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Interim Report for the Fresno Asthmatic Children's Environment Study (FACES)

ARB Contract Nos. 99- 322 and 99-323

by

Ira Tager
S. Katharine Hammond
Kathleen Mortimer
Romain Neugebauer
John R. Balmes
Mervi Hjelmroos-Koski
Mark van der Laan

School of Public Health
University of California, Berkeley
140 Warren Hall
Berkeley, CA 94720-7360

Helene Margolis
California Environmental Protection Agency
Sacramento, CA

Frederick W. Lurmann
Paul T. Roberts
Nicole Hyslop

Sonoma Technology, Inc.
Petaluma, CA

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Research Division
California Air Resources Board
Sacramento, CA

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PREFACE

FACES is designed to examine the acute and chronic health effects of particulate matter (PM) air pollution, in combination with other ambient air pollutants and bioaerosols on children with asthma who reside in the Fresno/Clovis area. Exposure assessment will include centrally located ambient monitors as well as neighborhood, home and some personal monitors. The detailed exposure monitoring will allow FACES to evaluate which components of air pollution, in combination with biological agents, influence the natural history of asthma. The detailed descriptive data collected as part of the health assessments will allow FACES to identify biological and environmental characteristics that make some children more susceptible to the health effects of air pollution.

Funding for FACES began in February 2000 for the health component and June 2000 for the exposure component. Data collection began in November 2000. To date (July 2002), approximately 200 children have been enrolled and nearly all of these children have completed between one and three two-week home-monitoring visits. Home intensive panels have been completed in 51 homes.

Preliminary analyses, using traditional regression analyses, suggest increases in ozone, PM2.5 and NO2 are associated with increases in the prevalence of asthma symptoms (cough or wheeze). The effects are similar in magnitude to those published from other asthma cohort studies. In future analyses, causal regression methods will be applied to more accurately estimate the health effects.

Data collection will continue until February 2005. At that point, 2.5 to 4 years of follow-up will have been completed on all children. ETS, NO2, ozone and dust samples will have been collected from all homes during each of three seasons. Children will have completed 2-weeks of pulmonary function monitoring several times during each season. These data will allow for the examination of season-specific responses to air pollutants and biological agents and the subsequent impact on pulmonary function and other health measures.

1. EXECUTIVE SUMMARY

1.1 PROJECT OVERVIEW

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 residing in the Fresno County region of California. (The term "natural history of disease" refers to how a disease progresses over the long-term once it has become manifest.) This region of California is notable for a high prevalence of asthma among an ethnically diverse population, and for high levels of ambient air pollution, especially PM, which makes it an appropriate location in which to address questions of how air pollution impacts this vulnerable population. A unique opportunity to address critical questions related to air pollution's effects on the long-term progression of asthma is presented by the U.S. EPA's enhanced air quality monitoring platform ("Supersite") in Fresno.

Asthma is a chronic airway inflammatory disease, which is characterized by reversible airway obstruction, non-specific airway hyper-responsiveness, and mucous 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 they are associated with which observed effects. There are few data available to assess how repeated day-to-day responses to air pollution affect long-term respiratory health/disease. However, there is mounting scientific evidence that non-transient inflammation, such as in the airways or the vascular system, underlies chronic respiratory and/or cardiovascular diseases. Evidence is also mounting that a key mechanism by which air pollutants and other airborne agents can adversely impact health is by promotion or induction of oxidative stress with or without inflammation. Thus it is important to define the probable linkage between short-term exposures-responses to health status in the longer-term. A better understanding is needed of the biological characteristics of asthma and the exposure characteristics that define subgroups who are more/less responsive to sets of exposures, or who experience larger effects associated with long-term exposures.

The Fresno Asthmatic Children's Environment Study is 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 use 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 can one identify specific sources of PM that 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 biological characteristics (e.g., asthma severity, genetics, nutrition) or exposure characteristics (e.g., activity patterns, housing characteristics) that define subgroups who are more (or less) responsive to a given acute exposure or set of exposures, or who experience larger effects associated with long-term exposures?

The project is comprised of two fully integrated components: an epidemiological health component (previously Part A) and an exposure assessment component (previously Part B). The overall study was designed as a 66-month project, which included a six-month protocol refinement period, and, in July 1999, was proposed as such to the Air Resources Board (ARB). 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 period. As requested by the ARB, this interim report represents a summary of the work accomplished through approximately the first two years of the project. [NB: The contract for Part A was effective February 2000 and finalized June 2000; the Contract for Part B was effective June 2000 and finalized October 2000; the contracts for both Part A and Part B end in February, 2003.] The report includes updates on the state-of-knowledge related to asthma and air pollution in the context of our study objectives, a reiteration of our specific hypotheses and aims, and a progress report on the key elements of the study. Detailed descriptions of study protocols have been provided in the directory Protocols. The original proposals are also on the CD-ROM included with this report. (Appendix CD1).

The first 30 months of FACES had brought some challenges. Overall, there has been significant progress and major accomplishments during this period. These are described in greater detail in the progress report, and are briefly summarized here.

1.2 PROGRESS TO DATE

1.2.1 Overall Project Accomplishments

The study team quickly formed a cohesive unit that has worked together positively and efficiently. This efficiency has contributed greatly to the overall positive progress achieved to date, and promises to ensure the successful completion of the study.

After extensive efforts by the investigators and Fresno-based staff to establish favorable community relationships, the greater Fresno community has come to embrace the study, and FACES has received favorable media attention. As described further in the next section, these positive relationships had facilitated participant recruitment. The FACES Field Coordinator and the investigators continue to foster positive working relationships not only with the media, but also with school districts, schools (public and private), the business community, and the community at large. The business community has been especially supportive of the study, and has contributed a significant level of in-kind support.

A major effort has been made to coordinate with and seek input from other researchers involved in studies that bear relation to FACES, most notably the Southern California Children's Health Study (CHS). Some of the areas of discussion have included lung function measurements, lung function growth curves, and analytic methods.

1.2.2 Study Design and Population

A series of health-related hypotheses were developed around the questions posed above. To test these 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 different seasons (with different air pollution and meteorological patterns), and; 2) a classical longitudinal component that allows an assessment of changes that occur as a result of the cumulative effects of acute responses.

Prior to development of our study design and subject recruitment strategy, investigators personally visited and met with Fresno health care professionals to assess their interest in collaboration and/or willingness to help us recruit study participants. We received strong support from physicians, other health care providers and community groups, all of whom agreed to directly or indirectly facilitate our accessing pediatric asthma patients. Unfortunately, a year later when we were beginning recruitment there had been a number of changes in national policies related to human subjects in research, and, at the local level, we encountered changes in personnel and attitude that lead to significant delays and shortfalls in recruitment. We spent a number of months trying to work with our original contacts, which included, but were not limited to, Valley Children's Hospital, Kaiser Hospital, asthma clinics, and the San Joaquin Valley Health Consortium. Once it became clear that we were not going to receive the support that had been promised, we developed a community-based recruitment strategy. Although the new strategy is far more labor intensive for the field team, it is slowly but effectively attracting participants to the study. To further increase the number of participants, we have slightly modified our participant inclusion/exclusion criteria: the eligible age range was increased from 10 to 11 years, the time in current residence was reduced from 12 to 3 months, and a more recent decision has been made to increase from 10 to 20 Kilometers the allowable distance of the residence from the Supersite. Our efforts to implement the original recruitment strategy and our shift to the revised strategy, including the rationale for each, are detailed in the Progress Report sections.

We obtained approval from the ARB management and staff in September, 2001, to implement the following revisions related to study participants. The fundamental study design has not changed. The original goal was to recruit up to 450 asthmatic children (ages 6-10 at enrollment) in groups of approximately 50 children per month over a period of nine-to-ten months in Year 1 (nominally September 2000 through August/September 2001) of the study. Each of these groups of 50 subjects would, shortly after their baseline examinations, participate in a 14-day panel involving daily follow-up. In Year 2, the 450 children would be randomly reassigned to nine reconstituted panels, the membership of which would remain fixed for the duration of the study. These panels would 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 would undergo detailed evaluations at baseline and every 6-months thereafter; these evaluations include a medical history, housing

characteristics, medication use, lung function testing, prick-skin testing and measures of somatic growth. The revisions included a shift down from a goal of 450 subjects to a goal of 300 subjects recruited in groups as large as possible each month until the goal was reached or until Summer/Fall 2002, whichever came sooner. From the approximately 300 children, eight panels, rather than nine, would be formed. As of this writing (8/20/02) 404 children have been screened, 325 were eligible, of which 221 have consented to participate in the study, and 200 have completed baseline interviews: recruitment will continue until December 2002 to take advantage of "back to school" increases in enrollment experienced in the past.

We do not believe the above noted changes will significantly impact our ability to meet the study objectives. 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 sharp contrast to the NCICAS compliance rate, our study population has had a compliance rate of greater than 85%. Another important distinction between the two studies is that in FACES we are using 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. Section **4.1** of the report discusses in depth sample size.

1.2.3 Health-Assessment Related Accomplishments

The primary health outcomes to be assessed for the day-to-day impacts of air pollution include asthma symptoms (e.g., wheeze, cough, etc.), lung function (PEFR, FEV1, FEF25-75, FEF75) and asthma medication use (a covariate in some analyses). Longer-term health outcomes of primary interest include: classification of asthma severity at the end of 4-years, changes in classification of asthma between successive 6-mo. evaluations in relation to specific response patterns to short-term fluctuations in air pollution, and changes in lung function growth over the 4-years of the study.

As noted above, the panel component of the study involves observation of each of eight groups of children during ten 14-day panels (a post-baseline panel, and one panel in each of three air pollution seasons, for each of the 3½ years of follow-up). During panel periods, participants are asked to provide daily data, including twice-daily lung-function tests, symptoms, medication use and time-location-activity patterns. The longitudinal component involves each subject undergoing detailed evaluations at baseline and every 6-months thereafter; these evaluations include a medical history, housing characteristics, medication use, lung function testing, and measures of somatic growth. Skin-prick allergy testing will be completed twice during the study period.

During the protocol refinement period and into year-one of the study, 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 (Appendix CD2).

Where possible, we used or adapted instruments from other studies, including the Southern California Children's Health Study (CHS), and NCICAS. 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. An abstract [Fallot et al., Appendix CD4] on this work was presented at the 2002 American College of Chest Physicians conference and a manuscript reporting on this work has been submitted to Chest for publication (Appendix CD4).

Another major accomplishment was the development of a strategy for classification of 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. Dr. John Balmes presented this work at the May 2002 annual meeting of the American Thoracic Society (Appendix CD4).

All of the detailed protocols are documented as Protocols (Appendix CD2). Another major accomplishment was the development of a secure, reliable and efficient database and a data entry and data tracking system that allows investigators at UCB direct access to data originating in Fresno.

Participating children and their families had, for the most part, complied with all aspects of the study. The exception to this was blood sampling, which has successfully been collected on only 29% of participants who had completed a baseline interview. The original purpose for the blood collection was to obtain DNA for future genetic studies and some markers of inflammation (e.g., C-reactive protein). An acceptable alternate source of DNA is buccal cells, the collection of which involves using a cytobrush to brush the inside of the cheek. This procedure is well tolerated by children and adults, and was implemented in July 2002. While the blood samples would have enhanced the study, their absence does not substantially diminish our ability to test our main hypotheses. Based on newly published data from the CHS and other asthma cohort studies, collection of DNA seemed imperative for this study.

Based on data entered as of June 30, 2002, 391 children had been screened, 314 were eligible, 236 of whom consented to participate and 195 children completed a baseline interview. Nearly all of the children have participated in at least one 14-day panel, and some have completed as many as four 14-day panels. Also completed are a large number of the scheduled participant follow-up contacts, including 131 3-month, 96 6-month, 89 9-month, 49 12-month, 29 15-month and 22 18-month interviews. Only 9 (0.05%) children have withdrawn from the study, most due to their moving out of the Fresno/Clovis area.

1.2.4 Exposure-Assessment Related Accomplishments

Accurate definition of the exposure-response relationship for each air contaminant of interest, with consideration of co-exposures, is central to the core study design and ultimately to the success of FACES. An underlying premise of FACES is that observed health effects are associated with specific exposures or sets of exposures. Furthermore, there are subsets of the population of asthmatic children who are more/less responsive to these different exposures. To identify these subsets of children, and to define the exposure characteristics of the children comprising the subsets, the exposure assessment program is targeted toward accurately estimating individual-level exposures on a *daily* basis. 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 exposure estimates will be based on microenvironmental models adjusted for indoor, outdoor, and activity patterns, and if possible personal exposures. Methods to adjust exposure assignments to account for proximity to roadways and traffic density will be explored because it is expected that these factors account for a significant portion of the within-community variation in ambient air quality and ultimately an individual's exposures.

The selection of environmental factors to be measured in FACES was based on the project's health hypotheses. A recent review of the literature did not indicate there should be any changes to the list of environmental measurements originally proposed. The air pollutants to be evaluated include: 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), and sulfur dioxide (SO_2). Different exposure metrics will be considered, including, but not limited to, daily 1-hour maximum, daily maximum 8-hour average, 24-hour average, and annual average. Environmental measurements will also be 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 (pollen grains, fungal spores, dog, cat, cockroach, and dust mite allergens), endotoxin and environmental tobacco smoke (ETS). In addition, meteorological factors (temperature, relative humidity and barometric pressure) may be important effect modifiers or potential confounders and therefore will be measured.

The scope of work contained in our original proposal was based on the most current information available in Spring, 1999, with regard to the measurements already being made at the U.S. EPA Fresno Monitoring Platform ("Supersite"), by the San Joaquin Valley $PM_{10}/PM_{2.5}$ Air Quality Study, and at routine air quality monitoring sites operated by the ARB and the local air quality monitoring district. It was also based on information provided to us by ARB staff and management that there would be two trailers available for neighborhood scale measurements through the ARB's Vulnerable Populations Research Program. In addition, we secured funding from the U.S. EPA Office of Transportation and Air Quality to implement monitoring of PAHs (polycyclic aromatic hydrocarbons), 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. This is described in Appendix 7.

Each of the main elements of the FACES environmental monitoring program for which FACES investigators are responsible is making good progress. The Supersite is the core long-

term environmental monitoring element of the study. It will provide the highly time resolved measurements for all exposures of interest over the entire study period. The data from the routine home measurements, the home-intensive sub-study, and from the mobile monitoring platforms (i.e., monitoring trailers) provide the ability to define the relationship(s) between air quality throughout the study area to the measurements at the Supersite. For FACES, seven additional measurements were initiated at the Supersite: PM_{10}-associated endotoxin and elements (metals are of specific interest), SO_2 continuous measurements with lower limits of detection, several bioaerosols (pollen grains, fungal spores, and endotoxin), and polycyclic aromatic hydrocarbons (PAHs). Additional quality control/quality assurance (QC/QA) was conducted by Sonoma Technology, Inc.

The aeroallergen sampler at the Supersite has been operating well since the beginning of the study, and the UCB laboratory has performed identification and counts of pollen and fungal spores on a bi-hourly basis for most days. One hundred-eleven different pollen types have been identified to date: 60% of those identified are from wind-pollinated plants, and 80% of these are known to produce allergenic pollen grains. Sixty-nine different fungal spore types have been identified, many of which are plant pathogenic fungi that have been associated with health problems. These detailed measurements are rarely available and will be critical to our gaining an understanding of the effects of aeroallergens on asthmatics, independently and in combination with ambient air pollutants.

The routine home measurements that occur during all panel periods at all homes include passive measures of nitrogen dioxide and nicotine (a measure of second hand smoke), and ozone during the high ozone season indoors at all homes and outdoors whenever the home has access to outdoor space for equipment placement. As part of the panel studies there is also a home 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. Overall, the Hammond laboratory at UCB is keeping up with processing all sample types, and is geared up to run analyses in batches. To date, 200 nicotine samples and 120 nitrogen dioxide samples have been analyzed. In addition, 460 dust samples have been weighed and aliquoted, and of these about 300 have been analyzed for each of five allergens.

The home-intensive element of the exposure assessment program, which involves a more comprehensive set of measurements for a subset of participants in each panel, began in February, 2002. For this effort, FACES investigators designed and constructed a Microenvironmental Exposure Monitoring System (MEMS), that consists of a freestanding rack that contains measurement devices for O_3, nicotine, fungal spores and pollen grains, PAHs, and a variety of PM-related measures. A great effort was made to ensure that each device was as quiet as possible. At each of two to five homes per panel, one unit is placed inside the home in the living room and one unit is placed outside the home. Despite its relatively imposing size, the majority of participants involved in the home intensive study have not indicated the unit poses any problems or is excessively obtrusive. The home-intensive is scheduled to continue through approximately January 2003, by which time we expect to have completed a total of 100 home visits, which includes some homes being visited twice, once in the "warm" season and once in the "cool" season.

An important element of the exposure monitoring program is the mobile monitoring trailers being provided by the ARB. These trailers provide key measurements for characterization of exposures in different neighborhoods throughout the study area, and the capacity to relate these exposures to the measurements at the Supersite. The trailers are instrumented such that each duplicates, to the extent possible, the measurements relevant to FACES, that are being made at the Supersite. Due to the labor intensity and costs of moving the trailers, one trailer will be moved to a new location in the study area approximately every six weeks, while the other will remain in one location for longer periods. Both will be set-up on school grounds, which will serve to characterize exposures both in a neighborhood and at the specific school.

1.2.5 Preliminary Data Analysis

A nucleus of FACES investigators have invested a substantial effort to develop the analytic framework to apply and evaluate causal analysis methods as detailed in the original proposal. The first stage of this effort was to examine the impact of treatment (medication use) on occurrence of symptoms, without further complicating the analyses by inclusion of air pollution. Dr. Kathleen Mortimer presented the results from this preliminary work at the Society for Epidemiologic Research in Palm Desert in June 2002. A manuscript is also being prepared and a summary of the presentation "Causal regression of asthma medication use and pulmonary function" can be found in Appendix 2.

Given that only limited data would be available by the time this interim report was to be prepared, the ARB and the FACES team agreed that the preliminary results were to at least demonstrate the capability of the team and the suitability of the data collected in FACES to provide results on the order of those observed in previous panel studies of asthmatics. Furthermore, it was agreed that we would provide this demonstration based on daily data collected at the Supersite and application of conventional analytic methods.

The analyses, which are presented in detail in Section 6, are restricted to data obtained between November 2000 and November 2001. We focused on the relationship between a set of daily air pollution measurements from the Supersite and the occurrence of symptoms (as reported on the EasyOne® portable spirometer). We limited the analyses to symptoms, as the daily pulmonary function data were still undergoing a rigorous quality assurance protocol performed by Drs. Tager and Balmes.

For the period for which the air pollution data were available (Nov 2000 – Nov 2001), 119 children had completed a two-week home-based health monitoring panel. Data for eighty-five percent (85%) of the possible 1287 child-days were available for inclusion in the analyses; missing child-days resulted from missing air pollution data or non-compliance. As described above, the EasyOne® has pre-programmed questions to which the children must respond in the morning and in the evening. For a number of reasons we chose to use symptoms as our primary outcome measure, as described in Section 6.1.

The pollutants and metrics we considered were $PM_{2.5}$ (24-hour average), NO_2 (24-hour average), and O_3 (maximum 8-hour average); Lag 0, and 2, 3, and 5-day moving averages were evaluated. We used logistic regression with the Generalized Estimating Equation (GEE) method.

S-Plus software was used in all analyses (the methods we used are not impacted by the recently reported problems with the back-fitting or convergence algorithms). Selection of the best model was based on the Akaike's Information Criterion (AIC). Single pollutant models were evaluated; all models were corrected for temperature and relative humidity, season, and day of the week (weekday vs. weekend day). For comparison with published data, our results are presented in increments of 10 $\mu g/m^3$ for $PM_{2.5}$ and in 10 ppb for NO_2 and O_3. For all of the pollutants, multi-day moving averages provided a better model fit than single day lags for the occurrence of symptoms. A 5-day moving average for 24-hour NO_2 showed a larger association with symptoms than did $PM_{2.5}$, but the effect estimate had less precision (NO_2 OR=1.33 p-value 0.15, $PM_{2.5}$ OR=1.09 p-value 0.09). In a non-seasonal analysis, a 3-day moving average of maximum 8-hour average ozone yielded an effect estimate (OR=1.08) quantitatively similar to $PM_{2.5}$ (OR=1.09), however, it had the least precision (p-value 0.25 versus .09 for $PM_{2.5}$). In a season specific (i.e., restricted to June, July, August) analysis of ozone the effect estimate increased as did its precision (OR=1.24 p-value 0.13). The magnitude of these results, while not final, are consistent with those reported in the literature.

An important observation that reinforced the need to use an alternate analytic method for our final analyses arose when we evaluated a model that included a main effect and an interaction term for "use of rescue medication in the hour before testing." In all instances, except for the annual average O_3 analysis, 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 increased 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.

The analyses conducted for this report did not include exploratory analyses, such as analysis of correlation of pollutants, evaluation of autocorrelation in models, or consideration of multi-pollutant models. We plan to proceed with the analysis plan as presented in our original application. We also plan to add simulation studies to verify the extent to which the causal modeling approaches are superior to those of non-causal approaches.

1.3 CONCLUDING REMARKS

The work to be accomplished during the second project period (with Parts A and B, combined) is as described in our original proposal(s). We do not anticipate the need for any further substantive modifications to the overall study design.

Based on the preliminary results from the limited data available for this report, which both demonstrate the suitability of the data and our ability as a team to generate and analyze that data, we are confident that FACES will meet its objectives. We are also very confident that FACES will yield important new information about the complex relationships between

environmental exposures and both short-term and medium-term effects in this highly vulnerable population, asthmatic children.

2. BACKGROUND

In our original application, we summarized the literature with regard to effects of particle air pollution on the occurrence and etiology of asthma. Our conclusion was the following:

> *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 PM2.5 and coarse fraction (PM10-2.5, 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. The clarification of elements 1-4 above are essential inputs into any overall risk evaluation of the health impacts of ambient air pollution on persons with asthma.*

For this interim report we have 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 have excluded consideration of cross-sectional studies. We also have reviewed the relevant section (Section 8) of the latest draft of the EPA criteria document for PM [U.S. Environmental Protection Agency, 2001]. 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 [U.S. Environmental Protection Agency, 2001] 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 \U.S. Environmental Protection Agency, 2001]

> "*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 U.S. Environmental Protection Agency, 2001].

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 [Segala, 1998; Tiittanen, 1999; Norris, 1999; Boezen, 1999; Hajat, 1999; Yu, 2000; Tolbert, 2000; Linaker, 2000; Roemer, 2000; Jalaludin, 2000; Thompson, 2001; Ostro, 2001; Friedman, 2001]. In relation to our previous review, these studies do not add important new insights into the nature and magnitude of the risk of exposure to air pollution. Selected studies are 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 [Norris, 1999; Yu, 2000]. Norris, *et al.* [Norris, 1999] observed an association between fine PM (at levels below the newly adopted NAAQS of 15 $\mu g/m^3$) and CO and daily emergency department visits for children with asthma. In a more extensive analysis, Yu and colleagues [Yu, 2000] 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 mg/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*. [Ostro, 2001] 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 [Friedman, 2001] 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} [Tolbert, 2000].

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) [Roemer, 2000]. Over 1000 children ages 6-12 years with asthma were observed daily for approximately 2 months during the winters of 1993 and 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 who were 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 [Tiittanen, 1999]. Various lags of $PM_{2.5}$, particle number in the range of 0.1-1.0 μm, PM_{10} and $PM_{10-2.5}$ 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 [Thompson, 2001]. 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 insight 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 [Gauderman, 2000]. Overall, the effects were strongest for NO_2, $PM_{10-2.5}$, 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 [Peters, 1999] 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 [McConnell, 2002] 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 [McConnell, 2002]. 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 [McConnell, 1999]. 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 of potentially 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 subset 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 [Downs, 2001]. 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 [Douwes, 2000]. 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* and in humans [U.S. Environmental Protection Agency, 2001]. 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 [Soukup, 2001]. 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 $PM_{10-2.5}$ 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 [Park, 2000], 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 [Liu, 2002]. Data from a birth cohort study have identified an association between levels of endotoxin in house dust and wheezing in the first year [Park, 2001], 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 very 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 ($PM_{10-2.5}$).

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*. [Casillas, 1999] 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) [English, 1999]. 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 [Wilkinson, 1999], 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 [Lin, 2002]. 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 [Venn, 2000]. 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 [Venn, 2001]. 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 was completed for a UC Berkeley senior thesis, and can be found in Appendix CD4.

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.

3. PROJECT OBJECTIVES, HYPOTHESES AND SPECIFIC AIMS

NOTE: At the time of the original submission, the health and exposure components of this project were submitted as separate proposals at the request of ARB. The investigative team always has considered this a single research project from its original design and in the manner in which the team has worked after the project funds were awarded. As part of the discussion for the preparation of this interim report, it was agreed jointly by ARB and the investigators that the two components should be recombined into a single interim report and there should be a single budget for the remaining 30 months of the project. In this section, we present the hypotheses as they were written in the original submissions. The first set of hypotheses relate specifically to the health outcomes component. The second set of hypotheses were developed for the exposure component but are directly relevant to the estimation of the exposure effects on the health of the study subjects. Both sets of hypotheses are presented exactly as they appear in the original proposal to provide perspective to those reviewers who may not be familiar with the original proposals, which are available on the enclosed compact disk.

3.1 HEALTH OUTCOMES HYPOTHESES

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 6-11 years of age 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 subsets 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 airway reactivity, etc.) of the responding subsets will 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, the analytic plan (Section 8) does include a description of the approach we would take to answer the question.)

3.1.1 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.

- **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.
  - **1.** 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.
  - **1.** These associations will not be influenced by ambient ozone concentrations.
  - **2**. These associations will be not be detected in asthmatic children repeatedly exposed (passively or directly) to environmental tobacco 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.

Hypothesis 2: There are specific biologic components (e.g., endotoxin, fungal spores) in the $PM_{10-2.5}$ (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 $PM_{10-2.5}$ 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 $PM_{10-2.5}$ mass concentration and exacerbations and transient declines in lung function that are observed in asthmatic children during the dry season (May-October).

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 asthmatic 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 environmental tobacco smoke and/or wood burning smoke in their homes.

3.1.2 Medium-term Effects (expected over 4-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.

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.

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}, are 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.

3.2 EXPOSURE HYPOTHESES

Exposure Hypotheses and Specific Aims

Hypothesis 1: The air pollutants of interest can be grouped into three categories on the basis of the principal determinants of their concentration.

(a) Group I (regional pollutants)
(b) Group II (neighborhood pollutants)
(c) Group III (home-specific agents)

Hypothesis 2: Although regional pollutants vary over large distances (>20 km), there is little variability of concentration within a region. These pollutants also have similar concentrations inside and outside a home. Among the pollutants which fall into this category are $PM_{2.5}$ sulfate, nitrate, ammonium, and secondary organic species.

Hypothesis 3: The primary determinants of the concentration of Group II agents are factors that vary from neighborhood to neighborhood. For instance, those pollutants whose primary source is traffic (e.g., EC) will be higher in neighborhoods near major traffic arteries than in those with little traffic. Similarly, pollen from particular plants will depend on the density of those plants in a neighborhood.

Hypothesis 4: Agents whose primary source are within the home fall into Group III. These agents include ETS, allergens from dogs, cats and cockroach, fungal spores, dust mites, and cockroaches, and endotoxin.

Hypothesis 5: Daily air pollution exposure of individual children can be estimated (modeled) with reasonable accuracy from

(a) ambient air pollution concentrations measured hourly and daily at a central site in the community;
(b) representative samples of indoor and outdoor pollutant concentrations measured infrequently at a child's home;
(c) representative samples of the time activity patterns at known locations for each child, obtained during each two-week panel of health effects;
(d) housing and school characteristics determined from questionnaires;
(e) annual traffic densities on roadways near a child's home and school; and
(f) vegetation near a child's home and school.

SPECIFIC AIMS

The overall objective of Part B of the study is to estimate the daily air pollution exposures of the study participants during each of the two-week health panels over the five-year period with a high degree of reliability. The specific aims of the study are as follows:

1. To augment ambient air quality measurements at the Fresno Supersite with agents of interest in this study, specifically, pollens, fungal spores, and endotoxins.
2. To evaluate the daily variability of Group I (regional) and Group II (neighborhood) agents using the Fresno Supersite air quality data.
3. To measure the concentrations of Group I (regional) agents indoors and outdoors at selected homes and to evaluate their relationship to concentrations measured at the Fresno Supersite.
4. To develop definitions of neighborhoods based on traffic density and vegetation patterns.
5. To measure the concentrations of Group II (neighborhood) agents indoors and outdoors at selected homes, to evaluate their relationships to concentrations measured at the Fresno Supersite, and to assess the extent to which neighborhood parameters account for differences between neighborhood and Fresno Supersite concentrations.
6. To survey (by questionnaire and diary) home-specific factors for Group III (home-specific) agents.
7. To develop and test models to predict neighborhood-scale concentrations of the Group II (neighborhood) agents.
8. To develop and test models to predict the daily variability of Group III (home-specific) agents from measured data and diary data.
9. To measure the concentration of selected agents (ETS, NO_2, and ozone) in the home of each child during selected two-week health study panels.
10. To survey (by questionnaire and diary) the principal locations of the study participants on each day of each two-week health study panels. To use the measurements made at the Fresno Supersite and homes and the questionnaire and diary data, as well as the models developed, to estimate the exposure of each child in the asthma health study to each agent of interest on each day during which the two-week health panels are conducted.

4. PROGRESS REPORT ON HEALTH COMPONENT

This section reviews the work that has been completed on this project as of the first 29 months of the study (February 13, 2000 through June 30, 2002) for the health component. The funds for the exposure component were not awarded until June 9, 2000, and therefore, this interim report covers work for the exposure component for the period June 9, 2000 through February 14, 2002. This reporting period was agreed upon jointly by ARB and the investigators (as per the January 11, 2002, letter from Richard Bode). Analyses of data are restricted to data available as of the last reporting date for each component.

4.1 DEVELOPMENT OF THE COHORT OF CHILDREN WITH ASTHMA

Our original proposal called for recruitment of 450 children during the first year of the study. The initial eligibility requirements included: **1**) a physician diagnosis of asthma; **2**) current asthma symptoms; **3**) utilization of or an active prescription for asthma medication; **4**) age 6-10 years; and **5**) residence within 10 kilometers of the Fresno First Street monitoring site.

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 would have involved relationships with kindergartens, grammar schools and possibly middle schools in two different school districts (Fresno and Clovis). The Children's Health Study utilized a great deal of resources to complete school-based recruitment, but, unlike FACES, was not restricted to the smaller 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 impose a range of financial and time constraints which we evaluated prior to our decision. Due to time constraints imposed on our project related to ARB's desire to have our project coincide to some extent with the 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, however, there was a 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. Finally, upon closer examination of the population serviced 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. Fortunately, our Field Coordinator had an extensive background in marketing, and 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 of 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 of eligible age. The Field Coordinator established a strong relationship with the head of the school nurse program who was very supportive of the project and encouraged the school nurses to distribute fliers and recruit children who frequently visit their offices for asthma care. FACES posters were hung in the school nurses' offices as a reminder. We 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) have developed an interest in the project and actively recruited participants. A summary of the number of patients recruited from each source is listed in Table 4.1.

In addition to changes in the recruitment method, we also made three changes to expand our pool of eligible children. In May of 2001, we expanded our age range to include 11 year old children. We considered this change due 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 want to include 11 year old children because of the possible confounding effects of smoking on

pulmonary function growth. Given the low prevalence of smoking among the 10 year old children we had recruited (0%), we reconsidered this decision. 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.

Table 4.1. Recruitment by referral source. (Based on data entered as of June 30, 2002.)

	Screened	Eligible	Enrolled
	# (%)	# (%)	# (%)
Schools	**142 (36.3)**	**113 (36)**	**68 (37.4)**
Daycare/preschools	**2 (0.5)**	**0**	**0**
Churches	**4 (1)**	**3 (1)**	**3 (1.6)**
TV	**131 (33.5)**	**106 (33.8)**	**57 (31.3)**
Radio	**1 (0.3)**	**0**	**0**
Newspaper	**21 (5.4)**	**19 (6.1)**	**14 (7.7)**
Medical Groups	**23 (5.9)**	**20 (6.4)**	**11 (6)**
Business	**5 (1.3)**	**5 (1.6)**	**4 (2.2)**
Health fairs/booths	**28 (7.2)**	**21 (6.7)**	**9 (4.9)**
Friends/family/staff referral	**34 (8.7)**	**27 (8.6)**	**16 (8.8)**
Total	**391 (100)**	**314 (100)**	**182 (100)**

Our original proposal called for the inclusion of only one child per family. This was done to increase the heterogeneity of exposure and decrease the workload on the participating families. In May of 2002, we removed that restriction and allowed age-eligible siblings to be included. We felt that tests of the primary hypothesis would benefit from a larger sample size and the inclusion of a small number of siblings would not have a substantial impact on the variation in some of our exposure measures. Prior to enrollment of the second siblings, the Field Coordinator discusses the time commitment with the family to ensure that they understand the burden and so that we don't end up losing both siblings in an attempt to increase our enrollment.

The final modification includes an expansion of the geographic area from 10 to 20 kilometers from the First Street monitoring site. Recent analyses of the spatial distribution of target pollutants for FACES suggest that expansion of our eligibility area to 20 km would not compromise the representitiveness of the ambient exposure assessment (Fred Lurmann, personal communication). This change will be implemented in July 2002. Models will be run with and without children recruited from this new region to determine how sensitive the effect estimates are to the inclusion/exclusion of these children. A summary of the eligibility criteria are present in Table 4.2.

Table 4.2: 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	Up to 2

For a variety of reasons, recruitment increased by the spring of 2002, and we are more optimistic that we will be able to recruit 225-250 patients by the winter of 2002. As of August 25, 2002, we have enrolled 200 children and will continue to implement our most successful recruitment strategies to boost enrollment. A local asthma specialist has offered to send letters to over 1000 age and zip code eligible children. We have provided the area newspaper (Fresno Bee) with some descriptive information, and these will be included in a cover story about asthma and air pollution. The paper has promised to mention FACES and provide information about how to get involved in the study. We will continue to use local TV advertisements, which have been one of our most successful methods of recruitment. When school begins in September, the schools will be asked to distribute our fliers to all children, as has been done in the past. Now that the FACES study has been established and recognized in the Fresno/Clovis area, parents may be more willing to participate.

Sample Size Considerations

In our original application, we identified subject-specific air pollution response parameters for symptoms and various measures of lung function as the principal response variables for the longitudinal analysis (see sections 8A and 8B of original application). We offered several examples of longitudinal analyses that account for the within and between-subject variability (see section 8C of original application). Therefore, the number of observations available for the analysis need to be considered in two separate contexts: data available from the panel studies needed to develop the subject-specific air pollution response parameters and data needed for the longitudinal analyses (asthma severity and lung function). The original target number was 450 subjects. This number was chosen based on the maximum number of subjects that we thought that we could study in the context of the design that we proposed and the level of anticipated funding and expected dropouts from the study. We estimated that losses to follow-up would be 20% (current loss to follow-up 4.4%--see Table 4.7 footnote), and 40% of the panel data would be missing (based on the experience of the NCICAS, current missing symptom data for FACES panel data is 15%). Thus, the numbers needed to carry out the study, as designed, are somewhat less than specified originally. We now consider the issue of sample size in relation to the panel study analyses and the longitudinal analyses.

In the original application (based upon the estimates noted above), we expected to have 34,000 observations from the panel studies. We indicated that we had no rational basis for making a sample size calculation for this part of the study. Based on our expected sample size of 250 subjects and the shortened duration of follow-up, we should have about 28,000 observations (83% of the original estimate of 34,000) based on the current estimates of loss to follow-up and missing panel data. Moreover, in Section 6, we present results that are nearly "statistically significant" with only 1287 observations. Therefore, sample size and power do not seem to be problematic for this part of the analysis. Although in that analysis, we did not specifically account for the dependent structure of the observations, we are confident that we will have more than enough power to detect the magnitude of changes reported by others. For example, Yu, Sheppard and colleagues [Yu, 2000], carried out a panel study of 133 children with asthma from the CAMP study who provided 7658 person-days of observations. In analyses that accounted for the within-subject correlations, these authors reported odd ratios for increased symptoms of ~1.13 for a 10mg/m^3 increase in PM_{10}. Since we anticipate have about 3½ times the number of

observations available to these authors, we will have no problems with power for this part of the analysis.

In our original application we used cigarette smoke exposure to estimate power for the longitudinal analysis of lung function. This was based on the fact that cigarette smoke represents a substantial particle exposure [Spengler, 1981]. We estimated the power to detect differences in levels of FEV_1 and FEF_{25-75} between children who were and were not responders to short-term increases in ambient air pollution based on estimates of the effect of exposure to maternal smoking during pregnancy and early life provided by Cunningham, *et al*. [Cunningham, 1994] from the Six Cities study. These authors observed a difference of 2.6% and 8.4% between exposed and unexposed boys (n=3254), largely in the age range covered by the proposed study, for FEV_1 and FEF_{25-75}, respectively. We assumed a simple linear, repeated measures regression {$FEV1_j$ (or $FEF25\text{-}75_j$)=β_o + β_1(Responder to PM)$_j$ +ε(j), j=1,…8, 6 month evaluations}. We carried out the estimate of power under a conservative scenario—i.e., under the assumption the correlation of ε(j)=0.75 that we will loose 20% of the sample during follow-up. We also assumed that after adjustment for relevant covariates, the correlations between the errors would be reduced to 0.50.

We used 3% and 8% as our estimated change for FEV_1 and FEF_{25-75}, respectively in the original proposal, and we retain these for this report. Based on those calculations (see section **8E** of the original application), we estimated that we had powers of 0.92 and 0.98, (misreported in that section as 98) respectively, for a sample size of 1000 observations in the responder and non-responded groups. Based on our current expected enrollment of 250 subjects and observed data losses that are far lower than were used in our original estimates, we expect to have at least 1892 observations. Based on completing the last baseline interview by December 2002 (or n=250, whichever comes first), the shortest follow-up times will be 24 months. If we assume that 20% of observations will be lost due either to unacceptable lung function data and losses to follow-up (missed appointments and dropouts), we will have 1514 observations. We further reduce the effective sample size by 50%. Based on the same calculations used in the original application, we estimate that we have a power 0.84 for an FEV_1 difference of 3% and a power of 0.97 for a 4% difference in FEV_1. The power for a 6%, 7% and 8% differences in FEF_{25-75} is estimated to be 0.76, 0.86 and 0.93, respectively. This estimate may be somewhat conservative, since it is based on a simple dichotomous "exposure" variable (short-term responder Y/N). In fact, the response variables available for analysis will be continuous.

Therefore, despite our having recruited fewer subjects than was proposed in the initial application and despite shorter follow-up times on some children, we still will have adequate power to detect changes similar in magnitude to those found for exposure to environmental tobacco smoke. We recognize that all power calculations are, at best, semi-informed guesses as to the precision with which we will be able to estimate the marginal changes that we have used for these calculations. We present these re-calculations to be consistent with our initial application and to demonstrate that, based on the criteria on which we were judged in the original submission, we remain in approximately the same position with regard to the effective amount of data available to test our hypotheses. Once we begin to evaluate the longitudinal data, we will be able to carry out simulations based on our observed data and possible covariate effects to get a more realistic estimate of the power of the longitudinal analyses.

4.2 DESCRIPTION OF THE COHORT

When potential participants call the FACES office to determine if they are eligible, they are first asked to provide the zip code and the age of the child and to indicate whether the child has already had a physician diagnosis of asthma. If the child does not meet the age, zip-code and asthma diagnosis criteria, a screening form is not administered. If the three criteria are met, interviewers complete the entire screening form and asks caller whether they would be interested in participation if their children are eligible. If callers are interested in participation, the interviewer informs them that they will be contacted by phone or mail to inform them if they are eligible. The Field Coordinator reviews the screening form and applies standardized criteria to determine eligibility. If the child is eligible, the interviewer calls the family to schedule an appointment.

For the purposes of this report, we had committed to presenting health data collected as of February 2002. However, given that our data systems are up-to-date and that recruitment has increased, we have decided to present information as of June 30, 2002. A total of 391 children were screened. Of these, 314 (80%) were eligible. Table 4.3 provides a summary of the reasons for ineligibility. A child may have more than one reason, so the numbers do not add up to the total number of ineligible children.

Table 4.3: Reason(s) for Ineligibility at Screening

Reason child was not eligible	#	%
Other medical conditions	31	7.9%
Did not meet definition of "current" asthma	11	2.8%
Did not agree to have passive monitors placed in home and/or have dust sample collected	11	2.8%
Had plans to move in next 24 months	13	3.3%
Did not sleep in the same household at least 5 nights/wk	13	3.3%
Had not lived in their current home at least 3 months	20	5.5%

Of the 314 children who were eligible, 236 (75%) agreed to participate. So far, of those who were eligible and consented, 195 have completed the baseline interview (as of June 2002).

Tables 4.4 and 4.5 report demographic characteristics of those who have been screened and/or enrolled in the study.

Table 4. 4 Description of screened participants
(Based on data entered as of June 30, 2002)

	Screened (n=391)	Eligible (n=314)	Consented (n=236)	Baselined (n=182)
Race				
White	144 (36.8)	116 (36.9)	85 (36)	74 (40.7)
Hispanic	162(41.4)	133 (42.4)	108 (45.8)	76 (41.8)
African-American	71 (18.2)	55 (17.5)	35 (14.8)	25 (13.7)
Other	14 (3.6)	10 (3.2)	8 (3.4)	7 (3.8)
Age				
5	17 (4.3)	11 (3.5)	8 (3.4)	6 (3.3)
6	87 (22.2)	67 (21.3)	47 (19.9)	31 (17)
7	66 (16.9)	54 (17.2)	40 (16.9)	29 (15.9)
8	68 (17.4)	51 (16.2)	37 (15.7)	32 (17.6)
9	82 (21)	69 (22)	54 (22.9)	44 (24.2)
10	52 (13.3)	48 (15.3)	39 (16.5)	32 (17.6)
11	19 (4.9)	14 (4.5)	11 (4.7)	8 (4.4)
Male (%)	58.1	58.3	57.2	58.2

Table 4.5: Demographics of the FACES Cohort at Baseline, n=182 (Based on data entered as of June 30, 2002)	# (%)
Income < $30,000 (%)	80 (44)
At least one parent employed	163 (90)
At least one parent completed high school	160 (88)
Respondent is a current smoker	18 (10)
Any smokers living in the home	42 (23)
Ever hospitalized for asthma	46 (25)
Ever prescribed oral steroids	111 (61)
Skin test positive to at least one antigen	107 (65)
Asthma severity (NHLBI) at baseline	
step 1	49 (27)
step 2	84 (46)
step 3	44 (24)
step 4	5 (3)
Height at baseline (in) (mean, sd)	52.5, 4.6
Weight at baseline (lbs.) (mean, sd)	75.7, 28.5
FEV1 (mean % predicted FEV1 at baseline (range, based on n=133)	1.06 (.51-1.59)

4.3 FOLLOW-UP OF THE COHORT AND MILESTONES REACHED

Preparation for each visit type includes designing data collection forms, Spanish translation, programming and pilot testing of data entry and double-data entry systems, development of tracking reports to identify children who are due to have a visit, and generation of contact records for logging the date/time of each attempted contact. Table 4.6 provides a list of the start dates for each type of visit.

Table 4.6: Milestones for Cohort

Visit / Protocol	Start date
Screening	September 2000
Baseline (Adult and child)	November 2000
Home panel (survey, 2-week monitoring) (scheduled for 1 panel/year/child)	November 2000
3-month telephone interview	February 2001
6-month clinic visit(adult and child)	May 2001
9-month telephone interview	August 2001
12-month clinic visit (adult and child)	November 2001
Home panels scheduled for 3 panels/yr/child	November 2001
15-month telephone interview	February 2002
18-month clinic visit (adult and child)	May 2002
Buccal cell collection (child and parents)	July 2002
Focus groups for economic component	July 2002

A summary of the completion rates for each visit can be found in Table 4.7.

Table 4.7 Completion Percentages by Study Visit Type
(Based on data entered as of June 30, 2002)

	Completed # (%)	Due Still within window # (%)	Overdue # (%)	Not yet Due # (%)
3-month	131 (71.6)	4 (2.2)	14 (7.7)	25 (13.7)
6-month	96 (52.5)	5 (2.7)	28 (15.3)	24 (24.6)
9-month	89 (48.6)	1 (0.5)	15 (8.2)	69 (37.7)
12-month	49 (26.8)	14 (7.7)	18 (9.8)	93 (50.8)
15-month	29 (15.8)	11 (6)	0	134 (73.2)
18-month	22 (12)	11 (6)	0	141 (77)

*Based on 182 enrolled, with 9 deactivated due to moving/dropping out of study at various points in time.

Included in Appendix 5 is a series of "Inventory Tables" which summarize some descriptive characteristics to date. Also included is a summary of the number of various types of samples that have been collected.

4.4 DEVELOPMENT OF AN ASTHMA SEVERITY CLASSIFICATION

Because we hypothesize that asthma severity is an important determinant of both short-term and medium-term responses of asthmatic children to air pollution exposures, we conducted a careful review of the current literature on the issue of asthma severity classification before we made a final decision on the definitions that we would employ. We present a brief synthesis of the key issues involved in the asthma severity classification scheme that we developed.

There appears to be universal acceptance of the basic concept embodied in the WHO/NHLBI guidelines that severity refers to the condition of the asthma at the time the condition is diagnosed/before any therapy is started [National Heart Lung and Blood Institute, 1997]. This might be called *UNDERLYING SEVERITY*. Beyond that point, the occurrence of symptoms, decreases in lung function and increased disability, in part, are issues of success or lack thereof of the treatment (control) of asthma. In our view, this is a somewhat simplistic and unrealistic view of what actually happens and makes no allowances for true changes in severity over time. Nonetheless, we retain elements of this approach, with some modification, since this classification is in such wide use throughout the world. Therefore, one principal outcome at any visit is not one of asthma severity, per se, but of control of asthma in keeping with the WHO/NHLBI concepts. For FACES, severity over time is best considered in terms of the characteristics of asthma that are most likely to be the underlying factors for current or future disability. In this context, two endpoints are of potential value: 1) the trajectory of lung function development (as we proposed in the original proposal) and; 2) changes in medication "step" (as per WHO/NHLBI—figure 7-6: *The long-term management of asthma: Treatments in the stepwise approach for infants and young children* or figure 7-4 for older children) [National Heart Lung and Blood Institute, 1997].

