-administered. The N is the number of non-missing values for that question except where otherwise specified; the unit of observation is child-day.

** These time/location/activity questions were asked in much more detail (both in time scale and type of activities specified) in the first versions of the diary (see Section 3.2.3.6) but because of the high level of missingness these questions were revised. The revised questions had much higher completion rates in the revised diary. Therefore, the results are only reported for the revised version.

4.1.4 Indoor Air Quality Conditions in Homes

4.1.4.1 Home Intensive Measurements

As described in Section 3.4, air quality conditions inside 84 homes of the FACES participants were measured during the 1-year Home Intensive study. Two to five homes from each two-week panel were sampled between February 2002 and February 2003. Separate 24-hr integrated samples were collected on 3 weekdays and 2 weekend days. A subset (26) of houses was sampled in two seasons. Another 58 houses were sampled in one season, for a total of 110 sets of home visits.

The extent of analyses of samples collected in the Home Intensive varied by compound. Light scattering data were processed for 11 or 12 days for each visit. $PM_{2.5}$ and PM_{10} mass were analyzed for 5 days of each visit. Samples of $PM_{2.5}$ sulfate, $PM_{2.5}$ nitrate, $PM_{2.5}$ EC, $PM_{2.5}$ OC, PAHs, PM_{10} metals and other trace elements, PM_{10} endotoxin, pollen grains, and fungal spores were typically analyzed for 2 or 3 days of each visit. Samples from at least one weekday and one weekend day were selected for analysis from each 5-day integrated sampling campaign. Sampling of PAHs indoors was conducted for seven months, starting in August 2002. The unanalyzed samples have been archived. This sampling and analysis strategy produced a data set with a widely varying number of samples, ranging from ~70 for PAHs to 1,234 for 24-hr light-

scattering measurements. Over 520 samples were analyzed for PM mass; 200 to 300 samples were analyzed for most other compounds. Comparisons of the PAH concentrations with those for other compounds is somewhat compromised by the small number of PAH samples and the limited seasonality of PAH samples (compared to other compounds).

Summary statistics for the PM, biological agents, PAHs, and PM_{10} metals and other trace elements are listed in Table 4.1.4-1. Figures 4.1.4-1 through 4.1.4-3 show the frequency distributions of indoor concentrations of the major compounds. The 10^{th}, 50^{th}, and 90^{th} percentile $PM_{2.5}$ mass concentrations were 6.9, 15.7, and 39.2 $\mu g/m^3$ inside FACES residences; the maximum 24-hr $PM_{2.5}$ mass concentration was 230 $\mu g/m^3$. The 10^{th}, 50^{th}, and 90^{th} percentile indoor PM_{10} mass concentrations were 15.9, 35.5, and 71.6 $\mu g/m^3$, and the maximum PM_{10} was 254 $\mu g/m^3$. The median distribution of chemical component concentrations indicates OC, NO_3, EC, and SO_4 composed 53.7%, 10.7%, 6.3%, and 6.2% of the $PM_{2.5}$ mass indoors, respectively. If the OC is multiplied by 1.4 to account for the hydrogen and oxygen associated with the organic carbon, the median indoor organic compound $PM_{2.5}$ (OM) concentration is 11.8 $\mu g/m^3$ and 75.2% of the $PM_{2.5}$ mass, which clearly indicates that indoor $PM_{2.5}$ primarily consists of organic compounds. The differences between the medians and means in the summary statistics and the frequency distribution plots show that the indoor concentration distributions are usually skewed, due to a relatively small number of high concentrations. The skewed distribution is observed in many other studies of indoor concentrations (261).

Indoor concentrations of biological agents varied widely. The median indoor concentrations of fungal spores were 67, 94, 182, 648, and 1094 spores/m^3 for alternaria, aspergillus+penicillium, agricultural fungi, cladosporium, and total fungi, respectively. The maximum indoor concentrations ranged from 621 spores/m^3 for alternaria to 10,166 spores/m^3 for total fungi. The median and maximum endotoxin concentrations indoors were 1.7 and 48 EU/m^3. The median and maximum total pollen concentrations indoors were 2.2 and 236 grains/m^3. Pollen levels were generally low and below detection levels, indoors on many of the home visits.

The PAH compounds constituted a relatively small fraction of the OM indoors. The median indoor concentrations of phenathrene and acenaphthene were 5.4 and 1.3 ng/m^3, and the median indoor concentrations of the other PAHs, excluding napthalene, were each less than 1 ng/m^3. Napthalene, which was found primarily in the gas phase rather than aerosol phase in the outdoor central site and school measurements, had a median indoor concentration of 433 ng/m^3. The maximum indoor PAH concentrations were 4 to 50 times the median concentrations. For example, the maximum 24-hr average indoor concentrations of flouranthene, indeno[1,2,3-cd]pyrene, flourene, acenaphthene, acenaphthylene, pyrene, benzo[ghi]perylene, phenathrene, and napthalene were 12, 13, 14, 15, 20, 30, 32, 72, and 1667 ng/m^3, respectively.

The most abundant PM_{10} trace metals inside residences were silica, aluminum, and iron; the median concentrations were 2.36, 0.68, and 0.35 $\mu g/m^3$, and the maximum concentrations were 20, 7.5, and 4.7 $\mu g/m^3$, respectively. The median indoor concentrations of nickel, vanadium, lead, and manganese were 0.0012, 0.0028, 0.0049, and 0.0071 $\mu g/m^3$ and the maximum indoor concentrations were 0.010, 0.027, 0.105, and 0.103 $\mu g/m^3$. The medium and maximum indoor concentrations of potassium, which is an indicator of wood smoke, were

0.4 and 4.4 μg/m^3. The levels of trace elements observed in FACES residences were within the ranges observed in other California residences (212, 224)

Summary statistics of the average indoor concentrations in residences, regardless of the number of visits, are shown in Table 4.1.4-1. The median and mean values are similar to those computed for all home visits. For example, the median indoor $PM_{2.5}$ concentration in 84 homes is 16.4 μg/m^3 compared to 15.7 μg/m^3 for 108 home visits. The median indoor PM_{10} concentration in 84 homes is 39.8 μg/m^3 compared to 35.5 μg/m^3 for 108 home visits. Overall, the median indoor concentrations averaged by residence are about 5% higher than those averaged over home visits. The indoor concentrations of total fungal spores, endotoxin, BAP, BBF, Zr, and Mn show the largest differences between home averages and home visit averages. These results suggest indoor concentrations in homes visited once were slightly higher on average than those homes visited twice.

4.1.4.2 Routine House Measurements

Routine environmental monitoring was conducted in every home as part of the panel visit until samples had been collected at least once from each of the three study seasons: spring (February to May); summer (June to September) and winter (October to January).

For many of the dust assays, the concentration of allergens was under the detection limit. For this reason, dust allergens were divided into categories corresponding with nondetectable, low, medium, and high concentrations.

Each panel visit was scheduled to be 14-days long. The passive sampling for NO_2, nicotine, and, during the ozone season, indoor and outdoor ozone, was occasionally longer than 14 days. All passive concentrations were calculated for the actual length of the sampling period.

The results of environmental samples from first visits completed by March 10, 2003, were assembled into a report for participants that is provided in Section 4.1.4.3. It reports the distribution of cockroach allergen in homes that reported cockroach problems at baseline, dog and cat allergen in homes with and without these pets, and second hand smoke concentrations in homes with and without smokers who lived in the home or were regular visitors.

4.1.4.2.1 Dust Samples

Two types of dust mites were collected: *Dermatophagoides pteronyssinus* (Der p) and *Dermatophagoides farinae* (Der f). Concentrations of both were often below the detection limit, although Der f had more values above the detection limit. A variable "dust mite" was created that was the maximum value of the two. As shown in Table 4.1.4-3, dust mite concentrations were not detectable in 77.9% of bed samples and 86.6% of floor samples. Only 4.8% of bed samples and 1.7% of floor samples had dust mite concentrations greater than 10 μg/g. As of March 10, 2003, all but 12 of 174 homes had wall-to-wall carpeting. The 12 homes without wall-to-wall carpeting had undetectable or low concentrations; however the average concentration of dust mite was too low to be detected in homes with and without wall-to-wall carpeting (see Figure 4.1.4-4).

Cockroach allergen levels were also very low, in fact, undetectable in 95.7% of bed samples and 85 % of floor samples. Of 32 homes in which cockroaches were reported to have been seen in the 12 months before the first home visit, only 12 had detectable levels of antigen (see Figure 4.1.4-7).

Both dog and cat allergen concentrations were higher than mite and cockroach. Dog allergen concentrations were high in 30.2% of samples from children's beds and 38.7% of samples from living room and kitchen floors. In the first visit report, pet dogs were present in about 22% of homes. Average levels were much higher in homes with dogs (123 μg/g) than in homes without dogs (8 μg/g); however, in 39.2% of homes with high levels of dog antigen (more than 10 μg/g), the residents did not own a pet dog (see Figure 4.1.4-6).

Cat allergen was found in all but 5% of both bed and floor samples. Bed samples tended to have higher concentrations; 34.4% of bed samples were more than 8 μg/g. Cat allergen concentrations were much higher in homes with cats 392 μg/g vs. 7 μg/g (see Figure 4.1.4-5) yet no cats were present in 23 of 54 homes with high concentration levels.

Our finding of both dog and cat allergen in homes without these pets has been observed in other studies (Ingram et al., 1995; Perzanowski et al., 1999). This is possibly explained by the observation that high levels of both of these allergens have been observed in schools (Perzanowski et al., 1999) and in public buildings, especially on upholstered surfaces (Custovic et al., 1996).

4.1.4.2.2 Endotoxin

Endotoxin levels are shown in Table 4.1.4-4. As of March 31, 2003, 211 bed samples and 113 floor samples had been assayed. The concentrations are skewed due to several very high concentrations. The maximum concentrations were more than 10 times the 75th percentile concentrations for both bed and floor samples The median concentration of endotoxin during this period was 52.5 EU/mg house dust for bed dust and 64.0 EU/mg for floor dust. The means were 82.5 EU/mg and 107.1 EU/mg, respectively. Median concentrations of endotoxin in bed dust were greatest in summer (62.0 EU/mg) and lowest in spring months (45.0 EU/mg). Endotoxin concentrations in floor dust were highest in winter (78.8 EU/mg) and lowest in spring (54.9 EU/mg). Levels of endotoxin in dust from floor samples were about 22% greater than those found in bed samples at median concentrations.

4.1.4.2.3 Passive Samples: Nicotine, NO_2 and Ozone

Fifty-seven of 237 nicotine samples (24.1%) had concentrations above the detection limit. The distribution of detectable concentrations is shown in Table 4.1.4-5. Nicotine levels were generally low; the levels in 75% of the samples with detectable concentrations were below 1 μg/m^3. (See also Figures 4.1.4-8 and 4.1.4-9).

The median concentration of NO_2 was 15.1 ppb (S.D.=13.4). Concentrations ranged from 0.6 ppb to 134.6 ppb. Figure 4.1.4-10 shows the distribution of NO_2 concentrations in

homes with and without gas stoves. NO_2 concentrations were generally greater in homes with gas stoves. Almost every home in the highest category (> 20 ppb) had a gas stove.

Indoor and outdoor ozone samples were taken in different months each year of the study (see Table 4.1.4-6). Prior to March 31, 2003, ozone was measured in homes as part of panel visits that occurred between August 29 and October 31, 2001. In 2002, ozone was measured during home visits that began between May 15 and October 4, 2002. (With the original protocol, there was some resistance to placement of the outdoor ozone sampling tripod in the yards of participants' homes. By this point in the study, there were only 87 outdoor ozone samples. By the end of 2004, there were 321 indoor ozone samples and 210 outdoor ozone samples. The mean indoor concentration of ozone (9.5 ppb) was about 32.7 ppb lower than the concentration right outside of the home (42.2 ppb). The current California 8-hr standard for ozone is 70 ppb. The highest two-week average indoor ozone concentration was 56 pbb. Two-week average concentrations of outdoor ozone were greater than 70 ppb in 21.8% of samples.

Table 4.1.4-7 shows the seasonal concentrations of NO_2 and indoor and outdoor ozone. There were too few nicotine samples above the detection limit for a seasonal comparison. The mean concentration of NO_2 rose from 11.3 ppb in the spring to 14.2 ppb in the winter. Mean indoor ozone concentrations were 7.8 ppb greater in summer (mean=11.4ppb, sd=18.2) than in winter (mean=3.2, sd=24.5). Outdoor ozone concentrations were 23.7 ppb greater in summer than in winter. In the summer, the 75^{th} percentile of outdoor ozone concentrations was 71.2 ppb, very near the current California standard for 8-hr average ozone.

4.1.4.2.4 Moisture Levels in Participants Homes as Measured at the Home Visit

As part of each home visit where passive samplers were placed in the home, interviewers took 3 moisture readings from the walls of a living area (usually the living room) and 3 moisture readings from the walls of the child's sleeping area or bedroom (see Appendix B, home visit folder *"Moisture Meter Measurements"*). The no-pins moisture meter (Professional Equipment, model #CT100, Hauppauge, NY) measures moisture content in the wall in which it is in contact on a scale of 0-30%. In each home, the moisture meter was placed on three walls in the living room and in the child's bedroom at the horizontal midpoint, 18-24 inches from the floor.

Priority was given: (1) to external walls, (2) walls adjoining a bathroom, kitchen or laundry room, and (3) walls shared with a bedroom, the living room, or dining room. The maximum of these three measurements was used in the data analysis (see Table 4.1.4-8)

The distribution of maximum moisture levels was very similar within each season strata for the living areas and the child's sleeping area. Furthermore, the seasonal means were quite similar.

As of July 1, 2005, 872 moisture measurements have been collected in living rooms and 862 measurements in the bedrooms of 294 participants. These measurements were collected in a total of 260 homes and 294 bedrooms of participants (there were sibling pairs in 34 of the homes). The maximum moisture measurements collected in the living rooms ranged from 3.0-30.0%, with a mean value of 8.9%. In the child's bedrooms, the maximum measurements ranged from 2.0-58.0% with a mean of 8.8%.

Survey-reported, visual evidence of moisture or mildew was detected in 8.8% of the living rooms and in 10.1% of the bedrooms. We divided the moisture measurements at the median into "higher" and "lower" categories. Visual evidence of moisture was significantly correlated with differing moisture levels ("higher" or "lower," as defined above) in both the living room and the child's bedroom. Spearman rank correlations between observation of moisture and higher moisture values were 0.88 and 0.79 for living areas and the child's sleeping area respectively. Each observation was summarized as the maximum of the three measurements taken.

4.1.4.3 First Visit Report of Routine Residential Measurements

Figures 4.1.4-4 through 4.1.4-10 summarize the routine household measurements obtained during the first visit to each home. This report and a cover letter explaining the categories were provided to all FACES participants whose homes were visited by March 10, 2003. The participants were also provided results for their own household. The number of samples available when this report was prepared is less than currently available in the database. The full report (customized for each participant) is in Appendix K.

Table 4.1.4-1. Summary statistics for indoor pollutant concentrations in FACES residences based on all 24-hr samples that exceeded the limits of detection.

Pollutant[1]	No. of cases	Minimum	10th Percentile	25th Percentile	Median	Mean	75th Percentile	90th Percentile	Maximum	Units
Particulate Matter										
$PM_{2.5}$ Mass	524	2.30	6.87	10.36	15.73	21.31	24.34	39.16	230.08	$\mu g/m^3$
PM_{10} Mass	528	4.39	15.93	24.29	35.50	41.87	51.13	71.60	253.68	$\mu g/m^3$
B_{scat}	1234	1.64	16.16	27.30	45.33	74.22	83.59	153.19	1184.12	Mm-1
$PM_{2.5}$ EC	254	0.09	0.39	0.53	0.99	1.69	1.70	2.69	34.56	$\mu g/m^3$
$PM_{2.5}$ OC	254	3.37	5.10	6.18	8.45	11.54	12.28	20.89	119.46	$\mu g/m^3$
$PM_{2.5}$ NO_3	156	0.43	0.59	0.93	1.68	2.49	3.17	5.29	23.98	$\mu g/m^3$
$PM_{2.5}$ SO_4	207	0.14	0.35	0.56	0.98	1.05	1.47	1.91	3.87	$\mu g/m^3$
Biological Agents										
ALTE	186	13.5	13.5	27.0	67.5	110.6	148.5	255.2	621.0	spores/m^3
AGFG	228	13.5	27.0	94.5	182	324	405	767	2889	spores/m^3
CLAD	239	13.5	175.5	357.8	648	1071	1360	2808	4401	spores/m^3
ASP	168	13.5	27.0	40.5	94.5	355	290	734	9599	spores/m^3
TOTFS	245	0.0	283.5	553.5	1094	1674	2433	3942	10166	spores/m^3
Endotoxin	366	0.0	0.55	0.95	1.73	2.92	3.79	6.07	47.73	EU/m^3
TOP	250	0.0	0.0	0.0	2.2	12.1	7.7	26.4	236.5	grains/m^3
Polycyclic Aromatic Hydrocarbons										
ACE	79	0.25	0.47	0.89	1.34	1.58	1.86	2.44	14.77	ng/m^3
ACY	74	0.08	0.16	0.22	0.41	1.74	1.19	3.63	20.19	ng/m^3
ANT	75	0.11	0.15	0.21	0.38	0.76	0.83	1.61	5.05	ng/m^3
BAA	53	0.03	0.06	0.11	0.31	0.49	0.69	1.34	2.40	ng/m^3
BAP	63	0.01	0.02	0.15	0.39	0.75	0.87	2.02	5.61	ng/m^3
BBF	59	0.02	0.05	0.14	0.32	0.68	0.87	1.81	3.85	ng/m^3
BGP	64	0.02	0.05	0.20	0.71	2.05	1.52	4.41	32.30	ng/m^3
BKF	60	0.00	0.01	0.04	0.12	0.41	0.48	1.47	2.74	ng/m^3
CRY	66	0.02	0.05	0.12	0.31	0.61	0.66	1.24	9.46	ng/m^3

Pollutant[1]	No. of cases	Minimum	10th Percentile	25th Percentile	Median	Mean	75th Percentile	90th Percentile	Maximum	Units
DBA	49	0.03	0.04	0.08	0.19	0.48	0.80	1.28	2.56	ng/m^3
FLT	81	0.13	0.36	0.56	0.75	1.62	1.33	4.51	12.21	ng/m^3
FLU	76	0.11	0.33	0.52	0.97	1.95	2.21	4.53	14.42	ng/m^3
ICP	45	0.24	0.43	0.62	0.85	1.70	1.98	3.57	12.78	ng/m^3
NAPST	66	92.97	189.55	328.71	433.46	529.34	610.21	973.8	1677.1	ng/m^3
PHE	78	1.88	2.67	3.75	5.38	9.89	8.08	25.43	72.91	ng/m^3
PYR	79	0.36	0.57	0.73	0.97	2.37	1.63	5.43	30.44	ng/m^3
PM_{10} Trace Elements										
AL	213	70.99	196.60	385.78	681.24	916.27	1180.41	1911.3	7511.1	ng/m^3
AS[1]	97	0.73	0.82	0.94	1.35	1.52	1.88	2.37	4.28	ng/m^3
AU[1]	7	1.48	1.48	1.54	1.77	1.97	2.42	2.87	2.94	ng/m^3
BA[1]	51	23.81	26.39	28.95	36.38	37.94	43.43	55.18	75.29	ng/m^3
BR	213	0.86	2.04	2.85	4.37	5.47	6.25	9.68	48.64	ng/m^3
CA	213	53.13	188.00	298.14	473.21	699.03	799.24	1415.9	10395.7	ng/m^3
CD[1]	1	6.72	0.00	0.00	6.72	6.72	0.00	0.00	6.72	ng/m^3
CL	213	9.38	57.91	119.07	212.50	382.40	401.40	793.34	5027.25	ng/m^3
CO	197	0.40	0.87	1.43	3.05	4.81	5.97	10.33	49.78	ng/m^3
CR	154	0.85	1.08	1.39	2.26	4.22	3.51	7.11	75.26	ng/m^3
CU	213	0.82	2.30	3.81	6.65	8.95	10.44	17.81	58.84	ng/m^3
FE	213	38.60	102.98	187.23	351.28	496.26	617.41	1033.3	4705.8	ng/m^3
GA[1]	12	0.87	0.89	1.06	1.16	1.13	1.24	1.29	1.32	ng/m^3
HG[1]	1	1.16	0.00	0.00	1.16	1.16	0.00	0.00	1.16	ng/m^3
IN[1]	2	6.84	6.84	6.84	7.60	7.60	8.36	8.36	8.36	ng/m^3
KP	213	57.35	159.19	245.61	405.48	513.03	614.05	919.3	4477.6	ng/m^3
LA[1]	13	30.73	31.22	31.96	35.29	36.55	38.55	43.34	55.66	ng/m^3
MG	110	45.09	49.49	58.59	78.63	93.51	108.62	149.25	508.88	ng/m^3
MN	212	0.75	2.06	3.60	7.09	10.37	13.01	21.08	102.70	ng/m^3
MO[1]	7	1.25	1.25	1.30	1.40	2.12	2.85	3.81	4.02	ng/m^3
NA[1]	94	224.37	248.72	273.02	329.82	408.33	424.81	687.29	1763.0	ng/m^3

Pollutant[1]	No. of cases	Minimum	10th Percentile	25th Percentile	Median	Mean	75th Percentile	90th Percentile	Maximum	Units
NI	185	0.40	0.54	0.75	1.18	1.58	1.78	3.11	9.93	ng/m^3
PB	134	2.51	2.95	3.59	4.87	6.64	7.23	9.93	104.82	ng/m^3
PD[1]	23	1.37	1.47	1.64	1.92	2.24	2.39	3.47	5.52	ng/m^3
PH[1]	31	6.52	6.92	10.82	23.95	70.03	85.32	171.55	591.55	ng/m^3
RB	168	0.45	0.55	0.79	1.27	1.63	1.96	3.10	9.29	ng/m^3
SB[1]	50	2.29	2.50	2.90	3.73	4.50	4.83	7.53	13.20	ng/m^3
SI	213	296.4	645.2	1157.1	2360.3	2943.7	3771.1	5830.8	19975.2	ng/m^3
SN[1]	86	2.79	3.15	3.84	4.42	5.42	6.33	8.93	16.24	ng/m^3
SR[1]	27	7.64	7.85	8.38	9.71	13.58	14.31	21.97	49.51	ng/m^3
SU	213	66.75	226.49	313.32	453.12	522.43	624.08	823.40	4344.6	ng/m^3
TI	203	1.61	11.90	22.36	43.02	85.82	68.92	114.35	6548.1	ng/m^3
TL[1]	8	1.11	1.12	1.15	1.31	1.49	1.74	2.28	2.40	ng/m^3
UR[1]	7	1.12	1.13	1.21	1.37	1.32	1.43	1.47	1.48	ng/m^3
VA[1]	99	1.11	1.47	1.94	2.85	3.77	4.54	7.35	26.94	ng/m^3
YT[1]	34	0.59	0.62	0.68	0.77	0.83	0.92	1.09	1.71	ng/m^3
ZN	213	4.04	10.94	15.93	26.01	34.60	39.79	66.13	294.61	ng/m^3
ZR	201	0.76	1.57	2.38	3.93	6.32	8.25	12.26	57.19	ng/m^3

[1] The majority of measured indoor concentrations for PM_{10} AS, AU, BA, CD, GA, HG, IN, LA, MO, NA, PD, PH, SB, SN, SR, TL, UR, VA, and YT were below the limit of detection. AG and SE were not detected in any samples.

Table 4.1.4-2. Summary statistics for the average indoor pollutant concentrations in FACES residences.

Pollutant[1]	No. of Residences	Minimum	10th Percentile	25th Percentile	Median	Mean	75th Percentile	90th Percentile	Maximum	Units
Particulate Matter										
$PM_{2.5}$ Mass	84	5.72	8.98	12.00	16.42	21.48	23.27	34.45	162.44	$\mu g/m^3$
PM_{10} Mass	84	8.71	18.53	28.01	39.79	42.69	50.27	75.27	183.71	$\mu g/m^3$
B_{scat}	84	7.42	22.99	36.87	52.77	72.4	79.8	139.7	803.0	Mm-1
$PM_{2.5}$ EC	83	0.21	0.46	0.72	1.07	1.55	1.55	2.41	11.35	$\mu g/m^3$
$PM_{2.5}$ OC	83	3.90	5.17	6.45	8.80	11.37	11.72	15.20	100.60	$\mu g/m^3$
$PM_{2.5}$ NO_3	69	0.43	0.59	1.03	1.88	2.20	3.02	4.06	8.58	$\mu g/m^3$
$PM_{2.5}$ SO_4	81	0.18	0.37	0.69	0.98	1.04	1.34	1.84	2.35	$\mu g/m^3$
Biological Agents										
ALTE	72	13.50	13.50	27.00	55.13	87.8	117.5	207.9	421.2	spores/m^3
AGFG	77	13.50	29.70	100	162	267	346	605	1370	spores/m^3
CLAD	77	108.0	251.1	388.4	823.5	1143	1421	2763	4145	spores/m^3
ASP	74	13.5	27.0	67.5	105.3	288.2	276.8	586.0	2835	spores/m^3
TOTFS	78	40.5	399	581	1333	1652	2282	3610	5103	spores/m^3
Endotoxin	84	0.18	0.75	1.38	2.57	3.06	4.21	6.10	11.61	EU/m^3
TOP	79	0.00	0.00	0.55	2.20	8.42	6.22	24.38	127.60	grains/m^3
Polycyclic Aromatic Hydrocarbons										
ACE	52	0.32	0.61	0.98	1.38	1.65	1.75	2.19	14.77	ng/m^3
ACY	49	0.08	0.18	0.22	0.47	1.21	0.96	2.13	13.54	ng/m^3
ANT	50	0.12	0.16	0.23	0.34	0.71	0.78	1.41	5.05	ng/m^3
BAA	32	0.03	0.05	0.13	0.34	0.49	0.69	1.06	2.40	ng/m^3
BAP	39	0.01	0.02	0.13	0.47	0.74	0.75	1.85	5.61	ng/m^3
BBF	34	0.02	0.04	0.15	0.42	0.67	0.86	1.66	3.24	ng/m^3
BGP	39	0.02	0.03	0.11	0.65	1.53	1.18	3.65	14.35	ng/m^3
BKF	35	0.00	0.01	0.01	0.10	0.34	0.47	0.90	2.74	ng/m^3
CRY	40	0.02	0.04	0.11	0.34	0.66	0.58	1.23	9.46	ng/m^3
DBA	30	0.03	0.04	0.06	0.22	0.41	0.72	0.93	1.52	ng/m^3
FLT	52	0.25	0.46	0.60	0.73	1.39	1.28	3.15	8.89	ng/m^3

Pollutant[1]	No. of Residences	Minimum	10th Percentile	25th Percentile	Median	Mean	75th Percentile	90th Percentile	Maximum	Units
FLU	50	0.27	0.33	0.52	0.89	1.69	1.91	4.93	9.53	ng/m^3
NAPST	41	93.0	175	314	402	489	546	909	1521	ng/m^3
PHE	51	2.21	2.73	3.77	4.90	8.51	6.78	14.72	69.64	ng/m^3
PYR	50	0.46	0.60	0.76	0.96	1.88	1.36	3.27	18.19	ng/m^3
PM_{10} Trace Elements										
AL	83	81.96	314	446	774	954	1125	1717	6203	
AS	59	0.73	0.82	0.95	1.35	1.47	1.83	2.16	4.06	ng/m^3
AU	6	1.48	1.48	1.50	1.71	2.00	2.63	2.91	2.94	ng/m^3
BA	37	23.81	24.87	28.47	36.41	36.44	41.36	48.90	70.60	ng/m^3
BR	83	1.13	2.53	3.29	4.56	5.52	6.03	8.36	29.21	ng/m^3
CA	83	62.52	217	362	505	721	891	1513	5576	ng/m^3
CD	1	6.72	0.00	0.00	6.72	6.72	0.00	0.00	6.72	ng/m^3
CL	83	33.30	93.2	146.1	234.8	402.6	447.7	745.1	3570.8	ng/m^3
CO	80	0.53	1.11	1.94	3.95	5.10	6.30	8.76	38.53	ng/m^3
CR	76	0.89	1.25	1.77	2.44	4.17	3.65	5.84	54.69	ng/m^3
CU	83	1.27	3.29	4.88	7.58	8.95	10.38	15.76	36.49	ng/m^3
FE	83	47	128	264	400	524	658	1026	3595	ng/m^3
GA	12	0.87	0.89	1.06	1.16	1.13	1.24	1.29	1.32	ng/m^3
HG	1	1.16	0.00	0.00	1.16	1.16	0.00	0.00	1.16	ng/m^3
ICP	29	242	405	569	850	1376	1590	3405	5498	ng/m^3
IN	2	6.84	6.84	6.84	7.60	7.60	8.36	8.36	8.36	ng/m^3
KP	83	80.01	215.0	311.7	433.0	520.2	609.2	1043.1	2098.2	ng/m^3
LA	13	30.73	31.22	31.96	35.29	36.55	38.55	43.34	55.66	ng/m^3
MG	65	45.09	54.60	62.38	81.50	91.94	107.16	136.99	300.40	ng/m^3
MN	83	1.03	2.65	5.09	8.56	10.99	13.54	20.29	77.38	ng/m^3
MO	7	1.25	1.25	1.30	1.40	2.12	2.85	3.81	4.02	ng/m^3
NA	62	229	256	288	335	403	489	658	1058	ng/m^3
NI	81	0.43	0.61	0.89	1.25	1.59	1.76	3.28	6.73	ng/m^3
PB	69	2.65	3.22	3.81	5.01	5.91	6.72	9.54	29.24	ng/m^3
PD	19	1.37	1.44	1.59	1.92	2.05	2.35	3.03	3.48	ng/m^3

Pollutant[1]	No. of Residences	Minimum	10th Percentile	25th Percentile	Median	Mean	75th Percentile	90th Percentile	Maximum	Units
PH	24	6.52	6.97	12.98	28.03	73.85	79.41	176.99	591.55	ng/m^3
RB	80	0.45	0.58	0.87	1.39	1.58	1.86	2.47	7.55	ng/m^3
SB	42	2.33	2.65	3.19	3.93	4.44	4.83	7.79	10.99	ng/m^3
SI	83	296	934	1643	2466	3073	3976	5757	16494	ng/m^3
SN	56	2.79	3.44	3.92	4.57	5.37	6.35	7.93	16.24	ng/m^3
SR	20	7.64	7.97	8.52	10.16	14.16	13.42	30.12	49.51	ng/m^3
SU	83	151	245	353	489	529	634	774	2445	ng/m^3
TI	80	5.95	20.00	30.97	46.63	77.34	73.20	113.27	1682.19	ng/m^3
TL	8	1.11	1.12	1.15	1.31	1.49	1.74	2.28	2.40	ng/m^3
UR	7	1.12	1.13	1.21	1.37	1.32	1.43	1.47	1.48	ng/m^3
VA	63	1.11	1.61	2.23	3.05	3.90	4.82	6.46	26.94	ng/m^3
YT	31	0.59	0.62	0.68	0.77	0.81	0.90	1.04	1.71	ng/m^3
ZN	83	4.66	13.18	17.35	27.79	34.50	43.31	53.46	186.32	ng/m^3
ZR	82	0.83	1.58	2.61	4.83	6.53	8.00	13.91	34.02	ng/m^3

1) The majority of measured indoor concentrations for PM10 AS, AU, BA, CD, GA, HG, IN, LA, MO, NA, PD, PH, SB, SN, SR, TL, UR, VA, and YT were below the limit of detection. AG and SE were not detected in any samples.

Table 4.1.4-3 Dust Concentrations: Samples Collected in the Home to March 31, 2003						
	BED			FLOOR		
	N	#	%	N	#	%
Dust Mite (µg/g) (DerF and DerP)*	456			417		
Not detectable		355	77.9		361	86.6
LOW (Less than 2 µg/g)		41	9.0		22	5.3
MEDIUM (2 to 10 µg/g)		38	8.3		27	6.5
HIGH (More than 10 µg/g)		22	4.8		7	1.7
Cockroach (µg/g) (BlaG)	415			360		
Not detectable		397	95.7		309	85.8
Detectable		18	4.3		51	14.2
Dog (µg/g) (CanF)	421			375		
Not detectable		9	2.1		5	1.3
LOW (Less than 1 µg/g)		117	27.8		84	22.4
MEDIUM (1 to 10 µg/g)		168	39.9		141	37.6
HIGH (More than 10 µg/g)		127	30.2		145	38.7
Cat (µg/g) (FelD)	360			339		
Not detectable		18	5.0		17	5.0
LOW (Less than 1 µg/g)		74	20.6		80	23.6
MEDIUM (1 to 8 µg/g)		144	40.0		148	43.7
HIGH (More than 8 µg/g)		124	34.4		94	27.7

Table 4.1.4-4 Endotoxin in House Dust (EU/mg)									
AS OF MARCH 31, 2003									
Sample Location	**Season**	**N**	**Mean**	**SD**	**Min**	**25th**	**50th**	**75th**	**Max**
Bed	*All to 3/03*	211	82.5	111.4	5.2	32.1	52.5	90.3	1029.5
	Spring	67	70.9	103.1	5.9	28.2	45.0	82.2	765.8
	Summer	66	88.4	104.2	5.2	40.3	62.0	101.2	179.7
	Winter	78	87.6	124.1	7.1	34.5	56.6	95.0	1029.5
Floor	*All to 3/31**	113	107.1	162.5	7.3	41.3	64.0	110.0	1378.9
	Spring	33	127.8	264.3	7.3	32.4	54.9	77.7	1378.9
	Summer	35	96.1	85.5	14.3	41.6	66.7	113.8	380.0
	Winter	45	100.4	101.4	18.5	50.4	78.8	116.0	672.0
AS OF MARCH 31, 2005									
Bed	*all to 03/05*	280	72.2	99.1	5.2	30.0	47.4	81.9	1029.5

* Floor samples of endotoxin taken after this date have not yet been analyzed.

Table 4.1.4-5 Distribution of Concentrations for 2-week passive samples taken in the home (November 30, 2000 to March 31, 2003)

	N	Mean	SD	Min*	10	25	50	75	90	Max
*Nicotine (µg/g)**	57	1.04	2.39	0.031	0.044	0.067	0.137	0.355	4.49	12.36
*NO_2 (ppb)**	322	13.3	13.4	0.6	4.4	6.6	9.7	15.1	25.2	134.6
Indoor Ozone (ppb) **	163	9.5	11.3	0.2	0.5	1.3	4.8	14.6	25.4	55.9
Outdoor Ozone (ppb) **	87	42.2	25.3	0.5	6.1	24.6	38.7	66.6	75.8	86.6

* Passive samplers were placed in the living area of the house for 2 weeks There were 180 values below the detection limit for nicotine during this period. They were not incorporated into the distribution and are only shown so that the distribution of detectable values can be observed. Values below the detection limit for NO_2 (1) and indoor ozone (12) were set to ½ the minimum value. The minimum value shown here is ½ the lowest value actually measured.

** Ozone was usually sampled in May through October (see Table 4.1.4-6).

Table 4.1.4-6 Periods that Ozone passive samplers were deployed (2000 to 2004)

Year	Begin	End
2001	08/29	11/29
2002	05/15	10/22
2003	05/28	10/16
2004	06/09	10/28

Table 4.1.4-7 Comparison of distributions by Study Season (November 30, 2000 to March 31, 2003)

	Season[1]	N	Mean	SD	Min	25th	50th	75th	Max
NO_2 (ppb)[2]	Spring	56	11.3	8.7	2.4	5.8	8.9	13.3	43.2
	Summer	131	13.2	9.9	2.6	6.7	10.2	16.5	74.2
	Winter	136	14.2	17.3	0.60	6.5	10.0	15.4	134.6
Indoor Ozone (ppb)[2]	Summer	118	11.4	11.5	0.14	2.3	7.2	18.2	48.0
	Fall*	40	3.2	4.4	0.14	0.54	1.5	4.1	17.9
Outdoor Ozone (ppb)[2]	Summer	64	48.2	26.4	0.47	34.6	48.6	71.2	86.6
	Fall*	21	24.5	8.7	9.5	19.3	27.2	31.1	35.0

Season is determined by the sampling period end-date. The months in which ozone was sampled varied each year (see Table4.1.4-6). Generally, the fall season refers to the month of October for ozone samples. Ozone was also measured in spring (May) in 2002 and 2003, but there were only 6 samples that were completed by the end of May.

Values below the detection limit for NO_2 (1) and indoor ozone (26) were set to ½ the minimum value. Therefore the minimum value shown here is ½ the minimum value actually measured.

Table 4.1.4-8 Distribution of Moisture Levels in Homes (November 28, 2000 to March 31, 2003)

	N	Min	25%	50%	Mean	75%	Max
Living Area							
Spring	279	4	7	9	8.85	10	19
Summer	265	3	7	8	8.57	9	25
Winter	328	3	8	9	9.14	10	30
Over all seasons	872	3	7	9	8.87	10	30
Child's Sleeping Area*							
Spring	275	4	8	9	8.95	10	27
Summer	259	2	7	8	8.57	9	58
Winter	328	2	8	9	8.82	10	31
Over all seasons	862	2	7	8	8.79	10	58

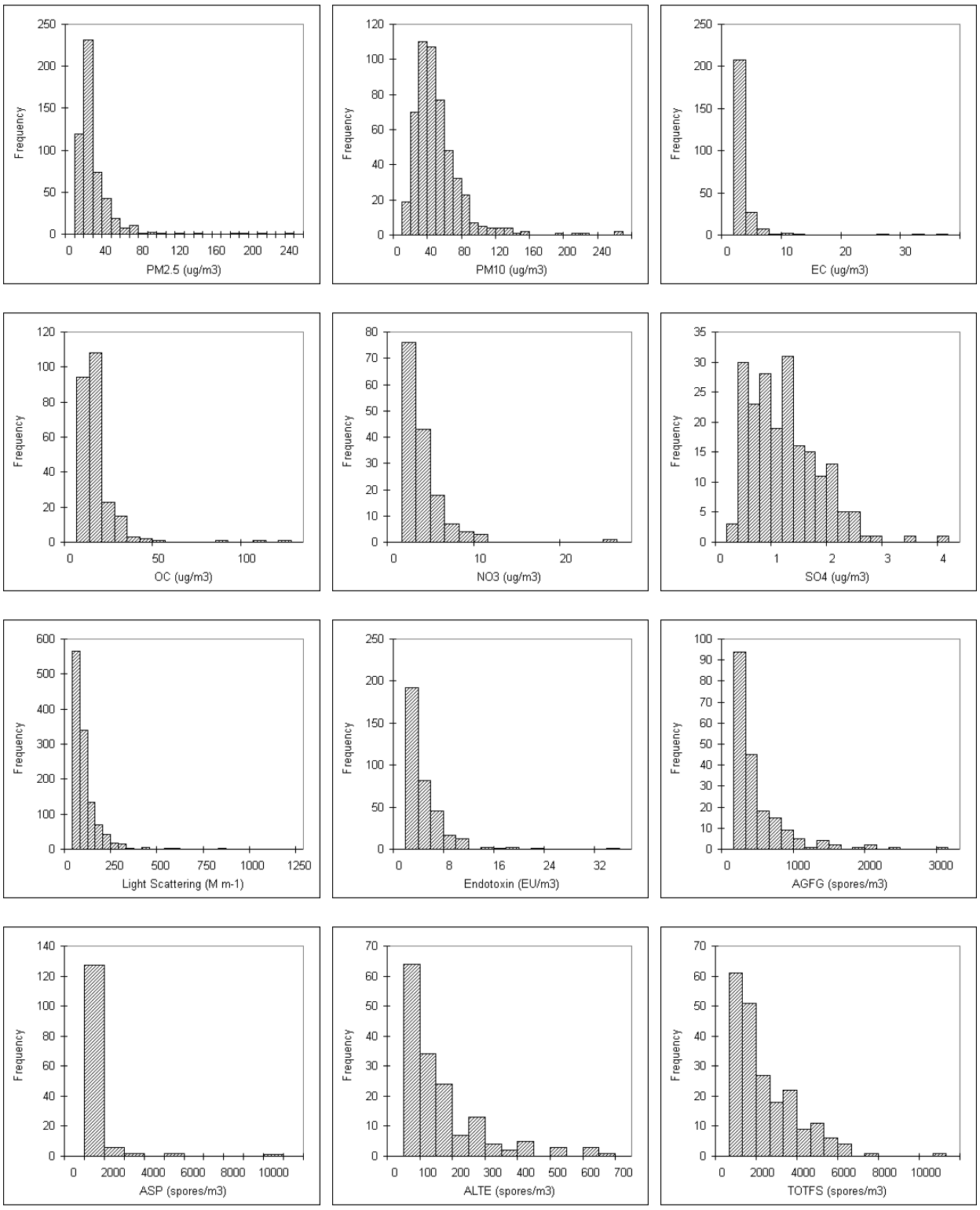


Figure 4.1.4-1. Frequency distribution of indoor concentrations of PM mass, PM chemical components, light-scattering, endotoxin .and fungal spores.

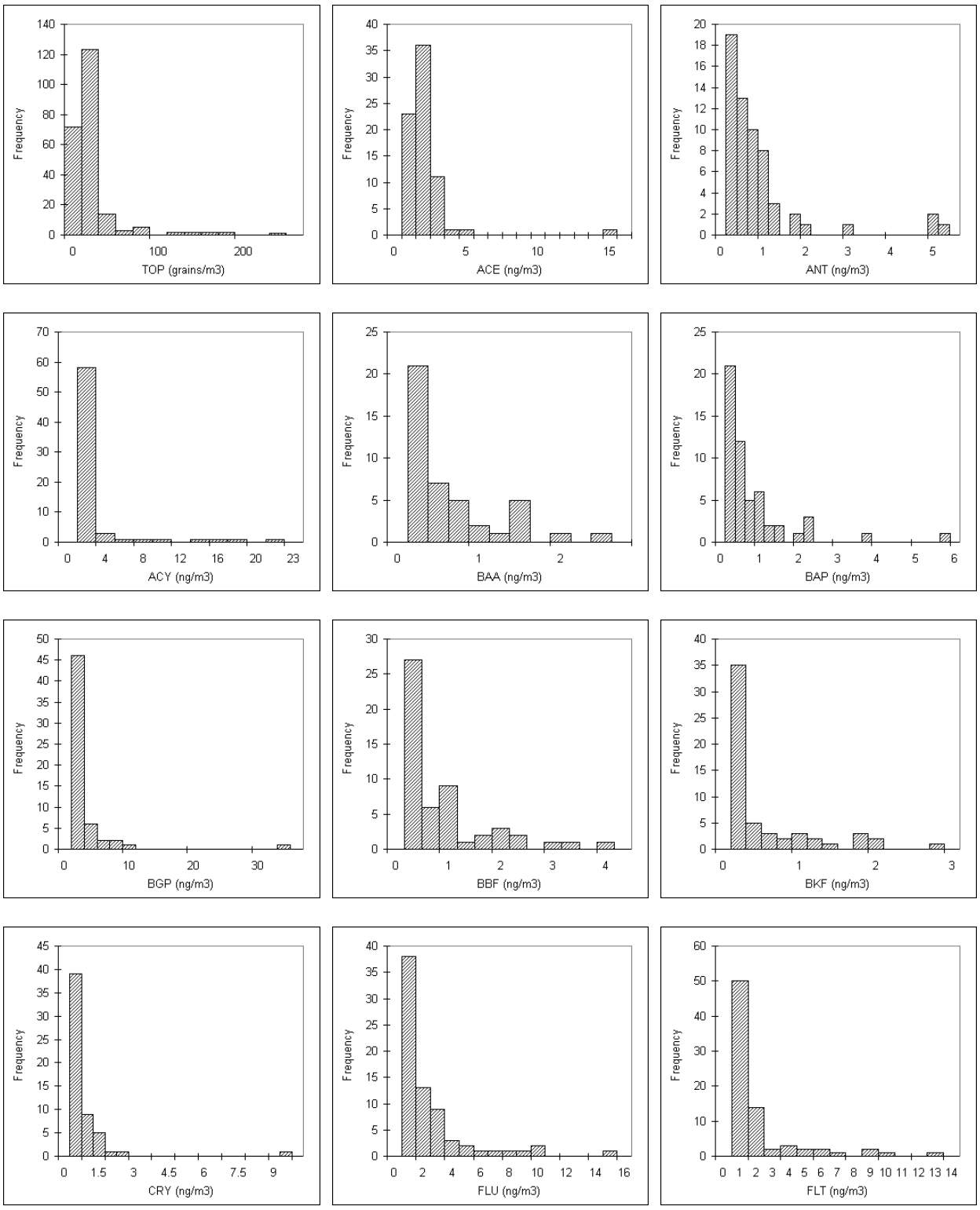


Figure 4.1.4-2. Frequency distribution of indoor concentrations of total pollens and selected polycyclic aromatic hydrocarbons (ACE, ANT, ACY, BAA, BAP, BGP, BBF, BKF, CRY, FLU, and FLT).

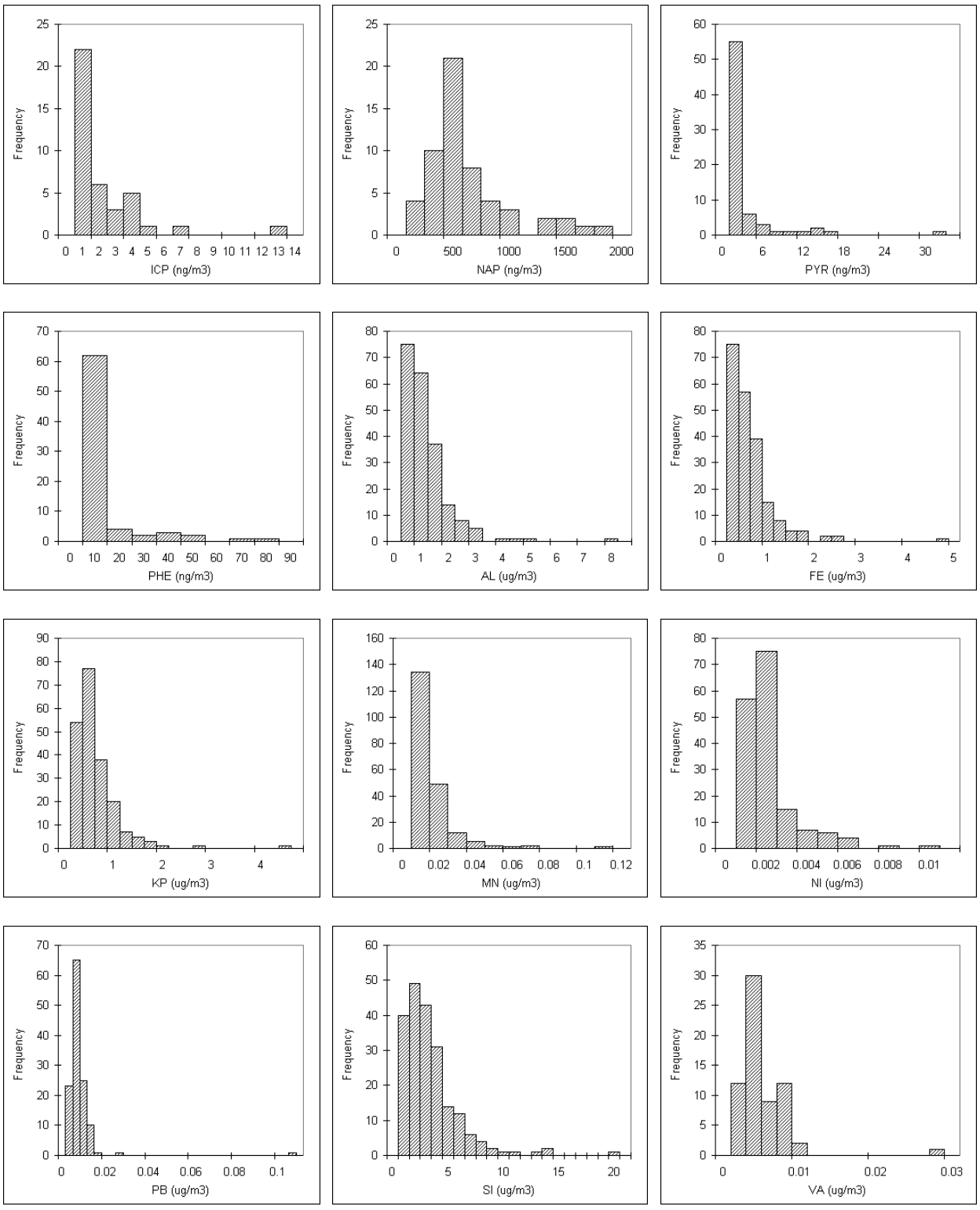
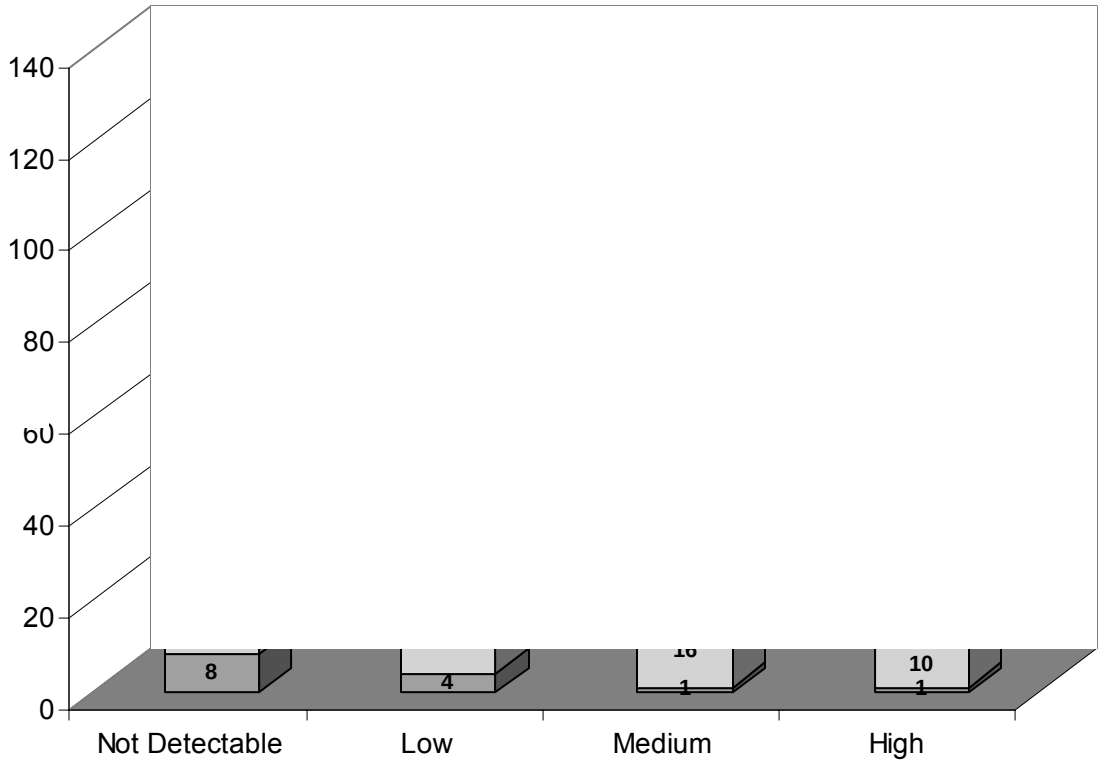


Figure 4.1.4-3. Frequency distribution of indoor concentrations of selected polycyclic aromatic hydrocarbons (ICP, NAP, PYR, and PHE) and trace metals (Al, Fe, K, Mn, Ni, Pb, Si, and Va).

Figure 4.1.4-4 Levels of Dust Mite Allergen ("Der-F" and "Der-P")in Household Dust: Comparison of Homes with and without Carpet

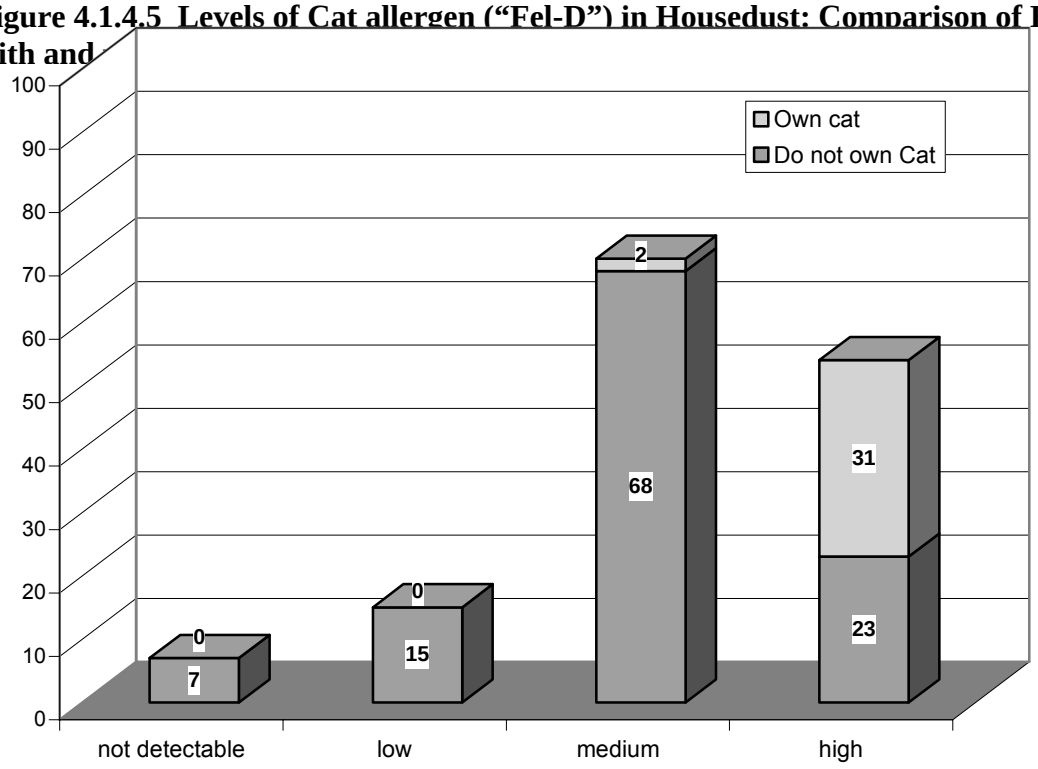


Low: less than 2 µg/g; ***Medium:*** 2 to 10 µg/g; ***High:*** more than 10 µg/g.

- Dust mite antigens were low and were below laboratory detection limits in 113 of 174 houses where it was collected.

Average level in homes without wall-to-wall carpet: Not detectable
Average level in homes with wall-to-wall carpet: Not detectable

Figure 4.1.4.5 Levels of Cat allergen ("Fel-D") in Housedust: Comparison of Homes with and

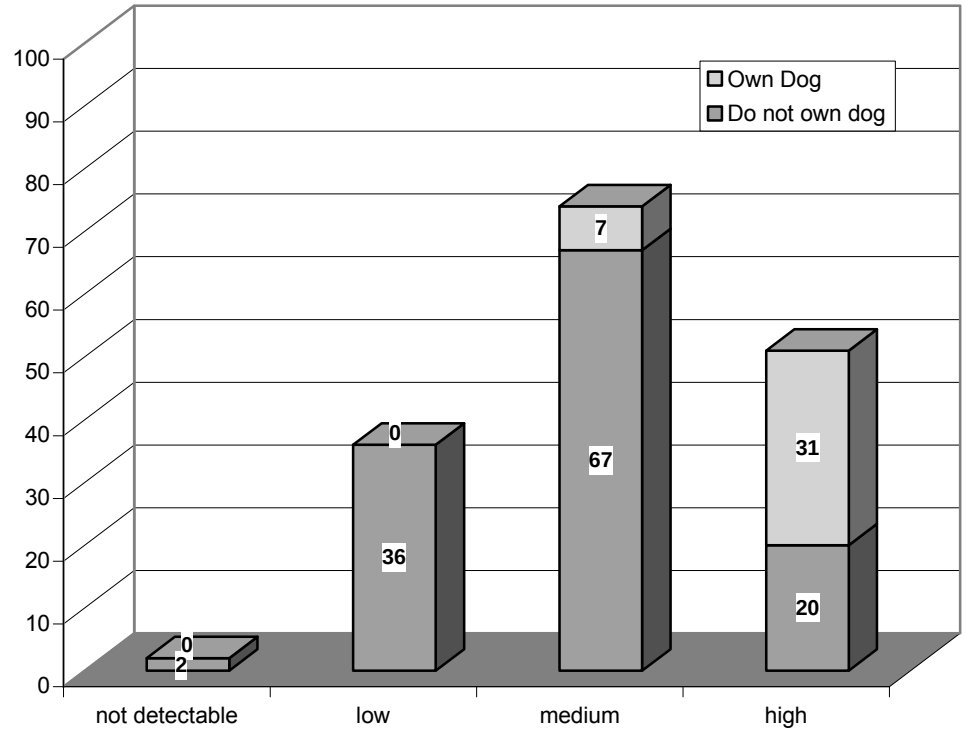


Low: less than 1 µg/g; ***Medium:*** 1 to 8 µg/g; ***High:*** more than 8 µg/g.

- Approximately 48% of homes had high levels of cat antigen.
- Nearly every home with a cat had high levels of cat antigen. However, about 40% of the homes with high cat antigen did not own a pet cat.

Average level in homes without cats: 7 µg/g.
Average level in homes with cats: 392 µg/g.

Figure 4.1.4-6 Levels of Dog Allergen ("Can-F") in Housedust: First Visit Samples

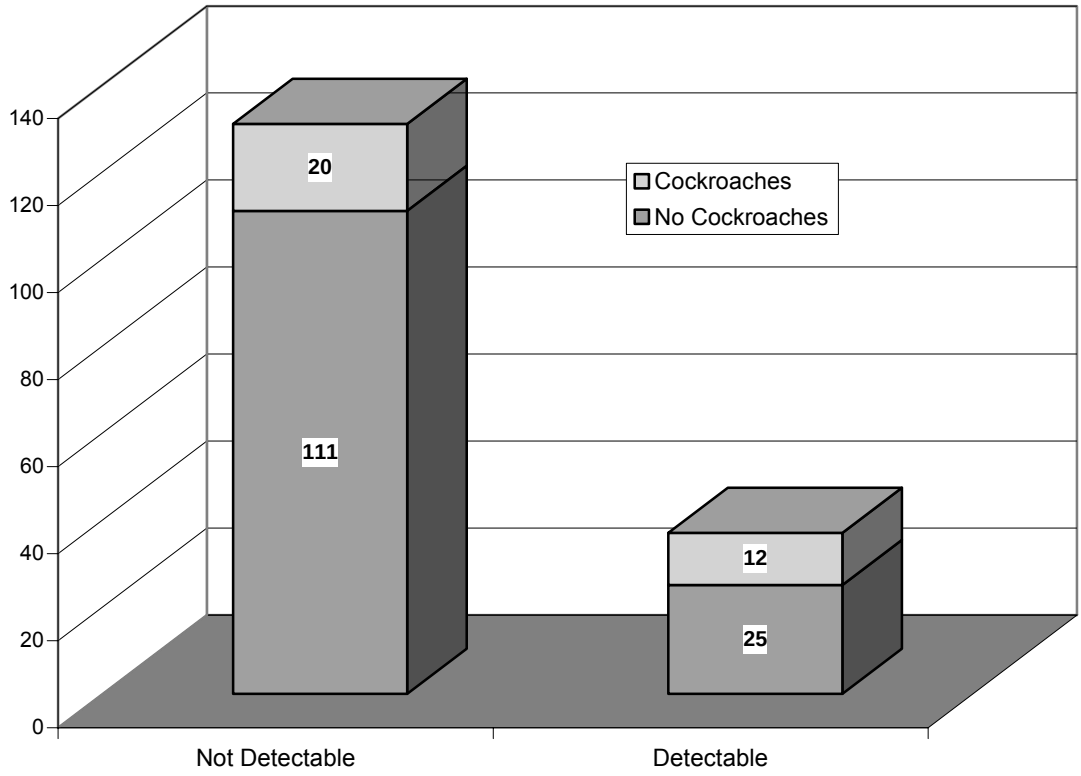


Low: less than 1 µg/g; ***Medium:*** 1 to 8 µg/g; ***High:*** more than 8 µg/g.

- About 22% of homes had pet dogs. Average levels were much higher in these homes (see below) However, about 40% of the homes with high dog antigen did not own a pet dog.

Average level in homes without dogs: 8 µg/g
Average level in homes with dogs: 123 µg/g

Figure 4.1.4-7 Levels of Cockroach Allergen ("Bla-G") in Housedust: Comparison of Homes with and without a History of Cockroaches

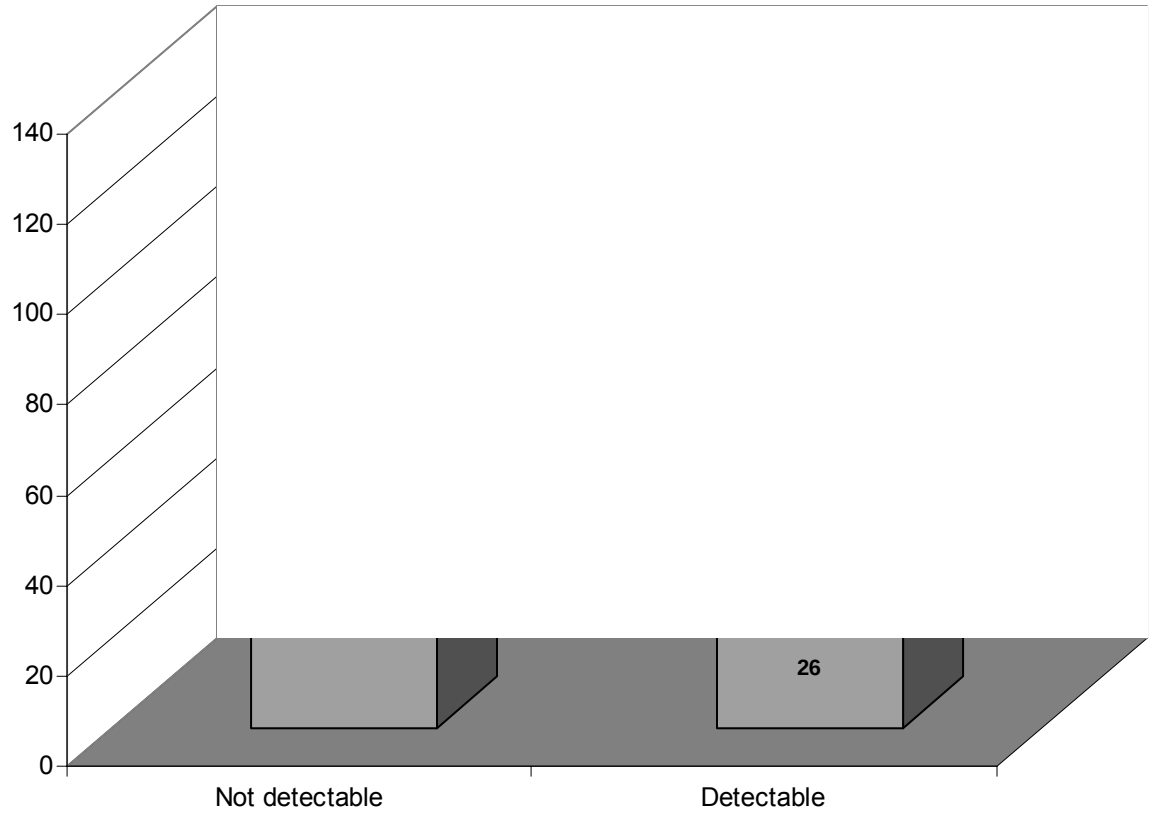


Categories: Not Detectable (too low to detect); Detectable

- Levels of cockroach antigen were too low to detect in 133 of 169 homes where it was tested.
- Of 32 homes that reported seeing cockroaches in the 12 months before the home visit, only 12 had detectable levels of antigen.
- Levels in the 37 homes with detectable concentrations varied from 4 to 395 µg/g and averaged 95 µg/g.

Average level in homes with cockroach history: Not detectable
Average level in homes with cockroach history: Not detectable

Figure 4.1.4-8 Levels of Nicotine from Secondhand Smoke: Comparison of homes with and without smokers

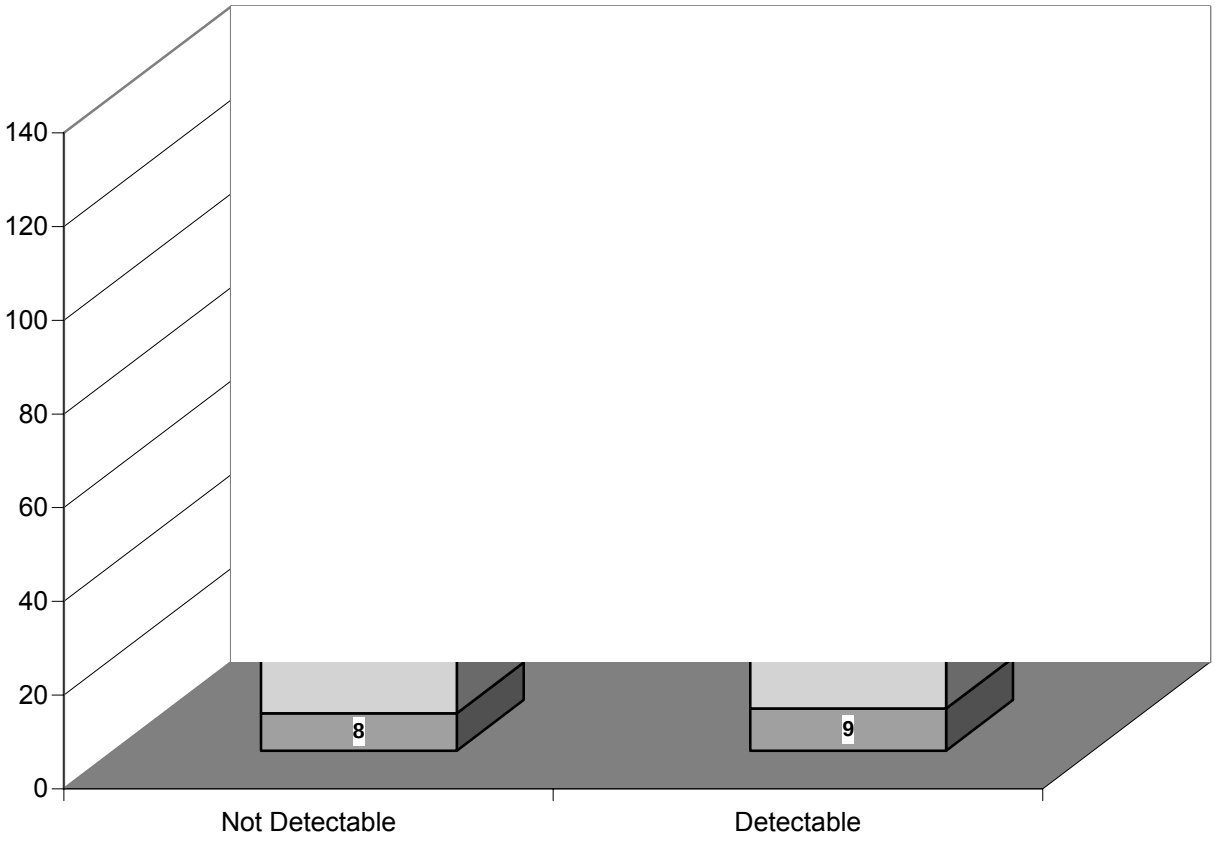


Categories: Not Detectable (too low to detect); Detectable

- There were detectable levels of nicotine in only 42 of 178 homes where samples were taken.

Average Concentration in Homes with and without Smokers: Too low to detect.

Figure 4.1.4-9 Levels of Nicotine from Secondhand Smoke inside Homes: Effect of "No Smoking Policy".