Our approach to asthma severity classification, to date, has been to try to distinguish the level of current control from underlying severity as much as possible. We considered the WHO/NHLBI classification scheme to be the best to use to capture current control, largely because of its wide acceptance, as noted above. The WHO/NHLBI scheme uses two major parameters, recent symptoms and lung function. The levels of these two parameters determine the step (from 1 to 4 on a scale of increasing severity) which, in turn, determines what type of medication is appropriate to control symptoms and improve lung function. We decided to consider separately these two asthma severity parameters because they may not vary with pollutant exposures in the same manner. Because it is unclear how to assess the severity of asthma across individuals with the same level of symptoms but different medication use (e.g., some using only inhaled bronchodilator while others are using bronchodilator plus a controller agent), we also decided to rate medication use separately from asthma symptoms. Moreover, change in medication step can be both an outcome variable and a potential confounder or effect – modifier of the response to pollutant exposures. Thus, while we used the WHO/NHLBI scheme as a starting point, we made major modifications as we developed the FACES scheme for the assessment of current asthma control.

To assess underlying severity we chose a scheme developed by Dr. Paul Blanc at UCSF for a longitudinal study of disability due to asthma [Blanc, 1993]. The Blanc scheme involves a 28-point scoring system which includes current symptoms, previous history of systemic steroid use, and previous history of health care utilization for asthma. In fact, this scoring system is weighted such that individuals with a previous history of hospitalization and intubation/mechanical ventilation for asthma exacerbations will be rated to have more severe asthma. We found the Blanc scheme attractive for a number of reasons. It provided a way to capture previous history of health care utilization for asthma at the time of enrollment of our subjects, its use has been validated, and it involves a numerical score. The main limitation of the Blanc score was that it was developed for use in adult asthma and it had not been previously applied to a pediatric population. We were fortunate to be able to work with Dr. Blanc to develop a modified version of his scheme that reflects current pediatric practice regarding asthma.

Lung function data were also used as an independent index of asthma severity. Only FEV_1 has been used to date, but PEFR and FEF_{25-75} data can be used as well. We modified the WHO/NHLBI step scheme approach to FEV_1 data to classify severity, and calculated a percent predicted of post-bronchodilator FEV_1.

To assess the range of asthma severity in the FACES subjects, we have compared the distribution of severity rating using the three different schemes described above. The modified Blanc scoring scheme, which includes both health care utilization and medication use items, appears to provide a better distribution of underlying asthma severity than the symptom/disability items from the WHO/NHLBI severity classification scheme. Neither the modified Blanc severity score nor the symptom/disability items from the WHO/NHLBI severity classification scheme predicts level of post-bronchodilator FEV_1 in FACES children, in part due to lack of variability of this parameter.

Another component of asthma severity classification that needs to be distinguished from underlying severity is that of severity of exacerbations of asthma. A scheme for classifying exacerbations reported by FACES subjects was developed using level of health care utilization required to treat the exacerbation (**step 1:** Increased symptoms or increased use of rescue medications; **step 2:** Increased symptoms with increase in inhaled corticosteroids or a short course of prednisone; **step 3:** Increased symptoms with an unscheduled visit to an Emergency Department or other health care provider; **step 4:** Increased symptoms with an overnight hospitalization).

The modified WHO/NHLBI classification scheme for symptoms, the modified Blanc score for pediatric asthma, the modified WHO/NHLBI classification scheme for FEV_1, and the asthma exacerbation severity scheme can be found in Appendix 3.

In summary, classification of asthma severity is difficult and complex because multiple factors (e.g., symptom level, medication use, health care utilization, and lung function) must be taken into consideration. While it is difficult to disentangle asthma severity from asthma control, the multi-component approach that we have developed for FACES appears to be reasonable for a longitudinal study of the effects of environmental exposures on asthma. The details of each definition are provided in Appendix 3.

4.5 HEALTH ASSESSMENTS

4.5.1 Assessment of Lung Function

4.5.1.1 Selection of Portable Spirometer/Development and Testing of EasyOne®

For both the panel and longitudinal components, lung function is a primary health outcome. Given that it is not feasible to do office-based lung function testing on a daily basis for several weeks, it was desirable to obtain an affordable and portable device that would give comparable measurements to a standard office spirometer. Key requirements included: **1**) the ability to record and store full flow-volume curves; **2**) a programmed series of medication and symptom questions; **3**) inclusion of quality control software and prompts to obtain acceptable and repeatable efforts; **4**) time and date stamping of all records; **5**) easy transfer of specific flows and volumes to a PC data base; **6**) approval for use in multiple patients; **7**) easy calibration; **8**) inclusion of an incentive program to maximize compliance; **9**) a reminder alarm and limitations on the times of day that entries can be collected; and **10**) compliance with the American Thoracic Society (ATS) criteria for spirometer performance. FACES is not an intervention study; therefore, we wanted to mask the results to avoid any influence on the children's behavior with respect to their asthma based on pulmonary function readings. The EasyOne ®(ndd Medical Technologies, Chelmsford, MA) met all of these criteria.

The EasyOne® portable spirometer 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. All sessions are time and date stamped. 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 requiring calibration.

A detailed description of the EasyOne® software and its use by the FACES cohort is included in Appendix CD4. In short, the devices were programmed with an alarm which activated during the time windows of 7am-9am and from 7pm-10pm to remind children to perform the tests. No tests can be performed outside of these windows. The spirometers used the same acceptability and reproducibility criteria noted previously (Appendix 4) 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 two of them meeting all of the reproducibility criteria. Data were saved for each of the three best efforts even if the acceptability and reproducibility 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 (Table 6.2). For each session, 500 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 or reproducibility criteria, the session was awarded 200 points. Over a 14-day period, a total of 14,000 points could be obtained.

To obtain an objective evaluation of the EasyOne's® reliability and validity, we performed a direct comparison between it and 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 summarized and submitted to *Chest* for publication (Appendix CD4). Based upon this evaluation, we conclude that the portable spirometer accurately and reliably measures lung function, relative to a "gold standard" clinic-based device. Although there was excellent agreement across key parameters, 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. Section 4.5.1.2 discusses our solution for this observation.

4.5.1.2 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, it was decided by Drs. Ira Tager (IT) and John Balmes (JB) that every curve from both spirometers should be reviewed.

The current QA/QC procedures now include the following:

- Review of every time volume and flow volume tracing from the Morgan spirometer by calling up all of the test data on the Morgan database. These reviews are done primarily by JB and to a lesser extent by IT. Since these data are obtained during a session that is supervised by a technician, strict criteria are used for acceptability (See Appendix 4 for these criteria) and only curves for which all measures of interest are valid are retained.

- Review every time-volume and flow volume curve of 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. These reviews are done primarily by IT and to a lesser extent by JB. All of these data are obtained in the homes of the children and without supervision of a technician. Therefore, some additional criteria are used. **1)** the review allows for the fact 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; **2)** coughing may occur during testing which reflects the clinical status of the child's asthma; therefore curves with the obvious evidence of coughs are retained; **3)** some curves provide valid measures of peak flow and FEV_1 but not measures of FEF_{25-75} or FEF_{75}, that are of interest to the study—peak flow and FEV_1 from such curves are retained.

To assure that there is consistency between JB and IT in the reviews, curves for which the interpretation is not absolutely clear are read by the person who did not carry out the initial evaluation but blinded as to the initial interpretation. In addition, JB and IT meet regularly to review criteria for difficult curves such that each applies the agreed upon decision rules for certain recurring patterns that lead to problematic interpretation—e.g., evidence of slight inhalation at the end of test or evidence of slight leaks at the beginning of tests.

4.5.2 Bronchodilator Protocol

During the baseline visit and all subsequent clinic visits (at 6-month intervals), children are asked to complete pre- and post-bronchodilator spirometry. This is a standard procedure in pulmonary function testing and allows for the mitigation of the effects of any recent exacerbations or alterations of baseline airway tone on levels of lung function. Albuterol is a medication to which most asthmatics have been exposed in the past and 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 four reasons: **1**) current guidelines for the diagnosis and management of asthma are based on tests of airways reversibility [National Heart Lung and Blood Institute, 1997]; **2**) methacholine testing, even the short protocols, is time consuming and has potential side effects; **3**) methacholine challenge will be contraindicated in asthmatic children with low levels of lung function (e.g., FEV_1 <80% predicted); and **4**) repeated methacholine testing at 6-month intervals is 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 (even a single baseline test) did not outweigh the practical and theoretical disadvantages. The research staff were trained by the study physicians on the proper administration of the albuterol. The details for bronchodilator administration are outlined in the Baseline Protocol (Table 8-1).

4.5.3 Allergen Skin Test Panel

There is extensive evidence to suggest that children who are allergic to indoor and outdoor allergens may respond differently to air pollutants than children who are not allergic to these antigens. To identify allergic children in our cohort, we have included a panel of 14

aeroallergens in our baseline assessment. Children who, for a variety of reasons, are not tested at baseline are tested during the 6-month visit. The selection of allergens for baseline testing was determined through discussions with the Mobile Asthma Clinic at VCH with additional modifications from UCSF-affiliated allergists familiar with Fresno area allergens. The list of allergens in the proposal (Appendix CD1) has been replaced by the panel described in the skin testing protocol (Appendix CD2). The distribution of positive responses to each allergen is presented in the inventory tables presented in Appendix 5.

At the central-site and during the home intensive visits, samples of airborne allergens are collected on a daily basis and analyzed on a bi-hourly basis. These samples will be analyzed and will be used to determine an appropriate panel of allergens for the second round of skin testing, planned for the 24-month interview.

4.5.4 Nutritional Assessment

We will examine whether dietary antioxidants or other nutrients provide short and/or long-term protective effects from air pollutants. A child's diet and use of vitamin supplementation may vary by age and by season; and, therefore, information will be collected twice during the study (at 6 and 24-month post baseline). Parents are asked to complete a brief nutritional survey of the child's diet and use of vitamin supplements. We use a dietary assessment tool that was developed and validated by the "Growing up Healthy" component of Nurses Health Study (NHS) for children in the age-range covered by this proposal. 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.

4.6 DEVELOPMENT AND TESTING OF DAILY DIARY AND HOME SURVEY QUESTIONNAIRE

The home survey is a modified version of the form used in the National Cooperative Inner-City Asthma Study (NCICAS). The layout of the home survey form was revised to have a format similar to all the FACES survey instruments. Some questions that were relevant only for east-coast urban populations were deleted. 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 is completed by visual inspection by the bilingual field staff. Some questions must be asked to the participant (i.e. how often is the fireplace used), and those questions were translated on the hardcopy of the form so that standardized wording would be used. In addition to the survey, FACES-specific forms were developed for EasyOne®, diary and ETS/NO_2/ozone sampler tracking forms, dust collection and moisture measurements. The interviewers and data entry clerks who use these forms also use the health data forms; and, therefore, coding is consistent across the health and exposure instruments (e.g. 1=Yes, 2=No.). Variable naming conventions, skip pattern rules and data cleaning procedures are identical to those described below in Section 4.7.

The two-week time activity diary was based on forms used in the ARB-funded Children's Health Study and several other large cohort studies. The exposure team determined the appropriate time-intervals for reporting activities (i.e. 6:00 am-9:00am, etc) based on information

about patterns of key air pollutants and children's "typical" school schedules. Every attempt was made to make the layout of the diary user-friendly, as this is one of the few self-administered forms used by FACES. Although we ask the parents to help with the completion of the form, each page has a place to indicate whether the mother, father and/or child completed the form.

The diary has not been translated into Spanish. One of our eligibility criteria is that the child speaks 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.

A coding scheme has been developed for daily activities (Table 4.8). Rather than enter detailed text, which would not be easily analyzed, we enter only the activity code and amount of time spent doing the particular activity. If an activity falls into multiple categories (e.g "went out to dinner"), then up to two codes can be entered in the field (e.g. 2,7). If necessary, we can refer back to the hardcopy for additional information.

Table 4.8 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

The home survey and diary have been implemented since the first home panels in November, 2000. Since the study began, we have made only minor revisions to the home visit forms. For example, after several months, it became clear that some questions could not always be ascertained by visual inspection, and now the interviewers indicate whether it was necessary to ask the participant or whether visual inspection was adequate. A new version of the forms was created and the necessary modifications were made to the data entry system.

Several minor revisions were also made to the time-activity diary. Currently, we are analyzing those data to evaluate the completeness and range of activities reported over the two-week periods. We also are evaluating the consistency of the symptom and medication data reported on the paper diaries with the symptoms reported by the child on the EasyOne® during the same interval. This analysis will help us determine whether further modifications to the format, content or instructions for the diary are necessary.

4.7 DATA MANAGEMENT PROCEDURES AND DOCUMENTATION

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

All of the interview data collected during clinic, telephone and home visits are recorded on hardcopy forms. Any coding that is needed (e.g. medication names), is completed by the interviewers prior to submission of the forms for editing. The Field Coordinator reviews all forms prior to data entry. If inconsistencies or missing data are noted, the family is called back within a day of the interview to retrieve the information. Only then are the forms forwarded to the data entry clerk. All data are entered directly into SAS data sets, Version 6.12. Data entry, with the exception of the two-week daily activity diaries, is completed in the Fresno office; and most of it is completed within one-week of collection. The diaries are sent to the Berkeley office and are coded by a research assistant and entered by a data entry clerk. Questions about particular coding problems are discussed with the Project Director or Principal Investigator prior to data entry.

In both offices, the data entry screens are programmed such that the screens look identical to the hardcopies. The clerk is instructed to enter the data only as they appear – if missing or incompletely coded information is found, s/he returns the form to the interviewer for resolution. Approximately every 10^{th} observation is double entered into separate data sets. The data manager runs reports to compare the original and quality control sample. If a batch (10 observations) has an error rate of >0.5%, the entire batch is to be reentered. This has not been necessary since we implemented this system.

The data from each visit are 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 will be analyzing 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 will not need to deal with data which 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 visit number, section of the form, and question numbers are embedded in the variable names. The first character refers to whether the visit was done in the clinic or telephone ("C" for clinic visits such as baseline, 6-month, etc.), the 2^{nd} character refers to the visit number (1 for baseline, 3 for 3-month), the third character is the section of the form (a=Asthma update). The next series of characters refer to the question number. For example, variable T9a_12b is question 12b from the first section of the 9-month telephone interview. This numbering system provides a concise and consistent method to identify the source of each data point, which is essential for data cleaning and analysis. Throughout all forms, a '.N' means that the data are not available due to programmed question skip patterns, a '.V' means that this question was not asked for a given version of the form, and '.M' means the data are missing due to interviewer error (e.g., they skipped a question and were not able to re-contact the family in a timely way). '.D' is used when the participant did not know the answer, '.R' is used if the participant refuses to answer a question or complete a part of the protocol.

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 (using PC Anywhere) and archived. A copy is burned onto a CD for additional off site storage. Files which are essential to the project (study form files, protocols, proposals, etc), are also copied onto the CD for archival and safe storage. The Berkeley server also has nightly tape back-up.

Data from the Morgan spirometer (used for clinic-based spirometry) are collected on a separate computer, but 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 are also FAX'ed to the Berkeley office for physician-review. The data files are transferred to the Berkeley server so that the tracings from all efforts (up to 8 each for pre and post-bronchodilator sessions) can be viewed by the physicians for additional grading when necessary. The actual data files are in a format which is proprietary and cannot be retrieved in electronic form. Therefore, the data from each effort must be manually data entered. This is done at the Berkeley office and stored on the server. Backup procedures are identical to those listed above for the interview data.

Data from the EasyOne® spirometer also is 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) are uploaded to the server using a customized cradle connection into an Access database. A query has been set up so that all records are compiled into a common database. When an EasyOne® spirometer is returned after a 2-week home panel, the same procedures are used to synchronize the data. This one common dataset is subject to backup procedures identical to those listed above for the interview data.

Study activity, tracking and quality control reports have been written and continue to evolve as the study becomes more complicated. These reports can be run from the Fresno or Berkeley servers, which allows both offices to have current information about study progress. For example, once a month, the Administrative Assistant in the Fresno office has been instructed to run a report that identifies all participants who are due for a visit during the following month. For each participant, these reports include current address information, windows for when visits are due, type of visit due, and key variables collected from previous visits which allow the interview to proceed more quickly. Log sheets are also produced on which the interviewers record the time, date and disposition of every attempt to contact the family. These can be reviewed by the Field Coordinator to ensure that difficult-to-track participants are being called at a variety of times, including evening hours. The Data Manager creates a weekly "Data Management Log" to summarize the status of all projects (e.g. new data entry screens, revisions to skip patterns, etc.) and distributes it to the Berkeley and Fresno offices so that everyone is 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 cleaning, resolution and analysis of all data sets. When analyses are undertaken (for reports, abstracts, publications), the data sets are "frozen" in different subdirectories so that analyses can be replicated using these files and are not influenced by on-going data entry. Data sets are also "frozen" for periodic data cleaning by the Project

Director, Data Manager and Research Associate. Frequencies, cross-tabulations and distributions of variables are reviewed and errors or inconsistencies are sent to the Fresno office for resolution. The Field Coordinator then responds in writing to all requests for modification. Edits are made from the Fresno server, and those data are copied back onto the Berkeley server for review. The copy on the Fresno system serves as the 'master' version.

All study forms were pilot tested before use on study participants. Over the course of the study, however, 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 labeled with the 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. When the forms are data entered, the first question that appears is the version number and then the skips and questions presented are modified accordingly. Electronic and hardcopies of all versions have been maintained for future reference.

4.8 MEETINGS WITH OUTSIDE QA/QC MONITOR

A contract was signed with Dave Bush, Senior Scientist (Technical & Business Systems Inc., Santa Rosa, CA) to perform QA/QC for the FACES study. Mr. Bush attended the External Advisory Panel meeting in February of 2001, and a FACES staff research meeting on July 11, 2001. On December 6, 2001, Mr. Bush performed a site-visit to the Fresno office. The Project Director and Field Coordinator met with him to discuss study procedures, the data management and editing process and quality control protocols. He met all staff members, surveyed the office layout, protocol manuals, data system, sampling equipment and samples logs. A copy of his summary report has been included in Appendix 6. In March, 2002, he performed QA audits of the two mobile trailers and also of the Home Intensive monitoring.

5. PROGRESS REPORT ON THE EXPOSURE ASSESSMENT

5.1 OVERVIEW OF EXPOSURE ASSESSMENT

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. There are few data available to assess how day-to-day responses to air pollution affect long-term respiratory health and disease; the Fresno Asthmatic Children's Environment Study (FACES) is attempting to address this problem. The assessment portion of the project is particularly aimed at developing estimates of each child's exposure to each pollutant and possible co-factors, such as pollen grains, fungal spores, and endotoxin, on each day of the study. This daunting task is being 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 each air pollutant 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 biological contaminants such as pollen grains, fungal spores, and endotoxin may influence the incidence, severity, and evolution of asthma in children. In this study, we are assessing the exposure of asthmatic children in Fresno, California to all these contaminants. It is important to note that PM 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 5.1-1 presents the agents which being measured and studied in FACES; these include PM and its constituents, pollutant gases, and bioaerosols.

Table 5.1-1. 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

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 secondarily caused by the temporal variations of emissions. 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 a regional scale (i.e., 20-50 km between cities) rather than on an urban-scale (10 km) or neighborhood-scale (1-2 km) (Chow et al., 1992, 1998). 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. Even though children spend less time indoors than adults, children still 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, including 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 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. Realistic characterization of human exposure to pollutants of potential relevance for asthmatics must account for indoor-outdoor differences in exposure concentrations 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 that will be collected at the Fresno Supersite during this study are ideally suited to specification of the ambient concentrations of pollutant that vary only on the regional scale. Ambient concentrations of $PM_{2.5}$ sulfate, nitrate, ammonium, and secondary organics throughout the Fresno study area are expected to go up and down as indicated at the central site (Fresno Supersite). Ozone concentrations at many locations in Fresno are expected to be similar to those at the central-site monitoring station.

Ambient concentrations of pollutants with neighborhood-scale variability are expected to be biased from the central site yet 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, $PM_{2.5}$OC, 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 (e.g., Solomon et al., 1996; Ludwig, 1994) 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 regarding 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 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 endotoxins 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 new measurements are needed to understand the phenomena and to ultimately develop models to accurately estimate concentrations on these scales.

Certain pollutants will 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 must be captured with a combination of housing questionnaires and indoor and outdoor measurements at the homes of interest. New measurements are especially needed 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 3.2.

5.1.1 Summary of Technical Approach

Most 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 the proposed study is designed to overcome these limitations by using a more comprehensive approach to exposure assessment.

The technical approach for the exposure analysis is to build databases and models to generate individual exposure estimates, rather than community average exposure estimates. The individual exposure estimates will be based on microenvironmental models adjusted for indoor, outdoor, and personal exposures and activity patterns. In addition, we plan to explore methods to adjust exposure assignments to account for proximity to roadways and traffic density because we expect these factors account for a significant portion of the within-community variation in ambient air quality.

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 5.1-2 and Figure 5.1-1):

1. The Fresno Supersite provides 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. To these we have added samplers to measure endotoxin, pollen grains, and fungal spores.

2. The ARB developed and deployed two mobile air monitoring trailers that are making, at schools and in selected neighborhoods in Fresno, measurements of 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, $PM_{2.5}$ metals, PM_{10} mass, and PM_{10} metals during the third and fourth years of the study.

3. During the two-week health panel studies, we are collecting integrated NO_2, SHS, and house dust allergen samples inside participants' homes and integrated ozone samples outside participants' homes. These measurements are being made in the first two years of the study. Ozone measurements will be confined to the extended ozone season (May-October).

4. During the second and third years of the study, we are making intensive air quality measurements during the panel studies at the homes of 100 participants. Two to five homes from each panel are being sampled for ozone, NO_2, light scattering by $PM_{2.5}$, $PM_{2.5}$ sulfate, $PM_{2.5}$ nitrate, $PM_{2.5}$EC, $PM_{2.5}$OC, PM_{10} mass, PM_{10} metals, PM_{10} endotoxins, pollen grains,

fungal spores, and SHS. All agents except SHS and NO_2 will be measured concurrently inside and outside the homes. Separate PM samples are being collected on 3 weekdays and 2 weekend days. A subset of houses (estimated 30-40) will be sampled in two seasons. Another 20-40 houses will be sampled in one season, for a total of 100 sets of home visits.

5. A pilot-scale personal sampling program will be conducted by UCB to collect NO_2, ozone, SHS, PM_{10} endotoxins, $PM_{2.5}$ mass, and PM_{10} mass on 25 participants during the two-week panel studies. Detailed time-activity diaries and household operating characteristics will be collected along with integrated 24-hr personal exposure samples.

6. Supplemental data will be provided by ongoing monitoring programs. Meteorological data will be provided by the National Weather Service (NWS) and ARB monitoring programs. Traffic count data will be provided for state and county roadways by CALTRANS.

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

Table 5.1-2. Agents being sampled and sample duration at various locations.

Location	Central Site	Two-Week Panel[2]		Exposure Intensive[3,4]		Personal	Schools
	Fresno Supersite (on-going)	Inside Home	Inside & outside Home	Inside Home	Outside home	Selected students	Selected sites[5]
Year(s) of study	1-5	1-3	2-3	2-3	2-3	2-3	2-3
No. of years	4	2	5 summer months	1	1		1
Agent:							
NO_2	H[1]	2W		2W[4]	2W	D	H[5]
NO	H[1]						H[5]
SO_2	H[1]						H[5]
Ozone	H[1]		2W	D – 8hr	D – 8hr	D	H[5]
PAH	H[1] D[6]			D	D		H[1,5] D[6]
Particle Number	H[1]						H[5]
Nicotine		2W		D		D	
House dust allergens & endotoxins		G					
Pollen Grains	D[2]			D	D		D[5]
Fungal Spores	D[2]			D	D		D[5]
PM_{10} endotoxins	D[2]			D	D	D	D[5]
Particle scattering	H[1]			H	H		H[5]
$PM_{2.5}$ mass	H[1]			D	D	D	H[5]
$PM_{2.5}$ ions	H[1]			D	D		H[5]
$PM_{2.5}$ OC/EC	H[1]			D	D		H[5]
PM_{10} mass	H[1]			D	D	D	H[5]
PM_{10} metals	D[5]			D	D		D[5]
PM black Carbon	H[1]						H[5]

Sample duration: H = hour, D = 1 day (24 hour, 8 p.m to 8 p.m), G = grab, 2W = 2-week

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

[2] Samples collected for 4 years during years 1-5; only 2 years to be analyzed

[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 to be provided by ARB

[6] PAH sampling and analysis for selected days sponsored by U.S. EPA.

The analyses of data collected in the study will first focus 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 will be carefully analyzed to characterize the within-community variability in concentrations of the different agents included in the study. We will identify the extent to which factors such as traffic density, neighborhood vegetation, housing characteristics, human time-activity patterns, and meteorology explain the observed variability in exposure concentrations. Relationships between agents will be fully explored to identify indicator species and metrics. We are especially interested in the relationships between the infrequently measured parameters and routinely collected parameters, and between biological agents and conventional pollutants.

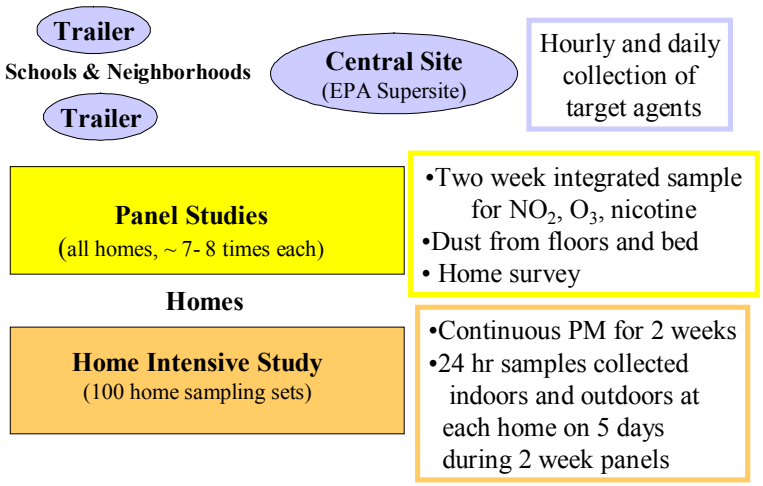


Figure 5.1-1. An overview of the air sampling during the FACES study. Daily data is collected at the Central Site and on the two trailers. Each subject has multiple measurements conducted at their home during the Panel Studies for home specific factors, e.g., allergens and endotoxin in the house dust and second hand smoke, and other measurements to characterize the home through the home survey and nitrogen dioxide and ozone measurements. A subset of homes has extensive measurements made indoors and out on 5 days during the two-week panel.

Figure 5.1-2 illustrates 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 are collected in the home of each child participating in the health panel; each day of that panel data will be 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 are collected at the Central Site and the trailers; 24 hour samples and continuous light scattering data are collected indoors and outdoors on five days at 2-5 homes from the health panel's part of the Home Intensive sampling; personal sampling will be collected on a subset of children from these homes on the same days.

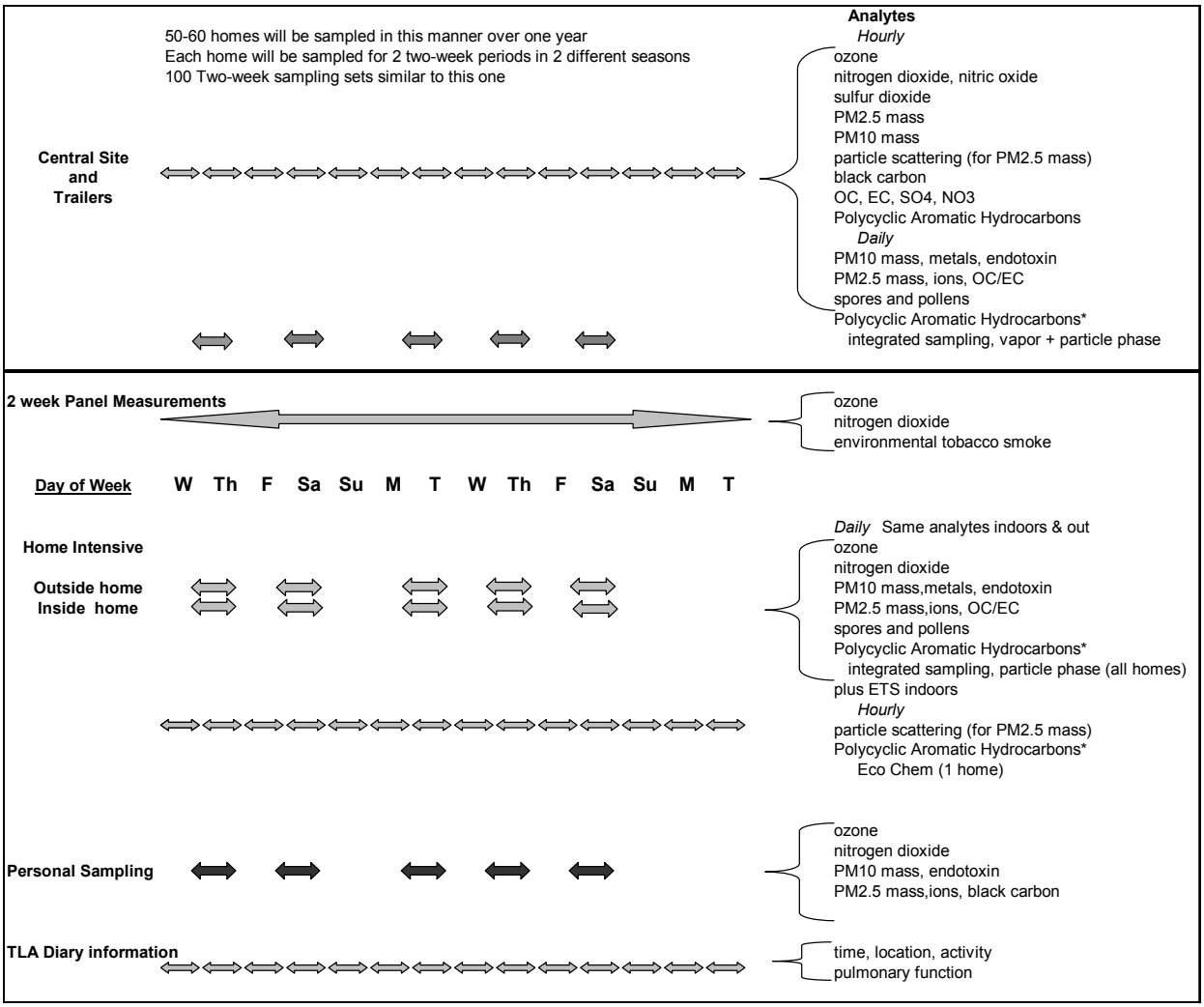


Figure 5.1-2. Time scale for sampling of air pollutants and biological agents during one home's two-week panel study.

The data will be analyzed to characterize relationships (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 scales of variability in concentrations will be ranked and categorized according to our three scales (regional, neighborhood, and residential). These analyses will lead to microenvironmental exposure models with parameters for each of the agents of concern in the study. The form of the models will depend on the spatial scale of specific pollutant variability. Model testing will be conducted using the personal sampling data. The database, models, and model estimates will be periodically delivered (in years 3, 4, and 5 of the study) to the health effects researchers so that they will be familiar with the data archive. The technical approach also involves closely monitoring how the data are used in the health analysis and review of the findings. The exposure team will provide feedback to the health analysis team to assure that data and model estimates are interpreted in appropriate ways.

Phase I has focused on the measurement of pollutants and biological agents at the Central Site, in the homes, and on the two mobile trailers. The goal has been to collect data that can be used to develop a model in Phase 2 that will estimate individual exposure. In the following sections we will describe the sample and data collection in the first year and a half at the Central Site, in the home surveys and two-week routine measurements, and in the home intensive survey. Finally, we present here some of the results of the measurements made at this point, with an emphasis on the daily variability, the spatial variability outdoors in Fresno, and the relationship between indoor and outdoor concentrations.

5.2 CENTRAL SITE MEASUREMENTS AND CONDITIONS

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. The section also summarizes preliminary results of the Central Site measurements.

5.2.1 Aerometric Measurements Conducted by ARB and DRI at the Central Site

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., 2000, and shown in **Table 5.2.1-1.** These measurements include gases, continuous PM mass and chemistry, particle number counts, continuous light scattering and light absorption, and meteorological measurements. 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 (from an R&P 2025 sampler); and pollen grains and fungal spores (Burkard BVST). The metals analysis is conducted by DRI while the endotoxin and bioaerosol analyses are conducted by UCB. Table 5.2.1-2 lists the elements, including the metals, that are determined by DRI's x-ray fluorescence analysis of Teflon filters collected by ARB at the Central Site. STI also operates a PAH samplers for determining 24-hr average gas-phase and particle-phase PAHs on an intermittent schedule.

5.2.2 Endotoxin Methods at the Central Site

Airborne endotoxin is collected on Teflon filters with a PM0 inlet. The samples are collected at a nominal 8.33 lpm flowrate for 24 hours. Initially the samples were collected from midnight to midnight, but in early 2002 the collection times were changed to 8 pm to 8 pm to coincide with the home intensive samples. Samples are returned to the laboratory, where they are 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 Appendix CD2—Protocols and SOPs for details of the method). In September 2001, Charles Perrino spent one week in Dr. Milton's laboratory training in the assay and performing replicate analyses, and we continue to be in contact with Dr. Milton, who serves as a consultant to this aspect of the study. Setting the assay up in the laboratory was hampered by our need for a laminar flow hood ($6,000), but we were able to get a small grant from COEH and order the hood in early 2002. The assay was then established in the laboratory, and a limited number of

airborne samples have been analyzed to date. Quality assurance includes analysis of reagent blanks and standard solutions with each plate of samples being analyzed; analysis of laboratory blanks, all of which have been less than detectable, field blanks, and field duplicates. Three sets of endotoxin duplicates were collected with the MEMs on March 11-16 (99 and 99D) and four sets of endotoxin duplicates were collected with the MEMS from March 20-30, 2002. In six of these seven duplicate sets the two measured values were within 0.1 EU/m^3, and the seventh was within 0.3; samples collected at several homes in Fresno on the same day typically varied over a range of 0.2 to 1.5 or 0.4 to 3.0 0.1 EU/m^3.

Table 5.2.1-1. 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., 2000.)

Observable and Method	Size Range	Avg Time	Period
Gases			
Nitrogen oxides (NO/NO_x) (TEI 42 chemiluminescence with internal converter)	Gas	5 min	1990 onward[a]
Ozone (API 400 UV absorption)	Gas	5 min	1990 onward[a]
Carbon monoxide (Dasibi 3008 infrared gas filter correlation)	Gas	5 min	1990 onward[a]
Reactive nitrogen (NO_y) (TEI 42C chemiluminescence with external converter)	Gas	5 min	12/15/99 to 3/31/03
Continuous Particle Mass and Chemistry			
$PM_{2.5}$ mass (ambient temperature Met One 1020 BAM)	<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	10 min	9/23/99 to 3/31/03
$PM_{2.5}$ SO_4^{-2} (ADI flash volatilization with SO_2 detector)	<2.5 μm	10 min	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	30 min	12/15/99 to 3/31/03
Particle-bound PAH (EcoChem Analytics PAS2000 w/UV radiation and photoelectric aerosol sensors)	<1 μm	5 min	9/30/99 to 3/31/03
Continuous Light Scattering and Light Absorption			
Total particle light scattering[c] (Radiance M903 nephelometer with smart heater at 530 nm)	<~30 μm	5 min	2/15/00 to 3/31/03
Single-wavelength light absorption[d] (McGee AE 14U aethalometer at 880 nm)	<2.5 μm	5 min	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	5 min	5/15/99 to 3/31/03
Meteorology			
Temperature (Met One CS500L platinum resistance sensor)	NA[b]	5 min	5/15/99 onward[a]
Relative humidity (Met One CS500L capacitance sensor)	NA[b]	5 min	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 5.2.1-2. 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

5.2.3 Sampling of Pollen and Fungal Spores

Burkard Seven Day Recording Volumetric Spore Trap (Burkard Manufacturing Co. Ltd., Rickmansworth, UK) with a flow rate of 10 l minute^{-1} is used for recording the regional concentration of pollen and fungal spores in Fresno. For practical sampling details, see the CD Protocols. The performance of the Burkard Seven Day Recording Volumetric Spore Trap (later as BSVT) is slightly improved from the original Hirst sampler (Hirst, 1952). This means that particles having 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 continuous air sampling devise is globally used to monitor the concentration of the airborne bioparticles, and also considered as the standard equipment for measurement of the airborne aeroallergens.

The height of the orifice above the ground level is 10.7 meters on the roof of the CARB 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 regionally representative of the flora since the prevailing winds at the sampling location are from northwest and southeast.

Three different adhesives for the deposition surface on the rotating drum were used during the past year:

1. Lubriseal adhesive (November-February) produced very thick and optically unsatisfactory deposition surface for pollen and fungal spores.
2. Mixture of Vaseline and Paraffin in Toluene (9:1:10) (February-May) 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 with
3. Silicon crease, 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 (Galan & Dominiques-Vilches, 1997).

The drum rotates 2 mm per hour and the weekly tape is cut into seven segments, each 48 mm long (tape width 19 mm) and corresponding to a 24 hr period. Tape segments are mounted onto microscopic slides with unstained glycerin jelly. Saffranine stained Gelvatol was used for mounting from November to February, unstained Gelvatol from February to May. The optical quality of the slides was noticeably improved when Gelvatol was replaced by Glycerin gelatin in May. Technical problems at the Central Site resulted in a loss of approximately 18 % of the data from the first 6 months period of sampling. A Nikon Eclipse 400 Brightfield microscope is used for identification.

5.2.3.1 Pollen Counts and Identification

For each 24-hour period 12 transverse strips are analyzed corresponding 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 2-hour mean pollen concentration per cubic meter of air using the following equation:

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

Where C = pollen concentration in pollen grains per cubic meter
N = Number of pollen 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)

Daily averages are calculated from the 2-hour mean pollen concentration values.

Pollen grains are identified at a magnification of 400x˚, in critical cases 1000x magnification with oil immersion is used. Pollen grains are identified at species or genera level; now 111 different types. Reference slides and available reference manuals (Hjelmroos et al. 1999, and the lit. cit. in it) have been used for identification. However, no reference literature in airborne pollen identification for California or the South West of the United States is available, therefore an extensive pollen reference collection for the area investigated is under preparation to facilitate the correct and reliable identification.

The different pollen types identified in Fresno are listed in Table 5.2.3-1. Of the 111 pollen types identified, approximately 60% belong to wind pollinated plants. About 80% of these plants are known to produce pollen grains causing allergies and might promote asthma.

Table 5.2.3-1. The different pollen types identified in Fresno.

***Acacia**	Fabaceae	****Platanus***
****Acer***	***Fagus**	***Poaceae**
****Aesculus***	Fern-Trilete	****Podocarpus***
Amelanchier/Rosaceae	****Fraxinus*** (type FR1)	Polypodiaceae
****Alnus***	****Fraxinus*** (type FR2)	****Populus***
****Ambrosia***	*Ginkgo*	****Prosopis***
*Apiaceae	*Helianthemum*	*Prunus*
***Artemisia**	*Ilex*	**Pseudotsuga*
*Asteraceae	Inaperturate	*Pyrus*
***Betula**	*Jasminium*	****Quercus***
*Brassicaceae	****Juglans***	Ranunculaceae
***Cannabaceae**	Lamiaceae	Rhamnaceae
****Carpinus***	*Lagerstroemia*	**Rhus**
****Carya***	Lauraceae	Rosaceae
***Caryophyllaceae**	*Larix	****Rumex***
**Castanea*	Leguminosae	Rutaceae
**Castaneopsis*	****Ligustrum***	***Salix**
****Casuarina***	****Liquidambar***	*Sambucus*
Cirsium-type	Liliaceae	****Schinus***
Cistaceae	*Liriodendron*	Schrophulariaceae
**Cedrus*	*Lonicera*	*Senecio*
****Celtis***	*Magnolia*	**Sequoia*
***Cerealea**	Monolete	***Simmondsia***
***Chenopodiaceae/Amaranth**	*Morus	*Syringa*
Cistaceae	*Myosotis*	*Sparganium*
Cinnamomum	****Olea***	Trilete
Cistaceae	****Ostrya***	*Thalictrum/Ranunculaceae*
**Cornus*	***Palmaceae/Arecaceae**	****Tsuga***
****Corylus***	Papaveraceae	*Taraxacum*-type
***Cupressaceae**	**Picea*	**Typha*
*Cyperaceae	**Pinus*	****Ulmus/Zelkova***
****Echium***	**Pistacia*	****Urtica/Parietaria***
****Eucalyptus***	*Pittosporum*	*Vitis*
Ephedra	****Plantago lanceolata***	*Xanthium*-type
*Ericaceae	****Plantago major***	Zygophyllaceae

* = wind-pollinated plant,
bold = documented aeroallergen

5.2.3.2 Fungal Spore Counts And Identification

Fungal spores are counted and identified at the magnification of x1000 and oil immersion. 20 fields of 92.16 μm^2, evenly spaced, are counted on each of the 12 transverse strips, corresponding the exposure for every second hour of the 24 –hour period. The number recorded is then converted to correspond to the actual concentration of fungal spores per cubic meter of air for the given period (see the formula for pollen conversion).

Reference literature (Hjelmroos et al., 1999, and the lit. cit. in it) and reference slide collection is used to support the correct identification. Most of the 69 fungal spore types

identified (Figure 5.2.3-2) belong to plant pathogenic fungi of which about many are known to cause health problems.

Table 5.2.3-2. The different fungal spore types and related bioparticles identified in Fresno from November 2000 to July 2001.

Acrodictys	*Fusariella*	*Pyrenospora*
Agrocybe	*Fusarium*	*Rhizopus*
Alternaria	*Fusicladium*	Rust
Arthinium	*Ganoderma*	*Septonema*
Ascomycetes	*Geotrichum*	Smut
Aspergillus/Penicillinium	*Gliomastic*	*Sordaria*
Asperisporum	*Gyrenospora*	*Spegazzinia*
Basidiomycetes	*Helicomyces*	*Sporidylocladiella*
Beltrania	Fungi Imperfecti gen.	*Sporodesmium*
Bipolaris	*Inocybe*	*Sporomiella*
Boletus	Leptosphaeria	*Stemphylium*
Botrytis	*Leptospaerulina*	*Tilletia*
Cercospora	*Monodictys*	*Torula*
Chaetomium	*Myxomycetes*	*Ustilago*
Cladosporium	*Nigrospora*	*Venturia*
Coprinus	*Oidium*	*Xylaria*
Corynespora	*Perenospora*	
Curvularia	*Periconia*	Other Fungi + Unknown
Dichotomonotropha	*Pestalotiopsis*	
Diplococcium	*Phoma*	Algae
Endophragmiella	Phycomycete	Hyphae
Epicoccum	Pithomyces	
Erysiphe	*Pleospora*	
Exosporium	*Puccinia*	
Exserohilum		

5.2.3.3 Nomenclature

Genus and species: the pollen or fungal spore morphology corresponds to a single species, *Genus*: the pollen or fungal spore morphology is common to more than one species of a genus *Pollen/Fungal Spore Type*: pollen or fungal spore morphology is common to more than one genus. The taxonomic nomenclature follows the Jepson Manual (3rd edition, Ed. James C. Hickman 1997) for higher plants and Ainsworth and Bisby's Dictionary (2001) for fungi.

5.2.3.4 Data Quality Control

A trip and a field blank follow each Burkard Drum sent to and from Fresno.. The field blank is removed from its container momentarily while the normal drum is loaded and unloaded. During different occasions two Continuous Recording Air Samplers are operated at the SuperSite next to the BVST.

The blank slides for pollen and fungal spores (Field and Trip blank) from Central Site have been analyzed for the first 13 month period. The number of airborne pollen and fungal

spores in each of the Field blanks has been extremely low, < 2 pollen or fungal spores per slide, the trip blanks have been completely empty.

Duplicate microscopic analysis has been conducted. About 3% of pollen and fungal spore analysis has been counted and identified a second time. The results are within the range of variability for such analysis. The differences in numbers are > $\pm$ 5% for each transverse, since 12 transverse strips are analyzed for each slide, this has little effect the final result. 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 stoke (20 fields per each of the 12 strokes). The pollen analysis is done for the whole length of each 12 strokes 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 nor fungal spores are homogeneously distributed on the deposition surfaces.

5.2.4 Air Quality Conditions at the Central Site

This section describes preliminary results for the continuous (5.2.4.1) and integrated (5.2.4.2) measurements at the Central Site. Section 5.2.4.3 illustrates some of the relationships between the continuous parameters and the integrated parameters. Although these presentations are based on just a few months of data collection, they illustrate the types of variations expected over a range of temporal scales for the complete study.

5.2.4.1 Continuously Measured Parameters

Of the continuously measured parameters mentioned in Section 5.2.1, central-site data are available and quality controlled for ozone, nitric oxide (NO), nitrogen dioxide (NO_2), carbon monoxide (CO), $PM_{2.5}$, PM_{10} , black carbon (BC), particle-bound polycyclic aromatic hydrocarbons (PAHS), and particle scattering (b_{sp}) for the period November 1, 2000, through April 30, 2002. Preliminary results for these data are presented below; these results illustrate the temporal range of outdoor exposures at the Central Site in Fresno. Data are also available and quality controlled for temperature and relative humidity, but results for these parameters are not presented in this report. Abbreviations and units are defined in **Table 5.2.4-1**; definitions of the various time averages for parameters are shown in **Table 5.2.4-2**.

Data are not yet available for SO_2, PM nitrate, PM sulfate, organic carbon, elemental carbon, PM metals, and particle number. The SO_2 monitor started operating later than the other monitors did and the data are not yet available. The PM nitrate and sulfate data are not yet available. Problems were encountered with the organic carbon/elemental carbon (OC/EC) monitor and this data is not yet available. The filters for metals analysis remain to be analyzed in the laboratory and particle number data still need to be quality controlled.

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 5.2.4-1** shows an illustrated box whisker plot. 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 there are data 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 also further identified with asterisks representing the points that fall within three times the interquartile range from the end of the box and circles representing points beyond this.

Table 5.2.4-1. Definitions of abbreviations used for air quality parameters and units.

Abbreviation	Definition	Units
b_{sp}	Light extinction coefficient due to scattering by particles	Mm^{-1}
BC	Black carbon	ng/m^3
BAM10	PM_{10} as measured by a Beta Attenuation Monitor	$\mu g/m^3$
BAM25	PM_{25} as measured by a Beta Attenuation Monitor	$\mu g/m^3$
PAHS	Particle bound polycyclic aromatic hydrocarbons	fA
O3	Ozone	ppb
NO	Nitrogen oxide	ppb
NO2	Nitrogen dioxide	ppb
CO	Carbon monoxide	ppm
Mm^{-1}	Inverse megameters	
Ppb	Parts per billion	
Ppm	Parts per million	
fA	Femto amperes	
$\mu g/m^3$	Micrograms per cubic meter	
ng/m^3	Nanograms per cubic meter	

Table 5.2.4-2. Definitions of time averages used in correlation matrices and box plots.

Time average symbol	Definition
_24	24-hour average concentration
_8	Daily maximum 8-hour average concentration
_1	Daily 1-hour maximum concentration

Seasonal characteristics

The box-whisker plots in **Figures 5.2.4-2 through 5.2.4-10** show the distributions of concentrations by month at the Central Site for ozone, NO, NO_2, CO, $PM_{2.5}$, PM_{10} , BC, PAHS, and b_{sp}. Three plots are shown for each parameter, one for the 24-hour average concentration, one for the daily maximum 8-hour average concentration, and one for the daily 1-hour maximum concentration. These plots show the seasonal patterns of the various parameters; the concentrations of some are highest during the summer months, while others are highest during the winter months.

Ozone concentrations (see Figure 5.2.4-2) increase each month from January through April, are highest during May through September, and then decrease during October through December. Note that the central boxes (showing the 25th to 50th 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 NO concentrations (see Figure 5.2.4-3) are the reverse of the distribution of the ozone concentrations; NO concentrations are lowest during the middle of the year (March through September) and highest during October through February. The NO distributions during October through February are statistically significantly different from the March through September distributions. The range of the monthly NO concentration distributions are very large: the medians cover a range of about a factor of 7 to 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 February, but a very narrow range of concentrations during each month, May through August.

The monthly distributions of NO_2 concentrations are shaped like the NO distributions, but with a very narrow range (see Figure 5.2.4-4). 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 NO_2 concentration distributions is only about a factor of 2.

The monthly distributions of CO concentrations (see Figure 5.2.4-5) are shaped like the NO distributions. The low months are April through September while the high months are October through February. The range of the monthly CO concentration distributions are large: the medians cover a range of about a factor of 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 $PM_{2.5}$ (see Figure 5.2.4-6) also 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 is very high when concentrations are high (November through February) and generally lower the rest of the year. Note, however, that there are two to three days with outlier $PM_{2.5}$ concentrations in July (individual points above the whisker).

The monthly distributions of PM_{10} (see Figure 5.2.4-7) show less of a seasonal pattern than the monthly distributions of $PM_{2.5}$. PM_{10} concentrations are somewhat higher during the winter months, but the boxes for all months overlap. Note that there are some outlier concentrations during most months, especially for the daily maximum 1-hour concentrations.

The monthly distributions of BC concentrations (see Figure 5.2.4-8) are shaped like the NO and CO distributions. The low months are March through October while the high months are November through February. The range of the monthly BC concentration distributions is large: the medians cover a range of about a factor of 5 to 8 between the low and high months. The whiskers of the monthly boxes indicate a fairly wide range of BC concentrations within the months of November through February and a narrower range of concentrations during the other months.

The monthly distributions of PAH concentrations (see Figure 5.2.4-9) are shaped like the NO, CO, and BC distributions. The low months are March through October while the high months are November through February. The range of the monthly PAH concentration distributions is very large: the medians cover a range of about a factor of 10 between the low and high months. The whiskers of the monthly boxes indicate a fairly wide range of PAH concentrations within the months of November through February and a narrower range of concentrations during the other months.

The monthly distributions of particle scattering (b_{sp}) (see Figure 5.2.4-10) are shaped like the NO, CO, BC, and PAH distributions. The low months are March through October while the high months are November through February. The range of the monthly particle scattering (b_{sp}) distributions are very large: the medians cover a range of about 10 between the low and high months. The whiskers of the monthly boxes indicate a very wide range of particle scattering (b_{sp}) within the months of November through February and a fairly narrow range during the other months.

Day-to-day characteristics

The time series plots in **Figures 5.2.4-11 through 5.2.4-19** show the daily 24-hour average concentrations at the Central Site for ozone, NO, NO_2, CO, $PM_{2.5}$, PM_{10} , BC, PAHS, and b_{sp}. These plots cover the period from November 1, 2000, through April 30, 2002. They show the daily average concentrations that are comparable to the distributions in the _24 box-whisker plots of Figures 5.2.4-2 through 5.2.4-10. Thus, these plots also show the seasonal patterns of the various parameters; the concentrations of some are highest during the summer months, while others are highest during the winter months.

Daily average ozone concentrations (see Figure 5.2.4-11) 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 about 50-65 ppb during the summer months. The range of daily average ozone concentrations is about a factor of five.

Daily average NO concentrations (see Figure 5.2.4-12) are very low with little day-to-day variation during the months of March through July. Daily average NO concentrations are much higher and vary significantly day-to-day during the months of October through January. Daily

average NO concentrations reach highs of about 60-120 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 5.2.4-13) show only a modest seasonal pattern with slightly lower concentrations during the months of March through August than other months. The daily average NO_2 concentrations typically range from about 10 ppb to about 35 ppb, with the full range from lowest to highest from about 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 CO concentration patterns (see Figure 5.2.4-14) are very similar to those for NO: low with only modest day-to-day variation during the period from late March into September and higher concentrations and larger variations during the rest of the year. Daily average CO concentrations reach highs of about 1.5-2.5 ppm during the winter months. The range of daily average CO concentrations between summer and winter is wide, typically about a factor of eight. Again note an occasional multi-day period of high concentrations (see the late-December 2000 period when both CO and NO_2 concentrations were high, for example).

Daily average $PM_{2.5}$ concentration patterns (see Figure 5.2.4-15) show low concentrations with low day-to-day variations during the April through September period with higher concentrations and higher variability during the rest of the year. Again note an occasional multi-day period of high concentrations, including the late-December 2000 period when both CO and NO_2 were also high. The range of daily average $PM_{2.5}$ concentrations between summer and winter is wide, typically about a factor of six.

Daily average PM_{10} concentration patterns (see Figure 5.2.4-16) show differences across the seasons. PM_{10} concentrations during the February through August period are slightly lower with a lower day-to-day variability than during the rest of the year. However, again note an occasional multi-day period of high concentrations, including the late-December 2000 period when CO, NO_2, and $PM_{2.5}$ concentrations were also high. The range of daily average PM_{10} concentrations between summer and winter is wide, typically about a factor of 6 to 10.

Daily average BC concentration patterns (see Figure 5.2.4-17) are very similar to those for NO and CO: low with only modest day-to-day variation during the period from March through September with higher concentrations and larger variations during the rest of the year. Daily average BC concentrations reach highs of about 5-8 $\mu g/m^3$ during the winter months. The range of daily average BC concentrations between summer and winter is wide, typically about a factor of 8 to 10. Again, note an occasional multi-day period of high concentrations, including the late-December 2000 period when CO, NO_2, $PM_{2.5}$, and PM_{10} concentrations were also high.

Daily average PAH concentration patterns (see Figure 5.2.4-18) are very similar to those for NO, CO, and BC: low with only modest day-to-day variation during the period from March through September with higher concentrations and larger variations during the rest of the year.

The range of daily average PAH concentrations between summer and winter is very wide, typically about a factor of 15 to 25. Again, note an occasional multi-day period of high concentrations, including the late-December 2000 period when CO, NO_2, $PM_{2.5}$, PM_{10}, and BC concentrations were also high.

Daily average b_{sp} patterns (see Figure 5.2.4-19) are very similar to those for NO, CO, BC, and PAH, but especially to the pattern for $PM_{2.5}$: low with only modest day-to-day variation during the period from April through September with higher concentrations and larger variations during the rest of the year. The range of daily average particle scattering between summer and winter is very wide, typically about a factor of 10 to 20. Again, note an occasional multi-day period of high concentrations, including the late-December 2000 period when CO, NO_2, $PM_{2.5}$, PM_{10}, BC, and PAH concentrations were also high.

Diurnal characteristics

The diurnal box-whisker plots in **Figures 5.2.4-20 through 5.2.4-28** show the distributions of concentrations by hour at the Central Site for ozone, NO, NO_2, CO, $PM_{2.5}$, PM_{10}, BC, PAHS, and b_{sp}. These plots show the diurnal distribution of concentration profiles and, thus, illustrate the range of concentrations and the diurnal pattern that occurs each day.

Figure 5.2.4-20 shows the diurnal distribution of ozone concentrations for the Central Site. No data is shown at 0400 PST when a daily calibration is typically performed. This pattern illustrates the typical daily emissions/photochemical pattern for ozone: ozone concentrations increasing in the morning daylight hours to a maximum at about 1400 or 1500 PST in the afternoon. This figure also illustrates the potential of high ozone exposures during afternoon outdoor activities. Note the wide range of concentrations each hour; some of this is due to using both winter and summer days in this plot.

Figure 5.2.4-21 shows the diurnal distribution of NO concentrations for the Central Site. No data is shown at 0400 PST when a daily calibration is typically performed. This pattern illustrates the typical pattern for NO with high NO concentrations during the morning and evening periods, indicating fresh emissions and low mixing heights. Note the wide range of concentrations each hour and the large number of individual values outside the whiskers (outside 1.5 times the interquartile range).

Figure 5.2.4-22 shows the diurnal distribution of NO_2 concentrations for the Central Site. No data is shown at 0400 PST when a daily calibration is typically performed. The characteristics of the NO_2 concentrations (i.e., the median and box indicating the 25^{th} and 75^{th} percentiles) are fairly flat with only modest variations during the daytime.

Figure 5.2.4-23 shows the diurnal distribution of CO concentrations for the Central Site. No data is shown at 0400 PST when a daily calibration is typically performed. The characteristics of the CO concentrations (i.e., the median and box indicating the 25^{th} and 75^{th} percentiles) are fairly flat with only modest variations across the day. Note the large number of individual values outside the whiskers (outside 1.5 times the interquartile range).

Figure 5.2.4-24 shows the diurnal distribution of $PM_{2.5}$ concentrations for the Central Site. The characteristics of the $PM_{2.5}$ concentrations (i.e., the median and box indicating the 25th and 75th percentiles) are fairly flat with only modest variations during the day; this is very similar to the profiles for CO. However, note the very large number of individual values outside the whiskers (outside 1.5 times the interquartile range).

Figure 5.2.4-25 shows the diurnal distribution of PM_{10} concentrations for the Central Site. The characteristics of the PM_{10} concentrations (i.e., the median and box indicating the 25th and 75th percentiles) are very flat with little variation during the day. However, note the large number of individual values outside the whiskers (outside 1.5 times the interquartile range).

Figures 5.2.4-26 and 5.2.4-27 show the diurnal distribution of BC and PAH concentrations for the Central Site. The characteristics of the BC and PAH concentrations (i.e., the median and box indicating the 25th and 75th percentiles) show a diurnal variation with higher concentrations during the morning rush hours and the evening. However, note the large number of individual values outside the whiskers (outside 1.5 times the interquartile range), especially at night.

Figure 5.2.4-28 shows the diurnal distribution of b_{sp} concentrations for the Central Site. The characteristics of the particle scattering concentrations (i.e., the median and box indicating the 25th and 75th percentiles) are fairly flat with modest variations during the day; this is very similar to the profile for $PM_{2.5}$. Also note the very large number of individual values outside the whiskers (outside 1.5 times the interquartile range).

The diurnal plots in **Figures 5.2.4-29 through 5.2.4-33** show the hourly average concentrations at the Central Site for ozone, NO, NO_2, CO, $PM_{2.5}$, PM_{10}, b_{sp}, BC, and PAHS. These plots show the average diurnal concentration profiles and, thus, illustrate the typical concentration pattern that occurs each day.

Figure 5.2.4-29 shows the average diurnal concentration patterns for ozone, NO, and NO_2. 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 increasing in the morning daylight hours to a maximum at about 1400 or 1500 PST in the afternoon. This also illustrates the potential of high ozone exposures during afternoon outdoor activities.

Figure 5.2.4-30 shows the average diurnal concentration patterns for NO and CO. These patterns are very similar in shape to each other, showing peaks in the morning and evening when emissions are the highest and mixing heights are low. Similar patterns for NO and CO with this shape are expected, since the concentrations of both of these pollutants are dominated by fresh motor vehicle emissions.

Figure 5.2.4-31 shows the average diurnal concentration patterns for $PM_{2.5}$, PM_{10}, and b_{sp}. These patterns are similar to each other with minimums in the late afternoon and peaks at night. As expected, average hourly PM_{10} concentrations are higher than those for $PM_{2.5}$.

Figure 5.2.4-32 shows the average diurnal concentration patterns for PAH and BC. These patterns are very similar in shape to each other, and to the patterns for NO and CO. PAH and BC diurnal concentrations show peaks in the morning and evening when emissions are the highest and mixing heights are low. Again, patterns with these shapes are expected, since the concentrations of both of these pollutants are likely dominated by fresh motor vehicle emissions (although wintertime fireplace emissions and some other sources likely also contribute).

Figure 5.2.4-33 shows the average diurnal concentration patterns for ozone, NO_2, and PM_{10}. These diurnal patterns illustrate several periods during a typical day when there will be different levels of outdoor exposure for these parameters. For example, note the high ozone exposure during the middle of the day when exposures for NO_2 and PM_{10} are relatively low, and the contrasting period in the evening when exposures are high for NO_2 and PM_{10}, but relatively low for ozone.

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

Relationships among continuously measured parameters

The scatter-plot matrices in **Figures 5.2.4-34 through 5.2.4-36** show two-parameter relative scatter plots between ozone, NO, NO_2, CO, $PM_{2.5}$, PM_{10} , BC, PAHS, and b_{sp} measured at the Central Site. Note that the relative distribution for each parameter is also shown as a bar chart. Separate plots are shown for the 24-hour average concentration, for the daily maximum 8-hour average concentration, and for daily 1-hour maximum concentration. These plots illustrate the relationships between the various parameters; some are related in a linear fashion, some in a non-linear fashion, while others appear to be unrelated.

Figure 5.2.4-34 shows the scatter-plot matrix for the 24-hour averaged data for the various parameters. There is a very tight linear relationship between $PM_{2.5}$ and particle scattering, and between CO and NO. There are good linear relationships between many of the other pollutants, excluding ozone. Some of the relationships with NO and NO_2 have fairly large scatter.

Figure 5.2.4-35 shows the scatter-plot matrix for the maximum 8-hour averaged data for the various parameters. As for the 24-hour data, there is a very tight linear relationship between $PM_{2.5}$ and particle scattering, and between CO and NO. Again, some of the relationships with NO and NO_2 have fairly large scatter. There are good linear relationships between many of the other pollutants, excluding ozone.

Figure 5.2.4-36 shows the scatter-plot matrix for the maximum 1-hour data for the various parameters. As for the 24-hour and 8-hour data, there is a very tight linear relationship between $PM_{2.5}$ and particle scattering, and between CO and NO. Again, some of the relationships with NO and NO_2 have fairly large scatter and there are good linear relationships between many of the other pollutants, excluding ozone.

The variations and relationships in Figures 5.2.4-2 through 5.2.4-36 illustrate a wide variety of patterns among the pollutants. These patterns depend on a range of factors, including source strength and location, seasonal sources (e.g. woodsmoke 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. These relationships will be explored in future data analysis and model development tasks.

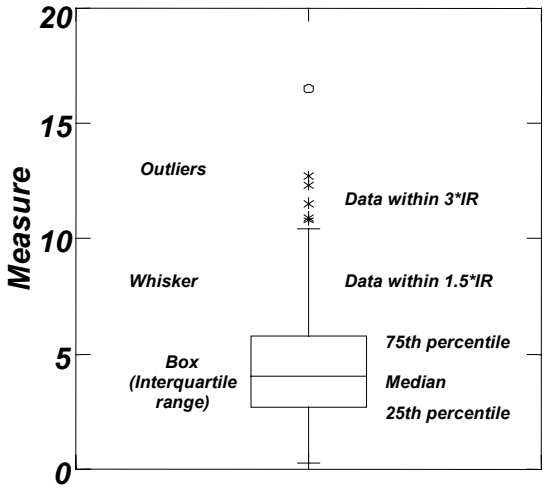


Figure 5.2.4-1. Illustration of a box whisker plot as defined by SYSTAT statistical software.

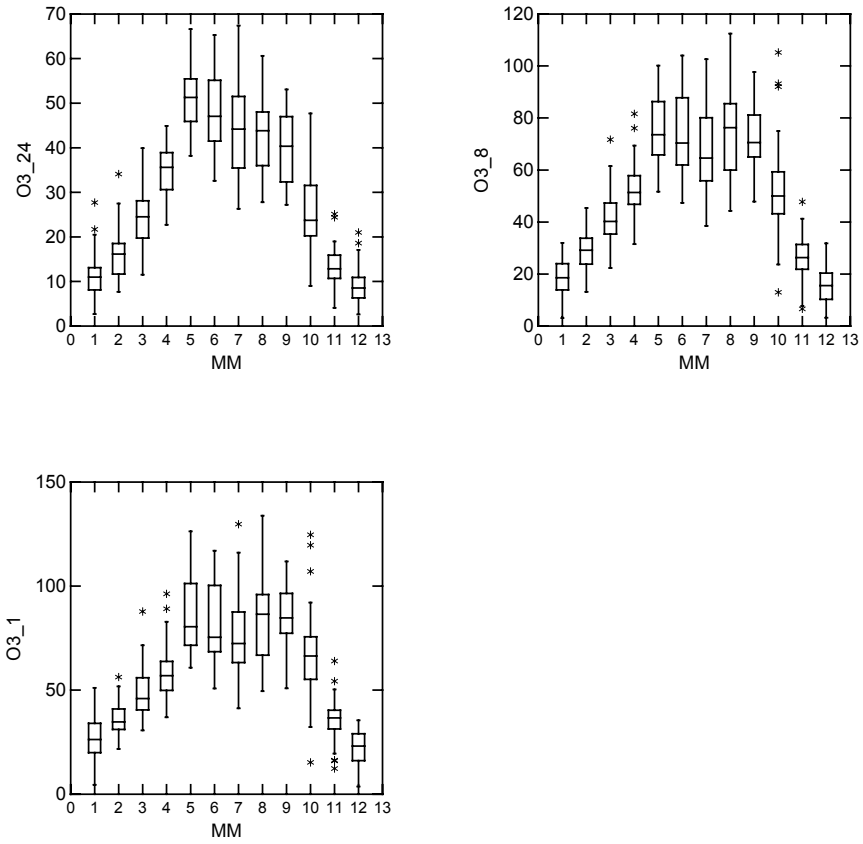


Figure 5.2.4-2. Monthly box whisker plots of ozone (O_3) at the Central Site (Fresno First Street) for November 1, 2000, through April 30, 2002. Shown are results for 24-hour average O_3 (O_3_24), maximum 8-hour O_3 (O_3_8), and maximum 1-hour O_3 (O_3_1) concentrations on each day; concentrations are in ppb. Note: the numbers (1-12) along the x-axis refer to months (January-December) and the data shown for May-October are only based on one year while the data for November-April are based on two years of sampling.

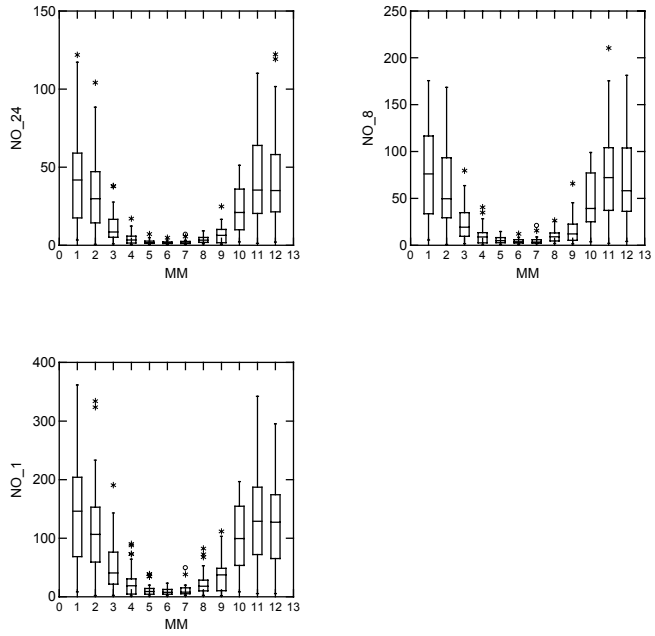


Figure 5.2.4-3. Monthly box whisker plot of nitric oxide (NO) at the Central Site (Fresno First Street) for November 1, 2000, through April 30, 2002. Shown are results for 24-hour average NO (NO_24), maximum 8-hour NO (NO_8), and maximum 1-hour NO (NO_1) concentrations on each day; concentrations are in ppb (see note to Figure 5.2.4-2).

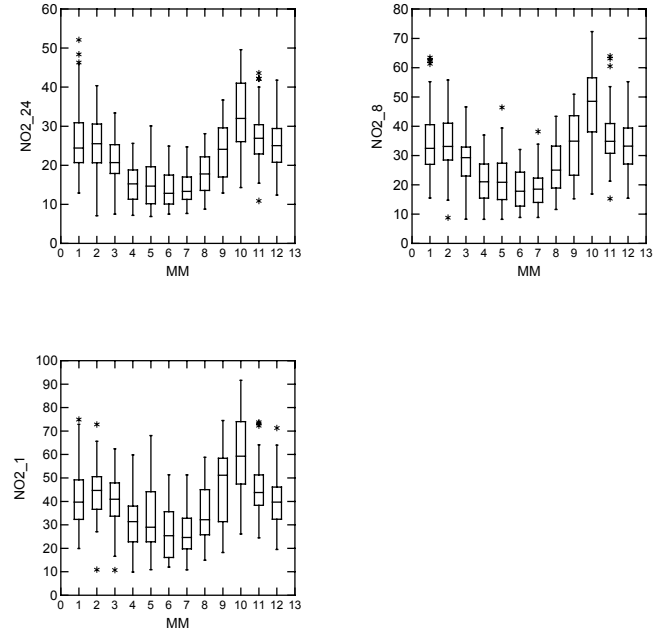


Figure 5.2.4-4. Monthly box whisker plot of nitrogen dioxide (NO_2) at the Central Site (Fresno First Street) for November 1, 2000, through April 30, 2002. Shown are results for 24-hour average NO_2 (NO_2_24), maximum 8-hour NO_2 (NO_2_8), and maximum 1-hour NO_2 (NO_2_1) concentrations on each day; concentrations are in ppb (see note to Figure 5.2.4-2)..

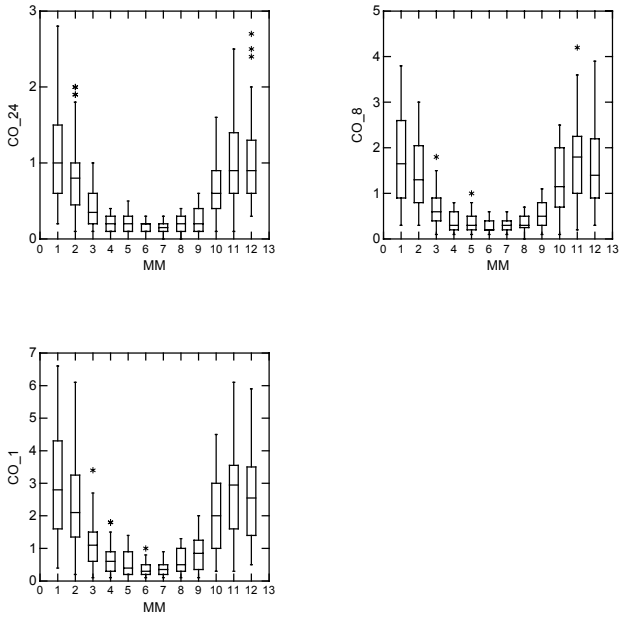


Figure 5.2.4-5. Monthly box whisker plot of carbon monoxide (CO) at the Central Site (Fresno First Street) for November 1, 2000, through April 30, 2002. Shown are results for 24-hour average CO (CO_24), maximum 8-hour CO (CO_8), and maximum 1-hour CO (CO_1) concentrations on each day; concentrations are in ppm (see note to Figure 5.2.4-2)..

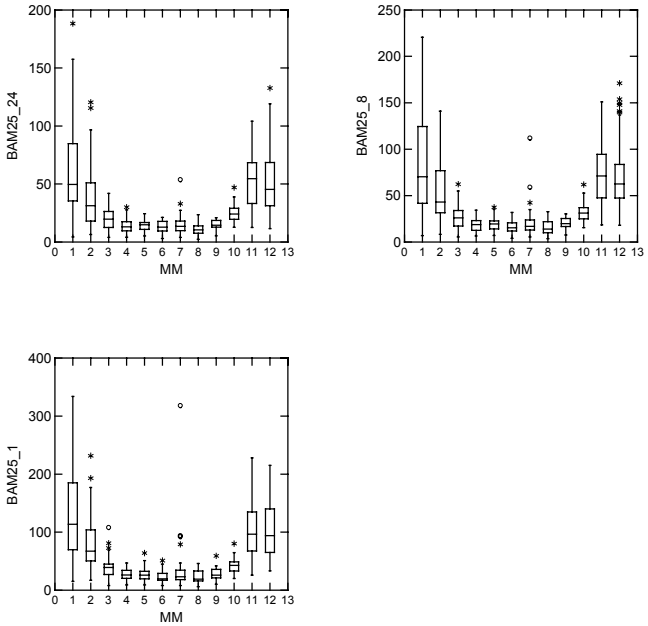


Figure 5.2.4-6. Monthly box whisker plot of $PM_{2.5}$ mass, as measured by the BAM, at the Central Site (Fresno First Street) for November 1, 2000, through April 30, 2002. Shown are results for 24-hour average $PM_{2.5}$ (BAM25_24), maximum 8-hour $PM_{2.5}$ (BAM25_8), and maximum 1-hour $PM_{2.5}$ (BAM25_1) concentrations on each day; concentrations are in $\mu g/m^3$ (see note to Figure 5.2.4-2).

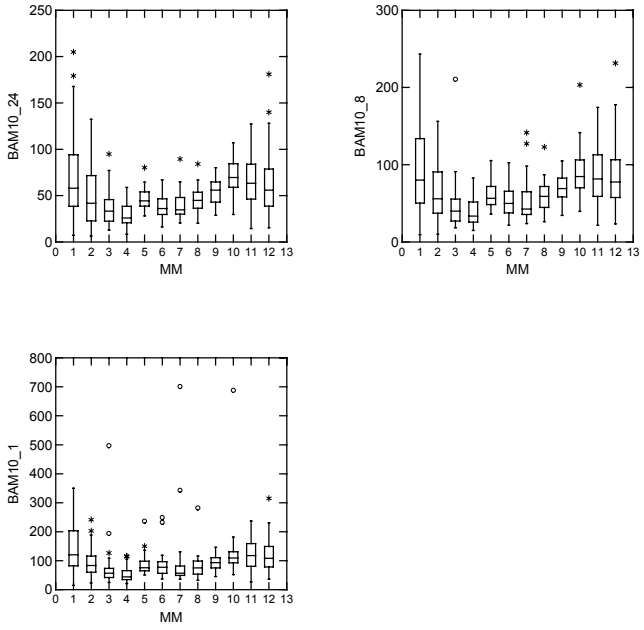


Figure 5.2.4-7. Monthly box whisker plot of PM_{10} mass, as measured by the BAM, at the Central Site (Fresno First Street) for November 1, 2000, through April 30, 2002. Shown are results for 24-hour average PM_{10} (BAM10_24), maximum 8-hour PM_{10} (BAM10_8), and maximum 1-hour PM_{10} (BAM10_1) concentrations on each day; concentrations are in $\mu g/m^3$ (see note to Figure 5.2.4-2).

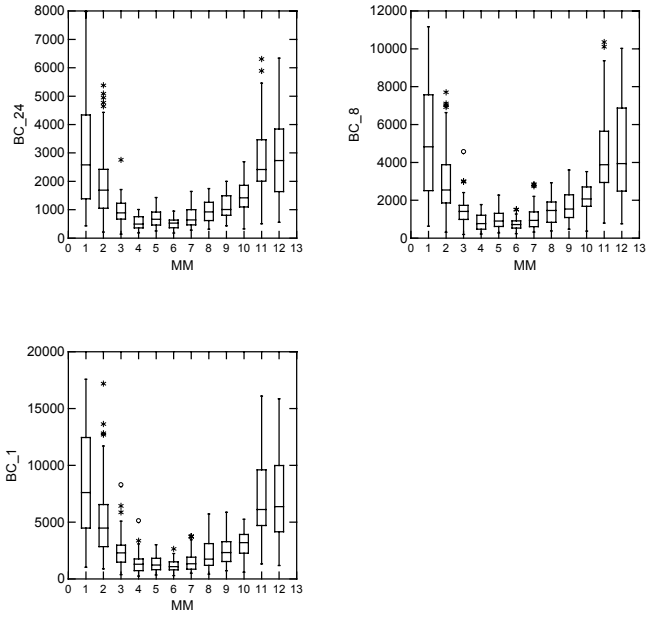


Figure 5.2.4-8. Monthly box whisker plot of black carbon (BC) at the Central Site (Fresno First Street) for November 1, 2000, through April 30, 2002. Shown are results for 24-hour average BC (BC_24), maximum 8-hour BC (BC_8), and maximum 1-hour BC (BC_1) concentrations on each day; concentrations are in ng/m^3 (see note to Figure 5.2.4-2).

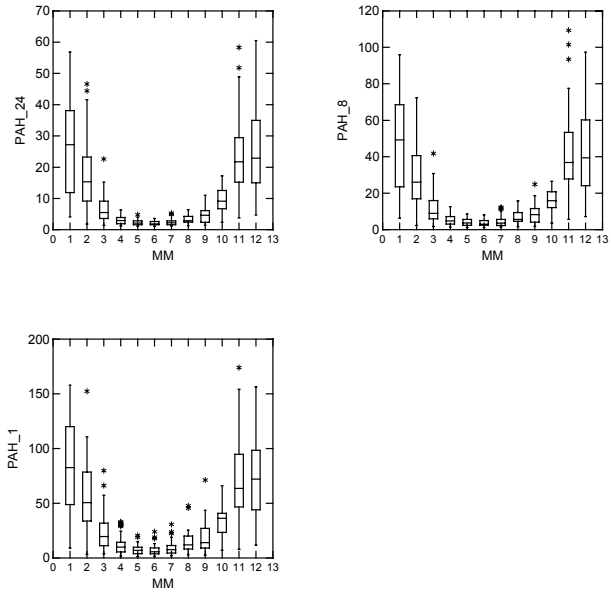


Figure 5.2.4-9. Monthly box whisker plot of particle-bound polycyclic aromatic hydrocarbons (PAH) at the Central Site (Fresno First Street) for November 1, 2000, through April 30, 2002. Shown are results for 24-hour average PAH (PAH_24), maximum 8-hour PAH (PAH_8), and maximum 1-hour PAH (PAH_1) concentrations on each day; concentrations are in relative units of fA. (see note to Figure 5.2.4-2).

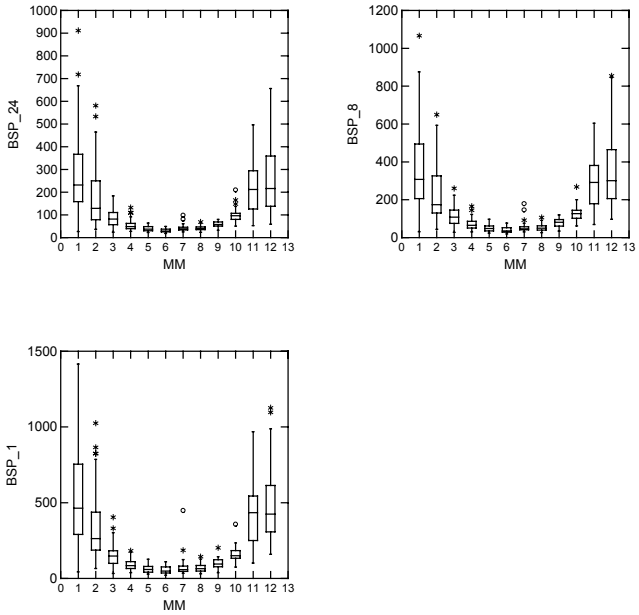


Figure 5.2.4-10. Monthly box whisker plot of particle scattering (BSP) at the Central Site (Fresno First Street) for November 1, 2000, through April 30, 2002. Shown are results for 24-hour average b_{sp} (BSP_24), maximum 8-hour b_{sp} (BSP_8), and maximum 1-hour b_{sp} (BSP_1) concentrations on each day; concentrations are in Mm^{-1} (see note to Figure 5.2.4-2).

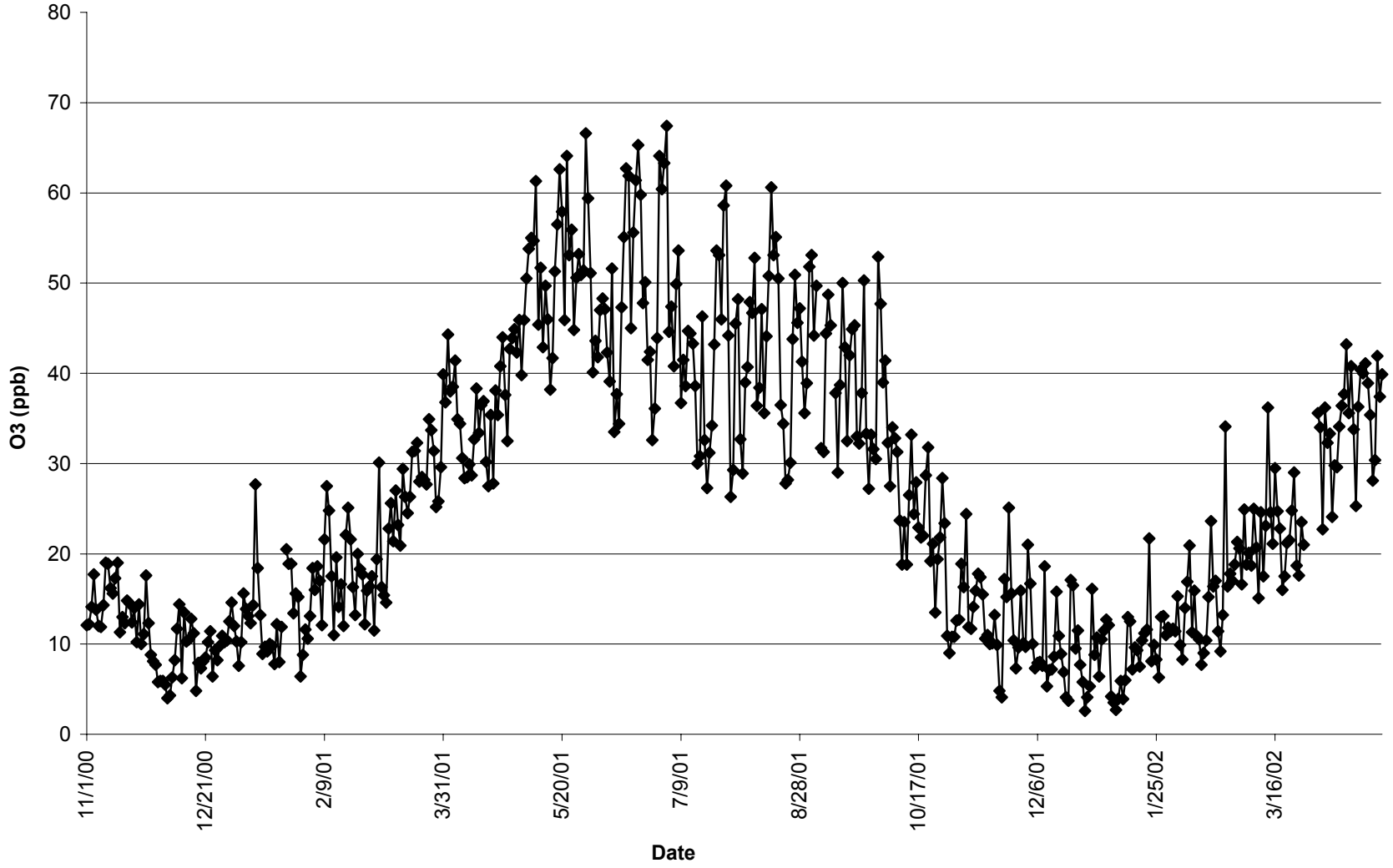


Figure 5.2.4-11. Daily (24-hour average) time series plot of ozone (O_3) at the Central Site (Fresno First Street) for November 1, 2000, through April 30, 2002; concentrations are in ppb.

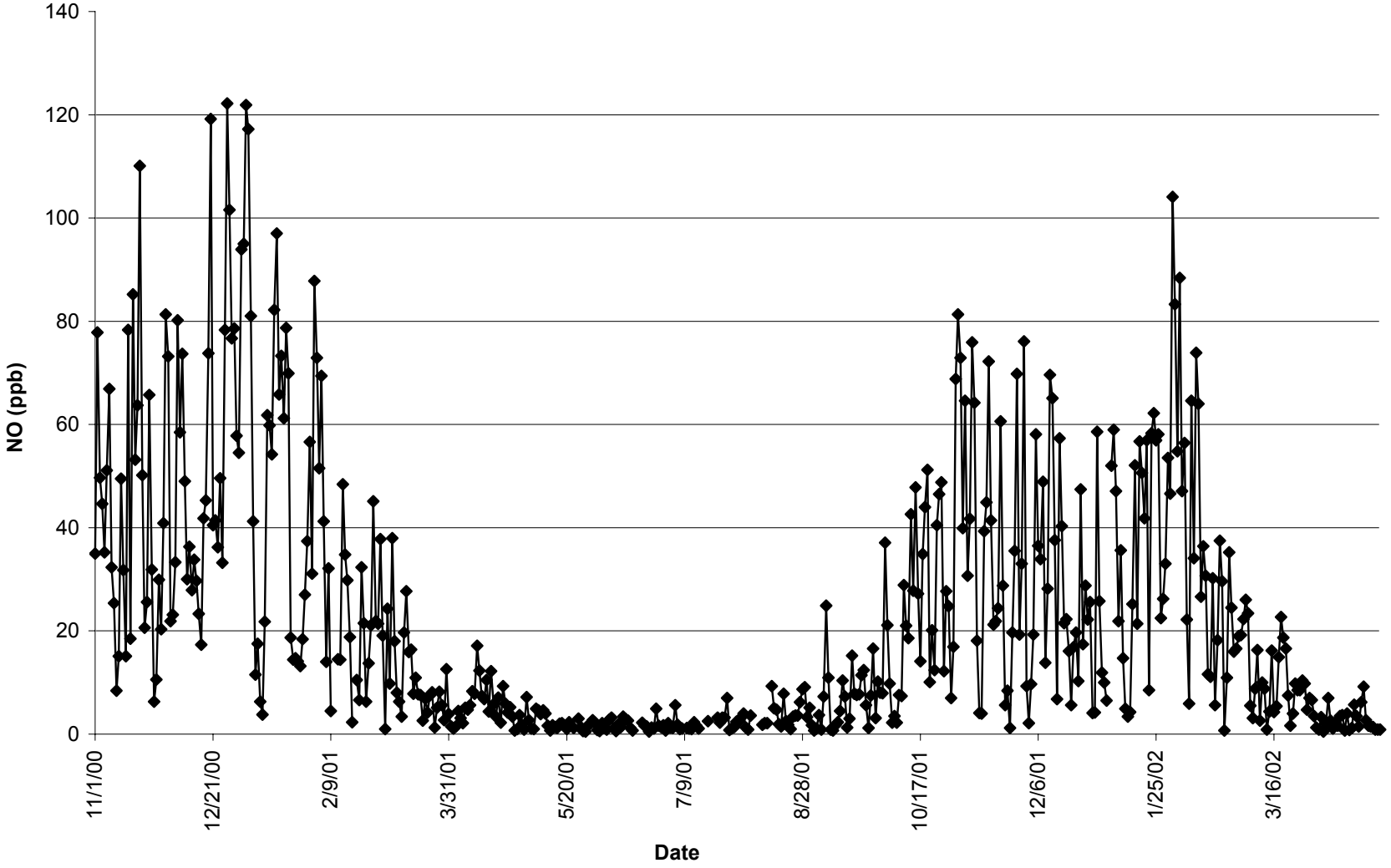


Figure 5.2.4-12. Daily (24-hour average) time series plot of nitric oxide (NO) at the Central Site (Fresno First Street) for November 1, 2000, through April 30, 2002; concentrations are in ppb.

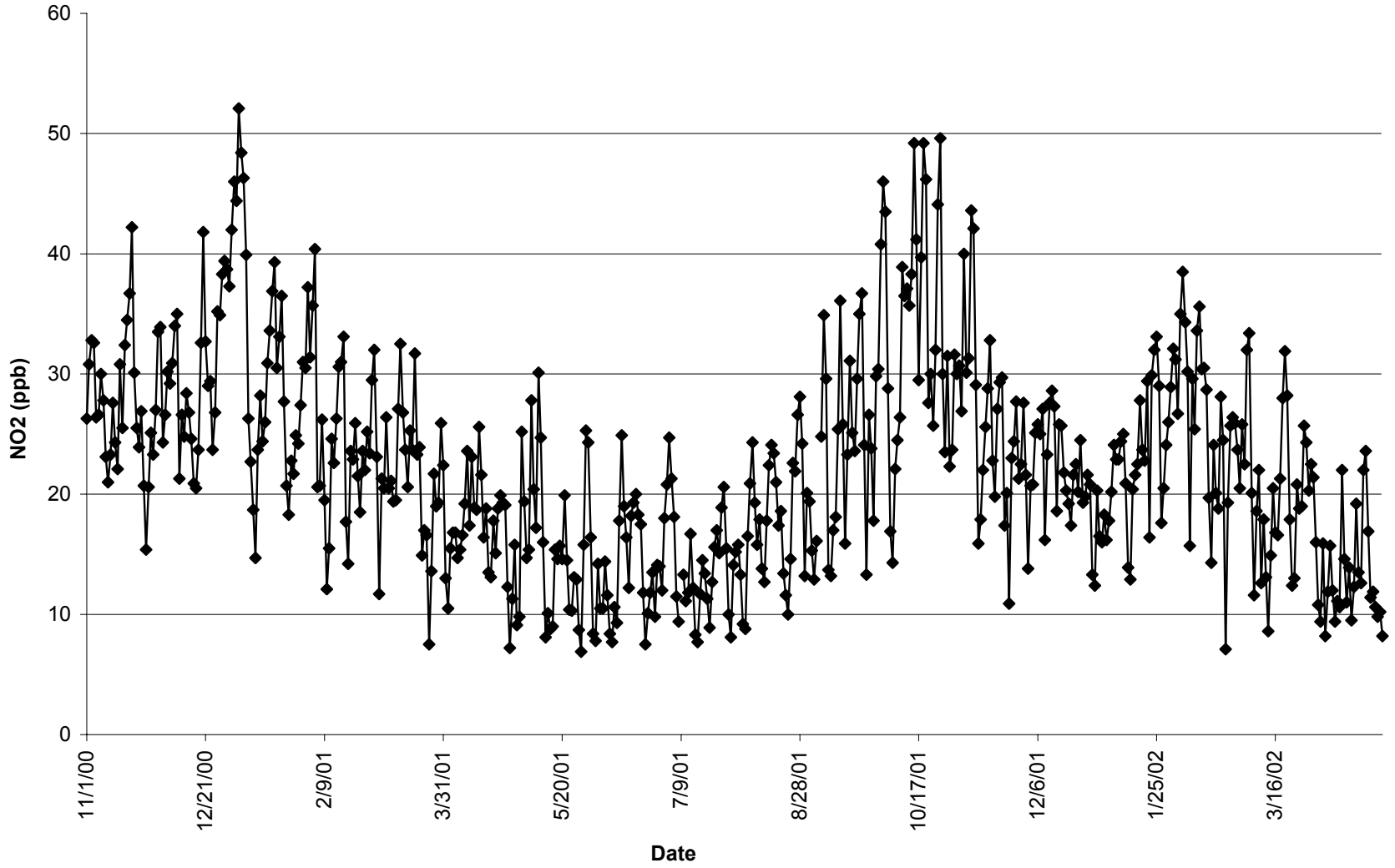


Figure 5.2.4-13. Daily (24-hour average) time series plot of nitrogen dioxide (NO_2) at the Central Site (Fresno First Street) for November 1, 2000, through April 30, 2002; concentrations are in ppb.