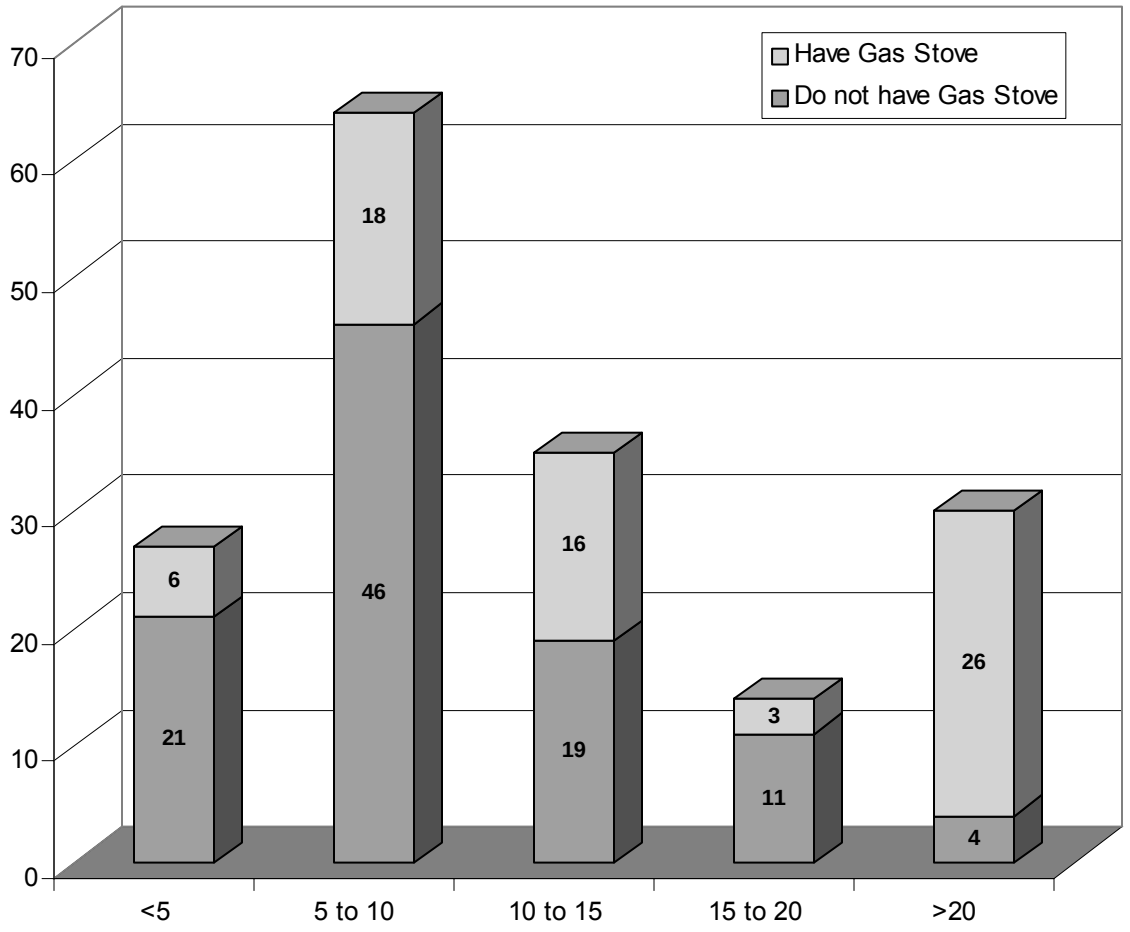


Categories: Not Detectable (too low to detect); Detectable

- Most parents do not allow any smoking inside their home.
- In the 36 homes where smokers had this policy, levels were about the same as in homes without smokers.

Average Concentration in Homes with and without Policy: Too low to detect

Figure 4.1.4-10 Levels of Nitrogen Dioxide (NO_2) inside Homes (ppb): Comparison of Homes with and without Gas Stoves



Categories: less than 5 ppb; 5-10 ppb; 10-15 ppb; 15-20 ppb; more than 20 ppb

- There are no universally agreed upon low, medium or high levels for indoor NO_2 based on health effects. For this reason, we have divided concentrations into 5 categories. At levels greater than 15 ppb, there are reports of increased asthma symptoms.
- NO_2 concentrations were generally greater in homes with gas stoves. Almost everyone in the highest category had a gas stove.

Average concentration in homes without gas stoves:	9.4 ppb
Average concentration in homes with gas stoves:	20.0 ppb

4.1.5 Indoor - Outdoor Pollutant Relationships at Residences

One of the main motivations for collecting Home Intensive measurement data was to assess relationships between indoor and outdoor compound levels in subjects' homes. The FACES participants spent more time on average inside their residences than at any other microenvironment, yet most of the data used to characterize their daily exposures were outdoor measurements (for economic and logistic reasons). Information on the differences and correlation between indoor and outdoor compound levels at FACES residences is important for understanding and assigning exposures.

Table 4.1.5-1 presents summary statistics for the 24-hr average concentrations measured outside residences in the Home Intensive Study. Scatter plots of indoor and outdoor concentrations of selected compounds are shown in Figures 4.1.5-1 through 4.1.5-4. Comparison with the indoor concentrations presented in Table 4.1.4-1 shows that the median and mean concentrations are higher outdoors than indoors for 60 and 55 of the 70 listed compounds, respectively. Notable exceptions are $PM_{2.5}$ OC and naphthalene concentrations that were higher indoor, on average. The maximum observed concentrations of compounds were distributed more evenly. The maximum 24-hr concentrations were higher outdoors than indoors for about half of the measured compounds, including $PM_{2.5}$ SO_4, $PM_{2.5}$ NO_3, endotoxin, total pollens, alternaria, agricultural fungi, cladosporium, acenaphthylene, anthracene, benz[a]anthracene, benzo[a]pyrene, benzo[b]flouranthene, benzo[k]flouranthene, flourene, manganese, lead, silicon, and vanadium. Conversely, the maximum indoor concentrations exceeded the maximum outdoor observations for other important compounds, such as $PM_{2.5}$ mass, PM_{10} mass, OC, EC, total fungi, naphthalene, pyrene, flouranthene , iron, and aluminum,

Summary statistics for the indoor-outdoor concentration ratios are show in Table 4.1.5-2. Figures 4.1.5-5 and 4.1.5-6 show the frequency distribution of indoor-outdoor ratios of selected compounds. The results clearly show a wide range of ratios of indoor to outdoor concentrations for many constituents. Because the distributions of ratios are skewed for many compounds, outliers were excluded from the concentrations used to compute the summary statistics. Even with outliers excluded, the mean ratios are 30% greater than the median ratios for half of the listed compounds. The mean indoor-outdoor ratios exceed the 75^{th} percentile values for certain biological agents, including endotoxin, total pollens, and aspergillus+penicillium, that are strongly influenced by small numbers of high ratios. Thus, for the purpose of evaluating relationships, we focus here on the median and inter-quartile range (IQR) of ratios.

The exclusion of outliers should not be interpreted to mean that the outliers are invalid or that the extremes in the exposures are unimportant. Quite the contrary, they are important and should be analyzed to identify factors or circumstances that may explain the extremes. Nevertheless, for purposes of analyzing general relationships in the data, outliers can obscure relationships and were excluded for selected analyses.

The median and IQR of indoor-outdoor ratios for numerous components of PM were quite similar. For example, median ratios for SO_4, light scattering, $PM_{2.5}$ mass, PM_{10} mass, and EC were 0.64, 0.72, 0.76, 0.76, and 0.82, respectively. The IQR of ratios were 0.49 to 0.80 for SO_4, 0.54 to 1.02 for $PM_{2.5}$ mass, and 0.65 to 1.07 for EC. The ratios for these parameters are more consistent than those for nitrate and OC, which are the two largest components of $PM_{2.5}$

mass. The ratios for nitrate are substantially lower than those for $PM_{2.5}$ mass, and the ratios for OC are substantially higher than those for $PM_{2.5}$ mass. The IQR of ratios for NO_3 was 0.17 to 0.50 with a median ratio of 0.30. The IQR of ratios for OC was 1.0 to 1.85 with a median ratio of 1.30, which clearly indicates indoor sources of OC in most homes. The similarity of the $PM_{2.5}$ mass ratios to those for SO_4 and EC may largely be due to the compensating effects of low ratios for nitrate and high ratios for OC. The low ratios for nitrate are most likely due to volatilization of aerosol ammonium nitrate in the warm indoor environments (262). Examination of the four temperature-resolved fractions of OC (not shown) that are provided with the detailed TOR carbon data (263) shows the largest indoor-outdoor concentration differences occur for carbon volatized at the lowest temperature step (120^{o}C). Elevated indoor-outdoor ratios for OC and, especially, the most volatile portion of OC in Fresno residences are consistent with other studies (e.g., (264)). However, the highly volatile portion of OC indoors may be partially an artifact resulting from collection of gaseous VOCs on quartz filters (265).

The median indoor-outdoor ratios for biological agents are 0.99 for endotoxin, 0.16 to 0.43 for fungal spores, and 0.02 for total pollens. The IQR of the ratios is 0.45 to 2.70 for endotoxin that is high compared to the IQR of ratios of 0.09 to 0.40 for total fungi and 0 to 0.10 for total pollens. The results indicate indoor sources of endotoxin exist in most FACES residences, and endotoxin levels in a few homes were extremely high compared to outdoor levels. For example, the 90th percentile and maximum indoor-outdoor ratios for endotoxin were 7.8 and 207, respectively. The next highest indoor-outdoor ratios for biological agents were found for aspergillus+penicillium (mean = 0.43, IQR = 0.17 to 0.90), which were noticeably higher than the ratios for other fungi. Taken as a group, the data indicate lower levels of fungal spores inside FACES residences than outdoors. The strength of the indoor fungi sources does not appear to be large enough to cause disproportionately high indoor exposures in most residences. The pollen levels indoors were extremely low compared to outdoors in almost all residences. The absence of strong indoor pollen sources and high outdoor pollen penetration losses due to the large size of pollen grains are the most probable reasons for the low indoor-outdoor ratios for pollens.

The indoor-outdoor ratios for PAHs, shown in Table 4.1.5-2, indicate the median ratios for 12 of 16 PAHs were less than one. The median ratios were 0.25 to 0.62 for chrysene, flourene, benz[a]anthracene, benzo[b]flouranthene, benzo[k]flouranthene, benzo[ghi]perylene, and flouranthene, which was lower than the median ratio for sulfate. These ratios suggest the indoor concentrations of these compounds are primarily from infiltration of ambient air. The median ratio of indeno[1,2,3-cd]pyrene, acenaphthylene, dibenz[a,h]anthracene, phenathrene, and benzo[a]pyrene were 0.66 to 0.81, which is greater than that for sulfate but lower than that for EC, suggesting some homes have indoor sources of these compounds. The median ratios for acenaphthene, anthracene, napthalene, and pyrene were 2.19, 1.92, 1.43, and 1.02, respectively, which clearly indicates the present of indoor sources of these compounds in most homes. The 90th percentile ratios for these four compounds were quite high, ranging from 3.9 for pyrene to 7.1 for acenaphthene.

For most PM_{10} trace elements, the median indoor-outdoor ratios were less than one, while the 75th percentile ratios were above one, as was the case for PM_{10} mass. It is convenient to stratify the data by the median ratio for PM_{10} mass (0.76). The median indoor-outdoor ratios for cobalt, iron, manganese, rubidium, silicon, aluminum, copper, titanium, vanadium, potassium,

lead, and calcium ranged from 0.41 to 0.76. These compounds represented more than half the mass of PM_{10} trace elements in most indoor and outdoor samples. The median ratios for nickel, strontium, barium, bromine, sodium, zinc, arsenic, tin, and zirconium ranged from 0.77 to 1.10, while the median ratio for chloride was 2.47. The indoor-outdoor ratios for chloride were surprisingly high. Some residences clearly have indoor sources of the latter ten trace elements. The upper tail of the distribution also extends to high ratios for certain compounds with median ratios below 0.76, such as silicon, aluminum, titanium, and calcium, as demonstrate by the 90^{th} percentile ratios that exceed two.

The correlations of the indoor to outdoor concentrations are shown in Table 4.1.5-3. The table provides the correlation coefficient (r) for all 24-hr samples and a subset of 24-hr samples with outliers removed, again because outliers can distort these relationships. Also, shown is the correlation of the average indoor and outdoor concentrations at residences, where the average may be based on from 2 to 24 samples at each residence. The correlation coefficient of concurrent 24-hr average $PM_{2.5}$ indoors and outdoors was 0.52 (outliers removed). The correlation coefficients, with outliers removed, of concurrent 24-hr average indoor and outdoor concentrations were 0.76, 0.74, 0.41, and 0.31 for EC, SO_4, NO_3, and OC, respectively. The correlation of indoor and outdoor light scattering was slightly higher (0.60) than for $PM_{2.5}$ mass, while the correlation for PM_{10} mass was lower (0.32). These results show that indoor-outdoor relationships are stronger for the nonvolatile components of $PM_{2.5}$ that lack significant indoor sources (i.e., SO_4 and EC) than volatile components like NO_3 or components with indoor sources like OC. For biological agents, the correlations were 0.30 for endotoxin, 0.40 for total pollen, and 0.19 to 0.37 for the various fungi (excluding outliers), indicating fairly weak relationships. For PAHs, benzo[a]pyrene, benzo[b]flouranthene, dibenz[a,h]anthracene, and benzo[k]flouranthene had correlations of 0.57, 0.73, 0.83, and 0.86 which were high compared to the correlations (-0.03 to 0.46) of other PAHs. The indoor-outdoor correlations of most trace elements were below 0.50; the exceptions were cobalt (0.54), lead (0.58), sulfur (0.58), and thallium (0.83). Overall, these correlations are consistent with results from other studies. They show modest relationships between indoor and outdoor levels for most compounds and stronger relationships for compounds without indoor sources. The modest correlations are generally consistent with expectations based on contributions to indoor concentrations from both ambient air infiltration and indoor sources.

Table 4.1.5-1.. Summary statistics for outdoor pollutant concentrations at FACES residences based on all 24-hr samples that exceeded the limits of detection.

Pollutant	No. of cases	Minimum	10th Percentile	25th Percentile	Median	Mean	75th Percentile	90th Percentile	Maximum	Units
Particulate Matter										
$PM_{2.5}$ Mass	527	2.49	8.72	12.18	19.29	24.25	30.11	47.84	107.42	$\mu g/m^3$
PM_{10} Mass	529	4.58	20.60	31.75	44.08	47.89	62.15	81.12	125.15	$\mu g/m^3$
B_{scat}	1248	3.42	19.52	30.58	58.12	90.61	119.29	227.55	460.55	Mm-1
$PM_{2.5}$ EC	257	0.14	0.43	0.58	1.07	1.44	1.90	2.98	7.56	$\mu g/m^3$
$PM_{2.5}$ OC	257	1.80	3.15	4.20	5.80	7.68	9.28	15.71	28.71	$\mu g/m^3$
$PM_{2.5}$ NO_3	212	0.75	1.91	2.80	4.55	6.70	8.85	14.81	30.35	$\mu g/m^3$
$PM_{2.5}$ SO_4	210	0.13	0.60	1.02	1.66	1.62	2.21	2.59	5.15	$\mu g/m^3$
Biological Agents										
ALTE	232	13.5	77.0	135.0	243	280	351	500	2187	spores/m^3
AGFG	234	13.5	174.2	418.5	925	1245	1647	2885	5927	spores/m^3
CLAD	234	189	1553	2511	4448	5070	6615	9142	24908	spores/m^3
ASP	212	13.5	40.5	81.0	263	389	527	864	3375	spores/m^3
TOTFS	236	54.0	2839.1	4394.3	6284	6886	8566	10676	25664	spores/m^3
Endotoxin	364	0.01	0.27	0.58	1.92	3.22	4.57	6.75	88.20	EU/m^3
TOP	256	0.00	8.80	18.70	63.8	193.3	227.2	456.2	3391.3	grains/m^3
Polycyclic Aromatic Hydrocarbons										
ACE	82	0.09	0.27	0.40	0.74	1.10	1.39	2.71	5.29	ng/m^3
ACY	80	0.09	0.19	0.28	0.46	3.50	3.54	10.04	39.53	ng/m^3
ANT	71	0.03	0.05	0.09	0.26	0.97	0.87	2.96	13.08	ng/m^3
BAA	55	0.03	0.07	0.35	0.60	0.97	1.03	2.44	5.47	ng/m^3
BAP	60	0.01	0.02	0.09	0.38	0.79	0.95	2.00	8.13	ng/m^3
BBF	61	0.02	0.09	0.34	0.70	0.92	1.17	2.08	4.37	ng/m^3
BGP	60	0.03	0.08	0.22	0.97	1.23	1.49	2.45	8.68	ng/m^3
BKF	62	0.00	0.01	0.06	0.36	0.63	1.00	1.72	3.14	ng/m^3
CRY	63	0.03	0.09	0.32	0.86	1.23	1.46	3.02	7.93	ng/m^3

Pollutant	No. of cases	Minimum	10th Percentile	25th Percentile	Median	Mean	75th Percentile	90th Percentile	Maximum	Units
DBA	52	0.03	0.04	0.11	0.31	0.52	0.79	1.25	2.05	ng/m^3
FLT	85	0.19	0.40	0.68	1.22	1.89	2.37	4.46	9.42	ng/m^3
FLU	84	0.50	1.11	1.52	2.87	4.25	5.38	9.05	23.63	ng/m^3
ICP	49	0.26	0.54	0.69	1.17	1.71	2.06	3.97	8.02	ng/m^3
NAPST	59	49.0	82.3	172.5	258.9	285.9	402.3	485.2	640.6	ng/m^3
PHE	82	1.03	1.69	3.74	6.25	9.76	11.46	22.28	61.00	ng/m^3
PYR	79	0.09	0.35	0.51	0.96	1.74	2.18	4.06	10.48	ng/m^3
PM_{10} Trace Elements										
AL	215	17.47	271.8	552	1299	1553	2027	3306	5816	ng/m^3
AS	107	0.72	0.86	1.04	1.41	1.73	2.07	3.09	5.31	ng/m^3
AU[1]	5	1.39	1.39	1.44	1.51	1.60	1.81	1.89	1.89	ng/m^3
BA	134	23.26	26.16	31.48	40.18	50.51	56.65	77.30	528.55	ng/m^3
BR	215	0.57	2.66	4.00	5.55	6.12	7.43	9.74	19.53	ng/m^3
CA	215	62.36	181.8	319.3	607.3	711.4	942.0	1385.3	5234	ng/m^3
CD[1]	1	5.34				5.34				ng/m^3
CL	211	6.03	17.36	32.53	70.02	316.98	432.60	783.10	3611.5	ng/m^3
CO	208	0.43	1.58	3.10	8.42	10.43	14.36	24.82	45.65	ng/m^3
CR	173	0.85	1.29	1.86	2.82	3.35	4.11	5.96	18.79	ng/m^3
CU	215	1.64	4.26	6.63	11.25	15.22	16.95	26.73	117.62	ng/m^3
FE	215	53.46	261.1	505.5	937.6	1105.1	1444.6	2224.5	4172.5	ng/m^3
GA[1]	6	0.87	0.89	1.05	1.12	1.10	1.19	1.23	1.23	ng/m^3
KP	215	93.38	224.09	384.82	575.29	664.83	819.56	1245.95	2104.65	ng/m^3
LA[1]	19	27.60	27.87	28.57	32.01	32.51	34.21	37.07	50.39	ng/m^3
MG	133	44.67	58.82	68.85	94.64	109.37	135.88	177.20	296.95	ng/m^3
MN	215	0.79	4.80	8.03	18.73	22.58	29.08	48.68	115.90	ng/m^3
MO[1]	27	1.22	1.27	1.30	1.49	1.63	1.87	2.22	2.49	ng/m^3
NA[1]	78	221.85	244.01	260.27	327.69	388.37	448.71	606.39	1236.28	ng/m^3
NI	196	0.40	0.65	0.94	1.46	1.80	2.26	2.83	23.58	ng/m^3

Pollutant	No. of cases	Minimum	10th Percentile	25th Percentile	Median	Mean	75th Percentile	90th Percentile	Maximum	Units
PB	193	2.48	3.42	4.15	5.79	7.37	8.49	10.82	125.97	ng/m^3
PD[1]	22	1.34	1.37	1.56	1.64	1.87	2.11	2.52	3.90	ng/m^3
PH[1]	28	5.59	7.77	10.10	24.40	28.97	42.10	59.90	65.06	ng/m^3
RB	190	0.48	0.79	1.22	2.34	2.85	3.85	5.65	11.52	ng/m^3
SB[1]	84	2.22	2.58	3.15	4.30	4.61	5.46	6.72	11.20	ng/m^3
SE[1]	7	8.46	8.49	8.71	9.51	9.57	10.29	10.98	11.12	ng/m^3
SI	215	232.06	952.22	1763.75	4332.94	5207.68	6999.13	10725.61	20348.41	ng/m^3
SN	97	2.79	3.40	4.13	5.25	6.08	7.09	9.83	17.04	ng/m^3
SR	79	7.54	8.14	8.80	10.23	12.83	13.25	16.72	99.19	ng/m^3
SU	215	101.24	298.02	399.76	629.11	620.57	792.66	945.93	1493.35	ng/m^3
TI	209	1.86	15.88	30.17	72.27	102.40	125.85	207.76	2558.00	ng/m^3
TL[1]	9	1.18	1.18	1.22	1.53	1.74	1.85	2.82	3.45	ng/m^3
UR[1]	21	1.06	1.12	1.20	1.32	1.37	1.38	1.78	1.95	ng/m^3
VA	117	1.17	1.74	2.71	4.38	5.26	6.90	8.98	36.28	ng/m^3
YT[1]	75	0.58	0.63	0.75	0.87	1.01	1.20	1.55	2.47	ng/m^3
ZN	215	4.21	11.64	17.01	27.39	30.80	39.94	54.80	131.77	ng/m^3
ZR	205	0.83	1.39	1.79	2.64	3.06	3.93	5.34	10.41	ng/m^3

1) The majority of measured outdoor concentrations for PM_{10} As, Au, Cd, Ga, La, Mo, Na, Pd, Ph, Sb, Se, Sn, Sr, Tl, Ur, and Yt were below the limit of detection. Ag, Hg, and In were not detected in any samples.

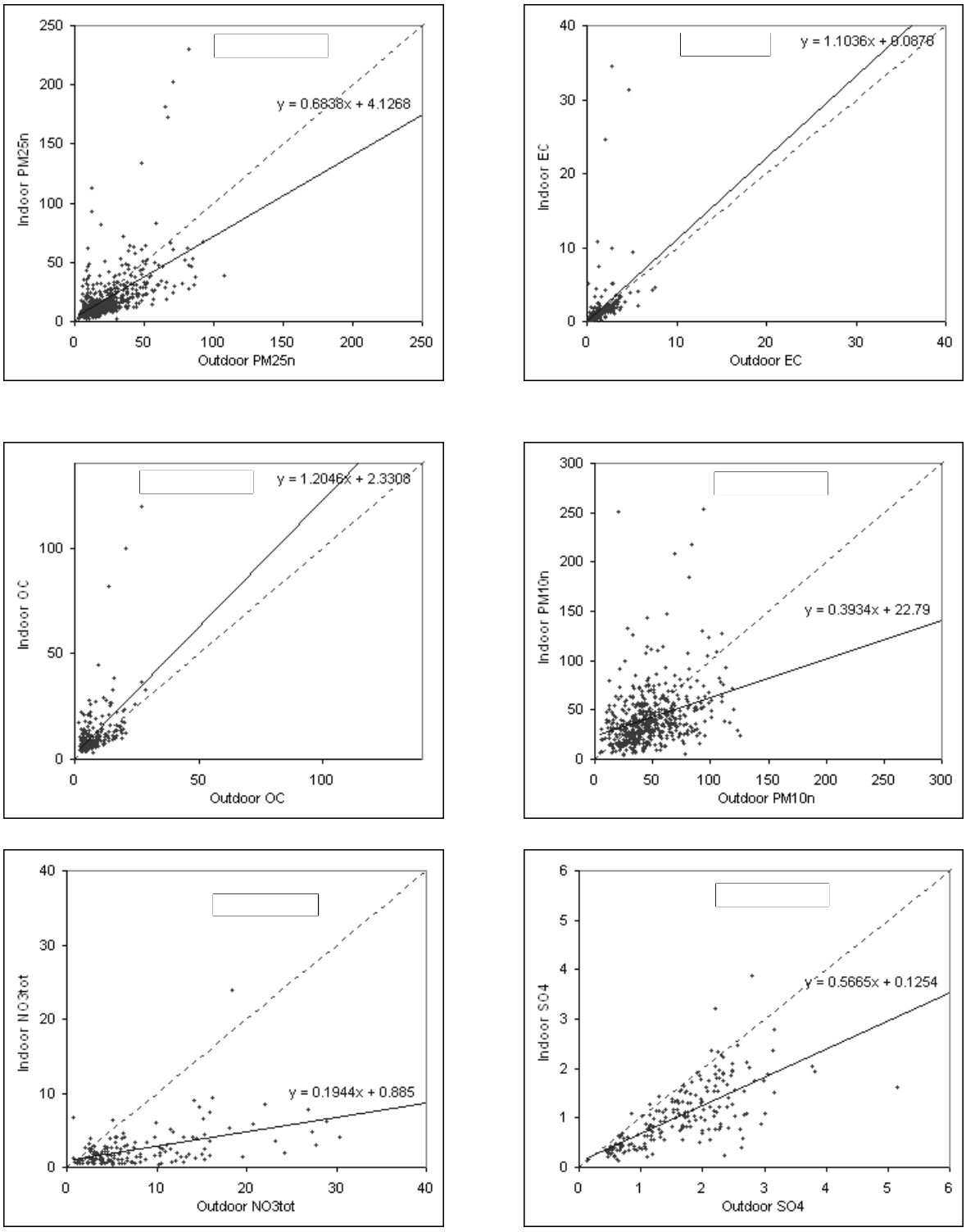


Figure 4.1.5-1. Comparison of indoor and outdoor 24-hr concentrations of particulate matter at FACES residences.

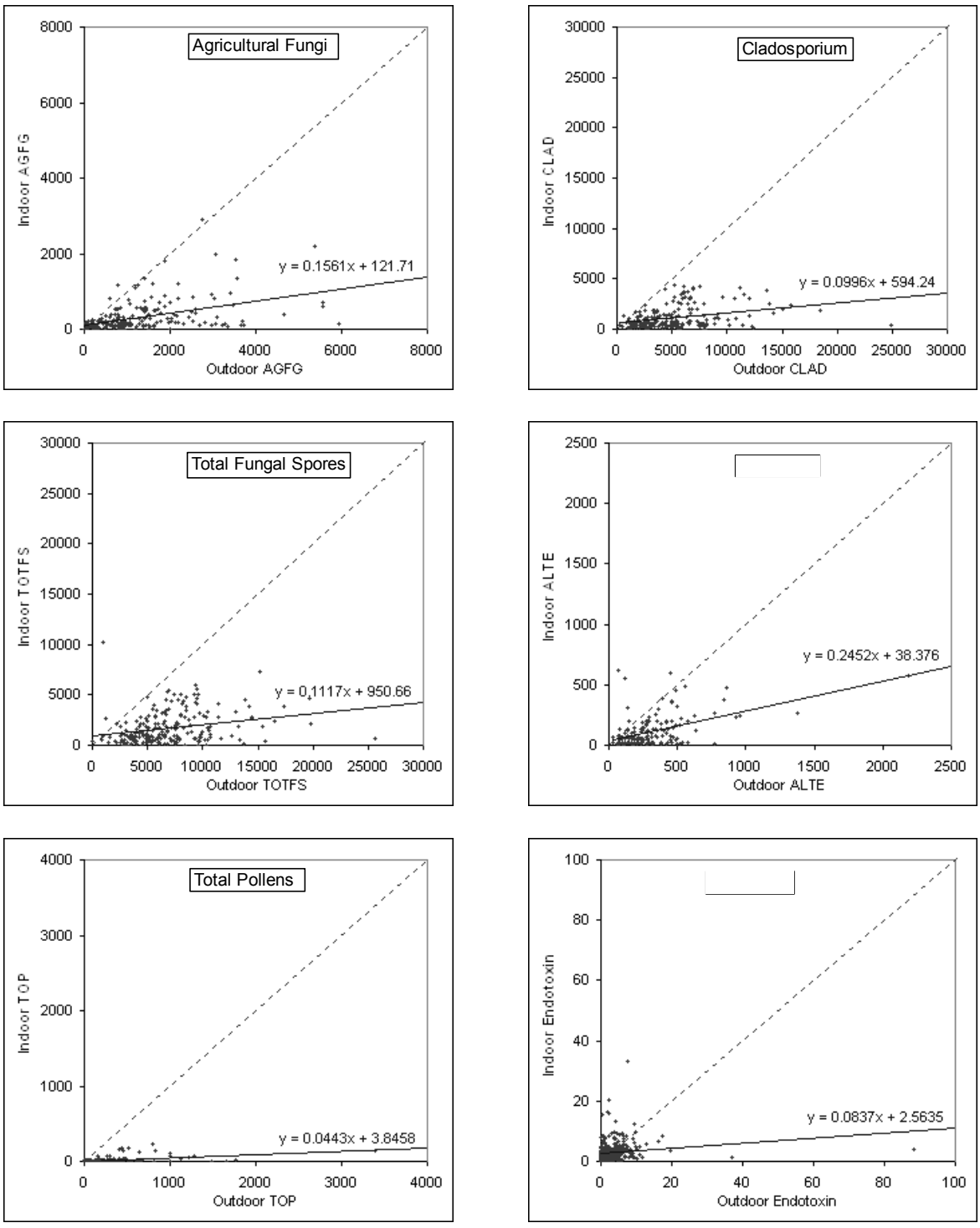


Figure 4.1.5-2. Comparison of indoor and outdoor 24-hr concentrations of biological agents at FACES residences.

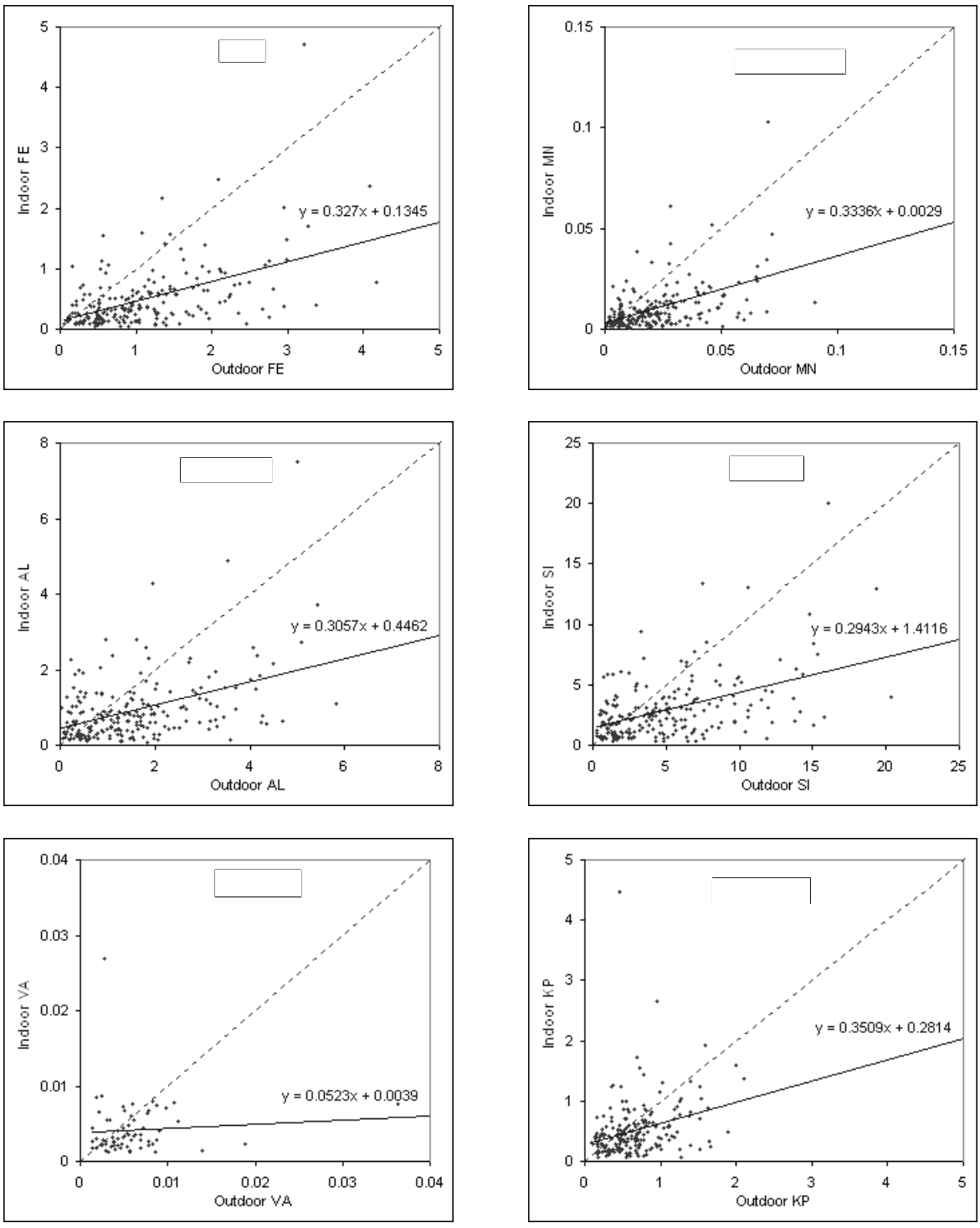


Figure 4.1.5-3. Comparison of indoor and outdoor 24-hr concentrations of PM_{10} trace elements at FACES residences.

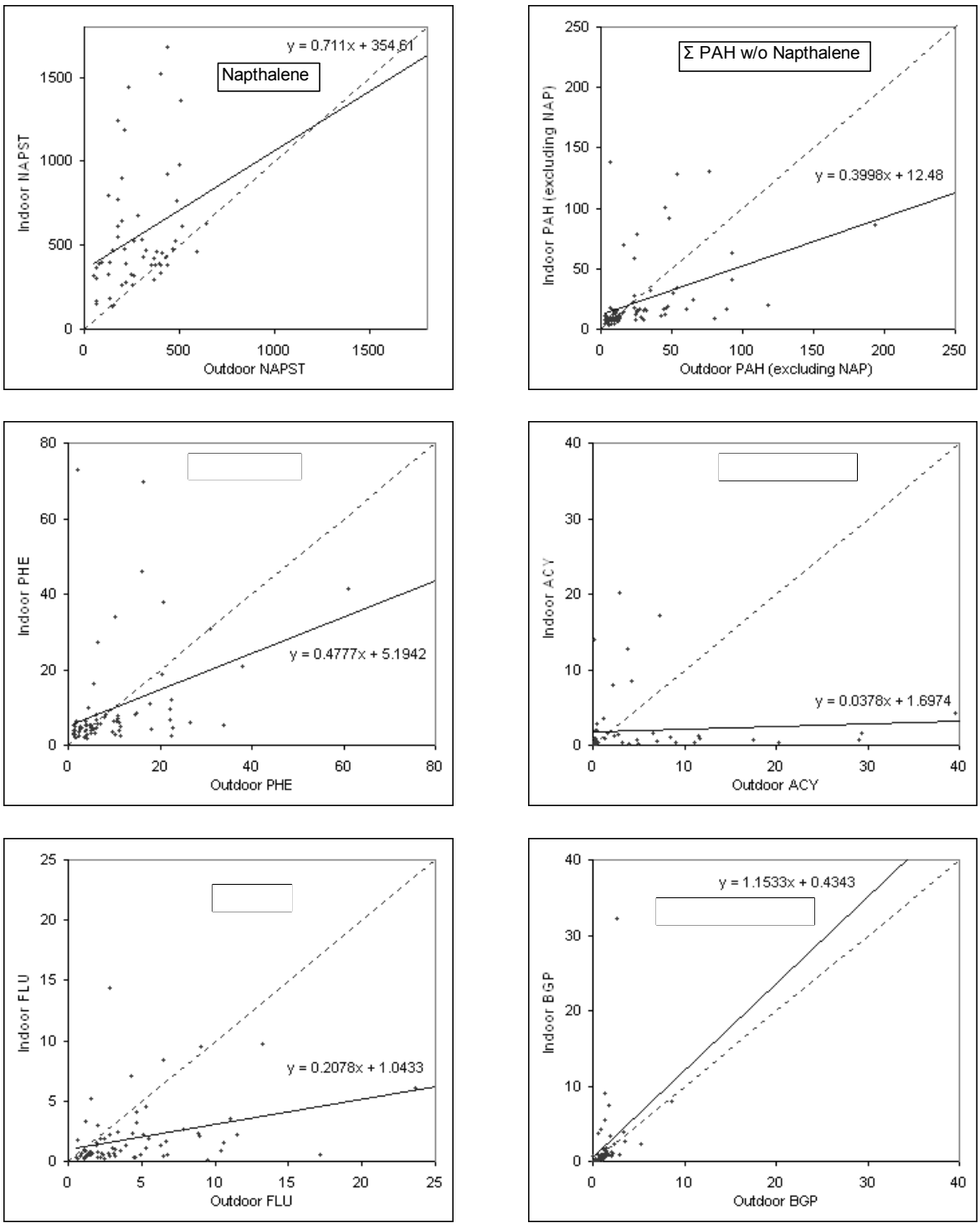


Figure 4.1.5-4. Comparison of indoor and outdoor 24-hr concentrations of selected polycyclic aromatic hydrocarbons at FACES residences.

Table 4.1.5-2. Summary statistics for the indoor/outdoor ratios in FACES residences based on concurrent 24-hr concentrations that were not outliers[2] and exceeded the limits of detection.

Pollutant[1]	No. of cases	Minimum	10th Percentile	25th Percentile	Median	Mean	75th Percentile	90th Percentile	Maximum
Particulate Matter									
$PM_{2.5}$ Mass	459	0.09	0.40	0.54	0.76	0.92	1.02	1.56	5.58
PM_{10} Mass	482	0.06	0.37	0.56	0.76	0.98	1.13	1.78	6.44
B_{scat}	1059	0.02	0.37	0.51	0.72	0.96	0.99	1.55	15.4
$PM_{2.5}$ EC	227	0.12	0.49	0.65	0.82	0.94	1.07	1.52	4.00
$PM_{2.5}$ OC	217	0.45	0.80	1.00	1.31	1.66	1.85	3.08	9.52
$PM_{2.5}$ NO_3	136	0.04	0.09	0.17	0.30	0.37	0.50	0.73	1.55
$PM_{2.5}$ SO_4	199	0.10	0.36	0.49	0.64	0.64	0.80	0.93	1.28
Biological Agents									
ALTE	143	0.03	0.06	0.14	0.27	0.37	0.50	0.77	2.50
AGFG	176	0.01	0.05	0.09	0.21	0.37	0.40	0.72	7.00
CLAD	181	0.00	0.04	0.08	0.16	0.25	0.33	0.50	2.26
ASP	119	0.02	0.07	0.17	0.43	1.26	0.90	2.23	25.0
TOTFS	204	0.00	0.04	0.09	0.20	0.31	0.40	0.58	7.25
Endotoxin	328	0.01	0.23	0.45	0.99	4.49	2.70	7.83	207
TOP	191	0.00	0.00	0.00	0.02	0.10	0.07	0.19	6.67
Polycyclic Aromatic Hydrocarbons									
ACE	64	0.13	0.49	1.12	2.19	2.89	3.58	5.93	19.29
ACY	52	0.03	0.08	0.45	0.69	1.30	1.51	3.51	6.66
ANT	49	0.21	0.41	0.82	1.92	2.91	3.92	7.08	11.72
BAA	37	0.07	0.10	0.18	0.35	0.73	0.93	1.88	4.53
BAP	46	0.10	0.33	0.48	0.81	1.66	1.43	2.19	26.3
BBF	47	0.03	0.18	0.28	0.46	0.65	0.90	1.27	2.65
BGP	49	0.07	0.30	0.41	0.62	0.88	0.93	1.32	9.92
BKF	51	0.14	0.22	0.29	0.47	0.82	0.73	1.12	12.0
CRY	49	0.05	0.09	0.17	0.25	0.59	0.74	1.32	5.60
DBA	39	0.29	0.41	0.48	0.76	0.93	1.27	1.57	2.75

Pollutant[1]	No. of cases	Minimum	10th Percentile	25th Percentile	Median	Mean	75th Percentile	90th Percentile	Maximum
FLT	64	0.05	0.17	0.28	0.62	0.91	1.32	1.87	5.56
FLU	63	0.01	0.10	0.22	0.34	0.48	0.66	0.86	2.91
ICP	33	0.15	0.35	0.48	0.66	1.08	1.54	2.46	3.70
NAPST	50	0.78	0.93	1.04	1.43	2.20	3.00	4.79	6.44
PHE	62	0.12	0.34	0.56	0.80	1.18	1.58	2.85	5.28
PYR	58	0.10	0.32	0.44	1.02	1.86	2.00	3.91	20.3
PM_{10} Trace Elements									
AL	192	0.04	0.20	0.34	0.57	1.36	0.97	2.77	57.4
AS	59	0.30	0.45	0.64	0.92	1.01	1.24	1.42	3.47
BA	37	0.28	0.47	0.56	0.79	0.87	1.14	1.42	1.85
BR	207	0.11	0.41	0.57	0.81	0.96	1.09	1.50	6.26
CA	184	0.06	0.26	0.47	0.75	1.24	1.54	2.93	6.60
CL	174	0.07	0.37	0.70	2.47	4.55	5.78	12.25	35.5
CO	172	0.04	0.12	0.21	0.41	0.58	0.69	1.43	3.61
CR	105	0.15	0.32	0.46	0.76	0.94	1.15	1.94	3.32
CU	182	0.06	0.23	0.36	0.57	0.78	0.95	1.63	3.71
FE	190	0.03	0.13	0.23	0.41	0.58	0.59	1.40	6.42
GA	3	0.73	0.73	0.79	1.00	0.99	1.18	1.24	1.24
KP	186	0.05	0.26	0.45	0.70	0.89	1.04	1.90	4.80
MG	72	0.25	0.38	0.54	0.74	0.89	1.22	1.46	2.93
MN	189	0.03	0.13	0.25	0.42	0.63	0.67	1.51	5.70
NA	34	0.46	0.68	0.81	0.89	1.01	1.23	1.51	1.81
NI	145	0.15	0.41	0.53	0.77	0.95	1.15	1.85	6.63
PB	117	0.35	0.45	0.57	0.73	0.82	0.96	1.29	3.13
PD	4	0.84	0.84	0.87	1.13	1.22	1.56	1.76	1.76
PH	10	0.12	0.18	0.28	0.44	0.73	0.65	2.10	2.51
RB	136	0.07	0.24	0.35	0.54	0.72	0.85	1.38	4.45
SB	17	0.48	0.54	0.59	0.90	0.99	1.13	1.91	2.31
SI	195	0.05	0.17	0.33	0.55	0.97	1.07	2.43	7.74
SN	39	0.46	0.58	0.78	1.01	1.09	1.31	1.63	2.74

Pollutant[1]	No. of cases	Minimum	10th Percentile	25th Percentile	Median	Mean	75th Percentile	90th Percentile	Maximum
SR	12	0.46	0.55	0.61	0.78	0.90	1.28	1.44	1.47
SU	196	0.13	0.46	0.61	0.78	0.83	0.93	1.14	3.15
TI	177	0.04	0.18	0.33	0.59	1.05	1.05	2.26	18.0
TL	3	0.70	0.70	0.76	0.94	0.98	1.22	1.31	1.31
UR	4	0.89	0.89	0.98	1.11	1.08	1.17	1.19	1.19
VA	62	0.15	0.30	0.49	0.70	0.93	0.95	1.66	4.59
YT	13	0.46	0.63	0.75	0.84	0.96	1.24	1.37	1.44
ZN	189	0.11	0.46	0.66	0.90	1.14	1.32	2.05	7.00
ZR	171	0.18	0.56	0.92	1.42	2.01	2.39	4.18	11.9

[1] Indoor/outdoor ratios were not computed for PM_{10} Ag, Mo, Hg, In, La, and Se because there were no concurrent indoor and outdoor samples with concentrations above the limit of detection.

[2] Excluded outliers are values below the 25^{th} percentile - 1.5*IQR and above the 75^{th} percentile +1.5*IQR.

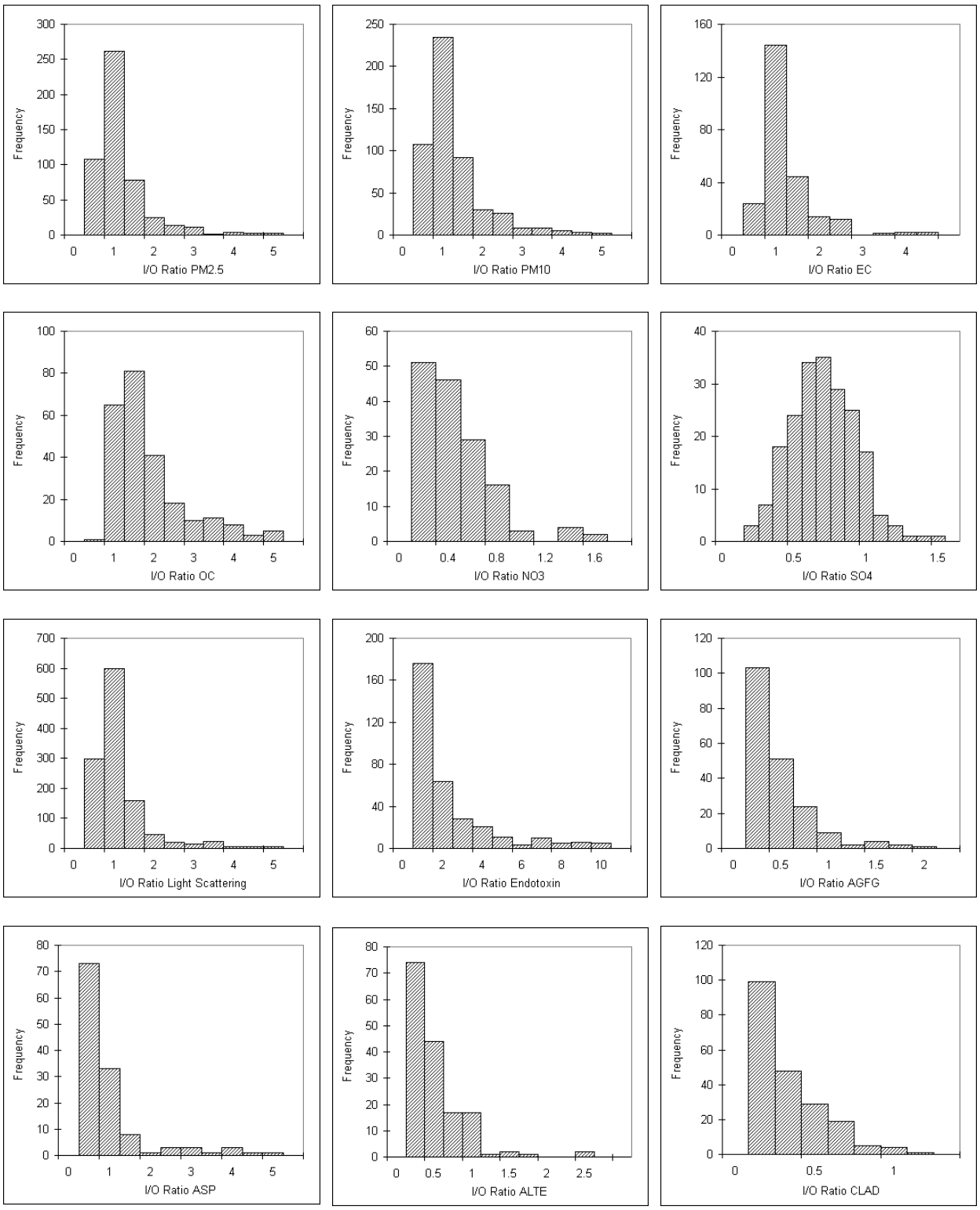


Figure 4.1.5-5. Frequency distribution of indoor/outdoor concentration ratios of PM mass, PM chemical components, light scattering, endotoxin. and fungal spores.

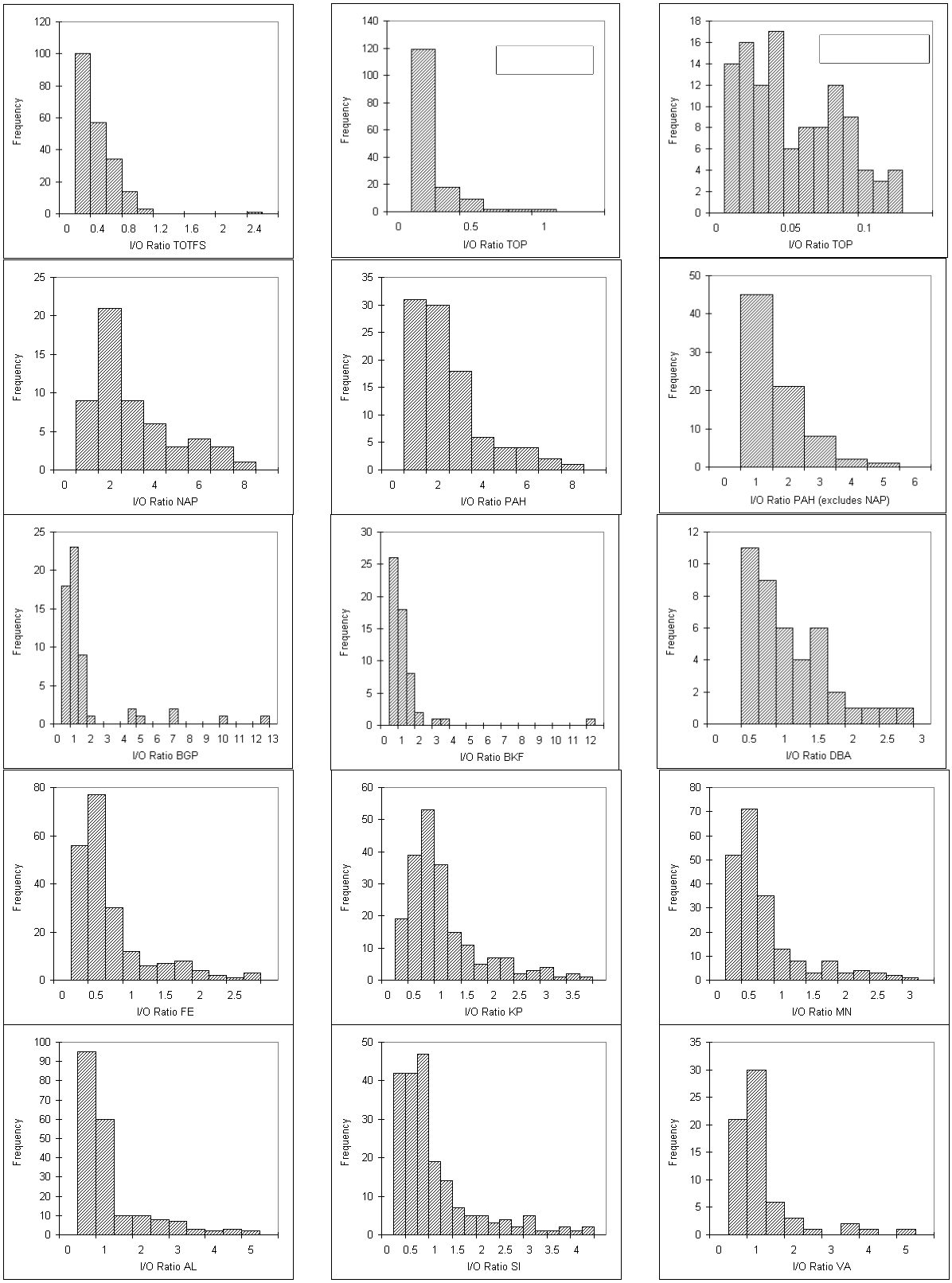


Figure 4.1.5-6. Frequency distribution of indoor/outdoor concentration ratios of total fungi, total pollens, polycyclic aromatic hydrocarbons and selected trace metals (Al, Fe, K, Mn, Al, Si, and Va).

Table 4.1.5-3. Correlation of indoor and outdoor concentrations at FACES residences.

Compound	Correlation Coefficient of All 24-hr Samples	Correlation Coefficient of 24-hr Samples Excluding Outliers[1]	Correlation Coefficient of Residence Average[2]		Compound	Correlation Coefficient of All 24-hr Samples	Correlation Coefficient of 24-hr Samples Excluding Outliers[1]	Correlation Coefficient of Residence Averages[2]
Particulate Matter					PM_{10} Trace Elements			
$PM_{2.5}$ Mass	0.54	0.52	0.63		AL	0.43	0.34	0.47
PM_{10} Mass	0.32	0.32	0.36		AS	0.33	0.36	0.43
$PM_{2.5}$ EC	0.37	0.76	0.51		BA	0.37	0.07	0.32
$PM_{2.5}$ OC	0.52	0.31	0.55		BR	-0.01	0.32	-0.03
$PM_{2.5}$ NO_3	0.47	0.41	0.50		CA	0.24	0.19	0.32
$PM_{2.5}$ SO_4	0.71	0.74	0.76		CL	0.29	0.32	0.28
B_{scat}	0.47	0.60	0.44		CO	0.49	0.54	0.51
Biological Agents					CR	-0.03	0.14	-0.02
ALTE	0.48	0.34	0.59		CU	0.54	0.35	0.40
AGFG	0.43	0.37	0.49		FE	0.50	0.41	0.52
ASP	0.07	0.23	0.16		GA	-0.25	-0.25	-0.25
CLAD	0.33	0.19	0.32		KP	0.30	0.36	0.37
TOTFS	0.26	0.32	0.30		MG	0.17	0.10	0.10
Endotoxin	0.15	0.30	0.36		MN	0.52	0.42	0.56
TOP	0.49	0.40	0.51		NA	0.06	0.18	0.10
Polycyclic Aromatic Hydrocarbons					NI	0.35	0.34	0.42
ACE	0.13	-0.03	0.22		PB	0.93	0.59	0.78
ACY	0.07	0.17	0.16		PD	0.68	0.68	0.68
ANT	0.08	0.45	0.17		PH	-0.25	0.07	-0.25
BAA	0.60	0.25	0.72		RB	0.48	0.37	0.52
BAP	0.85	0.57	0.90		SB	0.02	0.17	0.19
BBF	0.71	0.73	0.77		SI	0.46	0.34	0.48
BGP	0.36	0.76	0.44		SN	0.34	0.19	0.21
BKF	0.80	0.86	0.91		SR	0.79	-0.03	0.81
CRY	0.36	0.20	0.41		SU	0.39	0.58	0.39
DBA	0.82	0.83	0.82		TI	0.15	0.41	0.06
FLT	0.29	0.10	0.45		TL	0.83	0.83	0.83
FLU	0.33	0.35	0.58		UR	0.31	0.31	0.31
ICP	0.14	0.26	0.33		VA	0.07	0.25	0.07
NAP	0.30	0.38	0.33		YT	0.68	0.28	0.72
PHE	0.36	0.46	0.53		ZR	0.09	0.27	0.14
PYR	0.28	0.15	0.36		ZN	0.44	0.50	0.48

[1] Excluded outliers are values below the 25th percentile - 1.5*IQR and above the 75th percentile +1.5*IQR.

[2] This is the correlation of the average indoor to average outdoor concentrations at residences, where each residence average is based on from 2 to 24 24-hr values.

4.1.6 Spatial Variability in Ambient Air Quality

An important element of the FACES exposure assessment was investigation of the spatial variability in ambient concentrations. Many epidemiologic studies of air pollution health effects have assigned daily exposures of all participants in communities with populations similar to that of Fresno based on data from a single air monitoring station or the average from several air monitoring stations. Ignoring the spatial variability in exposure assignments can increase measurement error and reduce statistical power in health effects studies (266, 267). Measurements of ambient air quality were made at residences and schools in FACES (see Figure 4.1.6-1) to supplement those obtained at the central site and other routine air monitoring stations and to facilitate investigation of neighborhood- and urban-scale spatial variability in Fresno.

A number of approaches are available for characterization of spatial variability measurements. Some approaches that require relatively long temporal records at numerous locations (206) were not suitable for the FACES data set. The distinguishing feature of the FACES data set is that it contains measurements collected over a year at a large number (~85) of locations; however, the number of locations with contemporaneous daily measurements is small, typically 6 to 8, and the number of days with measurements at a specific location can be as few as 2. Because the day-to-day temporal variation in ambient air quality in Fresno is generally much larger than the spatial variation, an approach that minimizes the confounding effects of temporal variability is most suitable for the FACES data spatial analysis. The approach used for the spatial analysis had four elements. The first element involved visual inspection of the spatial patterns of concentrations on individual days. The second element involved statistical quantification of the spatial variability. The third element was the assessment of biases in concentrations relative to the central site concentrations. The fourth element was the investigation of associations of concentrations with various metrics of local traffic. The approaches and results are described below.

Exposure assignment error may also result from sampling, instrumentation, and laboratory analysis errors as well as ignoring spatial differences. The measurement precision information presented in Section 3.4 indicates than many of the FACES exposure parameters were measured to within ±10% or ±15%. Caution is needed in interpreting small differences in measurement made at different locations because it is not possible to distinguish between real spatial differences and the combination of sampling, instrumentation, and laboratory analysis errors. Only differences that exceed the measurement precision (which vary by species) can be interpreted at real spatial differences.

4.1.6.1 Visual observations of Spatial Patterns

Spatial plots of the 24-hr average concentrations of $PM_{2.5}$, PM_{10}, EC, OC, NO_3, SO_4, selected trace elements, and PAHs on individual Home Intensive sampling days were generated. The spatial maps are contained in Appendix L – Appendix Q in the electronic supplement. The maps were reviewed to assess the consistency and seasonality of patterns. It is convenient to consider the spatial patterns in terms of directional quadrants from the central site (northwest, northeast, southeast, and southwest as illustrated in Figure 4.1.6-1). Figures 4.1.6-2 through 4.1.6-4 show examples of patterns of 24-hr average $PM_{2.5}$ and PM_{10} mass concentrations. They

show circumstances in which PM concentrations are lower in the northwest and northeast quadrants than at the central site and in the southwest and southeast quadrants. They illustrate that $PM_{2.5}$ and PM_{10} concentrations in the outlying areas may only be half the values observed at the central site during the cool season when the highest $PM_{2.5}$ levels are observed. They suggest that spatial variations in PM mass across Fresno are smaller in the warm season than the cool season. They show that coarse PM is a significant fraction of PM_{10} in the warm season at virtually all locations, but not in the cool season. In the cool season, $PM_{2.5}$ mass is ~80% to 100% of PM_{10} mass at most locations.

Examples of the spatial distribution of $PM_{2.5}$ NO_3 and OC are shown in Figures 4.1.6-5 and 4.1.6-6. NO_3 and OC are the two largest constituents of $PM_{2.5}$ mass. These examples show cases where OC levels are consistent across the community and are lower in the outlying areas than at the central site. The seasonal shift in the relative abundance of the two constituents is evident—NO_3 levels exceed OC levels in the cool season, while OC levels are greater than NO_3 levels in the warm season at virtually all sites in these examples. NO_3 levels are so low in the warm season that it is difficult to discern the spatial pattern because measurement error becomes more important as the levels approach the detection limits.

Figure 4.1.6-7 and 4.1.6-8 show examples of the spatial distributions of $PM_{2.5}$ EC and SO_4. The EC levels at the central site are more than 30% higher than those at any other location on the three cool-season days shown. EC levels in the outlying areas can be much lower (e.g., ~80%) than at the central site in the cool season, particularly in the northeast quadrant. SO_4 levels are generally low, but are much lower in the cool season than in the warm season. SO_4 levels are more spatially uniform than EC levels, indicating the more regional nature of SO_4. The differences in spatial distributions illustrate expected differences between a prime aerosol (EC) and a secondary aerosol (SO_4) in the SJV (268).

Sample spatial plots of 15 trace-metals levels in PM_{10} are shown in Figures 4.1.6-9 and 4.1.6-10. The trace metals, which are potentially of concern for health analyses, include Ag, Au, Cd, Co, Cr, Cu, Fe, Hg, Mn, Mo, Ni, Pd, Va, Zn, and Zr. The data for four locations on a fall day (November 20, 2002) are quite consistent across the area, while the data for eight locations on a winter day (January 11, 2003) are consistent, with the exception of lower concentrations in the outlying northeast quadrant. Spatial patterns of numerous trace metals need to be interpreted cautiously because levels are often near the detection limits.

Figures 4.1.6-11 and 4.1.6-12 show examples of the spatial distribution of 13 representative PAHs on two winter days. Large spatial variations in most PAH species are evident. Central Fresno experiences higher levels on these days than do the outlying areas, much like the pattern for EC where "factor of five" differences occur. These characteristics are consistent with PAHs as primary aerosols.

4.1.6.2 Spatial Variability

The spatial variability in ambient concentrations was statistically characterized using the mean spatial coefficient of variation. For each pollutant, we first determined the daily spatial variability from all locations with valid measurements on that day using the coefficient of

variation (CV_t^i) and then average over all days to determine the mean spatial coefficient of variation (CV_t).

$$CV_t^i = \frac{\sqrt{\dfrac{m_t \sum_{x=1}^{m_t} (c_{xt}^i)^2 - \left(\sum_{x=1}^{m_t} c_{xt}^i \right)^2}{m_t (m_t - 1)}}}{\dfrac{1}{m_t} \sum_{x=1}^{m_t} c_{xt}^i} \qquad (4.1.6\text{-}1)$$

$$\overline{CV}^i = \frac{1}{n} \sum_{t=1}^{n} CV_t^i \qquad (4.1.6\text{-}2)$$

where: c_{xt}^i = concentration of species *i* at location *x* on day *t*.

m_t = the number of locations on day *t*.

CV_t^i = the spatial coefficient of variation of species *i* on day *t*.

$\overline{CV}^i$ = the mean spatial coefficient of variation of species *i*.

n = the number of days.

The CV calculations were made using the 24-hr average concentrations of pollutants in the cool and warm seasons as well as the entire year of the Home Intensive Study. Table 4.1.6-1 lists the mean spatial coefficient of variation for the cool season, warm season, and entire year. Data for days with valid data available from three or more locations were included. The minimum detection levels (MDL) were not substituted for zero values. The calculated CVs for species with concentrations frequently near the detection limit (e.g., numerous trace elements) may be large on a percentage basis but are usually quite small on an absolute basis. Figure 4.1.6-13 shows the mean spatial coefficients of variation of key PM constituents and gases for the three time periods. Figures 4.1.6-14 and 4.1.6-15 display the mean spatial coefficients of variation of trace elements and PAHs by rank on an annual basis.

The results show that SO_4 has the least spatial variability (14%) followed by PM_{10} mass (17%), and $PM_{2.5}$ mass (18%). Light scattering by particles has essentially the same spatial variability as $PM_{2.5}$ mass (18%-19%) on an annual basis. Similarly, PM_{10} sulfur (S) by XRF has low spatial variability (10%) confirming the result for SO_4. Four abundant elements in PM_{10}—iron, silicon, potassium, and calcium—showed spatial variability similar to that for PM_{10} mass. The mean spatial variations exceed the precision of these measurements indicating that the spatial variability is real but fairly small for $PM_{2.5}$ mass, sulfate, PM_{10} mass, and major crustal components of PM_{10}. We rank spatial variability low when it is less than 20%. This result is consistent with our original hypotheses for the spatial variation of $PM_{2.5}$ and sulfate.

Next, a group of species with annual spatial variability between 20% and 35% includes OC, EC, NO_3, NO_2, NO_x, ozone, CO, and endotoxin. Coarse PM and the following seven constituents of PM_{10} also have similar spatial variability: aluminum, bromine, cobalt, copper, manganese, strontium, and zinc. These gases and components of PM have real spatial variability that we rank as moderate. They include both primary and secondary species.

The spatial variability of NO, SO_2, all PAHs, and other measured PM_{10} trace elements was greater than 35%. The annual variability of continuous particle PAH, SO_2, and NO was 42%, 44%, and 55%, respectively. The mean spatial variability in PAHs ranged from 66% for pyrene and fluoranthene to 106% and 117% for dibenz[a,h]anthracene and anthracene. The high spatial variability of individual PAHs was not expected given the somewhat lower variability observed for continuous particle PAH, OC, and EC; the higher spatial variability suggests individual PAHs may be more specific indicators of certain combustion source types than continuous particle PAH, OC, and EC within the community. For other trace elements, the mean spatial variability ranged from 44% and 45% for chlorine and nickel to 122% to 164% for silver, gold, cadmium, gallium, mercury, indium, lanthanum, molybdenum, sodium, palladium, phosphorous, antimony, thallium, and uranium. Concentrations of the less abundant PAHs and later group of trace elements were often near or below the detection limits and strongly influenced the spatial variability percentage.

Most pollutants have similar spatial variability in the cool and warm seasons. Notable exceptions are OC, EC, ozone, and SO_2 which are more spatially varying in the cool season than in the warm season, and NO, CO and continuous particle PAH which are less variable in the cool season than in the warm season. These differences are probably related to seasonal variations in concentrations and source activities. For example, ozone is more variable in the cool season because it occurs at lower concentrations and is strongly influenced by NO_x scavenging from local sources in the cools season. Likewise, wood smoke emissions in the cool season increase the spatial variability of OC and EC relative to the warm season when transportation is the predominant source of these compounds. NO has more variability in the warm season because concentrations are lower and it reacts more quickly due to higher warm season ozone levels.

The relative ranking of outdoor pollutant concentration spatial variability is summarized in Table 4.1.6-2. The rankings generally confirm the expectations established at the beginning of the study.

4.1.6.3 Systematic Spatial Variation and Spatial Representativeness

For purpose of exposure assignments, we would like to know whether the spatial variability is purely random or whether there are consistent spatial patterns (or systematic spatial variations) that can be accounted for in an exposure model. Also, because the FACES exposure assessment design relies heavily on the daily central site measurements, the spatial differences in concentration relative to the central site values are important. We examined the spatial patterns of measured concentrations and categorized the variations by season, wind quadrants, and distance from the central site. The day-to-day variations in meteorological conditions have such a large effect on concentrations that we chose to focus on the ratio of concentrations (instead of absolute concentrations) at various locations in the community to those at the central site instead

of absolute concentrations. The ratio of local concentrations to those at the central site is an approximate and imperfect way to normalize the spatial data for meteorological differences. A statistical summary of the ratios is presented in Table 4.1.6-3.

Examining plots of the ratio of concentrations to those at the central site by direction quadrant and distance in 3-km increments showed evidence of notable concentration variations beyond 9 km north of the central site. For example, ozone concentration ratios increased with distance from the central site in the northwest and northeast directions, while $PM_{2.5}$, b_{scat}, EC, PAHs, NO_2, and PM_{10} concentration ratios decreased in the region 9 to 12 km northwest and northeast of the central site. Oddly, the $PM_{2.5}$, EC, PAHs, NO_2, and PM_{10} concentration ratios were often higher at sites 12 to 15 km north of the central site than those 9-12 km north of the central site. Gradients in concentration ratios with distance south of the central site were smaller than those north of the central site. For most species examined, stratification of the ratios into distance bins and quadrants resulted in large confidence intervals that encompassed the ratio of one. Thus, while the means show evidence of increases and decreases in concentration ratios with distance from the central site, they were not statistically significant.

The concentration ratios were examined by direction quadrant and season. Figures 4.1.6-16 and 4.1.6-17 show the mean ratios and 95% confidence intervals in the cool and warm seasons for representative pollutants. Many of the confidence intervals encompass 1.0, especially in the warm season, indicating that concentrations at other locations in the community are similar to those at the central site. In the cool season, the ratios are noticeably less than one (i.e., concentrations are lower than those at the central site) in the northeast quadrants for $PM_{2.5}$, b_{scat}, EC, OC, SO_4, PPAH, PM_{10}, NO, NO_2, NO_x, and CO. The ratios are also less than one in the northwest quadrant for PM_{10}, NO_3, NO, NO_2, NO_x, and CO in the cool season. Concentration ratios are greater than one (i.e., concentrations are higher than those at the central site) in the cool season for $PM_{2.5}$, B_{scat}, PPAH, endotoxin, NO, NO_x, and CO, in the southwest quadrant, and for PPAH, NO_3, and CO in the southeast. In the warm season, 24-hr average ozone levels are higher in the northwest region than at the central site. Endotoxin levels are higher at most other locations than those at the central site in the warm season, which perhaps reflects the closer proximity to agricultural emissions in the outlying areas compared to the city center. In the warm season, the ratios of numerous primary species, including NO, NO_x, PPAH, and CO, are higher than one in areas southwest and southeast of the central site. The ratios of most species northwest and northeast of the central site are close to one in the warm season; however, the ratios for EC are noticeably lower than one in the north in the warm season. Thus, there are clearly different patterns of concentrations relative to the central site in the warm and cool seasons.

Examining the ratios across seasons suggests a general pattern where PM, primary PM components, and concentrations of primary gases are higher than those at the central site in the area southwest and, to a lesser extent, southeast of the central site, and lower than those at the central site in the area northeast, and to a lesser extent, northwest of the central site. Most of the mean ratios for pollutants are within 1 ± 0.2. The exceptions are the mean ratios of NO, NO_x, CO, PPAH, and endotoxin which exceed 1.20 at locations sampled to the south of the central site, and means ratios of EC, NO, and NO_x which are below 0.80 in either the northeast or northeast areas.

Figures 4.1.6-17 and 4.1.6-18 show the median and mean ratios of 24-hr average concentrations at schools, residences, and other air quality stations in the community to those at the central site in Fresno. These figures show the median and mean $PM_{2.5}$ mass concentrations measured at all FACES locations away from the central site were 3% and 2% lower than the corresponding central site concentrations on average. The 95% confidence interval (0.97 to 1.00) of the mean (0.98) ratio for $PM_{2.5}$ was quite small, indicating that $PM_{2.5}$ levels in the neighborhoods around Fresno were well represented by the central site measurements. The median systematic variations in EC, OC, PM_{10}, PM coarse, NO, NO_2, and NO_x were between -6% and -13%, while the median systematic variations in SO_4, NO_3, b_{scat}, endotoxin, CO, SO_2, and ozone were between +2% and +13%. The mean values were slightly higher than the median biases for most of these parameters; the exceptions were NO, ozone, SO_2, and endotoxin which had mean systematic variations of 22%, 97%, and 38%, respectively. The central site measurements of NO, ozone, SO_2, and endotoxin are less representative of conditions in the community than other pollutants, such as $PM_{2.5}$ and PM_{10}.

The median systematic variations in PM_{10} trace metal concentrations measured at all other locations was between -15% for copper and +7% for nickel. The median systematic variations for vanadium, chromium, manganese, iron, cobalt, nickel, copper, zinc, aluminum, silicon, and lead were within these bounds. The median systematic variation in concentrations for the more abundant trace metals, such as iron, aluminum, and silicon, was 3% to 5%, which is within the measurement precision. The mean variations were slightly higher than the median variations for most elements. However, the mean systematic variations in PM_{10} chromium, cobalt, titanium, aluminum, vanadium, lead, selenium, and nickel were noticeably higher than the medians; the mean systematic variations were 23%, 27%, 28%, 32%, 46%, 51%, 52%, and 113%, respectively. Again, the central site measurements are less representative of conditions in the community for vanadium, lead, selenium, and nickel than most other trace metals.

The median and mean systematic variations for continuous particle PAH (PPAH) were +26% and +47%; however, PPAH was not measured at as many locations as individual PAHs. The median systematic variations in individual PAHs range from -44% for indeno[1,2,3-cd]pyrene to -3% for dibenz[a,h]anthracene. The median systematic variations in the more abundant PAHs were -32% for phenathrene, -14% for napthalene, and -9% for fluorene. The mean biases ranged from -24% for phenathrene to +42% for benz[a]anthracene and +80% for benzo[b]flouranthene. The mean systematic variations for naphthalene and fluorene were -14% and -1%, respectively. As might be expected from the high spatial variability of individual PAHs described above and the primary nature of PAHs, the variations relative to the central site measurements vary considerably by compound and the confidence intervals are quite wide. Thus, the central site individual PAH measurements are less representative of conditions in the community than other species, like $PM_{2.5}$ and PM_{10}.

Overall, it was concluded that exposure assignments for FACES participants could be improved by developing methods to account for the spatial patterns and systematic variations in ambient concentrations in the community. As described in Section 3.4.7, methods were developed to spatially map ambient concentrations for selected pollutants for use in the individual exposure model. The average spatial gradient maps shown in Section 3.4.7 were developed from the ratios of concentrations to the central site (described above) and capture the

principal characteristics of the spatial patterns revealed in the directional quadrant and distance analyses.

4.1.6.4 Pollutant Relationships to Traffic

The relationship between ambient concentrations and indicators of traffic activity were examined. The rationale was that the emission inventory suggests motor vehicles are the principal source of many of the pollutants measured in FACES (269). We examined the relationships of $PM_{2.5}$ mass, EC, OC, and the individual PAHs to 14 metrics of traffic activity assigned to each FACES residence, school, and other air quality station. As described in Section 3.4.6.3, the traffic metrics included

- A GIS estimate of traffic density based on annual average traffic volumes and a 90% concentration decay from the edge of the roadway to 150 m perpendicular to the roadway;
- A second GIS estimate of traffic density based on 90% concentration decay within 300 m of the edge of the roadway;
- Inverse distances from the nearest freeway, major arterial, minor arterial, and major collector;
- Inverse distance-weighted annual average traffic volume on the nearest freeway, major arterial, minor arterial, and major collector; and
- Inverse distance-squared-weighted annual average traffic volume on the nearest freeway, major arterial, minor arterial, and major collector.

Because the number of locations with measurements on any given day is small in FACES, we chose to pool all days for the analysis. Instead of using the absolute concentrations, which are strongly influenced by day-to-day meteorological variability, we chose to use the ratio of 24-hr average concentrations at various locations in the community to those at the central site. The ratios represent a normalized pattern of concentrations in the community, and we examined whether that pattern was related to the annual average traffic pattern. Regression analysis and analysis of variance using ratios stratified by season (cool and warm) were used.

Table 4.1.6-4 lists the coefficients of determination (r^2) for associations between traffic density and freeway traffic metrics and the pollutant ratios to the central site. For this data set, r^2 between 0.25 and 0.50 were considered to reflect moderate associations and r^2 greater than 0.50 were considered to reflect strong associations. First, none of the ratios for any of the pollutants considered were related to the traffic metrics specific to major arterials, minor arterials, and major collectors. Only traffic density, which incorporates all roads with traffic volume data, and freeway traffic metrics were related to the ratio of some of the pollutants. The ratios of $PM_{2.5}$, OC, acenaphthylene, benzo[k]flouranthene, chrysene, dibenz[a,h]anthracene, flouranthene, napthalene, and pyrene to the central site were not related to any of traffic metrics ($r^2 < 0.25$).

Significant statistical associations were found between the traffic metrics and EC and certain PAHs. The ratios of local EC concentrations to those at the central site were moderated related to the inverse of the distance to the nearest freeway in the cool season ($r^2 = 0.27$), but not

in the warm season. The EC ratios were also moderated related to the inverse distance-weighted traffic volume ($r^2 = 0.25$) and inverse-distance-squared weighted traffic volume ($r^2 = 0.26$) in the cool season. The ratios of local concentrations of several other compounds to those at the central site were moderately related to at least one traffic metric in at least one season, including those for acenaphthene ($r^2 = 0.34$ warm season), anthracene ($r^2 = 0.40$ cool season), flourene benzo[b]flouranthene ($r^2 = 0.41$ cool season), benz[a]anthracene ($r^2 = 0.49$ warm), and phenathrene ($r^2 = 0.61$ warm); however, these compounds were not consistently related to more than one traffic metric.

Stronger relationships to multiple traffic metrics were found for the ratios of benzo[a]pyrene , benzo[b]flouranthene, benzo[ghi]perylene, and indeno[1,2,3-cd]pyrene local concentrations to those at the central site. The ratios for benzo[b]flouranthene were related to traffic density with 300 m falloff ($r^2 = 0.65$), traffic density with 150 m falloff ($r^2 = 0.54$), and the inverse of the distance to nearest freeway ($r^2 = 0.52$) in the warm season. The ratios of benzo[a]pyrene , benzo[ghi]perylene, and indeno[1,2,3-cd]pyrene were similarly related to the same three traffic metrics in the warm season. Only the ratios of indeno[1,2,3-cd]pyrene were moderately related to inverse-distance-weighted traffic volume ($r^2 = 0.26$) in the cool season. The inconsistency in the results for the two seasons, and especially the lack of relationships in the cool season, was a concern. Because the number of PAH samples was much greater and the PAH concentrations were higher in the cool season than in the warm season, we expected that relationships between PAHs and traffic would be more evident and robust in the cool season than the warm, but this was clearly not the case for these four compounds.

Figures 4.1.6-19 and 4.1.6-20 show the relationships between the ratios of $PM_{2.5}$, EC, OC, phenathrene, benzo[a]pyrene , benzo[b]flouranthene, benzo[ghi]perylene, and indeno[1,2,3-cd]pyrene, and the traffic metrics to which the ratios were most strongly correlated. The graphical displays of the data do not show convincing relationships between the ratios of pollutants to the central site and the traffic metrics; they illustrate that the regressions are often strongly influenced by a small number of high points and that they show inconsistencies between seasons for numerous pollutants. Thus, using this analysis method, we do not find sufficiently consistent relationships of the suspected traffic-related pollutants to traffic metrics to justify using proximity to traffic as a variable in the individual exposure model.

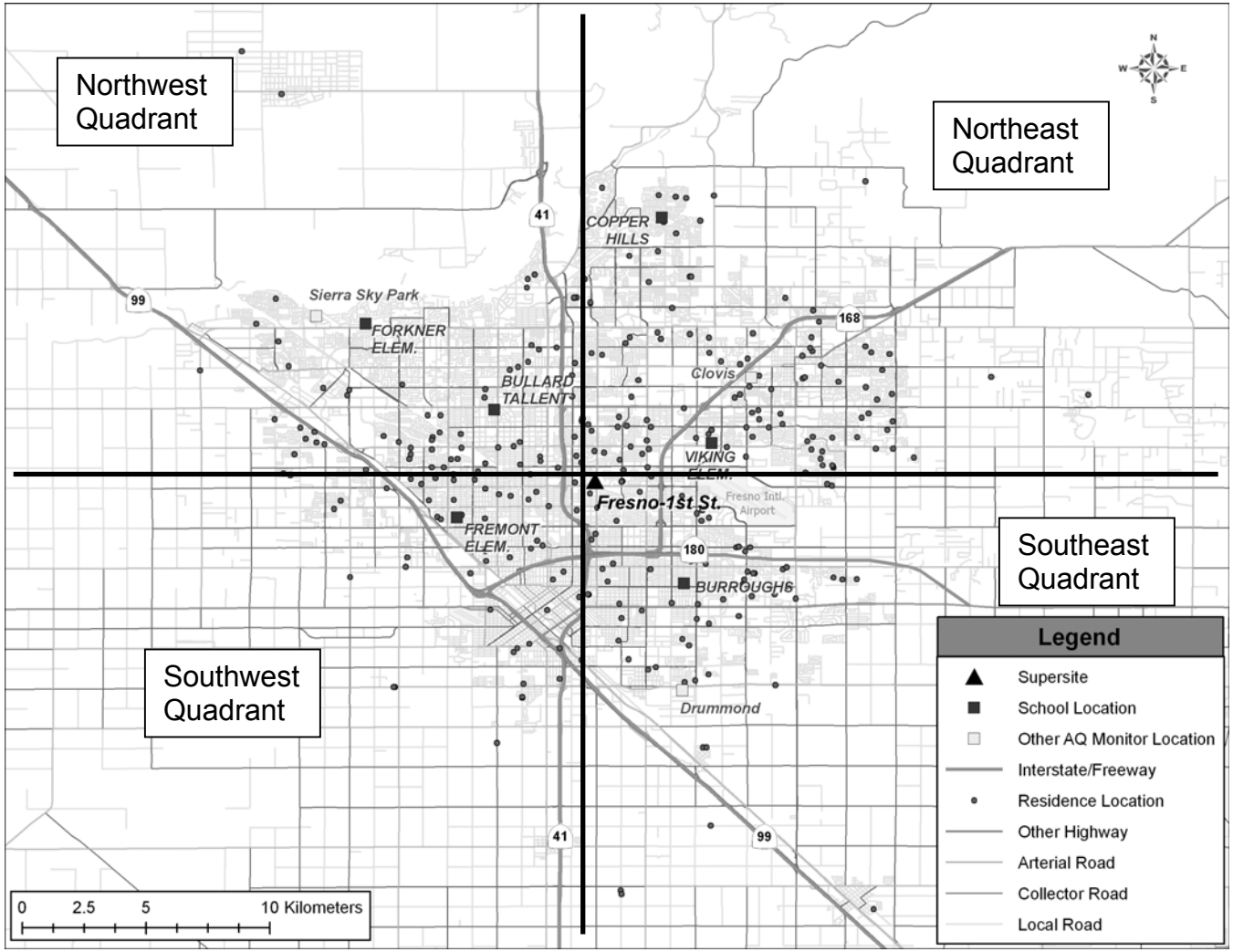


Figure 4.1.6-1. Map of air quality monitoring locations, FACES residences, and roadways in Fresno.

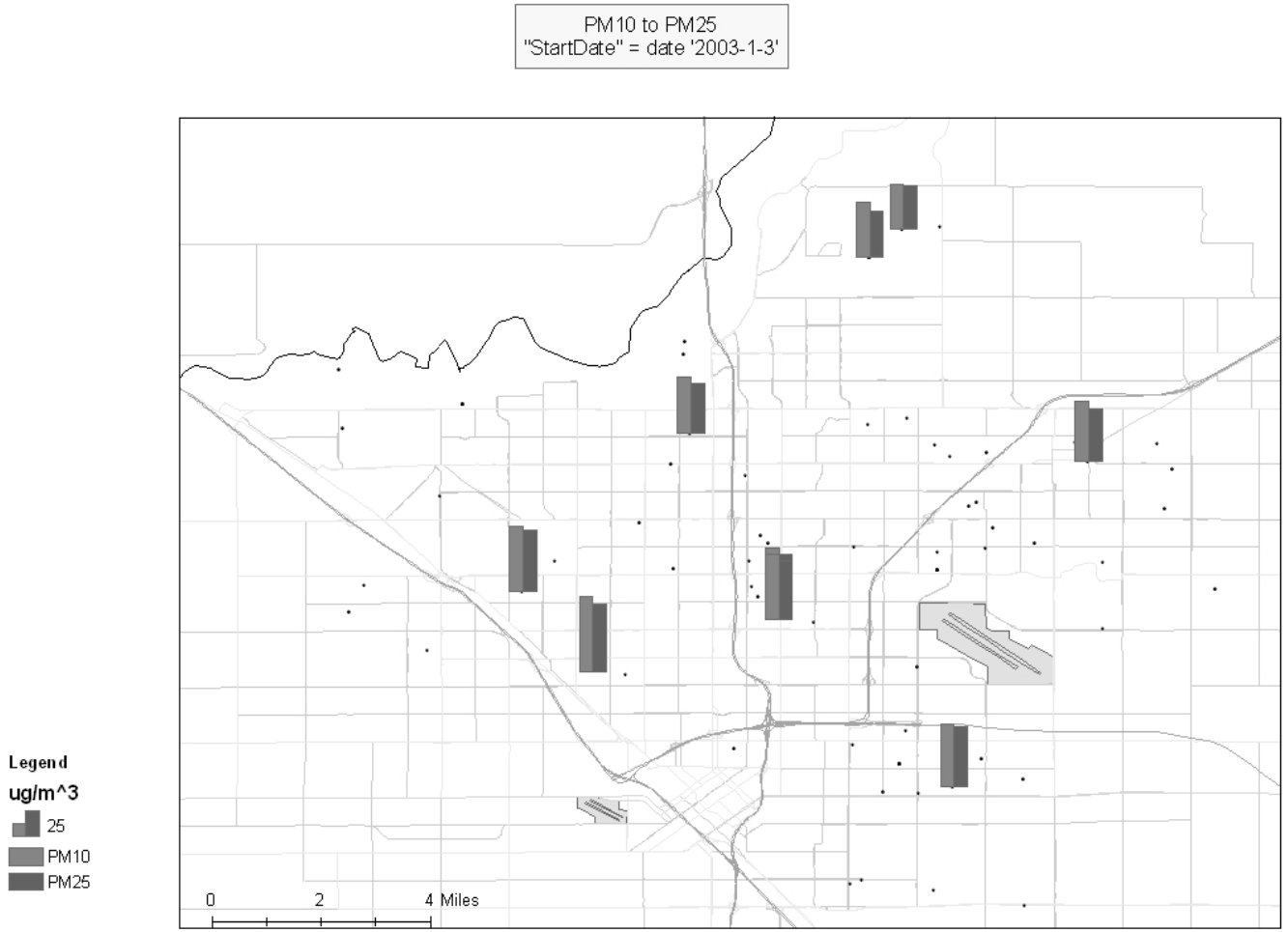


Figure 4.1.6-2. Typical spatial distribution of 24-hr average $PM_{2.5}$ and PM_{10} mass concentrations in FACES in the cool season; data shown are for 8 p.m. January 3 to 8 p.m. January 4, 2003.

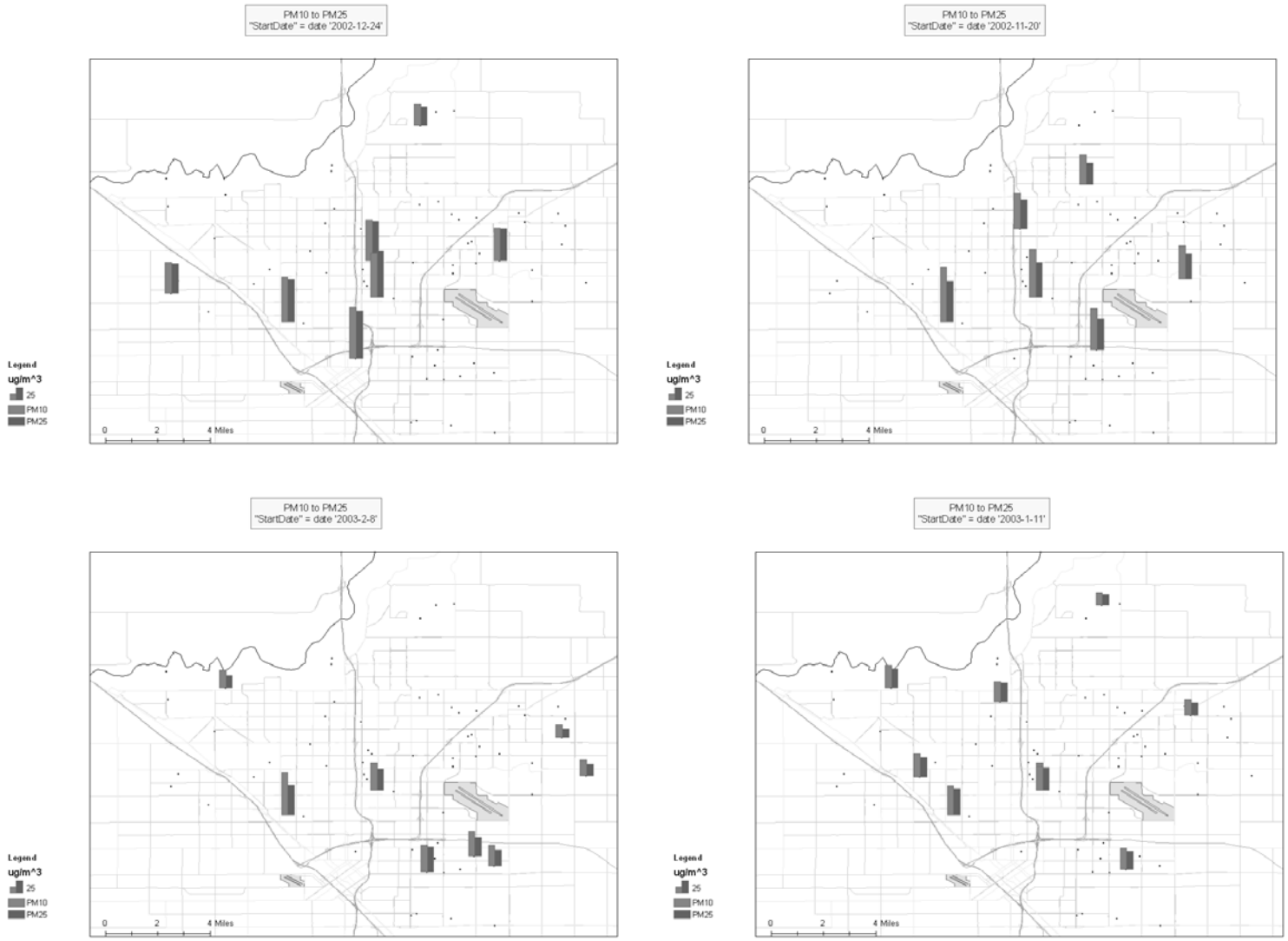


Figure 4.1.6-3. Spatial distribution of 24-hr average $PM_{2.5}$ and PM_{10} mass concentrations in FACES in the cool season; data shown are for November 20-21, 2002; December 24-25, 2002; January 11-12, 2003; and February 8-9, 2003.

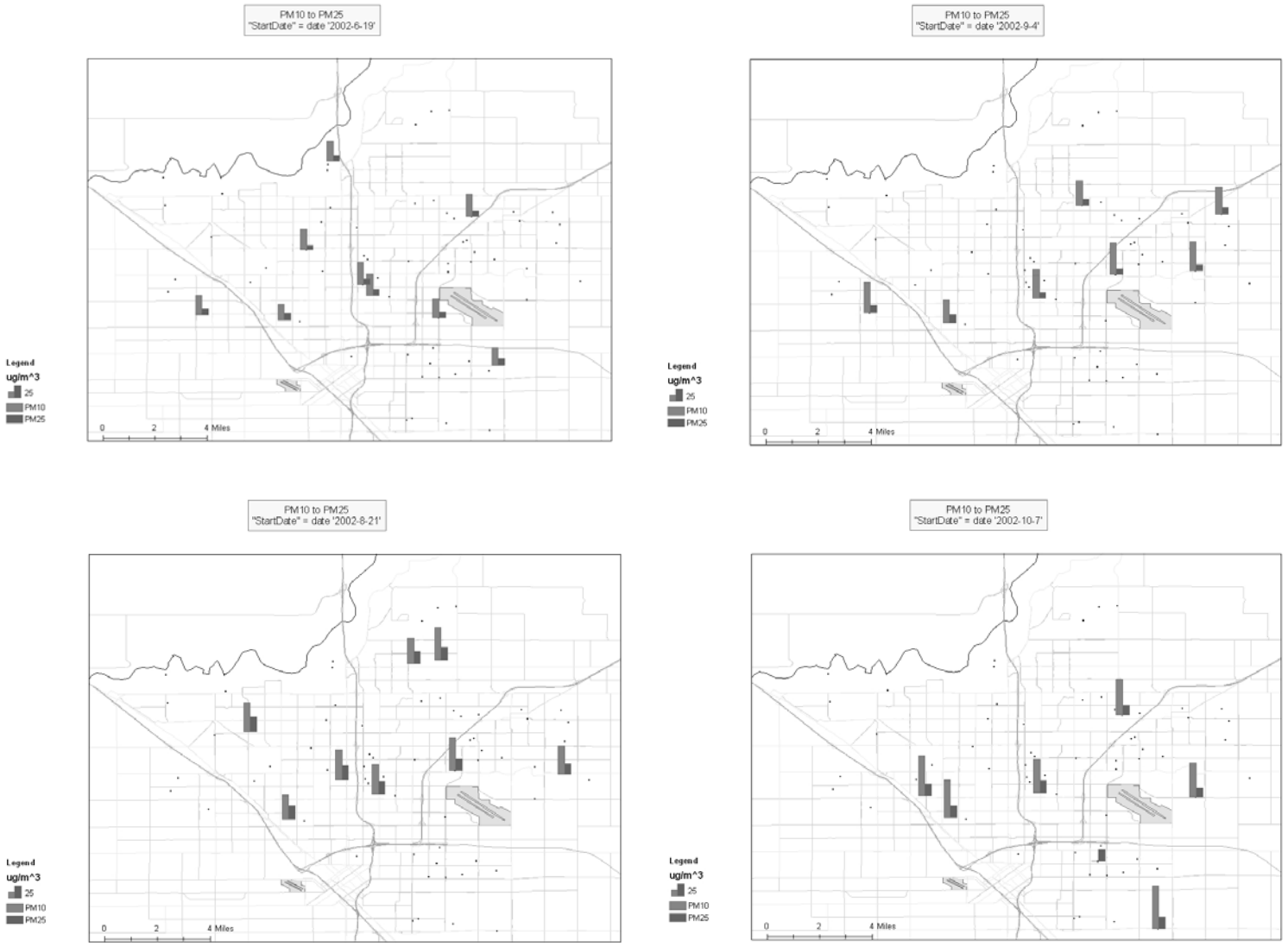


Figure 4.1.6-4. Spatial distribution of 24-hr average $PM_{2.5}$ and PM_{10} mass concentrations in FACES in the warm season; data shown are for June 19-20, August 21-22, September 4-5, and October 7-8, 2002.

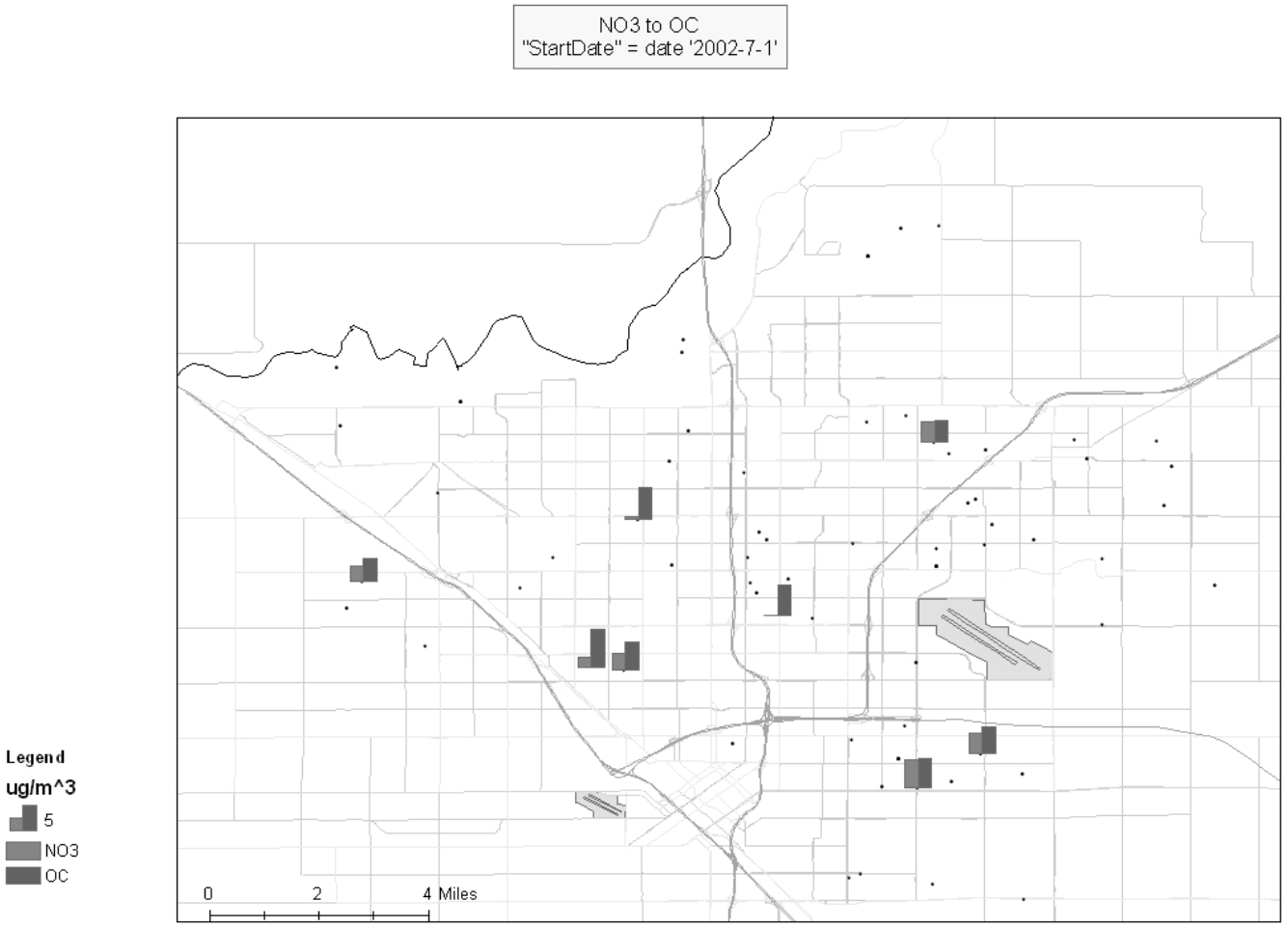


Figure 4.1.6-5. Spatial distribution of 24-hr average $PM_{2.5}$ NO_3 and OC concentrations in FACES in the warm season; data shown are for 8 p.m. July 1 to 8 p.m. July 2, 2002.

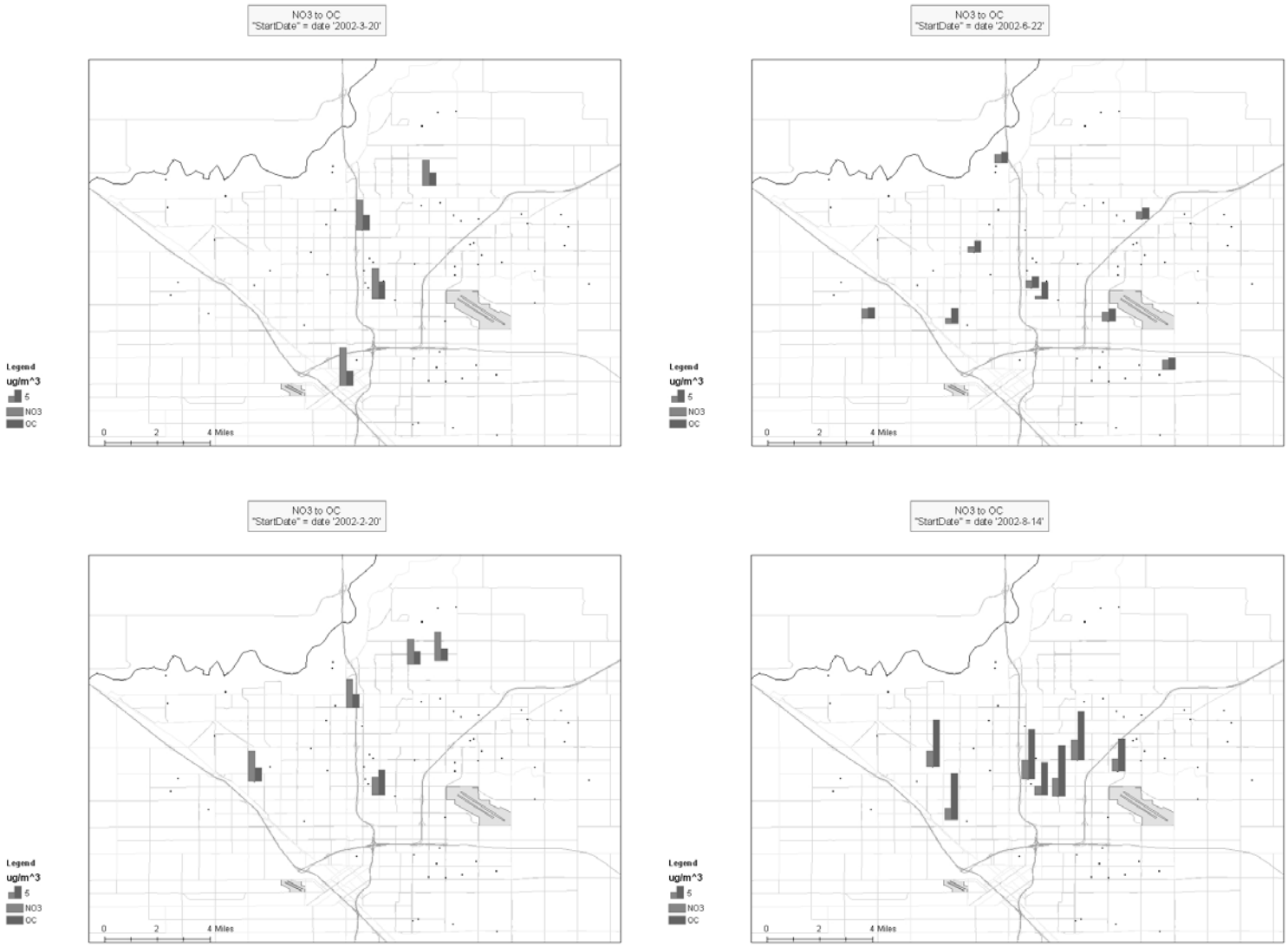


Figure 4.1.6-6. Spatial distribution of 24-hr average $PM_{2.5}$ NO_3 and OC concentrations in FACES; data shown are for February 20-21, March 20-21, June 22-23, and August 14-15, 2002.

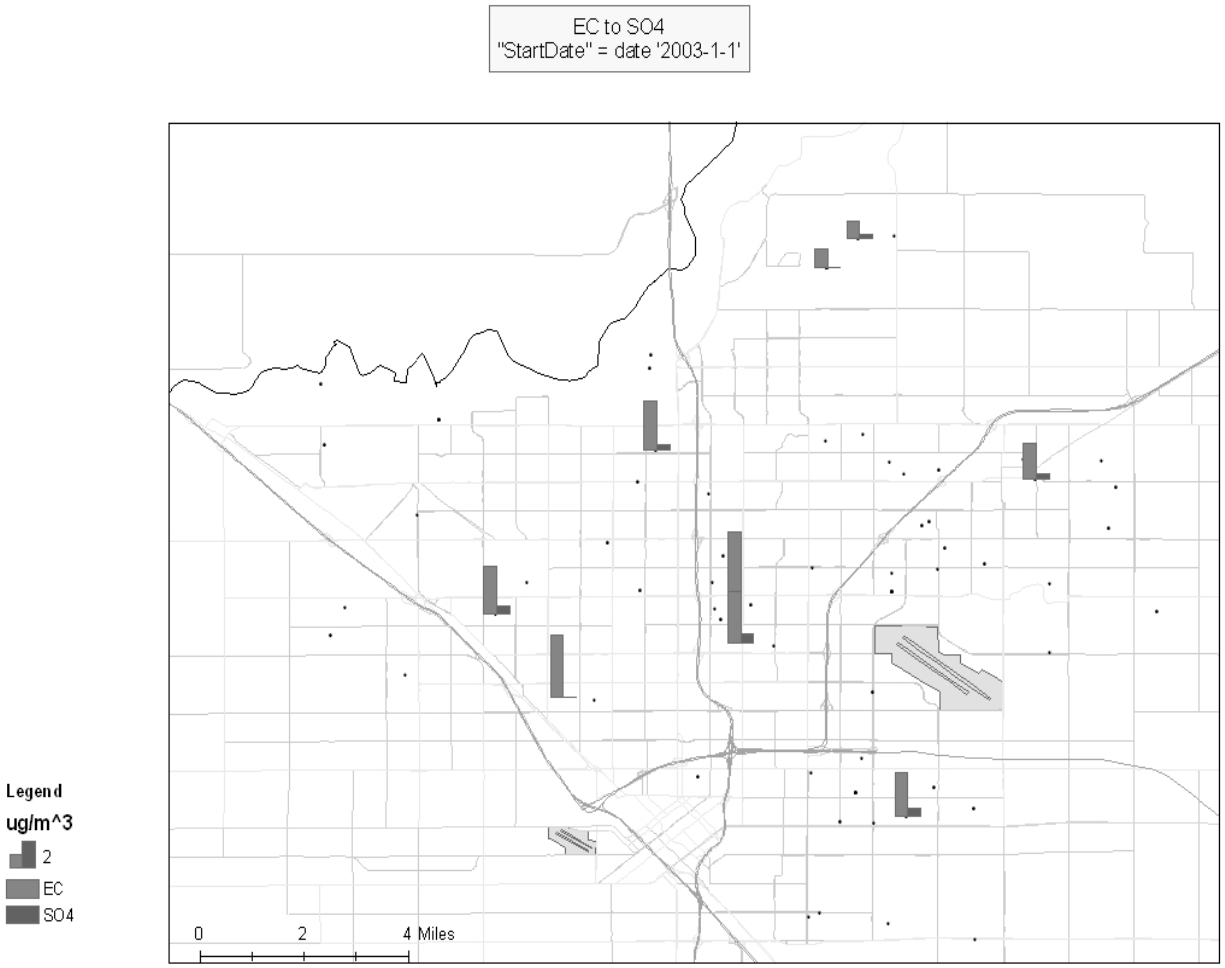


Figure 4.1.6-7. Spatial distribution of 24-hr average $PM_{2.5}$ EC and SO_4 concentrations in FACES in the cool season; data shown are for 8 p.m. January 1 to 8 p.m. January 2, 2003.

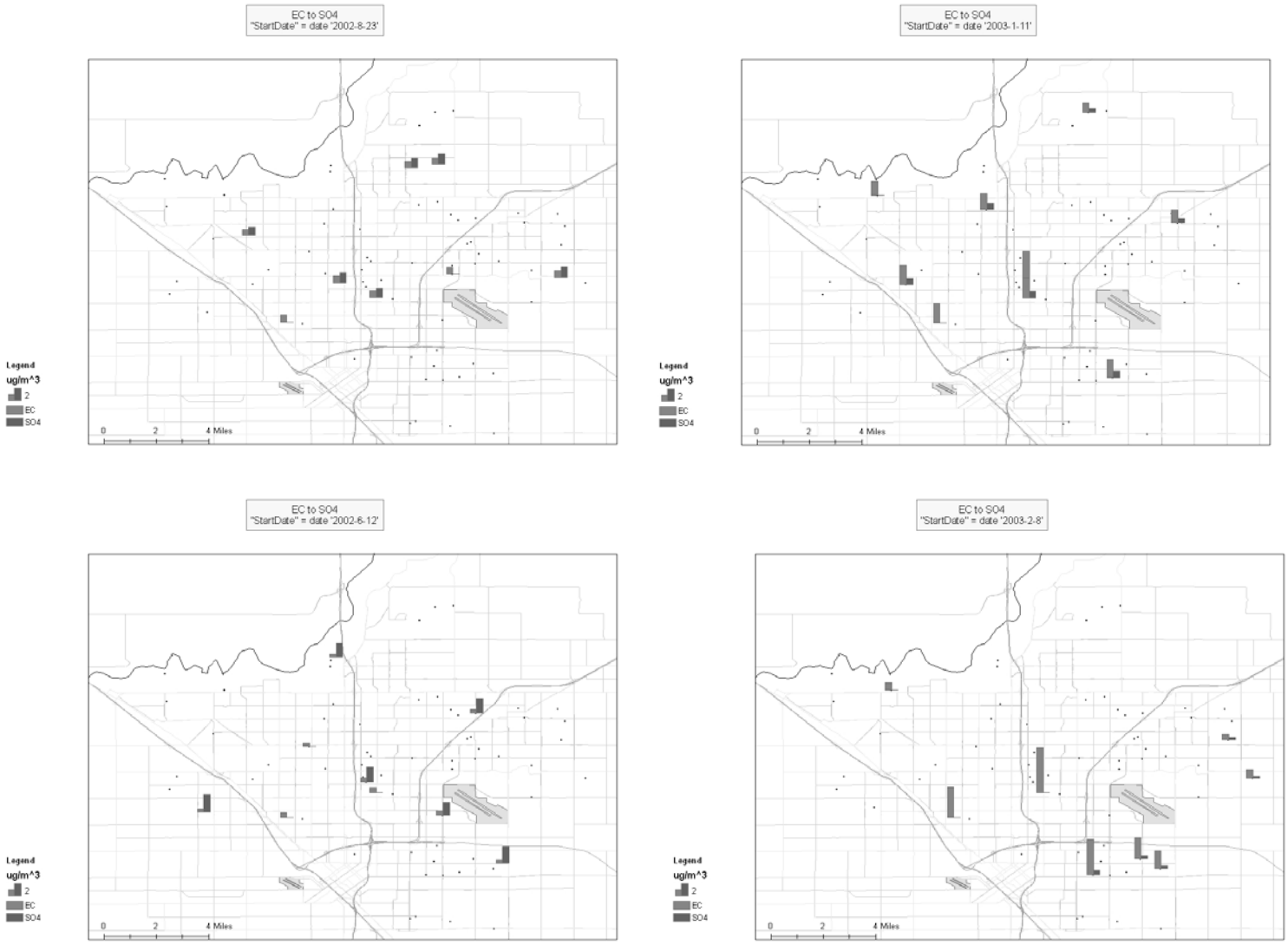


Figure 4.1.6-8. Spatial distribution of 24-hr average $PM_{2.5}$ EC and SO_4 concentrations in FACES; data shown are for June 12-13, 2002; August 23-24, 2003; January 11-12, 2003; and February 8-9, 2003.

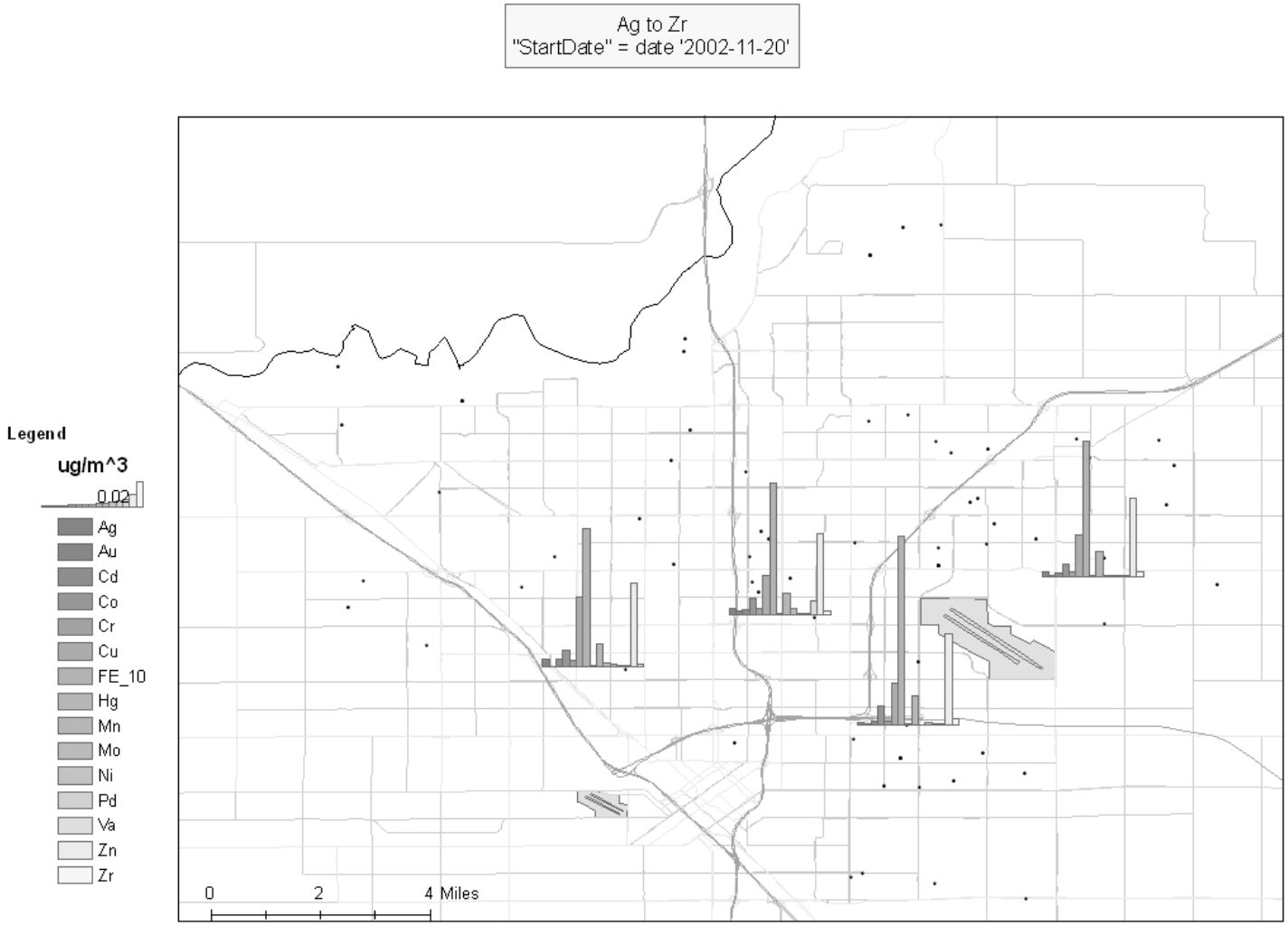


Figure 4.1.6-9. Spatial distribution of 24-hr average concentrations of 15 trace elements in FACES on November 20-21, 2002. Iron (FE) concentrations are displayed as one tenth their actual concentrations.

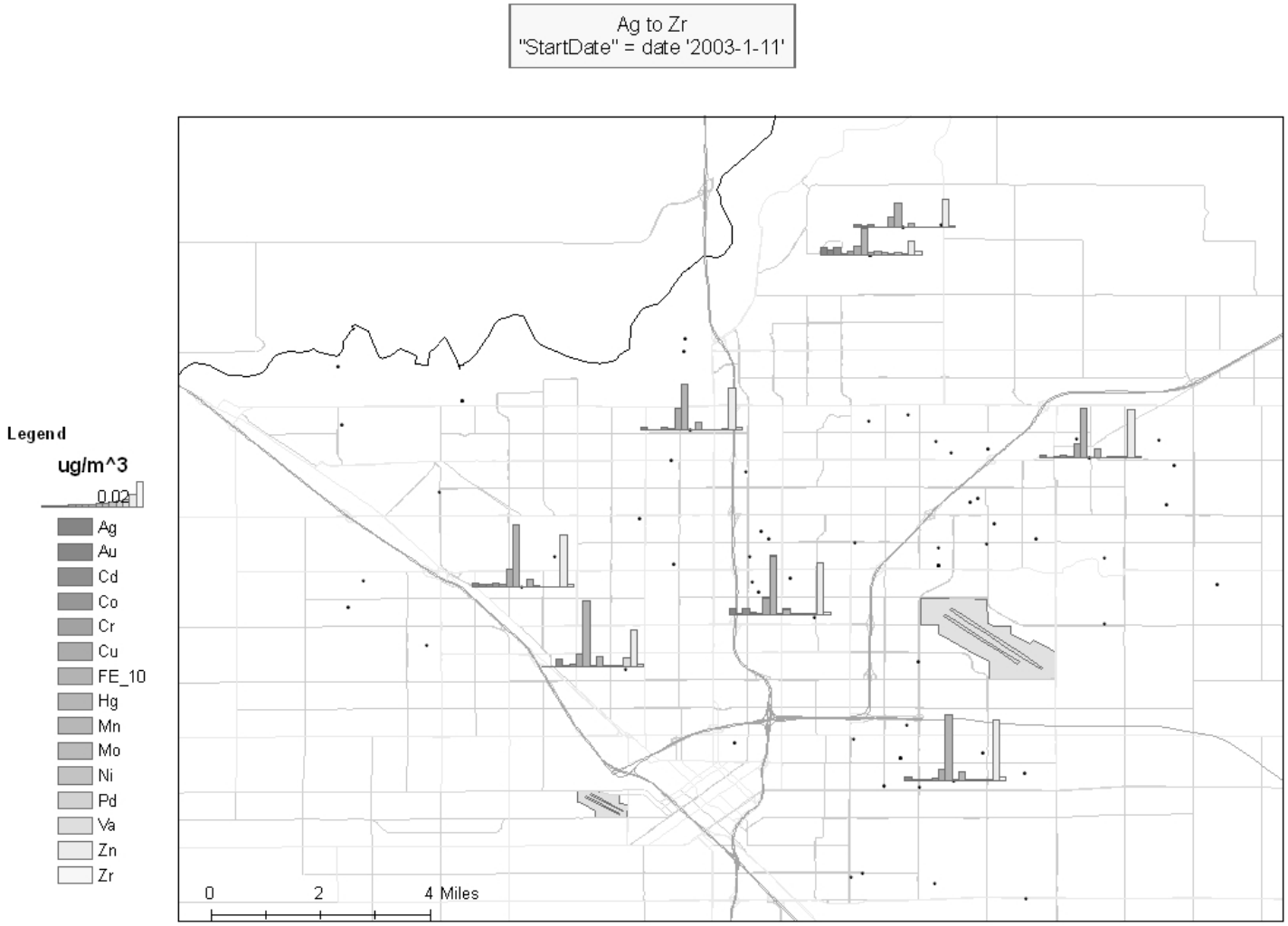


Figure 4.1.6-10. Spatial distribution of 24-hr average concentrations of 15 trace elements in FACES on January 11-12, 2003. Iron (FE) concentrations are displayed as one tenth their actual concentrations.

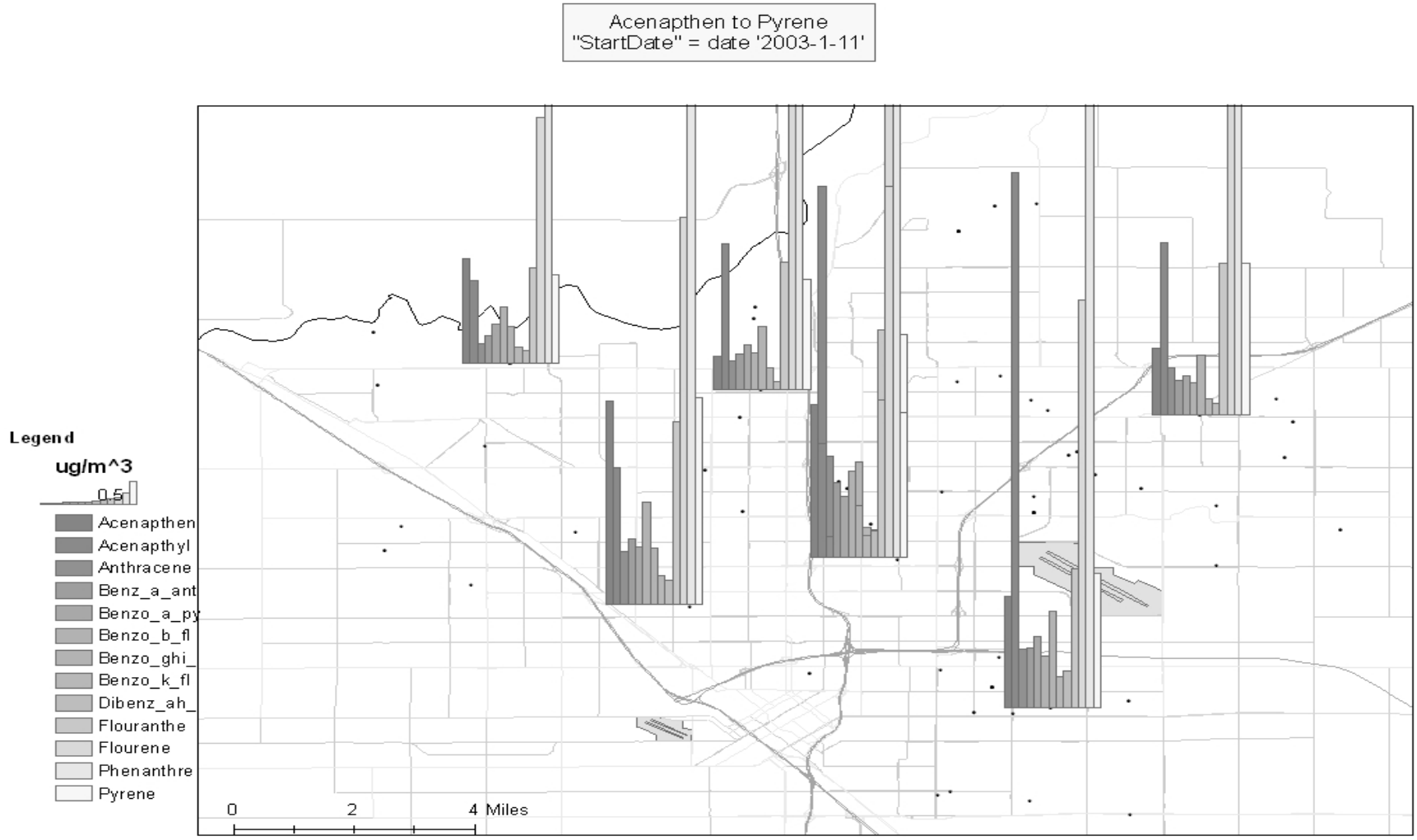


Figure 4.1.6-11. Spatial distribution of 24-hr average concentrations of 13 PAHs in FACES on January 11-12, 2003.

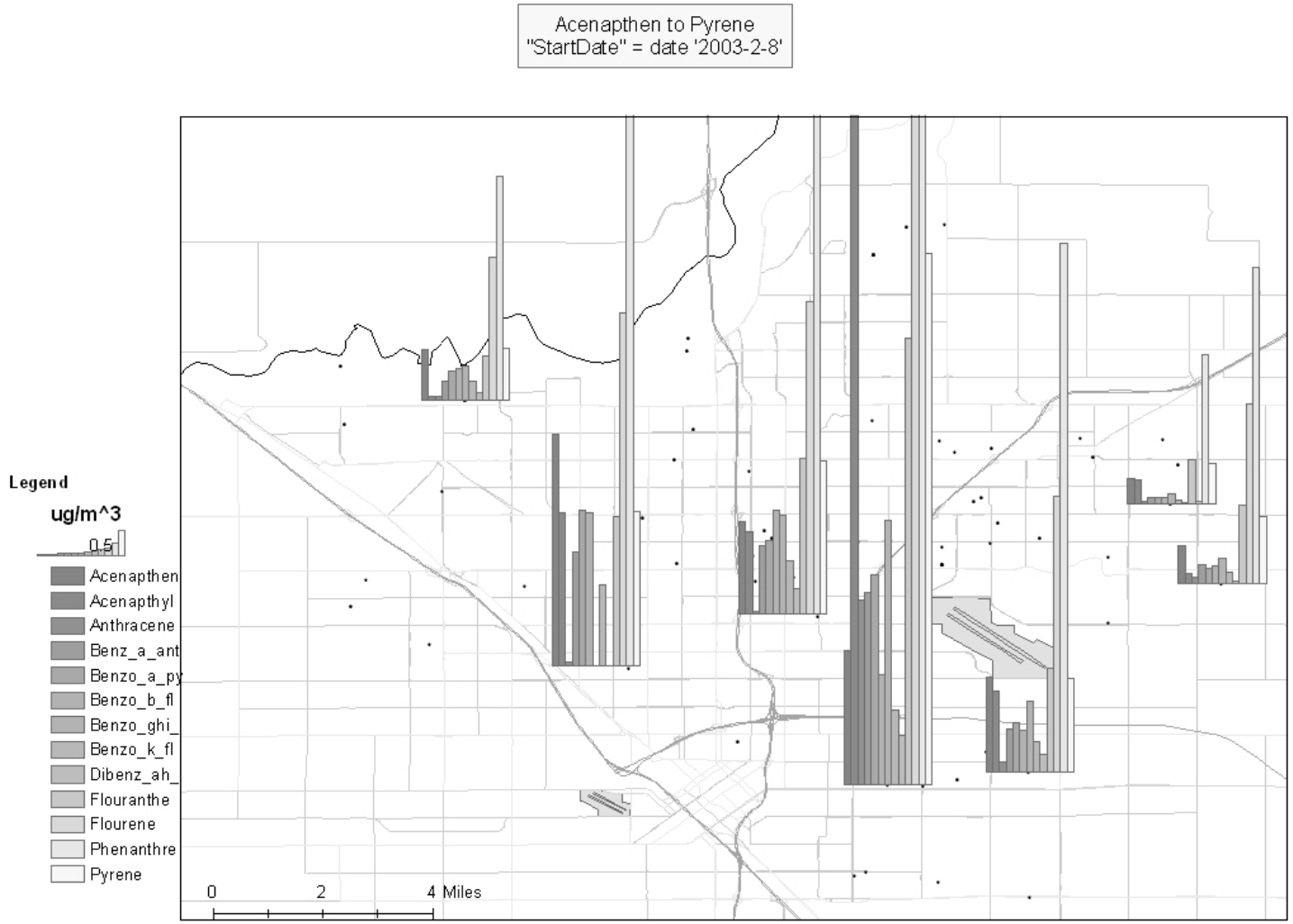


Figure 4.1.6-12. Spatial distribution of 24-hr average concentrations of 13 PAHs in FACES on February 8-9, 2003.

Table 4.1.6-1. Mean daily spatial coefficients of variation in 24-hr average concentrations in Fresno.

Pollutant	Annual	Cool Season				Warm Season			
	Mean Daily Spatial Coefficient of Variation	Mean Daily Spatial Coefficient of Variation	Standard Deviation of Daily CVs	No. Days	Average No. Sites per Day	Mean Daily Spatial Coefficient of Variation	Standard Deviation of Daily CVs	No. Days	Average No. Sites per Day
$PM_{2.5}$	0.18	0.18	0.11	189	4.2	0.18	0.09	128	5.0
Bscat	0.19	0.24	0.14	182	5.4	0.13	0.08	171	6.2
OC	0.24	0.31	0.19	121	3.9	0.18	0.07	84	4.0
EC	0.29	0.38	0.22	192	3.6	0.20	0.10	112	3.8
PPAH	0.42	0.35	0.14	164	3.0	0.50	0.14	105	3.0
SO_4	0.14	0.16	0.11	26	5.1	0.12	0.07	26	5.4
NO_3	0.28	0.28	0.15	158	3.6	0.28	0.14	112	3.8
PM_{10}	0.17	0.17	0.11	174	4.3	0.17	0.08	131	5.0
$PM_{2.5-10}$	0.30	0.30	0.19	134	3.0	0.30	0.10	100	3.0
Endotoxin	0.33	0.36	0.22	139	3.7	0.29	0.23	107	4.2
Gases									
NO	0.55	0.39	0.21	160	3.0	0.71	0.26	98	3.0
NO_2	0.21	0.20	0.06	506	4.6	0.22	0.07	366	4.3
NO_x	0.31	0.35	0.12	506	4.6	0.27	0.08	366	4.3
Carbon monoxide	0.31	0.27	0.11	515	4.5	0.34	0.12	366	4.5
Ozone	0.28	0.40	0.17	515	4.6	0.15	0.06	366	4.6
SO_2	0.44	0.62	0.30	115	3.0	0.26	0.17	87	3.0
Polycyclic Aromatic Hydrocarbons									
ACE	0.82	0.91	0.17	20	5.2	0.72	0.23	15	4.1
ACY	0.93	1.08	0.39	20	5.2	0.78	0.29	15	4.1
ANT	1.17	1.29	0.69	19	5.3	1.05	0.58	9	4.2
BAA	0.94	0.91	0.30	20	5.2	0.97	0.34	15	4.1
BAP	0.96	0.94	0.28	20	5.2	0.98	0.49	13	4.2
BBF	0.94	0.83	0.18	20	5.2	1.06	0.62	13	4.2

Pollutant	Annual	Cool Season				Warm Season			
	Mean Daily Spatial Coefficient of Variation	Mean Daily Spatial Coefficient of Variation	Standard Deviation of Daily CVs	No. Days	Average No. Sites per Day	Mean Daily Spatial Coefficient of Variation	Standard Deviation of Daily CVs	No. Days	Average No. Sites per Day
BGP	0.88	0.88	0.25	20	5.2	0.87	0.44	14	4.3
BKF	0.99	0.85	0.21	20	5.2	1.13	0.53	14	4.1
CRY	0.83	0.81	0.23	20	5.2	0.85	0.35	15	4.1
DBA	1.06	1.03	0.35	18	5.4	1.09	0.61	13	4.2
FLT	0.66	0.69	0.21	20	5.2	0.64	0.20	15	4.1
FLU	0.69	0.74	0.22	20	5.2	0.64	0.25	15	4.1
ICP	1.01	1.03	0.40	20	5.2	1.00	0.51	13	4.2
NAP	0.79	0.60	0.46	17	6.2	1.01	0.74	4	4.5
PHE	0.68	0.74	0.21	20	5.2	0.62	0.23	15	4.1
PYR	0.66	0.70	0.22	20	5.2	0.63	0.30	15	4.1
PM_{10} Trace Elements									
AG	1.50	1.43	0.45	124	3.7	1.57	0.36	52	4.7
AL	0.34	0.48	0.45	137	3.7	0.20	0.16	92	4.0
AS	1.07	0.80	0.48	135	3.7	1.34	0.45	72	4.2
AU	1.51	1.69	0.36	90	3.8	1.34	0.64	70	3.9
BA	0.93	0.98	0.54	129	3.7	0.88	0.42	91	4.0
BR	0.22	0.28	0.24	137	3.7	0.16	0.13	92	4.0
CA	0.20	0.23	0.14	138	3.7	0.17	0.13	92	4.0
CD	1.46	1.45	0.44	90	4.0	1.48	0.40	74	4.2
CL	0.45	0.39	0.24	138	3.7	0.50	0.39	92	4.0
CO	0.35	0.41	0.33	138	3.7	0.29	0.21	92	4.0
CR	0.65	0.78	0.51	138	3.7	0.52	0.32	92	4.0
CU	0.35	0.32	0.21	138	3.7	0.37	0.31	92	4.0
FE	0.20	0.22	0.15	138	3.7	0.17	0.15	92	4.0
GA	1.57	1.60	0.47	100	3.8	1.54	0.66	62	4.1
HG	1.48	1.41	0.60	84	4.0	1.55	0.51	81	4.0

Pollutant	Annual	Cool Season				Warm Season			
	Mean Daily Spatial Coefficient of Variation	Mean Daily Spatial Coefficient of Variation	Standard Deviation of Daily CVs	No. Days	Average No. Sites per Day	Mean Daily Spatial Coefficient of Variation	Standard Deviation of Daily CVs	No. Days	Average No. Sites per Day
IN	1.31	1.37	0.43	125	3.7	1.25	0.44	89	4.0
KP	0.17	0.18	0.11	138	3.7	0.16	0.13	92	4.0
LA	1.45	1.41	0.44	130	3.7	1.50	0.37	79	4.1
MG	1.06	1.25	0.49	119	3.8	0.88	0.42	89	4.0
MN	0.24	0.29	0.23	138	3.7	0.18	0.16	92	4.0
MO	1.22	1.39	0.51	118	3.8	1.05	0.57	90	4.0
NA	1.25	1.26	0.44	120	3.8	1.24	0.46	81	4.1
NI	0.44	0.51	0.34	138	3.7	0.38	0.29	92	4.0
PB	0.54	0.69	0.50	126	3.7	0.38	0.30	92	4.0
PD	1.46	1.44	0.44	116	3.8	1.48	0.41	72	4.2
PH	1.64	1.58	0.53	47	3.8	1.70	0.64	25	4.8
SB	1.26	0.99	0.49	128	3.7	1.54	0.36	65	4.4
SE	0.64	0.65	0.45	133	3.7	0.62	0.30	92	4.0
SI	0.19	0.21	0.15	138	3.7	0.18	0.15	92	4.0
SN	1.06	0.96	0.42	135	3.7	1.17	0.45	91	4.0
SR	0.34	0.46	0.38	138	3.7	0.22	0.16	92	4.0
SU	0.10	0.12	0.09	138	3.7	0.07	0.06	92	4.0
TI	0.45	0.61	0.47	138	3.7	0.29	0.30	92	4.0
TL	1.40	1.37	0.43	102	3.9	1.42	0.37	57	4.5
UR	1.39	1.42	0.56	113	3.8	1.36	0.44	83	4.1
VA	1.13	1.24	0.59	123	3.7	1.01	0.42	89	4.0
YT	1.11	1.25	0.53	117	3.8	0.96	0.44	90	4.0
ZN	0.22	0.23	0.16	138	3.7	0.21	0.17	92	4.0
ZR	0.51	0.59	0.40	135	3.7	0.42	0.33	92	4.0

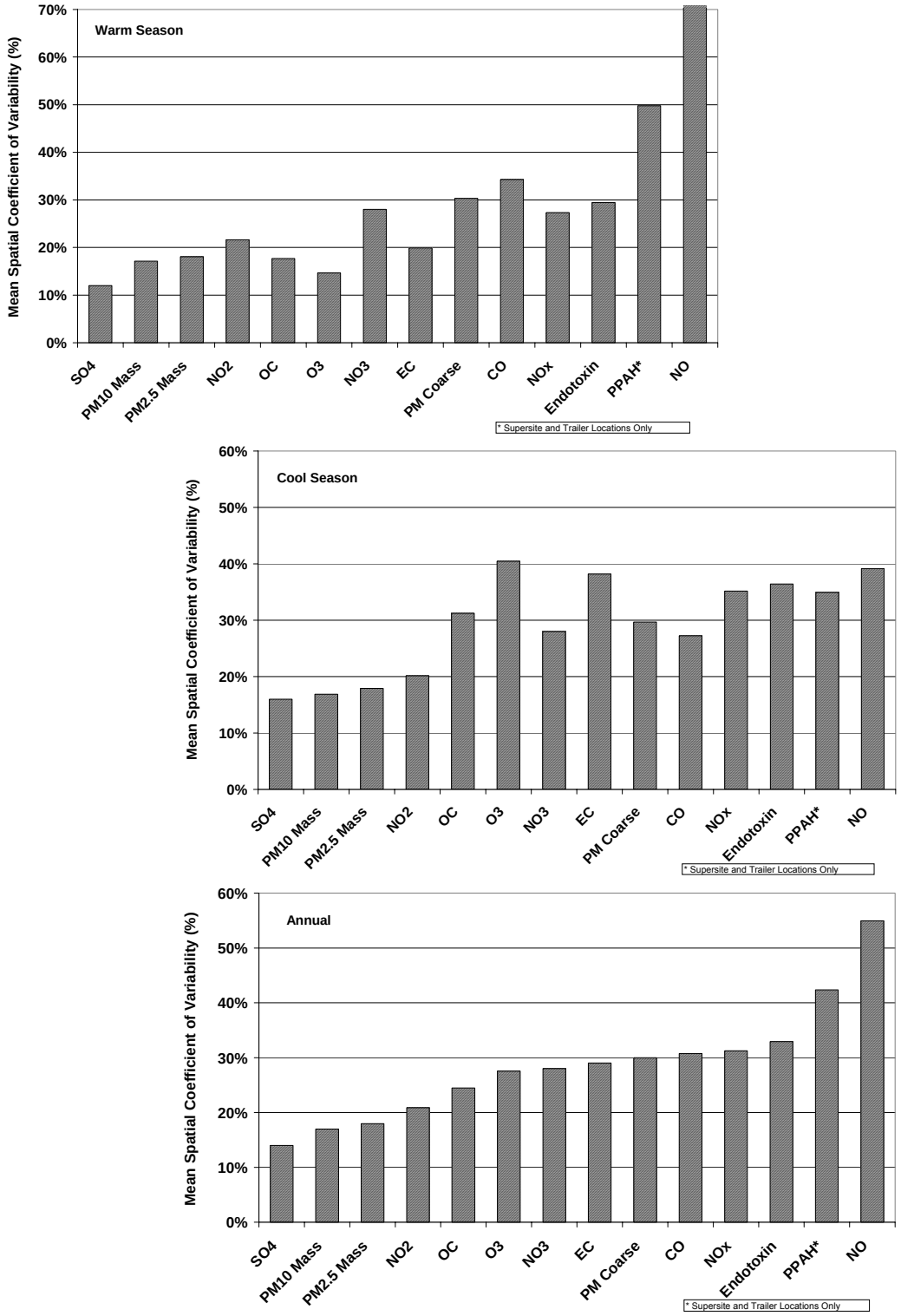


Figure 4.1.6-13. Mean spatial coefficient of variation in 24-hr concentrations of $PM_{2.5}$ mass, NO_3, OC, EC, SO_4, PPAH, PM_{10} mass, $PM_{2.5-10}$ mass, endotoxin, NO, NO_2, NO_x, CO, and ozone in Fresno in the warm season (top), cool season (middle), and annually (bottom). Error bars denote one standard deviation.