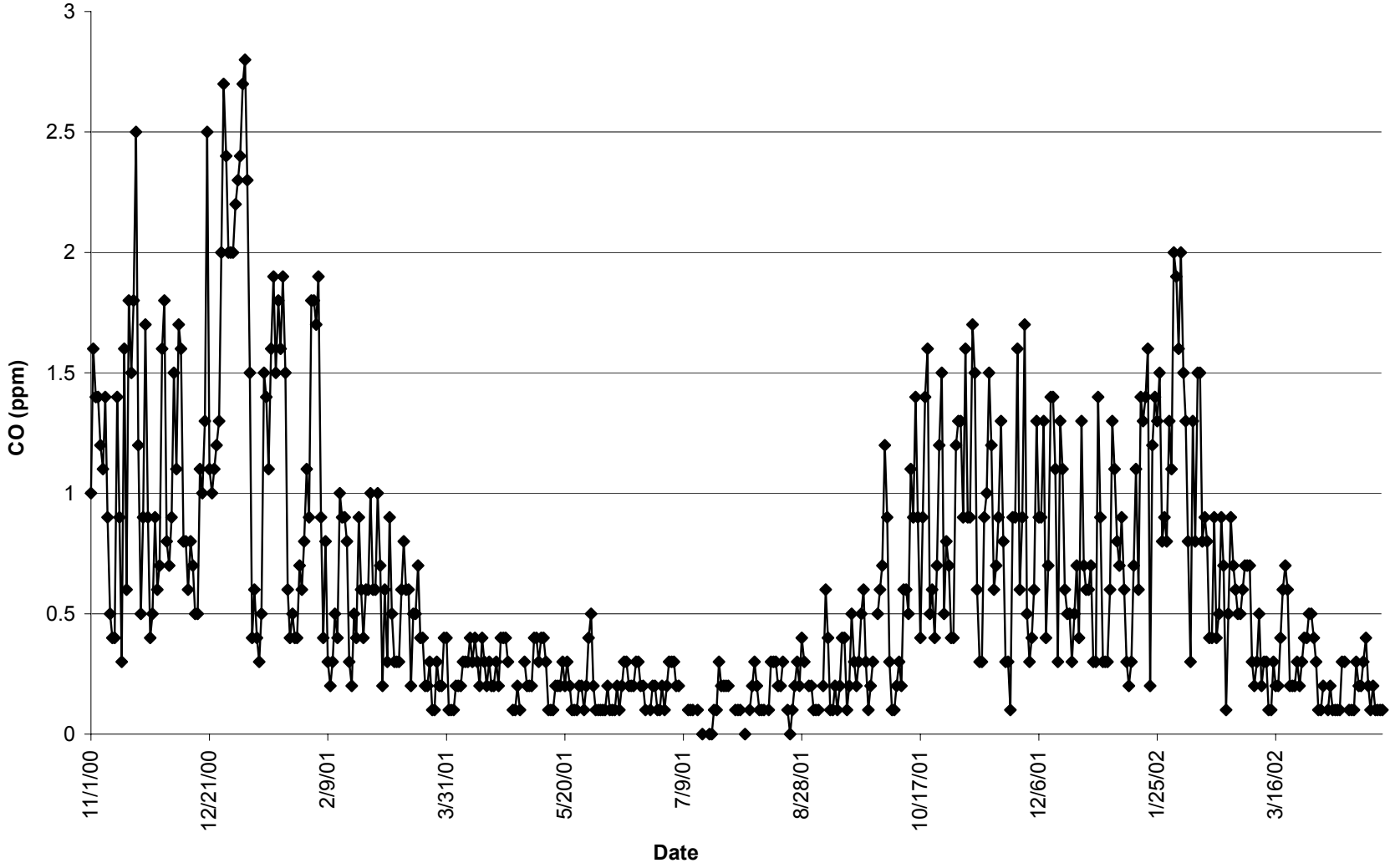


Figure 5.2.4-14. Daily (24-hour average) time series plot of carbon monoxide (CO) at the Central Site (Fresno First Street) for November 1, 2000, through April 30, 2002; concentrations are in ppm.

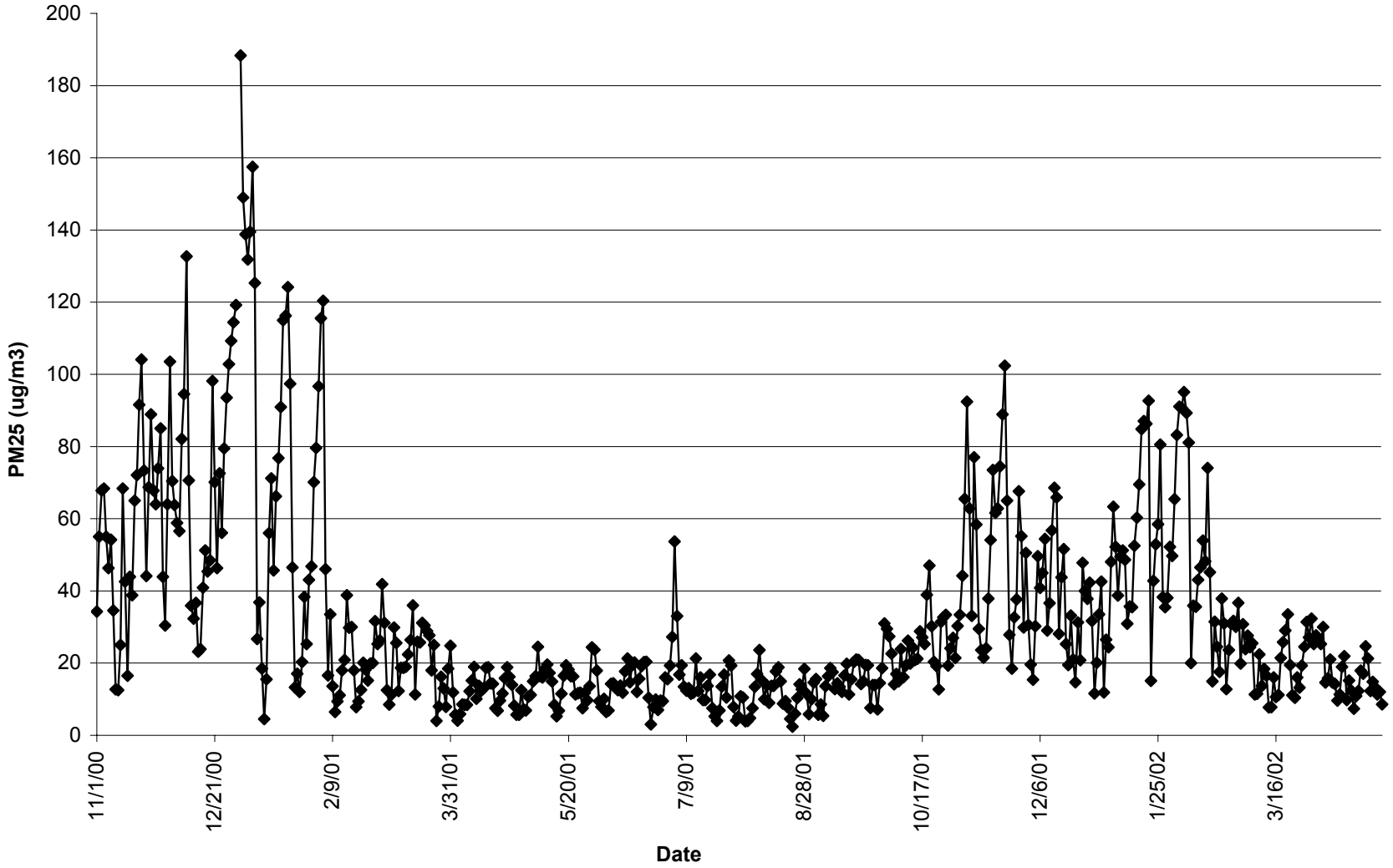


Figure 5.2.4-15. Daily (24-hour average) time series plot of $PM_{2.5}$ mass (PM25) at the Central Site (Fresno First Street) for November 1, 2000, through April 30, 2002; concentrations are in $\mu g/m^3$.

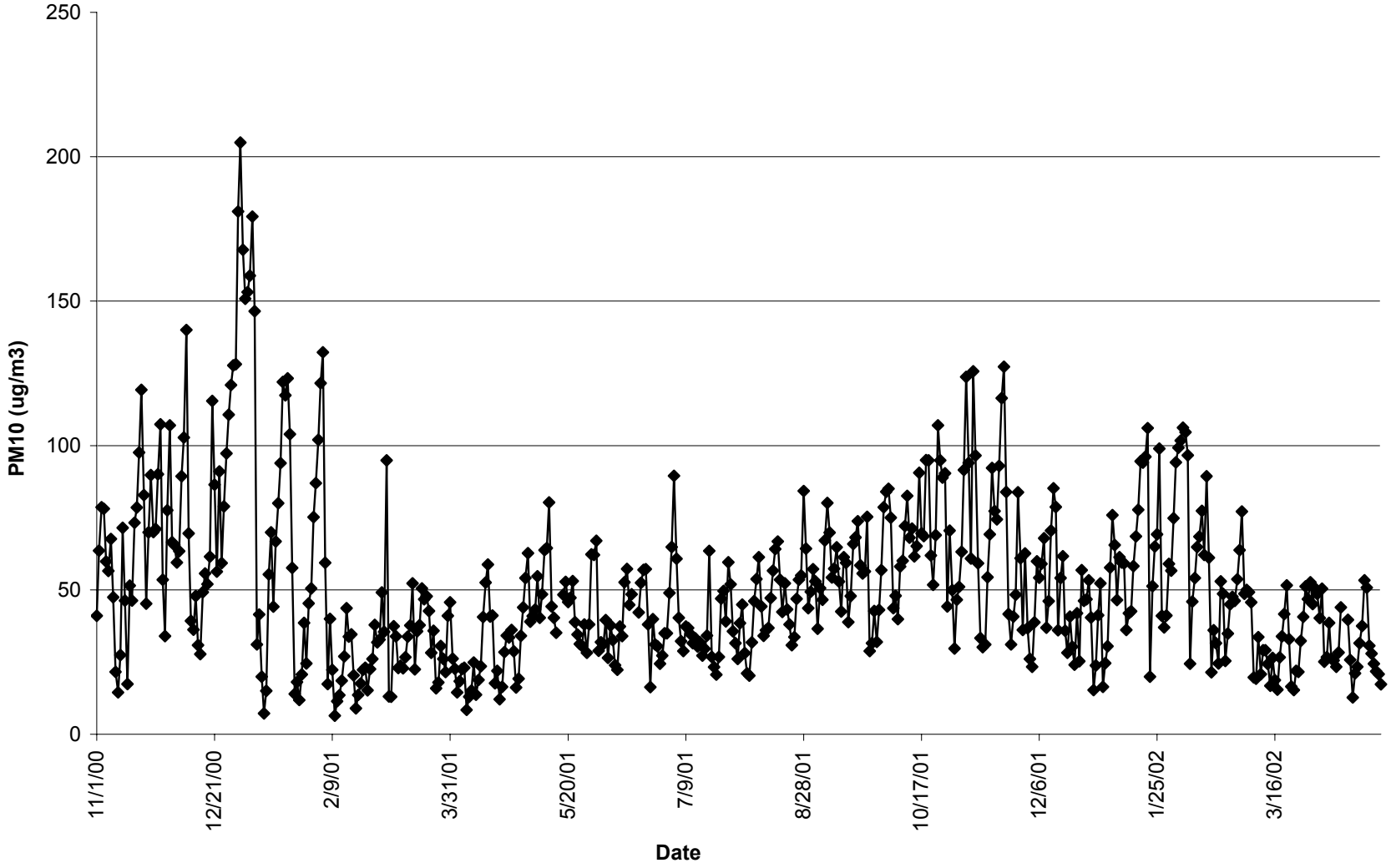


Figure 5.2.4-16. Daily (24-hour average) time series plot of PM_{10} mass (PM10) at the Central Site (Fresno First Street) for November 1, 2000, through April 30, 2002; concentrations are in $\mu g/m^3$.

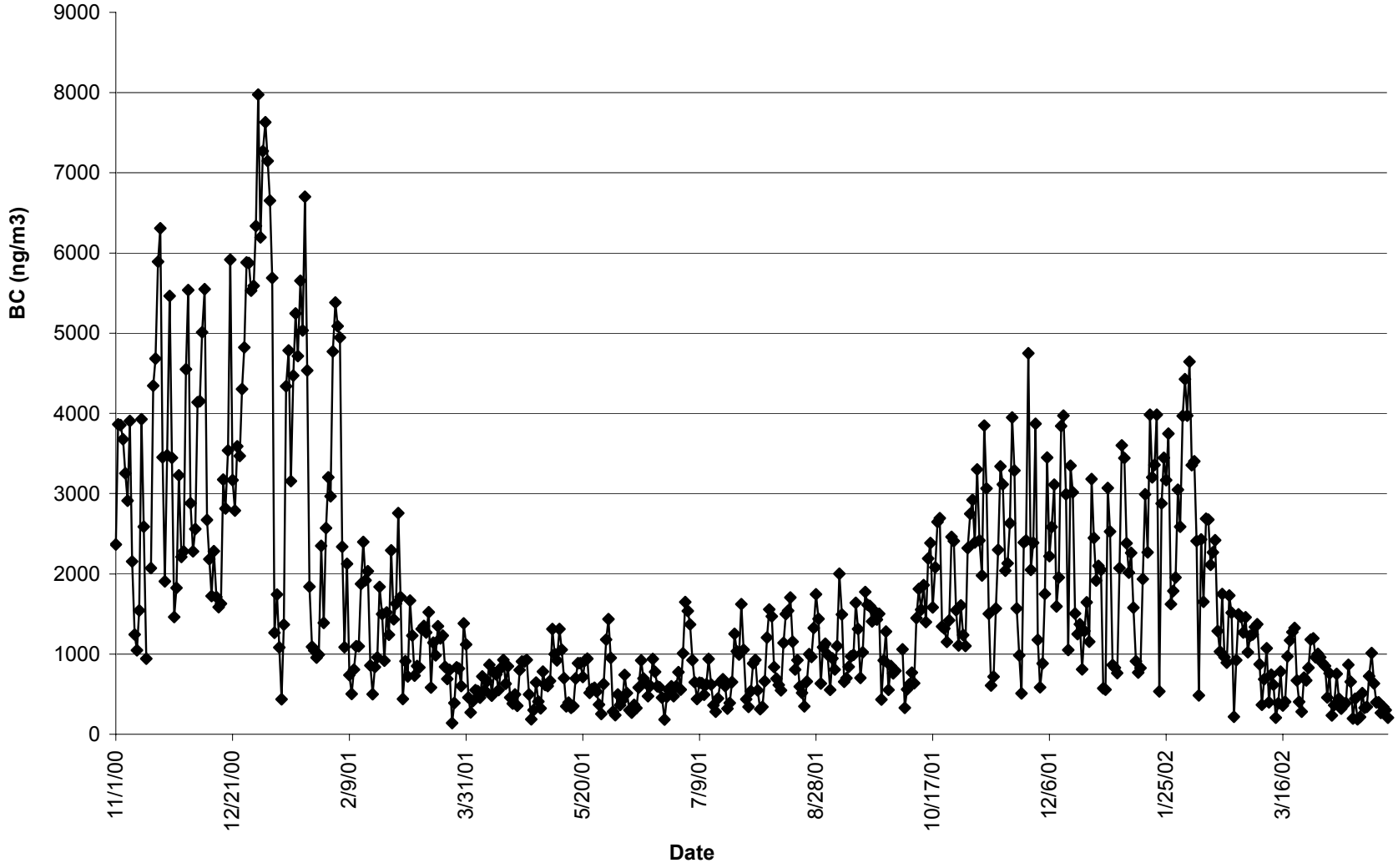


Figure 5.2.4-17. Daily (24-hour average) time series plot of black carbon (BC) at the Central Site (Fresno First Street) for November 1, 2000, through April 30, 2002; concentrations are in ng/m^3.

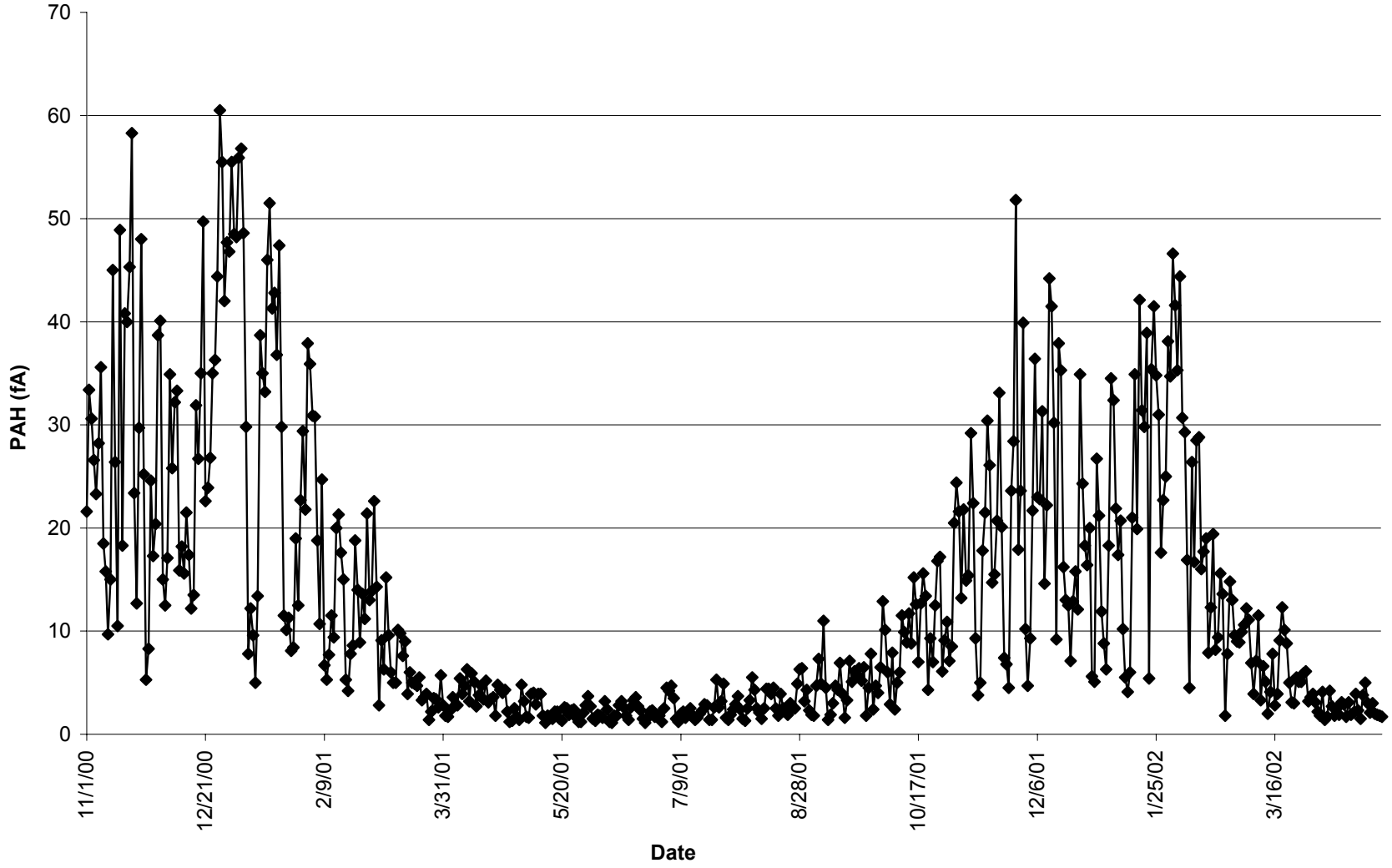


Figure 5.2.4-18. Daily (24-hour average) time series plot of particle-bound polycyclic aromatic hydrocarbons (PAH) at the Central Site (Fresno First Street) for November 1, 2000, through April 30, 2002; concentrations are in fA.

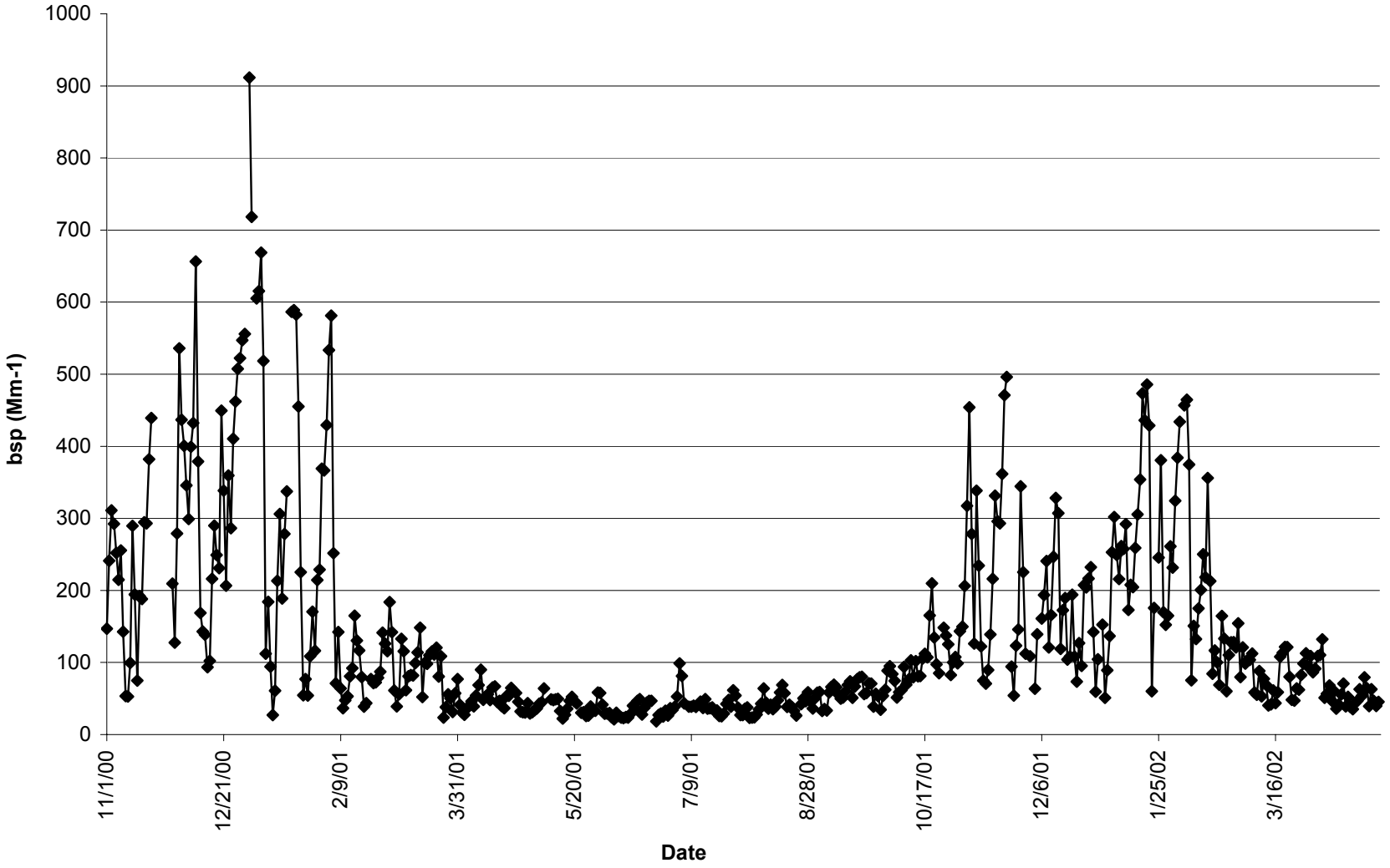


Figure 5.2.4-19. Daily (24-hour average) time series plot of particle scattering (b_{sp}) at the Central Site (Fresno First Street) for November 1, 2000, through April 30, 2002; concentrations are in Mm^{-1}.

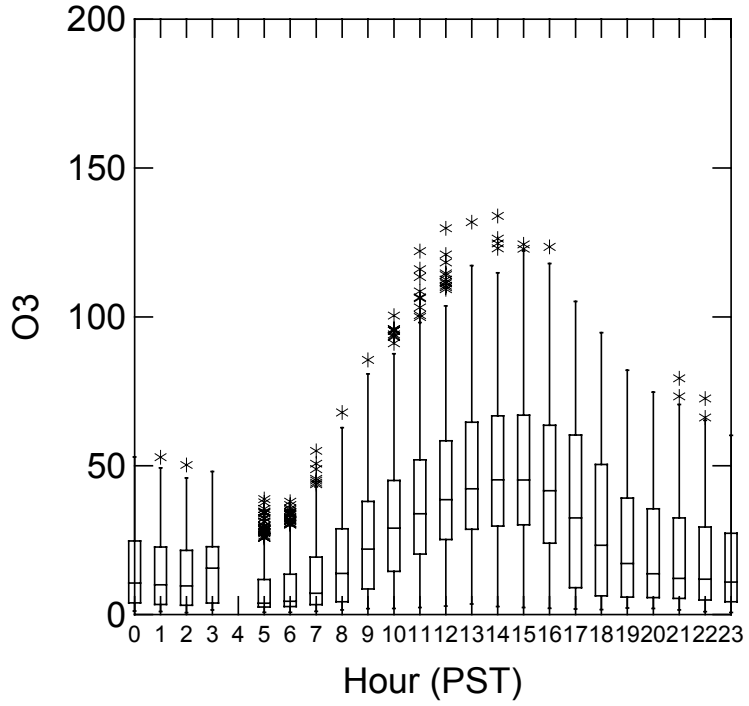


Figure 5.2.4-20. Diurnal box whisker plot of ozone (O_3) at the Central Site (Fresno First Street) for November 1, 2000, through April 30, 2002; concentrations are in ppb.

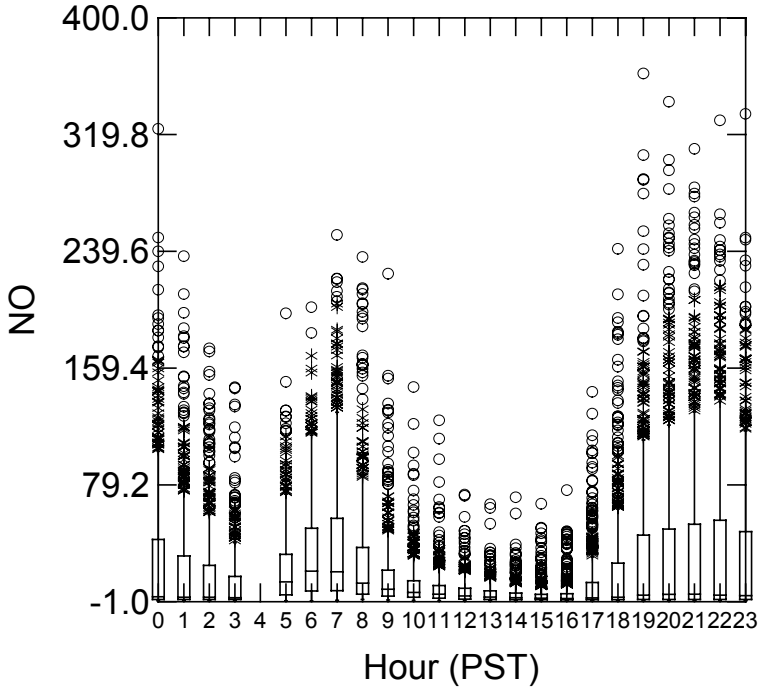


Figure 5.2.4-21. Diurnal box whisker plot of nitric oxide (NO) at the Central Site (Fresno First Street) for November 1, 2000, through April 30, 2002; concentrations are in ppb.

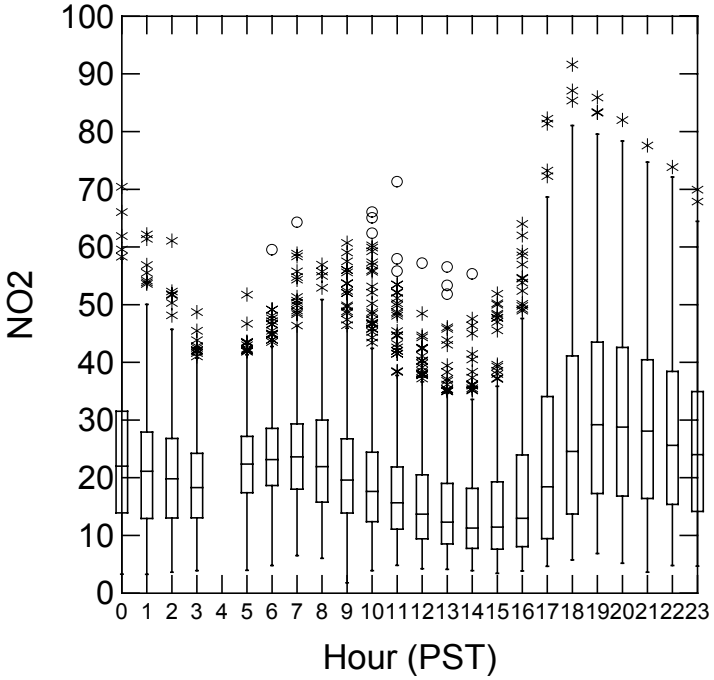


Figure 5.2.4-22. Diurnal box whisker plot of nitrogen dioxide (NO_2) at the Central Site (Fresno First Street) for November 1, 2000, through April 30, 2002; concentrations are in ppb.

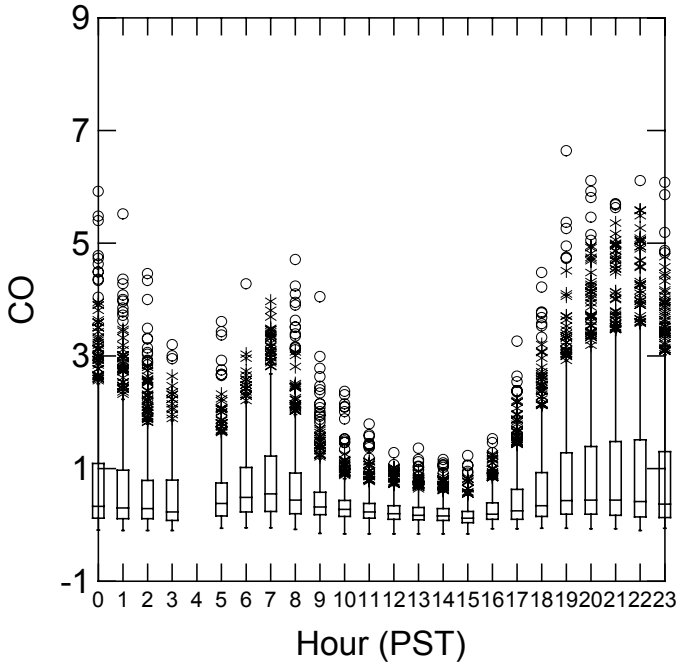


Figure 5.2.4-23. Diurnal box whisker plot of carbon monoxide (CO) at the Central Site (Fresno First Street) for November 1, 2000, through April 30, 2002; concentrations are in ppm.

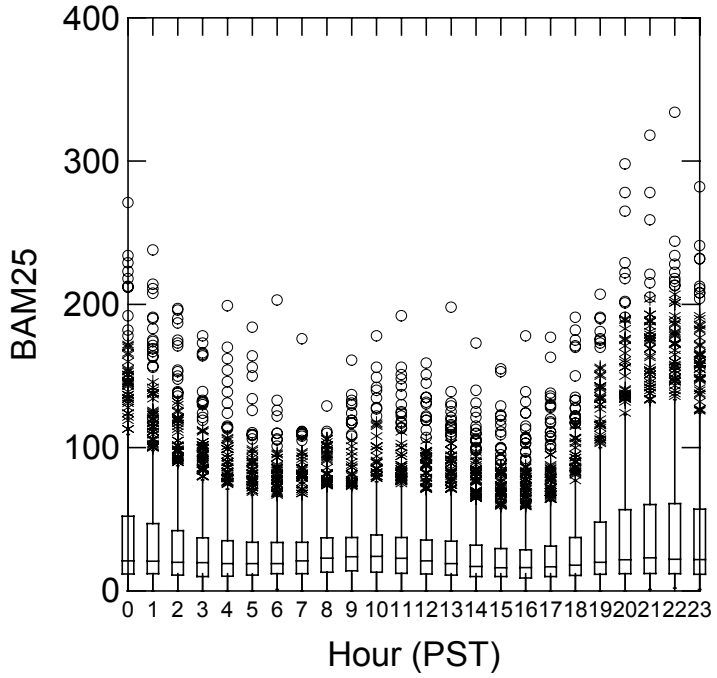


Figure 5.2.4-24. Diurnal box whisker plot of $PM_{2.5}$ mass (BAM25) at the Central Site (Fresno First Street) for November 1, 2000, through April 30, 2002; concentrations are in $\mu g/m^3$.

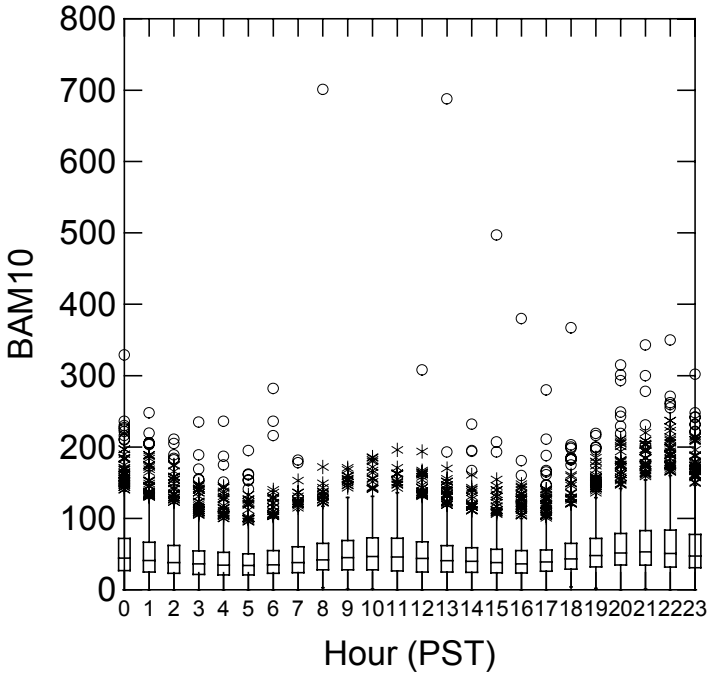


Figure 5.2.4-25. Diurnal box whisker plot of PM_{10} mass (BAM10) at the Central Site (Fresno First Street) for November 1, 2000, through April 30, 2002; concentrations are in $\mu g/m^3$.

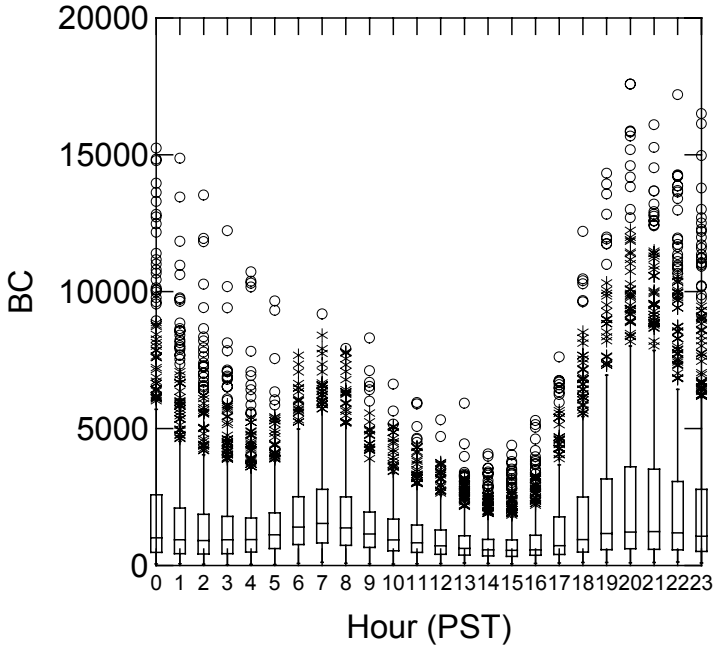


Figure 5.2.4-26. Diurnal box whisker plot of black carbon (BC) at the Central Site (Fresno First Street) for November 1, 2000, through April 30, 2002; concentrations are in ng/m^3.

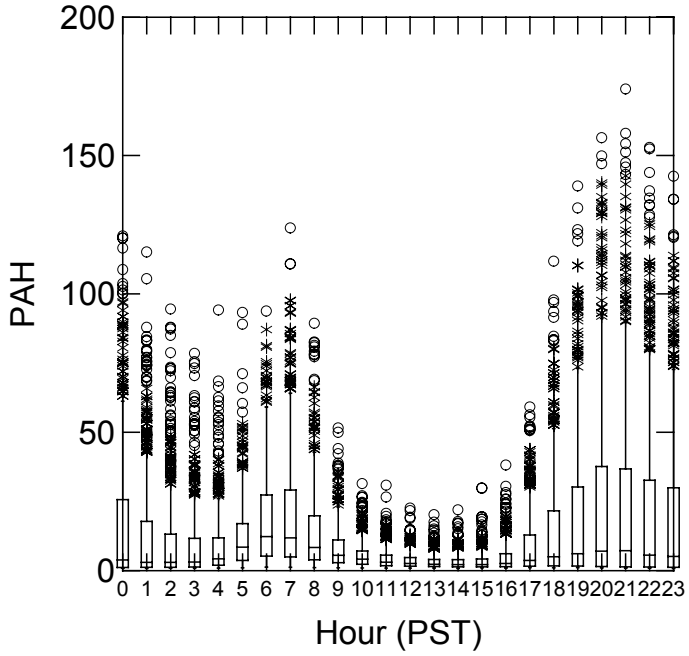


Figure 5.2.4-27. Diurnal box whisker plot of particle-bound polycyclic aromatic hydrocarbons (PAH) at the Central Site (Fresno First Street) for November 1, 2000, through April 30, 2002; relative concentrations are in fA.

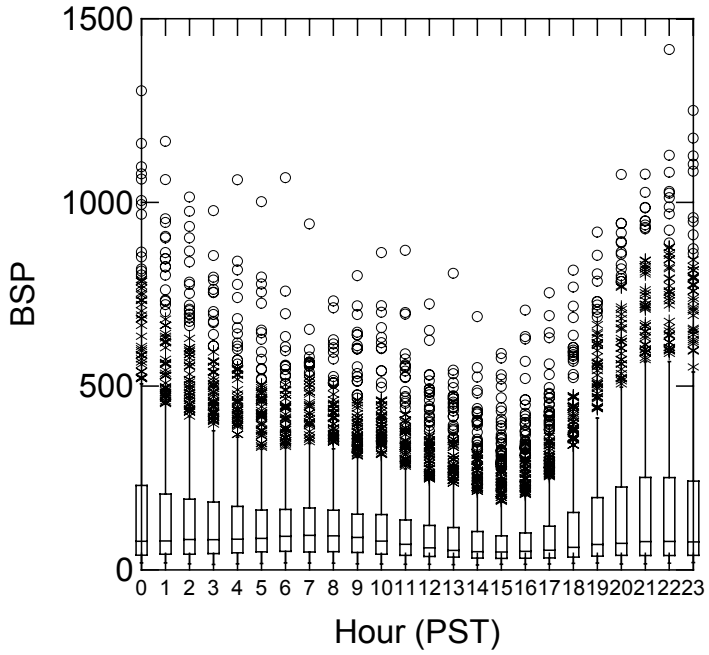


Figure 5.2.4-28. Diurnal box whisker plot of particle scattering (BSP) at the Central Site (Fresno First Street) for November 1, 2000, through April 30, 2002; concentrations are in Mm^{-1}.

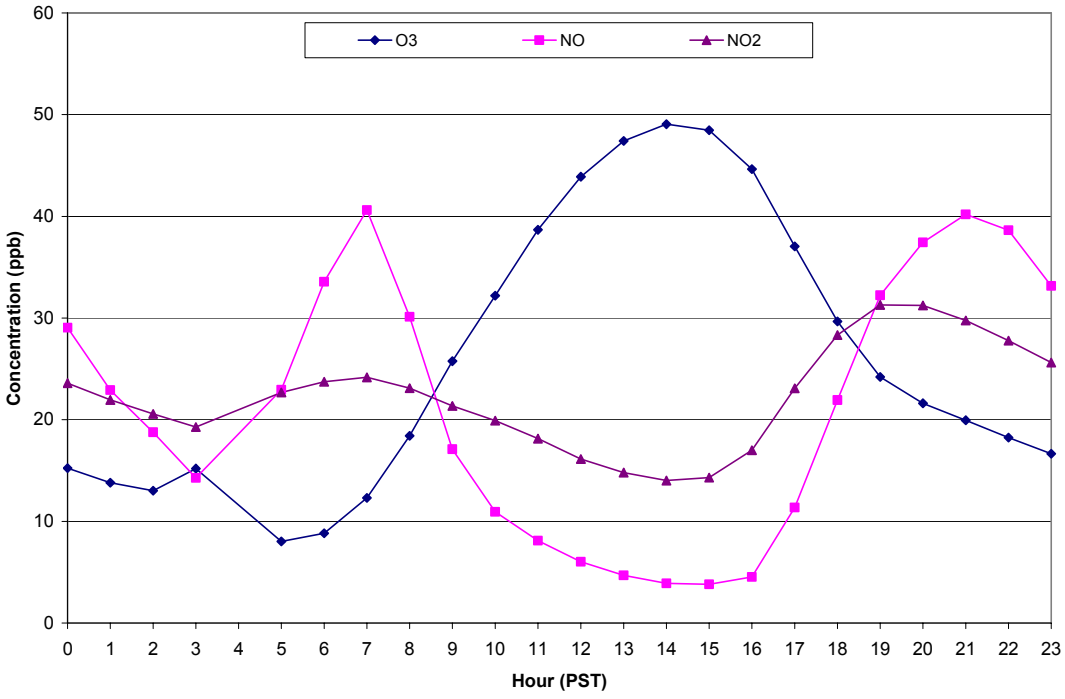


Figure 5.2.4-29. Average diurnal profile of ozone (O_3), nitric oxide (NO), and nitrogen dioxide (NO_2) at the Central Site (Fresno First Street) for November 1, 2000, through April 30, 2002.

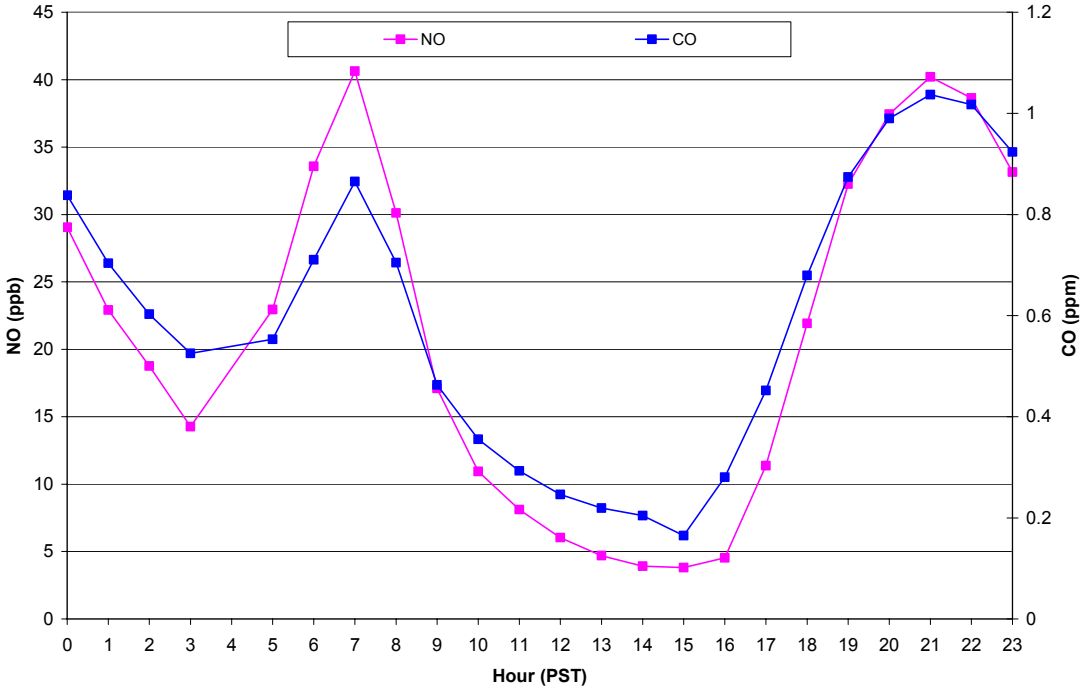


Figure 5.2.4-30. Average diurnal profile of nitric oxide (NO) and carbon monoxide (CO) at the Central Site (Fresno First Street) for November 1, 2000, through April 30, 2002.

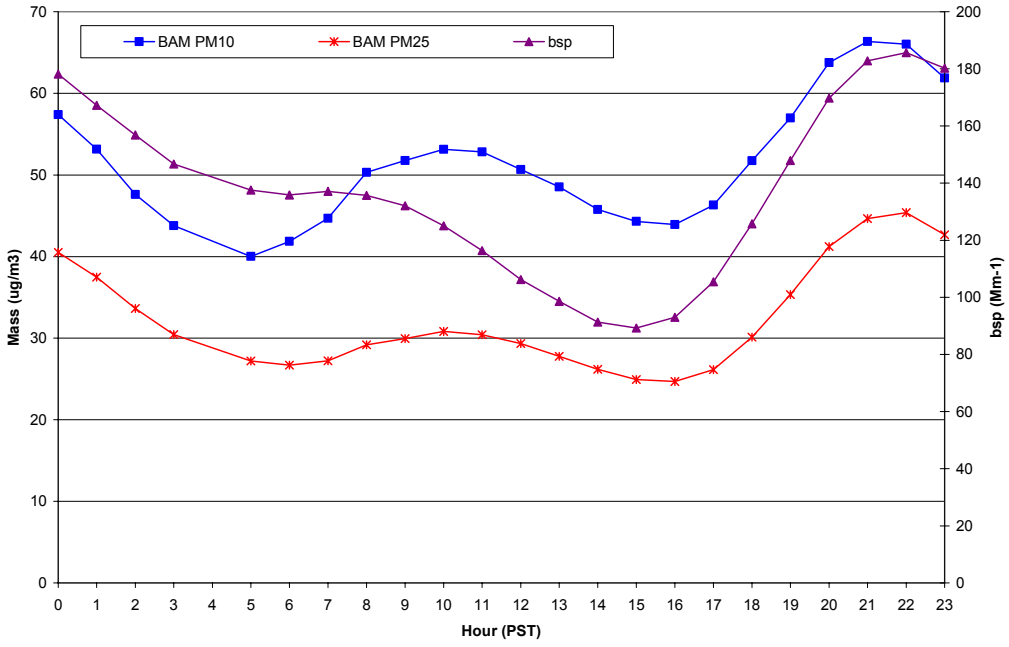


Figure 5.2.4-31. Average diurnal profile of $PM_{2.5}$ mass (BAM PM25), PM_{10} mass (BAM PM10), and particle scattering (bsp) at the Central Site (Fresno First Street) for November 1, 2000 through April 30, 2002.