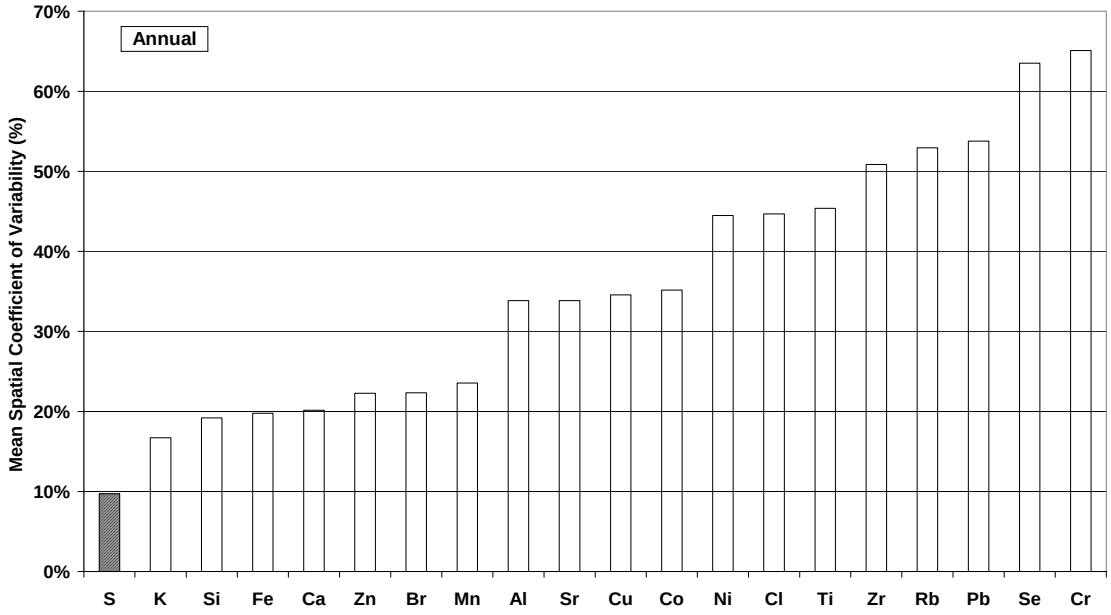


Figure 4.1.6-14. Mean spatial coefficient of variation in 24-hr PM_{10} elemental concentrations in Fresno. Error bars denote one standard deviation.

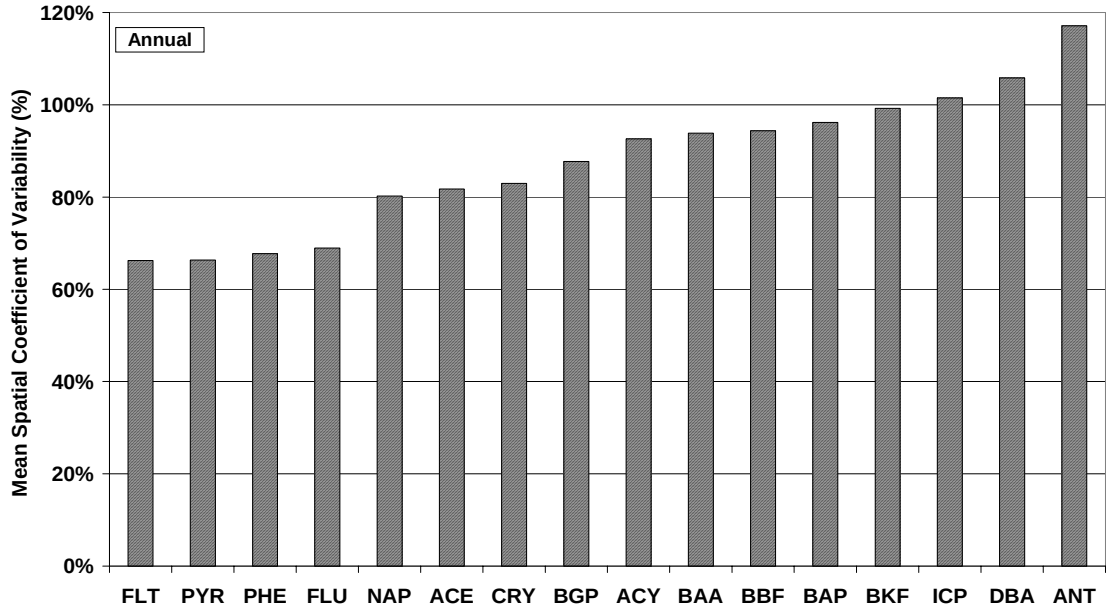


Figure 4.1.6-15. Mean spatial coefficient of variation in 24-hr PAH concentrations in Fresno. . Error bars denote one standard deviation.

Table 4.1.6-2. Relative ranking of outdoor pollutant concentration spatial variability in Fresno.

Rank of Mean Daily Spatial Coefficients of Variation		
Low (CV<20%)	Moderate (20%<CV <35%)	High CV > 35%
$PM_{2.5}$ Mass	OC	NO
B_{scat}	EC	SO_2
SO_4 and PM_{10} S	NO_3	PAHs
PM_{10} Mass	Endotoxin	PM_{10} Ag, As, Au, Ba, Cd
PM_{10} K, Si, Fe, Ca	NO_2, NO_x	PM_{10} Cl, Cr, Ga, Hg, In
	Ozone	PM_{10} La, Mg, Mo, Na, Ni
	CO	PM_{10} Pb, Pd, Ph, Sb, Se
	PM Coarse	PM_{10} Sn, Ti, Tl, Ur, Va
	PM_{10} Zn, Br, Mn	PM_{10} Yt, Zr
	PM_{10} Al, Sr, Cu, Co	

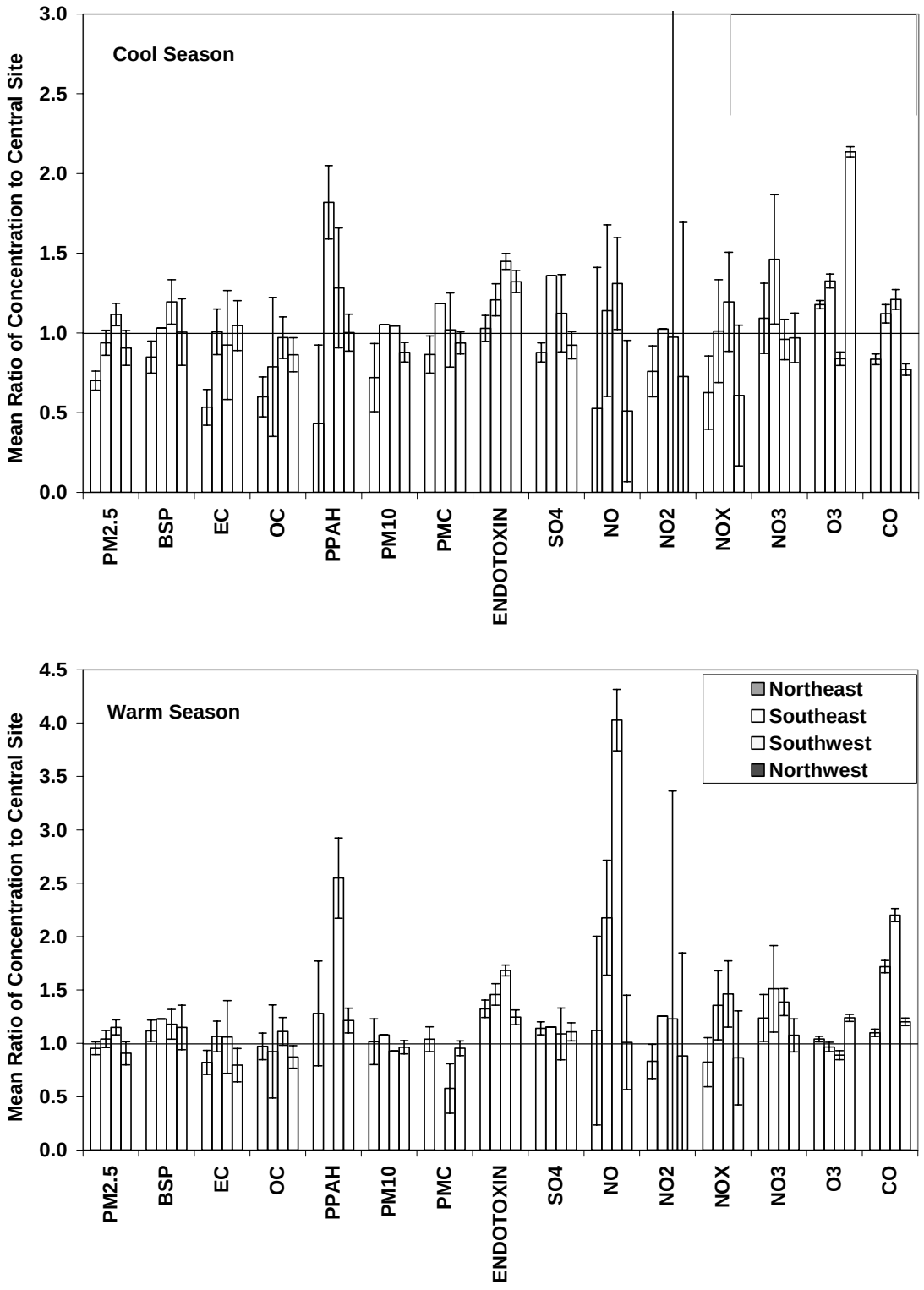


Figure 4.1.6-16. Mean ratios of 24-hr average concentrations at schools, residences, and other air quality stations in the community to those at the central site stratified by direction from the central site in the cool season (top) and warm season (bottom).

Table 4.1.6-3. Descriptive statistics of ratios of 24-hr average concentrations at schools, residences, and other air quality stations in the community to those at the central site in Fresno.

Parameter	No. of Cases	Median	Mean	Standard Deviation	Minimum	Maximum	Interquartile Range	95% CI Lower	95% CI Upper
$PM_{2.5}$	775	0.97	0.98	0.26	0.31	2.96	2.65	0.97	1.00
B_{scat}	650	1.06	1.09	0.39	0.06	4.98	4.92	1.06	1.12
EC	402	0.91	0.92	0.35	0.11	3.99	3.88	0.89	0.95
OC	104	0.91	0.94	0.26	0.39	2.36	1.97	0.89	0.99
NO_3	426	1.06	1.13	0.43	0.07	2.65	2.58	1.09	1.18
SO_4	57	1.03	1.06	0.23	0.48	2.14	1.66	1.00	1.12
PPAH	451	1.26	1.47	0.83	0.22	5.66	5.44	1.39	1.55
PM_{10}	787	0.94	0.96	0.25	0.31	2.90	2.58	0.94	0.98
$PM_{2.5-10}$	418	0.87	0.90	0.42	0.24	4.90	4.66	0.86	0.94
ENDO	527	1.08	1.38	1.22	0.24	18.40	18.17	1.27	1.48
Gases									
CO	1331	1.02	1.08	0.52	0.00	6.90	6.90	1.05	1.11
NO	1890	0.93	1.22	1.57	0.00	43.69	43.94	1.15	1.29
NO_2	1627	0.91	0.94	0.23	0.25	1.89	1.64	0.93	0.95
NO_x	2006	0.89	0.93	0.34	0.16	2.28	2.12	0.91	0.94
Ozone	2439	1.10	1.29	0.64	0.33	7.26	6.93	1.26	1.31
SO2	358	1.13	1.97	3.75	0.00	45.11	45.11	1.58	2.36
PM_{10} Elemental Concentrations									
AG	95	0.75	1.56	3.26	0.00	26.50	26.50	0.89	2.22
AL	455	1.05	1.32	2.55	0.00	46.99	46.99	1.08	1.55
AS	266	0.82	1.29	2.16	0.00	17.00	17.00	1.03	1.56
AU	95	0.11	1.20	2.83	0.00	16.00	16.00	0.62	1.77
BA	308	0.84	2.40	15.39	0.00	257.50	257.50	0.68	4.13
BR	421	1.00	1.04	0.53	0.00	7.86	7.86	0.99	1.09
CA	493	1.03	1.09	0.36	0.27	3.81	3.54	1.06	1.12
CD	104	0.34	0.84	1.32	0.00	7.18	7.18	0.59	1.10
CL	481	1.04	1.75	7.63	0.00	159.00	159.00	1.07	2.44
Co	386	1.05	1.27	1.42	0.00	18.88	18.88	1.12	1.41
CR	393	0.98	1.23	2.47	0.00	44.42	44.42	0.98	1.47
CU	482	0.93	1.10	1.05	0.14	14.76	14.62	1.00	1.19
FE	515	1.03	1.06	0.41	0.14	4.50	4.36	1.02	1.10
GA	79	0.26	0.78	1.05	0.00	6.00	6.00	0.54	1.01
HG	130	0.31	1.28	2.24	0.00	13.00	13.00	0.89	1.66
IN	184	0.58	1.36	3.11	0.00	33.00	33.00	0.90	1.81
KP	497	1.01	1.04	0.33	0.24	3.27	3.03	1.01	1.07
LA	125	0.63	1.75	4.50	0.00	35.50	35.50	0.96	2.55
MG	237	0.94	1.98	5.43	0.00	68.33	68.33	1.29	2.68
MN	490	1.03	1.14	0.59	0.00	5.33	5.33	1.09	1.19
MO	211	0.68	1.82	5.86	0.00	75.00	75.00	1.03	2.62
NA	163	0.67	1.71	3.32	0.00	23.43	23.43	1.19	2.22
NI	436	1.07	2.13	9.00	0.00	166.86	166.86	1.28	2.98

Table 4.1.6-3 continued

Parameter	No. of Cases	Median	Mean	Standard Deviation	Minimum	Maximum	Interquartile Range	95% CI Lower	95% CI Upper
PB	404	1.01	1.51	2.71	0.00	29.04	29.04	1.24	1.77
PD	97	0.24	1.31	2.80	0.00	18.00	18.00	0.74	1.87
PH	37	0.79	1.52	2.63	0.00	11.98	11.98	0.64	2.40
RB	357	1.06	1.34	1.50	0.00	13.50	13.50	1.18	1.49
SB	160	0.91	1.78	3.66	0.00	29.33	29.33	1.20	2.35
SE	434	1.00	1.52	2.32	0.00	31.00	31.00	1.30	1.74
SI	505	1.05	1.12	0.43	0.19	4.11	3.92	1.08	1.16
SN	245	0.81	1.56	3.16	0.00	32.67	32.67	1.16	1.96
SR	446	1.03	1.15	1.20	0.00	23.76	23.76	1.04	1.26
SU	453	0.97	0.95	0.17	0.20	1.84	1.63	0.93	0.96
TI	380	1.07	1.28	1.82	0.00	33.29	33.29	1.09	1.46
TL	86	0.84	1.62	2.63	0.00	17.00	17.00	1.05	2.18
UR	150	0.70	1.62	3.05	0.00	28.00	28.00	1.13	2.11
VA	209	0.85	1.46	3.60	0.00	37.00	37.00	0.96	1.95
YT	201	0.75	1.44	2.25	0.00	21.00	21.00	1.12	1.75
ZN	546	1.00	1.06	0.47	0.26	6.21	5.95	1.02	1.10
ZR	381	1.04	1.26	1.22	0.00	12.50	12.50	1.14	1.39
Polycyclic Aromatic Hydrocarbons:									
ACE	71	0.95	1.17	1.13	0.09	6.23	6.14	0.91	1.44
ACY	88	0.91	1.17	1.26	0.00	7.15	7.15	0.90	1.44
ANT	37	0.81	1.31	1.52	0.01	6.59	6.58	0.80	1.81
BAA	63	0.59	1.42	2.92	0.00	19.12	19.12	0.68	2.15
BAP	68	0.61	1.02	1.58	0.00	9.63	9.63	0.64	1.40
BBF	57	0.69	1.80	5.06	0.00	28.73	28.73	0.46	3.14
BGP	73	0.88	1.26	2.27	0.00	15.39	15.39	0.73	1.79
BKF	66	0.60	0.87	1.04	0.00	6.96	6.96	0.62	1.13
CRY	59	0.60	0.85	0.75	0.00	3.11	3.11	0.66	1.05
DBA	54	0.97	1.14	1.32	0.00	8.56	8.56	0.78	1.50
FLT	55	0.72	0.77	0.41	0.19	2.19	2.00	0.66	0.88
FLU	70	0.91	0.99	0.73	0.00	3.94	3.94	0.82	1.17
ICP	62	0.56	1.06	1.76	0.00	10.59	10.59	0.61	1.50
NAP	50	0.72	0.86	0.54	0.00	3.27	3.27	0.71	1.01
PHE	67	0.68	0.76	0.39	0.15	1.81	1.66	0.67	0.86
PYR	60	0.69	0.83	0.61	0.09	3.38	3.28	0.67	0.98
Pollen and Fungal Spores									
TOP	89	0.92	1.62	3.57	0.12	33.50	0.73	0.88	2.37
ALTE	88	3.64	4.59	3.82	0.80	28.26	3.46	3.79	5.39
AGFG	88	1.78	2.37	1.91	0.34	11.33	1.23	1.98	2.77
CLAD	88	1.18	1.32	1.14	0.31	11.40	0.38	1.08	1.56
TOTFS	88	1.27	1.39	0.93	0.30	9.14	0.38	1.20	1.59

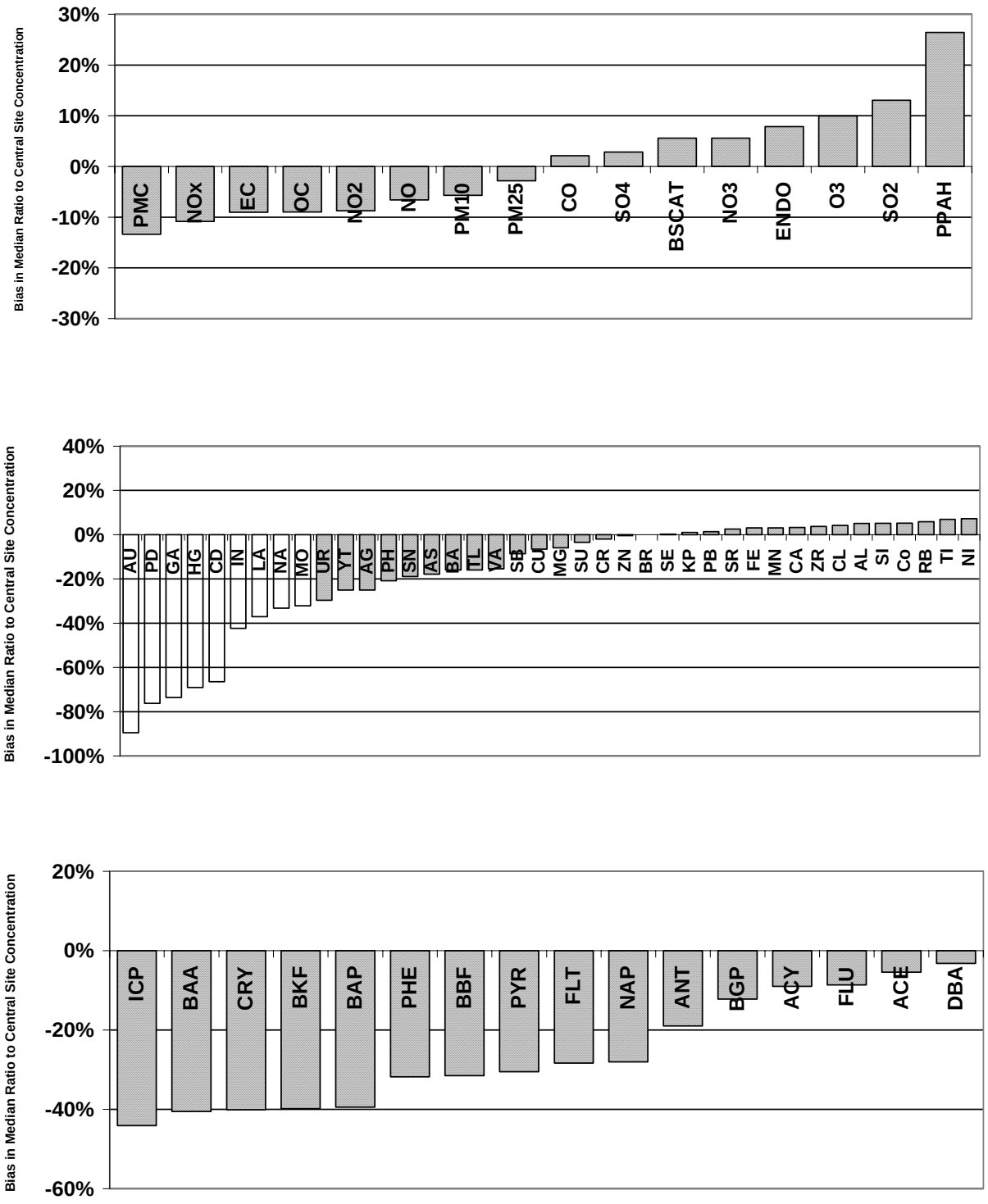


Figure 4.1.6-17. Bias in median ratios of 24-hr average concentrations at schools, residences, and other air quality stations in the community to those at the central site in Fresno.

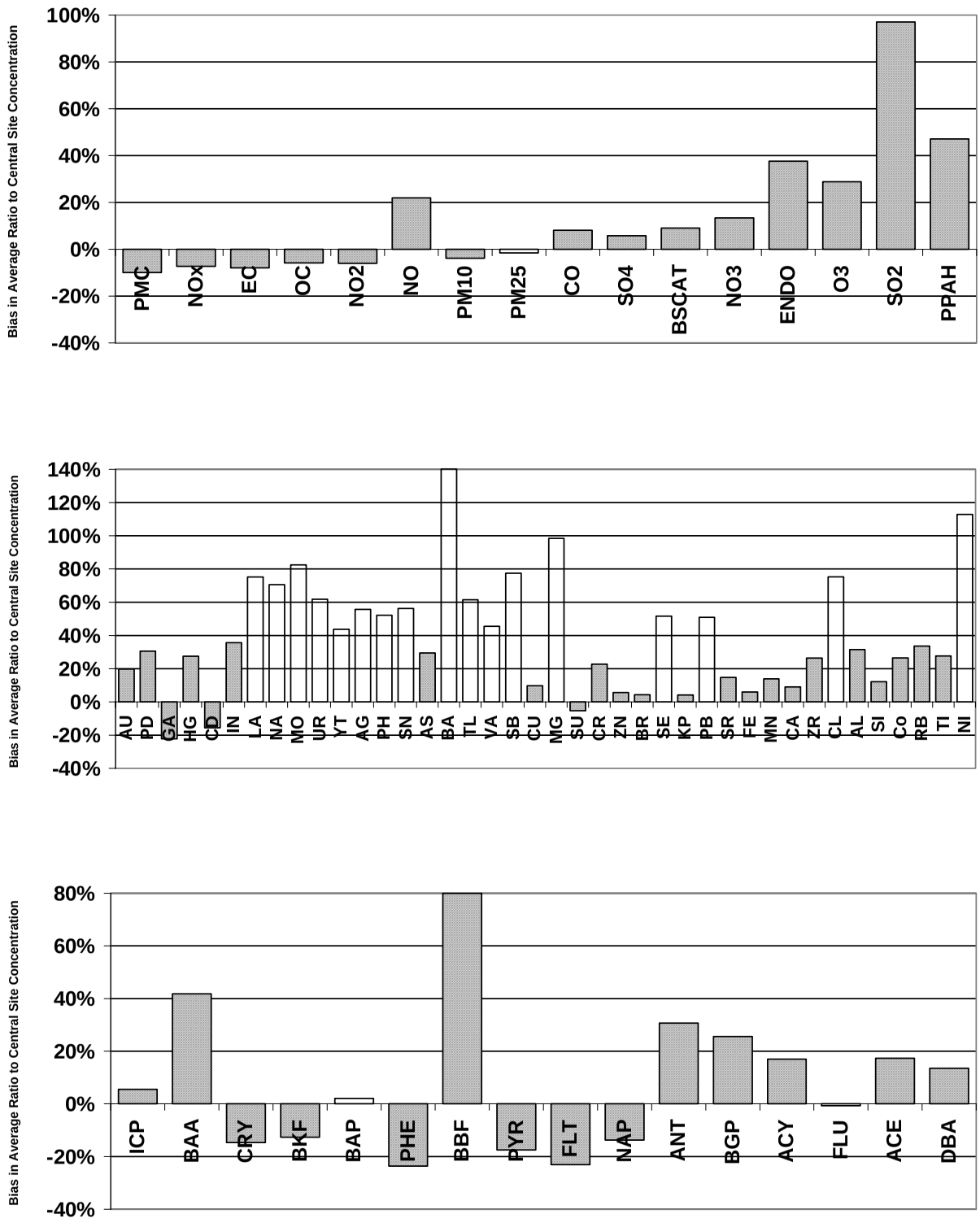


Figure4.1.6-18. Bias in mean ratios of 24-hr average concentrations at schools, residences, and other air quality stations in the community to those at the central site in Fresno.

Table 4.1.6-4. Coefficient of determination (r^2) for associations between traffic density and freeway traffic metrics, and the ratio of PM chemical component to central site levels across Fresno.

Chemical Component	Number of Cases		Traffic Density 150m Falloff		Traffic Density 300m Falloff		Inverse Distance to Nearest Freeway		Inverse Distance Weighted Traffic Volume on Nearest Freeway		Inverse Distance Squared Weighted Traffic Volume on Nearest Freeway	
		Warm	Cool	Warm	Cool	Warm	Cool	Warm	Cool	Warm	Cool	Warm
$PM_{2.5}$ Mass	385	354	0.015*	0.048*	0.000	0.054*	0.024*	0.026*	0.041*	0.026*	0.067*	0.141*
EC	171	211	0.153*	0.014*	0.164*	0.031*	0.271*	0.036*	0.254*	0.031*	0.268*	0.188*
OC	32	64	0.083	0.000	0.130+	0.000	0.129+	0.074+	0.163+	0.073+	0.091	0.151*
ACE	42	22	0.000	0.000	0.011	0.000	0.000	0.000	0.056	0.259*	0.343*	0.201+
Cool ACY	64	16	0.152*	0.036	0.190*	0.080	0.014	0.000	0.038	0.000	0.000	0.000
ANT	33	0	0.000	-	0.000	-	0.407*	-	0.159	-	0.010	-
BAA	35	22	0.000	0.000	0.000	0.004	0.000	0.499*	0.030	0.366*	0.030	0.000
BAP	42	19	0.000	0.491*	0.024	0.479*	0.050	0.515*	0.289*	0.331*	0.151*	0.000
BBF	38	15	0.000	0.546*	0.000	0.655*	0.049	0.525*	0.245*	0.294+	0.149+	0.000
BGP	47	19	0.000	0.567*	0.008	0.529*	0.052	0.461*	0.145*	0.268+	0.011	0.000
BKF	45	18	0.000	0.000	0.000	0.000	0.105+	0.049	0.145*	0.193+	0.057	0.122
CRY	31	27	0.009	0.000	0.060	0.007	0.048	0.306*	0.218*	0.224*	0.013	0.000
DBA	32	15	0.000	0.000	0.000	0.000	0.000	0.000	0.037	0.000	0.143+	0.000
FLT	28	24	0.104	0.000	0.072	0.000	0.039	0.000	0.167+	0.057	0.087	0.085
FLU	42	24	0.011	0.028	0.000	0.056	0.410*	0.007	0.258*	0.000	0.375*	0.030
ICP	39	19	0.000	0.561*	0.000	0.564*	0.000	0.487*	0.080+	0.268+	0.150*	0.000
NAP	45	0	0.181*	-	0.096+	-	0.000	-	0.000	-	0.000	-
PHE	44	22	0.019	0.000	0.000	0.000	0.064	0.000	0.156*	0.036	0.358*	0.617*
PYR	30	27	0.047	0.000	0.076	0.000	0.026	0.000	0.077	0.053	0.044	0.077

+ $p < 0.05$
* $p < 0.01$

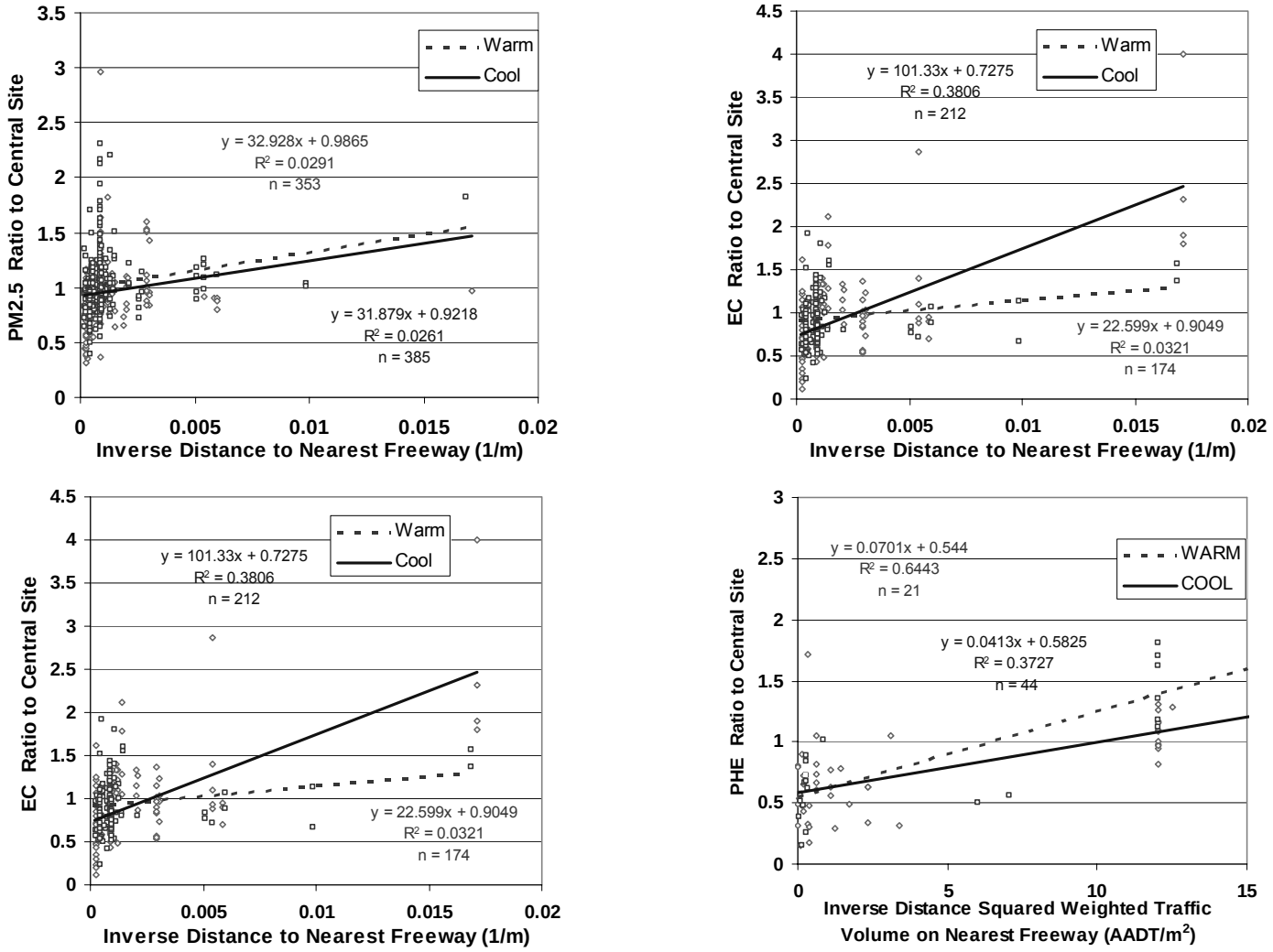


Figure 4.1.6-19. Relationship between freeway traffic indicators and the ratio of 24-hr average concentrations of $PM_{2.5}$ mass, EC, OC, and phenathrene (PHE) at residences and schools to concentrations at the central site in Fresno with a few outliers removed for display purposes.

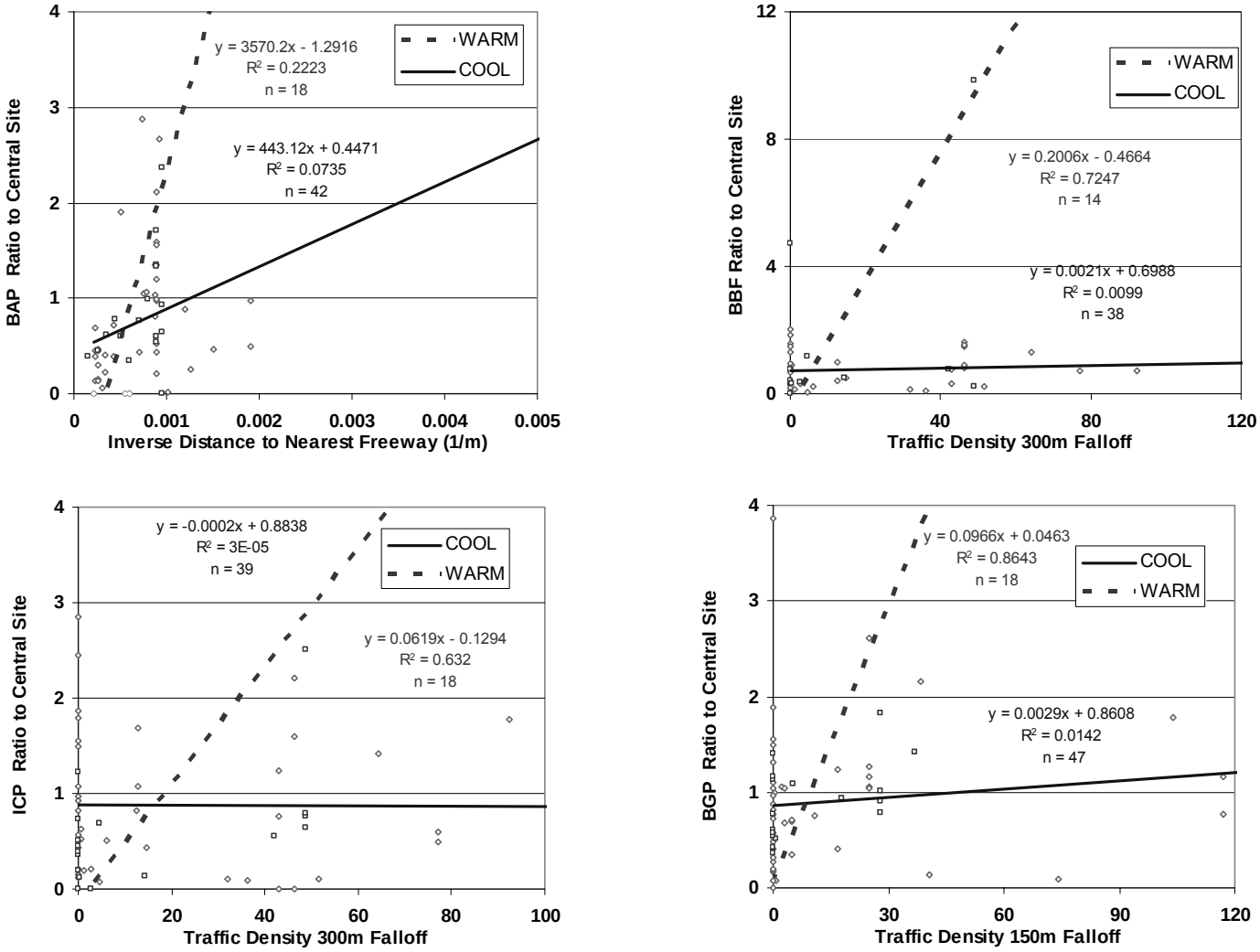


Figure 4.1.6-20. Relationship between freeway traffic indicators and the ratio of 24-hr average concentrations of selected PAHs at residences and schools to concentrations at the central site in Fresno with a few outliers removed for display purposes. The PAHs are benzo[a]pyrene (BAP), benzo[b]flouranthene (BBF), indeno[1,2,3-cd]pyrene (ICP), and benzo[ghi]perylene (BGP).

4.1.7 Exposure Modeling

As described in Section 3.4.7.2, the FACES individual exposure model is a microenvironmental model intended to characterize exposure of subjects to air pollution of outdoor origin. The model considers five microenvironments: indoors and outdoors at residences, indoors and outdoors at schools, and in vehicles. The model was applied to simulate the daily individual exposures of FACES participants to selected pollutants from November 2000 through March 2003. The simulated pollutants included commonly modeled species, such as ozone, NO_2, and $PM_{2.5}$, and biological agents for which little or no personal modeling is reported in the literature. Unfortunately, the individual exposure monitoring data that were needed to evaluate the accuracy and precision of the exposure model were not collected in FACES. Although evaluation of the performance of the model against actual personal monitoring data is not possible, comparisons can be made to the central site ambient exposures as a point of reference.

A principal objective of the modeling was to generate individual exposure estimates, rather than community mean exposure estimates, for use in the health analysis Individual exposure estimates are intended to account for individual differences in time activity, geographic location within the community, and household characteristics. Figure 4.1.7-1 illustrates the range of estimated 8-hr daily maximum individual exposure concentrations for FACES subjects on panel study days. It shows that on days when ambient ozone concentrations were high, the estimated 8-hr daily maximum individual exposure concentrations range from about 20 ppb to 60 ppb for FACES participants. It is common for the highest estimated personal ozone levels to be three times higher than the lowest estimate, indicating a large (e.g., threefold) range in the personal estimates.

Figures 4.1.7-2 through 4.1.7-6 illustrate the range of daily individual exposure concentrations estimated by the model for 24-hr ozone, NO_2, $PM_{2.5}$, EC, PM coarse, endotoxin, alternaria, agricultural fungi, and total pollen on panel study days. They also show the daily mean individual exposure estimates for all subjects and the central site concentrations on panel study days from November 1, 2000, to March 31, 2003. The mean individual exposure across all panel study days is compared to the corresponding mean central site concentrations in Table 4.1.7-1. The figures and table illustrate the three principal characteristics of the results:

1. On most days, individual exposure estimates vary between subjects by a factor of two for $PM_{2.5}$ mass and by a factor of three or more for other pollutants considered here. The large variations between subjects in estimated exposure to pollutants of ambient origin suggest that the use of central site ambient concentrations for individual exposure assignments in FACES may result in considerable exposure misclassification and assignment error. The magnitude of the error is unknown because the individual exposure model performance has not been evaluated against individual exposure observations.
2. The mean estimated individual exposure concentrations of pollutants of ambient origin are consistently lower than the central site ambient concentrations. On average, the mean individual exposure concentrations range from 15% of central site ambient concentrations

for total pollens to 59% of central site ambient concentrations for $PM_{2.5}$ mass. The pollutant ranking (from highest to lowest) for mean ratio of individual exposure to central site ambient concentrations is $PM_{2.5}$ mass, endotoxin, EC, agricultural fungi, NO_2, PM coarse, alternaria, ozone, cladosporium, and total pollen. The biases in individual exposure levels relative to central site ambient concentrations are primarily a result of lower indoor than outdoor concentrations caused by pollutant deposition on indoor surfaces and penetration losses. Spatial differences in ambient concentrations within the community and indoor chemical reactions may also contribute to the differences.

3. The between-subject variations in individual exposure estimates are generally greater for biological agents than conventional pollutants. For example, on a day with relative high pollen grain and fungal spore levels, the individual exposure estimates may range from 100 to 800 total pollen grains/m^3 and from 10 to 250 alternaria spores/m^3. In contrast, on a day when conventional pollutant levels are high, the individual exposure estimates may range from 40 to 80 $\mu g/m^3$ for $PM_{2.5}$ mass and from 8 to 25 ppb for NO_2. The variance between subjects for primary PM components, such as EC, is also considerably higher than those for $PM_{2.5}$ mass.

These findings represent the initial results of the FACES individual exposure modeling. Additional work is needed to evaluate the accuracy and precision of the exposure model for pollutants of outdoor origin, and additional development and evaluation work is needed to account for indoor source contributions to total individual exposures of FACES participants.

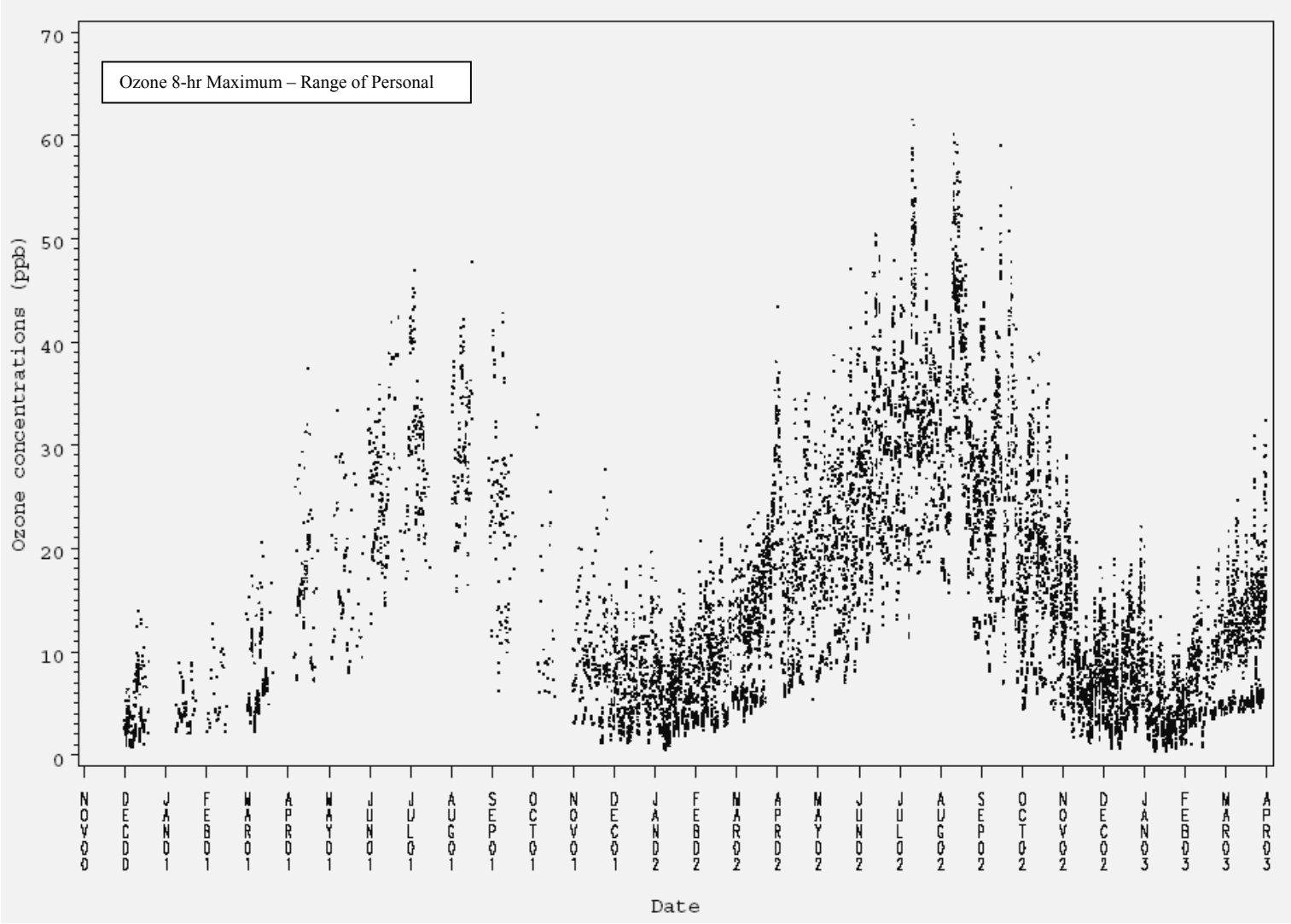


Figure 4.1.7-1. Range of estimated 8-hr daily maximum individual exposure concentrations for FACES subjects on days with panel studies from November 1, 2000, to March 31, 2003.

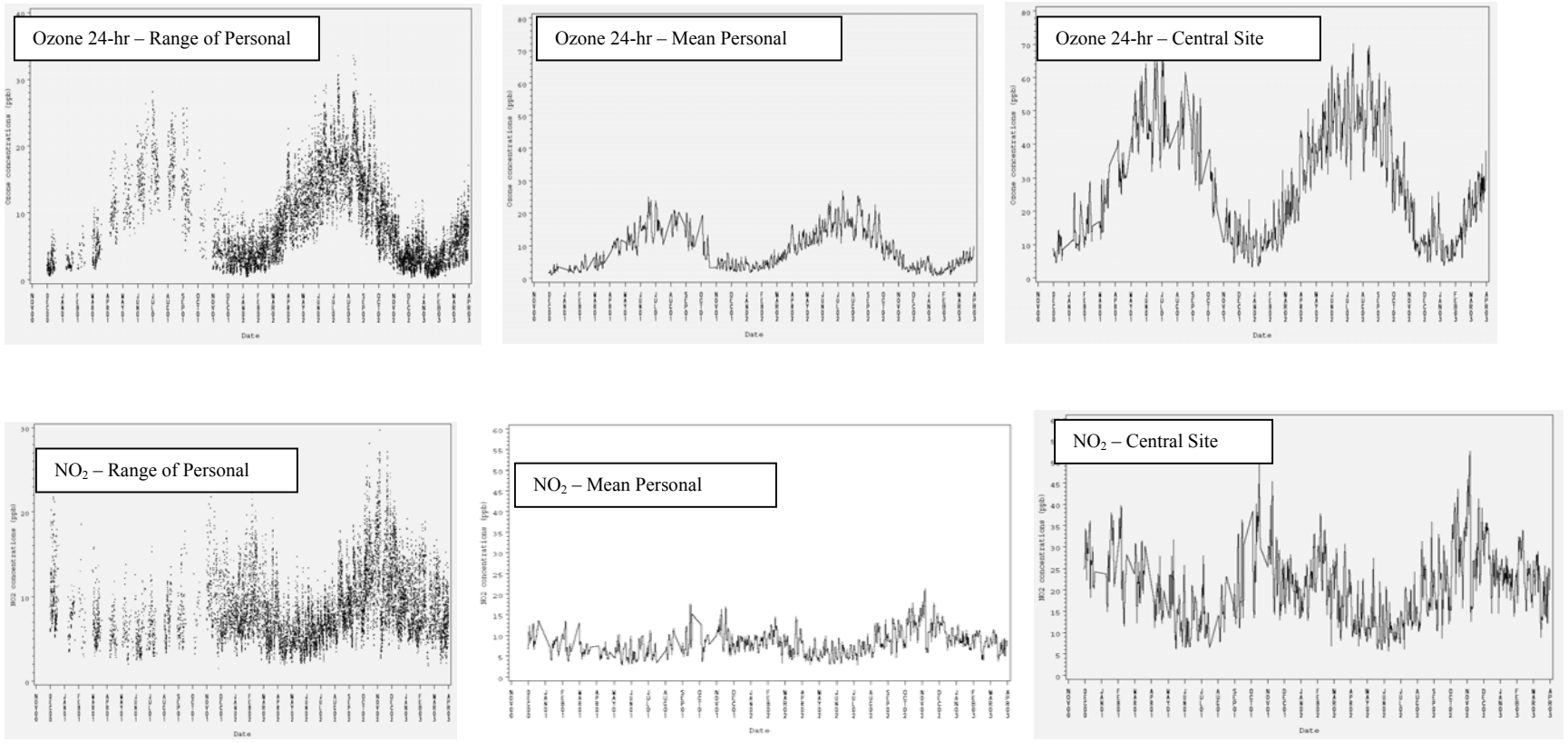


Figure 4.1.7-2. Range of individual exposure, mean individual exposure, and central site concentrations of ozone (top) and NO_2 (bottom) on days with panel studies from November 1, 2000, to March 31, 2003.

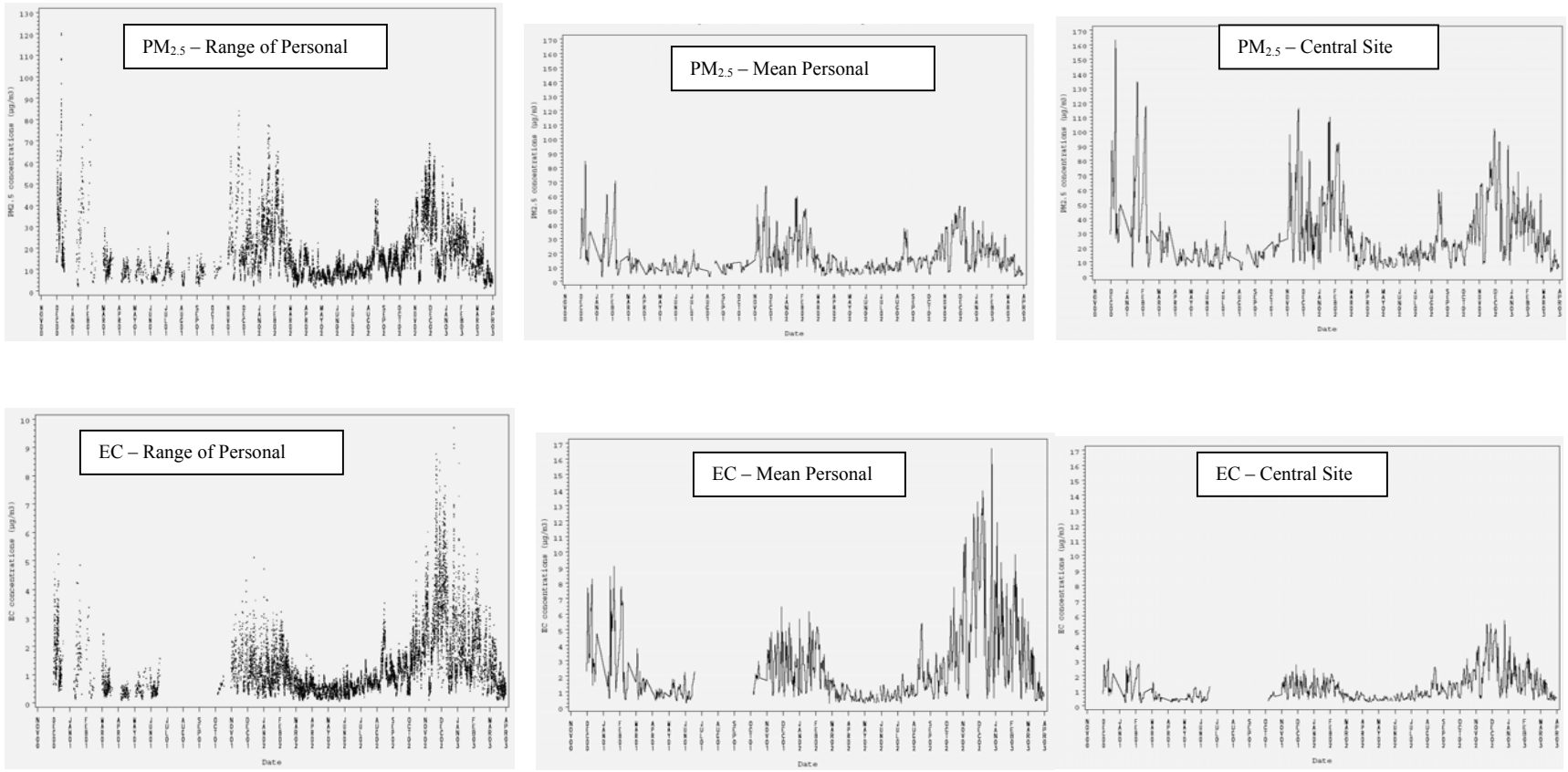


Figure 4.1.7-3. Range of individual exposure, mean individual exposure, and central site concentrations of $PM_{2.5}$ (top) and EC (bottom) on days with panel studies from November 1, 2000, to March 31, 2003.

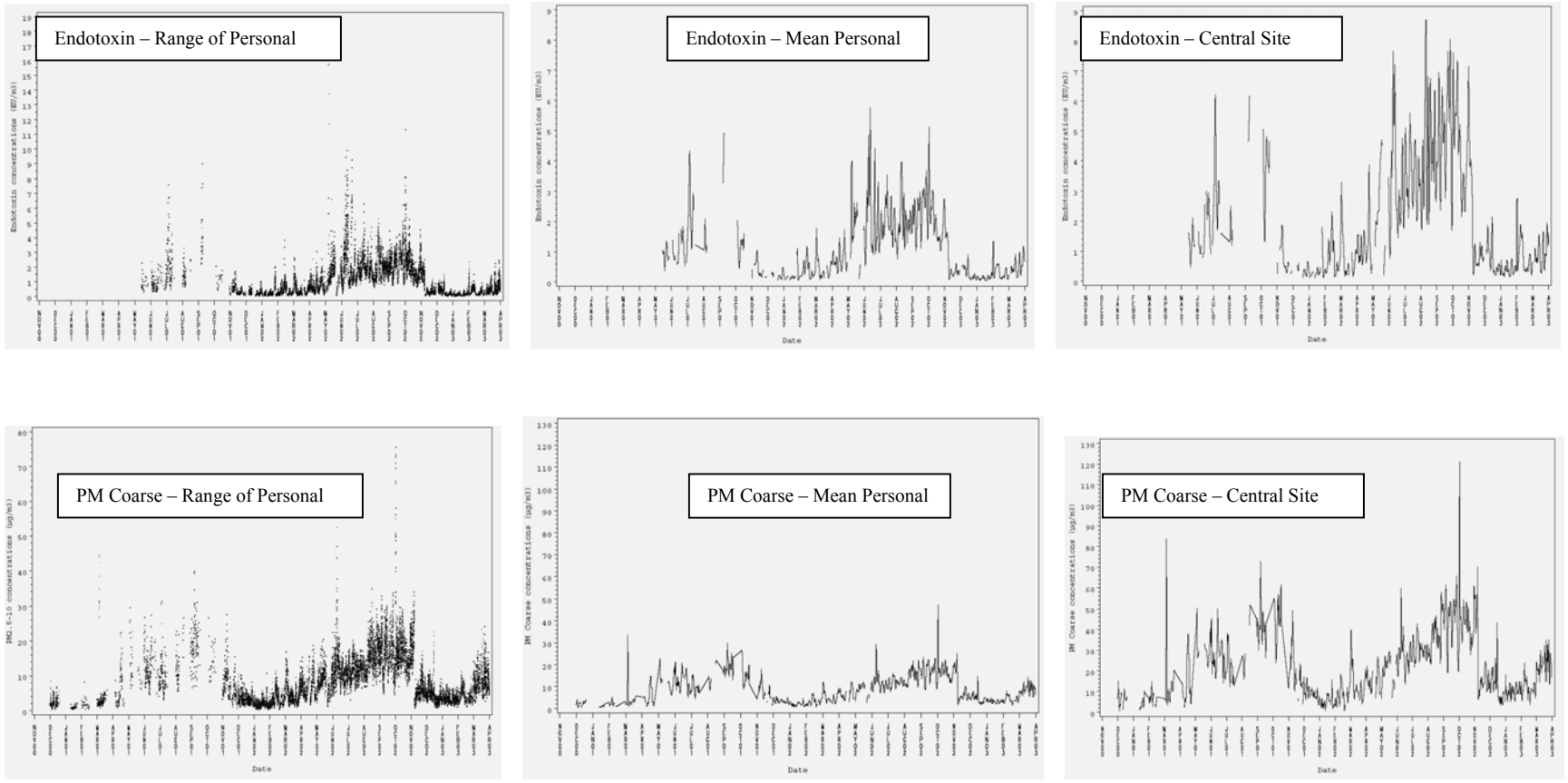


Figure 4.1.7-4. Range of individual exposure, mean individual exposure, and central site concentrations of endotoxin (top) and coarse PM (bottom) on days with panel studies from November 1, 2000, to March 31, 2003.

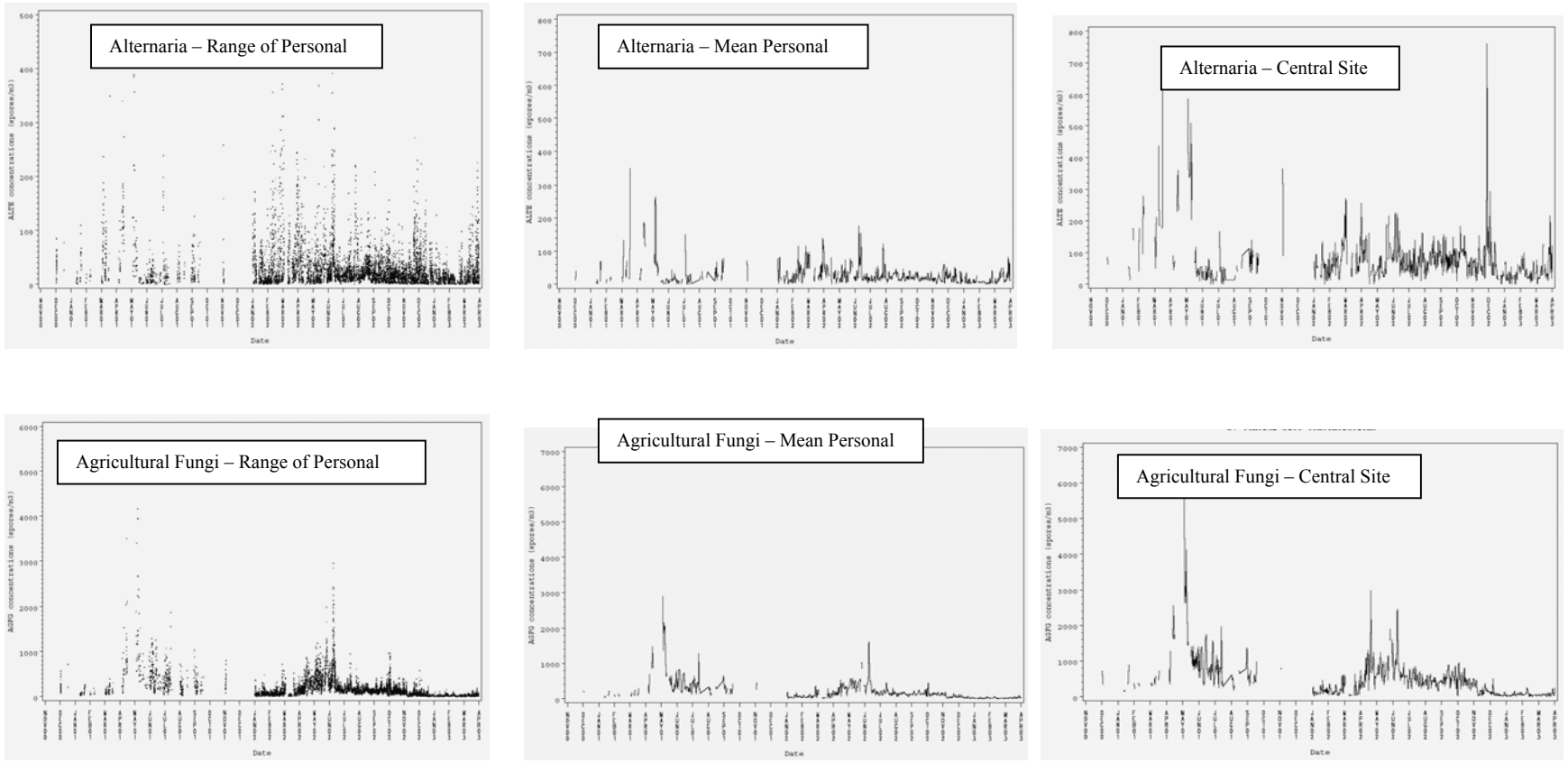


Figure 4.1.7-5. Range of individual exposure, mean individual exposure, and central site concentrations of alternaria (top) and agricultural fungi (bottom) on days with panel studies from November 1, 2000, to March 31, 2003.

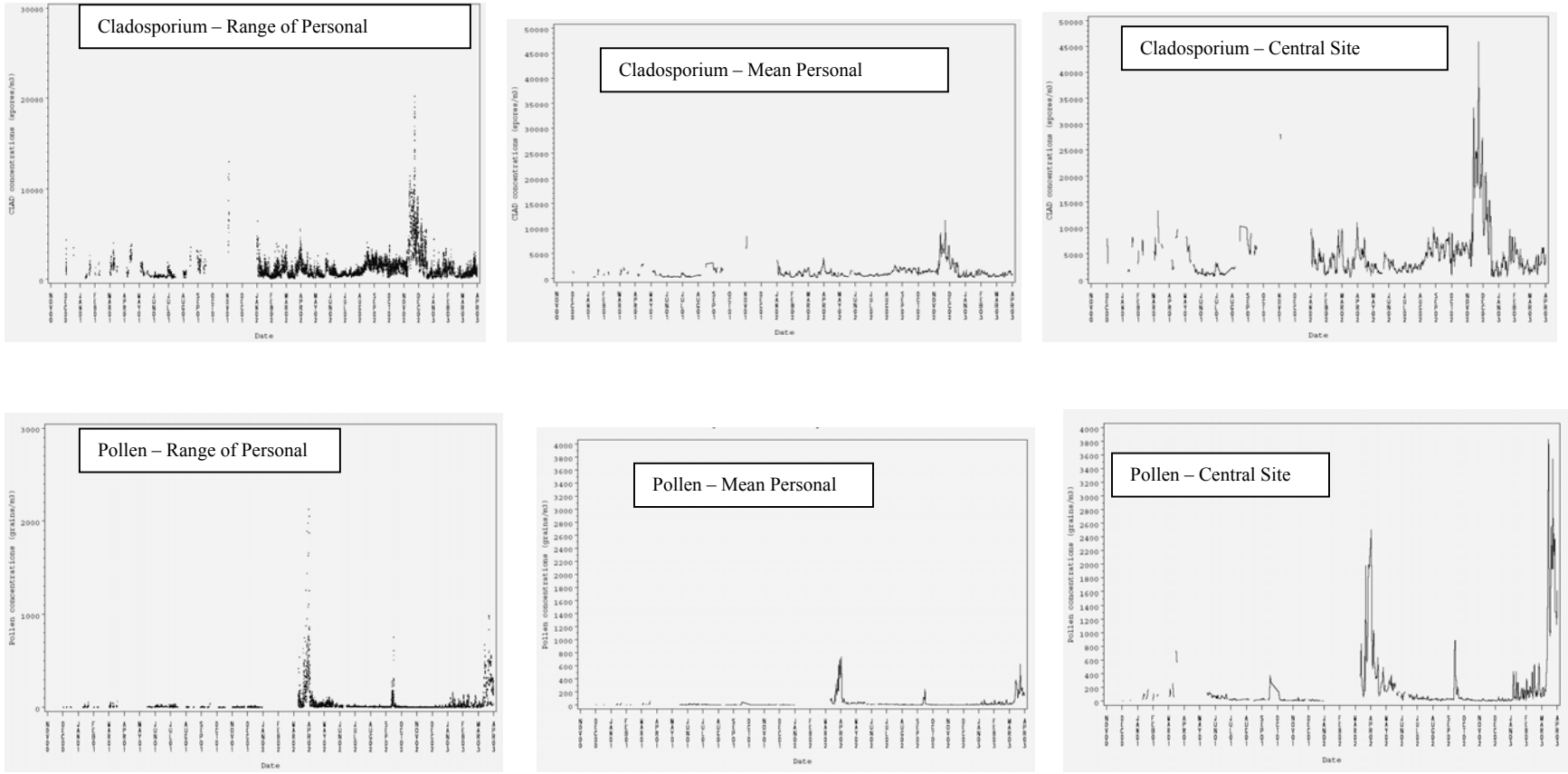


Figure 4.1.7-6. Range of individual exposure, mean individual exposure, and central site concentrations of cladosporium (top) and total pollen (bottom) on days with panel studies from November 1, 2000, to March 31, 2003.

Table 4.1.7-1. Comparison of mean estimated individual exposure and mean central site ambient concentrations on panel study days.

Pollutant (units)	No. Days	Individual exposure		Central Site Ambient Exposure		Personal Percent of Ambient
		Mean	Standard Deviation[a]	Mean	Standard Deviation	
Ozone (24-hr) (ppb)	731	8.88	5.97	28.2	16.8	31.5%
NO_2 (ppb)	731	8.25	3.04	20.7	8.3	39.9%
$PM_{2.5}$ ($\mu g/m^3$)	716	16.7	12.1	28.3	23.2	59.0%
EC ($\mu g/m^3$)	658	1.20	0.94	2.60	2.5	46.2%
PM Coarse ($\mu g/m^3$)	683	8.48	6.25	21.6	15.5	39.3%
Endotoxin (EU/m^3)	544	1.08	1.02	2.03	1.89	53.2%
Alternaria ($spores/m^3$)	532	27.2	33.4	79.4	85.7	34.3%
Agricultural Fungi ($spores/m^3$)	561	200.	280.	474.	545.	42.2%
Cladosporium ($spores/m^3$)	574	1216.	1213.	4702.	4880.	25.9%
Total Pollens ($grains/m^3$)	555	28.4	83.66	192.	473.	14.8%

[a] This is the standard deviation of the daily mean individual exposure estimates. It does not include the between subject variance.

4.1.8 Exposure Summary

4.1.8.1 Specific Aims

The following specific aims of the exposure component of the study were accomplished.

1. Ambient air quality measurements were augmented at the Fresno Supersite with trace metals and biological agents, specifically, pollen grains, fungal spores, and endotoxin.
2. The daily variability of pollutants and agents with regional-scale and neighborhood-scale spatial variability was evaluated using the Fresno Supersite air quality data.
3. The concentrations of pollutants and agents with regional-scale spatial variability were measured indoors and outdoors at selected homes and the relationships of concentrations outside selected homes to concentrations measured at the Fresno Supersite were evaluated.
4. The concentrations of pollutants and agents with neighborhood-scale spatial variability were measured indoors and outdoors at selected homes and the relationship of concentrations outside selected homes to concentrations measured at the Fresno Supersite were evaluated.
5. Home specific factors were collected by survey (by questionnaire and diary) to relate to home-specific agents.
6. Models were developed to predict neighborhood-scale concentrations of the pollutants and agents with neighborhood-scale spatial variability.
7. The concentrations of SHS, NO_2, and ozone were measured in the home of each child during selected two-week health study panels.
8. The principal locations of the study participants on each day of each two-week health study panels were surveyed (by questionnaire and diary).
9. The measurements made at the Fresno Supersite and homes, and the questionnaire and diary data, as well as the models developed, were used to estimate the exposure of each child in the asthma health study to selected agents of interest on each day during which the two-week health panels were conducted (from November 1, 2000 to March 31, 2003).

The following three specific aims were not addressed as planned.

10. To assess the extent to which neighborhood parameters account for differences between neighborhood and Fresno Supersite concentrations.
11. To develop definitions of neighborhoods based on traffic density and vegetation patterns.
12. To develop and test models to predict the daily variability of home-specific agents from measured data and diary data.

For specific aims 10 and 11, rather than classifying neighborhoods, we developed spatial models directly from the measurement data that provide a surface to make concentration estimates for locations throughout the community. For specific aim 12, nicotine was the only home-specific

agent with sufficient daily data to accomplish this aim and the nicotine levels were too low to obtain meaningful results.