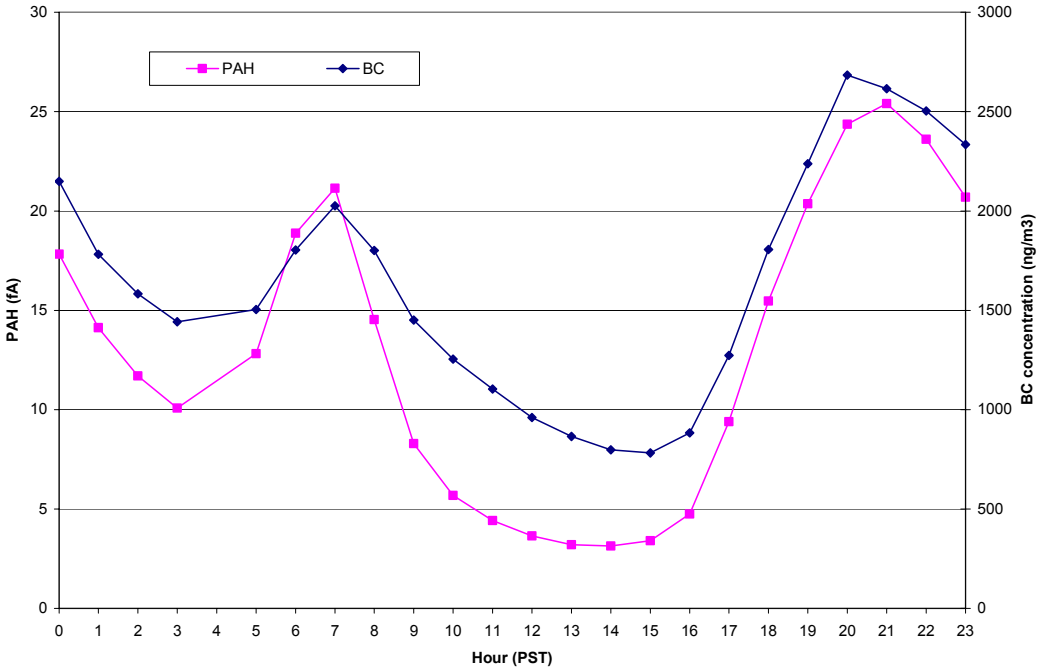


Figure 5.2.4-32. Average diurnal profile of particle-bound polycyclic aromatic hydrocarbons (PAH) and black carbon (BC) at the Central Site (Fresno First Street) for November 1, 2000, through April 30, 2002.

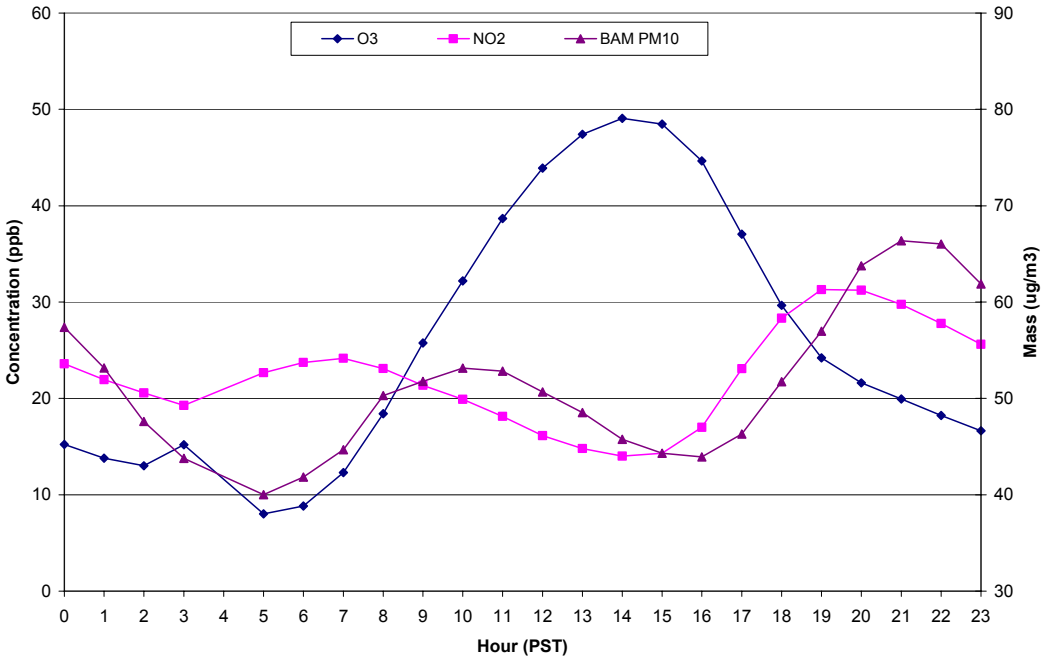


Figure 5.2.4-33. Average diurnal profile of ozone (O_3), nitrogen dioxide (NO_2), and PM_{10} mass (BAM PM10) at the Central Site (Fresno First Street) for November 1, 2000, through April 30, 2002.

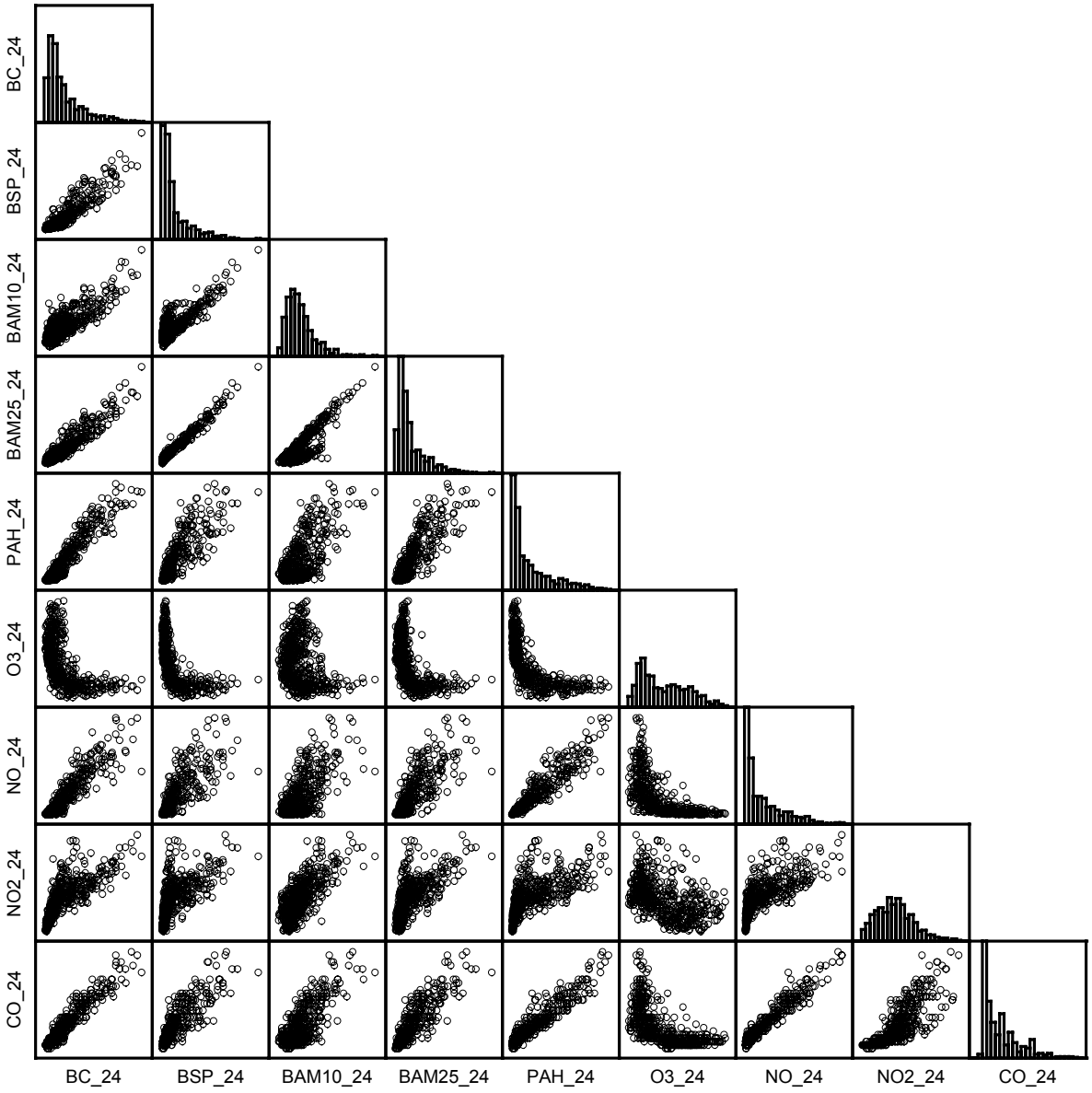


Figure 5.2.4-34. Scatter-plot matrix of 24-hour average concentrations at the Central Site (Fresno First Street) for November 1, 2000, through April 30, 2002. Shown are results for the following parameters: black carbon (BC_24), particle scattering (BSP_24), PM_{10} mass (BAM10_24), $PM_{2.5}$ mass (BAM25_24), polycyclic aromatic hydrocarbons (PAH_24), ozone (O_3_24), nitric oxide (NO_24), nitrogen dioxide (NO_2_24), and carbon monoxide (CO_24).

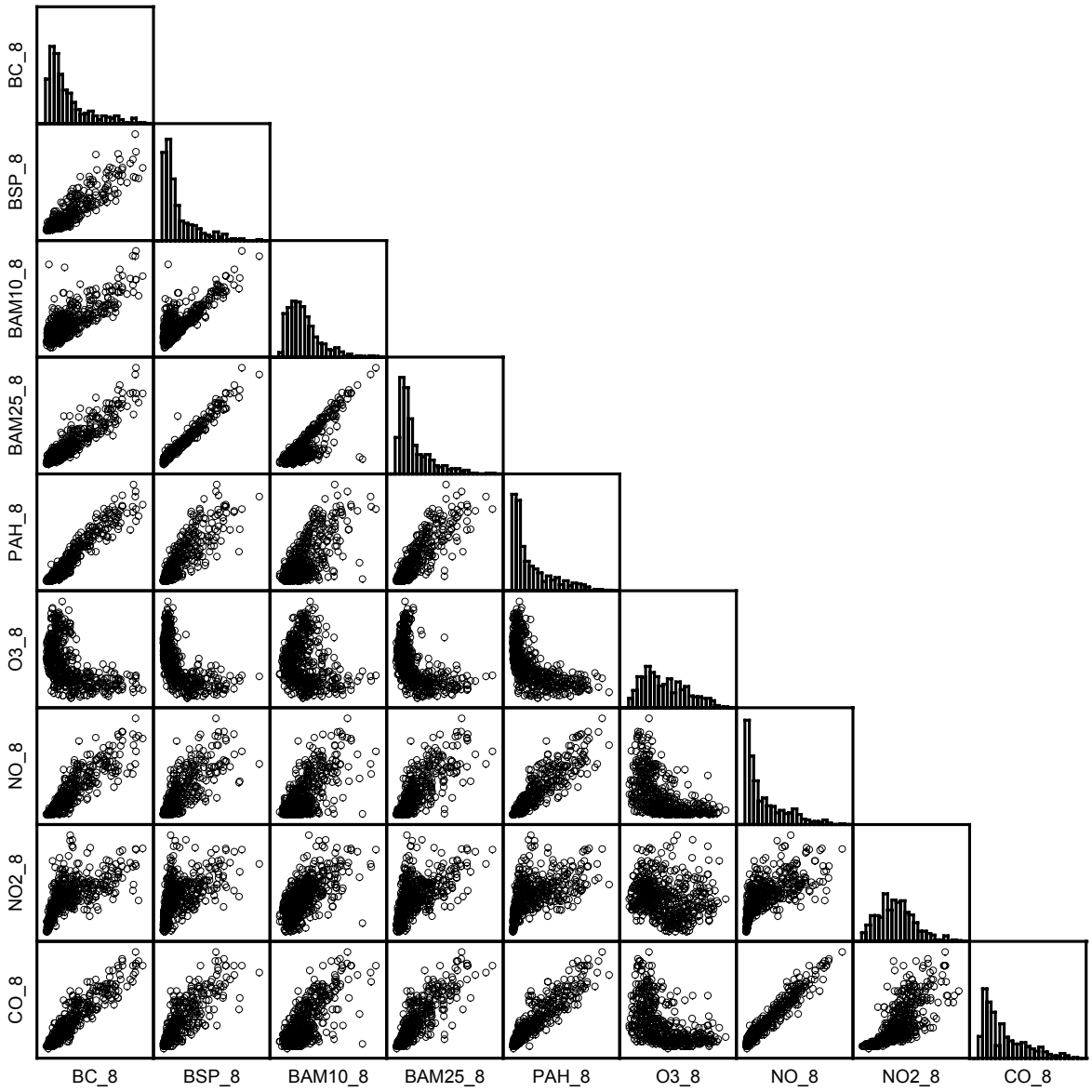


Figure 5.2.4-35. Scatter-plot matrix of maximum 8-hour average concentrations at the Central Site (Fresno First Street) for November 1, 2000, through April 30, 2002. Shown are results for the following parameters: black carbon (BC_8), particle scattering (BSP_8), PM_{10} mass (BAM10_8), $PM_{2.5}$ mass (BAM25_8), polycyclic aromatic hydrocarbons (PAH_8), ozone (O_3_8), nitric oxide (NO_8), nitrogen dioxide (NO_2_8), and carbon monoxide (CO_8).

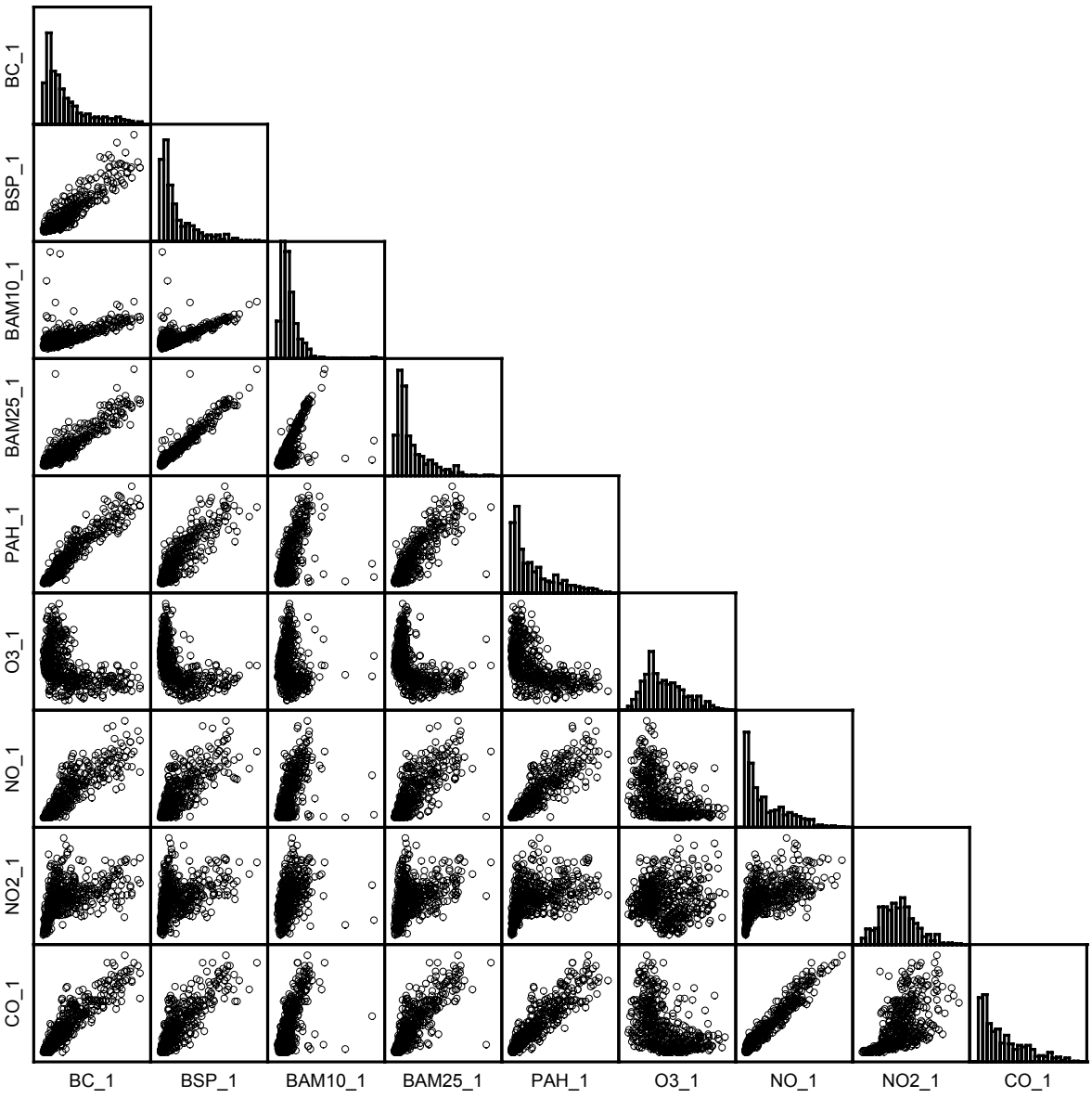


Figure 5.2.4-36. Scatter-plot matrix of maximum 1-hour concentrations at the Central Site (Fresno First Street) for November 1, 2000, through April 30, 2002. Shown are results for the following parameters: black carbon (BC_1), particle scattering (BSP_1), PM_{10} mass (BAM10_1), $PM_{2.5}$ mass (BAM25_1), polycyclic aromatic hydrocarbons (PAH_1), ozone (O_3_1), nitric oxide (NO_1), nitrogen dioxide (NO_2_1), and carbon monoxide (CO_1).

5.2.4.2 Integrated Measure

5.2.4.2.1 Endotoxin

Only a limited number of endotoxin samples from the Central Site have been analyzed to date; these have focused on those corresponding to the Home Intensive samples. However, clearly a large range in exposure can be seen in the ten samples analyzed from March, 2002 (see Figure 5.2.4.5.1-1), where the concentration of endotoxin in the samples ranged over an order of magnitude.

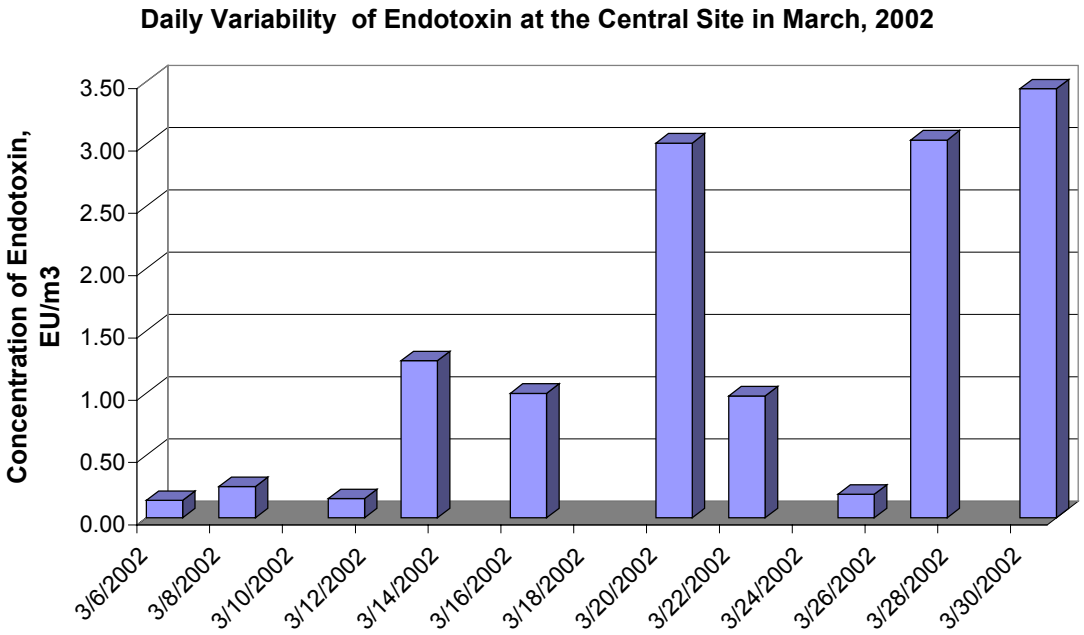


Figure 5.2.4.2.1-1. Concentration of airborne endotoxin measured at the Central Site on the ten days which correspond to home intensive sampling. Note that the concentration of endotoxin ranges from 0.14 to 3.4 endotoxin units per cubic meter.

5.2.4.2.2 Pollen Grains

All pollen in samples collected from November 15 2000 to the end of January 2002, have been counted and identified to date, with the exception of a 30 day period in April-May 2001 (Figure 5.2.4.2.2-1). The variety of species identified in Fresno is large and reflects the surrounding agricultural community. The main pollen season in 2001 started at the end of February. During the month of March the total daily pollen concentration exceeded 3500 pollen m^{-3}. By the end of May the total daily concentration decreased to ~200 pollen m^{-3}. There was a second, much weaker, pollen season from September through October with daily concentrations of 300 to 400 pollen m^{-3}.

The most dominant species was *Morus*, which started flowering during the first week of March (Figure 5.2.4.2.2-2). The maximum, extremely high, concentration of 2464 pollen m^{-3} was measured on March 21, and pollen grains were found throughout the month of April. *Morus* has a small pollen grain with a diameter of 18-19 microns; this pollen grain is known to cause serious respiratory problems (e.g., in Arizona, Halonen et al., 1997). During the spring flowering season (March-April) the daily pollen concentrations of ash (*Fraxinus*), sycamore/American plane tree (*Platanus*), olive (*Olea*), oak (*Quercus*) and nuts, especially pistacio (*Pistacia)* were high, between 250 and 300 pollen m^{-3}. The American Academy of Allergy, Asthma and Immunology suggests for trees the following definitions for low, moderate, high and very high: 0-14, 15-89, 90-1499 and >1500 pollen m^{-3}, respectively. All the species mentioned except *Pistacia* are known to cause respiratory problems. According to the literature, *Pistacia* (both the cultivated and the ornamental pistacio) has not been documented as an identified airborne pollen grain in this connection; thus, we know very little about its allergenicity although it is known that the nut itself can be a cause of food allergies. *Pistacia* seems to have a high content of starch particles; and on several occasions *Pistacia* pollen was observed to be broken, releasing its starch particles, or the pollen grain was "empty" but starch particles could be recognized on the same stroke.

The concentrations of grasses and weed pollen are moderate to high from March to the end of September. Spring is the main grass pollen season, from mid-March to the end of June. In May, daily concentrations can rise to 180 pollen m^{-3}. Grass pollen, with and without starch particles, and starch-particle-releasing grass pollen grains were observed throughout the year. Starch particles are <2 microns in diameter, released from hydrated pollen and documented to be allergen bearing at least for allergenic grasses (Grote et al., 2001; Marks, 2001). Grass continues flowering throughout the summer and fall; in Fresno the concentrations remained low to moderate during this period.

Ragweed occurred in September-October, but only in low to moderate concentrations. Also the concentrations of other weeds, such as Chenopods and *Amaranthus* were generally low to moderate during the summer and fall season.

Generally, during the springtime with the very high pollen concentrations, the day to day variation within the same species could be considerable. Generally, at the beginning of the pollen season the concentrations can increase tenfold from one day to another and over 500 times within a few days (e.g., *Morus*).

In general, the pollen concentrations seem to be very high in Fresno. Since the measurements have only taken place for one whole year, we cannot conclude whether this is typical for Fresno. However, on the basis of one pollen season, the diurnal pattern for the pollen concentrations and the timing of pollen release for different plants can be studied. Preliminary analysis of the data shows, for example, that the highest pollen concentrations can be expected between 11am and 2 pm in Fresno. However, the time of the pollen release is different and individual for each species depending on their ecological demands; for example, summer flowering grasses release their pollen around 10 a.m. and grasses flowering in the spring between 12 and 2 p.m.; of the two *Morus* species, one releases pollen between 8 a.m. and 10 a.m., and the other in the early afternoon. This information is very important for preventive healthcare.

After February 2002, only days with ongoing home intensive study have been analyzed for the Central Site and will be discussed later.

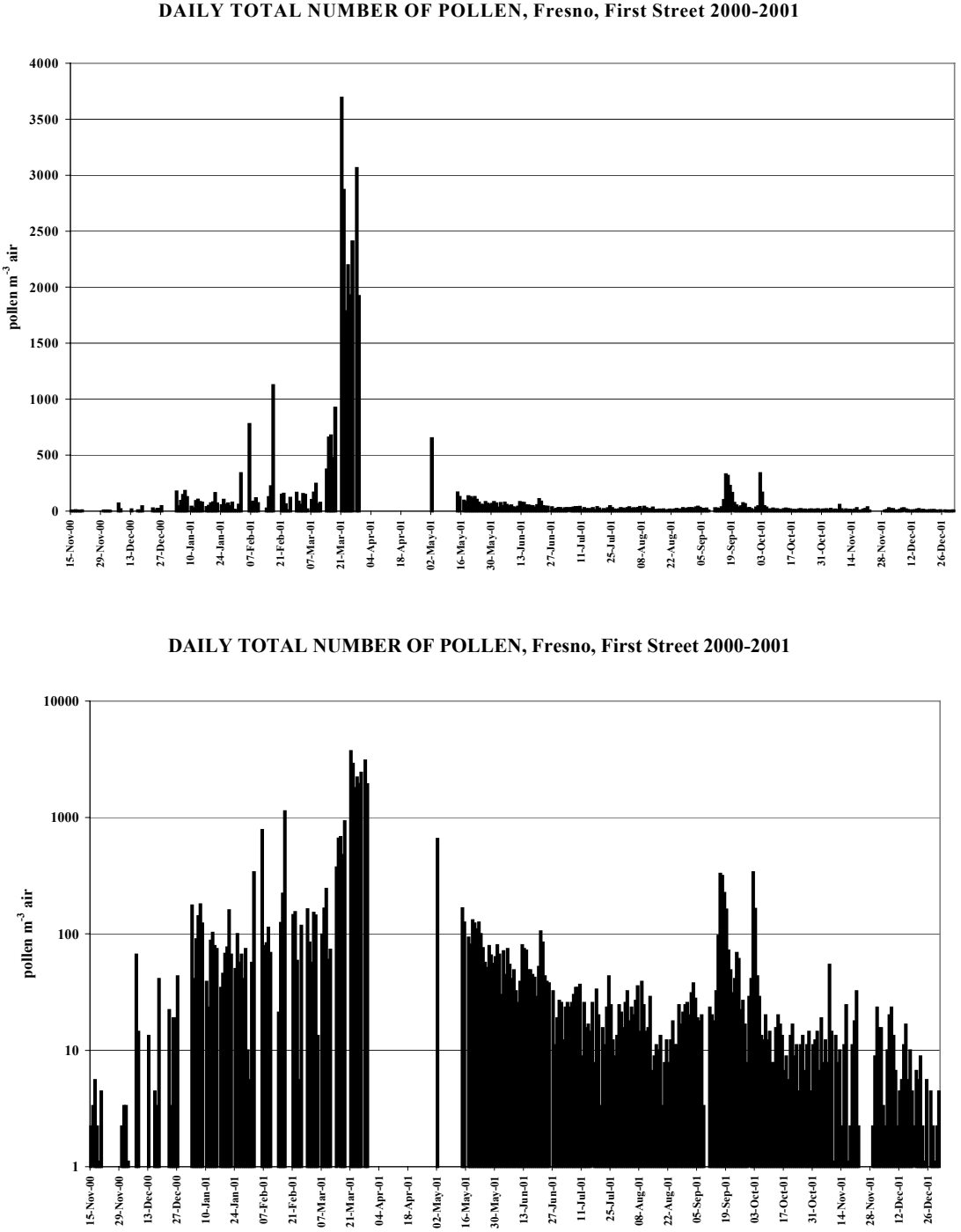


Figure 5.2.4.2.2-1. The daily total concentration of pollen grains at Fresno Central Site, November 2000–December 2001. In the lower diagram a logarithmic scale is used.

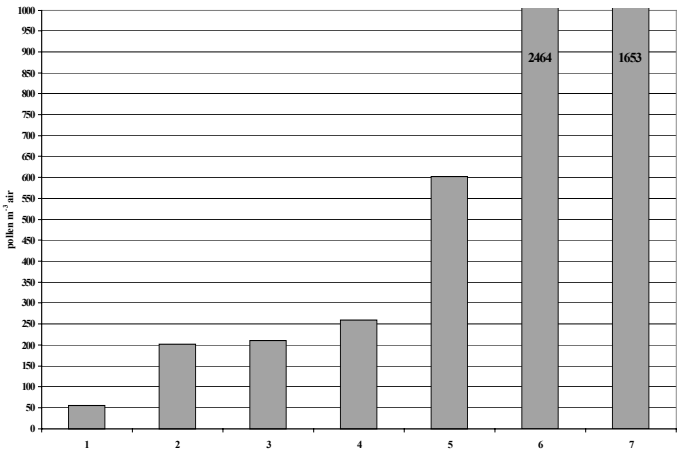


Figure 5.2.4.2.2-2. Total daily concentrations for *Morus* for seven consecutive days in March.

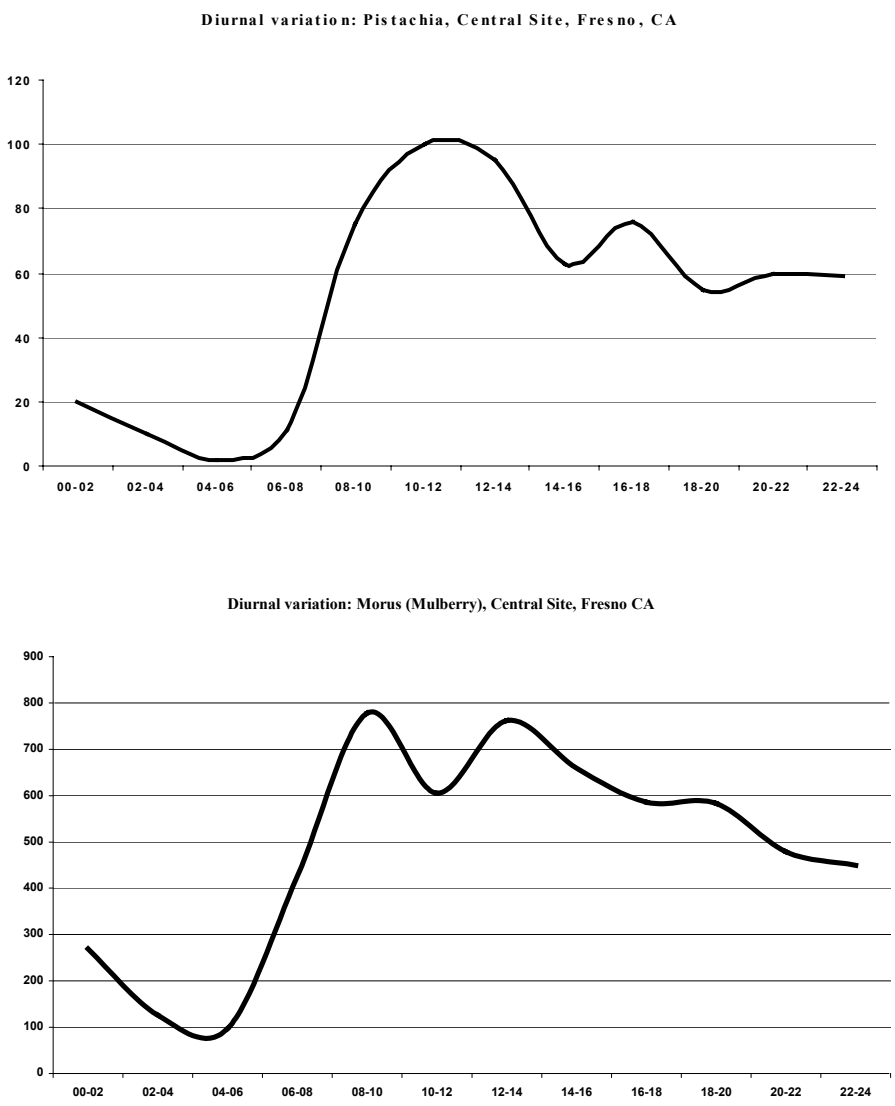


Figure 5.2.4.2.2-4. Example of two different diurnal patters for airborne pollen from the Central Site in Fresno.

5.2.4.2.3 Fungal spores

Fungal spores have been analyzed and identified from November 15, 2000, to the end of July 2001. During most of the analyzed period the concentrations are moderate to high (AAAI: moderate fungal spore concentrations, 6500-12999 spores m^{-3} air; high, 13000-49999 spores m^{-3} air; and very high, >50000 spores m^{-3} air) reaching the highest concentrations at the end of April and beginning of May (see Figure 5.2.4.2.3-1).

The most frequently found spore type was *Cladosporium* with values mostly ranging from 5000 to 32000 spores m^{-3} air. This season with moderate to very high numbers lasted from December to mid-May (see Figure 5.2.4.2.3-2). In May the concentrations decreased to less than 5000 spores m^{-3} air. *Cladosporium* is considered to be one of the most common and important allergenic fungi globally.

Alternaria is another important fungal aeroallergen and its concentrations were relatively high throughout the whole period, as shown in Figure 5.2.4.2.3-3. In Europe the aeroallergy service recommends 30-99 for moderate concentrations, 100-500 as high, and >500 as very high for *Alternaria*, since the size of the *Alternaria* spore is bigger than most of the airborne fungal spores. If we use the European scale the number of *Alternaria* in Fresno during the first part of 2001 would have been mostly high or very high. The highest concentrations were found from mid-March to the beginning of May, ranging from 600 to 1880 spores m^{-3} air. *Alternaria* values dropped suddenly in May; this might have been due to the increase of the mean daily temperature over $+25^{o}C$.

The spores from the plant pathogenic fungi were very common in Fresno. An example of a plant pathogenic fungal spore, *Ustilago*, is shown in Figure 5.2.4.2.3-4. Little is known about the relationship between these fungal spores and human respiratory health. Spores from agriculture-related fungal species increased in numbers in March and culminated in May and the numbers were low during the summer months. Their occurrence might correlate with farming activities.

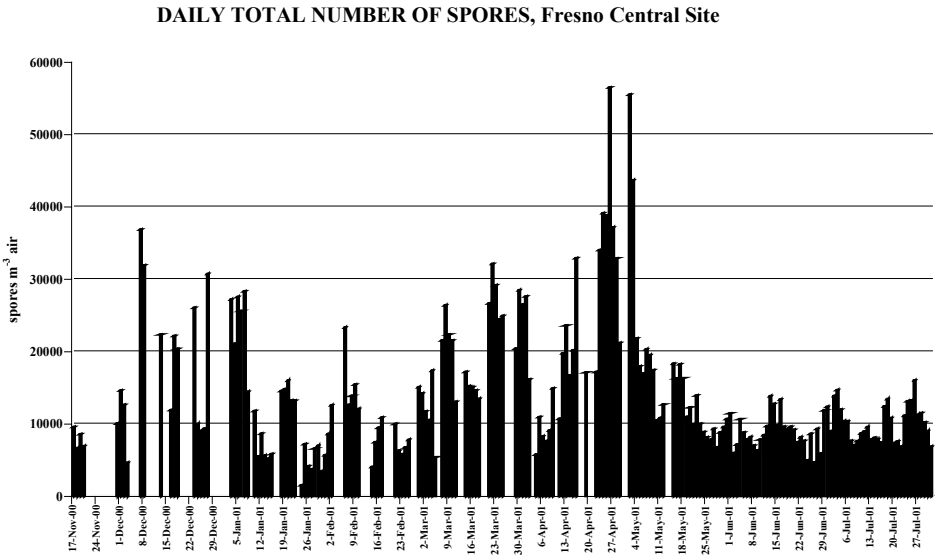


Figure 5.2.4.2.3-1. Daily total concentrations of fungal spores at the Fresno Central Site, July 2001.

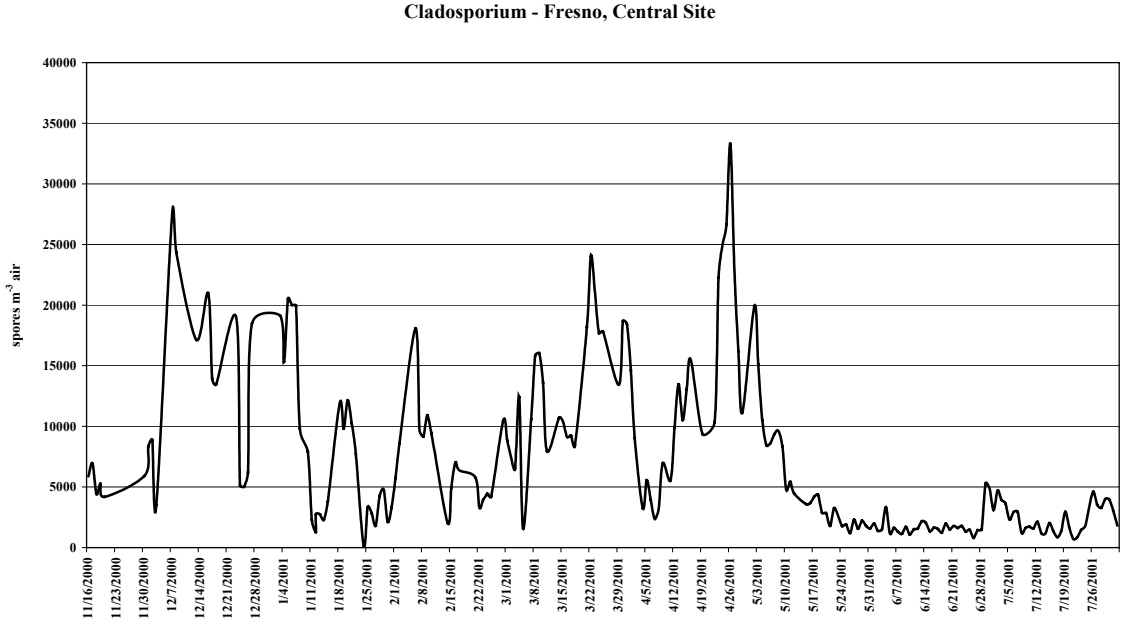


Figure 5.2.4.2.3-2. *Cladosporium* concentrations in Fresno Central Site.

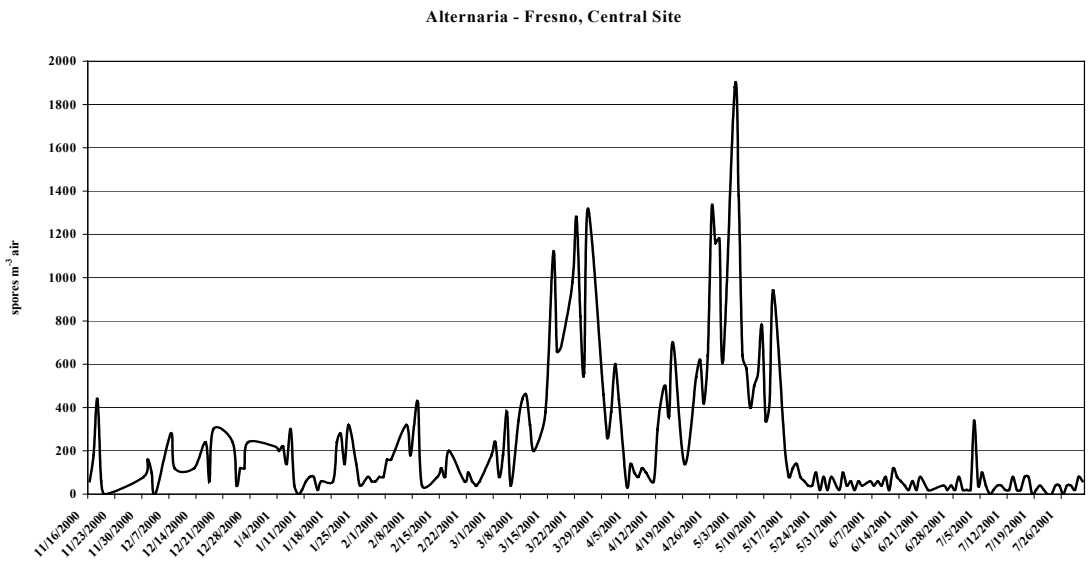


Figure 5.2.4.2.3-3. *Alternaria* concentrations in the Fresno Central Site.

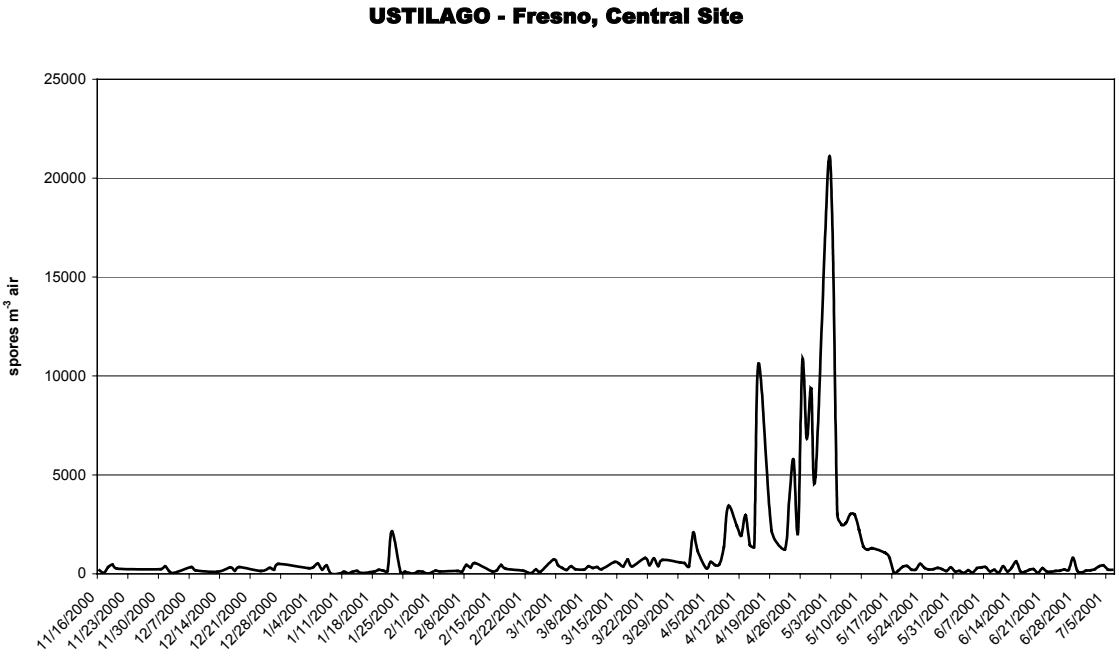


Figure 5.2.4.2.3-4. An example of a plant pathogenic fungal spore, *Ustilago*, and its concentrations at the Fresno Central Site.

5.3 SCHOOL MEASUREMENT SPECIFICATIONS

As indicated above, a major hypothesis guiding the design of the exposure component of FACES is that the air quality parameters of interest vary at different spatial scales in Fresno. In order to evaluate the extent of spatial variations, the FACES exposure assessment incorporates measurements at a large number of locations in the community, including numerous elementary schools. The specific objectives of the school monitoring are to characterize

- spatial gradients in ambient concentrations within the Fresno region and
- ambient concentrations at schools attended by FACES participants.

Data from the schools can be compared with those from the Central Site and from homes monitored in the Home Intensive in order to characterize the spatial gradients and understand differences between conditions at the schools and homes of subjects.

ARB elected to make measurements at elementary schools using two mobile trailers equipped with air pollution monitoring equipment. The mobile trailers were designed, constructed, deployed, tested, and operated by ARB. The FACES exposure team provided recommendations for the parameters to be measured and the sampling locations and durations. The principal recommendations of the FACES exposure team were to

- use instruments and samplers in the mobile trailers that are identical to those used at the Central Site in order to assure comparability of the data and minimize measurement bias;
- conduct an intercomparison study in order to evaluate the comparability of the mobile trailers and Central Site measurements; and
- measure air pollutants at schools attended by FACES participants for at least four weeks at a time. Specifically, it was recommended that sampling take place at one school for a relatively long time (more than six months) and at a series of other schools from four to eight weeks at a time.

The ARB accepted the recommendations and has committed to deliver quality-assured data for Fresno schools to the FACES project team for use in the exposure assessment.

Parameters Measured at the Schools

The FACES health scientists identified the high priority pollutants for examining asthma-air pollution interactions. Based on those priorities, the FACES exposure team recommended measuring the following parameters on an hourly basis at the schools: ozone, NO, NO_x, SO_2, CO, $PM_{2.5}$ mass, PM_{10} mass, EC, OC, lumped polycyclic aromatic hydrocarbons (PAHs), light scattering by particles, particle number, wind speed, wind direction, temperature, and relative humidity. In addition, daily measurements of PM_{10} mass, PM_{10} endotoxin, PM_{10} metals, speciated PM_{10} PAHs, pollen grains, and fungal spores were recommended. Note, the meteorological measurements are needed to allow interpretation of pollutant transport and source-receptor relationships for the various parameters being measured. The specific instruments and samplers recommended for these measurements are listed in **Table 5.3-1**.

In order to obtain data from the mobile trailers that are comparable to those at the Central Site, it is essential to have the same calibration, operation, and quality assurance procedures used in the trailers as are used at the Central Site. Following collection, the samples need to be handled with the same procedures and analyzed by the same laboratory as used for the Central Site. Common procedures are needed to minimize the role of instrument bias and measurement error in the evaluation of spatial gradients within the community. With faithful adherence to consistent procedures, differences in 1-hr and daily concentrations exceeding ±5% to 7% can be interpreted as real differences, not just inherent measurement error.

Table 5.3-1. Measurement equipment in the FACES mobile trailers.

Parameters	Reported Sample Duration (Data logger interval)	Instrument or Sampler Type	FACES Priority Agent
Ozone	Hourly (5 min)	API 400	Yes
NO, NO_x (for NO_2)	Hourly (5 min)	Teco 42	Yes
SO_2	Hourly (5 min)	Teco 43 (model to match Central Site)	Yes
CO	Hourly (5 min)	Dasibi 3008	Yes
Continuous PM_{10} mass	Hourly	PM_{10} BAM	Yes
Continuous $PM_{2.5}$ mass	Hourly	$PM_{2.5}$ BAM	Yes
PM_{10} mass, endotoxins, metals	Daily	PM_{10} sequential filter sampler	Yes
$PM_{2.5}$ nitrate	Hourly	R&P 8400N	Yes
$PM_{2.5}$ sulfate	Hourly	R&P 8400S	Yes
Black carbon	Hourly (15 min)	Anderson Aethelometer (model to match Central Site)	Yes
Elemental and organic carbon	Hourly	R&P Carbon Analyzer (model to match Central Site)	Yes
Light scattering by particles	Hourly (5 min)	Radiance Research Nephelometer	Yes
PAHs (lumped)	Hourly (5 Min)	EcoChem PAS 2000[1]	Yes
PAHs (speciated)	Daily (1 in 7)	sequential filter sampler[1]	Yes
Particle number	Hourly (5 min)	TSI Model 3022A Condensation Particle Counter	Yes
Pollens and spores	TBD	Burkhard (outdoor with wind vane)	Yes
Wind speed and direction	Hourly (5 min)	Met One	No
Temperature and relative humidity	Hourly (5 min)	Met One	No

[1] The PAH measurement equipment is funded by the EPA Office of Transportation and Air Quality.