4.1.8.2 Findings

The overall objective of the exposure study was to estimate the daily air pollution exposures of the study participants during each of the two-week health panels over the study period with a high degree of reliability. The daily exposure assignments were made using a data-driven modeling approach that accounted for spatial variations in ambient pollutants and agents, effects of home ventilation conditions on infiltration of ambient air to the indoor environment, and children's' daily time-use patterns. Spatial variations in ambient concentration and indoor-outdoor pollutant relationships were analyzed to develop the individual exposure model. The principal findings of the exposure study are as follows.

- The temporal and spatial variation of pollen grains and fungal spores are independent of other pollutants and agents measured in FACES and thus provide a significant opportunity to independently evaluate their associations with health outcomes.
- The day-to-day variations in ambient concentrations were large for most pollutants and agents in FACES, which provided the exposure variability needed to support the panel study design.
- The seasonal variations were large for many pollutants and agents, with median monthly ambient concentrations varying by factors of 5 to 10 between the lowest and highest months. The seasonal patterns of variations differed considerably for the different pollutants and agents. Pollens were highest in the spring; ozone was highest in summer; endotoxin was highest in the summer or fall, coarse PM was highest in the fall; and $PM_{2.5}$, EC, NO_3, PAH, NO, and CO were highest in the fall or winter. Total fungal spores (but not necessarily individual types of spores) were lowest in winter.
- Relatively large diurnal variations in ambient concentrations were observed which may provide further opportunity to link exposure differences to health outcomes. Factors of 4 to 5 differences between the lowest and highest average hourly concentration were observed for ambient ozone, EC, PAH, CO, NO, pollen grains and fungal spores.
- Apparent tracers exist for several of the important sources of ambient pollution, including ones for combustion sources (CO, NO, EC, and PAHs), soil dust (Si, Al, Fe, and Mn), and biological sources (endotoxins, fungal spores, and pollens) that could potentially support apportionment of health effects to sources.
- Spatial variations in daily ambient concentration ranged from barely detectable to large. The relative ranking shown in Table 4.1.6-2 confirmed most of our hypothesis regarding regional-scale and neighborhood-scale spatial variations in ambient concentrations. $PM_{2.5}$ mass, SO_4, b_{sp}, and PM_{10} mass, potassium, iron, silicon, and calcium had mean daily spatial coefficients of variation less than 20% and were classified as pollutants with regional-scale variations. $PM_{2.5}$ OC; EC; NO_3; coarse PM; PM_{10} zinc, bromine, manganese, aluminum, strontium, copper, and cobalt; endotoxin; CO; NO_2; NO_x; and ozone had mean daily spatial coefficients of variation between 20% and 35%, and were classified as pollutants with moderate neighborhood-scale variations. NO, SO_2, PAHs, fungal spores, pollens, and other measured trace elements were found to have large neighborhood-scale variations, with mean daily spatial coefficients of variation greater than 35%.

- Mean indoor concentrations of most (55 of 70) pollutants and agents were lower indoors than outdoors in FACES residences. Notable exceptions were OC and naphthalene concentrations that were higher indoors, on average; endotoxin was higher indoors than outdoors in the winter (November-March), but lower in other seasons. About half of the measured compounds had higher maximum concentrations indoors than outdoors. For example, the maximum indoor concentrations of $PM_{2.5}$ mass, PM_{10} mass, OC, EC, total fungi, naphthalene, pyrene, flouranthene, iron, and aluminum exceeded the maximum outdoor observations.
- Routine home measurements indicated dust mites and cockroach allergens were uncommon in floor and bed dust, while cat and dog allergens were very common in FACES residences, including those without these pets. Measurable endotoxin levels were common in house dust; median levels of endotoxin were 64 EU/mg in floor samples and 52 EU/mg in bed samples. Two-week average nicotine levels were low (<1 $\mu g/m_3$) in 95% of the homes. Two-week average NO_2 and ozone concentrations averaged 13 ppb and 9 ppb in FACES residences.
- The indoor and outdoor concentrations of SO_4, EC, benzo[b]flouranthene, dibenz[a,h]anthracene, benzo[k]flouranthene, and thallium were reasonably well correlated ($r = 0.73$ to 0.86). Indoor and outdoor concentration of $PM_{2.5}$, b_{sp}, benzo[a]pyrene, cobalt, and lead were moderately correlated with coefficients (r) between 0.5 and 0.6. The correlation coefficients for indoor and outdoor concentrations of all other compounds were less than 0.5. Window position and heating or air conditioning system use explained 70% of the variance in the indoor-outdoor ratio for SO_4, an important tracer of pollution of ambient origin.
- A personal microenvironmental exposure model was developed to estimate individual daily exposure to pollution and agents of ambient origin. It combined a model of spatial variations of outdoor concentrations with a single compartment steady-state indoor air quality model. Daily individual diary information on residence operating characteristics and subjects' activities was used along with ARB time-activity survey data to estimates time spent in various microenvironments each day.
- Results of the microenvironmental exposure model suggest individual exposures vary between subjects by a factor of two for $PM_{2.5}$ mass and by a factor of three or more for other pollutants considered on most days. The large variations in estimated exposure to pollutants of ambient origin between subjects suggest that the use of central site ambient concentrations for individual exposure assignments in FACES may result in considerable exposure misclassification and assignment error. The magnitude of the error is unknown because the individual exposure model performance has not been evaluated against individual exposure observations.
- The mean estimated individual exposure concentrations of pollutants of ambient origin are consistently lower than the central site ambient concentrations. On average, the mean individual exposure concentrations range from 15% of central site ambient concentrations for total pollens to 59% of central site ambient concentrations for $PM_{2.5}$ mass. The pollutant ranking (from highest to lowest) for mean ratio of individual exposure to central site ambient concentrations is $PM_{2.5}$ mass, endotoxin, EC, agricultural fungi, NO_2, PM coarse, *Alternaria*, ozone, *Cladosporium*, and total pollen. The differences in individual exposure levels relative to central site ambient concentrations are primarily a result of lower indoor than outdoor concentrations caused by pollutant deposition on indoor

surfaces and penetration losses; these losses from outdoors to indoors are also quite variable among the pollutants and bioaerosols, with median indoor to outdoor ratios ranging from 0.82 for EC to less than 0.02 for total pollen. Spatial differences in ambient concentrations within the community and indoor chemical reactions also contribute to the differences.

- The between-subject variations in individual exposure estimates are generally greater for biological agents than conventional pollutants. For example, on a day with relative high pollen grain and fungal spore levels, the individual exposure estimates may range from 100 to 800 total pollen grains/m^3 and from 10 to 250 *Alternaria* spores/m^3. In contrast, on a day when conventional pollutant levels are high, the individual exposure estimates may range from 40 to 80 $\mu g/m^3$ for $PM_{2.5}$ mass and from 8 to 25 ppb for NO_2. The variance among subjects for primary PM components, such as EC, is also considerably higher than the variance for $PM_{2.5}$ mass.
- Assessment of the overall accuracy and reliability of modeled individual exposure requires an extension of the model to account for indoor sources and collection of personal monitoring data for FACES subjects.

4.2 POLLUTION-RELATED HEALTH OUTCOMES

4.2.1 Descriptive Analyses of Cohort

The age distribution of children at each clinic visit from baseline to 54-months is shown in Table 4.2.1-1a. At baseline, children ranged in age from 6 to 12 years. (One child, who was 11 when screened, did not enter the study until s/he had turned 12 years old.). Children had a median age of 8 years at baseline. By the 54-month visit, children were as old as 15.

Table 4.2.1-1b shows the age distribution at each visit as of March 31, 2003. The age distributions are very similar to the distributions by July 2005. The mean age at 24-months was slightly younger (9.9 years vs. 10.2 years).

The demographic characteristics of the 315 children and their families at baseline are displayed in Table 4.2.1-2. FACES household incomes are similar to those of the entire Fresno community; 45.4% of households reported incomes of $30,000 or below. Relative to the larger community, high school degrees were reported more frequently by parents of FACES children; more than 90% of families had at least one parent with a high school degree. The percentage of participating household that owned their own home was identical to that in the larger community. Almost 96% of children were covered by health insurance, although 8.7% of children had coverage that was “self-paid”.

4.2.1.1 Health Characteristics at Baseline

At baseline, 22.5% of children reporting having been hospitalized for asthma in their lifetime, with 7.3% having been hospitalized in the 12 months prior to interview (Table 4.2.1-3). Only 5.7% of children had been put in the intensive care unit for asthma. Unscheduled medical

or emergency room visits in the 12 months before baseline occurred in more than half of the cohort.

Almost 80% of the cohort was on at least one controller medication (Table 4.2.1-3). A few (3.2%) were not taking any medications for their asthma, and 17.1% only took beta-agonists. Prednisone was taken at least once in the lifetime of 59.0% of the cohort and had been used by 37.5% of the cohort in the past 12 months.

Despite the prevalence of reported recent prednisone use, 75.8% of the children in the study were classified as having mild intermittent or mild persistent asthma when the Global Initiative for Asthma (GINA) classification scheme for symptoms was applied to assess severity at baseline. Unfortunately, we have no data on the distribution of all children with asthma in the study area with which to compare this distribution of severity.

Pulmonary function testing at baseline showed that, on average, most children had pre-bronchodilator FEV_1 and maximal midexpiratory flow (FEF_{25-75}) values close to those that would be predicted given their age, sex and race/ethnicity (4). Peak expiratory flow (PEF) values were 7% greater on average than predicted. FEF_{25-75} was the most variable pulmonary function measure and also was the measure with the largest (and most variable) response to bronchodilator administration (Table 4.2.1-4).

4.2.1.2 Asthma Symptoms at Baseline

Of the 315 children who began the study, 17 met our criteria for cough-variant asthma (Table 4.2.1-5). For those with a history of wheeze (92.7%), 37.3% had wheezed in the 2 weeks prior to baseline interview. Wheeze interrupted sleep in the past 2 weeks for 64.4% of the cohort. Wheeze led to school absences in the previous two weeks for 12.5% of the children and missed work for 8.1% of parents over the same time period. Persistent cough occurred in 72.6% of the cohort in the 12 months before baseline and for 32.8% in the past 2 weeks. Most children reported activity limitations in the past year. Coughing was common in the cohort. Almost 1/3 of participants had a cough, which lasted two or more days within the 2-weeks before the baseline interview.

A diagnosis of allergic rhinitis or eczema was reported by 32.6% and 17.0% of parents, respectively. Skin tests were performed at the baseline visit. Sixty-one percent of children tested had a positive reaction to at least one allergen (Table 4.2.1-6). More than 30% of children were skin-test positive to each of *Penicillium*, rye, *Alternaria*, olive and grass allergens. Approximately 20% of children tested positive to *Chladosporium*, dust mite and cat, which are common indoor aeroallergens. By comparison, sensitivity to cockroach antigen was found in 11% of the study population. The median value of the number of positive skin tests was 1.0 (interquartile range=4.0, range=13).

Among the 266 children who were skin-tested, we compared their skin test status with self-reported allergic rhinitis or hay fever. There were 28 children whose parents reported a diagnosis of hay fever or allergic rhinitis who were not skin-test positive to the allergen panel used in this study. There were 101 cases (42.3%) in which the parent reported there was no

diagnosis, yet the children were skin test positive to at least one allergen in the panel (Table 4.2.1-7).

4.2.1.3 Triggers

The 292 adults who reported that their children wheezed were asked about triggers of wheeze. The most commonly reported asthma triggers were weather, colds and flu, air pollution, pollens/grasses/trees and physical activity. There were no important differences in triggers over a lifetime and triggers in the past 12 months (Table 4.2.1-8).

4.2.1.4 Panel Visits

4.2.1.4.1 Symptoms and Medication use Reported in the Daily Diary

The diary administered as part of each panel visit contained questions about daily symptoms, school absences, lost work, medication use, exposures in the home and some general questions which related to time/location and activity. Table 4.2.1-9 gives the percent of "YES" responses to health questions asked in the diary. The most prevalent daily symptom was wheeze or cough (asked together), which was reported on 43.3% of panel-days. Shortness of breath was reported on 16.2% of panel days. On the panel-days where the child was in school, there were school absences on 5.4% of panel-days. A parent missed work because of this absence slightly more than half the time, on 2.6% of panel-days. The medication use questions on the diary did not specify whether a rescue medication or controller medication was used. Medication use was reported in the "A.M." and "P.M." 46.5% and 50.4% of the time, respectively.

4.2.1.4.2 Symptoms and Medication Use Data from the EasyOne®

During spirometry testing with the EasyOne®, each child was presented (on the EasyOne® screen) with two questions about symptoms (cough or wheeze since the last test) and two questions about rescue medications (use since the last test and use in the hour before the current test) (See Appendix D). These are reported below for both the morning test (completed within one hour of waking) and the evening test (completed at bedtime) (Table 4.2.1-10). Unlike the paper diary discussed above, wheeze and cough were distinguished. Children reported wheeze since bedtime on 36.5% of panel-days, and wheeze since the morning test at 41.2% of the evening spirometry tests. Cough was reported slightly more often, 44.6% since bedtime and 41.4% of panel-days since the morning test. Use of rescue medication in the time since the last test was more commonly reported in the evening (20.4%) than in the mornings (12.4%), probably because the child was sleeping in the interval since bedtime. Rescue medication during the hour before the test was reported for 8.9% of morning tests and 9.4% of evening tests.

Table 4.2.1-11 shows the responses for the EasyOne® questions by study season. (Note: in this study, seasons were defined as Winter (October through January), Spring (February through May) and Summer (June through September.). For both symptoms and rescue medication use, winter had the highest percent of positive responses, and summer the lowest.

Rescue medication in the hour before the test was essentially the same in the winter and spring. Cough and wheeze both had a high degree of seasonal variability with cough reported since the morning test being twice as prevalent on panel-days in winter than in summer.

Table 4.2.1-12 displays the distribution of counts each day for the A.M. EasyOne® questions. On average, there was less than one report of rescue medication use in the hour before the A.M. test (0.81) each day and a maximum of 6 reports on a given day. Daily counts for cough and wheeze were more frequent with maximums of 7 and 13 daily counts for wheeze and cough respectively.

4.2.1.4.3 Pulmonary Function During Study Panels

Table 4.2.1-13 shows the distribution of pulmonary function measures. For the "mean values, each observation represents the mean of two or three acceptable blows for a session based on investigator's review (IBT, LC). For example, there were 6,021 sessions with values for mean FEV_1. The mean over all of those observations was 1.53 mL. For the percent-predicted values, session means were adjusted for race/ethnicity age, sex and height (4).

Daily mean FEV_1 values reflect the characteristics of the population doing the test that day (e.g. age, race, sex and height) and the level of asthma morbidity in those participants. For each pulmonary function measure the mean and median values were very similar. Mean percent-predicted values were lower than their pre-bronchodilator counterparts from the baseline visit. For example, the mean value of percent-predicted FEV_1 was 97.9 %. The mean percent-predicted value of morning and evening FEV_1 during panel visits were 83.2 % and 86.8%, respectively. Since mean percent-predicted FEV_1 values for both morning and evening sessions were lower than those observed at baseline, diurnal variability probably does not account for the differences observed.

The differences between Morgan and EO after stratifying by age group and gender is shown in Table 4.2.1-14. The overall mean FEV_1 for both morning and evening EO sessions is lower than observed at the FO visit for the same age group/gender stratum. There are several reasons why we could have observed a difference between the average levels of lung function during the field office (FO) and panel visits: 1) The most obvious one relates to the fact that FO tests were done under supervision and with coaching. More than likely, this plays some role; 2) Many panel days were characterized by marked declines in lung function that followed one or more days of much higher lung function. These were undoubtedly due to exacerbations of asthma. Many such days are included in the calculation of the means for the panel days; 3) The EO spirometer ends the session as soon as it identifies 3 acceptable curves by its criteria. It is entirely possible that some children would have produced higher values, if they had been allowed to produce more than the 3 tracing. In a number of cases, based on the pattern of the curve sequence, would question whether better curves would have been produced, if subjects were allowed to go on beyond 3. In the end, it is not possible to distinguish between the 3 choices. In health children, it often is possible to detect a learning effect over several days, since there is a progressive increase in magnitude of the measures. This is not the case for children with asthma in whom lung function results could decline over several days due to worsening of their asthma. All this having been said, the differences between FO and panel data should not

have affected our acute exposure results, since they are based only on panel data. Similarly, the preliminary data on the association of responses to acute changes and lung growth also should not be affected directly panel responses are used to predict subsequent levels in FO measures. Even if the panel estimates are biased downward, the acute exposure response estimates would be unaffected, insofar as each child's downward bias is relative constant in any panel relative to the FO measurement that bound the panel.

Table 4.2.1-1a Age Distribution at each follow-up visit (November 28, 2000 to July, 2005)

Clinic Visit	N	Min	25%	50%	Mean	75%	Max
Baseline	315	6	6	8	8.1	9	12*
6-Month	229	6	7	9	8.5	10	12
12-Month	195	7	7	9	9.0	10	13
18-Month	173	7	8	9	9.4	11	13
24-Month	149	8	9	10	10.2	12	13
30-Month	119	8	9	11	10.6	12	14
36-Month	97	9	10	11	11.1	12	14
42-Month	65	9	10	12	11.6	13	14
48-Month	45	10	11	12	11.8	13	15
54-Month	16	10	11	13	12.7	14	15

* One child, who was screened for the study at age 11, did not do his baseline interview until he was 12 years old.

Table 4.2.1-1b Age Distribution at each follow-up visit (November 28, 2000 to March 31, 2003)

Visit	N	Min	25%	50%	Mean	75%	Max
Baseline	236	6	6	8	8.1	9	11
6-Month	147	6	7	9	8.6	10	12
12-Month	91	7	8	9	8.9	10	12
18-Month	67	7	8	10	9.5	11	12
24-Month	41	8	9	10	9.9	11	12

Table 4.2.1-2. Demographic characteristics in the Fresno population and in the FACES Cohort at Baseline			
	#	% in FACES	% in Fresno
INCOME (N=304)*			
less than $15,000	62	20.4	20.0
$15000-$30,000	76	25.0	23.2
$31,000-$50,000	76	25.0	23.1
more than $50,000	90	29.6	33.7
EDUCATION*			
Mother, high school education or greater (n=311)	264	84.9	69.0
Father, high school education or greater (n=302)	248	82.1	66.1
At least one parent completed high school (n=310)	281	90.6	----
HOME OWNERSHIP* (n=294)			
Home owned	166	56.5	56.5
CHILD'S HEALTH INSURANCE STATUS (N=311)**			
No insurance	13	4.2	10.7
From either parent's work	165	53.1	48.5
Government	106	34.1	37.7
Self-Pay	27	8.7	3.1
Child covered by health insurance	298	95.8	89.3**
RACE/ETHNICITY OF CHILD (N=15)***			
Hispanic	125	39.7	n/a
African-American	49	15.6	n/a
White	132	41.9	n/a
Asian	2	0.6	n/a
Other/Missing	7	2.2	n/a

* For income: Fresno County, 2000 Census from American Factfinder http://factfinder.census.gov/ The income categories were slightly different: less than $15,000, $15,000-$29,999; $30,000-$49,999; $50,000 or more.

** http://www.chis.ucla.edu -- results from 2001 and 2003 combined, computed for children aged 6 to 11 in Fresno County using AskCHIS.

*** Race/ethnicity data are defined differently than in the census and are therefore not comparable. The data were collected such that Hispanic origin and race were asked in the same question. People were allowed to select more than one race/ethnicity so could have described themselves, for example, as Hispanic and white, but were not required to do so.

Table 4.2.1-3 Health Characteristics at Baseline			
HEALTH UTILIZATION	N*	#	%
Ever hospitalized for asthma	315	71	22.5
Hospitalized for asthma in the past 12 months	315	23	7.3
Ever in intensive care unit for asthma	315	18	5.7
Unscheduled medical or emergency room visits in last 12 months	315	182	57.8
Unscheduled medical or emergency room visits in last 3 months	314	86	27.4
MEDICATION USE AT BASELINE			
Only on beta-agonists	315	54	17.1
On inhaled steroids/intal/cromolyn	315	230	73.0
On any controller medications	315	251	79.7
Not on any medication	315	10	3.2
Ever prescribed prednisone	305	180	59.0
Oral Prednisone in the last 12 months	309	116	37.5
ASTHMA SEVERITY (N=315)**	315		
mild intermittent		89	28.2
mild persistent		150	47.6
moderate		67	21.3
severe		9	2.9

* N=the number of non-missing answers for the question. An answer of "don't know" was considered to be missing. Other sources of missing data include revisions to the questionnaire after the start of the study.

** Uses severity index based on the Global Initiative for Asthma's Symptom Severity scale as described in Section 3.5.1.3 and in Appendix H.

*Table 4.2.1-4 Pulmonary Function at Baseline**			
	N*	Mean (s.d.)	Range
PERSONAL CHARACTERISTICS			
Standing height at baseline (inches)	315	51.7 (4.8)	(41.9-63.2)
Weight at baseline (lbs.)	315	72.5 (27.3)	(37.5-188.0)
PRE-BRONCHODILATOR PULMONARY FUNCTION			
*Forced Expiratory Volume 1-second(FEV_1) (% predicted)***	284	97.9 (17.8)	(54.4-147.2)
*Maximal mid-expiratory flow (FEF_{25-75}) (% predicted)***	285	93.3 (36.5)	(23.3-244.7)
*Peak expiratory flow rate (PEFR) (% predicted)***	285	107.3 (22.7)	(45.1-165.0)
*Forced vital capacity (FVC) (% predicted)***	285	102.1 (17.1)	(55.6 -155.7)
Mean FEV_1	293	1.64 (0.46)	(0.66 - 3.15)
Mean FEF_{25-75}	294	1.82 (0.70)	(0.45 - 4.03)
Mean PEFR	294	3.93 (1.17)	(1.45 - 7.45)
Mean FVC	294	1.99 (0.54)	(0.91 - 3.85)
CHANGE IN % PREDICTED VALUES WITH BRONCHODILATOR ADMINISTRATION			
*FEV_1 (% predicted)***	272	7.9% (11.1)	(-18.9 - 71.4)
*FEF_{25-75} (% predicted)***	273	31.7% (36.9)	(-40.1 - 252.2)
*PEFR (% predicted)***	273	7.8% (14.6)	(-25.0 - 81.1)

* Determined from sessions with 2 or more acceptable blows for the given pulmonary function measure based on acceptability criteria of study reviewers (JB and LC; (see Section3.5.1.1). The N is the number of non-missing values. If there were zero or one acceptable blows then the value was missing.

** Predicted values are based on Hankinson *et al*. (4).

Table 4.2.1-5 Asthma Symptoms Reported at Baseline			
	Ever	**Past 12 months**	**Past 2 weeks**
Wheeze or whistling in the chest	92.7	87.0	37.3
Wheeze limited child's speech	48.1	37.9	10.7
Trouble keeping up with other children because of wheeze	75.4	66.2	20.2
Child Missed school because of wheeze	64.9	57.6	12.5
Parent missed work because of child's wheeze	44.0	35.6	8.1
Wheezed while fighting or throwing a tantrum	32.8	29.3	7.9
Quit playing a sport or excused from gym because of wheeze	50.0	44.3	11.5
Sleep disturbed by wheeze	88.7	82.6	64.4
Cough lasting 2 or more days	----	72.6	32.8

Table 4.2.1-6. Skin Test Positivity: Percent positive to each allergen (N=266)	
Allergen	**%**
*Penicillium**	38.7
Rye	32.7
Alternaria	31.9
Olive	30.8
Grass	30.1
Mite	23.3
Cat	19.9
*Chladosporium***	19.8
Mugwort	19.5
Cockroach	11.3
Oak	10.9
Privet	9.38
Cedar	6.39
Dog	5.26
Juniper	2.26
Median Number of Positive Skin tests (IQR.)	2.57 (3.13)
Atopic	61.3

* N=62

** N=192; IQR=Interquartile Range

Table 4.2.1-7. Comparison of self-reported diagnosis of allergic rhinitis and skin-test results			
	Skin Test +	***Skin Test -***	Total
Diagnosis of allergic rhinitis	28 (18.8)	45	73
No diagnosis of allergic rhinitis	65	101 (42.6)	166
Total	93	146	239

Table 4.2.1-8 Wheezing triggers during lifetime and in the past 12 months				
	Ever		**In the past 12 months**	
	N*	***%***	***N****	***%***
Weather	278	87.1	260	88.1
Colds or flu	288	89.6	268	85.4
Air pollution	186	81.2	170	81.2
Pollens, grasses or trees	218	81.2	200	80.5
Physical activity	284	79.6	264	79.2
Windy conditions	241	71.4	224	69.2
*Cold air***	136	66.2	126	64.3
House dust	206	54.9	188	55.3
Outdoor smoke	224	55.8	206	51.0
Molds	165	55.2	153	50.3
Fields being plowed	149	53.0	137	48.2
Cigarette smoke	235	57.0	215	46.5
*Crops being sprayed***	142	51.4	128	43.8
*Wood smoke***	123	40.7	112	37.5
*Perfumes and odors***	129	36.4	117	34.2
Pets	238	35.7	222	28.8

* N=number of non-missing answers. "Don't Know" was considered to be missing. Of the 292 people who answered the question about weather as a trigger for their child's wheeze during their lifetime, (these questions were asked to the 292 respondents with children who had a history of wheeze), 14 gave an answer of "Don't Know". These 14 people were not asked the question about wheeze in the past 12 months. This question was also not asked to 4 people who did not wheeze in the last 12 months. (274 people reported wheeze in the past 12 months) therefore the N for this question is 260.

** Item added in November 2002.

Table 4.2.1-9 Frequency of "YES" Responses to Diary Questions			
	N*	#	%
Daily Symptoms			
Wheeze or Cough	6517	2821	43.3
Shortness of Breath	6458	1047	16.2
Chest Congestion	6465	684	10.6
Runny or Stuffy Nose	6462	2074	32.1
Head or Chest Cold or Flu	6411	470	7.3
*Absent from school today***	3684	188	5.4
*Mother or father missed work because of absence***	3684	97	2.6
Medication Use			
A.M. (Before 12 noon)	2033	946	46.5
P.M. (After 12 noon until bedtime)	2018	1017	50.4

* The diary is self-administered. The N is the number of non-missing values for that question, except where specified otherwise.

** N is students who had school that day.

Table 4.2.1-10 Percent of "YES" Responses to EasyOne® Questions (November 28, 2000 to March 31, 2003	
	%
EasyOne® Questions asked During Morning Session (N=6521)	
Wheezed since bedtime	15.8
Coughed since bedtime	27.5
Used rescue medication since evening test	12.4
Used rescue medication in the hour before morning test	8.9
EasyOne® Questions asked During Evening Session (N=7129)	
Wheezed since morning test	21.6
Coughed since morning test	41.4
Used rescue medication since morning test	20.4
Used rescue medication in the hour before the evening test	9.4

* N= Total number of panel-days

Table 4.2.1-11 Percent of "YES" Responses to EasyOne® Questions by Season* (November 28, 2000 to March 31, 2003			
	Winter	Spring	Summer
EasyOne® Questions asked During Morning Session			
Wheezed since bedtime	17.4	16.8	12.5
Coughed since bedtime	31.4	30.1	18.8
Asked during A.M. session: Used rescue medication since P.M. test	14.5	11.8	9.7
Used rescue medication in the hour before A.M. test	10.0	8.6	7.8
EasyOne® Questions asked During Evening Session			
Wheezed since morning test	23.4	23.2	17.6
Coughed since morning test	45.9	43.8	32.6
Used rescue medication since A.M. test	23.1	20.4	16.5
Used rescue medication in the hour before the P.M. test	10.1	8.7	9.0

* Winter=October through January; Spring=February through May; Summer=June through September. A.M.: Winter (n=3004); Spring (n=1811); Summer (n=1706). P.M.: Winter (n=3256); Spring (n=1987); Summer (n=1886).

Table 4.2.1-12 Distribution of Daily Counts (YES Responses to A.M. EasyOne® ***Questions) November 28, 2000 to March 31, 2003) (N=718 days)***							
Question	**Mean**	**S.D.**	**Min**	**25%**	**50%**	**75%**	**Max**
Wheezed since bedtime	1.44	1.41	0	0	1	2	7
Coughed since bedtime	2.49	2.26	0	1	2	4	13
Used rescue medication since P.M. test	1.22	1.26	0	0	1	2	8
Used rescue medication in the hour before A.M. test	0.81	1.06	0	0	1	1	6

Table 4.2.1-13 Distribution of Pulmonary Function Measures (November 28, 2000 to March 31, 2003)									
	N	**Min**	**10%**	**25%**	**50%**	**Mean**	**75%**	**90%**	**Max**
MEAN VALUES*									
Morning FEV_1 (L)	6021	0.202	0.876	1.14	1.50	1.53	1.88	2.20	4.05
Morning FEF_{25-75} (L/sec)	5612	0.156	0.619	0.956	1.47	1.52	2.00	2.73	6.21
Morning FEF_{75} (L/sec)	5612	0.037	0.282	0.447	0.710	0.776	1.03	2.05	2.82
Morning Peak Expiratory Flow (L/sec)	6065	0.390	1.88	2.62	3.53	3.56	4.45	5.23	13.9
Evening FEV_1(L)	6556	0.153	0.976	1.22	1.54	1.57	1.91	2.21	4.23
PERCENT-PREDICTED VALUES**									
Morning FEV_1 (L)	5851	10.8	54.3	70.3	84.2	83.2	96.9	108.0	334.5
Morning FEF_{25-75} (L/sec)	5468	5.9	31.0	47.9	68.1	71.5	90.9	113.7	302.2
Morning Peak Expiratory Flow (L/sec)	5890	11.7	54.7	74.2	91.9	90.7	107.1	123.2	392.1
Evening FEV_1(L)	6338	10.4	59.6	73.9	86.8	86.1	98.2	109.3	354.1

* The mean of acceptable values from each session based on investigator's review (IBT, LC) (see Section 3.5.1.1). For a mean to be calculated, there had to be at least two acceptable values for the session.

** The percent-predicted values were based on Hankinson et al. (4)

Table 4.2.1-14 Comparison of Morgan and EasyOne data stratified by gender and age group.												
	All available Morgan data (2+ acceptables)				*All available EO data (2+ acceptables), AM only*				*All available EO data (2+ acceptables), PM only*			
	Age at time of visit				*Age at time of visit*				*Age at time of visit*			
	6-7	*8-9*	*10-11*	*12+*	*6-7*	*8-9*	*10-11*	*12+*	*6-7*	*8-9*	*10-11*	*12+*
Spring												
males	35	47	39	8	30	35	34	7	31	37	35	8
n of sessions	43	56	43	8	334	429	322	63	387	465	329	68
mean	1.41	1.79	2.09	2.21	1.20	1.45	1.78	2.26	1.12	1.56	1.82	2.32
std	0.31	0.40	0.37	0.42	0.37	0.48	0.46	0.53	0.35	0.48	0.42	0.5
females	18	38	31	8	12	18	19	2	12	29	20	2
n of sessions	23	43	35	8	118	326	198	9	124	367	205	12
mean	1.38	1.62	2.02	2.74	1.23	1.35	1.61	1.93	1.25	1.41	1.72	1.99
std	0.40	0.34	0.39	0.35	0.37	0.40	0.53	0.26	0.37	0.39	0.45	0.21
Summer												
males	31	48	39	15	22	32	31	4	23	33	32	4
n of sessions	20	38	30	16	232	333	377	37	286	353	387	43
mean	1.43	1.76	2.25	2.44	1.06	1.61	1.90	2.36	1.15	1.67	1.92	2.29
std	0.34	0.36	0.40	0.48	0.32	0.44	0.47	0.50	0.33	0.40	0.43	0.48
females	21	36	33	6	11	23	24	7	12	23	24	2
n of sessions	16	29	38	6	139	269	275	32	165	300	322	33
mean	1.38	1.64	1.93	1.93	1.24	1.51	1.63	2.72	1.31	1.53	1.69	2.63
std	0.20	0.35	0.46	0.59	0.29	0.46	0.43	0.33	0.31	0.46	0.42	0.32
Winter												
males	38	32	45	22	28	41	37	9	29	41	38	9
n of sessions	26	38	48	27	360	466	529	63	396	499	559	89
mean	1.32	1.75	2.12	2.47	1.38	1.5	1.76	1.81	1.19	1.58	1.79	1.87
std	0.271	0.347	0.372	0.531	0.35	0.45	0.54	0.63	0.31	0.43	0.5	0.6
females	25	31	34	10	22	35	28	3	22	35	28	3
n of sessions	12	28	40	11	283	448	365	14	296	469	401	19
mean	1.38	1.725	2.08	2.56	1.13	1.51	1.79	2.14	1.18	1.53	1.81	2.18
std	0.41	0.35	0.40	0.70	0.37	0.38	0.53	0.22	0.35	0.35	0.47	0.19

*Table 4.2.1-15 Distribution of Daily Pulmonary Function Values by Season (November 28, 2000 to March 31, 2003)**												
	Winter				**Spring**				**Summer**			
	N	**25%**	**50%**	**75%.**	**N**	**25%**	**50%**	**75%.**	**N**	**25%**	**50%**	**75%.**
MEAN VALUES												
Morning FEV_1 (L)	2528	1.14	1.51	1.86	1799	1.11	1.42	1.82	1694	1.19	1.57	1.96
Morning FEF_{25-75} (L/sec)	2357	0.95	1.48	2.01	1643	0.90	1.36	1.90	1612	1.05	1.57	2.09
Morning FEF_{75} (L/sec)	2357	0.44	0.71	1.03	1643	0.42	0.67	0.98	1612	0.49	0.76	1.09
Morning Peak Expiratory Flow (L/sec)	2549	2.61	3.51	4.43	1816	2.500	3.34	4.28	1700	2.84	3.78	4.67
Evening FEV_1(L)	2720	1.23	1.54	1.87	1950	1.18	1.49	1.87	1886	1.24	1.60	1.98
%PREDICTED VALUES**												
Morning FEV_1 (L)	2474	70.4	84.3	96.3	1725	67.7	82.8	98.0	1652	72.1	85.1	97.0
Morning FEF_{25-75} (L/sec)	2316	48.0	68.5	90.6	1579	44.4	65.0	88.9	1573	51.1	70.8	93.2
Morning Peak Expiratory Flow (L/sec)	2493	74.3	91.9	106.7	1739	70.2	89.3	106.1	1658	78.3	93.8	108.9
Evening FEV_1(L)	2645	73.2	86.5	96.7	1860	72.8	86.3	100.2	1833	75.5	87.9	98.8

* Tables of raw lung function measures cannot be interpreted with respect to temporal trends, since the values have not been adjusted for difference in age, height, sex and race/ethnicity distributions over each period. The data are present solely for simple descriptive purposes. Winter=October through January; Spring=February through May; Summer=June through September. The mean of acceptable values from each session based on investigator's review (IBT, LC) (see Section 3.5.1.1). For a mean to be calculated, there had to be at least two acceptable values for the session otherwise the value was missing. ** The percent-predicted values were based on Hankinson et al. (4)

Table 4.2.1-16 Distribution of Daily Pulmonary Function Measures by Study Period (November 28, 2000 to March 31, 2003)									
	11/28/00 to 10/31/01			**11/01/01 to 10/31/02**			**11/01/02 to 03/31/03**		
	N	Mean	s.d	N	Mean	s.d	N	Mean	s.d
Morning FEV_1 (L)	1134	1.39	0.479	3166	1.56	0.518	1721	1.56	0.202
Morning FEF_{25} (L/sec)	1045	2.80	1.20	2978	3.14	1.19	1589	3.08	0.273
Morning FEF_{25-75} (L/sec)	1045	1.40	0.688	2978	1.56	0.726	1589	1.52	0.156
Morning FEF_{75} (L/sec)	1045	0.701	0.394	2978	0.803	0.438	1589	0.774	0.037
Morning Peak Expiratory Flow (L/sec)	1140	3.24	1.23	3187	3.66	1.26	1738	3.58	0.566
Evening FEV_1(L)	1211	1.44	0.443	3439	1.60	0.490	1906	1.61	0.344

* Tables of raw lung function measures cannot be interpreted with respect to temporal trends, since the values have not been adjusted for difference in age, height, sex and race/ethnicity distributions over each period. The data are present solely for simple descriptive purposes.
The mean of acceptable values from each session according to investigator's review (IBT, LC) (See section 3.5.1.1). For a mean to be calculated, there had to be at least two acceptable values for the session otherwise the value was missing.

4.2.2 Results of Short-term Effects Analyses

4.2.2.1 Introduction and Conventional Analyses

As noted in the section 3.6.8, we restricted our conventional and MSM $PM_{2.5}$ analyses to the months of October through February, since $PM_{2.5}$ levels were highest and quite variable during these months and were consistently low for the remainder of the year. Moreover, the range of values observed over the remainder of the year also are observed during the winter months. As noted, a total of 4032 panel observation days were available for this analysis. Of these days, there were 3111 acceptable FEV_1 measurements (for 696 days, FEV_1 data were not provided; for 225 days the FEV_1 tracings were not acceptable).

Figure 4.2.2-1 presents the daily time series for Central Site and estimated personal $PM_{2.5}$ for days on which FACES panels took place. The shaded area identifies the period for which $PM_{2..5}$ data were imputed.

Figure 4.2.2-2 shows the time series of individual subject FEV_1 mean values and the overall daily mean in relation to the time series for exposure to $PM_{2.5}$. It should be noted that there is not an obvious correspondence between the overall mean daily FEV_1 time series and the $PM_{2.5}$ time series.

Relatively few subjects each day used rescue medication or wheezed/coughed (Figure 4.2.2-3). The maximum number of subjects who reported rescue medication use in the hour before A.M. spirometry on any given day was 6. The maximum number who reported wheeze and cough was 7 and 13.

Based on data from the published literature, for both the conventional and MSM analyses, we investigated the effects of $PM_{2.5}$ lagged 0-7 days and 2-8 day moving averages on

A.M. FEV_1. We chose FEV_1, because it is a frequently used measure to evaluate lung function in asthma and is used in the international classification systems for asthma severity . All daily individual exposures were calculated from 8 A.M. to 8 A.M, since we are using A.M. FEV_1 as our outcome. Lag 0 in all analyses represented the 24-hour average $PM_{2.5}$ concentration from 8 A.M. the day before to 8 A.M. in the morning of the FEV_1 measurement. Therefore, what we call lag 0 would correspond to lag 1 in the published literature. In the published literature, lag 0 (meaning the day of the measurement or event) actually could include exposures that followed the measurement or event; we sought to eliminate this possibility. Our classification assures that temporal ordering is preserved, since we required that the morning lung function measurements only could be made between 7-9 A.M. each panel day (see description of EasyOne quality control).

Up to 425 potential confounders and effect modifiers of the effect of estimated individual exposure to $PM_{2.5}$ on FEV_1 were considered for inclusion in the analysis. These variables fell into the following categories[1] (see Appendix R for detailed list):

- The available, estimated individual exposure to pollutants (NO_2, elemental carbon (EC), endotoxin, total pollen counts, agricultural fungi, *Alternaria*, and *Chladosporium*[2]) and their time appropriate lags and moving averages. These correspond to "co-pollutants."
- Estimates of ambient exposure to pollutants from First Street Central Site when the corresponding estimated individual exposure estimates were not available (CO, NO, particle number (NP), PAH) and their time appropriate lags and moving averages. We did not consider exposures to organic carbon due to a large number of missing data values (3402 of 4032 panel observation days were missing).
- Meteorological variables: apparent temperature derived from 24-hour average relative humidity and temperature (270), the square of apparent temperature and its lags and moving averages; 2 P.M. wind speed
- Time variables: a counter beginning Nov 30, 2000 (1st panel day of the study) and ending March 8, 2003 (last panel for which estimated individual exposure estimates were available for inclusion in these analyses), a counter that began the first day of each panel and ended the last day of each panel, square of the time counter, year, month, day of week and panel number.
- Fixed Characteristics: home ownership, pets, atopic status, height, indicators for maternal smoking during pregnancy, low birth weight and/or prematurity, questionnaire-based report of smoking in household, race, sex, age, age diagnosed with asthma (2 years or less, > 2 years), asthma severity measured at baseline.
- Time-dependent characteristics, which were asked about at each follow-up visit. The answer from the most recent interview was used. These included : pets, height, age, and use of controller medication in the past 3 months.

For all variables, except the exposure ($PM_{2.5}$) and outcome (FEV_1), missing values were handled as follows: missing values were replaced with zeros and a complementary variable was created to indicate if the new value was measured/observed (indicator=1) or imputed/missing (indicator=0). The indicator variables were considered only if the indicator variable was selected with the t-statistic. Note that both the indicators alone ***and*** the product of the imputed covariates

[1] We did not consider exposures to organic carbon due to a large number of missing data values (3402 of 4032 panel observation days were missing).

with the corresponding indicator variable were considered in the data-adaptive model selection process. When either $PM_{2.5}$ or FEV_1 was missing, the observation was excluded.

Due to time and computing limitations and to improve the efficacy of the data-adaptive model selection by reduction of the variability of the model selected, we devised a method to reduce the number of potential confounders and effect-modifiers of the relation between $PM_{2.5}$ and A.M. FEV_1 to be considered. Univariate regressions with FEV_1 and $PM_{2.5}$ were carried out with all of the candidate variables, but only those with an associated with FEV_1 or $PM_{2.5}$ (p-value of the t-statistics adjusted for repeated measure ≤ 0.1) were considered for inclusion in the model. Based on this criterion, more than 200 variables were eligible to be considered by the deletion-substitution-addition (DSA) algorithm for inclusion in the conventional and MSM models. Differences in the number of variables depended on the number of variables that was significant at the 0.1 level for the different lags and moving averages of $PM_{2.5}$. The air pollution and meteorological variables that were considered for inclusion were all preceding lags (up to 7 days) and preceding moving averages (up to 8 days) up to the $PM_{2.5}$ metric (lag or moving average) that was of interest in a given model. For example, when the exposure of interest was $PM_{2.5}$ lagged 7 days, the model considered CO lag 8 through lag 14 and an 8-day moving average of CO (lag 7+…+lag 14)/8). In these conventional analyses, we did not include factors that could be "on the causal pathway" between daily estimated individual $PM_{2.5}$ exposure and daily levels of FEV_1. An exception was made in the case of apparent temperature (AT) because: 1) levels of $PM_{2.5}$ are unlikely to affect subsequent levels of AT, and 2) the importance of adjustment for the potential influence of AT on FEV_1 as it may be a confounder of the effect of $PM_{2.5}$. Lags 0, 1 of AT and 2-8 day moving averages of AT, which incorporate Lags 0 and 1 of AT, were included. Squares of these variables were also included. This overall strategy allows the data to determine which lag structure is most consistent with the data (simple lags, moving averages, polynomial distributed lags or combinations thereof) and is much more flexible than the usual strategy that restricts a model only to a single lag structure. Moreover, this permits co-pollutants to have different lag structures than the pollutant of primary interest in the same model.

We ignored responses to EasyOne question 5 (q5, "rescue medication use in the previous hour") in the conventional analysis, as its relation to FEV_1 depends on respiratory symptoms which are on the causal pathway between exposure to $PM_{2.5}$ and the morning FEV_1 measurement -- i.e., we want to know the effect of $PM_{2.5}$ on FEV_1 in the absence of rescue medication use. We could adjust for q5; then, we also would have to adjust for the confounders of q5 (i.e., symptoms). These latter variables would create problems, since they are again on the causal pathway between $PM_{2.5}$ and FEV_1. The major problem for conventional analyses comes from such time-dependent confounders that are on the causal pathway of interest. Strategies for dealing with this medication-use variable are discussed in detail in the MSM section that follows. It should be noted that, the conventional analysis would likely underestimate the effect of $PM_{2.5}$ (under the assumption that such an effect exists) as it does not account for rescue medication use.

After the final conventional models were selected by the data-adaptive model selection (DSA) procedure, we determined the robust standard errors of the $PM_{2.5}$ parameters. Due to time limitations and due to concerns about model misspecification, we considered only the independence and autoregressive (1) (AR (1)) variance-covariance structures for the Generalized Estimating Equations methodology, i.e. based on semi-parametric models. We used the

"Empirical" option of PROC Mixed in SAS (Version 9.1). This adjustment for repeated measures is essential for the correct estimation of the standard errors.

There was no evidence of an association between estimated individual exposure to $PM_{2.5}$ concentration at any lag or for any moving average and A.M. FEV_1 (Table 4.2.2-1). Table 4.2.2-1 and all of the subsequent tables in this section present the coefficients for each of the lags and moving averages that were tested in the DSA models along with all of the covariates listed above. Estimates of the precision of each coefficient is based on two assumed variance-covariance structures: 1) Independence--this structure assumes that each day's observations are independent from those of the previous days; and 2) Autoregressive type 1 (AR1) - this structure assumes that the correlation between daily observations declines as an exponential function of the distance between the days. Misspecification of the correlation structure usually does not lead to bias in the coefficients but can lead to over estimates of the precision around the parameter estimates—expressed in the tables as the standard error of the estimate (SE) from which confidence can be calculated. Parameter estimates are not shown for any of the other "co-pollutants" that could have entered the model, since none was statistically significant.

The above analyses were repeated with $PM_{2.5}$ data from the Central Site at First Street in Fresno. For these analyses, all estimated individual exposure variables were replaced with Central Site variables. Once again, there was no evidence of an association between $PM_{2.5}$ and A.M. FEV_1 at any lag or moving average or any combination of co-pollutants and meteorological variables (Table 4.2.2-2).

Because FEV_1 is a measure of lung function that depends to a substantial degree of subject effort, we repeated these analyses with two other measures of lung function: 1) FEF_{25-75} which does include an effort-dependent component but is more reflective of small airways function and has been found to be a more sensitive indicator of functional abnormalities in asthma; and 2) FEF_{75} which is an effort-independent measure of small airway (~2mm) function and a principal site of deposition of gaseous and particulate pollutants that penetrate deep into the lung. There were 2881 non-missing observations for $PM_{2.5}$ and each of these flow measures. For FEF_{25-75}, there was no evidence of an association between estimated individual exposure to $PM_{2.5}$ for any lag or moving average (Table 4.2.2-3). For FEF_{75}, lags from 4-7 days and moving averages from 5 to 8 days all had negative signs (Table 4.2.2-4); however, none was statistically significant. Moreover, point estimates for a decrement in FEF_{75} associated with a 10 $\mu g/m^3$ change in $PM_{2.5}$ for these latter lags and moving averages ranged between 1 and 10 ml/sec.

Mobile sources and wood burning are major sources for winter $PM_{2.5}$ in the study area. To try to distinguish between these sources, we repeated the FEV_1 analysis with winter time Central Site NO (estimated individual NO exposures were not available), which has a similar temporal pattern to that for $PM_{2.5}$ and EC (Figure 4.2.2-4) and is derived largely from mobile sources (as is EC) (269). All coefficients were negative (Table 4.2.2-5). The precision for the estimates for lag 7 and 8 were such that the p-values were <0.10 (Table 4.2.2-5, see boldface type). The estimated effects of a 10 ppb increase for these latter lags were decrements between 50 and 90 ml.

We also investigated the association between estimated individual exposure and Central Site NO_2 and FEV_1. NO_2 largely is derived from mobile sources in Fresno. Estimated personal NO_2 has a temporal pattern that is similar to $PM_{2.5}$ and EC, but the Central Site pattern is not as

pronounced. (Figure 4.2.2-5). Because of the latter observation, we included data for the entire year in this analysis. We added several additional variables for possible inclusion: $PM_{2.5-10}$ and 8-hour maximum O_3 and their various lags and moving averages, and indicators for season and months of the year. Table 4.2.2-6 presents the results for estimated individual exposure. All lags (except lag 0) under the independence variance-covariance structure were negative, but all were estimated at a low level of precision and did not support an association with decreased FEV_1. Estimates with Central Site data (Table 4.2.2-7) all had negative signs; several were highly precisely estimated with the independence variance covariance structure. The estimates for lags and moving averages under the independence structure ranged from a 17-27 ml and a 27-33 ml reduction, respectively, in FEV_1 per 10 $\mu g/m^3$ increase in $PM_{2.5}$. Although the results with moving averages under the AR(1) variance-covariance structure were estimated less precisely that those under the independence models, the estimates, in general, were larger than those under the latter model.

4.2.2.2 Influence of Medication Use on the Effect of Pollutants on Pulmonary Function

As noted earlier, it is likely that rescue medication use is on the causal pathway between exposure to a given pollutant and pulmonary function, which is one of the justification for using causal modeling approaches. To examine the influence of medication use on the association between the pollutants and FEV_1, we first conducted a series of conventional analyses. This summary is restricted to analyses for 2-day moving average of Central site measurements of NO_2, and morning FEV_1. Briefly, observations from the period of November, 2000 – March 2003 were included (i.e. all seasons) and model selection was based on AIC and significance of the covariates. This demonstration expands upon that analysis described later (section 4.2.4) only in that we added terms for medication use and/or excluding observations based on their value of medication use. All models were adjusted for race category, and height from closest clinic visit. Table 4.2.2-8 is a summary of fixed effects for various models.

We used a series of steps to determine if medication use was on the causal pathway between exposure to NO_2 and morning FEV_1 in our data. First, we used a logistic model to fit the association between NO_2 and medication use. A 10 ppb increase in the 2-day moving average of NO_2 was associated with an odds of 1.18 ($p=.10$) for use of rescue medication in the hour prior to the test. Second, we used a linear model to determine if medication use was associated with FEV_1. The observations with medication use reported had a mean FEV_1 that was 0.220 L lower than the observations with no medication use reported ($p < 0.0001$). For both of these models, adjustments for race and the repeated measures design were taken into account and an independent covariance structure was used. Despite the fact that we determined that medication use was significantly associated with the outcome (FEV_1) and exposure (NO_2) of interest and clearly is on the causal pathway, we report the models below to investigate the impact that adjustment for this factor would have on our results.

In summary, the overall effect of a 10 ppb increase in NO_2 was a .017 L decline in FEV_1 ($p = 0.08$, model A). In a separate model (Model B), medication was associated with a 0.05 L decline in FEV_1, which is counter-intuitive, since medication use should be associated with an *increase* in FEV_1. (Recall, the mean FEV1 is ~1.5 L, so this corresponds to a ~3.3% average decline in FEV_1.) When NO_2 and medication use were entered in the same model (model C), the coefficients reported in models A and B were unchanged. We examined whether the effect of

NO_2 on FEV_1 was different across levels of medication use (0/1) using two methods. First, we examined the interaction between NO_2 and medication use. The interaction term was not significant (model D, p = 0.24). Based on the main effect and interaction terms, the effect of a 10 ppb increase in NO_2 on those without medication use was a 0.018 L decline in FEV_1 (nearly identical to the effect when no interaction term was included). Among the medication use=1 observations, the effect of a 10 ppb increase in NO_2 was 0.0008 L- essentially no effect. In contrast, when we ran stratified models, the effect of NO_2 was significant in both groups. There was a 0.022 L decline among non users (Model E, p = 0.03) and a 0.049 L decline among in medication users (model F, p = .06) (Table 4.2.2-8).

4.2.2.3 Summary of Conventional Acute Analyses

None of the analyses based on estimated individual exposure to $PM_{2.5}$ or NO_2 demonstrated an association with decrements in FEV_1, FEF_{25-75} or FEF_{75} The most consistent negative associations were observed between Central Site NO_2 and FEV_1, with less precise negative associations with Central Site NO. It is not clear why Central Site measures for these two pollutants should be more strongly associated with decrements in FEV_1, when estimated individual exposure (to NO_2) showed no such associations. The extent to which measurement errors in individual exposure estimates contribute to this lack of association has not yet been explored. In the absence of personal monitoring data, any such exploration will have to be based on simulated measurement error scenarios. While the overall analyses do not provide compelling evidence for associations, they do seem to indicate that, if effects are going to be observed as we accumulate more data, markers for specific sources (in this case, mobile sources) are more likely to show effects than the omnibus $PM_{2.5}$ mass measurements. Our analyses of the association between traffic exposures and baseline lung function certainly support this contention. Given the differences in the spatial distribution of EC, this pollutant is an obvious target to address this issue. A more complete discussion of these results appears later in the report.

4.2.2.4 Preliminary Analyses of Symptom and Rescue Medication Outcomes (Presented previously as part of Interim Report - August 26, 2002)

As part of preliminary analyses presented as part of the Interim Report for this contract (filed on August 26, 2002) we carried out a conventional analysis with conventional methods for model fitting of the association between Central Site concentrations several ambient pollutants and asthma symptoms “after going to bed” (a good marker for asthma severity), using the first year of data. All analyses were carried out with S-Plus 2000 Professional Release 3 software. (NB: None of the back-fitting or convergence algorithms that created the problems in the National Morbidity, Mortality, and Air Pollution Study (NNMAPS) data were used for these analyses.) We used logistic regression with the Generalized Estimating Equation (GEE) methodology to estimate the association between daily concentrations of ambient pollutants and the morning report about any symptoms since bedtime. The steps followed for modeling each pollutant are listed in Table 4.2.2-9. At each step of the process that required a model selection choice, the best model based on the Akaike Information Criterion (AIC) was selected. All analyses were based on the assumption that the variance-covariance matrix for the residuals is diagonal (i.e. observations are independent). A formal test for residual autocorrelation was not

performed. However, it should be noted that if the model chosen for the covariance matrix is mis-specified, parameter estimates are still consistent and the confidence intervals reported are correct. Only single-pollutant models were evaluated. All models were corrected for weather (temperature and relative humidity) as well as an indicator of weekend vs. weekday, season and time (defined as the number of days since November 30, 2000 (the first day home panel spirometry was collected)).

For this summary, arbitrary increments of 10 $\mu g/m^3$ and 10 ppb were used for $PM_{2.5}$ and NO_2 and O_3, respectively, for comparison with published data. For each of the pollutants, multi-day moving averages provided a better model fit for the occurrence of symptoms than did models with single day lags. In models for which adjustment was made for meteorological factors, season, time and weekend day, 5-day moving average for 24-hour NO_2 showed a larger association with symptoms than did $PM_{2.5}$ but was estimated somewhat less precisely (i.e., wider confidence interval, Table 4.2.2-10). When data from all of the months were used, the effect estimate for a 3-day moving average of 8-hour O_3, adjusted for weather, time, weekend day and season, was quantitatively similar to that for $PM_{2.5}$ but was the least precisely estimated of the three pollutants (p-value 0.25). In contrast, when the analysis for O_3 was restricted to the summer months (June, July, August) the effect estimate for O_3, adjusted for weather, time and weekend day, increased to an OR of 1.24 and was more precisely estimated than the estimate for O_3 with data for the entire period.

These very preliminary analyses based on only a single year of panel data are consistent with the conventional analyses for $PM_{2.5}$ and NO_2 and FEV_1 and FEF_{25-75} in that NO_2 was more closely associated with symptoms than was $PM_{2.5}$. In addition, the ozone analyses indicated that we are likely to see associations with symptoms when we carry out analyses with a larger sample of data.

Table 4.2.2-1: Results of Conventional Analysis of Association Between Daily Levels in Estimated Personal $PM_{2.5}$ ($\mu g/m^3$) and A.M. FEV_1 (Liters)[*]

	Variance-Covariance Structure	
	Independence	**Autoregressive(1)**
	Parameter (SE)	**Parameter (SE)**
$PM_{2.5}$ Lags[+]		
0	+0.0002 (0.0010)[++]	+0.0005 (0.0008)
1	-0.0001 (0.0010)	+0.0003 (0.0008)
2	+0.0000 (0.0011)	+0.0004 (0.0008)
3	-0.0002 (0.0011)	-0.0003 (0.0008)
4	-0.0004 (0.0011)	-0.0004 (0.0008)
5	-0.0003 (0.0011)	-0.0004 (0.0009)
6	-0.0005 (0.0012)	-0.0010 (0.0009)
7	-0.0004 (0.0011)	-0.0004 (0.0008)
$PM_{2.5}$ Moving Averages (days)		
2	+0.0008 (0.0013)	+0.0008 (0.0015)
3	+0.0008 (0.0014)	+0.0011 (0.0019)
4	-0.0000 (0.0016)	+0.0006 (0.0023)
5	+0.0006 (0.0018)	+0.0006 (0.0028)
6	-0.0004 (0.0019)	-0.0001 (0.0029)
7	-0.0007 (0.0020)	-0.0006 (0.0030)
8	-0.0008 (0.0021)	-0.0006 (0.0029)

***** $PM_{2.5}$ forced into all models; only other variables selected were height, height^2 and age in various combinations which depended on the specific lag or moving average; N=3096 observations for 168 subjects

+ lag 0 starts refers to 8 A.M. day before the spirometry test session to 8 A.M. the morning of the test session; all A.M. panels had to be performed between 7 A.M. – 9 A.M.

++ Confidence intervals can be calculated by the addition and subtraction, respectively, of (1.96∗SE) of each coefficient.

Table 4.2.2-2: Results of Conventional Analysis of Association Between Daily Levels in Central Site $PM_{2.5}$ ($\mu g/m^3$) Concentrations and A.M. FEV_1 (liters)*		
	Variance-Covariance Structure	
	Independence	**Autoregressive(1)**
	Parameter (SE)	**Parameter (SE)**
$PM_{2.5}$ Lags+		
0	+0.0001 (0.0005)	+0.0002 (0.0004)
1	-0.0001 (0.0005)	+0.0001 (0.0004)
2	-0.0001 (0.0005)	+0.0002 (0.0004)
3	-0.0003 (0.0005)	-0.0002 (0.0004)
4	-0.0004 (0.0006)	-0.0002 (0.0004)
5	-0.0007 (0.0006)	-0.0005 (0.0005)
6	-0.0009 (0.0006)	-0.0007 (0.0005)
7	-0.0008 (0.0006)	-0.0004 (0.0005)
$PM_{2.5}$ Moving Averages (days)		
2	-0.0000 (0.0006)	+0.0003 (0.0007)
3	-0.0002 (0.0009)	+0.0002 (0.0014)
4	-0.0002 (0.0008)	+0.0003 (0.0011)
5	-0.0002 (0.0009)	+0.0002 (0.0014)
6	-0.0005 (0.0010)	-0.0002 (0.0014)
7	-0.0007 (0.0011)	-0.0006 (0.0016)
8	-0.0008 (0.0011)	-0.0006 (0.0015)

***** See footnote in Table 4.2.2-1

Table 4.2.2-3: Results of Conventional Analysis of Association Between Daily Levels in Estimated Personal Exposure to $PM_{2.5}$ ($\mu g/m^3$) and A.M. FEF_{25-75} (liters/second)*		
	Variance-Covariance Structure	
	Independence	**Autoregressive(1)**
	Parameter (SE)	**Parameter (SE)**
$PM_{2.5}$ Lags+		
0	+0.0008 (0.0016)	+0.0002 (0.0012)
1	+0.0009 (0.0017)	+0.0004 (0.0012)
2	+0.0007 (0.0017)	+0.0013 (0.0012)
3	+0.0005 (0.0017)	+0.0004 (0.0011)
4	-0.0002 (0.0018)	-0.0012 (0.0013)
5	-0.0001 (0.0019)	+0.0001 (0.0014)
6	-0.0003 (0.0019)	+0.0000 (0.0015)
7	-0.0002 (0.0019)	-0.0001 (0.0015)
$PM_{2.5}$ Moving Averages (days)		
2	+0.0008 (0.0019)	+0.0004 (0.0020)
3	+0.0009 (0.0022)	+0.0016 (0.0027)
4	+0.0016 (0.0026)	+0.0020 (0.0033)
5	+0.0013 (0.0029)	+0.0012 (0.0032)
6	+0.0012 (0.0032)	+0.0010 (0.0044)
7	+0.0005 (0.0032)	+0.0007 (0.0047)
8	+0.0008 (0.0035)	+0.0008 (0.0049)

***** See footnote in Table 4.2.2-1

+ See footnote in Table 4.2.2-1

Table 4.2.2-4: Results of Conventional Analysis of Association Between Daily Levels in Estimated Personal $PM_{2.5}$ ($\mu g/m^3$) Exposure and A.M. FEF_{75} (liters/second)*		
	Variance-Covariance Structure	
	Independence	**Autoregressive(1)**
	Parameter (SE)	**Parameter (SE)**
$PM_{2.5}$ Lags+		
0	+0.0004 (0.0009)	-0.0001 (0.0008)
1	-0.0003 (0.0009)	-0.0002 (0.0008)
2	+0.0000 (0.0010)	+0.0008 (0.0008)
3	-0.0003 (0.0010)	+0.0001 (0.0007)
4	-0.0008 (0.0010)	-0.0006 (0.0008)
5	-0.0007 (0.0010)	-0.0000 (0.0008)
6	-0.0008 (0.0011)	-0.0000 (0.0009)
7	-0.0007 (0.0010)	-0.0000 (0.0000)
$PM_{2.5}$ Moving Averages (days)		
2	+0.0002 (0.0011)	-0.0002 (0.0013)
3	+0.0003 (0.0013)	+0.0006 (0.0018)
4	-0.0002 (0.0014)	+0.0004 (0.0021)
5	-0.0005 (0.0016)	-0.0001 (0.0025)
6	-0.0007 (0.0017)	-0.0001 (0.0027)
7	-0.0008 (0.0018)	-0.0001 (0.0029)
8	-0.0009 (0.0019)	-0.0001 (0.0030)

***** See footnote in Table 4.2.2-1

+ See footnote in Table 4.2.2-1

Table 4.2.2-5: Results of Conventional Analysis of Association Between Daily Levels in Central Site NO (ppb) Concentrations and A.M. FEV_1 (liters)*		
	Variance-Covariance Structure	
	Independence	**Autoregressive(1)**
	Parameter (SE)	**Parameter (SE)**
NO Lags+		
0	-0.0003 (0.0004)	-0.0002 (0.0003)
1	-0.0005 (0.0004)	-0.0000 (0.0003)
2	-0.0004 (0.0004)	-0.0000 (0.0002)
3	-0.0004 (0.0004)	-0.0002 (0.0003)
4	-0.0004 (0.0004)	-0.0003 (0.0003)
5	-0.0005 (0.0005)	-0.0004 (0.0003)
6	-0.0007 (0.0004)	**-0.0005 (0.0003**)**
7	**-0.0009 (0.0005)**	**-0.0005 (0.0003)**
NO Moving Averages (days)		
2	-0.0006 (0.0005)	-0.0003 (0.0005)
3	-0.0007 (0.0007)	-0.0002 (0.0006)
4	-0.0009 (0.0009)	-0.0005 (0.0010)
5	-0.0011 (0.0010)	-0.0010 (0.0014)
6	-0.0014 (0.0012)	-0.0018 (0.0018)
7	-0.0015 (0.0013)	-0.0025 (0.0020)
8	-0.0018 (0.0014)	-0.0032 (0.0021)

***** See footnote in Table 4.2.2-1

+ See footnote in Table 4.2.2-1 **** Bold**: p <0.10

Table 4.2.2-6: Results of Conventional Analysis of Association Between Daily Levels in Estimated Personal Exposure to NO_2 (ppb) and A.M. FEV_1 (liters)*

	Variance-Covariance Structure	
	Independence	**Autoregressive(1)**
	Parameter (SE)	**Parameter (SE)**
NO_2 Lags+		
0	+0.0002 (0.0036)	-0.0005 (0.0022)
1	-0.0015 (0.0035)	+0.0017 (0.0021)
2	-0.0014 (0.0033)	-0.0009 (0.0025)
3	-0.0013 (0.0036)	+0.0002 (0.0025)
4	-0.0012 (0.0031)	-0.0003 (0.0024)
5	-0.0012 (0.0030)	+0.0006 (0.0024)
6	-0.0013 (0.0029)	+0.0002 (0.0025)
7	-0.0009 (0.0029)	+0.0014 (0.0022)
NO_2 Moving Averages (days)		
2	-0.0008 (0.0041)	+0.0013 (0.0034)
3	-0.0012 (0.0044)	+0.0003 (0.0050)
4	-0.0014 (0.0047)	+0.0005 (0.0065)
5	-0.0016 (0.0048)	+0.0001 (0.0076)
6	-0.0017 (0.0049)	+0.0006 (0.0084)
7	-0.0018 (0.0050)	+0.0008 (0.0089)
8	-0.0018 (0.0050)	+0.0017 (0.0092)

***** See footnote in Table 4.2.2-1

+ See footnote in Table 4.2.2-1

Table 4.2.2-7 Results of Conventional Analysis of Association Between Daily Levels in Central Site NO_2 (ppb) and FEV_1 (liters)*

	Variance-Covariance Structure	
	Independence	**Autoregressive(1)**
	Parameter (SE)	**Parameter (SE)**
NO_2 Lags+		
0	-0.0021 (0.0013)	-0.0013 (0.0009)
1	**-0.0027 (0.0013)** **	-0.0009 (0.0010)
2	**-0.0025 (0.0012)**	-0.0012 (0.0009)
3	*-0.0022 (0.0012)*	-0.0009 (0.0010)
4	-0.0018 (0.0012)	-0.0009 (0.0009)
5	-0.0017 (0.0013)	-0.0009 (0.0010)
6	-0.0018 (0.0013)	-0.0013 (0.0009)
7	-0.0018 (0.0013)	-0.0013 (0.0009)
NO_2 Moving Averages (days)		
2	*-0.0027 (0.0015)*	-0.0020 (0.0015)
3	*-0.0031 (0.0016)*	-0.0030 (0.0020)
4	*-0.0032 (0.0017)*	-0.0036 (0.0025)
5	*-0.0027 (0.0015)*	-0.0041 (0.0027)
6	*-0.0032 (0.0018)*	-0.0044 (0.0030)
7	*-0.0033 (0.0019)*	-0.0049 (0.0031)
8	*-0.0033 (0.0019)*	-0.0053 (0.0032)

***** See footnote in Table 4.2.2-1

+ See footnote in Table 4.2.2-1

**** Bold $p<0.05$;** *italics $0.05 \leq P \leq 0.10$*

Table 4.2.2-8: Traditional Models* of the Influence of Medication Use on the Effect of 2-day average NO_2 on A.M. FEV_1.

Model		Estimate	Stderr	t-value	prob
All observations					
A)	NO_2	-0.00171	0.00098	-1.74	0.0816
B)	Medication use	-0.04963	0.01365	-3.64	0.0003
C)	NO_2	-0.00172	0.00098	-1.76	0.0790
	Medication use	-0.04816	0.01340	-3.59	0.0003
D)	NO_2	-0.00189	0.00099	-1.91	0.0567
	Medication use	-0.08775	0.03639	-2.41	0.0159
	NO_2* medication use interaction	0.00181	0.00155	1.17	0.2422
Observations with medication use = 0					
E)	NO_2	-0.00217	0.00099	-2.19	0.0292
Observations with medication use = 1					
F)	NO_2	0.00486	0.00256	-1.90	0.0596

* All models adjusted for race category, height and repeated measurements using an AR(1) structure. NO_2=2-day moving average NO_2 from Central Site.

Table 4.2.2-9: Procedures for Analysis for a Given Pollutant

1. For all lag/moving averages, fit 3 models
   - Fit crude pollutant model
   - Fit pollutant seasons, binary term for weekend vs weekday, and fit temperature, relative humidity and day number with B-splines with a common degree and choose this degree based on AIC and no interior knots
   - Add to each of the previous models: rescue medication use (Q5) as a main term and an interaction with the pollutant and, if necessary, select a new common degree for the splines using AIC
2. For each lag/moving average, select one of the 3 models using AIC
3. Compute for these last models the AIC associated with the observations common to every lag/moving average model and select the best lag/moving average to use for that pollutant.