Sampling Locations and Durations

The exposure team surveyed approximately 20 candidate schools in Fresno and Clovis and provided recommendations to ARB for sampling locations and durations. The schools were selected based on the following four criteria:

1. Schools that are attended by FACES participants, preferably by more than one participant.
2. Schools that are located near the residences of children participating in the Home Intensive.
3. Schools that represent specific gradients in important parameters, such as near Highway 99, between Highway 99 and the Central Site, between the Central Site and the Clovis site, and between urban and rural areas.
4. Schools that represent a range of neighborhood-type situations, including near (both east and west of) Highway 41, near busy arterial streets, within a residential neighborhood away from busy streets, and near rural/agriculture use areas.

The ARB is deploying and operating the two mobile trailers at the schools for a 14-month period that partially overlaps the FACES Home Intensive sampling period. ARB contacted the schools and made arrangements to facilitate sampling on their premises. The recommended sampling strategy involves locating one trailer at a single school throughout the study and locating the other trailer at different schools for six- to eight-week periods. Fremont School, which is located west of the Central Site and east of Highway 99, was selected as the location for the long-term trailer. The short-term trailer is currently deployed at Bullard TALENT School which is located northwest of the Central Site. The recommended locations and schedule for the short-term trailer are shown in **Table 5.3-2**. Note that the start and end dates are contiguous; however, it will take about one week to move the trailer and initiate monitoring operations at each new location.

Table 5.3-2. Locations and schedule for the second mobile trailer**.**

School	Start Date	End Date
Bullard TALENT	June 1, 2002	July 22, 2002
Viking	July 22, 2002	September 9, 2002
Easterly or Burroughs	September 9, 2002	October 21, 2002
Maple Creek or Copper Hills (Clovis)	October 21, 2002	December 9, 2002
Forkner	December 9, 2002	January 27, 2003
Holland or McCardle	January 27, 2003	March 17, 2003
Cole (Clovis)	March 17, 2003	May 5, 2003
Miramonte (Clovis)	May 5, 2003	June 23, 2003
Easterly or Burroughs (other site)	June 23, 2003	August 11, 2003

5.4 ROUTINE HOME SURVEY AND SAMPLING

During each of the panel studies, several measurements and evaluations are conducted to assess home specific factors that will affect the exposure assessment. These include

- Home survey
- Exposure related questions on the daily diary
- Moisture measurements
- Collection of dust for measurement of allergens and endotoxin. The dust is 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 are 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

5.4.1 Methods

5.4.1.1 Moisture Protocol and Preliminary Results

A household survey was developed to gather information about each home, such as type of stoves, smoking policy, windows in child's home, signs of mold, etc. During each home panel, two home inspectors visit the home. One home inspector collects survey data about housing characteristics, while a second home inspector uses 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, each home will be visited three times a year during differing seasons.

5.4.1.2 Household Dust

5.4.1.2.1 Collection, Weighing, and Storing

We developed a new method to collect household dust. This method uses a commercial handheld vacuum cleaner (a Shark) connected to a modified industrial hygiene sampling cassette (see Figure 5.4 - 1). The cassette contains window screening on the front to sieve out large particles; dust is collected on a cellulose support pad. Dust is 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 is 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 CD2 - Protocols and SOPs. As noted in Table 7-3, the sampling time was increased from 2 minutes per sample to 4 minutes per sample in August 2001.

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

5.4.1.2.2 Allergens

We are analyzing five allergens: dog, cat, cockroach, and two kinds of dust mites. Enzyme-Linked Immunosorbent Assays (ELISA) is performed to determine the concentrations of allergens in house dust samples.

The dust samples (~ 50 mg) are 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 is coated with a capture monoclonal antibody (mAb) and placed in a refrigerator overnight. Allergen standard and dust extracts are added to the microplate and serially diluted with PBS-T by a multi-channel pipet on the plate. After incubation at room temperature, a detector mAb is added to the plate. Streptavidin peroxidase (for cat and mite allergens) or Peroxidase conjugated Goat anti Rabbit (for dog and cockroach allergens) is added to the plate after incubation. Finally, color developing solution is added to the plate; the intensity of the color developed in each well is proportional to the amount of the allergen present. The plate is read at 405 nm by a spectrophotometer. The allergen concentration in the sample is calculated by using the standard curve.

5.4.1.2.3 Endotoxin

We are using the Limulus amebocyte lysate (LAL) test 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 are extracted by sonication in 5ml of triethylamine phosphate (TAP) buffer for one hour. After extraction, the sample is serially diluted in endotoxin-free test tubes

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

5.4.1.3 Passive Samplers Collected in the Home

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

5.4.1.3.1 Nitrogen Dioxide

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

5.4.1.3.2 Ozone

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

5.4.1.3.3 Second-hand Smoke

Second-hand smoke (SHS) is sampled by collecting nicotine as a tracer. Nicotine is 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 filter. The sampler is approximately 1.5 inches in diameter and 1 inch high, made of plastic, and weighs half an ounce.

The nicotine is extracted from the filter in ethanolic water, the pH is adjusted with sodium hydroxide to free the nicotine molecule, which is then concentrated by liquid liquid extraction into heptane. A small aliquot of the heptane layer is then injected into a gas chromatograph with a nitrogen selective detector. Standards (0.01 ug/ml through 10 ug/ml) are run on each analysis day, as are 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 will be 0.02 ug/m^3, although greater sensitivity is possible if needed, and we have achieved lower levels routinely in selected studies. This method was developed in our laboratory, and we have used these passive samplers in hundreds of homes in California and thousands of homes across the United States. The method

has been successfully tested against other methods in an intercomparison study of several methods, and in fact, was the only passive sampler to perform effectively.

5.4.2 Results

5.4.2.1 Home Survey

To date, 243 home surveys have been conducted and 233 diaries have been returned to the office.

A good distribution of home sources was found in this population (see Table 5.4.2.1-1). Nearly half the families had a pet (23% had a dog and 19% had a cat), 45% had a gas stove, 53% had signs of mold or mildew. On the other hand, nearly all families had air conditioning, 95% had policies restricting or banning smoking in the home, and 64% said they used a fireplace at least one day per month. As of July 1, 2002, moisture measurements have been collected in the living rooms of 230 homes and in the bedrooms of 226 homes. These measurements were collected in a total of 140 homes. The maximum moisture measurements collected in the living rooms ranged from 4.0-30.0%, with a mean value of 9.2%. In the child's bedrooms, the maximum measurements ranged from 4.0-23.0% with a mean of 8.8%. Survey-reported, visual evidence of moisture was detected in 7.8% of the living rooms and in 17.9% of the bedrooms. At this point, visual evidence of moisture was not associated with differing moisture levels ("higher" or "lower," as defined above) with statistical significance in either the living room or the child's bedroom. This is due in part to the relatively small percentage of homes with survey-reported evidence of moisture. As we continue to collect moisture measurements in the homes, the resulting data will allow for the examination of multivariate associations between moisture and microbial growth across seasons and housing types. Eventually, we will examine the association between indoor moisture and its relationship to indoor biological agents and short and long term measures of asthma morbidity. The mean moisture measurements were 9.2 in the living rooms and 8.8 in the children's bedrooms.. The distribution of the highest moisture measurements are given in Figure 5.4.2.1-1.

* Table 5.4.2.1-1. Housing Characteristics of FACES Population.

Housing Characteristics	Number	Visit Type	Distribution of Reponses		
			Yes No. (%)	No No. (%)	.Missing No. (%)
Any Pets	184	B	80 (44)	101 (55)	3 (1)
Any cats	184	B	34 (19)	146 (79)	4 (2)
Any dogs	184	B	43 (23)	137 (75)	4 (2)
New cat last 3 mo.	99	6	5 (5)	92 (93)	2 (2)
New dog last 3 mo.	99	6	4 (4)	93 (94)	2 (2)
Gas stove (cooking)	184	B	82 (45)	98 (53)	4 (2)
Wood stove (heat)	184	B	3 (2)	173 (94)	8 (4)
Air conditioning	184	B	171 (93)	10 (5)	3 (2)
Air conditioning	99	6	93 (94)	4 (4)	2 (2)
Pests (last 12 months)	184	B	78 (42)	106 (58)	0
Water damage	184	B	44 (24)	136 (74)	4 (2)
Mold or mildew inside home	184	B	98 (53)	78 (42)	8 (5)
Fireplace use >=1day/month	236	H	151 (64)	85 (36)	0

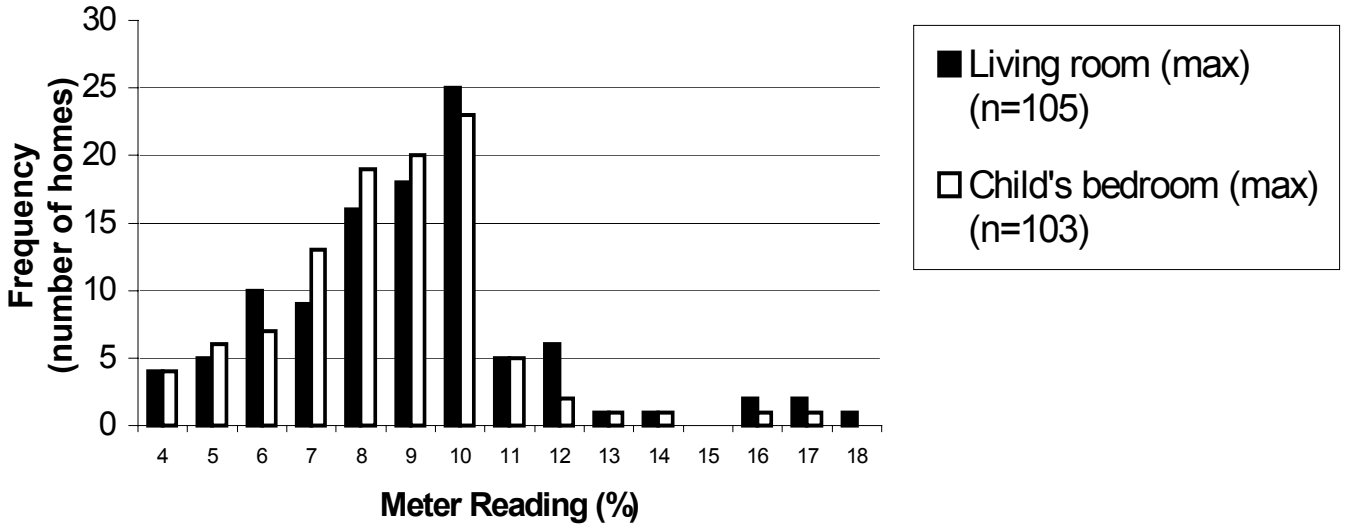


Figure 5.4.2.1-1. Distributions of highest moisture measurements.

5.4.2.2 House Dust

Dust samples are collected during each home visit from both the child's bed and one integrated sample from the kitchen and living room floors. As of May 31, 462 dust samples had been collected, weighed, and aliquoted for analysis for allergens and endotoxin.

5.4.2.2.1 House Dust—Allergens

There are five allergens being analyzed on each dust sample: cat, dog, cockroach, and two dust mite allergens. As of June 21, 1,355 allergen assays had been performed on the dust samples; detectable levels of each of these have been found in some homes. See Figure 5.4.2.2.1-1.

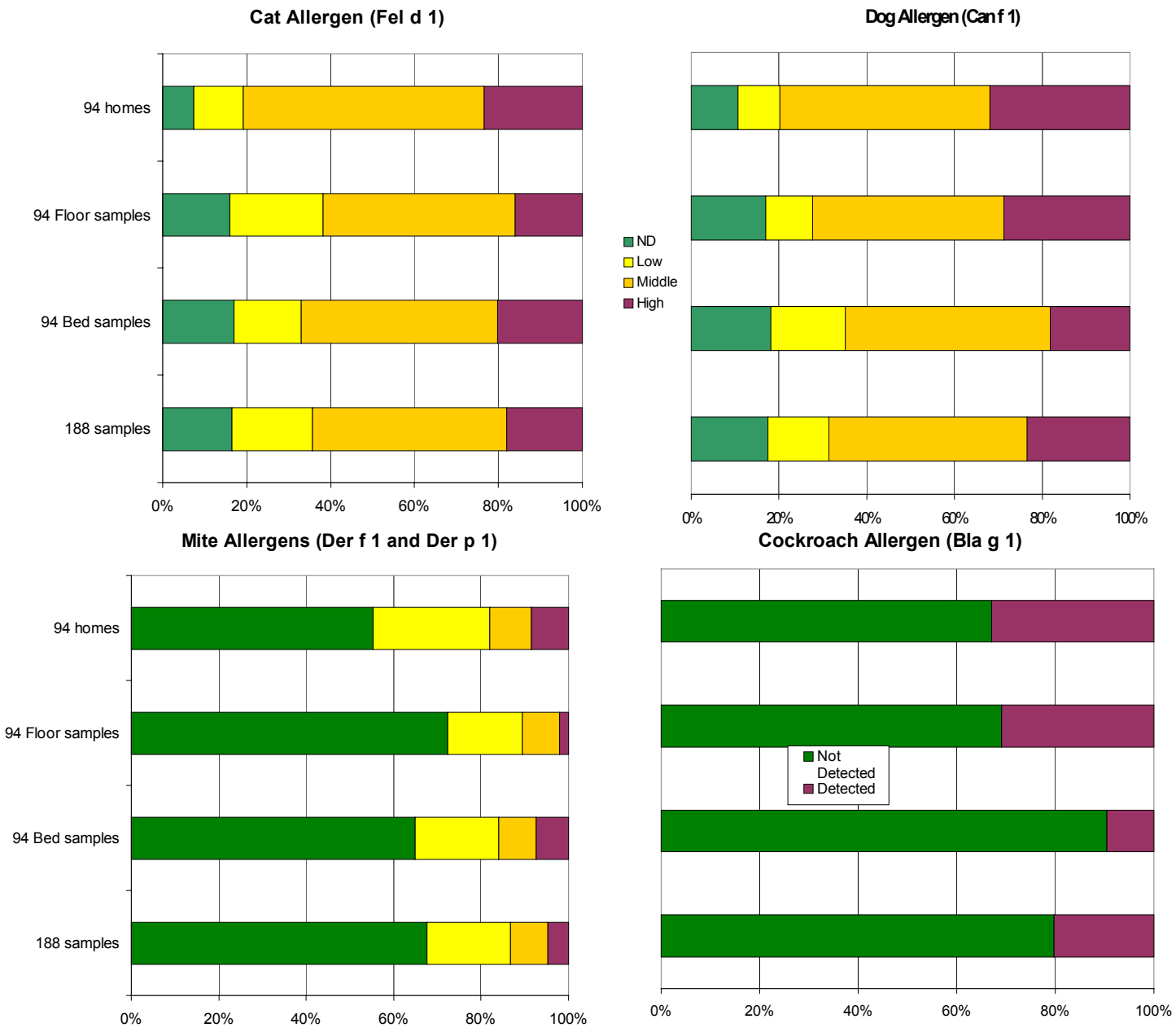


Figure 5.4.2.2.1-1. Concentrations of allergens in house dust. Low is defined as <1 ug/g dust for cat and dog; medium is 1-8 for cat, 1-10 for dog, and 2-10 for mite; high is > 8 for cat and > 10 for dog and mite. The distribution for "94 homes" uses the larger allergen value found in the floor and bed samples of each home, and the distribution for "188 samples" is the distribution for all samples collected in the 94 homes.

5.4.2.2.2 House Dust—Endotoxin

Dust samples are collected during each home visit. Twenty-seven of these have been analyzed, with the results as shown in Figure 5.4.2.2.2-1. These samples indicate that higher endotoxin concentrations were found on the dust from the floors than that from the beds, but the data are too few to reach definitive conclusions as this point. The concentrations found on the dust were all well above the detection limits.

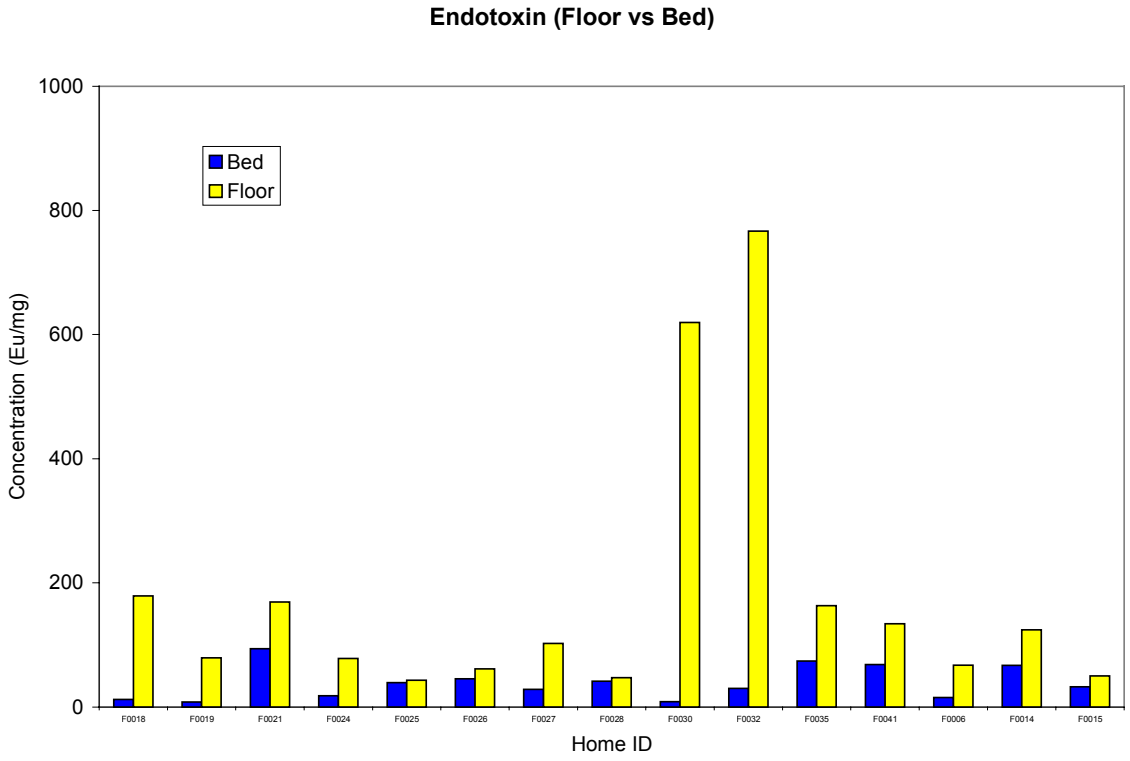


Figure 5.4.2.2.2-1. Endotoxin concentrations (endotoxin units per gram of dust) in floor dust and in dust collected from the bed, at 15 homes.

5.4.2.3 Second-hand Smoke

To date, 205 samples for second-hand smoke (SHS) have been analyzed. The results indicate much lower concentrations than are typically found in homes, which is consistent with the survey data suggesting 95% of FACES homes have "no smoking" policies. The concentrations ranged from less than 0.1 to 6.15 ug/m^3 ; and the distribution of nicotine concentrations are presented in Figure 5.4.2.3-2. The mean concentration was 0.10, with a standard deviation of 0.44 and a median of 0.03. Although the average concentration in the homes of nonsmokers was low (0.05 ug/m^3), the range was less than 0.1 to 1.1. ug/m^3. Among homes with smokers in residence, the mean was 0.64 ($\pm$ 1.83) and the range was less than 0.1 to 6.2ug/m^3; a random sample of homes in New York State found a mean of 2 and a median of 1 ug/m^3 in the homes of smokers (Leaderer and Hammond, 1991).

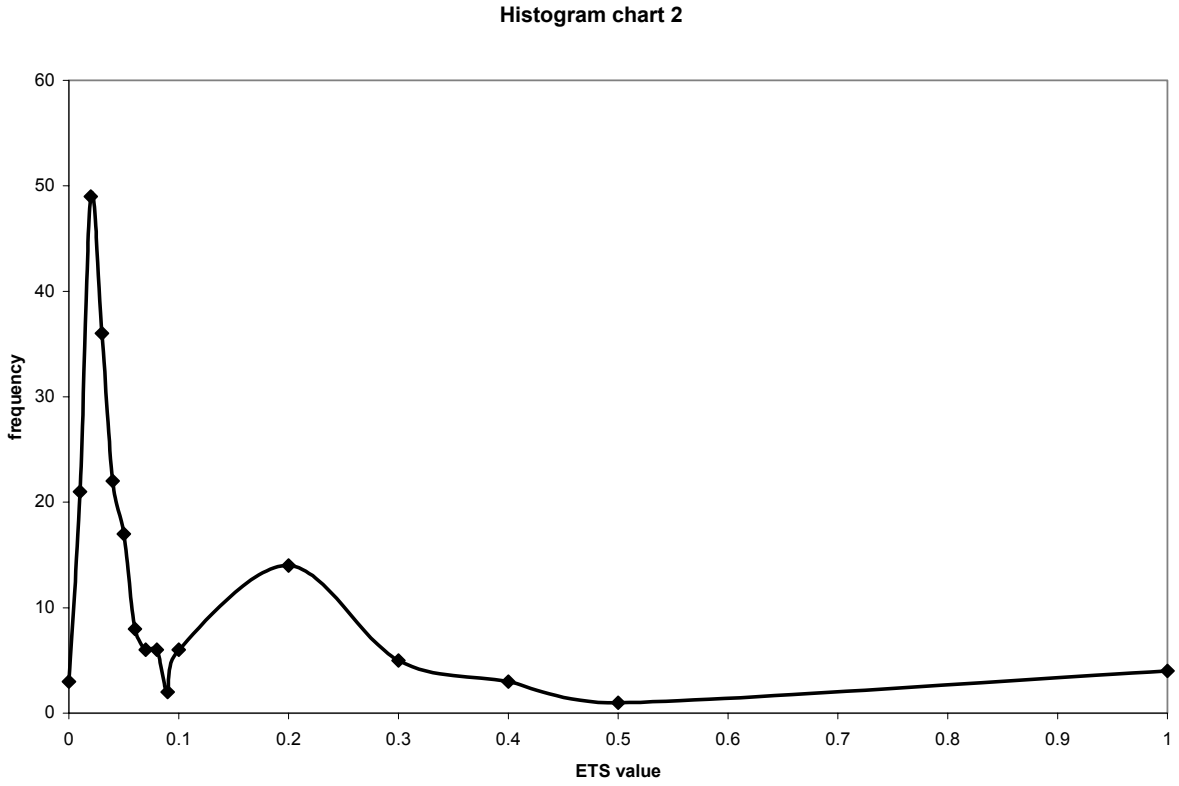


Figure 5.4.2.3-1. Distribution of nicotine concentrations (in micrograms per cubic meter) found in 205 homes. Based on a passive sampler exposed for two weeks. Note the bimodal distribution.

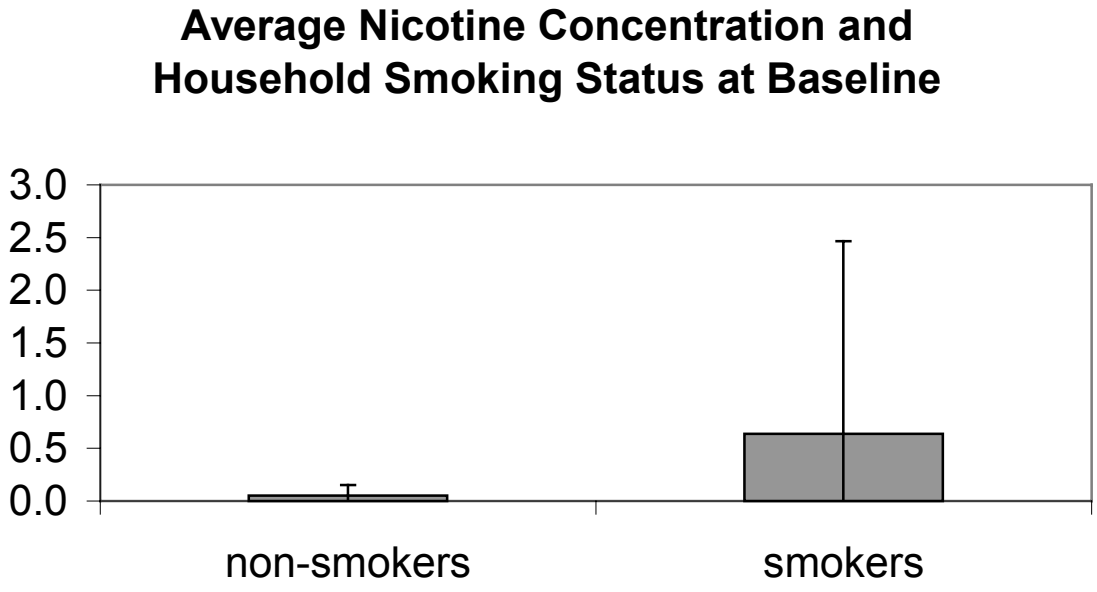


Figure 5.4.2.3-2. Nicotine concentrations ($\mu g/m^3$) in nonsmokers' homes compared with nicotine concentrations in the homes of smokers.

5.4.2.4 Nitrogen Dioxide

As of June 1, 2002, 184 nitrogen dioxide samples collected in the home had been analyzed. The mean concentration was 11.7 (±15.3) ppb, the median concentration was 8.1 ppb, and the range was 0.4 – 140 ppb. The distribution of the concentrations measured is presented in Figure 5.4.2.4.– 1; Figure 5.4.2.4-2 presents the monthly variability of concentrations.

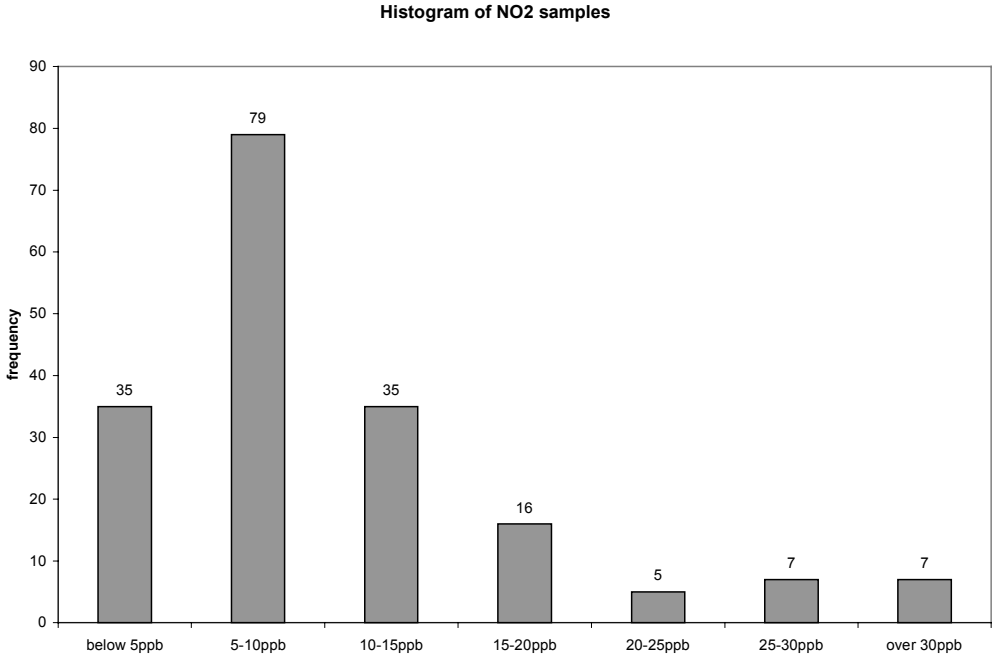


Figure 5.4.2.4-1. Distribution of two-week average NO_2 concentrations measured in homes during the panel studies.

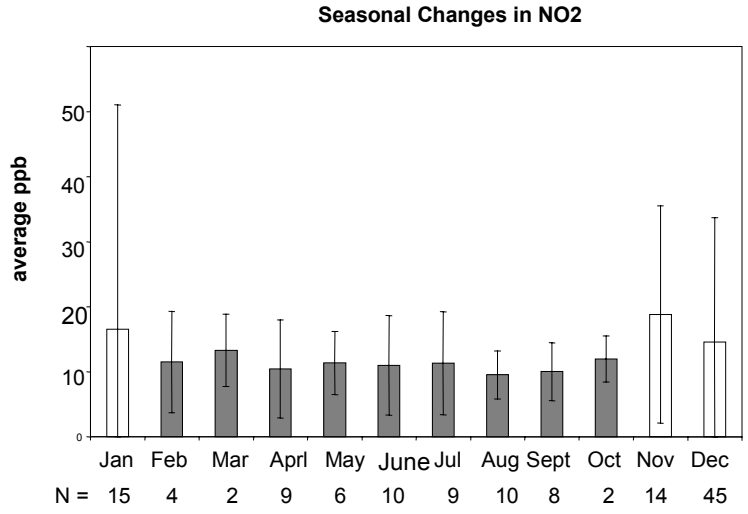


Figure 5.4.2.4-2. Monthly variation of two-week average NO_2 concentrations measured in homes during the panels.

5.4.2.5 Ozone

Sixty ozone samples were collected at the homes during the 2001 ozone season. These samples were collected both inside and outside the homes. The 14-day average concentrations ranged from less than detectable (i.e., less than 0.2 ppb) to 21 ppb., The data are preliminary, and will be analyzed in more detail when more data are available.

5.5 HOME INTENSIVE PROCEDURES

5.5.1 Sampling Strategy and Home Selection

Between 70 and 80 subjects will participate in the Home Intensive sampling. The participants are selected based on the location of the residences, housing characteristics (e.g., combustion sources such as a gas stove), and household smoking status. The residences are categorized by their proximity to roadways and reported use of indoor combustion devices. Homes where participants report smoking indoors are generally excluded from the Home Intensive sampling. Approximately 100 two-week home sampling visits will be conducted between February 2002 and 2003. The plan includes sampling in a subset of homes twice during different seasons. The Home Intensive sampling is conducted at three to five homes during each of 25 two-week panels.

5.5.2 Home Intensive Sampling Methods

The Home Intensive sampling equipment is shown in **Figure 5.5.2-1**. The four main components of the Microenvironmental Exposure Monitoring System (MEMS) are

- a timed, five-leg sampler that collects 24-hr filter samples;
- a nephelometer (Radiance Research, Model M903) that provides continuous 5-minute average particle light scattering measurements;
- a Continuous Recording Air Sampler for Glass Slides (Burkard Manufacturing Company Limited, Cat. No. 9100) that is used to collect pollen and fungal spores over 24 hours; and
- a timed, active ozone sampling system that collects 8-hr integrated ozone samples during the ozone season.

The MEMS has a footprint of 80 cm x 60 cm and a height of 150 cm. Figure 5.5.2-1 shows an indoor MEMS. The outdoor MEMS is identical except that it has an opaque Plexiglas roof and a Mylar cover over the pump box on the bottom for rain and sun protection. Twelve MEMS have been constructed and are deployed in the Home Intensive sampling program. The Home Intensive sampling procedures and equipment are explained in detail in the CD Protocols.

The filter sampling system consists of a pump, a timer, a flow manifold, and five Harvard-type impactors. **Table 5.5.2-1** specifies the targeted pollutants, filter media, filter preparation, and arrangement for each of the five impactors. The impactors use Teflon cassettes to secure the filter media in place. The cassettes are loaded with filters at the Fresno office inside a glove box with filtered air. Stainless steel screens and Teflon spacer rings provide

separation between stacked filters. Polyolefin drain disks support the filters, particularly when abrupt changes in pressure occur. The Harvard-type impactors were selected for use in the Home Intensive sampling because their performance is comparable to the Federal Reference Method (FRM) (Yanosky and MacIntosh, 2001) and they are well characterized for indoor and outdoor sampling (Turner et al., 2000). 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, requiring 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 is set using precise needle valves. The flow rates have been extensively characterized and are stable throughout a broad range of temperatures and filter particle loadings. The impactor flow rates are checked before and after each filter sample is collected using Gilmont rotameters, which have been calibrated against a primary standard. The average of these two measurements is used to calculate the total volume passed through each filter sample. The seven-day timers, which control 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.

The nephelometers obtain 5-minute average particle light scattering values, instrument temperature measurements, and relative humidity (RH) measurements. The nephelometers are stored in a weather-tight container with a fan to ventilate the enclosure and a heater to dry the air stream, when necessary. The heater is controlled by RH measurements and is set to start heating the incoming air stream when the outgoing air stream exceeds approximately 60% RH. The amount of heating increases as the RH increases, and this setting results in a maximum RH of approximately 70% for the air stream passing through the nephelometer. Heating both prevents water droplets from dominating the light scattering measurement and protects the instrument from moisture damage. Heating of the air stream may result in some volatilization of particles, and the heater operation must be considered when analyzing the data. The nephelometers contain a hard drive capable of storing approximately fourteen days of data. Particle light scattering values are calculated by measuring atmospheric scattering and subtracting Rayleigh scattering. Rayleigh scattering is adjusted for temperature measurements and the local average pressure. Nephelometer calibrations are checked before each measurement panel. The nephelometer zero values are first checked by passing the ambient air stream through a filter to eliminate the particles. Acceptable light scattering values for this filtered ambient air are $0 \pm 0.20 \times 10^{-6}$ $1/Mm^{-1}$. A precision point is then checked with a hydrofluorocarbon (HFC-143a) refrigerant, which has a moderate, approximately 90 Mm^{-1}, light scattering value. The nephelometer has a measurement range of 2000 Mm^{-1}; it is desirable to challenge any instrument with a standard that has a value of approximately 80% of the full range of the instrument, but a method has not been developed to calibrate particle-measuring equipment, such as the nephelometer, in the field.

The environmental enclosure for the nephelometer is a modified toolbox bolted to the MEMS scaffold (Figure 2-1a). The design of the MEMS nephelometer enclosure was based on the enclosures used at Fresno First Street and on the FACES trailers. Sample air enters 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 promote condensation of water vapor before the shelter to avoid condensation in the shelter and potential damage to the

nephelometer electronics. Air in the enclosure is continuously purged with a muffin fan, located at the top of the enclosure, which pulls 30 CFM (849 LPM) 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 is approximately 85 exchanges per minute, which is more than adequate. Although inlet effects are not a major concern with this instrument, the inlet diameter is large to minimize contact with the surfaces. Inlet effects are 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.

The Burkard Continuous Recording Air Sampler for Glass Slides (BCRAS) is used to collect airborne bioparticles, like pollen and fungal spores, and is operated on the same 24-hr cycles as the impactors. This sampler works on the same principle as that of the Burkard seven-day recording volumetric spore trap but is designed for continuous operation over a maximum period of 24 hours. Trapping efficiency is the same as that of the Burkard Recording Volumetric Spore Trap; airborne particles are separated from the air with an efficiency greater than 90% for particles with an aerodynamic diameter of 5 μm or more, except for very small spores when the efficiency is proved to be better than that of the seven-day volumetric trap (Stern et al., 1999). The BCRAS also gives a continuous record for indoor concentrations of particles other than pollen and fungal spores, such as human and animal skin cells, fibers, human and animal hair, etc. A constant flow rate of 10 LPM passes through a 1-mm-wide intake slit on the upper case of the instrument. The airborne particles are impacted onto a moving glass microscope slide below. The continuous movement of the slide carrier is set at 2 mm h^{-1} over 24 hours, and the total traveling distance of the slide is 48 mm. The trapping area of glass microscope slides is coated with Dow Corning 280A, which remains stable at high temperatures. The seven-day timer that controls the filter-sampling pump also initiates the Continuous Recording Air Sampler sampling. After exposure, the slides are mounted in glygerol gelatine and microscopically examined for enumeration and identification of pollen and fungal spores.

The active ozone sampling system is operated on the MEMS during the Fresno ozone season, May through October. The active ozone sampling system consists of a glass reaction tube coated with sodium nitrite, a miniature pump, a solenoid valve, and a timer. This active ozone sampling technique was developed and evaluated by Geyh et al. (1999). The flow through the ozone sampling system is controlled by a timer, which opens a solenoid valve on the inlet of the glass reactor and turns on the ozone pump. The 8-hr ozone samples are collected during the period when the highest ozone concentrations typically occur, 1000 to 1800 PDT, which is a subset of the 24-hr period sampled with the other media. These active-flow ozone tubes use the same chemical analysis technique as the passive-flow ozone measurements; the sodium nitrite is converted to sodium nitrate by ozone in the ambient air stream as it passes through the reaction tube. The generated sodium nitrate is measured in the laboratory, and the average ozone concentration is calculated from the measured nitrate concentrations (Geyh et al., 1999). The ozone pumps were borrowed from the University of Southern California and are operated at 65 ml/min. The ozone pump flow rates are checked before and after each panel.

Figure 5.5.2-1. Microenvironmental Exposure Monitoring System (MEMS).

Table 5.5.2-1. 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
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	PallFlex Tissue Quartz (2 stacked) Polyolefin Drain Disk	XAD4 Coating	UCB→ STI/Fresno→UCB

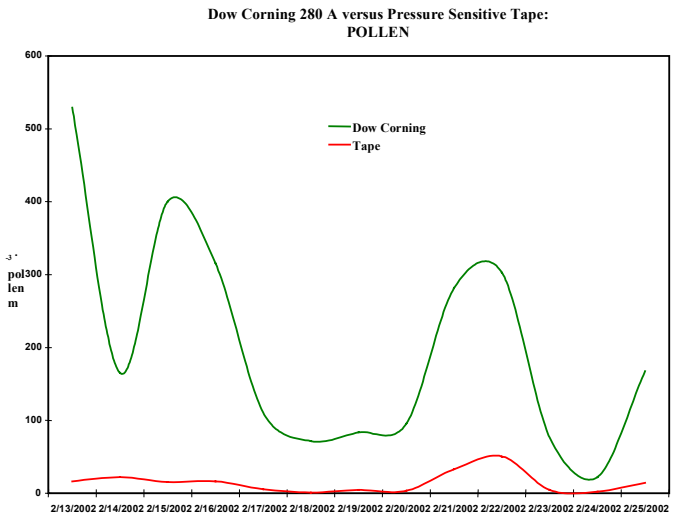
* PAH sampling is funded by the EPA Office of Transportation and Air Quality.

5.5.3 Methods and Quality Assurance for Pollen Grains and Fungal Spores

To evaluate the pollen and fungal spore concentration inside and outside the homes in Fresno we use Continuous Recording Air Sampler for Glass Slides (Burkard Manufacturing Company Limited, Cat. No. 9100). See the CD Protocols for the operating details. This sampler possesses the same sampling properties as the BSVT and the measuring results are known to be comparable (Stern et al. 1999).

This sampler has a flow rate of 10 l min^{-1} and collects the airborne material directly onto the adhesive coated microscopic slide. The slide travel is adjusted to 48 mm in 24 hours, which is equivalent to the speed of the drum in the BVST. The slides are labeled before exposure, and mounted with Glycerine gelatine after the collection.

Since attaching the Dow Corning 280A coated Melinex tape to the slides makes the slides too thick to fit into the sampler, a solvent-based pressure sensitive tape was used during the pilot study and the 3 first panels. This choice was made following the recommendation of one of the leading mycologists in the country (see also Razmovski et al. 1998). Even though the optical quality of the tape adhesive was superior when compared to any other sampling media, the adhesive was changed to Dow Corning 280A for the 4^{th} and subsequent panels (03.20.2002) due to the poor capture efficiency of the pressure sensitive tapes (Fig. 5.5.3-1).



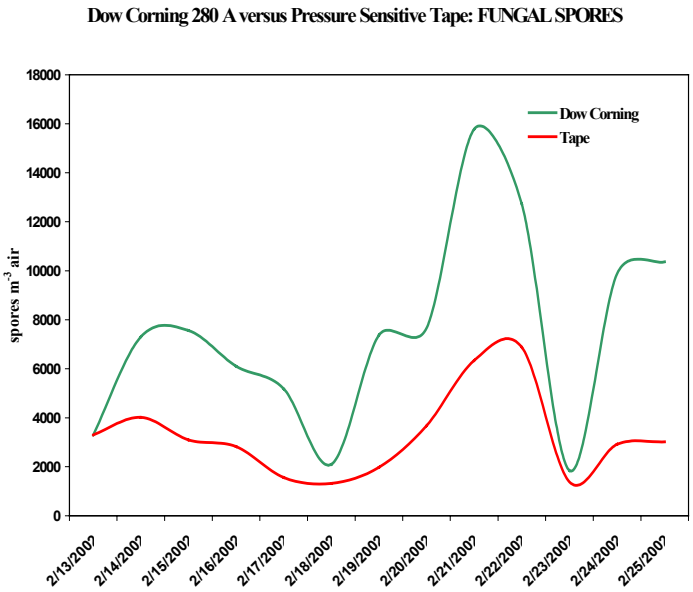


Fig 5.5.3-1. The capturing efficiency of the two different adhesive surfaces tested.

Details on the methods for pollen grain and fungal spore counting and identification are given in Section 5.2, under the Central Site. Due to the mechanical problems with the Continuous Recording Air Sampler ca 9% of the data from the 47 homes is missing.

DATA QUALITY CONTROL

The slide box for each home in the home intensive panels contains blank slides. The field blank is removed from its container momentarily while the normal slide is loaded and unloaded. Since the outdoor concentration of pollen and fungal spores is normally higher than that indoors the duplicate samples are collected mostly outdoors within the home intensive study (one subject in each panel). During different occasions two Continuous Recording Air Samplers are operated at the SuperSite next to the BVST. To ensure the repeatability, efficiency and comparability of the Continuous Recording Air Samplers, one BVST is operated outdoors on the ground level close to the Home Intensive outdoor MEMS during different seasons.

Blank Sample Data

The blank slides for pollen and fungal spores (Field and Trip blank) for the home intensive panels 4 and 5 have been analyzed. The number of airborne pollen and fungal spores in each of the Field blanks has been extremely low, <2 pollen or fungal spores per slide, the trip blanks have been completely empty.

Duplicate Data

The duplicate data for Continuous Recording Air Samplers has been analyzed for one panel. To date only the pollen analysis is completed. The data compare very well, however, the

Continuous Recording Air Samplers seem to be very sensitive to the wind, and when used outdoors they ultimately need to be supplied with a wind protection (Fig 5.5.3-2). In our study, wind protection was installed on the outdoor sampling unit at the time of the first Home Intensive panel (Feb 6, 2002).

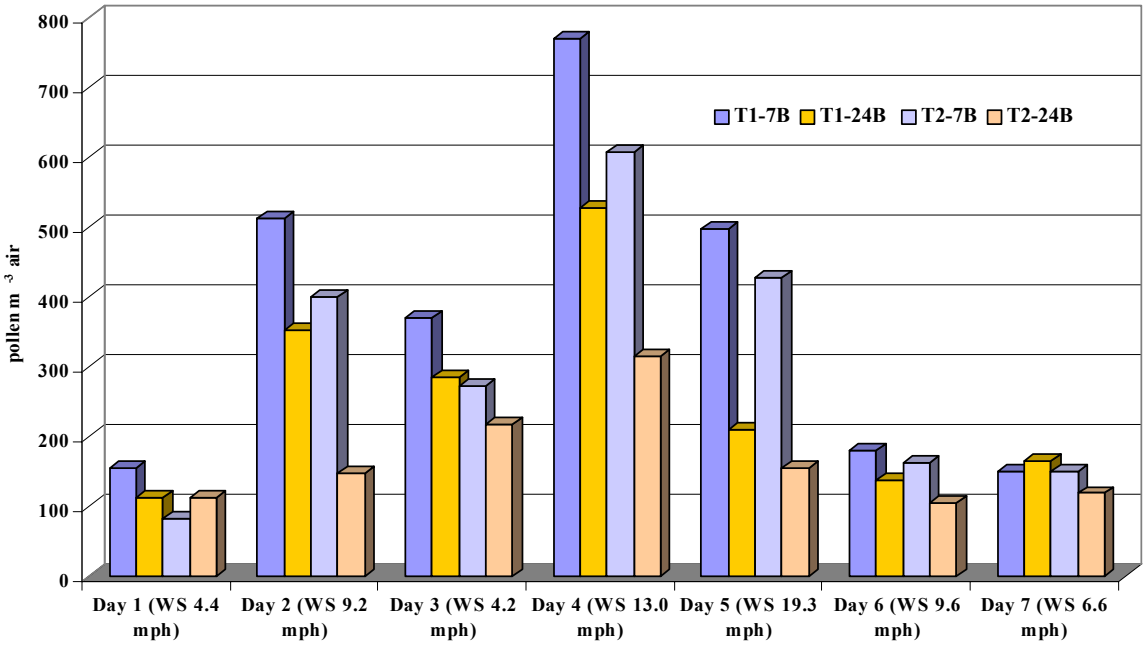


Fig. 5.5.3-2. Number of pollen collected with two collocated uncovered Continuous Recording Air Samplers and two BSVT – units during five different days. During the first two and the last two days the wind speed was over 4.5 m per sec. (adhesive used: Dow Corning 280A).

Comparison of samples

Comparing the Continuous Recording Air Sampler results with the simultaneous data from BVST from the same location, the number of pollen grains generally compares extremely well; however, the BVST seem to collect larger pollen grains (> 30 µm in Ø) about 25% more effectively (e.g., *Quercus* and *Pinus*). The results are fully comparable to the collection efficiency of pollen grains of smaller size and mass (e.g., *Morus*). Since the fungal spores are not yet completely analyzed, we do not know exactly how these two devices compare. Preliminary results indicate that the very small airborne bioparticles (< 5 µm) are collected more efficiently with the Continuous Recording Air Sampler than with the BSVT (see Figure 5.5.3 –3 through 5.5.3-6). The endotoxin analysis shows day-to-day variation similar to the daily total concentration for the MEMS samples (ARB1 and ARB2). Also the concentration differences between the two devices shows a similar trend which suggests that the pollen grains might transport endotoxin on their surface. The dimensional data for these three different pollen types, such as the mean values of the longest axis measurable of pollen orientation, longest axis measurable perpendicular to the length, and the total surface area, are given by Hjelmroos et al. (1999).