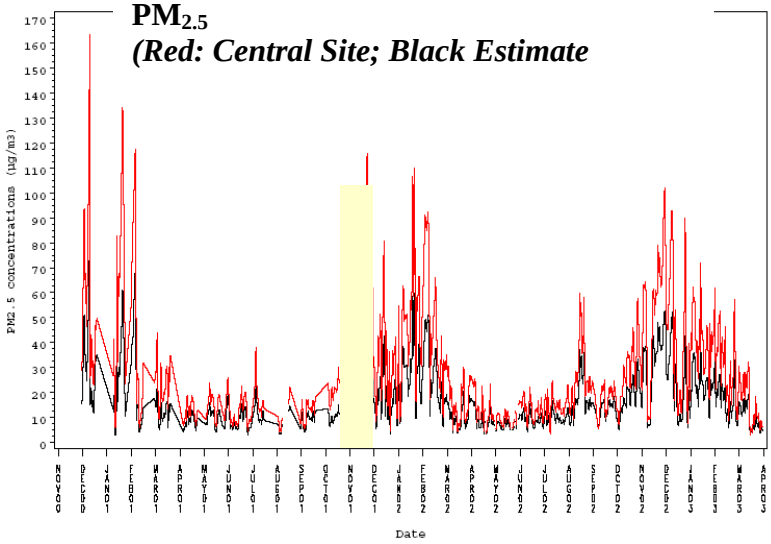
Table 4.2.2-10: Crude and Adjusted Odds Ratios For the Prevalence of Symptoms since bedtime*

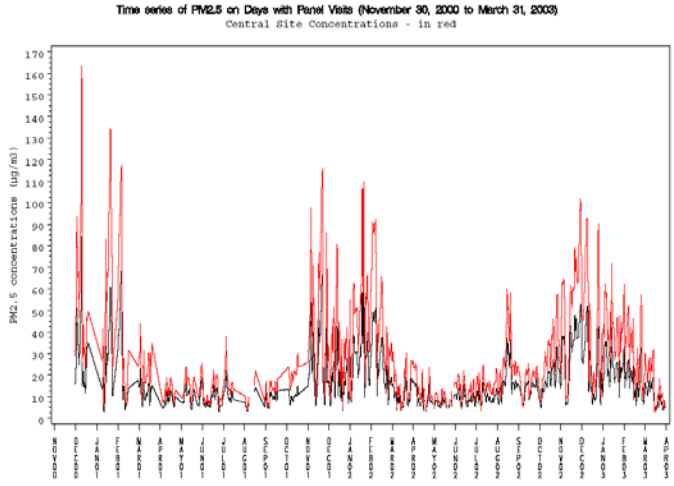
	November 2000 – November 2001 Odds Ratio (95% CI)*	
	Crude	**Adjusted for Weather/Weekend day/Season/Time**
$PM_{2.5}$ (24-hour) • 5 day mean	1.07 (0.98, 1.17)	1.09 (0.96, 1.23)
NO_2 (24-hour) • 5-day mean	1.25 (0.88, 1.78)	1.33 (0.77, 2.29)
O_3 (8-hour mean) • 3-day mean	0.92 (0.83, 1.02)	1.08 (0.86, 1.36)
June, July, August 2001 Odds Ratio (95% CI)**		
O_3 (8-hour mean) • 3-day mean**	1.09 (0.85, 1.38)	1.24 (0.85, 1.82)

***** Odds ratios are reported for 10μg/m^3 increase in $PM_{2.5}$ and a 10 ppb increase for O_3 and NO_2

****** Summer analysis does not include adjustment for season.

Figure 4.2.2-1: Time Series of Daily $PM_{2.5}$
(Red: Central Site; Black Estimate





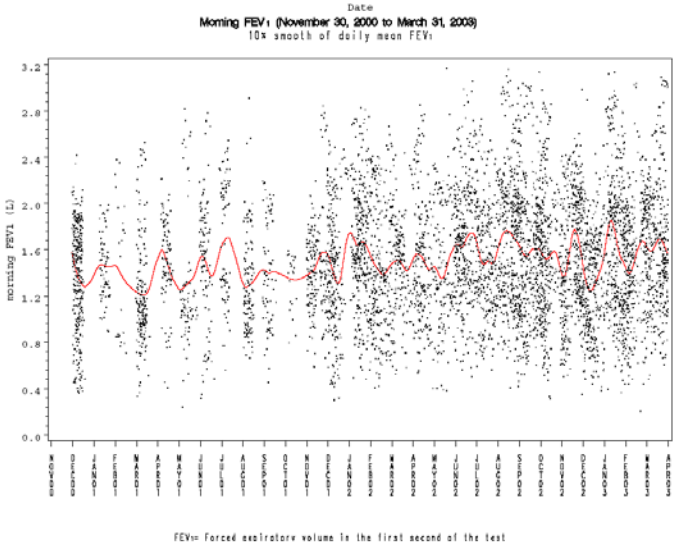
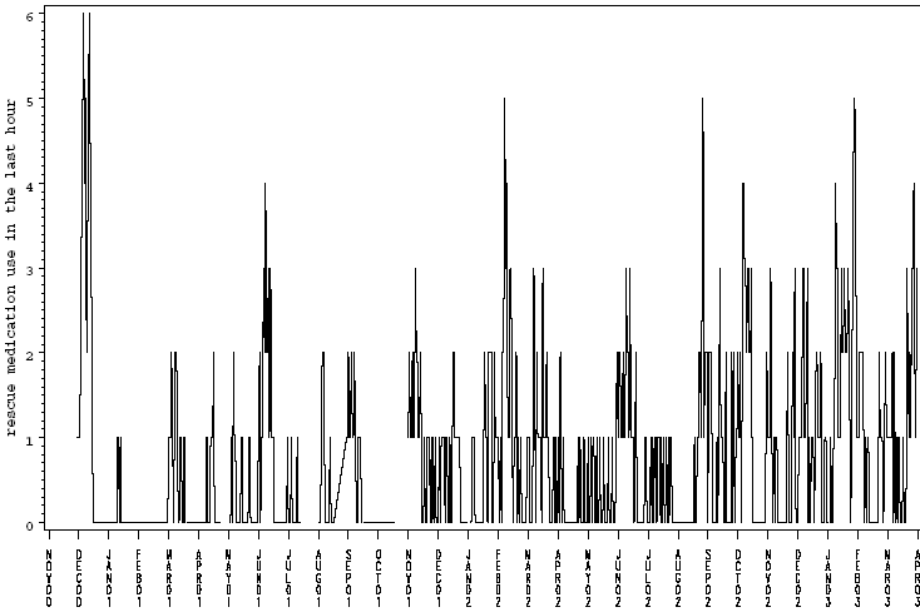
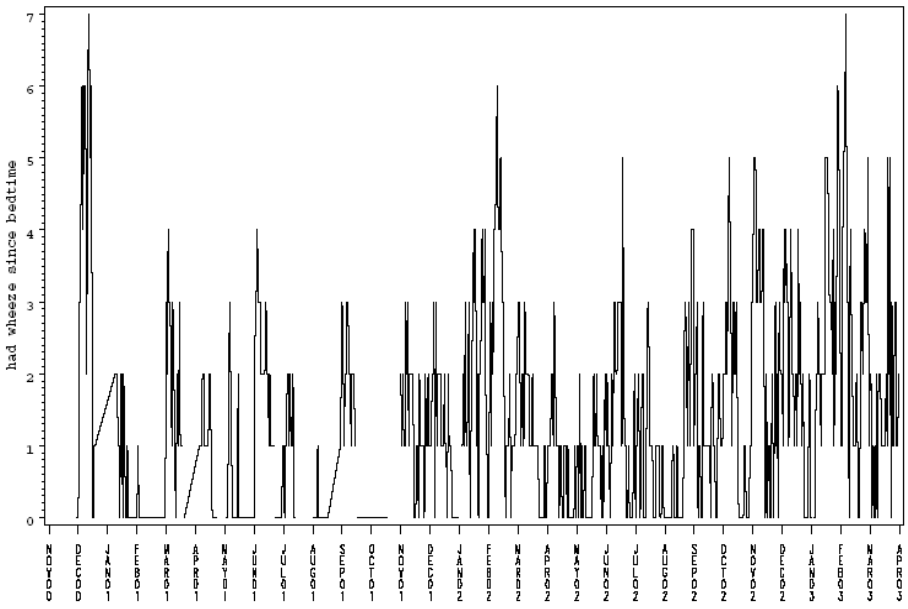


Figure 4.2.2-2: FEV1 and PM2.5 Time

Number of Children Who Reported Use of Rescue Medications
in the Hour Before the Morning Pulmonary Function Test



Had Wheeze Since Bedtime
as Reported During the Morning Pulmonary Function Test



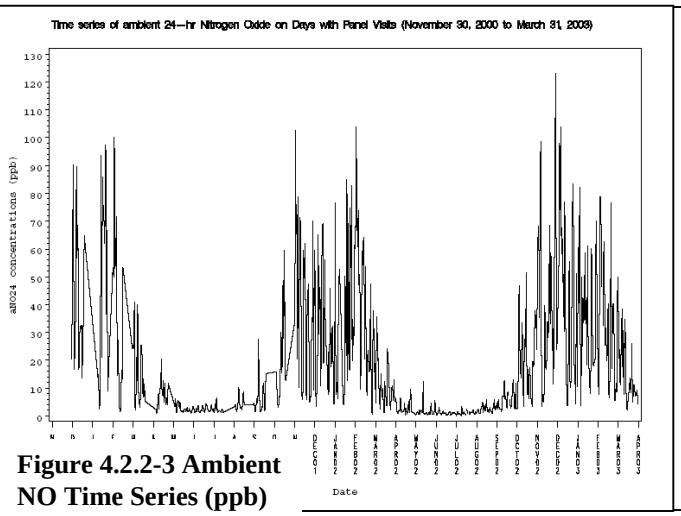


Figure 4.2.2-3 Ambient NO Time Series (ppb)

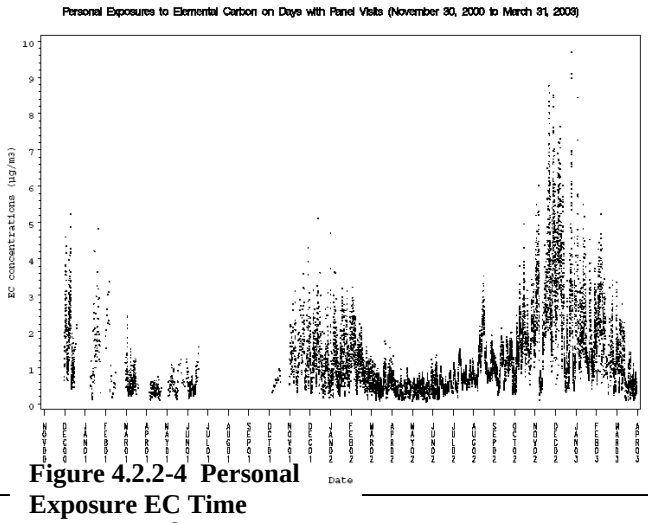


Figure 4.2.2-4 Personal Exposure EC Time Series (µg/m^3)

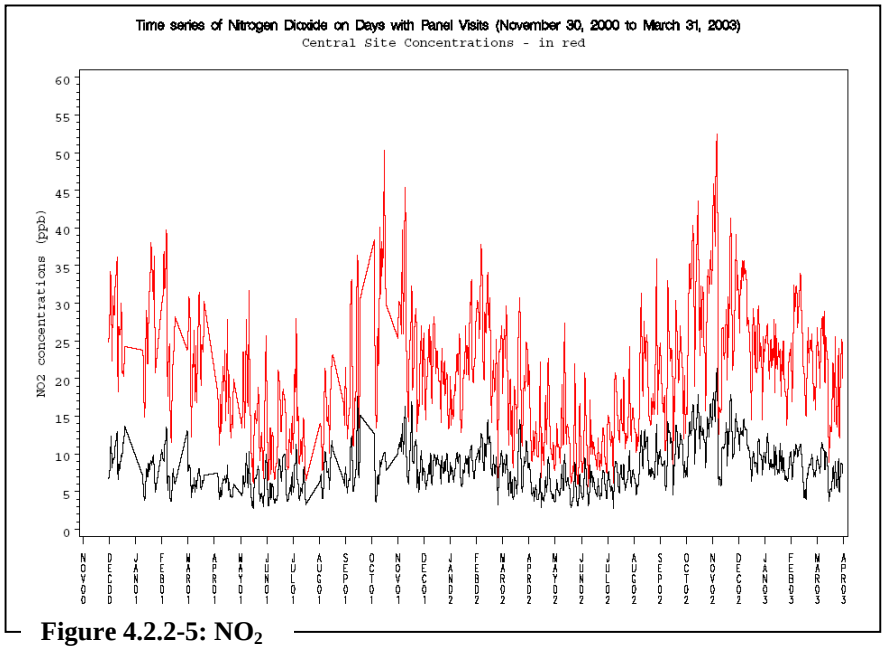


Figure 4.2.2-5: NO_2 Personal and Central Site (red)

4.2.3 Marginal Structure Model Analysis: (See section 3.6 for a summary and Appendix I for theoretical details of the statistical methods)**.**

The available data and list of potential candidate variables are described in Section 4.2.2 (also see Appendix R for list of candidate variables).

The goal of our MSM analyses is to evaluate the effect of $PM_{2.5}$ on FEV_1 had children in the cohort not used rescue medication (i.e., assess the effect of air pollution on FEV_1 through all causal pathways, except pathways which involve rescue medication use) and to take into account the potential for informative censoring of the health outcome (i.e. account for the fact that some of the "missingness" may be not random and, in particular, may be influenced by $PM_{2.5}$ exposure itself). The motivation is to remove any effect that use of rescue medication may have on amelioration of declines in lung function due to day-to-day increases in $PM_{2.5}$. While our main approach is that of a longitudinal analysis, we also carried out point-treatment analyses as well.

Before we present the actual analyses, we introduce the basic data structure for the longitudinal analysis and its modification for point-treatment analysis. The upper line of Figure 4.2.3-1 presents a longitudinal representation of the panel data. The exposures of interest (daily $PM_{2.5}$, rescue medication use in the one hour before A.M. lung function testing, indicators of censoring) are represented by 'A', while all other variables are represented with 'L'. These latter covariates include the outcome of interest and also two censoring variables, which also are considered as treatments: an indicator for completion of the EasyOne® (lung function test) session (DIDTEST) and an indicator of the acceptability of the FEV_1 measurement (ACCEPTABLE). Based on the history restricted MSM (HRMSM) methodology, we can use this longitudinal representation of the panel data to investigate the effect of an exposure regimen over "x" days, where the value for "x" is user-specified: (A(t),…,A(t+x-1)). This methodology accounts for time-dependent confounders collected between the exposure regimen of interest: L(t+1),…,L(t+x -1).

In the point-treatment representation of the panel data (lower line in Figure 4.2.3-1), these later time-dependent confounders are ignored; and this approach accounts only for variables collected prior to collection of the exposure regimen of interest: L(0)A(0)…L(t)A(t). The exception is "apparent temperature" at time t+x-2 and t+x-1 and the corresponding moving average (for the same reasons developed in section 4.4.2 on conventional analyses).

Although the point-treatment MSM approach ignores potential time-dependent confounders of the exposures of interest, it was implemented for ease of interpretation, since it is the MSM analysis that is closest to a conventional analysis of rescue medication use. Despite the limitation of the point-treatment approach, we implemented it for comparison with the longitudinal MSM approach to highlight the problems of more conventional approaches. In addition it will provide support to inferences based on the more complex longitudinal approach, which may appear as a black box for readers who are unfamiliar with MSM for longitudinal data.

Based on the longitudinal representation of the panel data, our inferences about the causal effects of interest (for a given history over "x" days of the exposures) are based on the estimation of causal parameters defined from the HRMSM and non-parametric MSM methodology applied to our problem and described in Appendix I. Briefly, the causal effects of the exposures of interest over "x" days are represented by the coefficients β of the following working causal

model: $\beta_0 + \beta_1$ MA[3](PM$_{2.5}$ over 'x' days) + β_2 SUM (rescue medication use over 'x' days) for the average counterfactual outcomes under all possible exposure regimens and if there were no censoring of the health outcome.

As noted in Appendix I, three estimators can be used to estimate the coefficients of MSMs in practice: the IPTW, G-computation and double robust (DR) estimators. Funding sources for MSM work largely came from two grants for which Dr. Mark van der Laan was the PI: 1) UC Industry-University Cooperative Research Program. The industry co-sponsor was Chiron. *Computationally Intensive Statistical Inference for Microarray Based Drug Discovery*; 2) NIH *Causal Inference and Longitudinal AIDS Studies*; and to a lesser extent from FACES. Based on this work, (251), we have established the importance of the ETA assumption for implementation of the three possible MSM estimation procedures. (Note that none of these estimators could be implemented with available public or commercial statistical software packages at the time of the submission of this report.) We have identified the central role of the ETA assumption for estimation of MSM coefficients with the IPTW estimator. The DR estimator was redefined so that its consistency property becomes robust to the ETA assumption. When the ETA assumption is violated, we established that both the DR and G-computation estimators can consistently estimate MSM coefficients under certain model assumptions. However, when the ETA assumption is heavily violated, the consistency of these two estimators will mostly rely on the model used, due to a lack of information in the data to explore the causal effects of interest. Thus, in practice, the ETA assumption is as important as the assumption of no unmeasured confounders, since otherwise, inference from MSMs will be based primarily on model assumptions rather than real information on the causal effect of interest contained in the data.

The above methodological work also suggested that violation of the ETA assumption is more likely with continuous treatments (exposures), such as air pollution. Therefore, at the start of our analyses, we had major concerns about the practical validity of the ETA assumption in our data. Due the large amount of time needed to develop complex software to implement these estimators, we, therefore, chose first to develop, test and implement the software for the G-computation estimators of the effects of interest. The decision to put our effort in to implementation of software for this estimator rather than for the DR estimator was based on the fact that the G-computation estimator is a necessary building block to implement the DR estimator. Based on the work presented in this report, we have evaluated the validity of the ETA assumption in our data. Our initial concern about its validity problem is not supported by the data (i.e., ETA is **not** violated for rescue medication and only minimally violated for $PM_{2.5,}$ in part because we restricted the analysis to the winter months). Thus, we will focus our efforts on the implementation of the IPTW estimator of the causal effects of interest in this study in work to be done during the augmentation period for this contract.

The following steps were followed to implement the G-computation estimate of the causal effects of interest in the longitudinal MSM approach:

- **Data reduction:** This step is necessary to allow a practical implementation of G-computation estimation in longitudinal studies with many covariates (271). This step aims to summarize the time-dependent confounding represented by $L^*(t+1)\ldots L^*(t+x-1)$ (which is composed of many variables) and baseline confounding into a more concise

[3] We considered only moving averages in the MSM analyses.

representation, $L^*(t)$ (far fewer variables) without loss of the necessary information required for the *sequential randomization assumption* (no unmeasured confounding) to hold. This data reduction step is based on generalized linear models for the treatments (exposures): $PM_{2.5}$ (general linear), rescue medication use (MEDUSE, logistic), whether an EasyOne® session was performed without regard to the acceptability of the data (DIDTEST, logistic), and whether there at least two acceptable FEV_1 measures (ACCEPTABLE, logistic).

- The models were selected based on a deletion/substitution/addition (DSA) algorithm with cross-validation and the L2 loss function: (Model constraints: *maximum of 2-way interactions, maximum sum of power in each term=2, maximum number of terms=10*. See Appendix I.)
- The set of potential confounders were defined as a) past covariates based on subject-matter considerations and with missing values imputed with 0's, (except for $PM_{2.5}$, rescue medication use and the outcome, FEV_1-see section 4.4.2); b) indicator variables for variables imputed with 0's; and c) past exposures. The "past" of each variable considered was defined as lag 0 through 7 and moving averages over 2 to 8 days. This initial set of potential time-dependent confounders was reduced to a smaller subset of potential confounders, based on the level of association of each variable in the initial set with the outcome of interest (FEV_1)-- based on t/z-statistics adjusted for repeated measurements (p-value <=0.1). (See Appendix R for list of the complete list of covariates**)**
- The linear part of the model for $PM_{2.5}$,MEDUSE, DIDTEST and ACCEPTABLE defines a new "aggregate" time-dependent variable (i.e., measured for each observation collected at time t) W1(t), W2(t), W3(t) and W4(t), respectively (e.g., for one of the analyses and for rescue medication, the linear model selected by DSA was: W2(t)=*pq5(t)+q3(t)+q5L1(t)+q2(t)+pq5L1(t)+q3L1(t)*) (q5=rescue medication use in the one-hour before morning lung function testing, q2=wheeze since bedtime, q3=cough since bedtime; prefix, *p*, designates evening measurements; suffix, *L1*, designates "lag 1").

The steps above give rise to the reduced longitudinal data structure:

$L^*(0)$ A(0) $L^*(1)$ A(1) $L^*(2)$ A(2) $L^*(3)$ A(3) $L^*(4)$ A(4) (see Figure 4.2.3-1 for color code)
Where: $L^*(2t)$=W1(2t) and $L^*(2t+1)$=(W2(2t+1), W3(2t+1), W4(2t+1) FEV_1) [See footnote 4]

- **Model selection of the QFx part of the likelihood of the reduced data** (For full explanation of the QFx part of likelihood, see Appendix I.)
  Under the sequential randomization assumption, the QFx part of the likelihood of the reduced data represents the distribution of the time-dependent process $L^*(t)$ given past observed covariates. We used Gaussian and logistic models to estimate the QFX part of the likelihood in our analyses:

[4] The designation "(2t)" and "(2t+1)" refer to even(always A.M.) and odd (always P.M.) time points to ensure that the measure of $PM_{2.5}$ exposure always precedes the measure of rescue medication use and FEV_1.

- f(W1(2t)/ past W1, past W2, past W3, past W4, past FEV1, past $PM_{2.5}$, past MEDUSE, past DIDTEST, past ACCEPTABLE, time variables, meteorology)[5]
- f(W2(2t+1)| past W1, past W2, past W3, past W4, past FEV1, past $PM_{2.5}$, past R, past did test, past acceptable, time variables)
- f(W3(2t+1)|past W1, past W2, past W3, past W4, past FEV1, past $PM_{2.5}$, past R, past did test, past acceptable, time variables)
- f(W4(2t+1)| past W1, past W2, past W3, past W4, past FEV1, past $PM_{2.5}$, past R, past did test, past acceptable, time variables)
- f(FEV1(2t+1)| past W1, past W2, past W3, past W4, past FEV1, past $PM_{2.5}$, past R, past did test, past acceptable, time variables)

Model 'e' represents the test of the hypothesis that past $PM_{2.5}$ and rescue medication use cause direct or indirect (through past W1-W4 variables) changes in FEV_1. Confounders of these causal relations are incorporated into the analysis through W1 and W2. Correction for informative censoring due to failure to provide acceptable measures of FEV_1 is included in the analysis through W3 and W4.

The model selection procedure was carried out with the DSA algorithm with cross-validation and the L2 loss function: maximum of 2-way interactions; maximum sum of power in each term=2; maximum number of terms=10.

- G-computation estimation based on the aforementioned three QFx models was reported only when the QFx part of the likelihood indicated a causal effect. Confidence intervals were then computed by bootstrapping.[6]

The procedures described above were used for all MSM longitudinal analyses. For the presentation of the results, we present only the exposure parameters of interest, since the parameter estimates for other terms (covariates) in the models selected by the DSA are not of particular interest. We do indicate which variables were selected into the models in selected instances.

4.2.3.1 General Comments about the Presentation of the MSM Data

Since the estimates for the final models for each longitudinal MSM involves several steps, the results will be presented in the same order for each analysis:

1. Data Reduction: We present the variables that, in a linear combination, make up the W that defines each L^* (See figure 4.2.3-1 above) that, in turn, explain the confounding structure for each of the "treatments". As explained above, each 'W' carries with it the confounder information contained in the linear combination that best describes it. These variables correspond to the variables selected by the model selection procedure applied to the treatment mechanisms.

[5] "Past" designates lags up to 7 days and moving averages from 2-8 days. Lag 0 defines the 24 hours prior to the morning spirometry session. Past FEV_1 is included in the function W1, since level of FEV_1, in so far as it reflects overall asthma status, could impact time spent outdoors and, therefore, estimated personal exposure to $PM_{2.5}$.
[6] In fact, no confidence intervals are presented, since there were no parameter estimates for $PM_{2.5}$ or R that suggested an effect.

2. Next we present each of the models that define the conditional distribution of L^*, given past, observed variables. These models correspond to the models for the QFx part of the likelihood of the reduced observed data. These models are used to obtain the G-computation estimate of the MSM parameters that represent the causal effect of interest (see Appendix I). When Ws appear as independent variables (moving averages, lags), they carry with them all of the information of the linear combination of confounder variables which define them -- i.e. the information content of these variables is contained in the Ws.
3. Lastly, we present the final fitted MSM for the mean counterfactual FEV_1 that results from all of the antecedent steps. This is the causal model from which we make inferences. However, we do not present the parameter estimates for such models when the QFx models obtained from step 2 do not indicate any effect of the air pollution exposures considered.

At each step of the process, we specify the number of candidate variables available for consideration in each application of the DSA algorithm. In addition, all models considered at each step were limited to models with a maximum of 10 terms, with the sum of powers not greater than 2 for a single variable or interaction (maximum of two-way interactions). In some cases, we made exceptions to this rule and considered models of size up to 20 terms; these are noted specifically. The number of candidate variables available for each step is the same, however, we reduced this number by limiting our selection to variables that were associated with the outcome (i.e., a p-value < 0.1.). The number of variables actually used in the DSA decreased for models of longer moving averages, because fewer variables are associated with the outcome as we look at exposure that were more distal to the outcome. For example: When we look at a lag 0 effect, most of the candidate variables are very close in time to the outcome (a maximum of 7 time points separate them) and are more likely to be correlated with that outcome. When we look at the effect of a moving average over 7 days, the candidate confounders are separated by 8 to 14 days from the outcome, and therefore are less correlated with that outcome. Table 4.2.3-1 presents an example for individual exposure to $PM_{2.5}$ and morning FEV_1, the interpretation of which is discussed in the specific section below.

In addition to the longitudinal MSMs, we carried out point-treatment MSM models as noted above. Based on the point-treatment representation of the panel data, our inferences about the causal effect of interest (for a given history over "x" days of the exposures) are based on the estimation of causal parameters defined with a MSM that represents the causal effect adjusted for all confounders. Estimation of such causal effects can be done through conventional least square regression for association models. Indeed, in the point-treatment MSM approach, the association model for the conditional mean outcome, given the exposures ("treatments") of interest and all confounders, defines parameters which can be interpreted as adjusted causal effects -- i.e., a least square regression can provide a fit for the MSM in this point-treatment approach. We used the model selection procedure (i.e. DSA) previously described for the longitudinal MSM approach to adjust properly for confounders of the effect of interest. However, in each regression model that represents the adjusted causal effects of the exposures over "x" days where x=1,…,7, we forced in marginal terms that correspond to the appropriate moving average of $PM_{2.5}$ and rescue medication use over "x" days. We report the coefficients associated with each term, and we indicate which variables were selected into each model.

4.2.3.2 Effect of Estimated Individual exposure to $PM_{2.5}$ and Rescue Medication Use on A.M. FEV_1

As noted in Table 4.2.3-1, there was no evidence in the longitudinal MSM for an effect of $PM_{2.5}$ or rescue medication at any lag or any moving average on A.M. FEV_1.

The results for the point-treatment model are presented in Table 4.2.3-2[7]. There was no evidence of an effect of individual exposure $PM_{2.5}$ on morning FEV_1. In fact, all of the parameter estimates had a positive sign. Moreover, there was no consistent effect of rescue medication on morning FEV_1, and, in all cases, the sign in front of the coefficient for the first order term for rescue medication use was negative. We also carried out a point-treatment analysis that permitted up to 20 variables to be included in the models at each step. The results were essentially the same as those in Table 4.2.3-2 and are not presented.

We were concerned that the results in Tables 4.2.3-1 and 4.2.3-2 could have been due to the fact that we did not adjust properly for all of the confounders of the effect of rescue medication use. To address this problem, we carried MSM analyses where rescue medication in the hour before the morning FEV_1 was the outcome -- i.e., adjustment for confounders of the effect of rescue medication use on A.M. FEV_1 is not an issue in this analysis. In the longitudinal MSM, there was no evidence that $PM_{2.5}$, either directly or through another variable, caused the use of rescue medication (Table 4.2.3-3). Past use of rescue medication was the only main variable associated with rescue medication use in the hour before A.M. lung function testing. The analysis was repeated with the point-treatment approach (Table 4.2.3-4). There was no evidence that individual exposure to $PM_{2.5}$ at any moving average caused an increased use of rescue medication in the hour prior to the morning lung function testing. On the basis of these two analyses with rescue medication as the outcome, we do not think that that the failure to find causal relations between $PM_{2.5}$ and FEV_1 is due to the failure to capture fully the confounders of rescue medication use -- i.e., we find no evidence that $PM_{2.5}$ is exerting an effect on FEV_1 through an effect on rescue medication use. An analysis that allows for up to 20 variables in the models leads to identical conclusions and is not presented. Moreover, in a subsequent analysis (see section 4.4.3.4) with NO_2 that used data from the entire year (i.e., many more observations), we found that when we did not force the pollutant term (NO_2) into the model, the DSA algorithm did not select NO_2 in any model. Therefore, the significance of pollutant terms in the treatment models must be interpreted in this context.

4.2.3.3 Effect of Exposure to Central Site Concentrations of $PM_{2.5}$ and Rescue Medication Use on A.M. FEV_1

The estimation of individual exposure has unmeasured measurement error, which, in the absence of personal monitoring, we cannot estimate properly. It is possible that measurement error led to sufficient bias such that exposure effects were not detected. To address this issue, we carried out analyses in which we used exposures based on the Central Site data. These analyses seemed appropriate, since the vast majority of studies of the effects of acute changes in air

[7] These models look complex, because they are presented explicitly, unlike what is done usually in the published literature when splines or non-parametric smoothes are used. These latter models are just as complex, but the actual representation (e.g, designation of specific variables) of the function form of the model is not presented—just the coefficient in front of the exposure is given.

pollutants on health outcomes have used data from area-wide monitors. The longitudinal MSM with Central Site $PM_{2.5}$ did not show any relation between $PM_{2.5}$ and A.M. FEV_1 at any moving average. We repeated the analysis with a point-treatment model (Table 4.2.3-6). This analysis also showed no evidence for a relation between Central Site concentrations of $PM_{2.5}$ and A.M. FEV_1 (Table 4.2.3-6). All but one of the coefficients for rescue medication use had a negative sign and were statistically significant for an inverse effect. The one exception was the 6-day moving average that included a square term for rescue medication that would lead to a positive association with A.M. FEV_1. An analysis that allows for up to 20 terms in the models gave identical results.

As was the case for individual exposure to $PM_{2.5}$, we carried out longitudinal and point-treatment MSM analyses with rescue medication use as the outcome. In neither analysis was there any suggestion of a relation between Central Site levels of $PM_{2.5}$ at any moving average and use of rescue medication in the one-hour before A.M. lung function testing (results not shown).

4.2.3.4 Effect of Estimated Individual exposure to $PM_{2.5}$ and Rescue Medication Use on A.M. FEF_{25-75}.

As noted in the methods section, FEV_1 is a measure that is determined largely by effort, especially in young children. Therefore, we carried out MSM analyses with FEF_{25-75}. As noted previously, the former has been found to be a more sensitive measure of lung function abnormality in asthma and the latter is a measure that depends solely on mechanical properties of small airways (~2mm).

The longitudinal MSM for FEF_{25-75} showed a *positive* relation between lag 2 of individual exposure to $PM_{2.5}$; rescue medication did not enter the model (Table 4.2.3-7). However, this positive coefficient only can be interpreted by looking at the effect of W1 in the models for W2-W4—i.e., estimated individual exposure to $PM_{2.5}$ was not included in any of the QFx models and, therefore, had no relation through any of the Ws.

The point-treatment analysis also failed to show any relation between $PM_{2.5}$ at any moving average and A.M. FEF_{25-75} (Table 4.2.3-8). The main effects parameters for rescue medication use were all negative and most were statistically significant.

4.2.3.5 Effect of Exposure to Central Site Concentrations of NO and Rescue Medication Use on A.M. FEV_1

As noted previously, the sources of wintertime $PM_{2.5}$ in Fresno are derived largely from mobile sources and wood burning. To determine if a more specific marker for mobile sources would give different results, we carried out longitudinal and point-treatment MSM analyses with Central Site NO (estimated individual exposure data were not available at the time of this submission). In the longitudinal MSM, a 6-day moving average of 24-hour NO did enter the model for A.M. FEV_1; however, the sign of the coefficient was *positive* and not significant at $p < 0.05$. (Table 4.2.3-9). Point-treatment MSM did not reveal any significant associations with 24-hour Central Site NO concentrations at any moving average.

4.2.3.6 Effect of Exposure to Estimated Individual exposure and Central Site Concentrations of NO_2 and Rescue Medication Use on A.M. FEV_1

NO_2 also is derived largely from mobile sources in Fresno (269). In addition, NO_2 does not have the distinct seasonal pattern that is seen with NO and $PM_{2.5}$, as shown previously. Therefore, this analysis covered all months of the year.

Although an interaction between lag 3 of the previous day's estimated individual exposure to NO_2 and W1 (data reduction for estimated individual exposure to NO_2) were included in the QFx model for rescue medication use, W2, (positive sign which indicates increased rescue medication use with increased exposure to NO_2), the final longitudinal MSM model for FEV_1 did not include any term for estimated individual exposure to NO_2 (Table 4.2.3-11). The point-treatment model for NO_2 also failed to show any effect of estimated individual exposure to NO_2 on A.M. FEV_1 (Table 4.2.3-12).

Since most of the signs for rescue medication use were negative and significant in the above NO_2 analyses (Tables 4.2.3-11, 4.2.3-12), we carried out analyses in which rescue medication use in the hour before the A.M. lung function testing was the outcome. The longitudinal MSM did not show any effect of estimated individual exposure to NO_2 on use of rescue medication in the one-hour before A.M. lung function testing (Table 4.2.3-13). The point-treatment MSM also did not show any effect of estimated individual exposure to NO_2 on rescue medication use. Of note is the observed associations between estimated individual exposure to to NO_2 and *Cladosporium* concentrations (net negative association), the agricultural group of fungi (net positive association for month of December) and endotoxin (net negative association) observed for the data reduction step for W1 in the longitudinal MSM (Table 4.2.3-11). The positive association with *Cladosporium* is driven largely by the spike in concentration for this species that is centered on December in winter of 2002-2003 (Figure 4.2.3-2). The negative association with the agricultural group is not as obvious from Figure 4.2.3-2, since its association with NO_2 is the sum of interactions with 3 and 6-day moving averages (negative association), panel number since the start of the study (positive association) and the presence of an actual measure of *Cladosporium* (Table 4.2.3-11) These associations were not seen with winter time $PM_{2.5}$. These results point to the need to consider exposures to fungi and endotoxin in the evaluation of effects of exposures to anthropogenic pollutants. The point-treatment analysis also failed to show an effect of estimated individual exposure to NO_2 on FEV_1 (Table 4.2.3-12), and, in the case of the 5-day moving average, there was a significant positive relation with A.M. FEV_1 (Table 4.2.3-12). Individual exposure to *Cladosporium*, the agricultural group of fungi and endotoxin were not selected for any point-treatment model.

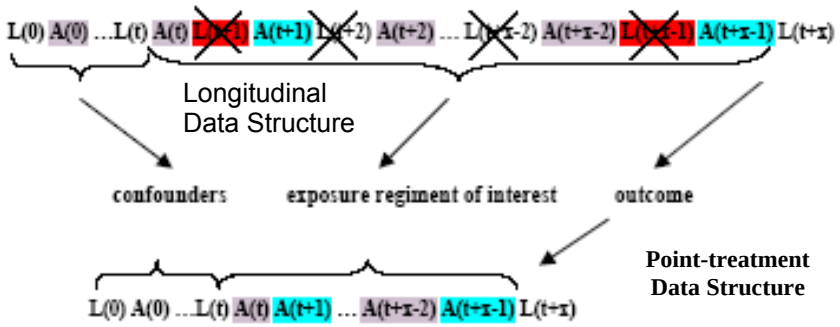
As with exposure to $PM_{2.5}$, we carried out an analysis for which use of rescue medication was the outcome and estimated individual exposure to NO_2 was the exposure of interest. In the longitudinal MSM, there was no relation between estimated individual exposure to NO_2 and use of rescue medication in the one hour before A.M. lung function testing (Table 4.2.3-13). In contrast, the point-treatment MSM found positive relations between all moving averages of estimated individual exposure to NO_2 and rescue medication use (Table 4.2.3-14). Moving averages of 3, 4, 5 and 6-day NO_2 had coefficients that were statistically significant. If, contrary to fact, all children experienced a 1 ppb increase in estimated personal 3 and 6-day moving average exposure to NO_2, the odds of the use of rescue medication in the one hour before lung function testing would be 1.033 (95% CI: 1.014, 1.053) and 1.054 (1.029, 1.080), respectively.

(These estimates ignore stratum-specific effects implied by the other covariates in the model, which are interpreted as interaction effects in an MSM model.) As noted previously, we when did not force NO_2 into the model, no lag or moving average of NO_2 was selected for inclusion in the model by the DSA algorithm. Therefore, these results need to be interpreted cautiously.

We also carried out analyses based on effects of Central Site NO_2 on A.M. FEV_1. The longitudinal MSM again showed that estimated individual exposures to *Cladosporium*, the agricultural group of fungi and endotoxin were associated with Central Site NO_2. The net signs for these associations were the same as those for estimated individual exposure to NO_2. As was the case for personal NO_2, there was no evidence of a relation between exposure to 24-hour Central Site NO_2 and A.M. FEV_1 in this model. The point-treatment MSM demonstrated significant negative coefficients for the 2-day through 5-day moving averages -- the 6- and 7-day averages were of similar magnitude to the other averages, but were not statistically significant (Table 4.2.3-16). These coefficients indicate that, if contrary to fact, the subjects had received an estimated daily individual exposure of 10 ppb *less*, A.M. FEV_1 would increase by approximately 24-32 ml per day (point estimates). This represents an increase of 1.6-2.3% for the daily average FEV_1 for the subjects. However, for moving averages from 3 to 6 days, the models indicate that, if contrary to fact all children used rescue medication, A.M. FEV_1 would *decrease* by approximately 200-250 ml (point estimates). The 2- and 7-day moving average models indicate that use of rescue medication in the hour before lung function testing is related to an increase in FEV_1, and the size of the increase decreases with age at baseline and is increased in the month of December. However, the net effect in these models for rescue medication use are not consistent. For the 2-day moving average model, the effect of rescue medication would be to *decrease* A.M. FEV_1 for all subjects 6 years and older -- i.e., most of our subjects at baseline (median 8, range 6-12 years; see Section 4.2.1 for full description of ages). The 7-day moving average model indicates that rescue medication would lead to a *decrease* in A.M. FEV_1 for all subjects 7.5 years and older (Somewhat more than 50% of our subjects, see Section 4.2.1 for full description of ages).

MSM analyses also were conducted with exposure to Central Site NO_2 with rescue medication use as the outcome. The longitudinal MSM did not show any effect of Central Site NO_2 on use of rescue medication in the hour before lung function testing. In the point-treatment MSM, the coefficients for the effect of exposure to Central Site NO_2 on rescue medication use in the hour before lung function testing were all positive but were estimated with relatively poor precision.

Figure 4.2.3-1—Data Structure for



Not highlighted:

- Morning FEV_1
- Time-dependent confounders of the effect of $PM_{2.5}$ (e.g., other pollutants, weather variables, time variables) and variables that affect both the outcome and the censoring indicators

Highlighted in…

- Grey= $PM_{2.5}$ 24-hour average (lags and moving averages)
  Red= time-dependent confounders of the effect of rescue medication on FEV_1 (e.g., previous evening FEV_1, rescue medication, wheeze and cough)

Blue= Rescue medication one hour before the morning

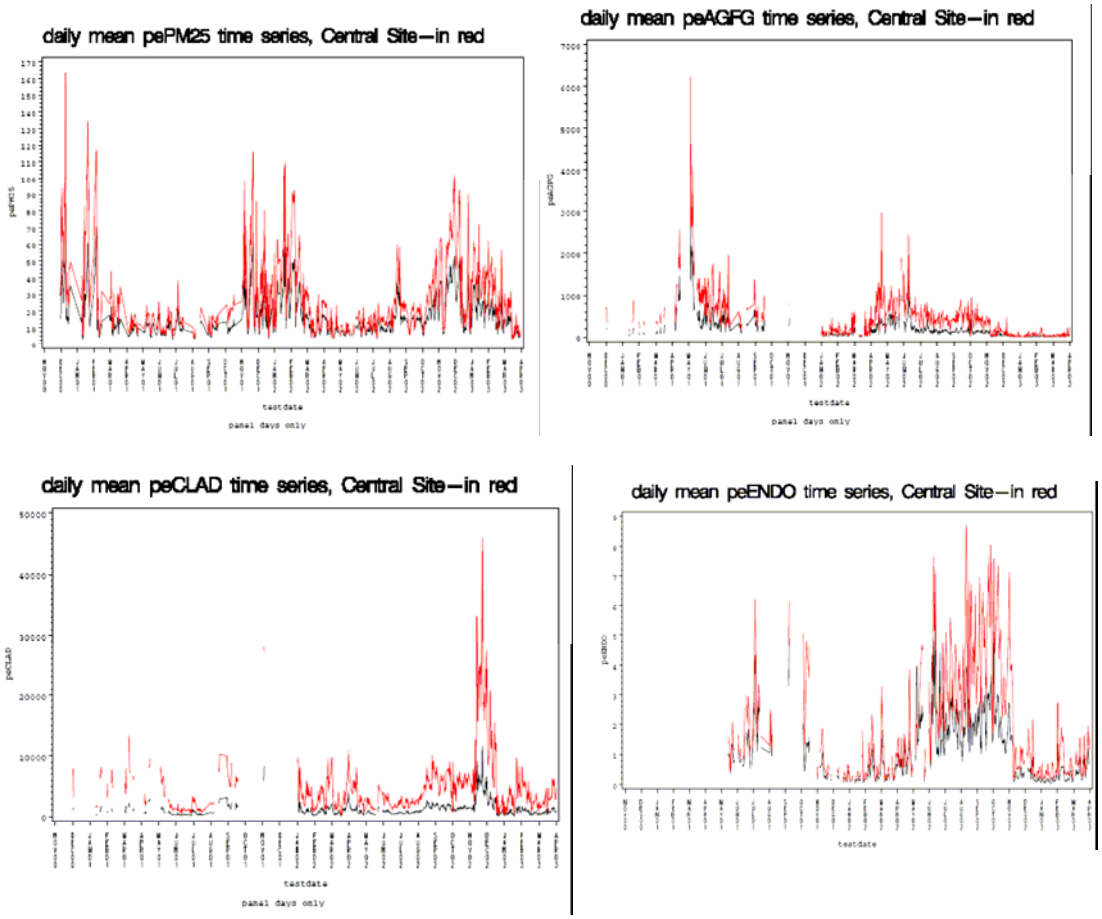


Figure 4.2.3-2: Time Series for Estimated Personal and Ambient Exposure to NO_2 *Chladosporium* and Agricultural Fungi for Panel Days

Table 4.2.3-1: **Longitudinal MSM Results for Effect of Estimated Personal Exposure to $PM_{2.5}$ on A.M. FEV_1**

(Prefix **p**=evening measurement; **In**=Yes if information is available, No if information is missing --; **pe**="personal" exposure estimate; Suffix **L**=lag (L2=lag 2); **A**=moving average (A2=2-day moving average); Variables: **RMed**=rescue medication use in 1-hour before A.M. test; **pRmed**=rescue medication use 1 hour before evening sesion; **wheeze**=wheeze since bedtime; **pwheeze**=wheeze reported during evening session; **cough**=cough since bedtime; **pcough**=cough reported in evening session; **fev1**=mean fev1 (from at least two acceptable measurements) during AM session; ;**pfev1**= fev1 measurement during the evening session; **didtest**=attempted an A.M. EasyOne session; **accept2**= at least 2 acceptable FEV1 measurements; ageV= age during panel visit; **panel visit number** = number according to scheduled not completed visits; **day of panel** = numbered 1-14;**day of study** (1=start of study); indicator variables for **day of week** (1=Sunday), **month** (1=January); **atopic**=skin test positive to at least one of tested antigens); **endo**=endotoxin; **agrg**=agricultural fungi group; **clad**=cladosporium)

DATA REDUCTION STEP:

- **W1**→***"Personal" $PM_{2.5}$*** ~ panel visit number + question about home ownership answered + FEV_1 L8 +panel visit^2 (65 candidate variables, 4018 observations)
  - *Interpretation*: best linear combination associated with $PM_{2.5}$ from among 65 variables
- **W2**→ ***Rescue Medication (RMed)*** ~ pRMed + cough + wheeze + pRMedL1 +coughL1 (72 candidate variables, 3336 observations)
  - *Interpretation*: best linear combination associated with rescue medication use in hour before test; pq5 L1=R use 2 nights prior to test from among 72 candidate variables
- **W3**→ ***Didtest***~ FEV_1 + coughA2 +wheezeL1∗ age at visit} +{ FEV_1A2∗FEV_1A7} + {panel visit number∗ FEV_1L7} + own home +$pFEV_1^2$ + {$pFEV_1$L4 ∗ FEV_1A2} + {q2L1∗q3L4} + {q3L2∗FEV_1A2} (72 candidate variables, 4032 observations)
  - *Interpretation*: best linear combination associated with attempted performance of an EasyOne session from among 72 candidate variables
- **W4**→***Accept2***~$pFEV_1$ + FEV_1A2 (72 candidate variables, 3336 observations)
  - *Interpretation*: best linear combination associated with completion of 2 acceptable FEV_1 measures from among 72 candidate variables

2. MODELS FOR QFX PART OF LIKELIHOOD (SEE APPENDIX H) FOR EACH W

- **W1**~ W1L1 + FEV_1 + day of panel + day of panel^2 + W1L2 + Thursday + Friday + day of study
  - *Interpretation*: variables best associated with W1 from among *55 candidate variables*; lags of W1 indicate associations with previous days' $PM_{2.5}$ and all other variables contained in W1; inclusion of FEV_1 reflects time dependent effects of FEV_1 on estimated personal exposure to $PM_{2.5}$, time variables reflect temporal trends and day of week effects.
- **W2**~ W2A2 + rmedL1 + {FEV_1A2∗W3A2} + {W2L2∗W3L2} + {rmedL2∗W2A2}
  - *Interpretation*: variables best associated with W2 from among *54 candidate variables*; previous rescue medication use, FEV_1 and attempt of an EasyOne session most associated
- **W3**~W2L2^2 + W2^2 + W3L1 + {rmedL1∗FEV_1A2} + {rmedL1∗W2} + {W2L2∗W3L2} + {W2L2∗W3L2} + {W2L1∗W2A2} +{W2L1∗W2} + {W2L2∗ W2L1}
  - *Interpretation*: various combinations of factors related to rescue medication use and level of FEV_1 most important from among *55 candidate variables*
- **W4**~FEV_1A2 + W4A2 + W3 + W3^2 + W3L1 + Sunday + Saturnday + day of panel
  - *Interpretation*: previous EasyOne® session, level of FEV_1 and days of week most important among *56 candidate variables*

FINAL MODEL FOR FEV_1:

- FEV_1~FEV_1A2 +W4^2 +{ FEV_1L1∗ FEV_1A2} + {W(4)∗ FEV_1A2}
  - *Interpretation*: **No direct effect of $PM_{2.5}$ or rescue medication**; previous FEV_1 and factors which affect completed test most important; **no effects of $PM_{2.5}$ or rescue medication which acts through other summary variables**

Table 4.2.3-2: **Point-Treatment MSM Results for the Effect of Personal Exposure to $PM_{2.5}$ and Rescue Medication Use on A.M. FEV_1 ($PM_{2.5}$ and Rescue Medication Use Forced in to the Model)***

TWO-DAY MOVING AVERAGE $PM_{2.5}$ (55 candidate variables, 2549 observations)

- FEV1~***"Personal" $PM_{2.5}$A2*** + rmedA2+ age at visit + {FEV_1L2∗FEV_1L3} + {age at visit∗FEV_1A2} +{FEV_1L2∗pFEV_1L2} + {FEV_1L3∗pFEV_1L3} + {FEV_1A2∗pFEV_1A2} + {wheezeL2∗December}
  - **$pePM_{2.5}A2$ = +0.00048(0.00076); rmedA2 = -0.13050 (0.04097)**

THREE-DAY MOVING AVERAGE $PM_{2.5}$ (46 candidate variables, 2118 observations)

- FEV_1~p$PM_{2.5}$A3 + rmedA3 + FEV_1L3^2 + FEV_1A2^2 + age at visit + FEV_1L4^2 +FEV_1L3+ FEV_1L4
  - **$PM_{2.5}A3$ = +0.00036 (0.00096); rmedA3 = -0.17199 (0.05760)**

3. **FOUR-DAY MOVING AVERAGE $PM_{2.5}$** (38 CANDIDATE VARIABLES, 1758 OBSERVATIONS)

- FEV_1~$PM_{2.5}$A4 + rmedA4 +FEV_1L4^2 +FEV_1L4 + age at visit + FEV_1L5^2 +FEV_1A2^2 +FEV_1L5 + $rmedA4^2$+ atopic + January + FEV_1A2 + age at $visit^2$ +
  - **$PM_{2.5}A4$ = +0.00103 (0.00110); rmedA4 = -0.63598 (0.21281); $rmedA4^2$ = +0.55321 (0.22395)**

4. **FIVE-DAY MOVING AVERAGE $PM_{2.5}$** (29 CANDIDATE VARIABLES, 1465 OBSERVATIONS)

- FEV_1~$PM_{2.5}$A5 + rmedA5 + FEV_1L5^2 + FEV_1L51+ age at visit + FEV_1L6^2 + FEV_1A2^2 (29 candidate variables, 1465 observations)
  - **$PM_{2.5}A5$ = +0.00077 (0.00130); rmedA5 = -0.22829 (0.08645)**

SIX-DAY MOVING AVERAGE $PM_{2.5}$ (23 candidate variables, 1214 observations)

- FEV_1~$PM_{2.5}$A6 + rmedA6 + FEV_1L6^2 + FEV_1L6 + age at visit + FEV_1L7^2 + FEV_1L7 + month12 + atopycat + $rmedA6^2$ + home ownership question answered + January
  - **$PM_{2.5}A6$ = +0.00205 (0.00154); rmedA6 = -0.69601 (0.26865); $rmedA6^2$ = +0.59318 (0.27885)**

5. **SEVEN-DAY MOVING AVERAGE $PM_{2.5}$** (19 CANDIDATE VARIABLES, 1002 OBSERVATIONS)

- FEV1~$PM_{2.5}$A7 + rmedA7 + FEV_1L7^2 + FEV_1L7 + age at visit + December +atopic + home ownership question answered + $rmedA7^2$ + $atopic^2$ + age at $visit^2$ + January
  - **$PM_{2.5}A7$ = +0.00221 (0.00176); rmedA7 = -0.60822 (0.29837); $rmedA7^2$ = +0.47323 (0.31823)**

*See Table 4.2.3-1 for variable names and conventions.

Table 4.2.3-3: Longitudinal MSM Results for Effect of Estimated Personal Exposure to $PM_{2.5}$ on Use of Rescue Medication in the Hour Before A.M. Lung Function Testing*

DATA REDUCTION STEP:

- **W1**→$PM_{2.5}$ ~wheezeL7 (53 candidate variables, 4018 observations)
- **W3**→Didtest~coughA3 + wheezeL3 + rmedA8 + rmedL8 + wheezeL5+ prmeda4^2 + prmedL3 (53 candidate variables, 4032 observations)

6. MODELS FOR QFX PART OF LIKELIHOOD (SEE APPENDIX H) FOR EACH W

- **W1**~W1L1 + rmed + day of panel + $PM_{2.5}L3^2$ + December + (day of panel^2 + $PM_{2.5}L4^2$ + February + March (82 candidate variables, 3098 observations)
- **W3**~W3L1 + {rmedL1∗day of panel) + {W1∗W3L1} (83 candidate variables, 2877 observations)

7. FINAL MODEL FOR RESCUE MEDICATION USE IN THE 1-HOUR BEFORE A.M. EASYONE

- **Rmed**~rmedA6 + rmedL1 (81 candidate variables, 1070 observations)

Table 4.2.3-4: Point-Treatment MSM Results for Effect of Estimated Personal Exposure to $PM_{2.5}$ on Use of Rescue Medication in the Hour Before Morning Lung Function Testing*

TWO-DAY MOVING AVERAGE $PM_{2.5}$ *(48 candidate variables, 3322 observations)*

- Rmed~"Personal" $PM_{2.5}$A2 + rmedL2 + prmedL2 + rmedL5 + wheezeA3 + wheezeA5^2
  - **"Personal" $PM_{2.5}$A2 = +0.00423 (0.00572)**

THREE-DAY MOVING AVERAGE $PM_{2.5}$ *(42 candidate variables, 3322 observations)*

- Rmed~"Personal" $PM_{2.5}$A3 + rmedL3 + wheezeL3 + rmedL6 + rmedL4 + rmedL5 + rmedA4^2
  - **"Personal" $PM_{2.5}$A3 = +0.00570 (0.00674)**

FOUR-DAY MOVING AVERAGE $PM_{2.5}$ *(36 candidate variables, 3322 observations)*

- Rmed~"Personal" $PM_{2.5}$A4 + rmedL4 + prmedL4 + rmedL6 + rmedL5 + rmeda3^2 + wheezeL4 + prmedA8^2 +wheezeA5^2 + rmedL8
  - **"Personal" $PM_{2.5}$A4 = +0.01096 (0.00789)**

FIVE-DAY MOVING AVERAGE $PM_{2.5}$ *(25 candidate variables, 3322 observations)*

- Rmed~"Personal" $PM_{2.5}$A5 + rmedL5 + prmedL5 + rmedL8
  - **"Personal" $PM_{2.5}$A5 =+0.01341 ((0.00897)**

SIX-DAY MOVING AVERAGE $PM_{2.5}$ *(17 candidate variables, 3322 observations)*

- Rmed~"Personal" $PM_{2.5}$A6 + rmedL6 + prmedL9
  - **"Personal" $PM_{2.5}$A6 = 0.01437 (0.00994)**

SEVEN-DAY MOVING AVERAGE $PM_{2.5}$ *(10 candidate variables, 3322 observations)*

- Rmed~"Personal" $PM_{2.5}$A7 + rmedL8 + prmedL7 + prmeda3 + prmedL9 + rmedL7 + rmeda2^2 + wheezeL7 + prmeda2^2
  - **"Personal" $PM_{2.5}$A7 = +0.01680 (0.01052)**

*See Table 4.2.3-1 for variable names and conventions.

Table 4.2.3-5: Longitudinal MSM Results for Effects of Exposure to Central Site Levels of $PM_{2.5}$ and Rescue Medicine Use on A.M. FEV_1 *

8. DATA REDUCTION STEP

- **W1**→***Central site $PM_{2.5}$***~{Central Site NO_2A8∗December} + December + {panel visit number∗December} + NO_2A7 + January + {NO_2A7∗NO2a8} + {panel visit number∗January} + {FEV_1L8∗NO_2A7} + {NO2A8∗January} +{$pFEV_1$L8∗January} *(67 candidate variables, 4032 observations)*
- **W2**→ ***Rmed***~prmed + cough + rmedL1 + wheeze1 + prmedL1 + coughL1 *(74 candidate variables, 3336 observations)*
- **W3**→ ***Didtest***~ $paFEV_1$ + coughA2 + {wheezeL1∗age at panel visit} + {$paFEV_1$A2∗FEV_1A7} + {panel visit number∗$pFEV_1$L7} + own home + $pFEV_1^2$ + {$paFEV_1$L4∗FEV_1A2} + {wheezeL1∗coughL4}+ {coughL2∗FEV_1A2} *(72 candidate variables, 4032 observations)*
- **W4**→***accept2***~$paFEV_1$ + FEV_1A2 (74 candidate variables, 3336 observations)

9. MODELS FOR QFX PART OF LIKELIHOOD (SEE APPENDIX H) FOR EACH W

- **W1**~W1L1 + rmedA2^2 + ($pePM_{2.5}$L7 + $PM_{2.5}$L6 + $PM_{2.5}$ + year 2000 + Monday + W1L2 + Saturday + October *(55 candidate variables, 2548 observations)*
- **W2**~W2A2 + rmedL1 + FEV_1A2 + W2L2 + rmedL2 + W3L2 + W3L1 + W2L2^2 + W2A2^2 *(54 candidate variables, 2282 observations)*
- **W3**~W2L2^2 + W2^2 + W3L1 + {rmedL1∗FEV_1A2} + {rmedL1∗W2} + {W2L2∗W3L1} +{W2L2∗W3L2) + {W2L1∗w2A2} + {W2L1∗W2} + {W2L2∗W2L1} *(55 candidate variables, 2282 observations)*
- **W4**~FEV_1A2 + W4A21 + W31 + W3^2 + W3L1 + Sunday + Saturday + day of panel +W3L1^2 *(56 candidate variables, 2282 observations)*

10. FINAL MODEL FOR FEV_1

- FEV_1~FEV_1A2 + W4^2+ {FEV_1L1∗FEV_1A2} +{W4∗FEV_1A2} *(54 candidate variables, 1986 observations)*

*See Table 4.2.3-1 for variable names and conventions.

Table 4.2.3-6: Point-Treatment MSM Results for Effect of Exposure to Central Site Levels of $PM_{2.5}$ on A.M. FEV_1

TWO-DAY MOVING AVERAGE $PM_{2.5}$ *(58 candidate variables, 2562 observations)*

- FEV_1~$PM_{2.5}$A2 + rmedA2 + age at visit + {aFEV_1L2∗FEV_1L3} + {age at visit∗FEV_1A2} +{FEV_1L2∗pFEV_1L2} + {FEV_1L3∗paFEV_1L3} + {FEV_1A2∗paFEV_1A2} + {wheezeL2∗December}
  - **$PM_{2.5}$A2 = +0.00012 (0.00038); rmedA2 = -0.12869 (0.04084)**

THREE-DAY MOVING AVERAGE $PM_{2.5}$ (*46 candidate variables, 2130 observations)*

- FEV_1~$PM_{2.5}$A3 + rmedA3 + FEV_1L3^2 + FEV_1A2 + age at visit + FEV_1L4^2 +FEV_1L3
  - **$PM_{2.5}$A3 = -0.00006 (0.00048); rmedA3 = -0.17174 (0.05748)**

FOUR-DAY MOVING AVERAGE $PM_{2.5}$ *(38 candidate variables, 1769 observations)*

- FEV1~$PM_{2.5}$A4 + rmedA4+ FEV_1L4^2 + FEV_1L4 + age at visit + FEV_1L5^2 + FEV_1A2^2 + FEV_1L5 + $rmedA4^2$ + atopic + January
  - **$PM_{2.5}$A4 = +0.00014 (0.00056); rmedA4 = -0.63179 (0.21050)**

FIVE-DAY MOVING AVERAGE $PM_{2.5}$ *(29 candidate variables, 1475 observations)*

- FEV_1~$PM_{2.5}$A5 + rmedA5 + FEV_1L5^2 + FEV_1L5 + age at visit + FEV_1L6^2 +FEV_1A2^2
  - **$PM_{2.5}$A5 = +0.00005 (0.00008); rmedA5 = -0.22395 (0.08552)**

SIX-DAY MOVING AVERAGE $PM_{2.5}$ *(22 candidate variables, 1223 observations)*

- FEV_1~$PM_{2.5}$A6 + rmedA6 + FEV_1L6^2 + FEV_1L6 + age at visit + FEV_1L7^2 +FEV_1L7 + atopic + December + $rmedA6^2$ + asked question about home ownership + January
  - **$PM_{2.5}$A6 = +0.00057 (0.00087); rmedA6 = -0.66539 (0.26523); $rmedA6^2$ = +055692 (0.27446)**

SEVEN-DAY MOVING AVERAGE $PM_{2.5}$ *(19 candidate variables, 1010 observations)*

- FEV_1~$PM_{2.5}$A7 + rmedA7 + FEV_1L7^2 + FEV_1L7 + age at visit
  - **$PM_{2.5}$A7 = +0.00028 (0.00091); rmedA7 =0.20045 (0.10422)**

*See Table 4.2.3-1 for variable names and conventions.

Table 4.2.3-7: Longitudinal MSM Results for Effects of Estimated Personal Exposure to $PM_{2.5}$ and Rescue Medicine Use on A.M. FEF_{25-75} *

11. DATA REDUCTION STEP

- **W1**→***"Personal" $PM_{2.5}$***~ asked home ownership question + age at visit^2 + $pFEF_{25-75}L8$ + $pFEF_{25-75}L8^2$ + coughL3 + wheezeA6 + coughA5^2 *(48 candidate variables, 4018 observations)*
- **W2**→***Rescue Medication (Rmed)*~** prmedA2^2 + wheeze + cough + prmed + asked home ownership question + age at visit *(53 candidate variables, 3336 observations)*
- **W3**→***didtest***~ coughA2 + $pFEF_{25-75}$ + wheezeL1 + ageV^2 + coughL2 + $FEF_{25-75}L1$ + INAown +$pFEF_{25-75}L7$ + $FEF_{25-75}A7$ *(72 candidate variables, 4032 observations)*
- **W4**→***accept2 FEF_{25-75} measurements***~ $pFEF_{25-75}$ + $pFEF_{25-75}^2$ + $FEF_{25-75}L1$ + $pFEF_{25-75}L1$ + $pFEF_{25-75}L1^2$ +age at visit + coughL1 + $FEF_{25-75}L1^2$ + $FEF_{25-75}L3$ + $FEF_{25-75}L3^2$ *(53 candidate variables, 3336 observations)*

12. MODELS FOR QFX PART OF LIKELIHOOD (SEE APPENDIX H) FOR EACH W

- **W1**~{panel day∗W1L2} + W3L1^2 + W1A2 + panel day^2 + {W1L1∗W2L1} + {FEF_{25-75}∗FEF_{25-75}L1} *(55 candidate variables, 2064 observations)*
- **W2**~W2A2 + {rmedL1∗FEF_{25-75}A2} + {W2L2∗W1A2} *(54 candidate variables, 2064 observations)*
- **W3**~W3L1 + W2^2 + {rmedL2∗Saturday} + {W2L2∗W2A2} + {W2L2∗W2L1} + {W2∗W3L1} + {W3L1∗W2A2} *(55 candidate variables, 2877observations)*
- **W4**~W4A2 +FEF_{25-75}A2 + $FEF_{25-75}A2^2$ + W3 + W3L1 + W3L2^2 + W4L2 + Saturday + W3^2 + FEF_{25-75}L1 *(56 candidate variables, 2064 observations)*

13. FINAL MODEL FOR FEF_{25-75}

- FEF_{25-75}~ FEF_{25-75}A2 + W2^2 + W4^2 + $FEF_{25-75}A2^2$ + $PM_{2.5}$L2 + Tuesday *(54 candidate variables, 1731 observations)*
  - **"Personal" $PM_{2.5}$L2 = +0.00155 (0.00052)**

Table 4.2.3-8: Point-Treatment MSM Results for Estimated Personal Exposure to $PM_{2.5}$ on A.M. FEF_{25-75} *

TWO-DAY MOVING AVERAGE $PM_{2.5}$ *(45 candidate variables, 2369 observations)*

- FEF_{25-75}~"Personal" $PM_{2.5}A2$ + rmedA2 + $FEF_{25-75}L2^2$ + $pFEF_{25-75}L2^2$ + $FEF_{25-75}L4^2$ +age at visit + $FEF_{25-75}A3$ + $FEF_{25-75}L3^2$
  - **"Personal" $PM_{2.5}A2$ = +0.00044 (0.00115); rmedA2 = -0.19775 (0.07364)**

THREE-DAY MOVING AVERAGE $PM_{2.5}$ *(41 candidate variables, 1971 observations)*

- FEF_{25-75}~"Personal" $PM_{2.5}A3$ + rmedA3 + $pFEF_{25-75}L3^2$ + $FEF_{25-75}L4^2$ + age at visit +$FEF_{25-75}L3^2$ + {age at visit∗$FEF_{25-75}A2$} + {wheezeL3∗age at visit} + {$FEF_{25-75}L3$∗wheezeL3} + {age at visit∗$paFEF_{25-75}L3$} + {$FEF_{25-75}L4$∗$paFEF_{25-75}L3$} + {$paFEF_{25-75}L4$∗$paFEF_{25-75}L5$}
  - **"Personal" $PM_{2.5}A3$ = +0.00082 (0.00138); rmedA3 = -0.19129 (0.08032)**

FOUR-DAY MOVING AVERAGE $PM_{2.5}$ *(34 candidate variables, 1636 observations)*

- FEF_{25-75}~"Personal" $PM_{2.5}A4$ + rmedA4 + $FEF_{25-75}L42$ + $paFEF_{25-75}L5^2$ + age at visit +$FEF_{25-75}A2$ + $FEF_{25-75}L5^2$
  - **"Personal" $PM_{2.5}A4$ = +0.00155 (0.00164); rmedA4 = -0.28916 (0.12046)**

FIVE-DAY MOVING AVERAGE $PM_{2.5}$ *(29 candidate variables, 1358 observations)*

- FEF_{25-75}~"Personal" $PM_{2.5}A5$ + rmedA5 + $FEF_{25-75}L5^2$ + $FEF_{25-75}L5$ + $FEF_{25-75}L6^2$ +age at visit + $pFEF_{25-75}L5^2$ + $FEF_{25-75}L7^2$ + $FEF_{25-75}A3^2$ + $rmedA5^2$ + $FEF_{25-75}A2^2$ + $FEF_{25-75}L7$
  - **"Personal" $PM_{2.5}A5$ = +0.00216 (0.00198); rmedA5 = -0.98985 (0.33791); $rmedA5^2$ = +0.88487 (0.40598)**

SIX-DAY MOVING AVERAGE $PM_{2.5}$ ***(26 candidate variables, 1125 observations)***

- FEF_{25-75}~"Personal" $PM_{2.5}A6$+ rmedA6 + $FEF_{25-75}L6^2$ + age at visit + $pFEF_{25-75}L6^2$ + $FEF_{25-75}L8^2$ + $FEF_{25-75}a3^2$ + $rmedA6^2$ + $paFEF_{25-75}L6$ + $FEF_{25-75}L7^2$ + $FEF_{25-75}A2$ + ageasth
  - **"Personal" $PM_{2.5}A6$ = +0.00258 (0.00245); rmedA6 = -1.23963 (0.39230); $rmedA6^2$ = +1.20259 (0.44923)**

SEVEN-DAY MOVING AVERAGE $PM_{2.5}$ *(22 candidate variables, 928 observations)*

- FEF_{25-75} ~"Personal" $PM_{2.5}A7$ + rmedA7 + $FEF_{25-75}L7^2$ + age at $visit^2$) + {$FEF_{25-75}L7$∗age at visit} + {age at visit∗rmedA7} + {rmedA7∗asked home ownership question} + {$pFEF_{25-75}L7^2$ + ageasth + {age at visit∗age of asthma diagnosis} + $rmedA7^2$ + {age of diagnosis∗$FEF_{25-75}A2$}

o **"Personal" $PM_{2.5}A7$ = +0.00219 (0.00267); rmedA7 = +2.49797 (0.78775); {age at visit∗rmedA7} = -0.36736 (0.07876); $rmedA7^2$ = +0.89747 (0.41726)**

*See Table 4.2.3-1 for variable names and conventions.