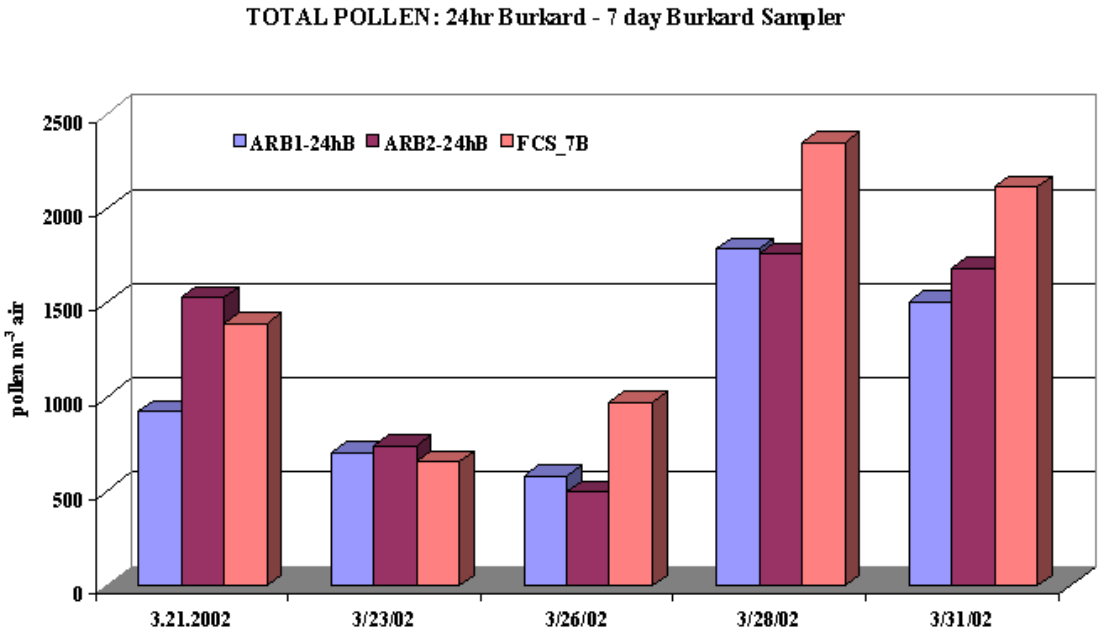


Figure 5.5.3-3. Total daily pollen concentrations collected at the Central Site with two collocated covered Continuous Recording Air Samplers (ARB 1, ARB2) and the BSVT (FCS_7B).

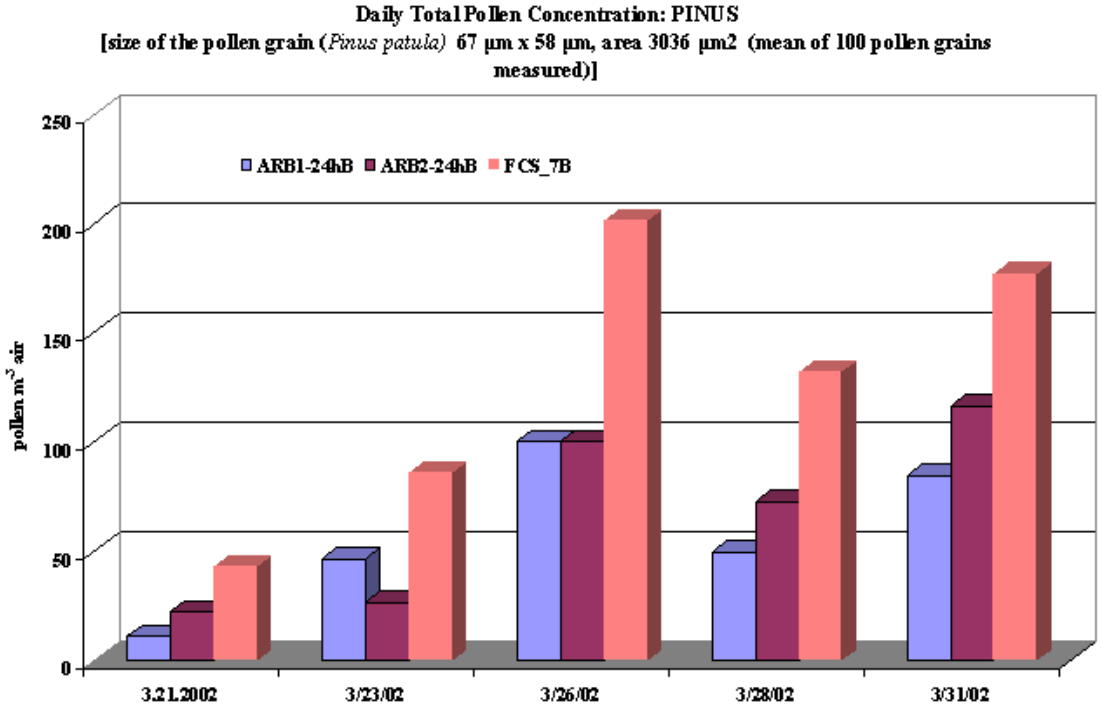


Figure 5.5.3-4. Total daily *Pinus* pollen concentrations (>30 microns) collected at the Central Site with two collocated covered Continuous Recording Air Samplers (MEMS ARB 1, ARB2) and the BSVT (FCS_7B).

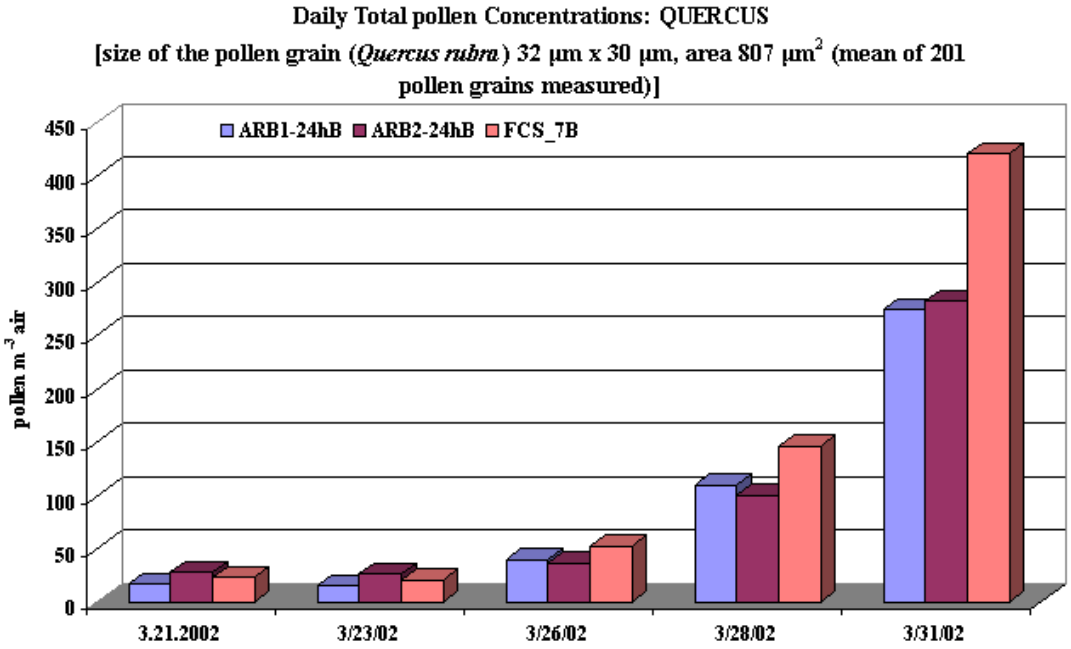


Figure 5.5.3-5. Total daily *Quercus* pollen concentrations (>30 microns) collected at the Central Site with two collocated covered Continuous Recording Air Samplers (ARB 1, ARB2) and the BSVT (FCS_7B).

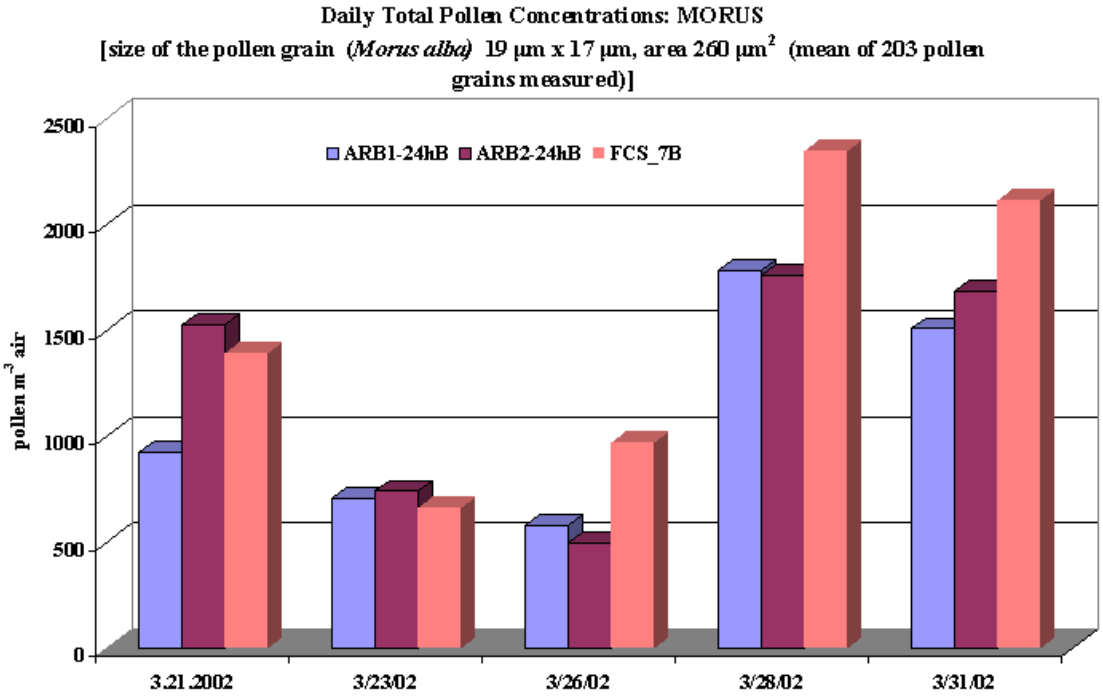


Fig.5.5.3-6. Total daily small pollen grain (*Morus*) concentrations collected at the Central Site with two collocated covered Continuous Recording Air Samplers (ARB 1, ARB2) and the BSVT (FCS_7B).

Duplicate microscopic analysis

About 3% of pollen and fungal spore slides have been counted and identified a second time. The results are within the range of variability for such analysis. The differences in numbers are > $\pm$ 5% for each transverse, since 12 transverse strips are analyzed for each slide; this has little effect on the final result. In the fungal spore analysis the difference in the daily total spore count for each species can be closer to 5% since the count is made in separate fields on the stoke (20 fields per each of the 12 strokes). The pollen analysis is done for the whole length of each 12 strokes, and the difference between replicate counts becomes very small. It is normal that slight differences between different counts can be observed because neither pollen nor fungal spores are homogeneously distributed on the deposition surfaces.

5.5.4 Home Intensive Procedures

Home Intensive sampling, documentation, laboratory, and data management procedures have been developed to facilitate communications among the FACES team, thoroughly document the sampling activities, and ultimately produce high quality data. The Home Intensive sampling and laboratory procedures are described in detail in Appendix CD2—Protocols and SOPs.

5.5.4.1 Home Intensive Sampling Schedule

Home Intensive panels begin every two weeks, always on a Wednesday, and end twelve days later on a Monday. The sampling schedule is shown in **Table 5.5.4-1**. Samples are collected over five 24-hr periods during each panel. The schedule is designed with a full day between samples during which each home in that panel is visited to download data, perform filter changes, and conduct flow checks on the pumping system. The schedule is also designed with two full days between Home Intensive panels during which the equipment is removed, quality-assured, maintained, and reinstalled in the next participants' homes. The equipment setup appointments last approximately 45 minutes, the intra-panel visits last approximately 1 hour, and the equipment removal visits last approximately 45 minutes.

Before each panel begins, several arrangements and equipment checks must be performed in the office:

- Scheduling home visits at each home to set up the equipment.
- Performing calibration checks on the nephelometers.
- Checking the BCRAS for proper start-up and operation.
- Verifying the current time on the timers for both the pump and the ozone samplers, and programming the timers for the first few sampling days.
- Checking and adjusting, if necessary, the flow rates of the ozone pumps.
- Installing clean impaction plates into each of the impactors.
- Applying mineral oil to the impaction plates.
- Loading filters into impactor cassettes.
- Compiling and organizing the paperwork.

These preparations are essential to keep the sampling on schedule and ensure the quality of the data.

Table 5.5.4-1. Home Intensive sampling schedule for each two-week panel.

Home Visit Window	Integrated Sample Collection	Activity
Tuesday-Wednesday 8 p.m.		Install sampler, load new samples, set to run starting Wednesday 8 p.m.
	Wednesday 8 p.m.-Thursday 8 p.m.	Pump and sampler operates
Friday before 8 p.m.		Unload used and load new samples, check sampler, collect nephelometer data
	Friday 8 p.m.-Saturday 8 p.m.	Pump and sampler operates
Monday before 8 p.m.		Unload used and load new samples, check sampler, collect nephelometer data
	Monday 8 p.m.-Tuesday 8 p.m.	Pump and sampler operates
Wednesday before 8 p.m.		Unload used and load new samples, check sampler, collect nephelometer data
	Wednesday 8 p.m.-Thursday 8 p.m.	Pump and sampler operates
Friday before 8 p.m.		Unload used and load new samples, check sampler, collect nephelometer data
	Saturday 8 p.m.-Sunday 8 p.m.	Pump and sampler operates
Monday		Unload used samples, check sampler, collect nephelometer data, remove sampler

MEMS units are typically set up at participants' homes on Tuesday or Wednesday. Before the MEMS units are set up, the participant is asked to sign a consent form if it has not already been signed. The MEMS units are then installed inside and outside each home. The inside MEMS is set up in the room where the family spends most of its time, typically the family room. Several scientific and practical considerations are made when locating the MEMS. The indoor considerations include avoiding windows, doors, vents, and pollution sources; installing close to a power outlet; and locating the sampler centrally in the room, away from walls and corners. **Figure 5.5.4-1** shows two MEMS installed at one participant's home. Note that although the MEMS are set up against the walls, the inlets for the impactors, nephelometers, and Burkard samplers are by design over 40 cm from the walls. The outside MEMS is set up in an open area of the back yard. Outdoor considerations include avoiding overhangs, large trees, fences, and pollution sources; setting up in a secure place, close to a power outlet; and aligning the MEMS to minimize impactors' exposure to the sun. **Figure 5.5.4-2** shows a MEMS installation outside a Home Intensive participant's home.

Figure 5.5.4-1. Duplicate MEMS inside a participant's home.

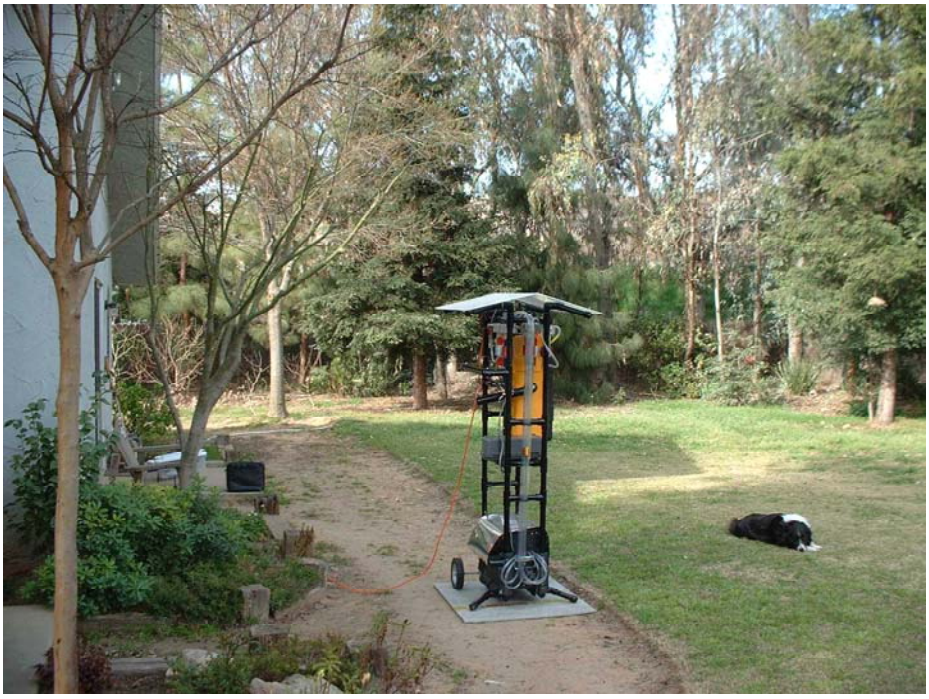


Figure 5.5.4-2. A MEMS installed outside a participant's home.

During each home visit, several steps are taken to prepare MEMS units for the integrated sampling periods, ensure that they are operating correctly, and document the sampler operation. Some steps are unique to the first visit:

- Photographing the MEMS units in position inside and outside the homes.
- Inspecting the power supply.

Most of the steps are repeated during each home visit:

- Scheduling the next home visit.
- Loading and/or unloading a microscope slide into the BCRAS.
- Loading and/or unloading an ozone tube into the sampler.
- Wiping off the impaction plates and reapplying mineral oil to the impaction plates.
- Measuring the pre-sampling flow rates through the five Harvard-type impactors using five rotameters simultaneously. If necessary, adjusting the flow rates.
- Measuring the post-sampling flow rates through the five Harvard-type impactors using five rotameters simultaneously.
- Verifying the current time and programs on the timers for both the filter and ozone sampling systems.
- Uploading the nephelometer data to a laptop computer.
- Checking the reasonableness of the nephelometer particle scattering and RH values.
- Checking the nephelometer fans and heater.
- Documenting the setup, sample identification numbers, elapsed time meter reading, and flow rates.

At the end of the Home Intensive panel, the MEMS are removed from the participants' homes and returned to the office for performance checks before being redeployed. Some specific tasks that are performed at the conclusion of each panel include

- Checking the flow rates of the ozone pumps.
- Performing calibration checks on the nephelometers.
- Washing and drying the impaction plates.
- Shipping the filters used to collect $PM_{2.5}$ mass, PM_{10} mass, PAHs, endotoxins, and ions collected during the panel to the U.C. Berkeley laboratory for analysis.
- Shipping the BCRAS slides collected during the panel to the U.C. Berkeley laboratory for analysis.
- Shipping the ozone samples collected during the panel to Johns Hopkins University for analysis.
- Photocopying the documentation and sending the originals to STI for data entry.
- Shipping the OC/EC and metals samples to DRI in batches every three months.

The Home Intensive sampling schedule and procedures are described in detail in Appendix CD2—Protocols and SOPs.

5.5.4.2 Home Intensive Documentation

Several types of documentation are maintained for the Home Intensive sampling including consent forms, home information forms, gift certificate receipt acknowledgement forms, flow check forms, follow-up questionnaires, and panel reports. This documentation is compiled by site in binders until the completion of a Home Intensive panel. At the completion of each panel, the documentation is photocopied and the originals are sent to STI.

The consent, home information, and gift certificate forms are maintained for each Home Intensive participant. Each participant is asked to sign a consent form before MEMS are set up at a home. The consent form describes the Home Intensive sampling and liability for the sampling. The FACES staff uses a home information sheet to list the Home Intensive participant's address and appointment times. Each Home Intensive participant is given three $25 gift certificates to cover the electrical costs and inconveniences of operating the equipment. The participants are asked to sign a form to acknowledge the receipt of each gift certificate.

The instrument and sample information is collected on a flow check form, as shown in **Figure 5.5.4-3**. One form is completed for each set of samples collected by a MEMS. Stickers are used to label the integrated samples. The required rotameter settings for a 10 LPM flow rate are listed next to the rotameter readings. The rotameter readings are recorded before and after any necessary pre- and post-sampling adjustments. The flow check form also includes several reminders for performing instrument checks. The sampling time is determined from the difference between the elapsed time recorder (ETR) readings which register the total amount of time the pump was running. The required rotameter settings for a 10 LPM flow rate are listed next to the rotameter readings. The rotameter settings were determined using a certified flow transfer standard. The rotameter readings are recorded before and after any necessary pre- and post-sampling adjustments. The rotameter readings are recorded before any necessary adjustments as a quality control measure to track the performance of the sampling lines.

Activity information is collected from the Home Intensive participants during each 24-hr sampling period. The follow-up questionnaire is shown in **Figure 5.5.4-4**. Elevated indoor nephelometer b_{sp} values can often be attributed to these activities as shown in Figure **5.5.4-5**. The arrows indicate the period during which the particular activity was reported to have occurred and do not indicate the actual start/end time of the activity. Several of the peaks in b_{sp} appear to result from the indoor activities. It is interesting to note the decay rates in the b_{sp} values after each of the indoor source events; the 5-minute resolution of the nephelometer data will be useful in estimating the ventilation rates in the homes.

At the completion of each Home Intensive panel, the field manager writes and distributes a report. The report describes the sampling locations, the vegetation, any unusual circumstances, and any sampling problems at each home. The reports also include overall panel information such as pre- and post-sampling equipment checks and summaries of sample shipments to the laboratories for analysis. Any on-going equipment characterizations or problems are also summarized. These reports facilitate communications among the FACES investigators and aid in quality control of the data.

Flow Check Form

I.D. Information
Tech Initials _____ _____
Subject I.D. _____
PEMS # _____
In ☐ **Out** ☐ **Field Blanks** ☐
Cassette Loading Date_____
Sample Date Start _____
Sample Date End _____
HI Loading Date _____
HI Loading Time _____ **am/pm**

Pre-Sample Flow Check
Date _____
Day _____
Time_____**am/pm**
Pressure _____
E.T.R. (hrs)_____
Ozone I.D. #

Post-Sample Flow Check
Date _____
Day _____
Time_____**am/pm**
Pressure_____
E.T.R. (hrs)_____
Delta (hrs)_____

Leg #	Identification	Nominal Rotameter (mm)	Pre-Sampling Rotameter (mm) Bank 1 ☐ Bank 2 ☐	Adjusted Reading	Post-Sampling Rotameter (mm) Bank 1 ☐ Bank 2 ☐
1 (Red)	Place L1A label here FRONT Place L1B label here BACK	136 ± 6mm (Bank 1) 135 ± 7mm (Bank 2)	(L1)_____	_____	(L1)_____
2 (Orange)	Place L2 label here	136 ± 6mm (Bank 1) 137 ± 7mm (Bank 2)	L2)_____	_____	(L2)_____
3 (Yellow)	Place L3A label here FRONT Place L3B label here BACK	139 ± 6mm (Bank 1) 138 ± 7mm (Bank 2)	(L3)_____	_____	(L3)_____
4 (Green)	Place L4 label here	138 ± 6mm (Bank 1) 137 ± 7mm (Bank 2)	(L4)_____	_____	(L4)_____
5 (Blue)	Place L5A label here FRONT Place L5B label here BACK	138 ± 6mm (Bank 1) 137 ± 7mm (Bank 2)	(L5)_____	_____	(L5)_____

Comments:

Comments:

***Elapsed Timer Reading – record to nearest hundredth hour**

Burkard Label
Burkard Label Here

Check Box Upon Completion

1. **Mechanical timer is set to correct day and time of day?** ☐
2. **Tabs are set for 8 p.m. to 8 p.m. on sample days?** ☐ **Neph bsp and RH values within range?** ☐
3. **Digital timer is set correctly for O_3 sampling?** ☐ **Neph data downloaded?** ☐

Figure 5.5.4-3. Sample flow check form.

FOLLOW-UP QUESTIONNAIRE

FACES HOME INTENSIVE FOLLOW-UP QUESTIONNAIRE FOR EACH FILTER SAMPLING PERIOD

Version 1.2 (1/25/2002)

FACES Participant ID# _____
Home Visit No. _____
House Address – Street _____
City _____ St. _____ Zip _____
Technician Name _____ No. _____
Survey Completion Date _____ (mm/dd/yy)
Filter Sampling Period Start Date _____ End Date _____

Did the Activity Occur In Any Room of the House During the Time Period? Enter **Y**=Yes, **N**=No, or **DK**=Don't Know							
Activity	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
Was a vacuum used?							
Did anyone smoke tobacco products (cigarettes, cigars or a pipe)?							
Were any windows or doors open for more than 30 minutes?							
Was a gas stove burner on for more than 10 minutes?							
Was a gas oven on for more than 10 minutes?							
Was a kerosene heater used?							
Was a wood stove used?							
Was a fireplace used?							
Were candles burned?							
Was incense burned?							
Was an oil lamp used?							
Was a stove used for frying?							

Figure 5.5.4-4. Home Intensive sampling period follow-up questionnaire.

Did the Activity Occur In Any Room of the House During the Time Period? Enter **Y**=Yes, **N**=No, or **DK**=Don't Know							
Activity	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
Was a stove used for charring food?							
Was an oven used for automatic cleaning?							
Was a wall or floor gas heater used?							
If the heating system was controlled by a thermostat, what was the temperature setting (**Temp** in degrees F or **DK**)?							
If the heating system was controlled manually, was it turned on and off (**ON** or **OFF**)?							
If the air conditioning system was controlled by a thermostat, what was the temperature setting (**Temp** in degrees F or **DK**)?							
If the air conditioning system was controlled manually, was it turned on and off (**ON** or **OFF**)?							
Were there any unusual activities or conditions (**Y, N,** or **DK**)?							
Describe unusual activities:							

Figure 5.5.4-4. Home Intensive sampling period follow-up questionnaire (concluded).

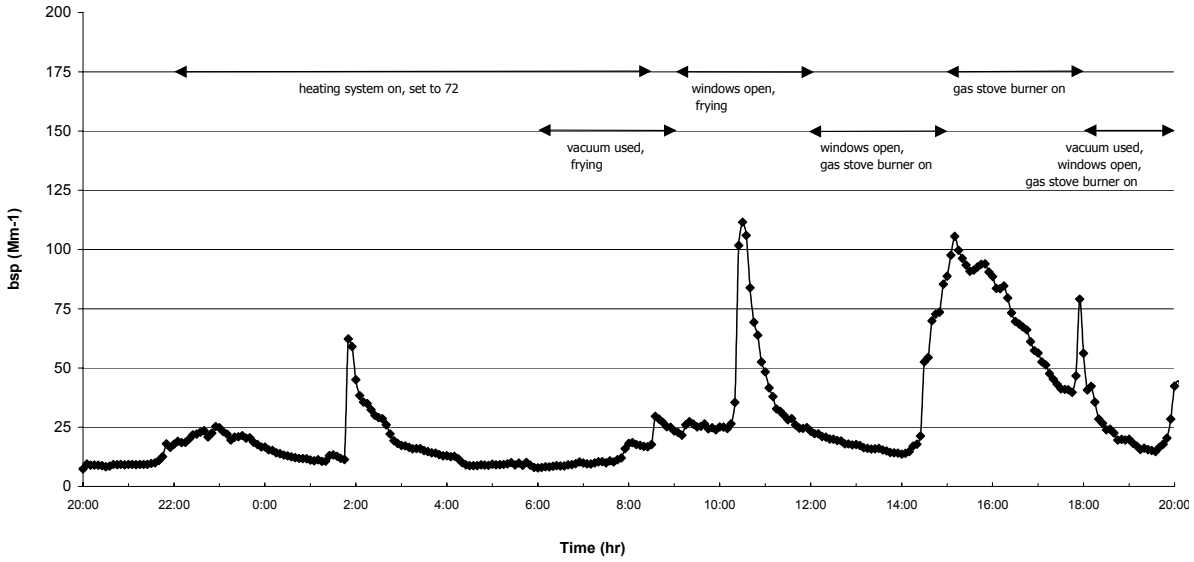


Figure 5.5.4-5. Nephelometer particle scattering (b_{sp}) data for one 24-hr sample period in the third panel at Residence 91. Activities that occurred during the 24-hr period and could affect the indoor air quality are noted on the top of the plot**.**

5.5.4.3 Home Intensive Data Management

Two Microsoft Access databases are currently maintained to store the continuous monitoring data and the sampling information. The continuous monitoring data from the nephelometers are downloaded during each home visit, usually every other day. The data are uploaded to STI's data management system, where they are ingested into the Microsoft Access database. The data are converted from end-time to start-time as they are ingested. In the database, automatic screening criteria are applied to the data. The automatic screening criteria include flagging data with excessive point-to-point jumps and extremely high values. The data are then plotted on graphs and posted on the Internet site (password-protected). An example graph from the Internet is shown in **Figure 5.4.4-6**. Each graph shows one week of data from Tuesday through Monday, and two complete graphs are generated for each participant in a panel. The b_{sp} and RH data for inside and outside the home are plotted along with the QC codes for each parameter. The y-axis scale is irrelevant for the QC codes. QC codes are only plotted when they are non-zero, and the level at which they are plotted on the y-axis is designed simply to make them visible. The QC values that are plotted indicate data that failed the screening criteria. The screening criteria are conservative and are simply used to highlight data for further review, not invalidate data. These graphs are reviewed each time they are updated and printed when a complete week of data is displayed on the plots. The graphs provide an efficient means of surveying the data and identifying any instrument, power, or data acquisition problems. Problems identified with the data or database are fixed quickly.

The sampling information database stores a variety of information including the filter identification, flow check, instrument identification, and participant activity information. At the completion of each panel, all the completed forms from the panel are photocopied, and the originals are sent to STI. The documentation is transferred into the database using MicrosoftAccess electronic forms; an example electronic flow check form is shown in

Figure 5.5.4-7. The forms facilitate data entry and help minimize errors. A few quality assurance measures are applied to the database: (1) summaries of the database status are maintained to confirm that all the documentation is accounted for in the database and files; (2) spot checks are performed to verify the data entry; and (3) summaries of the participants' activities are compiled to confirm the reasonableness of the activities (e.g., air conditioning not used in February). In addition, many of the activities at individual households are reviewed monthly when the metals samples are selected for analysis.

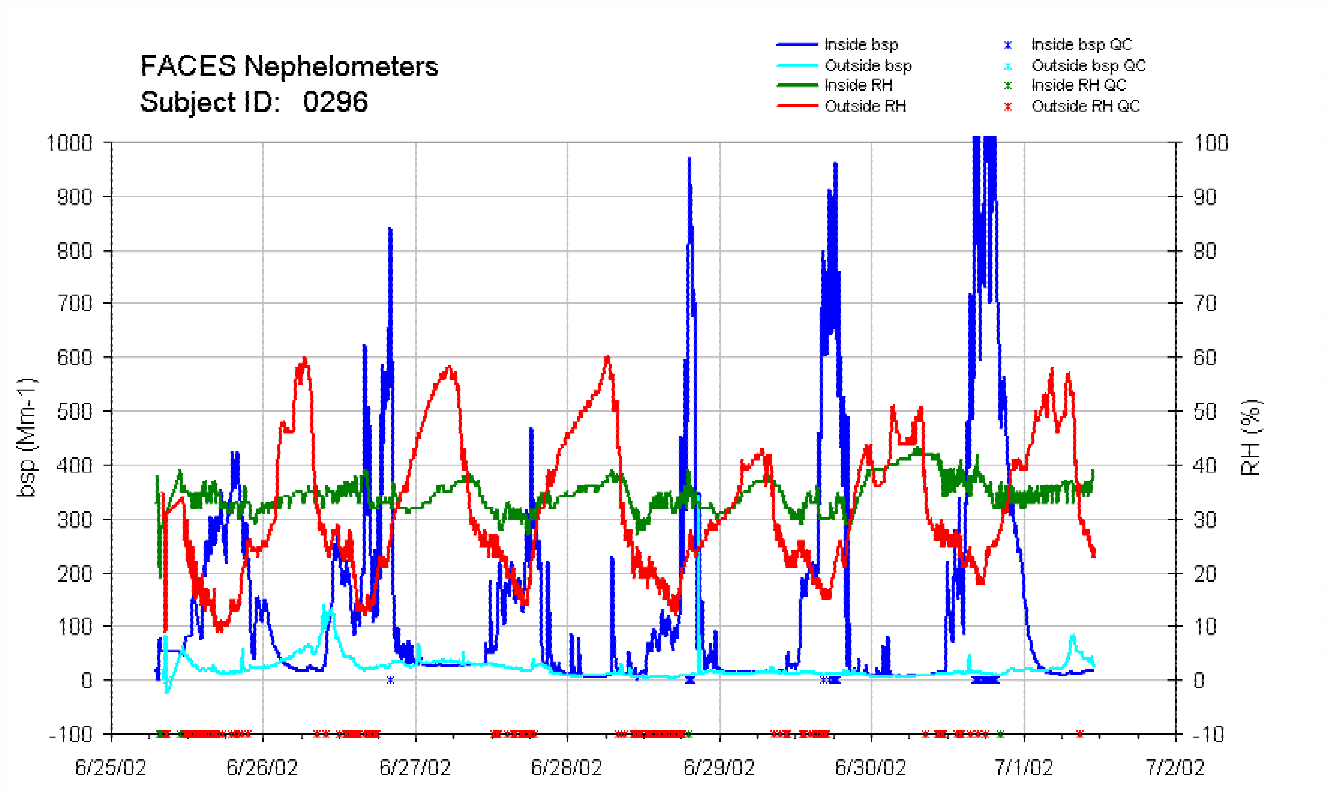


Figure 5.5.4-6. Example of a nephelometer data graph posted on the Internet.

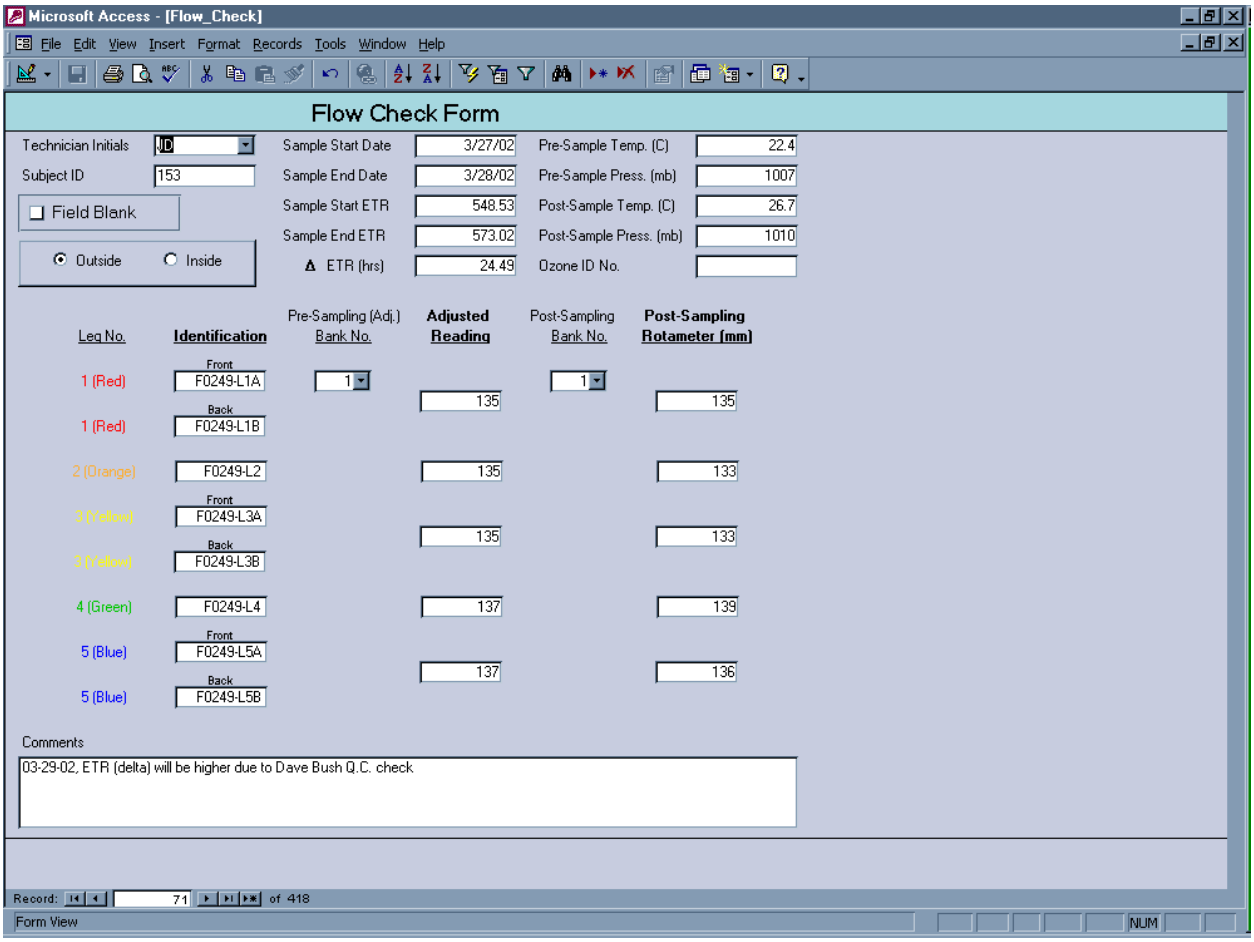


Figure 5.5.4-7. Microsoft Access electronic flow check form used to enter the sampling information.

5.5.5 Home Intensive Quality Assurance

Several practices are being implemented to ensure the quality of the FACES Home Intensive data:

- A pilot study was performed in January at the homes of two FACES employees to develop, refine, and test the procedures and equipment.
- Data are reviewed and validated on a timely and routine basis.
- Ten percent of the samples are designated quality-control samples, which includes blanks and duplicates.
- MEMS are operated at the Central Site during different seasons to establish relationships between the MEMS and the Central Site measurements.
- The MEMS instruments are thoroughly checked, maintained, and calibrated every two weeks.

- The sampling procedures have been reviewed and approved by several advisors including the FACES independent auditor, ARB, and EPA.

In addition to the quality assurance discussion in this section, please see the discussion in Section 5.7, which includes comparisons between the Home Intensive data and the Central Site data.

5.5.5.1 Nephelometer Data Quality Control

Nephelometer data are reviewed at several points to confirm that the instruments are operating properly, the data are accurate, and there is agreement among the instruments at nearby sites. Nephelometer data are uploaded from the instruments at each site visit and ingested into a database where they are automatically screened for common problems, such as large point-to-point variations. Any data that fail the screening criteria are flagged with an appropriate quality control code. The particle scattering and RH data are then plotted on time-series graphs and posted on the Internet. The graphs are reviewed whenever they are updated, typically every other workday. At this time, any data gaps are identified and the missing data are pursued. This routine data review ensures that nephelometer instrument problems are identified and resolved quickly.

The nephelometer data are validated on a monthly basis. The data are graphed in a validation software program, and the complete data set obtained by a particular instrument are reviewed together. The data collected at the different houses around Fresno are compared for consistency in b_{sp} values and general patterns. The validation also includes flagging data when the instruments are stabilizing at a new site, being maintained, or are malfunctioning. In addition, the calibration data are reviewed and summarized. If necessary, slope and offset values are applied to the data. The panel reports include information about the performance of the nephelometers and are useful in validating the data.

Additional quality control is performed on the nephelometer data when the two metals samples, out of the five collected at each site, are selected for analysis. The metals samples are selected every three months. The continuous nephelometer data along with the sampling information data are used to select the metals samples to be analyzed. Several factors are considered when selecting the metals samples for analysis including any sampling problems affecting the metals samples or any other samples, the availability of nephelometer data, the day of week of the samples (i.e., weekday or weekend), the indoor and outdoor pollution levels as recorded by the nephelometers, and any unusual activities. These factors are evaluated by reviewing the nephelometer data, the activity data, and panel reports. In the review process, any discrepancies between these sources are identified and resolved.

5.5.5.2 Pilot Study data

A pilot study was conducted in January 2002 at the homes of two FACES employees. The MEMS were set up in the two homes, identified as 1901 and 481, on January 25, 2002. The locations of the two pilot study homes are shown in **Figure 5.5.5-1**. Nephelometer data were collected continuously from January 25 through January 31 and are displayed in **Figure 5.5.5-2**. Several of the peaks in b_{sp} inside can be attributed to activities noted in the follow-up questionnaires. The follow-up questionnaires are summarized in **Table 5.5.5-1**. Table 5.5.5-1 only includes the activities for which one of the homes answered yes at any time and does not

include heating and air conditioning information. The activity questionnaires indicate that candles were burned at Residence 481 for several hours on January 25 and January 26, and the times when the candles were burned on these two days correspond to significant peaks in b_{sp} in Figure 5.5.5-1. At home 1901, a few of the spikes in b_{sp} can be attributed to frying on the stove.

Three integrated samples were collected on January 25, 28, and 30, 2002. Note that the start date of the sampling period is always used to identify samples in this report, although the 24-hr sampling period includes two calendar dates. The PM_{10}, $PM_{2.5}$, OC, and EC concentrations are displayed in **Figures 5.5.5-3** and **5.5.5-4**. Note that the mass concentrations have not yet been adjusted for the volatilized nitrate concentrations. The day-to-day patterns among the different pollutants are very consistent. These consistencies are a testament to the quality of the equipment, sample handling, and laboratory analyses. Differences in the outdoor concentrations measured at the two homes can be attributed to their proximities to roadways. Residence 481 is located on the north side of Fresno west of Hwy 41, and Residence 1901 is located slightly east of Highway 99. The outdoor PM_{10}, $PM_{2.5}$, OC, EC, and b_{sp} values are consistently and significantly higher at Residence 1901, which is likely due to its proximity to Highway 99. The I/O ratios are not the same from sample to sample or home to home because there are some strong, intermittent indoor sources that can dominate the indoor concentrations at these two homes. In the absence of these indoor sources, the indoor concentrations are less than the outdoor concentrations. Extremely high PM_{10}, $PM_{2.5}$, OC, and EC concentrations were observed inside home 481 on January 25, which is the period when candles were burned.

The pilot study was extremely useful in refining the procedures, training the field staff, testing the data processing systems, and identifying potential problems. The data obtained in the pilot study are reasonable and consistent. Section 5.7 discusses and illustrates the comparisons between the pilot data and the Central Site data.

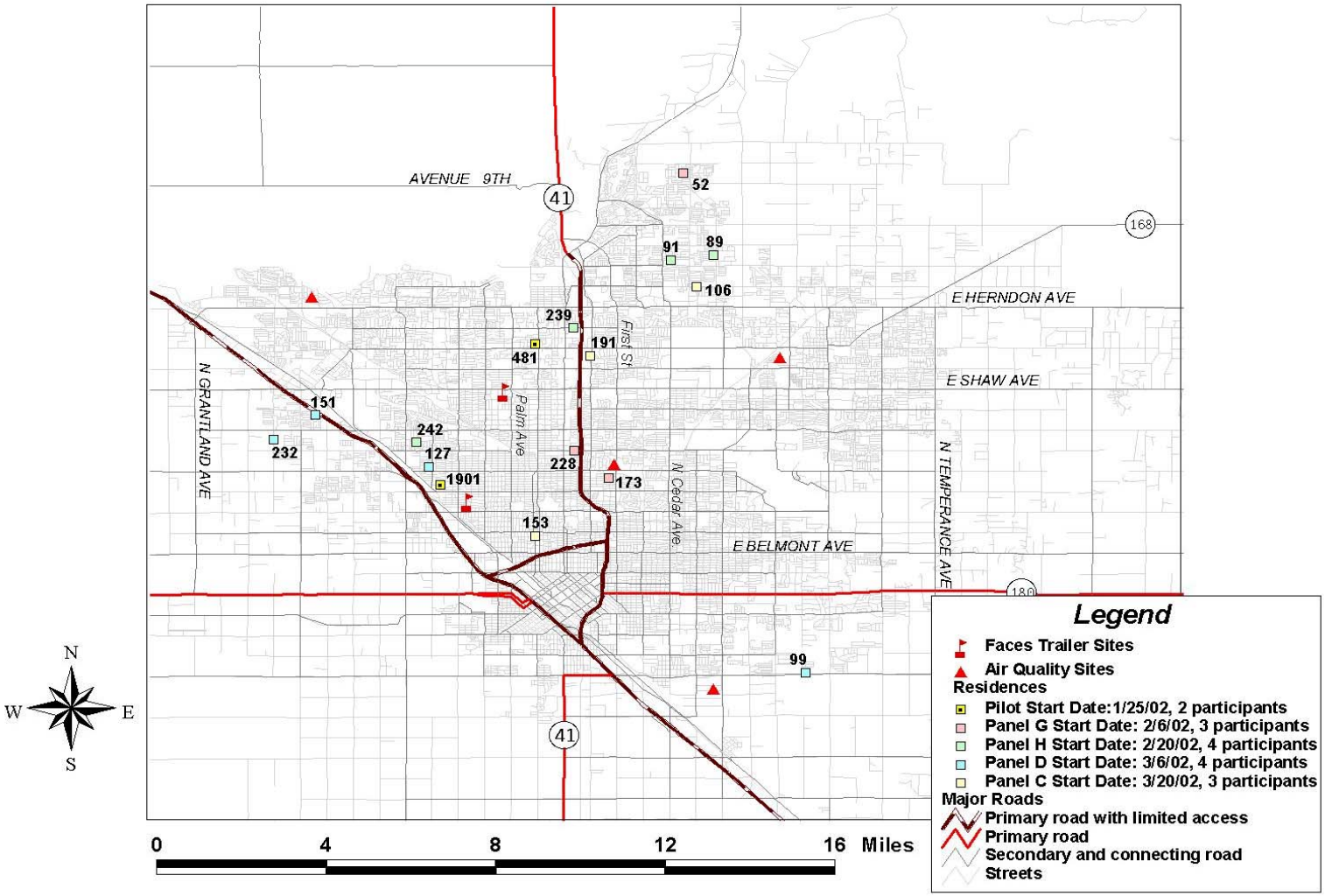


Figure 5.5.5-1. The integrated samples have been analyzed and are discussed in this report for the pilot and Home Intensive participants shown on this map. The map also shows the Central Site and other air quality monitoring sites and the trailer sites.