Table 4.2.3-9: Longitudinal MSM for Effects of Exposure to 24 Hour Central Site Concentrations of NO and Rescue Medicine on A.M. FEV_1*

14. DATA REDUCTION STEP

- **W1**→24-hrNO~{panel visit number∗"central"NO_2A8*} + {NO_2A8∗Decmeber} + December + {FEV_1L8∗pNO_2A8} + {pFEV_1L5∗pFEV_1A2} + panel visit number1 + panel visit number^2 + {FEV_1L8∗January} *(67 candidate variables, 4015 observations)*
- **W2**→Rescue Medication~prmed + cough + rmedL1 + wheeze + prmedL1 + coughL1 *(74 candidate variables, 3336 observations)*
- **W3**→didtest~ pFEV_1 + coughA2 + {wheezeL1∗age at visit} + {pFEV_1A2∗FEV_1A7} + {panel visit number∗pFEV_1L7} + own home + pFEV_1^2 + {pFEV_1L4∗FEV_1A2} + {wheezeL1∗coughL4} + {coughL2∗FEV_1A2} *(74 candidate variables, 4032 observations)*
- **W4**→at least 2 acceptable FEV_1 measurements~pFEV_1 + FEV_1A2 *(74 candidate variables, 3336 observations)*

15. MODELS FOR QFX PART OF LIKELIHOOD (SEE APPENDIX H) FOR EACH W

- **W1**~ W1L1 + {FEV_1∗24-hrNOL7) + {W41∗24-hrNOA6} + {panel day∗W1L1} + {Thursday∗Day of Study} + panel day + {Decenber∗year 2000} + {year 2002∗Day of study} + {Monday∗24-hrNOA2} + {24-hrNOL7*January} *(55 candidate variables, 2833 observations)*
- **W2**~W2A2 + rmedL1 + {FEV_1A2∗W3A2} + {W2L2∗W3L2} + {rmedL2∗W2A2} + {rmedL1∗January} *(54 candidate variables, 2282 observations)*
- **W3**~W2L2^2 + W2^2 + W3L1 + {rmedL1∗FEV_1A2} + {rmedL1∗W2} + {W2L2∗W3L1} + {W2L2∗W3L2} + {W2L1∗W2A2} + {W2L1∗W2} + {W2L2∗W2L1} *(55 candidate variables, 2282 observations)*
- **W4**~FEV_1A2 + W4A2 + {W3L1∗FEV_1A2} + {FEV_1L1∗W31}+ {Saturday∗January} + {FEV_1L2∗Sunday} + {24-hrNOL4∗Sunday} + {panel day∗W1L1} + {W3L1∗w4A2} + {W31∗W4L2} *(56 candidate variables, 2274 observations)*

FINAL MODEL FOR FEV_1

- FEV_1~FEV_1A2 + W4^2 + 24-hrNOA6 + FEV_1L1 + December + W2^2 *(54 candidate variables, 1941 observations)*
    - 24-hrNOA6 = +0.00045 (0.00036)

*See Table 4.2.3-1 for variable names and conventions.

Table 4.2.3-10: Point-treatment MSM Results for Exposure to 24 Hour Central Site Concentrations of NO on A.M. FEV_1*

TWO-DAY MOVING AVERAGE NO *(58 candidate variables, 2450 observations)*

- FEV_1~24-hrNOA2 + rmedA2 + FEV_1L2^2 + {FEV_1L2∗age at visit} + age at visit + FEV_1L3^2 +{FEV_1L2∗FEV_1A2} + FEV_1L3
  - **<u>24-hrNOA2</u> = -0.00042 (0.00037); <u>rmedA2</u> = -0.13948 (0.04573)**

THREE-DAY MOVING AVERAGE NO (46 candidate variables, 2102 observations)

- FEV_1~24-hrNOA3 + rmedA3 + FEV_1L3^2 + FEV_1A2^2 + age at visit + FEV_1L4^2 + FEV_1L3 + FEV_1L4
  - **<u>24-hrNOA3</u> = -0.00047 (0.00049); <u>rmedA3</u> = -0.16759 (0.05734)**

FOUR-DAY MOVING AVERAGE NO (38 candidate variables, 1735 observations)

- FEV_1~24-hrNOA4 + rmedA4 + FEV_1L4^2 + FEV_1L4 + age at visit + FEV_1L5^2 +FEV_1A2^2 + FEV_1L5 + FEV_1A2 + atopy + January + $rmedA4^2$
  - **<u>24-hrNOA4</u> = -0.00020 (0.00064); <u>rmedA4</u> = -0.59762 (0.21437); <u>$rmedA4^2$</u> = +(0.51184 (0.22540)**

FIVE-DAY MOVING AVERAGE NO (29 candidate variables, 1439 observations)

- FEV_1~24-hrNOA5 + rmedA5 + FEV_1L5^2 + FEV_1L5 + age at visit +FEV_1L6^2 + FEV_1A2^2 + January + atopic + FEV_1A2 + FEV_1L6
  - **<u>24-hrNOA5</u> = -0.00015 (0.00079); <u>rmedA5</u> = -0.20770 (0.08302)**

SIX-DAY MOVING AVERAGE NO (23 candidate variables, 1185 observations)

- FEV_1~24-hrNOA6 + rmedA6 + FEV_1L6^2 + FEV_1L6 + age at visit + FEV_1L7^2 + FEV_1L7 + atopic + month
  - **<u>24-hrNOA6</u> = +0.00006 (0.00092); <u>rmedA6</u> = -0.20247 (0.09326)**

SEVEN-DAY MOVING AVERAGE NO (19 candidate variables, 975 observations)

- FEV_1~24-hrNOA7 + rmedA7 + FEV_1L7^2 + FEV_1L7 + age at visit + atopic + December + asked home ownership question + $rmedA7^2$ + $atopy^2$ + $age\ at\ visit^2$ + month
  - **<u>24-hrNOA7</u> = +0.00140 (0.00124); <u>rmedA7</u> = -0.57550 (0.29238); <u>$rmedA7^2$</u> = +0.42631 (0.30945)**

*See Table 4.2.3-1 for variable names and conventions.

Table 4.2.3-11: Longitudinal MSM Results for Estimated Personal Exposure to NO_2 and Rescue Medicine Use on A.M. FEV_1—Estimates Over All Seasons*

16. DATA REDUCTION STEP

- **W1**→24-hrNO_2~{DAY OF STUDY∗INApeCLADA6} + {INACLADA3∗INACLADA6} + {panel visit number∗day of studye + {age at visit∗asked home ownership question} + {panel visit number∗INApeCLADA6} + {December∗INAAGFG} + {December∗INApeENDOA8} + {asked home ownership question∗INApeAGFG} + {own a home ∗ asked home ownership question} + INACLAD (*76 candidate variables, 7658 observations)*
- **W2**→Rescue Medication~rmedL1 + wheeze + cough + asked home ownership question + rmedA3 + coughA42 (79 candidate variables, 6315 observations
- **W3**→DIDTEST~$pFEV_1$ + coughA2 + wheezeL1 + FEV_1L1 + $pFEV_1^2$ + $pFEV_1L7$ +FEV_1A7 + own + panel visit number + $coughL^2$ *(79 candidate variables, 7700 observations) (This model was somewhat unstable)*
- **W4**→ accept2~$paFEV_1$ + {$pFEV_1L1$∗INAAGFG} + $paFEV_1^2$ + asked home ownership question ∗INACLADL1} + {FEV_1L5∗own1} + {panel visit number∗December} + {wheezea41∗own a home} + FEV_1A2 + {$paFEV_1L1$∗$paFEV_1A2$

17. MODELS FOR QFX PART OF LIKELIHOOD (SEE APPENDIX H) FOR EACH W

- **W1**~W1L1 + rmedL1 + FEV_1^2 + Monday + year2001 + May + $W1L1^2$ + January + W1L2 + Thursday *(63 candidate variables, 4490 observations)*
- **W2**~rmedL1 + W2A2 + {FEV_1A2∗rmedA2} + {W4L1∗rmedA2} + {pNO_2L3∗W1L1} + W2L2 *(62 candidate variables, 4294 observations)*
    - {NO_2L3∗W1L1} = **+0.00132 (0.00033)**
- **W3**~{W2L2∗W3L1} + {rmedL1∗W2} + {FEV_1A2∗rmedA2} + W3L1+ {W2L2∗W2A2} + {rmedL11∗W3A2} + $W2^2$ + {W2L1∗W2A2} + {W21∗W3L1} + {W3L2∗W3L1} *(63 candidate variables, 4328 observations)*
- **W4**~FEV_1A2 + $W4L1^2$ + December + FEV_1A2^2 + W4A2 + Saturday + W3L2 + $W3L2^2$ + Sunday + Wednesday *(64 candidate variables, 4328 observations)*

FINAL MODEL FOR FEV_1

- FEV_1~FEV_1A^2 + FEV_1L1^2 + $W4A^2$

*See Table 4.2.3-1 for variable names and conventions.

Table 4.2.3-12: Point Treatment MSM Results for Effect of Estimated Personal Exposure to NO_2 on A.M. FEV_1 *

TWO-DAY MOVING AVERAGE NO_2 (*66 candidate variable, 4805 observations)*

- FEV_1~pNO_2A2 + rmedA2 + {FEV_1L2∗FEV_1L3} + {age at visit∗FEV_1A2} + age at visit + {FEV_1L2∗$paFEV_1L2$} + {FEV_1L3∗$paFEV_1L3$} + {FEV_1A2∗$pFEV_1A2$}
  - **pNO_2A2 = -0.00127 (0.00250); rmedA2 = -0.16410 (0.04209)**

THREE-DAY MOVING AVERAGE NO_2 *(59 candidate variables, 3973 observations)*

- FEV_1~pNO_2A3 + rmedA3 + FEV_1L3^2 + FEV_1A2^2 + age at visit + FEV_1L4^2 + FEV_1L3 + FEV_1L4 + asked home ownership question+ FEV_1A2 + December + age at $visit^2$
  - **pNO_2A3 = -0.00253 (0.00296); rmedA3 = -0.20232 (0.04316)**

FOUR-DAY MOVING AVERAGE NO_2 *(51 candidate variables, 3285 observations)*

- FEV_1~pNO_2A4 + rmedA4 + FEV_1L4^2 + FEV_1L4 + age at visit + FEV_1L5^2 + FEV_1A2^2 + FEV_1L5 + asked home ownership question + FEV_1A2 + $January^2$
  - **pNO_2A4 = -0.00376 (0.00366); rmedA4 = -0.22851 (0.05328)**

18. **FIVE-DAY MOVING AVERAGE NO_2** *(46 candidate variables, 2726 observations)*

- FEV_1~pNO_2A5+ rmedA5 + FEV_1L5^2 + {FEV_1L5∗age at visit} + age at visit + {FEV_1L6∗$paFEV_1L6$} + {FEV_1L5∗FEV_1A2} + {FEV_1L5∗FEV_1L6} + {December∗rmedA5} + {age at visit∗rmedA5}
  - **$peNO_2A5$ = -0.00087 (0.00366); rmedA5 = +0.77356 (0.28397); {December∗rmedA5} = -0.38051 (0.10663); {age at visit∗rmedA5} = -0.10612 (0.03461)**

19. **SIX-DAY MOVING AVERAGE NO_2** (*42 candidate variables, 2252 observations)*

- FEV_1~pNO_2A6 + rmedA6 + FEV_1L6^2 + FEV_1L6 + age at visit + FEV_1L7^2 + FEV_1L7 + FEV_1A2^2 + FEV_1A2 + asked home ownership question+ December + age at $visit^2$

pNO_2A6 = -0.00225 (0.00447); rmedA6 = -0.24508 (0.06603)

20. **SEVEN-DAY MOVING AVERAGE NO_2** *(36 candidate variables, 1853 observations)*

- FEV_1~pNO_2A7 + rmedA7 + FEV_1L7^2 + FEV_1L7 + age at visit + FEV_1L8 + FEV_1L8^2+ asked home ownership question + December + day of study

o **pNO_2A7 = +0.00105 (0.00507); rmedA7 = -0.26699 (0.07839)**

*See Table 4.2.3-1 for variable names and conventions.

Table 4.2.3-13: Longitudinal MSM for the Effect of Personal Exposure to NO_2 on Rescue Medication Use in the Hour Before A.M. Lung Function Testing*

DATA REDUCTION STEP:

- **W1**→"personal" NO_2~ prmedA5 *(54 candidate variables, 7658 observations)*
- **W3**→didtest~coughA3 + rmedA8 + rmedL8 + wheezeL3 + coughA3^2 + prmedL4 + prmedA4 + wheezeL5 + prmedL2 + wheezeL1 *(54 candidate variables, 7700 observations)*

21. MODELS FOR QFX PART OF LIKELIHOOD (SEE APPENDIX H) FOR EACH W

- **W1**~W1L1^2 + rmedA6 + rmed + W1L2^2 + rmedA3 + W3A3 + W3L2 + W3L4^2 + W1L4^2 *(90 candidate variables, 1757 observations)*
- **W3**~{W1∗W3L} + {rmedL8∗W1L5} + {W1∗rmedA8} + {W3L1∗rmedA7} + {rmed∗June} + {W3L5∗W3L2} + {W3L3∗W3A6} + {rmedL1∗winter} + {rmedL8∗W3L8} *(91 candidate variables, 1087 observations)*

22. FINAL MODEL FOR RESCUE MEDICATION USE IN THE 1-HOUR BEFORE A.M. EASYONE

- rmed~rmedA6+rmedL1 (*89 candidate variables, 1992 observations)*

Table 4.2.3-14: Point Treatment MSM for the Effect of Personal Exposure to NO_2 on Rescue Medication Use in the Hour Before A.M. Lung Function Testing*

23. **TWO-DAY MOVING AVERAGE NO_2** (49 CANDIDATE VARIABLES, 6274 OBSERVATIONS)

- rmed~"personal" NO_2A2 + rmedL2 + prmedL2 + rmedL5 + coughL2 + rmedL6 + coughA5 + wheezeL3
  - **$\underline{pNO_2A2}$ = +0.02366 (0.01716)**

24. **THREE-DAY MOVING AVERAGE NO_2** (44 CANDIDATE VARIABLES, 6274 OBSERVATIONS)

- rmed~"personal" NO_2A3+ rmedL4 + wheezeL3 + rmedL6 + rmedA4 + rmedL5 + rmedL3 + rmedL8 + prmedL3 + wheezeL8 + wheezeL4
  - **$\underline{pNO_2A3}$ = +0.03249 (0.01888)**

25. **FOUR-DAY MOVING AVERAGE NO_2** (37 CANDIDATE VARIABLES, 6274 OBSERVATIONS)

- rmed~"personal" NO_2A4 + rmedL4 + wheezeL4+ rmedL5 + rmeda2^2 + rmedL6 + rmedL8 + prmedL4 + rmeda3 + wheezeL8 + rmeda7
  - **$\underline{pNO_2A4}$ = +0.03917 (0.02081)**

26. **FIVE-DAY MOVING AVERAGE NO_2** (30 CANDIDATE VARIABLES, 6274 OBSERVATIONS)

- rmed~"personal" NO_2A5 + rmedL5 + rmedL8 + rmedL6 + wheezeL5 + rmedA2^2 + prmedL5 + rmeda7^2
  - **$\underline{pNO_2A5}$ = +0.04541 (0.02245)**

27. **SIX-DAY MOVING AVERAGE NO_2** (20 CANDIDATE VARIABLES, 6274 OBSERVATIONS)

- rmed~"personal" NO_2A6 + rmedL6 + rmedL8
  - **$\underline{pNO_2A6}$ = +0.05262 (0.02420)**

28. **SEVEN-DAY MOVING AVERAGE NO_2** (20 CANDIDATE VARIABLES, 6274 OBSERVATIONS)

- rmed~"personal" NO_2A7 + rmedL7 + rmedL8 + rmeda3 + rmedL9 + wheezeL7 + prmedL7 + "personal" NO_2MA7^2 + rmeda2^2
  - **$\underline{peNO_2A7}$ = +0.16366 (0.10525); $\underline{peNO_2MA7^2}$ = -0.00525 (0.00501)**

*See Table 4.2.3-1 for variable names and conventions.

Table 4.2.3-15: Longitudinal MSM Results for Exposure to 24 Hour Central Site Concentrations of NO_2 and Rescue Medicine Use on A.M. FEV_1on A.M. FEV_1—Estimates Over All Seasons*

DATA REDUCTION STEP

- **W1**→24-hrNO_2~{Time∗INACLADA7} + {INACLADa4∗INACLADA7} + Time + {INACLAD∗INAENDO3} + {December∗INAENDOA8} + {INAENDO∗INAENDOL2} + {December∗INACLAD} + {own∗wheezeA2} (69 candidate variables, 7700 observations)
- **W2**→Rescue Medication~rmedL1 + wheeze + cough + asked home ownership question + rmedA3 + cougha4^2 (72 candidate variables, 6315 observations)
- **W3**→DIDTEST~paFEV 1 + coughA2 + wheezeL1 + FEV_1L1 + $pFEV_1^2$ + $pFEV_1$L7 + FEV_1A7 + own home + panel visit number + coughL2 (72 candidate variables, 7700 observations)
- **W4**→accept2~$pFEV_1$ + $pFEV_1$L1 + $pFEV_1^2$ + coughA3 + FEV_1L2 + FEV_1L2^2 + asked home ownership questions+ coughA3^2 + FEV_1L1 + $pFEV_1A2^2$ (72 candidate variables, 6315 observations)

29. MODELS FOR QFX PART OF LIKELIHOOD (SEE APPENDIX H) FOR EACH W

- **W1**~W1L1+ {rmed1∗Friday} + {FEV_1L2∗summer} + {Wednesday*year2} + {year3∗spring} + {January∗year3} + {pNO_2L1∗Saturday} + {Wednesday∗April} + {June∗year2} + {Tuesday∗June} (63 candidate variables, 4066 observations)
- **W2**~rmedL1 + W2A2 + {W3L1∗FEV_1A2} + {W1L2∗W2L2} + {FEV_1L1∗W3L1} + {January∗rmedA2} (62 candidate variables, 4328 observations)
- **W3**~{rmedL1∗W2} + {FEV_1L1∗rmedA2} + W3L1 + W2$L2^2$ + $W2^2$ + {W2L2∗W3L1} + {rmedL1∗W3A2} + {W3L1∗W3A2} + {W2∗W3L1} (63 candidate variables, 4490 observations)
- W4~W4L1 + {FEV 1L2∗FEV 1a21} + FEV_1A2 + W3L1 + {W3L1∗W3} + W3 + FEV_1L2∗W4A2} + {W3L1∗W2A2} (64 candidate variables, 4328 observations)

FINAL MODEL FOR FEV_1

- FEV_1~FEV_1L1 + FEV_1L1^2 + $W4^2$ + FEV_1A2^2 + $W2^2$ +W3L1+ December + rmed

*See Table 4.2.3-1 for variable names and conventions.

Table 4.2.3-16: Point Treatment MSM for Effect of Exposure to Central Site NO_2 on A.M. FEV_1*

30. **TWO-DAY MOVING AVERAGE NO_2** (49 CANDIDATE VARIABLES, 6274 OBSERVATIONS)

- FEV_1~NO_2A2+rmedA2 + age at visit +{FEV_1L2∗FEV_1L3} + {age at visit∗FEV_1A2} + {FEV_1L2∗paFEV$_1$L2} + {FEV_1L3∗pFEV1L3} + {FEV_1A2∗pFEV$_1$A2} + INAown + {FEV_1A2∗INAown} + {age at visit∗rmedA2} + {age at visit∗pFEV$_1$L2}
  - **pNO_2A2 = -0.00238 (0.00082); rmedA2 = +0.34248 (0.17106); {age at visit∗rmedA2} = -0.06005 (0.02106)**

31. **THREE-DAY MOVING AVERAGE NO_2** (55 CANDIDATE VARIABLES, 4006 OBSERVATIONS)

- FEV_1~NO_2A3 + rmedA3 + FEV_1L3^2 + FEV_1A2^2 + age at visit + FEV_1L4^2 + FEV_1L3 + FEV_1L4 + INAown + paFEV$_1L3^2$ + paFEV$_1$L3
  - **NO_2A3 = -0.00250 (0.00106); rmedA3 = -0.19911 (0.04598)**

32. **FOUR-DAY MOVING AVERAGE NO_2** (50 CANDIDATE VARIABLES, 3314 OBSERVATIONS)

- FEV_1~NO_2A4 + rmedA4 + FEV_1L4^2 + FEV_1L4 + age at visit + FEV_1L5^2 + FEV_1A2^2) + FEV_1L5 + INAown + FEV_1A2
  - **NO_2A4 = -0.00297 (0.00129); rmedA4 = -0.22742 (0.05540)**

33. **FIVE-DAY MOVING AVERAGE NO_2** (44 CANDIDATE VARIABLES, 2751 OBSERVATIONS)

- FEV_1~NO_2A5 + rmedA5 + FEV_1L5^2 + FEV_1L5 + age at visit + FEV_1L6^2 + FEV_1A2^2 + FEV_1L6 + FEV_1A2 + INAown
  - **NO_2A5 = -0.00302 (0.00149); rmedA5 = -0.24879 (0.06684)**

34. **SIX-DAY MOVING AVERAGE NO_2** (4 CANDIDATE VARIABLES, 2274 OBSERVATIONS)

- FEV_1~NO_2A6 + rmedA6 + FEV_1L6^2 + FEV_1L6 + age at visit + FEV_1L7^2 + FEV_1L7 + FEV_1A2^2 + FEV_1A2 + INAown
  - **NO_2A6 = -0.00323 (0.00180); rmedA6 = -0.24786 (0.07237)**

35. **SEVEN-DAY MOVING AVERAGE NO_2** (36 CANDIDATE VARIABLES, 1872 OBSERVATIONS)

- FEV_1~NO_2A7 + rmedA7 + age at visit^2 + {age at visit∗FEV_1A2} + {FEV_1L7∗FEV_1L8} + {FEV_1L7∗paFEV$_1$L7} + {age at visit∗rmedA7} + INAown + {month12∗rmedA7} + {FEV_1A2∗INAown}
  - **NO_2A7 = -0.00294 (0.00218); q5Q7 = +1.39935 (0.46842); {ageV∗q5A7} = -0.18547 (0.05632); {month12∗q5A7} = +0.09869 (0.04461)**

*See Table 4.2.3-1 for variable names and conventions.

Table 4.2.3-17: Point Treatment MSM for the Effect of Exposure to Central Site NO_2 on Rescue Medication Use in the Hour Before A.M. Lung Function Testing

36. **TWO-DAY MOVING AVERAGE NO_2** (49 CANDIDATE VARIABLES, 6315 OBSERVATIONS)

- rmed~NO_2A2 **+** rmedL2 + prmedL2 + rmedL5 + wheezeL2 + rmedL6
  - **NO_2A2 = +0.00479 (0.00811)**

37. **THREE-DAY MOVING AVERAGE NO_2** (44 CANDIDATE VARIABLES, 6315 OBSERVATIONS)

- rmed~NO_2A3+ {wheezeL4∗rmedL4} + rmedL3 + {coughL5∗ rmedL6} + {wheezeL3∗coughL3} + {coughL3∗coughA4} + {rmedL6∗coughA3} + {rmedL5∗rmedL8}
  - **NO_2A3 = +0.00973 (0.00913)**

38. **FOUR-DAY MOVING AVERAGE NO_2** (37 CANDIDATE VARIABLES, 6315 OBSERVATIONS)

- rmed~NO_2A4 + wheezeL4 +rmedL5 + rmedL4 + rmedA2^2 + rmedL6 + rmedL81+ prmedL4 + rmedA3 + wheezeL8 + rmedL9
  - **NO_2A4 = +0.01171 (0.00976)**

39. **FIVE-DAY MOVING AVERAGE NO_2** (30 CANDIDATE VARIABLES, 6315 OBSERVATIONS)

- rmed~NO_2A5 + rmedL5 + rmedL8 + wheezeL5 + rmedL6 + rmedA2^2 + prmedL5 + rmedA7^2 + prmedA5
  - **NO_2A5 = +0.01397 (0.01078)**

40. **SIX-DAY MOVING AVERAGE NO_2** (20 CANDIDATE VARIABLES, 6315 OBSERVATIONS)

- rmed~NO_2A6 + rmedL6 + rmedL8 + wheezeL6
  - **NO_2A6 = +0.01562 (0.01138)**

41. **SEVEN-DAY MOVING AVERAGE NO_2** (13 CANDIDATE VARIABLES, 6315 OBSERVATIONS)

- rmed~NO_2A7 + rmedL7 + rmedL8 + rmedL9 + prmedL7 + rmedA3 + wheezeA3 + wheezeA2 + wheezeL7 + wheezeA2^2
  - **NO_2A7 = +0.01557 (0.01173)**

*See Table 4.2.3-1 for variable names and conventions.

4.2.4 Methods and Analysis of Chronic Effect of Acute Responses on Pulmonary Function Growth

This section includes a discussion of the preliminary methods and analysis for the assessment of the influence of short-term responses to daily air pollution on the longer-term pulmonary function growth. *The data presented here are for demonstration purposes only and are not intended to represent the final analyses on the questions addressed or the full range of questions that will be addressed as we collect and analyze more data.* We restricted this summary to one outcome, one exposure and a limited set of covariates for selection by the DSA algorithm.

We hypothesized that children with large declines in pulmonary function due to acute effects of a given pollutant would have slower lung function growth over a 6-month period or longer. (NB: In this analysis, negative coefficients are consistent with declines in pulmonary function). To assess the acute effect, we used daily measurements from the EasyOne® spirometer which were performed by the child at home during the two week panel sessions with data collected over the period November 30, 2000 through March 31, 2003 (i.e. the interval for which we have daily exposure data). All exposures are based only on Central Site measurements. To assess lung function growth, we used data from the every 6-month field office visits, restricted to the period November 2, 2000 through September 2, 2003 (i.e. field office visits that occurred before the first panel day and up to 6 months after the last panel day for which we have daily exposure data). For this example, we refer to these measures as $FEV_{1(1)}$ for time 1 and $FEV_{1(2)}$ for measurements taken during the next field office visit. The "exposure" of interest for this longer-term or chronic analysis is the child-specific acute effect measured during a two-week panel of home monitoring of pulmonary function, which took place in the 6 to 12-month interval between two field office visits. All analyses are based on spirometry data that were reviewed by investigators (JB, LC, and IT) and determined to be acceptable. PROC MIXED (SAS version 9.1) was used to account for the fact that children contributed up to 14 days of data for each panel and may have contributed more than one panel. We included a random effects term for NO_2.

Based on the results of the conventional analyses, we selected "NO_2, lag 1" as our primary acute model of interest. We repeated the analysis using the model selected through the DSA algorithm (which included only height-squared and NO_2 lag 1) to obtain a subject and panel-specific estimate of the effect of 1-day lagged NO_2 on the daily morning mean pulmonary function (FEV_1) over a panel of up to 14 days in length. We used the independent covariance structure, and indicated that the measures were nested within ID and panel. We output a coefficient, NO2_ESTIMATE, that summarized each child's increase or decrease in FEV_1 response to changes in NO_2 during the two-week panel. This coefficient is calculated by summing the overall fixed NO_2 effect and the child/panel-specific random effect. A negative value for NO2_ESTIMATE corresponds to lowered FEV_1.

To evaluate the effect of the acute response (NO2_ESTIMATE) on lung function growth over a 6-month interval, we defined $FEV_{1(2)}$ as the outcome and considered the following covariates, using the DSA algorithm: $FEV_{1(1)}$, height(centered), sex, race and home visit panel number. We selected this very short list of covariates for two reasons. First, during the NIH grant

writing period, we began this chronic analysis using traditional model selection techniques, which suggested that these covariates may be important. Second, due to time constraints, we used these prior modeling results to inform us as to what covariates should be considered by the DSA algorithm. As with acute models, we considered model with up 10 terms, up to 2-way interactions and the sum of the powers in each term could not exceed 2. Missingness was assumed to be random.

There were 5995 child-days included in the models, based on data from 570 panels from 215 children. Children completed as few as one and as many as six panels. Slightly fewer than 60% of the child-days were from boys. The overall effect estimate was –0.002 L (se=.0007, p= 0.005) per ppb of NO_2, which corresponds to an average 2.4% decline in mean FEV_1 per IQR (12 ppb) increase in 1-day lagged NO_2. The individual short-term NO_2 effects (NO2_ESTIMATE) ranged from -0.067 to +0.065, with a median of –0.002 liters L. A boxplot of the distribution is found in Figure 4.2.4-1.

There were 343 observations for which we had available data (i.e., a panel completed between two field office visits). A total of 155 children contributed from 1 to 5 pairs of field office visits for which there was at least one panel period completed in between the visits. The DSA algorithm selected the following model for FEV_1 at time 2 : $FEV_{1\ (1)}$(squared), NO2_ESTIMATE and $height_2$ (centered), all $p < .0001$. The statistical significance of the findings and magnitude of the coefficients were unaffected by the choice of covariance structure. The coefficient for the NO2_ESTIMATE was 6.12 (SE=1.34, p <0 .0001). The median effect was 6.5, with a range of (-.38,19.06). A boxplot of the estimate can be found in Figure 4.2.4-2. A positive coefficient in this case means that children who had a positive or null acute response to NO_2 had greater pulmonary function growth over time. To put it another way, the more negative the acute response was to NO_2, the slower the pulmonary function growth over a 6-month interval. Therefore, for a child of median height and average $FEV1_{(1)}$, an IQR (0.015) decrease in NO2_ESTIMATE (i.e., the FEV_1 acute change in response to daily NO_2), resulted in a corresponding 0.092 L decrease in FEV_1 at time 2. Given a mean $FEV_{1(2)}$ of 1.86 L, this corresponds, on average, to a 4.9% decline in FEV growth.

As noted above, the analyses are preliminary and are used for demonstration purposes only. These results, however, suggest that the acute effect of NO2 exposure during a two-week panel have a longer-term impact on pulmonary function growth between office visits (usually 6 months). We will explore some methodological issues related to these models and will explore the chronic effects of other pollutants.

Table 4.2.4-1: Distribution of Selected Variables for Demonstration of Approach to "Chronic" Analysis

	Mean (SD)	**Range**
FEV_1 at time $_1$ (liters)	1.76(.45)	(.74, 2.15)
FEV_1 at time $_2$(liters)	1.85 (.50)	(.81,3.49)
FEV_1 growth ($t_2 - t_1$)	.09(.22)	(-.78,.74)
Age (years)	8.7 (1.6)	(6.0, 12.0)
Days between field office visits	199(39)	(137,365)
Height (cm)	135.2 (11.9)	(110, 163)

Figure 4.2.4-1: Distribution of the acute response to 2-day lag NO2- Sum of Fixed and Random Effects

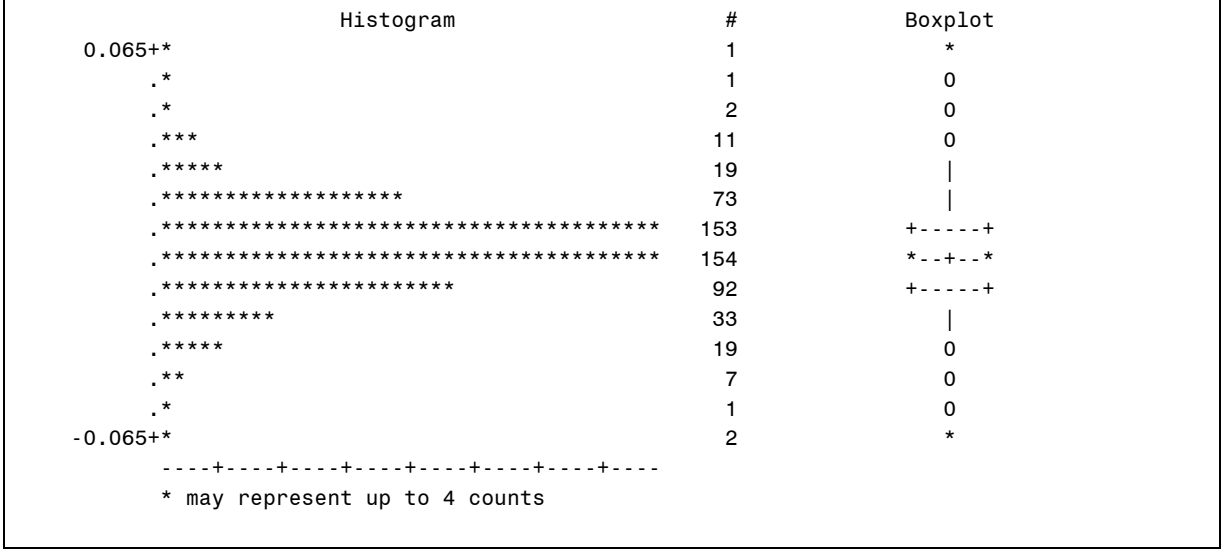
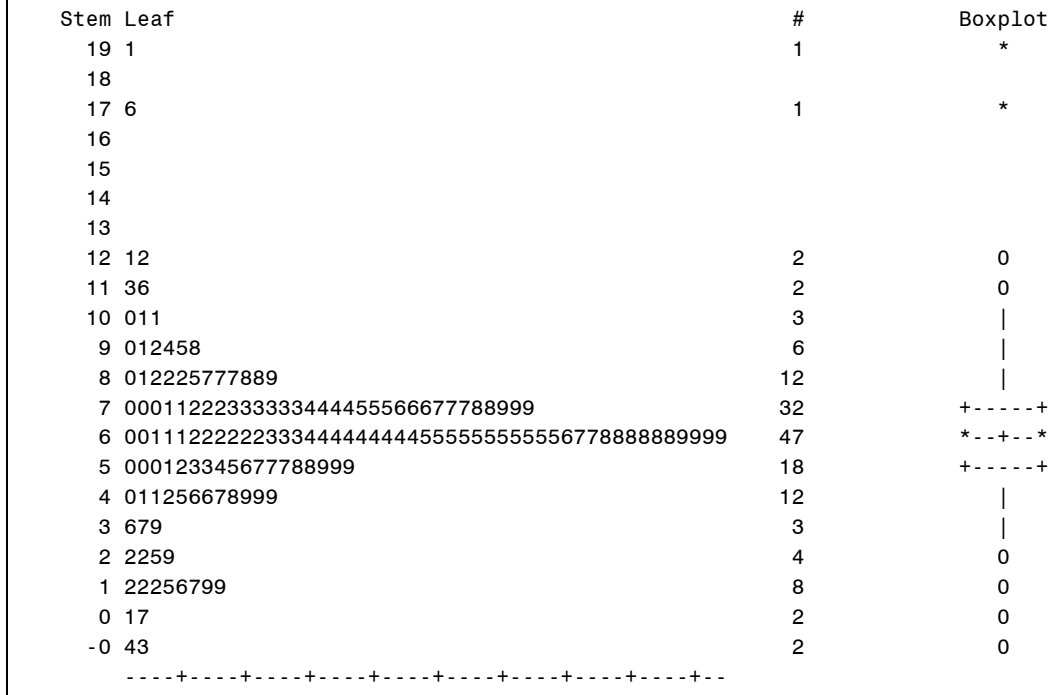


Figure 4.2.4-2: Distribution of Chronic Response to Acute NO_2 Effect – Sum of Fixed and Random Effects



4.2.5 Altered Pulmonary Function Associated with Highway Traffic Near Residence

As described in Section 3.4.6, we carried out cross-sectional analyses to evaluate the association between highway traffic near the children's residence and their pulmonary function at baseline. The draft manuscript can be found in Appendix J. In summary, exposure variables considered were distance of residence to the nearest highway, annual average daily traffic count (AADT) on that road, and the inverse-distance-weighted annual average daily traffic count (IDWT; computed as AADT/distance). The heavy-duty vehicle (i.e., vehicles with ≥ 6 axles) fraction of the inverse-distance weighted total vehicle count (IDWTH) was used as a surrogate measure of diesel-related exposures.

Multiple linear regression was used to evaluate the relationships between the children's baseline pulmonary function and the surrogate measures of traffic-related exposures. For 214 subjects, race-sex-specific equations (4) were used to calculate percent predicted lung function values (pre-bronchodilator) for forced vital capacity (FVC), forced expiratory volume in 1 second (FEV_1), the ratio of FEV_1 to FVC (FEV_1/FVC%), peak expiratory flow rate (PEFR), and forced expiratory flow between 25 and 75% of vital capacity (FEF_{25-75}). A reference equation for the ratio of FEF_{25-75} to FVC (FEF_{25-75}/FVC) was not available; therefore, the raw data for FEF_{25-75}/FVC, natural log transformed, were used in all analyses. Initially, stepwise multiple regression was used to identify possible confounders (sex, age, standing height, race/ethnicity, atopic status (based on skin-prick test), allergy history, demographic characteristics of the family, second-hand smoke exposure, activity patterns (number of indoor or outdoor sports), home characteristics and time-dependent variables (symptoms or medications use within 2 weeks prior to spirometry, 24-hour average ambient air pollution levels, 24-hour average temperature and humidity the day of exam).

There were few statistically significant associations; however, FEV_1/FVC, PEFR, and FEF_{25-75} %predicted and FEF_{25-75}/FVC tended to be positively associated with longer distance-to-road and negatively associated with traffic measures that capture traffic intensity (AADT, IDWT, and IDWTH). The IDWT was associated more consistently associated with deficits in pulmonary function than were AADT or distance to highway. Presented in Table 4.2.5-1 are results for IDWT and IDWTH. The coefficients for FEF_{25-75}/FVC showed the largest decrement and were the most precisely estimated. Over a IQR (73.7) in IDWT, the %predicted FEV_1/FVC% was diminished by 0.6 % (95% CI: -1.13%, -0.02%), and there was a -2.6 percent difference in FEF_{25-75}/FVC (95% CI: -4.79%, -0.47%). The FEF_{25-75}/FVC ratio has the interpretation of the reciprocal of the time constant of the lung (244), similar to Meade's $Vmax_{50}$ / (VC ∗$Pst(L)_{50}$) (i.e. instantaneous flow at 50% divided by vital capacity time elastic recoil pressure at 50% of vital capacity) and is reflective of intrinsic airway size (272). The FEF_{25-75}/FVC ratio has been shown to be a very sensitive indicator of the state of the airways in children with asthma (245).

To test the hypothesis that one subgroup of children with asthma who might be more sensitive to effects of MVE on lung function would be those with low FEF_{25-75}/FVC ratio, we included an interaction term between the ratio and the IDWT. There was a significant interaction between the FEF_{25-75}/FVC ratio and IDWT and all measures of lung function, except for FVC% predicted, i.e., measures of flow but not volume. (Table 4.2.5-2) The positive sign in front of

the interaction term indicates that higher levels of FEF_{25-75}/FVC ratio (i.e., faster time constants) are associated with a diminished association between traffic measures and %predicted FEV_1, FEV_1/FVC%, PEFR and FEF_{25-75}. The observation that all measures of lung function, except FVC were significantly inversely associated with traffic intensity is of interest since increases in FVC have been associated with asthma (273, 274) and have been attributed to a developmental increase in alveolar size or number which could reflect a stimulus related to airway inflammation such that increased lung volume and decreased airway size go hand in hand (274). It also may be that any other factor that affects airway size (e.g., *in utero* exposure to tobacco smoke (275) enhances the susceptibility of children with asthma to the adverse effects of pollutants derived from MVE.

In conclusion, these analyses support the hypothesis that traffic-related exposures, as defined on proximity of residences to roadways, are associated with declines in pulmonary function in these asthmatic children. asthmatic children with smaller FEF_{25-75}/FVC ratios were more sensitive to traffic-related exposures in that they had lower measures of flow. Although it can be hypothesized that these children are likely to also be more sensitive to other pollutants, that remains to be seen and will be explored in our data. Future analyses also will include the panel and longitudinal data to examine the impact of traffic exposure on longer-term pulmonary function growth. We will also expand our analyses to identify other subgroups of asthmatic children who may be more vulnerable to the health effects of these pollutants. Identification of these subgroups will inform regulators as they develop environmental health policies, as well as physicians and other health care professionals as they design appropriate clinical interventions.

Table 4.2.5-1. Association betwee highway traffic exposure metrics and measures of pulmonary function. [a,b]		
	Traffic Measure	**Coefficient 95% (CI)** [c]
FVC *%predicted*	*IDWT*	0.75 (-0.24, 1.73)
	IDWTH	0.07 (-0.46, 0.60)
FEV_1 *%predicted*	*IDWT*	-0.11 (-1.14, 0.92)
	IDWTH	-0.05 (-0.61, 0.52)
FEV_1/FVC% *%predicted*	*IDWT*	-0.57 (-1.13, -0.02)*
	IDWTH	-0.21 (-0.52, 0.10)
PEFR *%predicted*	*IDWT*	-1.01 (-2.45, 0.43)
	IDWTH	-0.44 (-1.22, 0.33)
FEF_{25-75} *%predicted*	*IDWT*	-1.58 (-3.64, 0.48)
	IDWTH	-0.40 (-1.54, 0.73)
FEF_{25-75}/FVC *Percent difference*	*IDWT*	-2.63 (-4.79, -0.47) *
	IDWTH	-1.06 (-2.25, 0.13) #

[a] Effect estimates are adjusted for the covariates noted in text if their partial R^2 was ≥ 0.01, p≤ 0.05 with traffic in the model.

[b] Mean value of FEF_{25-75}/FVC, natural log transformed, used in analyses; results are in terms of percent difference.

[c] Regression coefficients are scaled to the interquartile range for each traffic measure as follows: 73.7 AADT/meter for IDWT and 4.89 for IDWTH. # p<0.1; * p<0.05

Table 4.2.5-2: Interaction Between FEF_{25-75}/FVC Ratio and Measures of Exposure to MVE From Freeways		
% Predicted	Coefficient [a] (SE)	Partial R^2
FEV_1		
IDWAADT	-0.105 (0.020)	0.15
(Ratio[+] ∗ IDWAADT)	+0.158 (0.031)	0.15
PEFR		
IDWAADT	-0.136 (0.024)	0.15
(Ratio[+] ∗ IDWAADT)	+0.192 (0.034)	0.15

[a] See footnotes in Table PS8; [+] FEF_{25-75}/FVC ratio

5. INTEGRATED SUMMARY AND CONCLUSIONS

5.1 GENERAL SUMMARY RELATED TO COHORT

Despite many obstacles, we were able to recruit 315 children with asthma into the study. As of June 30, 2005, 240 remain active in the cohort at the time of this report[8]. Seventy-two percent of the cohort is composed of children with persistent asthma, based on generally accepted classification criteria. Over 20% have been hospitalized for their asthma at some time (7% in the 12 months prior to baseline interview), 57% have visited an emergency facility (27% in the 12 months prior to baseline interview) and 80% were taking a controller medication. Therefore, although the cohort is somewhat smaller than was our original target, we have recruited a group of children with asthma with sufficient disease severity, such that, if as a group, they are susceptible to air pollution, we should be able to detect it. This comment is based on the fact that both the size of the cohort and the number of follow-up observations that we have accumulated already are as large or larger than several published studies that have reported associations with air pollution exposures and symptoms or lowered lung function.

5.2 GENERAL SUMMARY OF CONCLUSIONS FROM EXPOSURE COMPONENT

One major objective of the exposure study was to estimate the daily air pollution exposures of the study participants during each of the two-week health panels throughout the study period with a high degree of reliability. The daily exposure assignments were made using a data-driven modeling approach that accounted for spatial variations in ambient pollutants and agents, effects of home ventilation conditions on infiltration of ambient air to the indoor environment, and children's daily time-use patterns. Spatial variations in ambient concentration and indoor-outdoor pollutant relationships were analyzed to develop the personal exposure model. The principal findings of the exposure study are as follows.

1. There was substantial temporal and spatial variability for pollutants and components of the bioaerosols:
   - The temporal and spatial variation of pollen grains and fungal spores are independent of other pollutants and agents measured in FACES and thus provide a significant opportunity to independently evaluate their associations with health outcomes.

   - The day-to-day variations in ambient concentrations were large for most pollutants and bioaerosols components in FACES, which provided the exposure variability needed to support the panel study design.

   - The seasonal variations in concentrations were large for many pollutants and agents, with median monthly ambient concentrations varying by factors of 5 to 10 between the lowest and highest months. The seasonal patterns of variations differed considerably for the different pollutants and bioaerosols components. **1)** Pollens were highest in the spring; **2)** ozone was highest in summer; **3)** endotoxin was highest in the summer or fall, **4)** coarse

[8] Analyses are restricted up to March 31, 2003.

PM was highest in the fall; and **5)** $PM_{2.5}$, EC, NO_3, PAH, NO, and CO were highest in the fall or winter. Total fungal spores (but not necessarily individual types of spores) were lowest in winter.

- Relatively large diurnal variations in ambient concentrations were observed which may provide further opportunity to link exposure differences to health outcomes. Four to five-fold differences between the lowest and highest average hourly concentration were observed for ambient ozone, EC, PAH, CO, NO, pollen grains and fungal spores.

- Apparent tracers exist for several of the important sources of ambient pollution, including ones for combustion sources (CO, NO, EC, and PAHs), soil dust (Si, Al, Fe, and Mn), and biological sources (endotoxins, fungal spores, and pollens) that potentially could support apportionment of health effects to sources.

- Spatial variations in daily ambient concentration ranged from barely detectable to high. The relative ranking shown in Table 4.1.6-2 confirmed most of our hypotheses with regard to regional-scale and neighborhood-scale spatial variations in ambient concentrations. $PM_{2.5}$ mass, SO_4, b_{sp}, and PM_{10} mass, potassium, iron, silicon, and calcium had mean daily spatial coefficients of variation less than 20% and were classified as pollutants with regional-scale variations. $PM_{2.5}$ OC; EC; NO_3; coarse PM; PM_{10} zinc, bromine, manganese, aluminum, strontium, copper, and cobalt; endotoxin; CO; NO_2; NO_x; and ozone had mean daily spatial coefficients of variation between 20% and 35%, and were classified as pollutants with moderate neighborhood-scale variations. NO, SO_2, PAHs, fungal spores, pollens, and other measured trace elements were found to have large neighborhood-scale variations, with mean daily spatial coefficients of variation greater than 35%.

- Mean indoor concentrations of most (55 of 70) pollutants and agents were lower indoors than outdoors in FACES residences. Notable exceptions were OC and naphthalene concentrations that were higher indoors, on average; endotoxin was higher indoors than outdoors in the winter (November-March), but lower in other seasons. About half of the measured compounds had higher maximum concentrations indoors than outdoors. For example, the maximum indoor concentrations of $PM_{2.5}$ mass, PM_{10} mass, OC, EC, total fungi, naphthalene, pyrene, flouranthene, iron, and aluminum exceeded the maximum outdoor observations.

- Routine home measurements indicated dust mites and cockroach allergens were uncommon in floor and bed dust, while cat and dog allergens were very common in FACES residences, including those without these pets. Measurable endotoxin levels were common in house dust; median levels of endotoxin were 64 EU/mg in floor samples and 52 EU/mg in bed samples. Two-week average nicotine levels were low (<1 $\mu g/m_3$) in 95% of the homes. Two-week average NO_2 and ozone concentrations averaged 13 ppb and 9 ppb respectively, in FACES residences.

- The indoor and outdoor concentrations of SO_4, EC, benzo[b]flouranthene, dibenz[a,h]anthracene, benzo[k]flouranthene, and thallium were reasonably well

correlated (r = 0.73 to 0.86). Indoor and outdoor concentration of $PM_{2.5}$, b_{sp}, benzo[a]pyrene, cobalt, and lead were moderately correlated with coefficients (r) between 0.5 and 0.6. The correlation coefficients for indoor and outdoor concentrations of all other compounds were less than 0.5. Window position and heating or air conditioning system use explained 70% of the variance in the indoor-outdoor ratio for SO_4, an important tracer of pollution of ambient origin.

2. A personal microenvironmental exposure model was developed to estimate individual daily exposure to pollution and agents of ambient origin. It combined a model of spatial variations of outdoor concentrations with a single compartment steady-state indoor air quality model. Daily individual diary information on residence operating characteristics and subjects' activities was used along with ARB time-activity survey data to estimates time spent in various microenvironments each day. Validation of this model was not possible, since resources were not sufficient to support personal monitoring. Therefore, at this time, we cannot comment on the validity of the model and the measurement errors (magnitude and sources) related to it.

    - Results of the microenvironmental exposure model suggest that personal exposures vary between subjects by a factor of two for $PM_{2.5}$ mass and by a factor of three or more for other pollutants considered on most days. The large variations in estimated exposure to pollutants of ambient origin between subjects suggest that the use of central site ambient concentrations for individual exposure assignments in FACES may result in considerable exposure misclassification and assignment error. The magnitude of the error is unknown because the individual exposure model performance has not been evaluated against personal exposure observations.

    - The mean estimated personal exposure concentrations of pollutants of ambient origin are consistently lower than the central site ambient concentrations. On average, the mean estimated individual exposure concentrations range from 15% of central site ambient concentrations for total pollens to 59% of central site ambient concentrations for $PM_{2.5}$ mass. The pollutant ranking (from highest to lowest) for mean ratio of personal exposure to central site ambient concentrations is $PM_{2.5}$ mass, endotoxin, EC, agricultural fungi, NO_2, PM coarse, *Alternaria*, ozone, *Cladosporium*, and total pollen.

3. The differences in individual exposure levels relative to central site ambient concentrations are primarily a result of lower indoor than outdoor concentrations caused by pollutant deposition on indoor surfaces and penetration losses; these losses from outdoors to indoors are also quite variable among the pollutants and bioaerosols, with median indoor to outdoor ratios ranging from 0.82 for EC to less than 0.02 for total pollen. Spatial differences in ambient concentrations within the community and indoor chemical reactions also contribute to the differences.

4. The between-subject variations in individual exposure estimates are generally greater for biological agents than conventional pollutants. For example, on a day with relative high pollen grain and fungal spore levels, the individual exposure estimates may range from 100 to 800 total pollen grains/m^3 and from 10 to 250 *Alternaria* spores/m^3. In contrast, on a day when conventional pollutant levels are high, the personal exposure estimates may range from

40 to 80 μg/m^3 for $PM_{2.5}$ mass and from 8 to 25 ppb for NO_2. The variance among subjects for primary PM components, such as EC, is also considerably higher than the variance for $PM_{2.5}$ mass.

Assessment of the overall accuracy and reliability of modeled personal exposure requires an extension of the model to account for indoor sources and collection of personal monitoring data for FACES subjects.

5.3 SUMMARY FOR ANALYSES OF POLLUTANT EFFECTS ON LUNG FUNCTION:

5.3.1 General Comments

Before we summarize and discuss the implications of the analyses that we have carried out related to lung function, we need to need to explain to the readers a number of limitations related to these analyses. This is of particular importance, given that many of our analyses, overall, do not seem to support associations (causal or otherwise) between daily changes in $PM_{2.5}$ and daily changes in FEV_1 or FEF_{25-75} in a group that has been considered to be "susceptible" to effects of air pollution. In this context, we stress that the results related to health effects are preliminary. Many additional analyses, both conventional and MSM, remain to be completed. Further refinements may be made to the estimates of individual exposure. Thus, the results in this report may be revised after further analyses are undertaken as part of the ongoing work on this project over the next 4.5 years.

5.3.1.1 Associations with Daily changes in Air Pollutants

Our conventional analyses carried out to-date do not support an association between $PM_{2.5}$--based either on our estimates of individual exposure or exposure based on Central Site data—and A.M. measures of FEV_1 or FEF_{25-75}. It is possible that restriction of the analyses to the "winter" months (October-February) is responsible, in part, for the lack of association. However, this seems unlikely for a number of reasons: 1) There is over a 10-fold range of variability in the daily levels of $PM_{2.5}$ during this period compared to an average of less than 3-fold variation during other months of the year; 2) During the winter months, $PM_{2.5}$ levels often exceed Federal standards and are, in general, much higher than levels in studies that have reported associations with measures of lung function; 3) We had over 3000 repeated measures with valid exposure and lung function measures for FEV_1 and 2800 for analyses for FEF_{25-75}. These latter numbers are in the range of those for studies that have show positive associations. It is possible that there is sufficient measurement error in our estimates of individual exposure—whose validity we could not check due to lack of funding for personal monitoring—such that we were not able to detect associations. This seems very unlikely to be the sole explanation, since analyses with Central Site data also failed to suggest any associations. We had null results with both the longitudinal and point treatment MSM.

We do not think that the null associations between $PM_{2.5}$ and measures of lung function could be explained solely by unmeasured confounding or failure to capture fully the effects of

the covariates that we did evaluate. First, unmeasured confounding would have to be very large to alter the results. The large numbers of confounders that we evaluated with a reasonable degree of model complexity, also makes it unlikely that unmeasured confounders are the sole problem. In addition, the MSM analyses took into account the potential confounding effects due to other pollutants, components of $PM_{2.5}$ and bioaerosols in a manner that does not lead to the colinearity problems that occur with conventional, conditional analyses.

In support of these conclusions with respect to $PM_{2.5}$ we cite a paper from the Children's Health Study (276). This cross-sectional study of asthma medication use and symptoms did not find an association with $PM_{2.5}$ with either monthly prevalence of medication use or wheeze in winter month (September-February), which is very similar to our data. Moreover, this study did not find associations with NO_2 on an annual or winter specific basis for medication use or wheeze. Stratification by time spent outdoors (above and below median) did not alter the results for NO_2 but did provide a suggestion of an effect for wheeze for $PM_{2.5}$. In our own preliminary data based on conventional analyses (see Section 4.2.2.3), Only further analyses will provide a more definitive explanation for our results, since $PM_{2.5}$ mass may not be the most relevant measure (in contrast to PM components and other pollutants) with which to address the health outcomes for this study.

Based on daily exposure throughout the year, our conventional analyses with NO_2 did observe an inverse association between Central Site 2-8 day moving averages and FEV_1. (We did not complete analyses for FEF_{25-75} or FEF_{75} in time for the submission of this report). The estimated effect was between a 3-6% reduction in FEV_1 for a 10 ppb increase in the 2-8 day moving averages, conditional on fixing the other covariates in the model and at a population mean FEV_1 of 1.50 L (the results do not suggest that one moving average had a larger effect than any other). We did not find any such associations with estimated personal exposure to NO_2. We did not find support for these observations in the longitudinal MSM or in the point treatment MSM for either estimated personal exposure or exposure based on Central Site data when the DSA alone selected variables into the model. However, when we forced NO_2 into the point treatment MSM[9], we did observe inverse associations with the moving averages and FEV_1. The interpretation for the these analyses is that, if contrary to fact, the population of asthmatic children were exposed to a 10 ppb lower level of NO_2 on any day, FEV_1 would be increased approximately 1.6-2.3% for the subsequent day, which depends on the specific lag or moving average that is chosen. The fact that the DSA algorithm did not select NO_2 at any lag or moving averages imposes a note of caution on the validity of these findings.

There are several possible explanations as to why we observed associations with NO_2 that we did not observe with $PM_{2.5}$. Since we used data from all seasons for NO_2, we had a larger sample size. However, for the reasons stated for $PM_{2.5}$, the sample size alone is not likely to be the explanation. While the range of daily levels for NO_2 is not as great as that for $PM_{2.5}$— although the spatial variability is greater[10]-- the specificity of NO_2 as a marker for the relevant sources is likely to be better. In Fresno/Clovis, mobile sources are the major sources for NO_2.

[9] There is no logical way to determine how to force NO_2 into the longitudinal MSM due to the existence of time-dependent confounding. Therefore, no analyses in which NO_2 was forced into the longitudinal model could be attempted.

[10] The greater spatial variability for NO_2 would be expected to make exposure estimates based on Central Site data less accurate (i.e., subject to greater misclassification than those for $PM_{2.5}$.

The fact that a mobile source emission component has effects on lung function is supported by our cross-sectional analyses of various traffic metrics with baseline lung function. These latter analyses found that, except for FVC, inverse distance weighted (from residence) traffic density on freeways and major connecting roadways was inversely associated with lung function. This association was largest and most precisely estimated for the FEF_{25-75}/FVC ratio, a measure of intrinsic air way size. It is interesting to note that, although the longitudinal MSM did not find effects for NO_2, the data reduction step for NO_2 showed that both estimated individual exposures and Central Site NO_2 were associated with concentrations of endotoxin, *Cladosporium* and agricultural fungi (estimated individual exposure only). Each of these components of the Fresno ambient bioaerosol have different typical seasonal patterns (*Cladosporium*: November peak and variability for the months February-May; endotoxin: May through November; agricultural fungi: April and May). Based on these observations, it appears that NO_2 not only is a marker for mobile sources, but that use of the full year's data also captures important contributions from the bioaerosols components, which was not captured in the winter-only $PM_{2.5}$ analyses. Our analyses, so far, do not allow us to determine if the bioaerosol components make independent contributions to adverse effects on FEV_1 and/or have important interactions with anthropogenic pollutants. These latter analyses will be conducted as part of our ongoing work. Nonetheless, the analyses highlight the importance of the consideration of effects of bioaerosols in the assessment of health effects related to anthropogenic pollutants.

The fact that estimated individual exposure to NO_2 was not associated with FEV_1, whereas Central Site concentrations were associated with FEV_1 does require comment. As we have noted, we do did not have funds to carry out personal monitoring to evaluate the measurement errors in our estimated individual exposure assignments. Therefore, the extent to which measurement error resulted in extreme bias to the null is not known. Given the lack of even a suggestion of an association makes measurement error unlikely to be the only explanation for the differences. Differences in spatial variability between $PM_{2.5}$ and NO_2 also are not a likely explanation for why we failed to find any association with $PM_{2.5}$. $PM_{2.5}$ has less spatial variability than NO_2: 18% compared to approximately 20-35%. This would favor fewer exposure errors for $PM_{2.5}$ based on Central Site data than for NO_2. In addition, the spatial variability of NO_2 is similar to that for EC, OC, and NO_x which suggests better specificity for NO_2 as a marker for the health-relevant components of the ambient air pollutant mixture (e.g., mobile sources). We did find weak additional support for the specificity of NO_2, in that 6 and 7 day lags for NO were estimated with reasonable precision; however, neither the longitudinal, point treatment or moving averages in the conventional analyses support the association with FEV_1.

A further suggestive piece of evidence in support of NO_2 as a marker of health-relevant air pollutants comes from a preliminary test of our hypothesis related to the relation between response to short-term increases in daily pollutant levels and growth of lung function. To our knowledge, no research has ever been presented on this question. We found that an inter-quartile decrease (more negative) in the parameter estimate for the association between daily increase in NO_2 and FEV_1 was associated, on average, with a 4.9% decline in FEV_1 over a given six to twelve-month interval. These observations are consistent with those from the Children's Health Study on the relation between community levels of NO_2 and lung function growth. However, we reiterate our caution about the interpretation of our results, given the preliminary nature of these chronic models. Additional model fitting and longer follow-up is needed to more completely

evaluate this effect. These observations will be explored further as we follow the cohort and carry out more detailed analyses on both morning and evening lung function.

With regard to our findings relative to the use of rescue medication in the hour before lung function measurement, we feel that it is important to be able to estimate the effects of ambient pollutants with any effects of medication use removed. Although it is not an issue of central concern for the study, it is nevertheless important—i.e., to the extent that medication effects might mitigate adverse responses of lung function and symptoms, the true adverse impacts of air pollution on children with asthma will be underestimated. The naïve (not fit with DSA) conventional and MSM analyses conducted to date consistently have shown inverse associations between rescue medication use in the hour before morning testing and lung function. In the naïve, conventional analyses this was the case regardless of whether rescue medication use was considered by itself with no other covariates or in models with lung function and other covariates. These analyses suggest that rescue medication use is a marker for more severe asthma with lower levels of lung function. The negative sign could reflect inadequate control for the confounding effects of symptoms. An alternative explanation for the negative association is that ozone and summertime photochemistry are more important drivers of the use of medications than are wintertime pollutant conditions. This can be seen clearly in the previously cited CHS paper (276). In that paper, analyses restricted to September-February showed inverse associations between monthly prevalence of wheeze and ozone and acids related to photochemicat reactions (nitric, acetic and formic). These issues will be explored further in our ongoing analyses.

Our MSM analysis in which rescue medication was the outcome did not suggest that we failed to properly adjust for symptoms related to its use. In addition, the final model for rescue medication never included the pollutant variable, either directly or through one of the linear combinations that summarized the pollutant variable or the successful performance of pulmonary function testing. In the point treatment model with rescue medication as the outcome and 2-8 day moving averages of estimated individual exposure to NO_2 as the pollutant, there were significant associations with moving averages of 3-6 days, with a suggestive trend such that the longer the average, the greater the odds of rescue medication use in the hour before lung function testing. A similar set of associations was seen with Central Site NO_2; however, the size of the point estimates for NO_2 moving averages were much lower and much less precisely estimated than was the case with the estimated individual exposure moving averages. The linear summary of the confounders of rescue medication use (which included symptom variables) was never selected by the DSA algorithm in the model for FEV_1 in longitudinal MSM analyses. In every table that summarizes the point-treatment MSMs, rescue medication was forced into the model. This makes it very difficult to interpret the negative sign in front of the coefficient related to it. Given the small number of subjects (median 5%) who used rescue medication in the hour before A.M. testing on any given day, it is difficult at this point to speculate on if and how rescue medication use modifies the effects of each pollutant on health outcomes. A demonstration of the influence of medication use on the traditional model of NO_2 and FEV_1 is presented in Section 4.2.2.2. However, the fact that summertime was included in the NO_2 analysis might provide a explanation of why we did see some associations with NO_2 and medication use. As noted we have not analyzed symptoms as an outcome.

5.3.2 Comments on the Analyses Presented

This section reviews a number of limitations related to these analyses. This is of particular importance, given that many of our analyses, overall, do not seem to support associations (causal or otherwise) between daily changes in $PM_{2.5}$ and daily changes in FEV_1 or FEF_{25-75} despite the fact that other literature suggests asthmatics are more "susceptible" to the effects of air pollution.

First and foremost, the analyses are far from complete in several respects:

- Factors related to the data available at the time that analyses for this report were begun:
  - Incomplete set of exposure data: Exposure data at the Central Site were available through August, 2004. However, the exposure team only had sufficient resources to process data through March 31, 2003. Obviously, this reduced the sample size available for these preliminary analyses. It is not likely that more data would change the inferences with respect to $PM_{2.5}$, since the number of observations that were available to us for the winter season was large (3,111 morning sessions with acceptable lung FEV_1 data and 2,881 morning sessions with acceptable FEF_{25-75} data. However, additional data might have provided more robust support for the findings with NO_2—i.e., with more data, NO_2 might have been selected into the MSM models.
  - Relatively limited duration of follow-up for many subjects: Of the total of 1,088 panel visits, only 342 (31%) represent follow up of 30 months or longer and only 45% represent 24 months or longer follow-up. This limited follow-up time can be attributed directly to the delays in the recruitment of the cohort due to the limited support that was received from community partners—contrary to their promises made and our expectations during the study design period.
- Limited range of pollutants examined: The main reasons for the limited analyses were: 1) The amount of time required to carry out the MSM analyses limited the number of analyses that we could perform, given the time constraints for the submission of this report; and 2) When we did not find any associations (causal or otherwise) between $PM_{2.5}$ and morning measurements of FEV_1, FEF_{25-75}, or rescue medication use one-hour before the morning test, we felt obligated to carry out some additional analyses to try to clarify our findings. We plan to carry out analyses with EC, $PM_{2.5-10}$ and ozone (in that order) as part of our ongoing analyses under a contract extension from ARB and under funding from our newly funded 4.5 year NIH grant (Division of Lung Diseases, National Heart, Lung and Blood Institute) that should begin in April, 2006. We also plan to carry out extensive additional analysis with all of our measured pollutants and bioaerosols (first priority is endotoxin) as part of our ongoing work under our NIH grant and additional analysis with PAHs as part of a three-year grant that is funded for this work from the Mickey Leland National Toxics Research Center (K. Hammond and I Tager, co-PIs). In addition, we have to address analyses that relate to asthma symptoms. It is entirely possible that symptom analyses will lead to different results from those for lung function, since it is well known that lung function and asthma symptoms may not be highly correlated. Extensive analyses of symptoms will be conducted. All of the analyses noted here also have to be carried out with the results from the evening panel data. This report includes our explanatory analyses of the role of rescue medication on the pollutant effect on pulmonary function but additional analyses are needed.

- No analyses with $PM_{2.5-10}$: We did not carry out either season-specific or year-round analyses with exposure to coarse PM. We also did not consider models in which both coarse PM and $PM_{2.5}$ were considered as treatments and in which interactions between the two could be tested.
-
- No analysis with components of $PM_{2.5}$: In particular, we did not carry out analyses with EC or with PM nitrate, which might have provided better specificity with respect to relevant components of $PM_{2.5}$ that relate to health effects. The reasons for this and our plans to address this need have been specified above.
- No analyses with endotoxin as primary exposure: We did not include analyses in which endotoxin was a primary exposure of interest in combination with $PM_{2.5}$. This is relevant, given published data that we cited in the Background section on *in vitro* endotoxin effects associated both with fine and coarse PM toxicity. The reasons for this and our plans to address this need have been specified above.
- No analysis with O_3: We did not carryout any analysis with summer time O_3 as the principal exposure of interest. This was an important omission, for the reasons given above. This is a very high priority analysis that will be carried out as soon as possible.
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- Factors related to the analysis methods:
  - "Final" Model Complexity: For both the conventional and MSM analyses, in general, we limited the model complexity to a maximum of 10 terms, maximum power of 2 and interactions whose sum of powers was 2. Although several analyses with up to 20 terms did not change the results in any analysis, we did not have time to explore higher polynomial models. Thus, it is possible that we did not capture fully the complexities of potential confounding by meteorology and the other pollutants/bioaerosols that were included in the analyses. However, given that the first and second-order meteorology and co-pollutant terms never were identified by the DSA as important covariates and that the analyses for $PM_{2.5}$ are restricted to a given season, it is unlikely that our null findings can be attributed to residual confounding by more complex terms. Sex-specific analyses, were evaluated by the inclusion of an interaction term (sex*pollutant) in all models. Thus far, no significant interactions have been found but we will continue to explore these and other important interactions with other health outcomes and pollutants. Finally, although we dealt with co-pollutants as confounders, we did not carry out any analyses in which we allowed more than one pollutant/bioaerosols to be a primary exposure. All of these analyses will be carried out as part of our ongoing work.

  Implementation of the MSMs: We applied the DSA algorithm to select models for the conventional analyses and to select nuisance parameters in the MSM analyses (data reduction and QFX) but not for the final MSM model. The software to implement the marginal structural model selection has not been developed as yet. As we noted, G-computation is sensitive to the proper specification of the models. We have not yet implemented the IPTW and double robust estimators. The latter estimator is more

robust to model mis-specification, and IPTW requires fewer model assumptions relative to G-computation. We already have determined that for $PM_{2.5,}$, there is minimum violation of the experimental treatment assignment assumption. This will permit us to carry out ITPW analyses that require fewer model assumptions and are easier to understand.

- Factors related to incomplete analyses of the health outcome data for acute exposures:
  - The current analyses have focused on A.M. FEV_1, with some limited exploration of FEF_{25-75}. We have not completed any analyses with FEF_{75} or FEF_{25-75}/FVC. We have not analyzed any lung function data from the P.M. lung function sessions, nor have we analyzed morning-evening and within-session variability in relation to pollutant and bioaerosol exposures.
  - We have not analyzed the effects of rescue medication during the nighttime hours for which we have somewhat more data and more variability than for medication use in the one-hour before A.M. testing. We have not explored the effect of daytime medication use on evening lung function.
  - We have not carried out analyses to evaluate the relation between differences in pre- and post-bronchodilator measures of lung function with respect to exposures to air pollutants and the bioaerosols. Similarly, pollutant effects on various symptoms of asthma and with asthma severity have not been completed.

All of the above will be carried as part of our ongoing worked funded by the ARB contract extension and NIH.

These issues need to be kept in mind relative to the interpretation of the analyses reported herein.

One final comment that relates to a comparison between the results of the conventional and marginal structural models is necessary. In our view, the longitudinal MSM is the "gold standard" for our analyses, since this approach accounts for the time-dependent confounding in the data—a situation that cannot be addressed properly by conventional analyses when the time-dependent confounders are also on the causal pathways between the pollutant and health outcome. Therefore, we remain circumspect with regard to the NO_2 findings. Moreover, even in the point-treatment MSM, NO_2 was not selected in the model unless it was "forced" into it. This suggests to us that (for the analyses we reported) NO_2 is acting, potentially, as a surrogate for some other variable or set of time-specific variables that are associated with decrements in FEV_1. Finally, we remind the reader that the interpretation of the coefficients from the conventional and MSM approaches differ and; therefore, direct comparison between them is not possible. For the conventional model (e.g., Table 4.2.2-7**)**, the coefficient in front of NO_2 is interpreted as the mean outcome change associated with each ppb change in NO_2 when all other strata are fixed. In contrast, the coefficient in front of NO_2 in the point treatment model (e.g., Table 4.2.3-16) is interpreted as follows: If contrary to fact, the entire population experiences a ppb change in NO_2, then the mean FEV_1 would be that many ml or lower. [For both models, a unit change in NO_2 is ppb.]

5.3.3 Summary Accomplishments Relative to Specific Aims

5.3.3.1 Specific Aims for Exposure Component

The following specific aims of the exposure component of the study were accomplished.

1. Ambient air quality measurements were augmented at the Fresno Supersite with trace metals and biological agents, specifically, pollen grains, fungal spores, and endotoxin.
2. The daily variability of pollutants and agents with regional-scale and neighborhood-scale spatial variability was evaluated using the Fresno Supersite air quality data.
3. The concentrations of pollutants and agents with regional-scale spatial variability were measured indoors and outdoors at selected homes and the relationships of concentrations outside selected homes to concentrations measured at the Fresno Supersite were evaluated.
4. The concentrations of pollutants and agents with neighborhood-scale spatial variability were measured indoors and outdoors at selected homes and the relationship of concentrations outside selected homes to concentrations measured at the Fresno Supersite was evaluated.
5. Home specific factors were collected by survey (by questionnaire and diary) to relate to home-specific agents.
6. Models were developed to predict neighborhood-scale concentrations of the pollutants and agents with neighborhood-scale spatial variability.
7. The concentrations of ETS, NO_2, and ozone were measured in the home of each child during selected two-week health study panels.
8. The principal locations of the study participants on each day of each two-week health study panels were surveyed (by questionnaire and diary).
9. The measurements made at the Fresno Supersite and homes, and the questionnaire and diary data, as well as the models developed, were used to estimate the exposure of each child in the asthma health study to selected agents of interest on each day during which the two-week health panels were conducted (from November 1, 2000 to March 31, 2003).

The following three specific aims were not addressed as planned:

10. To assess the extent to which neighborhood parameters account for differences between neighborhood and Fresno Supersite concentrations.
11. To develop definitions of neighborhoods based on traffic density and vegetation patterns.
12. To develop and test models to predict the daily variability of home-specific agents from measured data and diary data.

For specific aims 10 and 11, rather than classification of neighborhoods as we had planned originally, we developed spatial models directly from the measurement data that provide a surface to make concentration estimates for locations throughout the community. After careful consideration, we believe the spatial mapping approach is superior to the neighborhood

classification approach that was envisioned at the outset of the study. In particular, the creation of smooth spatial surfaces eliminates any arbitrary designations of "neighborhood".

For specific aim 12, nicotine was the only home-specific agent with sufficient daily data to accomplish this aim. However, the prevalence of smoking in homes was too low to obtain meaningful estimates of variability of exposure to second hand smoke. At the outset of the study we expected that there would be a significant number of homes where day-to-day variations in SHS levels might be important for subject exposures and their daily symptoms. Fortunately for the subjects, we did not find many homes with nicotine levels above the limits of detection (which are quite low) or relevant day-day variations. Had we had these data in advance, we would not have offered this specific aim as part of the exposure assessment.

5.3.3.2 Specific Aims for the Health Component

We report on work to-date for the hypotheses offered in the original application. These hypotheses remain the guiding hypotheses for our research. They will be pursued fully with funding from three sources: 1) A several month extension of the original contract by ARB; 2) a new 4.5-year award from the Division of Lung Diseases, National Heart, Lung and Blood Institute, NIH that should begin sometime in April, 2006 (date subject to change based on more direct communication from NIH); and 3) three-year award from the Mickey Leland National Toxics Research Center to continue our PAH work.

Hypothesis 1: Chemical components of particle air pollution that have immuno-enhancing properties (i.e., polyaromatic hydrocarbons (PAH) in diesel exhaust) are associated with symptom onset and severity and short-term reductions in lung function in a seasonally dependent pattern (and sub hypotheses).

In pursuit of the aim, a number of elements have been addressed: 1) We have developed spatial maps for our PAH data (work funded through EPA) and received funding to obtain additional years of PAH data through a three-year award from the Mickey Leland National Toxics Research Center. We have developed estimated individual exposure estimates for EC—EC is a good marker for mobile source emissions and, in parts of our study area, for diesel emissions. Our analysis of traffic metrics that included the heavy duty vehicle fraction represents the beginning of this work. We have developed the algorithm for classification for asthma severity that will be required for these analyses. In addition, we have developed estimated individual exposure estimates for pollens and endotoxin that are likely to be important exposure to consider with respect to this aim. The work that we report here lays the ground work for addressing the overall hypothesis and the sub-hypotheses.

Hypothesis 2: There are specific biologic components (e.g., endotoxin, fungal spores) and specific anthropogenic components (e.g., latex particles from road tire dust) in the $PM_{2.5-10}$ (coarse) fraction that are associated with exacerbations of symptoms and short-term, reversible decrements of lung function in a subset of asthmatic children and these associations are strongest during the months of April through September, when $PM_{2.5-10}$ constitutes a major fraction of the PM_{10} mass (and sub-hypotheses).

We have developed spatial maps and estimated individual exposure estimates for the bioaerosols and $PM_{2.5-10}$ that are the focus of these analyses We have developed the algorithm for classification for asthma severity that will be required for these analyses. The analyses for $PM_{2.5}$, NO_2 and NO included in this report evaluated the possible contribution of the bioaerosols and coarse PM to any associations observed for these three pollutants. None was observed; however, we did observe associations between endotoxin and fungal spores and Central Site NO_2, observations that provide a justification for the inclusion of this hypotheses and further exploration of these associations.

Hypothesis 3: Components of particle air pollution that are markers for the oxidative potential of particle air pollution (e.g., transition metals) are associated with more severe symptoms and short-term, reversible decrements in lung function in a subset of asthma children (and sub-hypotheses).

We carried out initial analyses of the spatial distribution and indoor-outdoor distributions of these metals. These data provide the groundwork for the analyses to address this hypothesis.

5.3.3.3 Medium-Term Effects (Expected over Four Years of observation)

Hypothesis 4: The subsets of asthmatic children who respond with short-term deficits in lung function to components of particulate air pollution (alone and/or in conjunction with other ambient air pollutants) will show relatively slower age-sex-specific growth of lung function than asthmatic children who do not so respond. (sub-hypotheses).

We have made a preliminary test of this hypothesis with NO_2 looking at 6- to 12-month growth in FEV_1. The preliminary results presented in this report provide the very intriguing suggestion that this hypothesis might be supported when more complete analyses with a variety of pollutants and combinations are carried out for the panel data. If so, this would be the first report of a direct connection between responses to acute fluctuations in ambient pollutant concentrations and long-term adverse effects on asthma. Testing of this hypothesis will remain a priority for our future work.

Hypothesis 5: The subset of asthmatic children who respond either to the immuno-adjuvants in particulate air pollution or the oxidizing properties of particle air pollution will have greater asthma-related morbidity {increased frequency and severity of attacks of asthma, more likely to be classified as severe asthma (e.g., NHLBI/WHO classification), and have more medical interventions {e.g., increased use of quick relief medications, higher doses of anti-inflammatory medication, need for medical care}.

We have created the asthma classification system that we need to carry out these analyses and have developed the data framework for the specific analyses. The latter was done as part of preliminary work on hypothesis 4 as note above.

Overall Summary of Work on Hypotheses: We have carried out a large amount of the work that is necessary to test the hypotheses. What remains is to collect sufficient data over time for additional exposure estimates and health outcomes and to further refine the estimated

individual exposure. We have obtained a long-term funding to complete this work that includes an ongoing collaborations with ARB to continue to provide Central Site data for this work.

One final comment relates to the extent of the analyses that we have performed for this report. We could have carried out a larger number of conventional analyses and covered more of the analyses that are inherent in our hypotheses. We chose not to follow this tact for several reasons: 1) As presented in the report, we have documented that that some important factors for this study are part of the causal pathways of interests (e.g., rescue medication use). Inclusion of factors on the causal pathway leads to bias in conventional analyses and exclusion of them leads to incomplete assessment of the air pollution effects of interest; 2) Our data exhibit time-dependent confounding, as we have demonstrated. Use of conventional analyses in the face of time-dependent confounding leads to biased estimates of effect, as we have demonstrated in our data (3); 3) Incorporation of highly correlated co-pollutants is problematic in conventional analyses, despite a number of methods that have been offered to address this issue (277). Inclusion of these co-pollutants can lead to biased coefficients for the pollutant of interest. We are seeking funds from NIH to carryout formal source-apportionment analyses to address this issue, in part. Given these constraints, we are reluctant of report conventional analyses until we have carried out parallel analyses with MSMs, which are not subject the problems noted above and produce unbiased or certainly less biased estimates of pollutant/bioaerosol effects. It would create considerable confusion if we were to report results with conventional analyses that we couls not support with our MSM analyses that are our "gold standard" analysis techniques. Our preference is to present conventional and MSM analyses in parallel and to discuss reasons for any differences in inferences that could arise from these two different approaches to analysis.

6. REFERENCES

1. Mortimer KM, Fallot A, Balmes JR, Tager IB. Evaluating the use of a portable spirometer a study of pediatric asthma. Chest 2003;123:1899-1907.
2. Robins JM, Hernan MA, Brumback B. Marginal structural models and causal inference in epidemiology. Epidemiology 2000;11:550-60.
3. Mortimer KM, Neugebauer R, van der Laan MJ, Tager IB. An Application of Model Fitting Procedures for Marginal Structural Models. American Journal of Epidemiology 2005;in press.
4. Hankinson JL, Odencrantz JR, Fedan KB. Spirometric reference values from a sample of the general U.S. population. American Journal of Respiratory Critical Care Medicine 1999;159:179-87.
5. Koren H. Association between criteria air polluants and asthma. Environmental Health Perspective 1995;103(103(S6)):235-242.
6. Miller R. Breathing freely: the need for asthma research on gene-environment interactions. Am J Public Health 1999;89:819-821.
7. Nicolai T. Air pollution and respiratory desease in children: What is the clinically relevant impact? Pediatric Pulmonology 1999;18S:9-13.
8. Weiss KB, Wagener DK. Geographic variations in US asthma mortality: small-area analyses of excess mortality, 1981-1985. American Journal of Epidemiology 1990;July 132:S107-15.
9. Utell MJ, Looney RJ. Environmentally induced asthma. Toxiclogy Letters 1995;82/83:47-53.
10. Sporik R, Chapman MD, Platts-Mills TAE. Review: House dust mite exposure as a cause of asthma. Clin Exp Allergy 1992;22:897-906.
11. Delfino RJ, Coate BD, Zeiger RS, Seltzer JM, Street DH, Koutrakis P. Daily asthma severity in relation to personal ozone exposure and outdoor fungal spores. American Journal of Respiratory and Critical Care Medicine 1996;154:633-41.
12. Halonen M, Stern DA, Wright AL, Taussig LM, Martinez FD. *Alternaria* as a major allergen for asthma in children raised in a desert environment. American Journal of Respiratory and Critical Care Medicine 1997;155:1356-61.
13. Michel O, Kips J, Duchateau J, Vertongen J, Robert L, Collet H, et al. Serverity of asthma is related to endotoxin in house dust. American Journal of Respiratory and Critical Care Medicine 1996;154:1641-6.
14. Strachan DP, Cook DG. Parental Smoking and childhood asthma: longitudinal and case control studies. Thorax 1998;53:295-301.
15. Platts-Mills TAE, Woodflok JA, Chapman MD, Heymann PW. Changing concepts of allergic disease. Journal of Allergy and Clinical Immunology 1996;98:s297-s306.
16. Humbert M, Durham SR, Ying S, Kimmitt P, Barkans J, Assoufi B, et al. IL-4 and IL-5 mRNA and protein in bronchial biopsies from patients with atopic and nonatopic asthma: Evidence against "intrinsic" asthma as being a distinct immunopathologic entity. American Journal of Respiratory and Critical Care Medicine 1996;154:1497-1504.
17. White MC, Etzel RA, Wilcox WD, Lloyd C. Exacerbations of childhood asthma and ozone pollution in Atlanta. Environmental Health Perspectives 1994;1:56-68.

18. Schwartz J, Slater D, Larson TV, Pierson WE, Koenig JQ. Particulate air pollution and hospital emergency room visits for asthma in Seattle. American Journal of Respiratory and Critical Care Medicine 1993;147:826-31.
19. Neas LM, Dockery DW, Koutrakis P, Tollerud DJ, Speizer FE. The association of ambient air pollution with twice daily peak expiratory flow rate measurements in children. American Journal of Epidemiology 1995;141(2):111-22.
20. Mortimer KM, Neas LM, Dockery DW, Redline S, Tager IB. The effect of summer ozone on inner city children with asthma. European Respiratory Journal 2002;19:699-705.
21. Hoek G, Dockery DW, Pope A, Neas L, Roemer W, Brunekreef B. Association between PM10 and decrements in peak expiratory flow rates in children: reanalysis of data from five panel studies. European Respiratory Journal 1998;11:1307-11.
22. Koenig JQ, Larson TV, Hanley QS, Robelledo V, Dumler K, Checkoway H, et al. Pulmonary function changes in children associated with fine particulate matter. Environmental Research 1993;63:26-38.
23. Delfino FJ, Zeigerm RS, Seltzer J, Street DH. Symptoms in pediatric asthmatics and air pollution: Differences in effects by symptom severity, anti-inflammatory medication use and particulate averaging time. Environmental Health Perspective 1998;106:751-761.
24. Cassino C, Ito K, Bader I, Ciotoli C, Thurston G, Reibman J. Cigarette smoking and ozone-associated emergency department use for asthma by adults in New York City. American Journal of Respiratory and Critical Care Medicine 1999;159:1773-9.
25. Peters A, Dockery DW, Heinrich J, Weichmann HE. Medication use modifies the health effects of particulate sulfate air pollution in children with asthma. Environmental Health Perspective 1997;105:430-5.
26. Mortimer KM, Tager IB, Dockery DW, Neas LM, Redline S. The effect of ozone on inner-city children with asthma: identification of susceptible subgroups. American Journal of Respiratory and Critical Care Medicine 2000;162:1838-45.
27. Beeson WL, Abbey DE, Knutsen SF. Long-term concentrations of ambient air pollutnants and incident lung cancer in California adults: results from the AHSMOG study. Environmental Health Perspective 1998;106:813-23.
28. Infante-Rivard C. Childhood asthma and indoor environmental risk factors. American Journal of Epidemiology 1993;137:834-44.
29. Holt PG, Yabuhara A, Prescott S, Venaille T, Macaubas C, Holt BJ, et al. Allergen recognition in the origin of asthma. In: Chadwick DJ, Cardew G, editors. The Rising Trends in Asthma: Ciba Foundation Symposium 206. New York: John Wiley, & Sons; 1997. p. 35-55.
30. Lange P, Parner J, Vestbo J, Schnohr P, Jensen G. A 15-year follow-up study of ventilatory function in adults with asthma. New England Journal of Medicine 1998;339:1194-200.
31. U.S. Environmental Protection Agency. Particulate Matter Research Needs for Human Health Risk Assessment to Support Future Reviews of the National Ambient Air Quality Standard for Particulate Matter--EPA/600/R-97/132F. Research Triangle Park: National Center for Environmental Assessment, U.S. E.P.A.; 1998 January 15, 1998. Report No.: EPA/600/R-97/132F.
32. U.S. Environmental Protection Agency. Ozone Research Needs to Improve Health and Ecological Risk Assessments--EPA/600/R-98/031. Research Triangle Park: National

Center for Environmental Assessment, U.S. E.P.A.; 1998 March 31, 1998. Report No.: EPA/600/R-98/031.
33. Kimber I. Allergy, Asthma and the environment: an introduction. Toxicology Letters 1998;102-103:301-306.
34. Koren H, O'Neill M. Experimental assessment of the influence of atmospheric pollutants on respiratory disease. Toxicology Letters 1998;102-103:317-321.
35. Seltzer J, Bigby BG, Stulbarg M, Holtzman MJ, Nadel JA, Ueki IF, et al. O_3-induced change in bronchial reactivity to methacholine and airway inflammation in humans. Journal of Applied Physiology 1986;60:1321-6.
36. Diaz-Sanchez D, Tsien A, Casillas A, Dotson AR, Saxton A. Enhanced nasal cytokine production in human beings after in vivo challenge with diesel exhaust particles. Journal of Allergy and Clinical Immunology 1996;98:114-23.
37. Diaz-Sanchez D, Tsien A, Fleming J, Saxon A. Combined diesel exhaust particulate and ragweed allergen challenge markedly enhances human in vivo nasal ragweed-specific IgE and skews cytokine production to a T helper cell 2-type pattern. Journal of Immunology 1997;158:2406-13.
38. U.S. Environmental Protection Agency. Integrative Synthesis of Key Points: PM Exposure, Dosimetry, and Health Effects. In: Air Quality Criteria for Particulate Matter Vol III of III. Washington, D.C.: National Center for Environmental Assessment Office of Research and Development, U.S. EPA; 1996. p. 13-1 to 13-28.
39. Peters A, Wichmann HE, Tuch T, Heinrich J, Heyder J. Respiratory health effects are associated with the number of ultrafine particles. American Journal of Respiratory and Critical Care Medicine 1997;155:1376-83.
40. Pekkanen J, Timonen KL, Ruuskanen J, Reponen A, Mirme A. Effects of ultrafine and fine particles in an urban air on peak expiratory flow among children with asthmatic symptoms. Environmental Research 1997;74:24-33.
41. Delfino RJ, Zeiger RS, Seltzer JM, Street DH. Symptoms in pediatric asthmatics and air pollution: Differences in effects by symptom severity, anti-inflamatory medication use and particulate averaging time. Environmental Health Perspectives 1998;106:751-61.
42. Dockery DW, Speizer FE, Stram DO, Ware JH, Spengler JD, Ferris BG. Effects of inhalable particles on respiratory health of children. American Review of Respiratory Disease 1989;139:587-94.
43. Ghio AJ, Samet JM. Metals and Air Pollution Particles. In: Holgate ST, Samet JM, Koren HS, Maynard RL, editors. Air Pollution and Health. New York: Academic Press; 1999. p. 635-51.
44. Ostro BD, Lipsett MJ, Wiener MB, Selner JC. Asthmatic responses to airborne acid aerosols. American Journal of Public Health 1991;81:694-702.
45. Monn C, Becker S. Cytotoxicity and induction of proinflammatory cytokines from human monocytes exposed to fine (PM2.5) and course particles (PM10-2.5) in outdoor and indoor air. Toxicology and Applied Pharmacology 1999;155:245-52.
46. Tsien A, Diaz-Sanchez D, Ma J, Saxon A. The organic component of diesel exhaust particles and phenathrene, a major polyaromatic hydrocarbon constituent, enhances IgE production by IgE-secreting EBV-transformed human B cells *in vitro*. Toxicology and Applied Pharmacology 1997;142:256-63.
47. Miguel AG, Cass GR, Weiss J, Glovsky MM. Latex allergens in tire dust and airborne particles. Environmental Health Perspectives 1996;104:1180-6.

48. Diaz-Sanchez D, Dotson AR, Takenaka H, Saxon A. Diesel exhaust particles induce local IgE production in vivo and alter the pattern of IgE messenger RNA isoforms. Journal of Clinical Investigation 1994;94:1417-25.
49. Zemp E, Elsasser S, Schindler C, Kunzli N, Perruchoud A, Domenighetti G, et al. Long-term ambient air pollution and respiratory symptoms in adults (SAPALDIA Study). American Journal of Respiratory and Critical Care Medicine 1999;159:1257 - 1266.
50. Jammes Y, Delpierre S, Delvolgo MJ, Humbert-Tena C, Burnet H. Long-term exposure of adults to outdoor air pollution is associated with increased airway obstruction and higher prevalence of bronchial hyperresponsiveness. Archives of Environmental Health 1988;53:372-377.
51. Detels RD, Tashkin DP, Sayre JW, Rokaw SN, Coulson AH, Massey FJ, et al. The UCLA population studies of chronic obstructive pulmonary disease. Chest 1987;95:594-603.
52. Abbey DE, Burchette RJ, Knutsen SF, McDonnell WF, Lebowitz MD, Enright PL. Long-term particulate and other air pollutants and lung function in nonsmokers. American Journal of Respiratory and Critical Care Medicine 1998;158:289-98.
53. McDonnell WF, Abbey DE, Nishino N, Lebowitz MD. Long-term ambient ozone concentration and the incidence of asthma in nonsmoking adults: the AHSMOG Study. Environmental Research 1999;80:110-21.
54. Braun-Fahrlander C, Vuille JC, Sennhauser FH, Neu U, Kunzle T, Grize L, et al. Respiratory health and long-term exposure to air pollutants in Swiss schoolchildren. Swiss Study on Childhood Allergy and Respiratory Symptoms with Respect to Air Pollution, Climate and Pollen. American Journal of Respiratory and Critical Care Medicine 1997;155:1042-9.
55. Dockery DW, Cunningham J, Damokosh AL, Neas LM, Spengler JD, Koutrakis P, et al. Health effects of acid aerosols on North American children: respiratory symptoms and illness. Environmental Health Perspective 1996;104:500-505.
56. Roemer W, Hoek G, Brunekreef B, Haluszka J, Kalandidi A, Pekkanen J. Daily variations in air pollution and respiratory health in a multicentre study: the PEACE project Pollution Effects on Asthmatic Children in Europe. European Respiratory Journal 1998;12:1354-61.
57. Peters JM, Avol E, Gauderman WJ, Linn WS, Navidi W, London SJ, et al. A study of twelve Southern California communities with differing levels and types of air pollution. II. Effects on pulmonary function. American Journal of Respiratory and Critical Care Medicine 1999;159:768-75.
58. McConnell R, Berhane K, Gilliland F, London SJ, Vora H, Avol E, et al. Air pollution and bronchitic symptoms in Southern California children with asthma. Environmental Health Perspectives 1999;107:757-60.
59. U.S. Environmental Protection Agency. Air Quality Criteria for Particulate Matter--Third External Review Draft. EPA 600/P-99/002aC. Research Triangle Park; 2001. Report No.: EPA 600/P-99/002aC.
60. Segala C, Fauroux B, Just J, Pascual L, Grimfeld A, Neukirch F. Short-term effect of winter air pollution on respiratory health of asthmatic children in Paris. Eur Respir J 1998;11:677-85.

61. Tiittanen P, Timonen KL, Ruuskanen J, Mirme A, Pekkanen J. Fine particulate air pollution, resuspended road dust and respiratory health among symptomatic children. Eur Respir J 1999;13:266-73.
62. Norris G, YoungPong SN, Koenig JQ, Larson TV, Sheppard L, Stout JW. An association between fine particles and asthma emergency department visits for children in Seattle. Environ Health Perspect 1999;107:489-93.
63. Boezen HM, van der Zee SC, Postma DS, Vonk JM, Gerritsen J, Hoek G, et al. Effects of ambient air pollution on upper and lower respiratory symptoms and peak expiratory flow in children. Lancet 1999;353:874-8.
64. Hajat S, Haines A, Goubet SA, Atkinson RW, Anderson HR. Association of air pollution with daily GP consultations for asthma and other lower respiratory conditions in London. Thorax 1999;54:597-605.
65. Yu O, Sheppard L, Lumley T, Koenig JQ, Shapiro GG. Effects of ambient air pollution on symptoms of asthma in Seattle-area children enrolled in the CAMP study. Environ Health Perspect 2000;108:1209-14.
66. Tolbert PE, Mulholland JA, MacIntosh DL, Xu F, Daniels D, Devine OJ, et al. Air quality and pediatric emergency room visits for asthma in Atlanta, Georgia, USA. American Journal of Epidemiology 2000;151:798-810.
67. Linaker CH, Chauhan AJ, Inskip HM, Holgate ST, Coggon D. Personal exposures of children to nitrogen dioxide relative to concentrations in outdoor air. Occup Environ Med 2000;57:472-6.
68. Roemer W, Hoek G, Brunekreef B, Clench-Aas J, Forsberg B, Pekkanen J, et al. PM10 elemental composition and acute respiratory health effects in European children (PEACE project). Pollution Effects on Asthmatic Children in Europe. Eur Respir J 2000;15:553-9.
69. Jalaludin BB, Chey T, O'Toole BI, Smith WT, Capon AG, Leeder SR. Acute effects of low levels of ambient ozone on peak expiratory flow rate in a cohort of Australian children. Int J Epidemiol 2000;29:549-57.
70. Thompson AJ, Shields MD, Patterson CC. Acute asthma exacerbations and air pollutants in children living in Belfast, Northern Ireland. Arch Environ Health 2001;56:234-41.
71. Ostro B, Lipsett M, Mann J, Braxton-Owens H, White M. Air pollution and exacerbation of asthma in African-American children in Los Angeles. Epidemiology 2001;12:200-8.
72. Friedman MS, Powell KE, Hutwagner L, Graham LM, Teague WG. Impact of changes in transportation and commuting behaviors during the 1996 summer olympic games in Atlanta on air qulaity and childhood asthma. Journal of the American Medical Association 2001;285:897-905.
73. Gauderman WJ, McConnell R, Gilliland F, London S, Thomas D, Avol E, et al. Association between air pollution and lung function growth in Southern California children. American Journal of Respiratory and Critical Care Medicine 2000;162:1383-90.
74. McConnell R, Berhane K, Gilliland F, London SJ, Islam T, Gauderman WJ, et al. Asthma in exercising children exposed to ozone: a cohort study. Lancet 2002;359:386-91.
75. Downs SH, Mitakakis TZ, Marks GB, Car NG, Belousova EG, Leuppi JD, et al. Clinical importance of Alternaria exposure in children. American Journal of Respiratory and Critical Care Medicine 2001;164:455-9.

76. Douwes J, Zuidhof A, Doekes G, van der Zee SC, Wouters I, Boezen MH, et al. (1-->3)-beta-D-glucan and endotoxin in house dust and peak flow variability in children. American Journal of Respiratory and Critical Care Medicine 2000;162(4 Pt 1):1348-54.
77. Soukup JM, Becker S. Human alveolar macrophage responses to air pollution particulates are associated with insoluble components of coarse material, including particulate endotoxin. Toxicology and Applied Pharmacology 2001;171:20-6.
78. Park JH, Spiegelman DL, Burge HA, Gold DR, Chew GL, Milton DK. Longitudinal study of dust and airborne endotoxin in the home. Environmental Health Perspectives 2000;108:1023-8.
79. Liu AH. Endotoxin exposure in allergy and asthma: Reconciling a paradox. Journal of Allergy and Clinical Immunology 2002;109:379-92.
80. Park J-H, Gold DR, Spielgelman DL, Burge HA, Milton DK. House dust endotoxin and wheeze in the first year of life. American Journal of Respiratory and Critical Care Medicine 2001;163:322-8.
81. Casillas AM, Hiura T, Li N, Nel AE. Enhancement of allergic inflammation by diesel exhaust particles: permissive role of reactive oxygen species. Ann Allergy Asthma Immunol 1999;83(6 Pt 2):624-9.
82. English P, Neutra R, Scalf R, Sullivan M, Waller L, Zhu L. Examining associations between childhood asthma and traffic flow using a geographic information system. Environmental Health Perspectives 1999;107:761-7.
83. Wilkinson P, Elliott P, Grundy C, Shaddick G, Thakrar B, Walls P, et al. Case-control study of hospital admission with asthma in children aged 5- 14 years: relation with road traffic in north west London. Thorax 1999;54:1070-4.
84. Lin S, Munsie JP, Hwang SA, Fitzgerald E, Cayo MR. Childhood asthma hospitalization and residential exposure to state route traffic. Environmental Research 2002;88:73-81.
85. Venn A, Lewis S, Cooper M, Hubbard R, Hill I, Boddy R, et al. Local road traffic activity and the prevalence, severity, and persistence of wheeze in school children: combined cross sectional and longitudinal study. Occupational and Environmental Medicine 2000;57:152-8.
86. Venn AJ, Lewis SA, Cooper M, Hubbard R, Britton J. Living near a main road and the risk of wheezing illness in children. American Journal of Respiratory and Critical Care Medicine 2001;164:2177-80.
87. U.S. Environmental Protection Agency. EPA Green Book - 8-Hour Ozone Area Standard, http://www.epa.gov/air/oaqps/greenbk/gnsum.html. Website; 2004 September 27.
88. California Environmental Protection Agency. Review of California Ambient Air Quality Standard for Ozone. Sacramento, Ca; 2004.
89. Stieb DM, Beveridge RC, Brook JR, Smith-Doiron M, Burnett RT, Dales RE, et al. Air pollution, aeroallergens and cardiorespiratory emergency department visits in Saint John, Canada. J Expo Anal Environ Epidemiol 2000;10:461-77.
90. Ross MA, Persky VW, Scheff PA, Chung J, Curtis L, Ramakrishnan V, et al. Effect of ozone and aeroallergens on the respiratory health of asthmatics. Arch Environ Health 2002;57:568-78.
91. Tobias A, Galan I, Banegas JR, Aranguez E. Short term effects of airborne pollen concentrations on asthma epidemic. Thorax 2003;58(8):708-10.

92. Galan I, Tobias A, Banegas JR, Aranguez E. Short-term effects of air pollution on daily asthma emergency room admissions. European Respiratory Journal 2003;22:802-8.
93. Hagen JA, Nafstad P, Skrondal A, Bjorkly S, Magnus P. Associations between outdoor air pollutants and hospitalization for respiratory diseases. Epidemiology 2000;11:136-40.
94. Delfino RJ, Gong H, Linn WS, Hu Y, Pellizzari ED. Respiratory symptoms and peak expiratory flow in children with asthma in relation to volatile organic compounds in exhaled breath and ambient air. J Expo Anal Environ Epidemiol 2003;13(5):348-63.
95. Delfino RJ, Gong H, Linn WS, Pelizzari ED, Hu Y. Asthma symptoms in Hispanic children and daily ambient exposures to toxic and criteria air pollutants. Environmental Health Perspectives 2003;111:647-56.
96. Chen C, Chock DP, Winkler SL. A simulation study of confounding in generalized linear models for air pollution epidemiology. Environ Health Perspect 1999;107:217-22.
97. McConnell R, Berhane K, Gilliland F, Molitor J, Thomas D, Lurmann F, et al. Prospective Study of Air Pollution and Bronchitic Symptoms in Children with Asthma. Am J Respir Crit Care Med 2003;168(7):790-797.
98. Janssen NA, Brunekreef B, van Vliet P, Aarts F, Meliefste K, Harssema H, et al. The relationship between air pollution from heavy traffic and allergic sensitization, bronchial hyperresponsiveness, and respiratory symptoms in Dutch schoolchildren. Environ Health Perspect 2003;111(12):1512-8.
99. Brauer M, Hoek G, Van Vliet P, Meliefste K, Fischer PH, Wijga A, et al. Air pollution from traffic and the development of respiratory infections and asthmatic and allergic symptoms in children. American Journal of Respiratory and Critical Care Medicine 2002;166:1092-8.
100. Brauer M, Hoek G, van Vliet P, Meliefste K, Fischer P, Gehring U, et al. Estimating long-term average particulate air pollution concentrations: application of traffic indicators and geographic information systems. Epidemiology 2003;14(2):228-39.
101. Nicolai T, Carr D, Weiland SK, Duhme H, von Ehrenstein O, Wagner C, et al. Urban traffic and pollutant exposure related to respiratory outcomes and atopy in a large sample of children. European Respiratory Journal 2003;21:956-63.
102. Kim JJ, Smorodinsky S, Lipsett M, Singer BC, Hodgson AT, Ostro B. Traffic-related air pollution near busy roads. American Journal of Respiratory and Critical Care Medicine 2004;570:520-6.
103. Risom L, Moller P, Loft S. Oxidative stress-induced DNA damage by particle air pollution. Mutation Research 2005; doi: 10.1016/j.mrfmmm.2005.06.012.
104. Lai CH, Liou SH, Lin HC, Shih TS, Tsai PJ, Chen JS, et al. Exposure to traffic exhausts and oxidative DNA damage. Occup Environ Med 2005;62:216-22.
105. Li N, Sioutas C, Cho A, Schmitz D, Misra C, Sempf J, et al. Ultrafine particulate pollutants induce oxidative stress and mitochondrial damage. Environmental Health Perspectives 2003;111:455-60.
106. Xia T, Korge P, Weiss JN, Li N, Venkatesen MI, Sioutas C, et al. Quinones and aromatic chemical compounds in particulate matter induce mitochondrial dysfunction: implications for ultrafine particle toxicity. Environ Health Perspect 2004;112:1347-58.
107. Brunekreef B. Epidemiological evidence of effects of coarse airborne particles on health. European Respiratory Journal 2005;26:309-18.

108. Lin M, Chen Y, Burnett RT, Villeneuve PJ, Krewski D. The influence of ambient coarse particulate matter on asthma hospitalization in children: case-crossover and time-series analyses. Environmental Health Perspectives 2002;110:575-81.
109. Delfino RJ, Quintana PJ, Floro J, Gastanaga VM, Samimi BS, Kleinman MT, et al. Association of FEV1 in asthmatic children with personal and microenvironmental exposure to airborne particulate matter. Environmental Health Perspectives 2004;112:932-41.
110. Delfino RJ, Zeiger RS, Seltzer JM, Street DH, McLaren CE. Association of asthma symptoms with peak particulate air pollution and effect modification by anti-inflammatory medication use. Environmental Health Perspectives 2002;110:A607-17.
111. von Klot S, Wolke G, Tuch T, Heinrich J, Dockery DW, Schwartz J, et al. Increased asthma medication use in association with ambient fine and ultrafine particles. European Respiratory Journal 2002;20:691-702.
112. Jalaludin BB, O'Toole BI, Leeder SR. Acute effects of urban ambient air pollution on respiratory symptoms, asthma medication use, and doctor visits for asthma in a cohort of Australian children. Environ Res 2004;95(1):32-42.
113. Gent JF, Triche EW, Holford TR, Belanger K, Bracken MB, Beckett WS, et al. Association of low-level ozone and fine particles with respiratory symptoms in children with asthma. Journal of the American Medical Association 2003;290:1859-67.
114. Horak F, Jr., Studnicka M, Gartner C, Spengler JD, Tauber E, Urbanek R, et al. Particulate matter and lung function growth in children: a 3-yr follow-up study in Austrian schoolchildren. European Respiratory Journal 2002;19:838-45.
115. Gauderman WJ, Avol E, Gilliland F, Vora H, Thomas D, Berhane K, et al. The effect of air pollution on lung development from 10 to 18 years of age. New England Journal of Medicine 2004;351:1057-67.
116. National Research Council. Research Priorities for Airborne Particulate. Washington, D.C.: The National Academies Press; 2004.
117. National Academy on An Aging Society. Childhood Asthma. Washington, D.C.; 2003 June, 2003.
118. Johnson PRS, Graham JJ. Final particular National Ambient Air Quality Standards: Public Health Impact on populations in the Northeastern United States. Environmental Health Perspectives 2005;113:1140-7.
119. Gilliland FD, Berhane K, Rappaport EB, Thomas DC, Avol E, Gauderman WJ, et al. The effects of ambient air pollution on school absenteeism due to respiratory illnesses. Epidemiology 2001;12:43-54.
120. California Environmental Protection Agency. Review of the California Ambient Air Quality Standards for Particulate Matter and Sulfates. Sacramento, CA; 2001.
121. Wong EY, Gohlke J, Griffith WC, Farrow S, Faustman EM. Assessing the health benefits of air pollution reduction for children. Environmental Health Perspectives 2004;112:226-32.
122. Wagner EM, Liu MC, Weinmann GG, Permutt S, Bleecker ER. Peripheral lung resistence in normal and asthmatic subject. American Review of Respiratory Disease 1990;141:584-8.
123. Carroll N, Morton EA, James A. The structure of large and small airways in nonfatal asthma. American Journal of Respiratory and Critical Care Medicine 1993;147:405-8.

124. Bousquet J, Jeffery PK, Busse WW, Johnson M, Vignola AM. Asthma. From bronchoconstriction to airways inflammation and remodeling. American Journal of Respiratory and Critical Care Medicine 2000;161:1720-45.
125. Schelegle ES, Miller LA, Gershwin LJ, Fanucchi MV, Van Winkle LS, Gerriets JE, et al. Repeated episodes of ozone inhalation amplifies the effects of allergen sensitization and inhalation on airway immune and structural development in Rhesus monkeys. Toxicol Appl Pharmacol 2003;191:74-85.
126. Tunnicliffe WS, Burge PS, Ayres JG. Effect of domestic concentrations of nitrogen dioxide on airway responses to inhaled allergen in asthmatic patients. Lancet 1994;344:1733-6.
127. Jorres R, Nowak D, Magnussen H. The effect of ozone exposure on allergen responsiveness in subjects with asthma or rhinitis. American Journal of Respiratory and Critical Care Medicine 1996;153:56-64.
128. Jenkins HS, Devalia JL, Mister RL, Bevan AM, Rusznak C, Davies RJ. The effect of exposure to ozone and nitrogen dioxide on the airway response of atopic asthmatics to inhaled allergen: dose- and time-dependent effects. American Journal of Respiratory and Critical Care Medicine 1999;160:33-9.
129. Chen LL, Scannell C, Tager IB, Peden DB, Christian DL, Ferrando RE, et al. Effect of ozone on the inflammatory response to inhaled allergen in allergic asthmatic subjects. Chest 2004;125:2328-35.
130. Salvi S, Blomberg A, Rudell B, Kelly F, Sandstrom T, Holgate ST, et al. Acute inflammatory responses in the airways and peripheral blood after short-term exposure to diesel exhaust in healthy human volunteers. American Journal of Respiratory and Critical Care Medicine 1999;159:702-9.
131. Nel AE, Diaz-Sanchez D, Ng D, Hiura T, Saxon A. Enhancement of allergic inflmmation by the interaction between diesel exhaust particles and the immune system. Journal of Allergy and Clinical Immunology 1998;102:539-54.
132. Diaz-Sanchez D, Garcia MP, Wang M, Jyrala M, Saxon A. Nasal challenge with diesel exhaust particles can induce sensitization to a neoallergen in the human mucosa. Journal of Allergy and Clinical Immunology 1999;104:1183-8.
133. Gilliland FD, Li YF, Saxon A, Diaz-Sanchez D. Effect of glutathione-S-transferase M1 and P1 genotypes on xenobiotic enhancement of allergic responses: randomised, placebo-controlled crossover study. Lancet 2004;363(9403):119-25.
134. Strange RC, Spiteri MA, Ramachandran S, Fryer AA. Glutathione-S-transferase family of enzymes. Mutation Research 2001;482(1-2):21-6.
135. Samet JM, Cohen AJ. Air Pollution and Lung Cancer. In: Holgate ST, Samet JM, Koren HS, Maynard RL, editors. Air Pollution and Health. New York: Academic Press; 1999. p. 849-50.
136. Hayes JD, Strange RC. Potential contributuion of the glutathione S-transferase supergene family to resistance to oxidative stress. Free Radical Research 1995;22:193-207.
137. Ward PA, Warren JS, Johnson KJ. Oxygen radicals, inflammation, and tissue injury. Free Radical Biology and Medicine 1988;5:403-8.
138. Poli G. Introduction--serial review: reactive oxygen and nitrogen in inflammation(1,2). Free Radical Biology and Medicine 2002;33:301-2.
139. Gilmour PS, Donaldson K, MacNee W. Overview of antioxxidant pathways in relation to the effects of air pollution. European Respiratory Monograph 2002;21:241-61.

140. Li N, Kim S, Wang M, Froines J, Sioutas C, Nel A. Use of a stratified oxidative stress model to study the biological effects of ambient concentrated and diesel exhaust particulate matter. Inhalation Toxicology 2002;14:459-86.
141. Wood LG, Gibson PG, Garg ML. Biomarkers of lipid peroxidation, airway inflammation and asthma. European Respiratory Journal 2003;21:177-86.
142. Hoidal JR. Reactive oxygen species and cell signaling. American Journal of Respiratory Cell and Molecular Biology 2001;25:661-3.
143. Baulig A, Garlatti M, Bonvallot V, Marchand A, Barouki R, Marano F, et al. Involvement of reactive oxygen species in the metabolic pathways triggered by diesel exhaust particles in human airway epithelial cells. American Journal of Physiology Lung Cellular and Molecular Physiology 2003;285:L671-9.
144. Nauseef WM, Clark RA. Granulocyte Phagocytosis. In: Mandell GL, Bennett JE, Dolin R, editors. Principles and Practices of Infectious Diseases: Fifth Edition. New York: Churchill Livingston; 2000. p. 89-112.
145. Vargas L, Patino PJ, Montoya F, Vanegas AC, Echavarria A, Garcia de Olarte D. A study of granulocyte respiratory burst in patients with allergic bronchial asthma. Inflammation 1998;22(1):45-54.
146. Barnes PJ, Chung KF, Page CP. Inflammatory mediators of asthma: update. Pharmacological Reviews 1998;50:515-96.
147. Ma JY, Ma JK. The dual effect of the particulate and organic components of diesel exhaust particles on the alteration of pulmonary immune/inflammatory responses and metabolic enzymes. Journal of Environmental Science and Health Part C Environmental Carcinogenesis and Ecotoxicological Reviews 2002;20:117-47.
148. Shukla A, Timblin C, BeruBe K, Gordon T, McKinney W, Driscoll K, et al. Inhaled particulate matter causes expression of nuclear factor (NF)-kappaB-related genes and oxidant-dependent NF-kappaB activation in vitro. American Journal of Respiratory Cell and Molecular Biology 2000;23:182-7.
149. O'Grady NP, Preas HL, Pugin J, Fiuza C, Tropea M, Reda D, et al. Local inflammatory responses following bronchial endotoxin instillation in humans. American Journal of Respiratory and Critical Care Medicine 2001;163:1591-8.
150. Hiura TS, Kaszubowski MP, Li N, Nel AE. Chemicals in diesel exhaust particles generate reactive oxygen radicals and induce apoptosis in macrophages. The Journal of Immunology 1999;163:5582-91.
151. Becker S, Soukup JM, Gilmour MI, Devlin RB. Stimulation of human and rat aleveolar macrophages by urban air particulates: Effeccts of oxidant radical generation and cytokine production. Toxicology and Applied Pharmacology 1996;141:637-48.
152. Monn C, Naef R, Koller T. Reactions of macrophages exposed to particles <10 microm. Environ Res 2003;91(1):35-44.
153. Monick MM, Hunninghake GW. Activation of second messenger pathways in alveolar macrophages by endotoxin. European Respiratory Journal 2002;20:210-22.
154. Romieu I, Sienra-Monge JJ, Ramirez-Aguilar M, Tellez-Rojo MM, Moreno-Macias H, Reyes-Ruiz NI, et al. Antioxidant supplementation and lung functions among children with asthma exposed to high levels of air pollutants. American Journal of Respiratory and Critical Care Medicine 2002;166:703-9.
155. Romieu I, Sienra-Monge JJ, Ramirez M, Moreno-Macias H, Reyes-Ruiz NI, del Rio-Navarro BE, et al. Genetic polymorphism of *GSTMI* and antioxidant supplementation

influence lung function in relation to ozone exposure among asthmatic children in Mexico City. Thorax 2004;59:8-10.
156. Trenga CL, Koenig JQ, Williams PV. Dietary antioxidants and ozone-induced bronchial hyperresponsiveness in adults with asthma. Archives of Environmental Health 2001;56:242-9.
157. Park JH, Spiegelman DL, Gold DR, Burge HA, Milton DK. Predictors of airborne endotoxin in the home. Environmental Health Perspectives 2001;109:859-64.
158. Gereda JE, Leung DY, Thatayatikom A, Streib JE, Price MR, Klinnert MD, et al. Relation between house-dust endotoxin exposure, type 1 T-cell development, and allergen sensitisation in infants at high risk of asthma. Lancet 2000;355(9216):1680-3.
159. Michel O, Ginanni R, Duchateau J, Vertongen F, Le Bon B, Sergysels R. Domestic endotoxin exposure and clinical severity of asthma. Clinical and Experimental Allergy 1991;21:441-8.
160. Braun-Fahrlander C, Riedler J, Herz U, Eder W, Waser M, Grize L, et al. Environmental exposure to endotoxin and its relation to asthma in school-age children. New England Journal of Medicine 2002;347:869-77.
161. Baldini M, Lohman IC, Halonen M, Erickson RP, Holt PG, Martinez FD. A Polymorphism* in the 5' flanking region of the CD14 gene is associated with circulating soluble CD14 levels and with total serum immunoglobulin E. American Journal of Respiratory Cell and Molecular Biology 1999;20:976-83.
162. Koppelman GH, Reijmerink NE, Colin Stine O, Howard TD, Whittaker PA, Meyers DA, et al. Association of a promoter polymorphism of the CD14 gene and atopy. American Journal of Respiratory and Critical Care Medicine 2001;163:965-9.
163. Haider SC, Sommerfeld A, Baldini M, Martinez F, Wahn U, Nickel R. Evaluation of the CD14 C-159T polymorphism in the German Multicenter Allergy Study cohort. Clinical and Experimental Allergy 2003;33:166-9.
164. Whitekus MJ, Li N, Zhang M, Wang M, Horwitz MA, Nelson SK, et al. Thiol antioxidants inhibit the adjuvant effects of aerosolized diesel exhaust particles in a murine model for ovalbumin sensitization. The Journal of Immunology 2002;168:2560-7.
165. Diaz-Sanchez D. The role of diesel exhaust particles and their associated polyaeromatic hydrocarbons in the induction of allergic airway disease. Allergy 1997;52:52.
166. Pandya RJ, Solomon G, Kinner A, Balmes JR. Diesel exhaust and asthma: hypotheses and molecular mechanisms of action. Environmental Health Perspectives 2002;110 Suppl 1:103-12.
167. Wiley JA, Robinson JP, Cheng Y-T, Piazza T, Stork L, Pladsen K. Study of Children's Activity Patterns: Final Report. Sacramento: California Air Resources Board; 1991 September, 1991. Report No.: A733-149.
168. Seinfeld JH, Pandis SN. Atmospheric chemistry and physics: from air pollution to global change. New York, New York: J. Wiley and Sons, Inc.; 1998.
169. Chow JC, Liu CS, Cassmassi J, Watson JG, Lu J, Pritchett LC. A neighborhood-scale study of source contributions in Rubidoux, California. Atmospheric Environment 1992;26A:693-706.
170. Chow JC, Watson JG, Lowenthal DH, Egami RT, Solomon PA, Thuillier RH, et al. Spatial and temporal variations of particulate precursor gases and photochemical reaction products during SJVAQS/AUSPEX ozone episodes. Atmospheric Environment 1998;32:2835-2844.

171. Solomon PA, Chow JC, Watson JG, Gilles J, Egami D, Magliano KL, et al. 1995 Integrated monitoring study: spatial and temporal variability of PM_{10} during the fall saturation study - preliminary results. In: Proceedings of the Air & Waste Management Association and U.S. Environmental Protection Agency 11th International Symposium on Measurement of Toxic and Related Air Pollutants; 1996; Pittsburgh, PA: Air & Waste Management Association; 1996.
172. Ludwig FL. A procedure for determining representative monitoring sites for photochemical model evaluation studies. In: Solomon PA, Silver TA, editors. Planning and Managing Regional Air Quality Modeling and Measurement Studies. Boca Roton, FL: Lewis Publisher; 1994.
173. Watson JG, Chow JC, Bowen JL, Lowenthal DH, Hering S, Ouchida P, et al. Air quality measurements from the Fresno Supersite. Journal of the Air & Waste Management Association 2000;50:1321-1334.
174. Hirst JM. An automatic volumetric spore trap. Annales of Appl Biol 1952;39:257-265.
175. Hirst JM. Changes in atmospheric spore content: diurnal periodicity and the effects of weather. Transactions British Mycol Soc 1953;36:375-392.
176. Nilsson SAIN, S. and Praglowski, J. (Eds.). Erdtman's Handbook of Palynology. 2nd ed ed. Copenhagen, Denmark:: Munksgaard; 1992.
177. Galán C, Domíniques-Vilches E. The capture media in aerobiological sampling. Aerobiologia 1997;13:155-160.
178. Erdtman G. The acetolysis method. A revised description 561-564. Svensk Bot Tidskr 1960;54:561-564.
179. Sterling M, Rogers C, Levetin E. An evaluation of two methods used for microscopic analysis of airborne fungal spore concentrations from the Burkard Spore Trap. Aerobiologia 1999;15:9-18.
180. Käpylä M, Penttinen A. An evaluation of the microscopical counting methods of the tape in Hirst-Burkard pollen and spore trap. Grana 1981;20:131-141.
181. Hjelmroos M, Benyon F, Culliver S, Jones A, Tovey E. Airborne Allergens. Interactive Identification of allergenic pollen and fungal spores. In: Institute of Respiratory Medicine Limited, Sydney, Australia; 1999.
182. Hjelmroos-Koski M, Macher JM, Hammond SK, Tager I. Assessment of pollen grain and fungal spore exposures for an epidemiological study of asthma in children. submitted.
183. Horner WE, Helbling A, Salvaggio JE, S.B L. Fungal allergens. Clin Microbiol Rev 1995;8:161-179.
184. Pedersen BV, Moseholm L. Precision of the daily pollen count. Identifying sources of variation using variance component models. Aerobiologia 1993;9:15-26.
185. Gundel LA, Lee VC, Mahanama KRR, Stevens RK, Daisey JM. Direct determination of the phase distributions of semi-volatile polycyclic aromatic hydrocarbons using annular denuders. Atmospheric Environment 1995;29:1719-1733.
186. Hickman JCE. The Jepson Manual. Higher Plants of California, 3rd ed. Berkeley, CA: University of California Press; 1996.
187. Greuter W, McNeill J, Barrie FR, Burdet, H.-M. D, V., Filgueiras TS, et al. (Eds.) July-August . International Code of Botanical Nomenclature (Saint Louis Code) adopted by the Sixteenth International Botanical Congress St. Louis, Missouri, July-August 1999. Königstein, Germany: Koeltz Scientific Books; 2000.

188. Mabberley DJ. The Plant-Book. A portable dictionary of the vascular plants. 2nd ed. ed. Cambridge, UK: Cambridge University Press; 2002.
189. Kirk PM, Cannon PF, David JC, Stalpers JAE. Ainsworth and Bisby's Dictionary of the Fungi. 9th ed. ed. Oxon, UK.:: CAB International; 2001.
190. Caka FM, Eatough DJ, Lewis EA, Tang H, Hammond SK, Leaderer BP, et al. An intercomparison of sampling techniques for nicotine in indoor environments. Environmental Science and Technology 1990;24:1196-1203.
191. Hyslop NM, Vaughn DL, Roberts PT, Lurmann FW, Hammond SK. Quality assurance project plan for Fresno PAH sampling; 2002 August.
192. Lurmann FW, Roberts PT, Hyslop NP, Hammond K, Perrino C, Jenske D, et al. Environmental monitoring in Fresno to support PAH assessment for the FACES project, phase 1: implementation of measurement systems. Report; 2002 July.
193. Yanosky JD, MacIntosh DL. A comparison of four gravimetric fine particle sampling methods. Journal of the Air & Waste Management Association 2001;51(6):878-884.
194. Turner WA, Olson BA, Allen GA. Calibration of sharp cut impactors for indoor and oudoor particle sampling. Journal of the Air & Waste Management Association 2000;50:484-487.
195. Stern MA, Allitt U, Corden J, Millington WT. The investigation of fungal spores in intramural air using a Burkard continuous recording air sample. Indoor Built Environ 1999;8:40-48.
196. TeleAtlas Eagle Geocoding Technology. Eagle™ Geocoding Technology. In; 2004.
197. Peters JM, Avol E, Berhane K, Gauderman J, Gilliland F, Jerrett M, et al. Epidemiologic investigation to identify chronic effects of ambient pollutants in southern California. Final report; 2004 May.
198. Wu J, Funk T, Lurmann FW, Winer A. Improving spatial accuracy of roadway networks and geocoded addresses. Transactions in GIS 2005;9:585-601.
199. Zhu YF, Hinds WC, Kim S, Sioutas C. Concentration and size distribution of ultrafine particles near a major highway. Journal of the Air & Waste Management Association 2002;52:1032-1042.
200. Ott W, Thomas J, Mage D, Wallace L. Validation of the simulation of human activity and pollutant exposure (SHAPE) model using paired days from the Denver, CO Carbon Monoxide Field Study. Atmospheric Environment 1988;22:2101-2113.
201. McCurdy T. Estimating human exposure to selected motor vehicle pollutants using the NEM series of models: lessons to be learned. Journal of Exposure Analysis and Environmental Epidemiology 1995;5:533-550.
202. MacIntosh D, Xue J, Ozkaynak H, Spengler J, Ryan PB. A population-based exposure model for benzene. Journal of Exposure Analysis and Environmental Epidemiology 1995;5:375-403.
203. Burke JM, Zufall MJ, Ozkaynak H. A population exposure model for particulate matter: case study results for PM2.5 in Philadelphia, PA. Journal of Exposure Analysis and Environmental Epidemiology 2001;11:470-489.
204. Fruin SA, St. Denis MJ, Winer AM, Colome SD, Lurmann FW. Reductions in human benzene exposure in the California South Coast Air Basin. Atmospheric Environment 2001;35:1069-1077.

205. Wu J, Lurmann F, Funk T, Winer A, Lu R, Turco R. Development of an individual exposure model for use in epidemiological studies: application to the Southern California Children's Health Study. Atmospheric Environment 2004;35.
206. Mulholland JA, Butler AJ, Wilkinson JG, Russell AG. Temporal and spatial distributions of ozone in Atlanta: regulatory and epidemiologic implications. Journal of Air and Waste Management Association 1998;48:418-426.
207. Jarrett M, Arain A, Kanaroglou P, Beckerman B, Potoglou D, Sahsuvaroglu T, et al. A review and evaluation of intra-urban exposure models. Journal of Exposure Analysis and Environmental Epidemiology 2004.
208. Koutrakis P, Briggs SLK, Leaderer BP. Source apportionment of indoor aerosols in Suffolk and Onondaga Counties, New York. Environmental Science and Technology 1992;26:521-527.
209. Koontz M, Evans WC, Wilkes CR. Development of a model for assessing indoor exposure to air pollutants; 1998.
210. Ebelt ST, Brauer M, Wilson WE. A comparison of health effects from exposure to ambient and non-ambient particles. In: 2003 AAAR PM Meeting, Particulate Matter: Atmospheric Sciences, Exposure and the Fourth Colloquium on PM and Human Health. Pittsburgh, PA; 2003.
211. Wilson WE, Mage DT, Grant LD. Estimating separately personal exposure to ambient and nonambient particulate matter for epidemiology and risk assessment: why and how. Journal of Air and Waste Management Association 2000;50:1167-1183.
212. Clayton CA, Perrit RL, Pellizzari ED, Thomas KW, Whitmore RM, Wallace LA, et al. Particle total exposure assessment methodology (PTEAM) study: Distributions of aerosol and elemental concentrations in personal, indoor and outdoor samples in a Southern California community. Journal of Exposure Analysis and Environmental Epidemiology 1993;3:227-250.
213. Liu DL, Nazaroff WW. Modeling pollutant penetration across building envelopes. Atmospheric Environment 2001;35:4451-4462.
214. Thatcher TL, Layton DW. Deposition, resuspension and penetration of particles within a residence. Atmospheric Environment 1995;29:1487-1497.
215. Thornburg J, Ensor DS, Rodes CE, Lawless PA, Sparks LE, Mosley RB. Penetration of particles into buildings and associated physical factors. Part 1: model development and computer simulation. Aerosol Science and Technology 2001;34:284-296.
216. Murray DM, Burnmaster DE. Residential air exchange rates in the United States: empirical and estimated parametric distributions by season and climatic region. Risk Analysis 1995;15:459-465.
217. Long CM, Suh HH, Koutrakis P. Characterization of indoor particle sources using continuous mass and size monitors. Journal of Air and Waste Management Association 2000;50:1236-1250.
218. Yamanaka S. Decay rates of nitrogen oxides in a typical Japanese living room. Environmental Science Technology 1984;18:566-570.
219. Nazaroff WW, Gadgil AJ, Weschler CJ. Critique of the use of deposition velocity in modeling indoor air quality. In: Modeling of Indoor Air Quality Exposure; 1993; Philadelphia, PA: American Society for Testing and Materials; 1993. p. 81-104.
220. Reiss R, Ryan, P.Barry, Koutrakis P. Modeling ozone deposition onto indoor residential surfaces. Environmental Science & Technology 1994;28:504-513.

221. Reiss R, Lurmann FW, Roberts PT, Schoell BM, Geyh AS, Koutrakis P. A pilot personal ozone study in southern California for validation of a microenvironmental model. In: Air & Waste Management Association and U.S. Environmental Protection Agency Conference on Measurement of Toxic and Related Air Pollutants, Research Triangle Park, NC, May 16-18; 1995.
222. Reiss R, Ryan PB, Koutrakis P, Tibbetts S. Ozone reactive chemistry on interior latex paint. Environmental Science & Technology 1995;29:1906-1912.
223. Ozkaynak H, Xue J, Spengler J, Wallace L, Pellizzari E, Jenkins P. Personal exposure to airborne particles and metals: results from the Particle Team Study in Riverside, California. Journal of Exposure Analysis and Environmental Epidemiology 1996;6:57-78.
224. Ozkaynak H, Xue J, Weker R, Butler D, Koutrakis P, Spengler J. The Particle Team (PTEAM) Study: analysis of the data, final report, vol. III. Final report; 1996 May.
225. Wallace L. Indoor particles: a review. Journal of the Air & Waste Management Association 1996;46:98-126.
226. Colome SD, Wilson AL, Tian Y. California Residental Indoor Air Quality Study, Volume 2: Carbon monoxide and air exchange rate: a univariate and multivariate analysis. Final report; 1994.
227. Sarnat JA, Koutrakis P, Suh HH. Assessing the relationship between personal particulate and gaseous exposures of senior citizens living in Baltimore, MD. Journal of Air and Waste Management Association 2000;50:1184-1198.
228. Allen R, Larsen T, Sheppard L, Wallace L, Liu LJS. Use of real-time light scattering data to estimate the contribution of infiltrated and indoor-generated particles to indoor air. Environmental Science and Technology 2004;37:3484-3492.
229. Fruin S. Characterizing black carbon inside vehicles: implications for refined exposure assessments for diesel exhaust particulate matter [Doctoral thesis]. Los Angeles, CA: University of California at Los Angeles; 2003.
230. Fruin SA, Winer AM, Rodes CE. Black carbon concentrations in California vehicles and estimation of in-vehicle diesel exhaust particulate matter exposures. Atmospheric Environment 2004;38:4123-4133.
231. Rodes CE, Sheldon L, Whitaker D, Clayton A, Fitzgerald KM, Flanagan J, et al. Measuring concentration of selected air pollutants inside California vehicles. Final report; 1998.
232. Shikiya DC, Liu CS, Kahn MI, Juarros J, Barcikowski W. In-vehicle air toxics characterization study in the South Coast Air Basin. Report; 1989.
233. American Thoracic Society. Standardization of Spirometry-1994 Update. American Journal of Respiratory and Critical Care Medicine 1995;152:1107-36.
234. Enright PL, Linn WS, Avol E, Margolis H, Gong HJ, Peters J. of spirometry test performance in children and adolescents: experience in a large field study. Chest 2000;118:665-71.
235. Redline S, Wright E, Kattan M, Kercsmar C, Weiss K. Short-term compliance with peak flow monitoring: results from a study of inner city children with asthma. Pediatric Pulmonology 1996;21:203-210.
236. Kunzli N, Lurmann F, Segal M, Ngo L, Balmes J, Tager IB. Association between lifetime ambient ozone exposure and pulmonary function in college freshman--Results of a pilot study. Environmental Research 1997;72:8-23.

237. Fujinaka L, Hyde D, Plopper C, Tyler W, Dungworth D, Lollini L. Respiratory bronchiolitis following long-term ozone exposure in bonnet monkeys: A morphometric study. Experimental Lung Research 1985;8:167-190.
238. Tyler W, Tyler N, Last J, Gillespie M, Barstow T. Comparison of daily and seasonal exposures of young monkeys to ozone. Toxicology 1988;50(b):131-44.
239. Tager IB, Balmes J, Lurmann F, Ngo L, Alcorn S, Kunzli N. Effect of chronic exposure to ambient ozone on lung function in young adults. Epidemiology 2005;16:DOI: 10.1097/01.ede.0000183166.68809.b0.
240. Blomberg A, Krishna MT, Bocchino V, Biscione GL, Shute JK, Kelly FJ, et al. The inflammatory effects of 2ppm NO_2 on the airways of healthy subjects. American Journal of Respiratory and Critical Care Medicine 1997;156:418-24.
241. Luppi F, Romagnoli M, Fabbri LM. The Global Initiative for Asthma guidelines: An update. European Respiratory Journal 2004;13:57-61.
242. Blanc PD, Jones M, Besson C, Katz P, Yelin E. Work disability among adults with asthma. Chest 1993;104:1371-7.
243. Spahn JD, Cherniack R, Paull K, Gelfand EW. Is forced expiratory volume in one second the best measure of severity in childhood asthma? American Journal of Respiratory and Critical Care Medicine 2004;169:784-6.
244. Tager IB, Weiss ST, Munoz A, Welty C, Speizer FE. Determinants of response to eucapneic hyperventilation with cold air in a population-based study. American Review of Respiratory Disease 1986;134:502-8.
245. O'Connor GT, Sparrow D, Demolles D, Dockery D, Raizenne M, Fay M, et al. Maximal and partial expiratory flow rates in a population sample of 10- to 11 yr-old school children: Effect of volume history and relation to asthma and maternal smoking. American Journal of Respiratory and Critical Care Medicine 2000;162:436-9.
246. Sin DD, Man SFP. Chronic obstructive pulmonary disease as a risk factor for cardiovascular morbidity and mortality. Proc Am Thorac Soc 2005;2:8-11.
247. Calverley PMA. Effects of corticosteroids on exacertabations of asthma and chronic obstructive lung disease. Proc Am Thorac Soc 2004;1:161-6.
248. Neyman J. On the application of probability theory to agricultural experiments. translated in Statistical Science 1923:465.
249. Fisher RA. The Design of Experiments. Edinburgh; 1951.
250. Rosenbaum P, Rubin D. The central role of the propensity score in observational studies for causal effects. Biometrika 1983;70:41-55.
251. Neugebauer R, van der Laan MJ. Why prefer double robust estimators in causal inference? Journal of Statistical Planning and Inference 2005;129:405-426.
252. Neugebauer R, van der Laan MJ. Locally efficient estimation of nonparametric causal effects on mean outcomes in longitudinal studies. U.C. Berkeley Division of Biostatistics Working Paper Series 2003.
253. Robins JM. Data, design, and background knowledge in etiologic inference. Epidemiology 2001;12:313-320.
254. Robins JM. A new approach to causal inference in mortality studies with sustained exposure periods -application to control of the healthy worker survivor effect. Mathematical Modelling 1986;7:1393-1512.

255. Neugebauer R, van der Laan MJ. G-computation Estimation of Nonparametric Causal Effects on Time-Dependent Mean Outcomes in Longitudinal Studies. U.C. Berkeley Division of Biostatistics Working Paper Series 2005.
256. Robins JM. Robust estimation in sequentially ignorable missing data and causal inference models. In: Proceedings of the American Statistical Association Section on Bayesian Statistical Science; 1999; Alexandria, VA, 2000; 1999. p. 6-10.
257. van der Laan MJ, Dudoit S. Unified Cross-Validation Methodology For Selection Among Estimators and a General Cross-Validated Adaptive Epsilon-Net Estimator: Finite Sample Oracle Inequalities and Examples--. 2003.
258. Sinisi SE, van der Laan MJ. Loss-based cross-validated deletion/substitution/addition algorithms in estimation. 2004;Working paper 143.
259. National Heart Lung and Blood Institute. National Asthma Education and Prevention Program, Expert Panel Report 2: Guidelines for the Diagnosis and Management of Asthma. Bethesda, MD: National Institutes of Health; 1997. Report No.: 97-4051c.
260. Tager IB, Kunzli N, Lurmann FL, Ngo L, Segal M, Balmes J. Part II: An approach to retrospective estimation of lifetime ozone exposure using a questionnaire and ambient monitoring data (California sites). Research Report. Cambridge: Health Effects Institute; 1998 1998. Report No.: 81.
261. Samet JM, Spengler JD. Indoor air pollution: a health perspective. Baltimore, MD: The Johns Hopkins University Press; 1991.
262. Lunden MM, Revzan KL, Fischer ML, Thatcher TL, Littlejohn D, Hering SV, et al. The transformation of outdoor ammonium nitrate aerosols in the indoor environment. Atmos. Environ. 2003;37(39-40):5633-5644.
263. Chow JC, Watson JG, Pritchett LC, Pierson WR, Frazier CA, Purcell RG. The DRI thermal/optical reflectance carbon analysis system: description, evaluation and applications in U.S. air quality studies. Atmospheric Environment 1993;27A:1185-1201.
264. Claiborn C, Pang Y, Finn D, Gundel L, Larson T, Liu L-J. The fine particle organic carbon measurement artifact and its implication for exposure assessment. In: 12th Conference of the International Society of Exposure Analysis; 2002 August 11-15, 2002; Vancouver, BC; 2002.
265. Turpin BJ, Saxena P, Andrews E. Measuring and simulating particulate organics in the atmosphere: problems and prospects. Atmospheric Environment 2000;34(18):2983-3013.
266. Zeger SL, Thomas D, Dominici F, Samet JM, Schwartz J, Dockery D, et al. Exposure measurement error in time-series studies of air pollution: concepts and consequences. Environ Health Perspect 2000;108:419-26.
267. Pinto JP, Lefohn AS, Shadwick DS. Spatial variability of PM2.5 in urban areas in the United States. Journal of the Air & Waste Management Association 2004;54(4):440-449.
268. Chow JC, Watson JG, Lowenthal DH, Chen L, Magliano KL. Particulate carbon measurements in California's San Joaquin Valley. Chemosphere 2005;62(3):337-48.
269. San Joaquin Valley Unified Air Pollution Control District. Extreme ozone attainment demonstration plan. Fresno, CA; 2004 October.
270. Steadman RG. A Universal Scale of Apparent Temperature. J Appl Meteor 1984;23:1674-1687.
271. Yu Z, van der Laan MJ. Double Robust Estimation in Longitudinal Marginal Structural Models. U.C. Berkeley Division of Biostatistics Working Paper Series. Working Paper 132 2003.

272. Mead J. Dysanapsis in normal lungs assessed by the relationship between maximal flow, static recoil, and vital capacity. American Review of Respiratory Disease 1980;121:339-42.
273. Weiss ST, Tosteson TD, Segal MR, Tager IB, Redline S, Speizer FE. Effects of asthma on pulmonary function in children. A longitudinal population-based study. American Review of Respiratory Disease 1992;145:58-64.
274. Merkus PJ, van Essen-Zandvliet EE, Kouwenberg JM, Duiverman EJ, Van Houwelingen HC, Kerrebijn KF, et al. Large lungs after childhood asthma. A case-control study. American Review of Respiratory Disease 1993;148:1484-9.
275. Tager IB, Ngo L, Hanrahan JP. Maternal smoking during pregnancy: Effects on lung function during the first 18 months of life. American Journal of Respiratory and Critical Care Medicine 1995;152:977-83.
276. Millstein J, Gilliland F, Berhane K, Gauderman W, McConnell R, Avol E, et al. Effects of ambient air pollutants on asthma medication use and wheezing among fourth-grade school children from 12 Southern California communities enrolled in The Children's Health Study. Arch Environ Health 2004;59:505-14.
277. Zeka A, Schwartz J. Estimating the independent effects of multiple pollutants in the presence of measurement error: an application of a measurement-error-resistant technique. Environ Health Perspect 2004;112(17):1686-90.