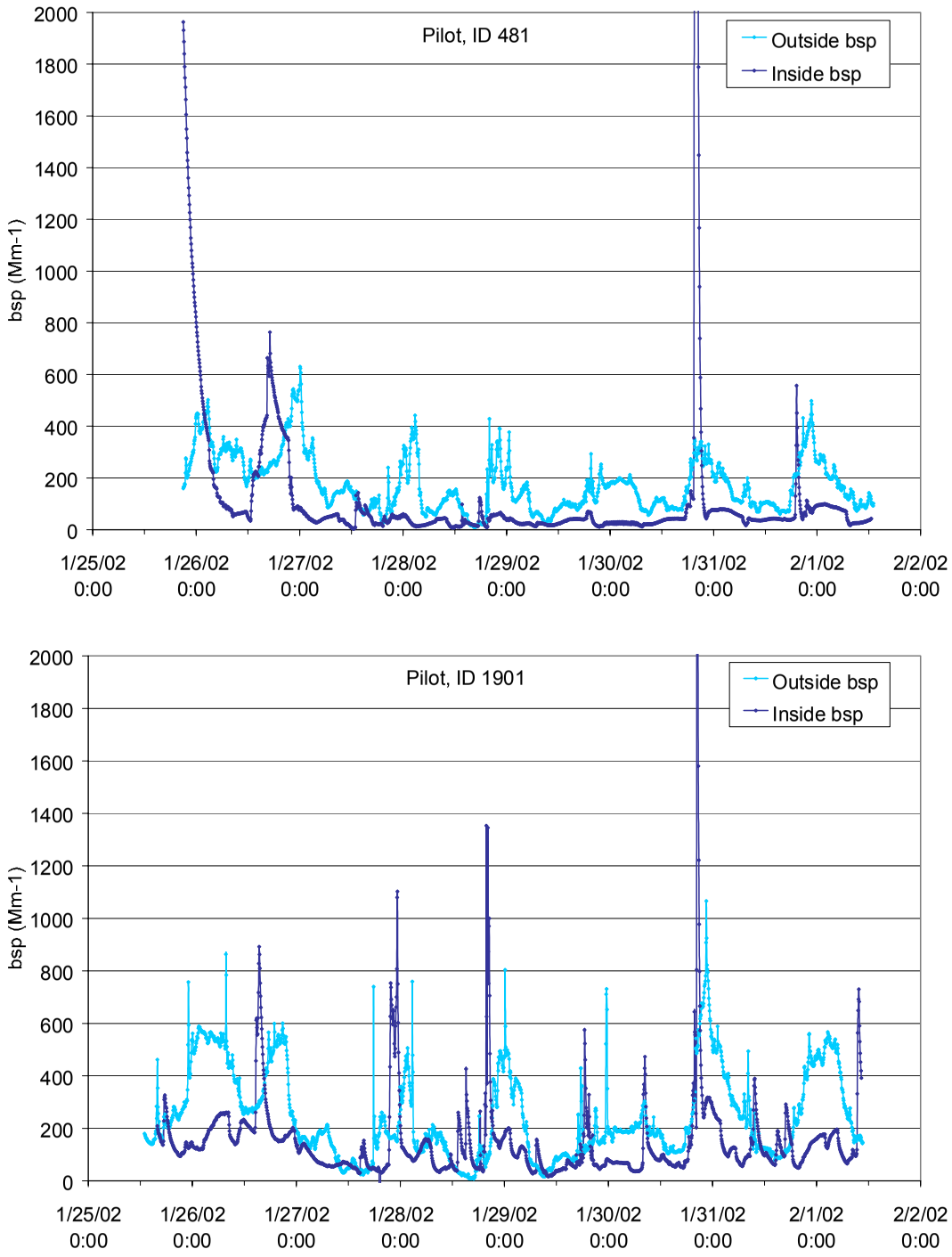


Figure 5.5.5-2. Light scattering by particles values (b_{sp}) measured inside and outside the two pilot study homes.

Table 5.5.5-1. Summary of activities noted on the follow-up questionnaires from the homes of the two pilot participants.

				Time (PST)						
Residence ID	StartDate	EndDate	Activity	2000 to 2200	2200 to 0600	0600 to 0900	0900 to 1200	1200 to 1500	1500 to 1800	1800 to 2000
481	1/25/02	1/26/02	Candles Burned	Yes	-	-	-	Yes	Yes	-
481			Fireplace Used	-	-	-	-	-	-	-
481			Vacuum Used	-	-	-	Yes	-	-	-
481			Frying on Stove	-	-	-	-	-	-	-
481			Windows Open	-	-	-	-	-	-	-
481	1/28/02	1/29/01	Candles Burned	-	-	-	-	-	-	-
481			Fireplace Used	-	-	-	-	-	-	-
481			Vacuum Used	-	-	-	-	-	-	Yes
481			Frying on Stove	-	-	-	-	-	-	-
481			Windows Open	-	-	-	-	-	-	-
481	1/30/02	1/31/02	Candles Burned	-	-	-	-	-	-	-
481			Fireplace Used	-	-	-	-	-	-	-
481			Vacuum Used	-	-	-	-	-	-	-
481			Frying on Stove	-	-	-	-	-	-	-
481			Windows Open	-	-	-	-	-	-	-
1901	1/25/02	1/26/02	Candles Burned	-	-	-	-	-	-	-
1901			Fireplace Used	-	-	-	-	-	-	-
1901			Vacuum Used	-	-	-	-	-	-	Yes
1901			Frying on Stove	-	-	Yes	-	-	Yes	-
1901			Windows Open	-	-	-	-	Yes	-	-
1901	1/28/02	1/29/02	Candles Burned	-	-	-	-	-	-	-
1901			Fireplace Used	-	-	-	-	-	-	Yes
1901			Vacuum Used	-	-	-	Yes	-	-	-
1901			Frying on Stove	-	-	Yes	-	Yes	-	-
1901			Windows Open	-	-	-	-	-	-	-
1901	1/30/02	1/31/02	Candles Burned	-	-	-	-	-	-	-
1901			Fireplace Used	Yes	-	-	-	-	-	Yes
1901			Vacuum Used	-	-	-	-	-	-	-
1901			Frying on Stove	Yes	-	Yes	-	-	Yes	-
1901			Windows Open	-	-	-	-	-	-	-

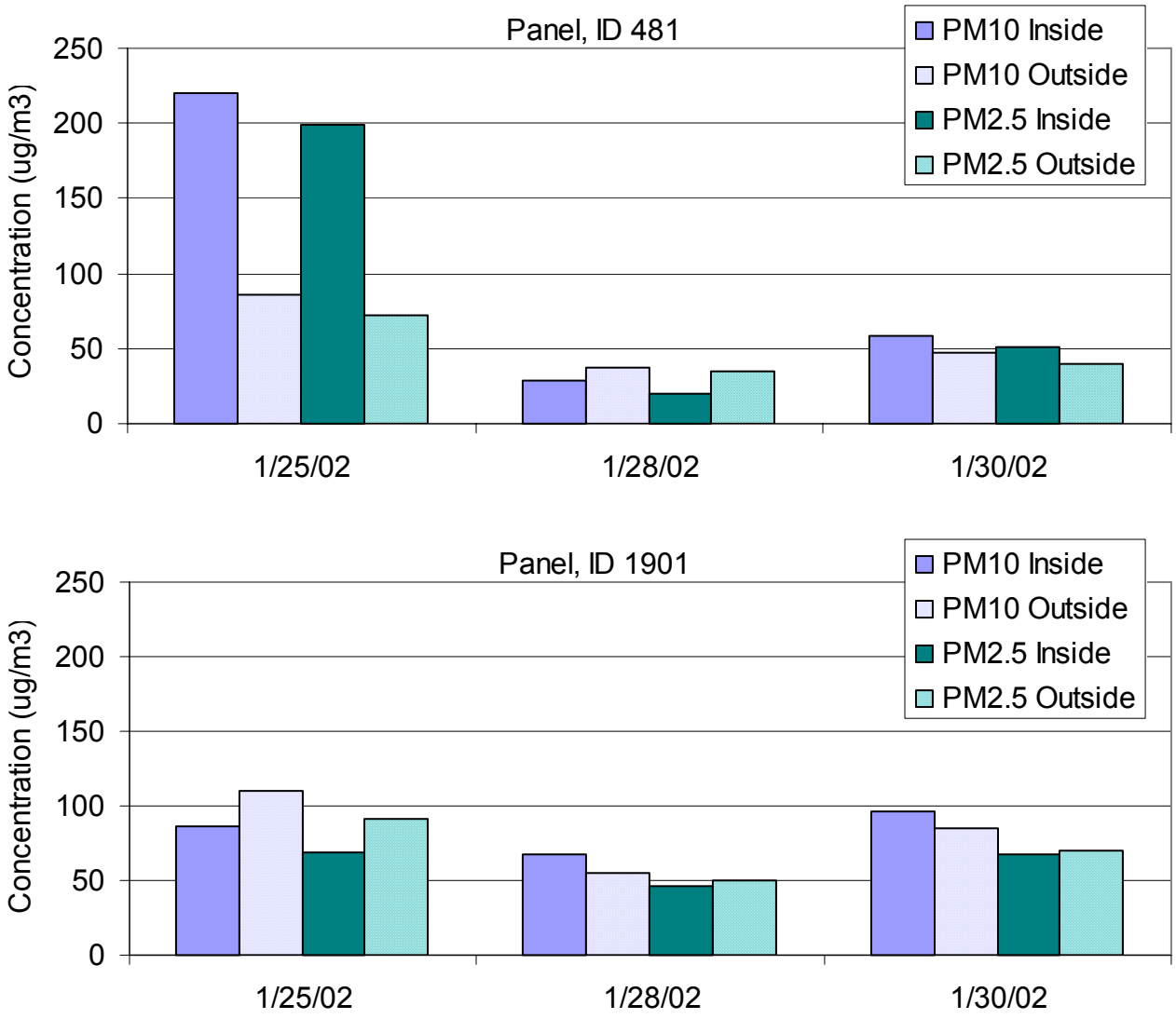


Figure 5.5.5-3. Uncorrected PM_{10} and $PM_{2.5}$ mass concentrations measured inside and outside the two pilot study homes.

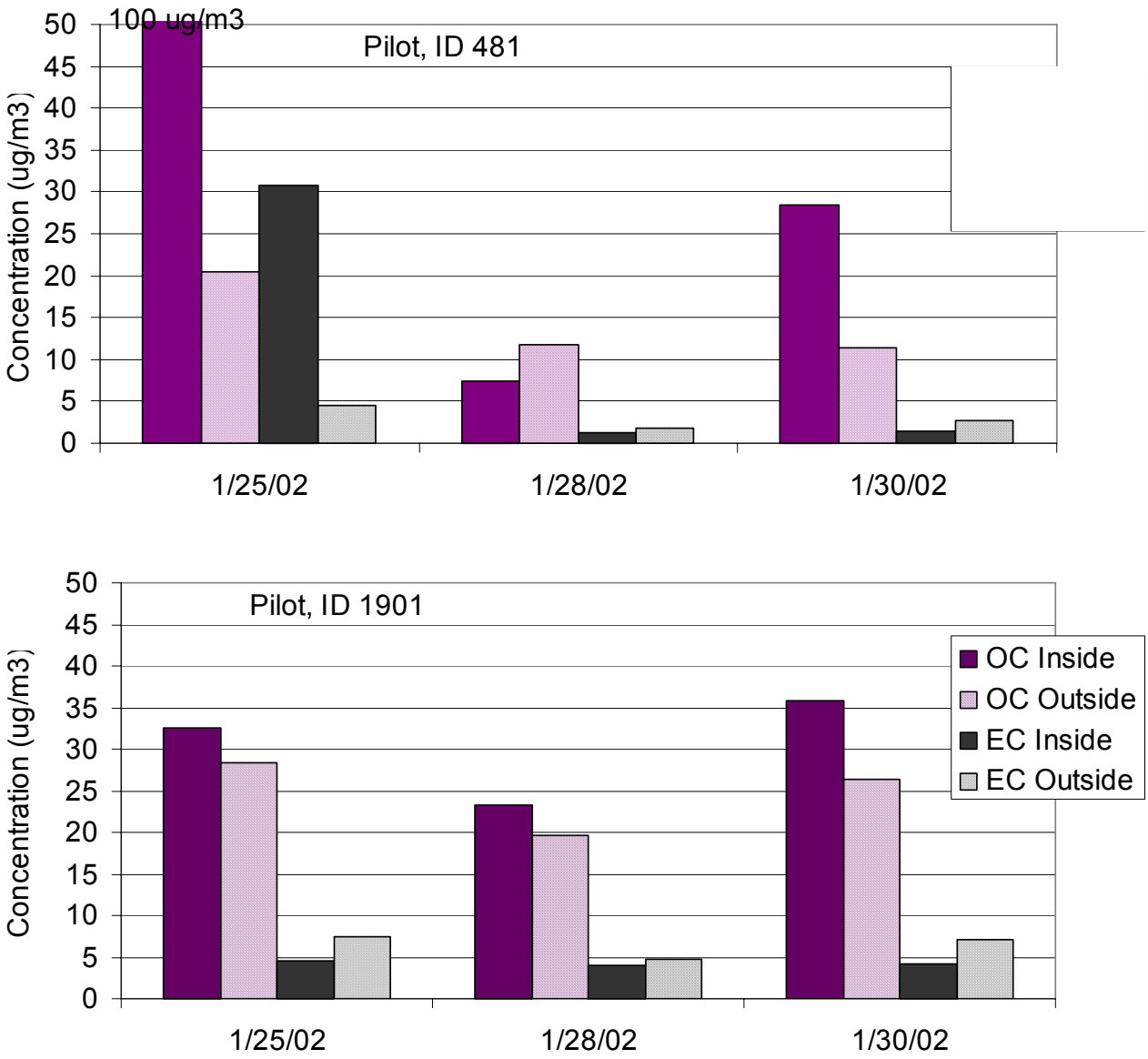


Figure 5.5.5-4. Organic and elemental carbon concentrations measured inside and outside the two pilot study homes. One inside OC concentration is off-scale and the value, 100 μg/m^3, is noted on the bar.

5.5.5.3 Blank Samples

A complete set of blank samples is being collected during each panel. The blank filter samples are collected as trip blanks, where the sample is transported to the site, removed momentarily from its container, and then transported back to the office when the routine samples are both loaded and unloaded. The blank ozone samples are collected as field blanks; the sample is set up and left at the site for the same time period as the normal sample, but the sample is not opened to ambient air and flow is not passed through the sample.

A small number of blank filter samples have been analyzed to date. **Tables 5.5.5-2 and 5.5.5-3** list the concentrations and standard deviations for the PM mass and OC/EC blank samples. These statistics must be regarded with caution because the number of samples is so low. The concentrations were calculated by assuming a flowrate of 10 LPM for 24 hours. No EC was detected on any of the blank filters. The average concentrations and standard deviations for the five blank samples analyzed by XRF are listed in **Table 5.5.5-4**.

Several quality assurance steps are taken at the beginning of each day of filter weighing: calibrating the balance with a calibration weight, zeroing the balance, and weighing four quality control filters (for details, see the weighing protocol in CD2-Protocols and SOPS). The quality control filters usually agree with their historical weights within 4 micrograms. Field blanks were collected during the pilot study and are being collected throughout the home intensive study. Problems were identified during the weighing of filters from the pilot study, but these were addressed. The four field blanks from the pilot study had an average weight gain of 60 micrograms; the six field blanks collected during the first home intensive panel had a mean weight gain of 14 micrograms, with a standard deviation of 4; and the eight field blanks evaluated since then have a mean weight gain of 2 ± 5 micrograms. These filter blanks correspond to an airborne concentration of 1 $\mu g/m^3$ for the first set of home intensive samples and 0.1 $\mu g/m^3$ for the second set of home intensive samples. The 82 filters, which collected $PM_{2.5}$ and have post weights, had average weight gains of 263 micrograms; the corresponding 81 PM_{10} filters had an average weight gain of 447 micrograms; and, the corresponding filter blanks for these samples had an average weight gain of 2 micrograms, or, less than 1% of the average for $PM_{2.5}$ and less than half a percent for PM_{10} filters The blank filter mean was only 3% of the minimum weight gain for these 163 filter samples, which was 64 micrograms. If the limit of detection, LD, is defined as the mean plus two standard deviations of the blank filter values, the LD would be 12 micrograms collected, which corresponds to less than 1 $\mu g/m^3$.

Table 5.5.5-2. Blank PM mass filter averages and standard deviations, expressed in terms of weight and concentration, for the four samples analyzed to date.

Group Species	Number	Mass (μg/filter)	Mass ($\mu g/m^3$)
Pilot Study	4	60 ±8	4.2 ±0.6
First Panel	6	14 ±4	1.0 ±0.3
Second and Third Panels	8	2 ±5	0.1 ±0.3

Table 5.5.5-3. Blank OC/EC filter averages and standard deviations, expressed in terms of weight and concentration, for the five samples analyzed to date. No EC was detected on any of the blank filters.

Species	OC (μg/filter)	OC (μg/m^3)
Number of samples	5	
Average	1.8	0.13
Standard Deviation	2.2	0.15

Table 5.5.5-4. Average concentrations and standard deviations for the five blank samples analyzed by XRF to date. The species are identified by their elemental symbols.

Species	Al	Si	P	S	Cl	K	Ca	Ti	V	Cr
Average blank concentration (ng/m^3)	8.31	24.1	3.59	1.77	10. 6	0.217	6.24	0.104	0.129	0.063
Blank standard deviation (ng/m^3)	7.18	36.0	4.30	2.43	20.0	0.385	9.19	0.233	0.289	0.140
Species	Mn	Fe	Co	Ni	Cu	Zn	Ga	As	Se	Br
Average blank concentration (ng/m^3)	0.043	5.83	0.449	0.340	0.165	0.693	0.328	0.021	0.108	0.057
Blank standard deviation (ng/m^3)	0.096	12.3	0.595	0.474	0.254	1.27	0.385	0.047	0.150	0.112
Species	Rb	Sr	Y	Zr	Mo	Pd	Ag	Cd	In	Sn
Average blank concentration (ng/m^3)	0.118	0.04	0.108	0.074	0.047	0.369	0.097	0.574	0.078	0.660
Blank standard deviation (ng/m^3)	0.165	0.09	0.242	0.109	0.094	0.826	0.217	0.786	0.111	0.909
Species	Sb	Ba	La	Au	Hg	Tl	Pb	U		
Average blank concentration (ng/m^3)	1.53	12.0	9.44	0.578	0.381	0.142	0.329	0.153		
Blank standard deviation (ng/m^3)	1.92	7.04	13.0	0.726	0.549	0.170	0.413	0.227		

5.5.5.4 Duplicate Samples

Collocated MEMS have been operated outside several homes and inside one home during the first five months of the Home Intensive as shown in **Table 5.5.5-5**. Collocated MEMS will be operated inside or outside at least three more participants' homes during the reamainder of the Home Intensive sampling. In addition, MEMS are operated intermittently at the Central Site. These collocated measurements will help establish relationships between the Home Intensive and Central Site measurement techniques. It is essential that the comparability and precision of the measurement techniques be demonstrated before the data are used to determine spatial trends. Two MEMS have been operated at the Central Site during two panels as shown in Table 5.5.5-5. The MEMS will be operated at the Central Site for two panels again in fall/winter 2002.

The collocated data generally compare well. They are highly correlated ($R^2 > 0.99$) and the differences between the duplicate data appear to be mostly random rather than systematic. **Figures 5.5.5-5 and 5.5.5-6** display a time series plot and a scatter plot of the duplicate b_{sp} data

from Residence 91. The time series plot displays only one week of data while the scatter plot includes approximately two weeks of data. The b_{sp} data track extremely well although there does appear to be a slight systematic bias. Calibration slope and offset values have not been applied to the data at this stage, and the calibration information may correct for this slight bias. At the conclusion of the home intensive sampling, the semi-weekly calibrations will be evaluated along with the duplicate data. Slopes and offsets will be applied when necessary. **Figure 5.5.5-7** displays the $PM_{2.5}$ OC and EC concentrations for each duplicate sampling period at Residence 91. Note that the duplicate MEMS was accidentally unplugged by the participant before the filter samples started on October 2, 2002. **Figure 5.5.5-8** shows the PM_{10} silicon, aluminum, and iron concentrations for the two metals samples selected for analysis. The agreement between the duplicate samples is excellent, and the differences appear to be random and not systematic. **Figures 5.5.5-9** and **5.5.5-10** display a time series plot and a scatter plot of the duplicate b_{sp} data from Residence 99. The b_{sp} values are comparable, but the R^2 value of 0.93 is moderate. **Figure 5.5.5-11** displays the $PM_{2.5}$ uncorrected mass, PM_{10} uncorrected mass, EC, and OC concentrations for the duplicate samples at Residence 99. **Figure 5.5.5-12** shows the PM_{10} silicon, aluminum, and iron concentrations for the March 16, 2002 metals samples selected for analysis. The duplicate samples compare extremely well and again do not show obvious systematic bias. **Figures 5.5.5-13 through 5.5.5-16** compare the duplicate nephelometer and filter data for two MEMS operated at the Central Site.

Overall, the collocated sampler data compare extremely well and demonstrate that the Home Intensive instruments are operating consistently and the Home Intensive procedures are adequate to obtain reproducible data. Duplicate samplers will be operated intermittently during the remainder of the Home Intensive sampling to further demonstrate comparability and quantify the precision.

Table 5.5.5-5. Summary of duplicate samplers operated in the Home Intensive as of June 27, 2002.

Group ID	StartDate	QC Samplers
G	02/06/02	
H	02/20/02	Duplicate MEMS outside Residence 91
D	03/06/02	Duplicate MEMS outside Residence 99
C	03/20/02	Two MEMS operated at the Central Site
A	04/03/02	Two MEMS operated at the Central Site
F	04/17/02	Duplicate MEMS outside Residence 231
G	05/01/02	
B	05/15/02	Duplicate MEMS in and outside Residence 278
H	05/29/02	
E	6/12/02	
A	6/26/02	One MEMS operated at the Central Site

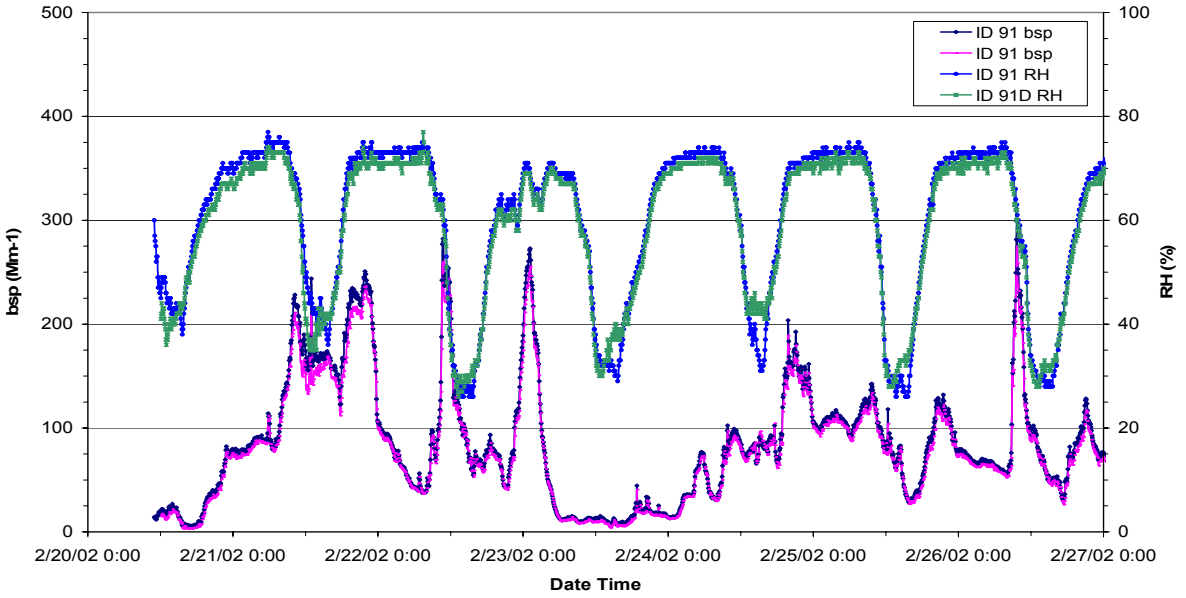


Figure 5.5.5-5. Light scattering by particles and relative humidity data from the collocated nephelometers outside Residence 91.

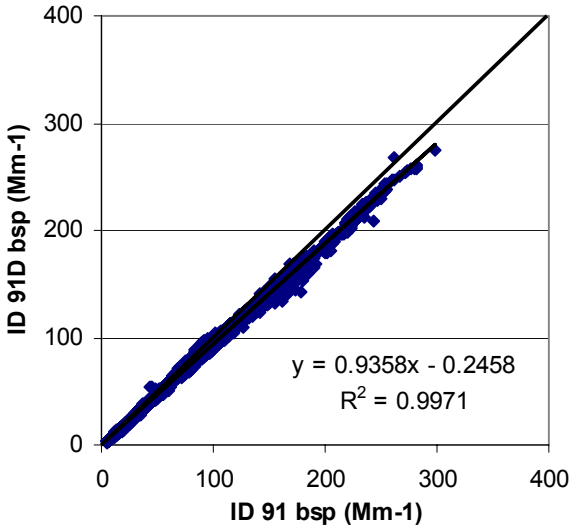


Figure 5.5.5-6. Comparison of 5-minute average light scattering by particles measured by nephelometers collocated at Residence 91 from February 20 to March 4, 2002. A total of 2845 pairs of data are included in this plot.

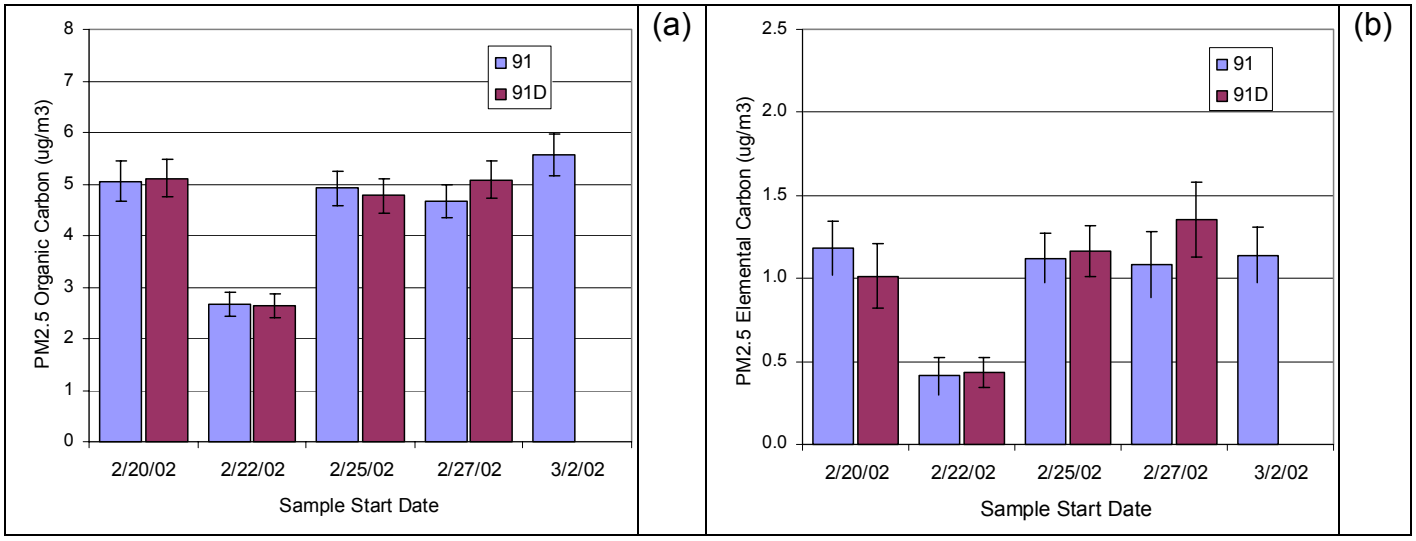


Figure 5.5.5-7. (a) $PM_{2.5}$ OC and (b) $PM_{2.5}$ EC concentrations measured by two collocated samplers outside Residence 91. Note that the duplicate MEMS (91D) was accidentally unplugged by the participant before the filter samples started on March 2, 2002.

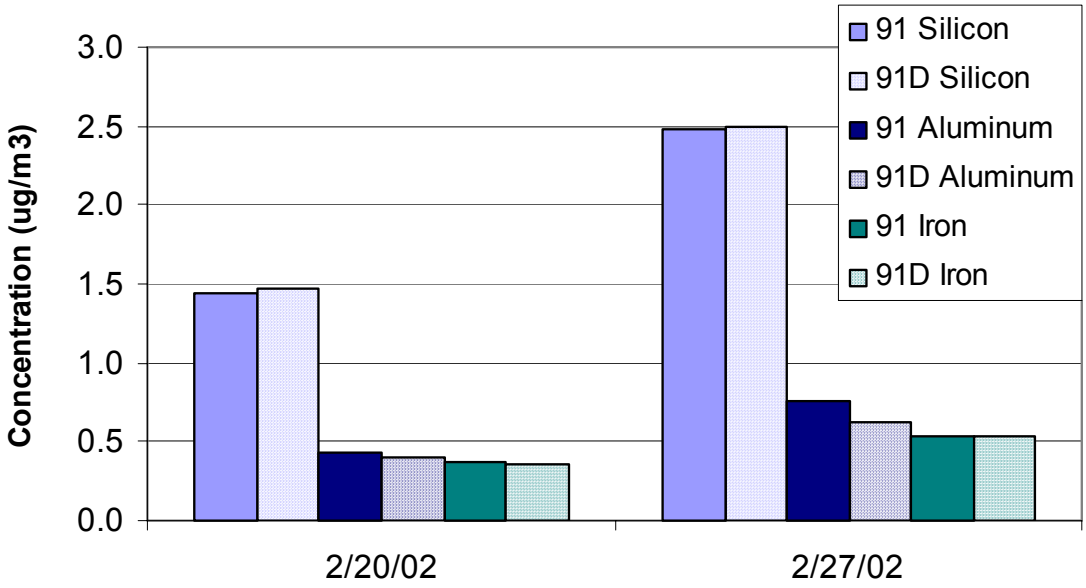


Figure 5.5.5-8. PM_{10} silicon, aluminum, and iron concentrations measured by two collocated samplers outside Residence 91.

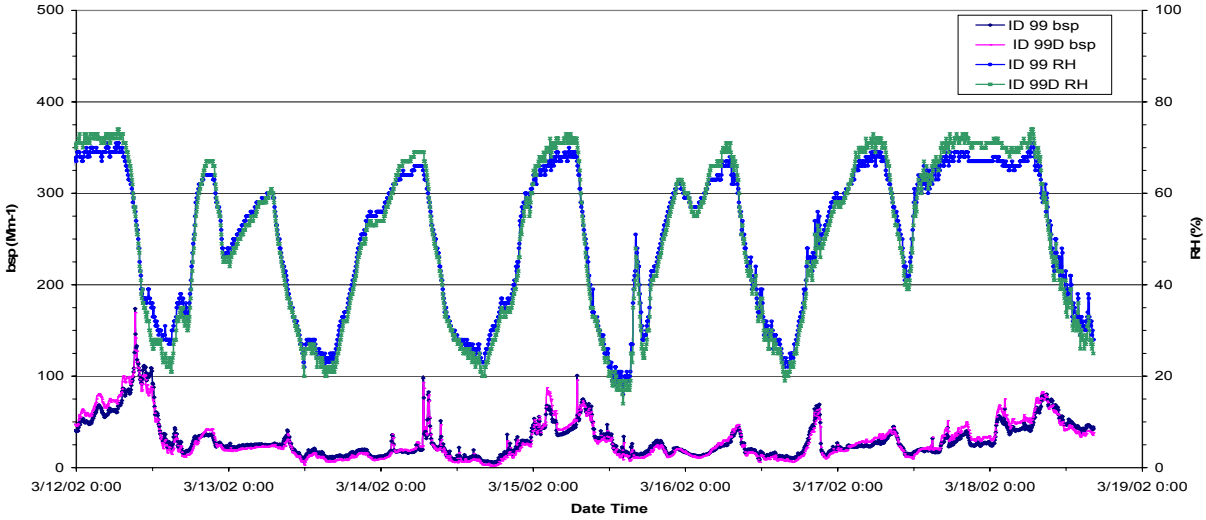


Figure 5.5.5-9. Particle scattering and relative humidity data from the collocated nephelometers outside Residence 99.

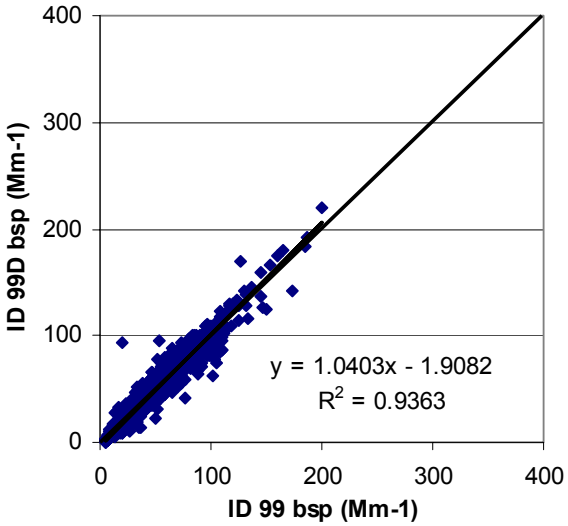


Figure 5.5.5-10. Comparison of 5-minute average light scattering by particles measured by nephelometers collocated at Residence 99 from March 6 to 18, 2002. A total of 2947 pairs of data are included in this plot.

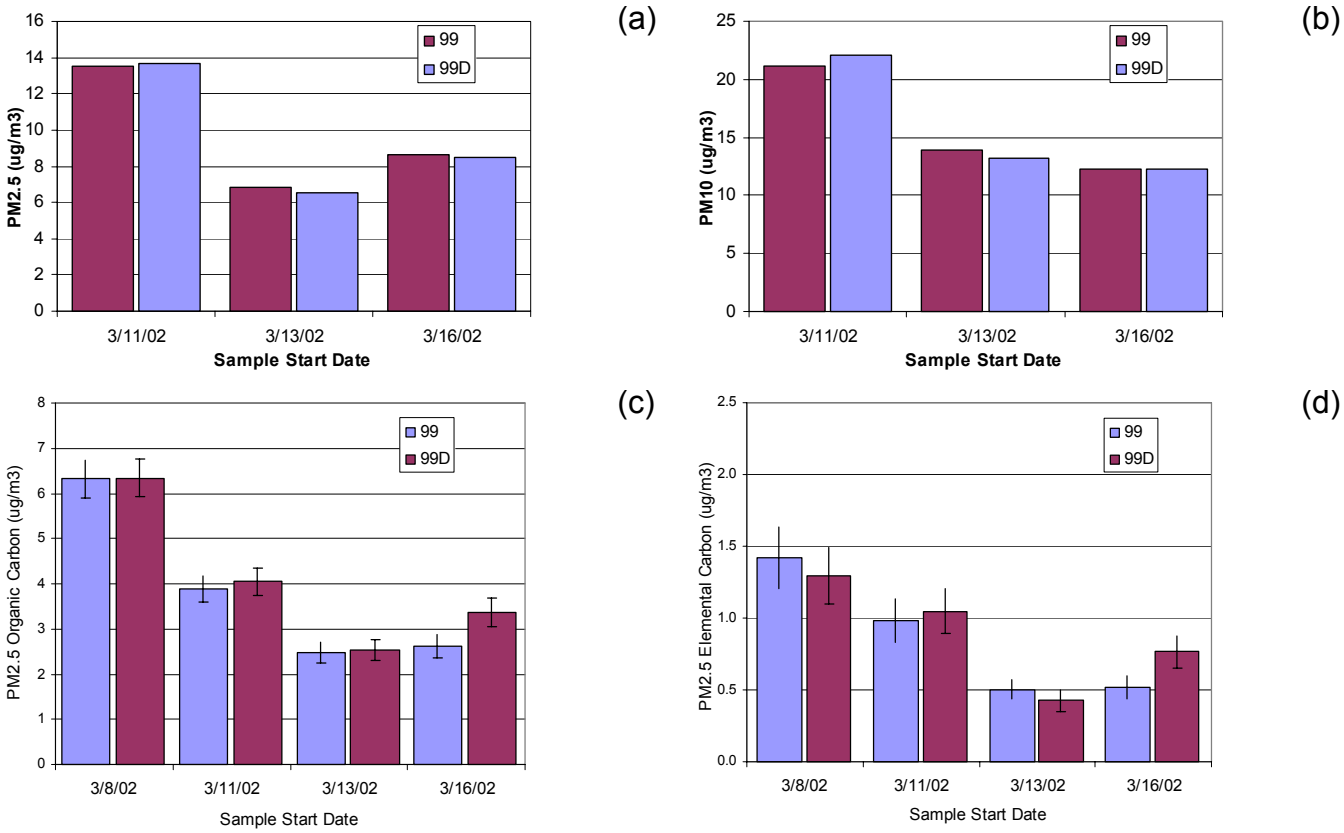


Figure 5.5.5-11. (a) $PM_{2.5}$ uncorrected mass, (b) PM_{10} uncorrected mass, (c) $PM_{2.5}$ OC, and (d) $PM_{2.5}$ EC concentrations measured by two collocated samplers outside Residence 99.

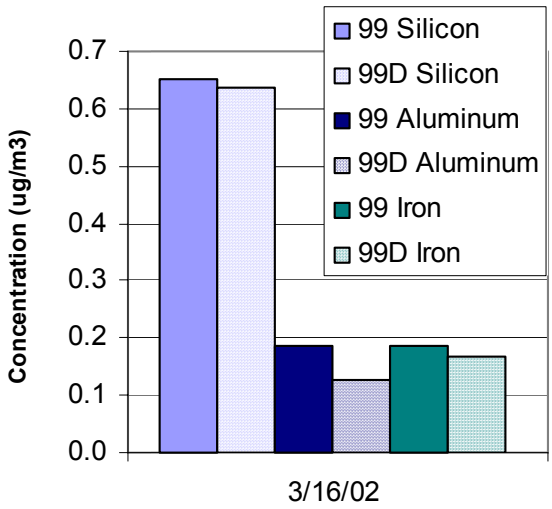


Figure 5.5.5-12. PM_{10} silicon, aluminum, and iron concentrations measured by two collocated samplers outside Residence 99.

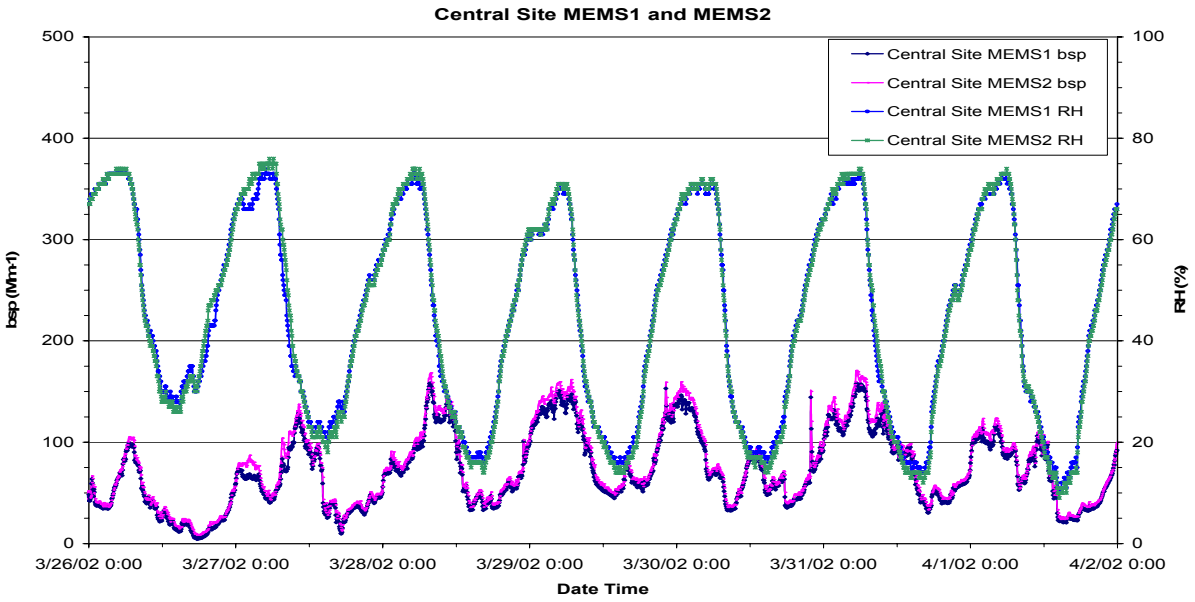


Figure 5.5.5-13. Light scattering by particles and relative humidity data from collocated nephelometers at the Central Site.

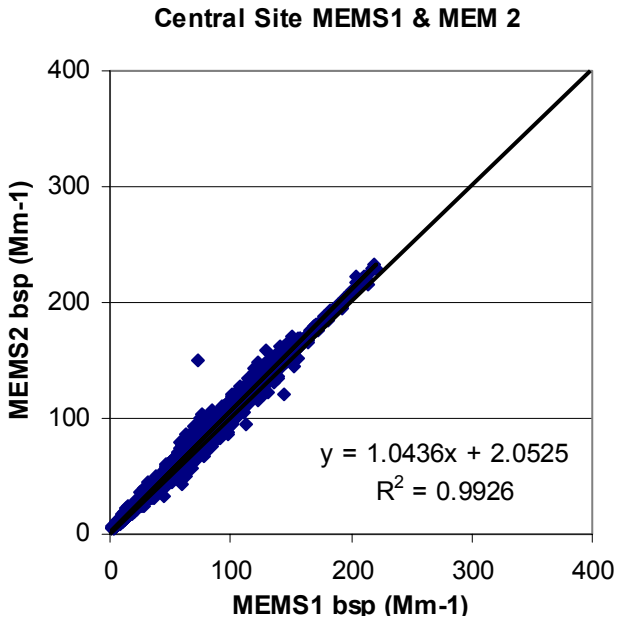


Figure 5.5.5-14. Comparison of 5-minute average light scattering by particles measured by nephelometers collocated at the Central Site for 12 days in March 2002. A total of 3617 pairs of data are included in this plot.

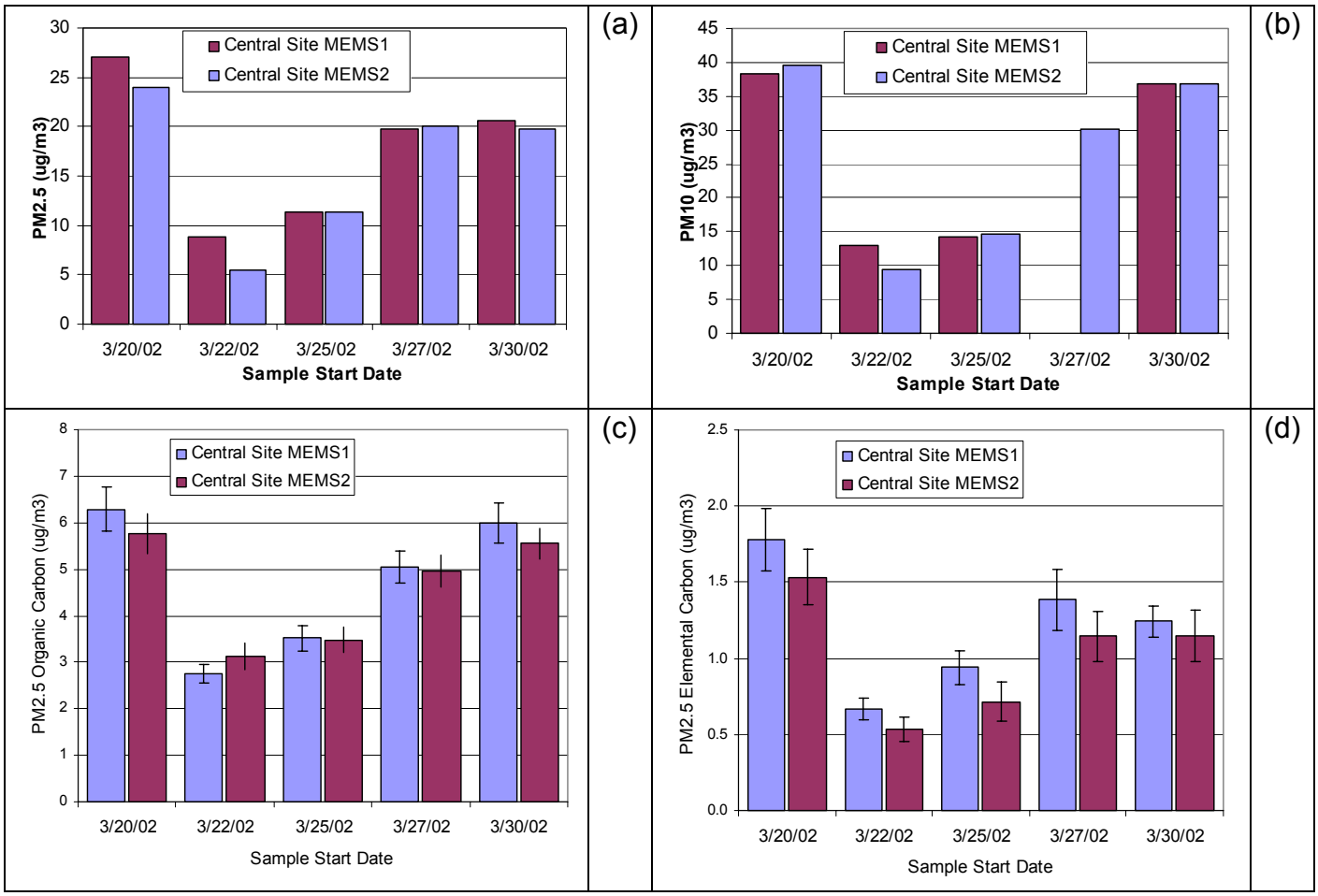


Figure 5.5.5-15. (a) $PM_{2.5}$ uncorrected mass, (b) PM_{10} uncorrected mass, (c) $PM_{2.5}$ organic carbon, and (d) $PM_{2.5}$ elemental carbon concentrations measured by two collocated samplers at the Central Site.

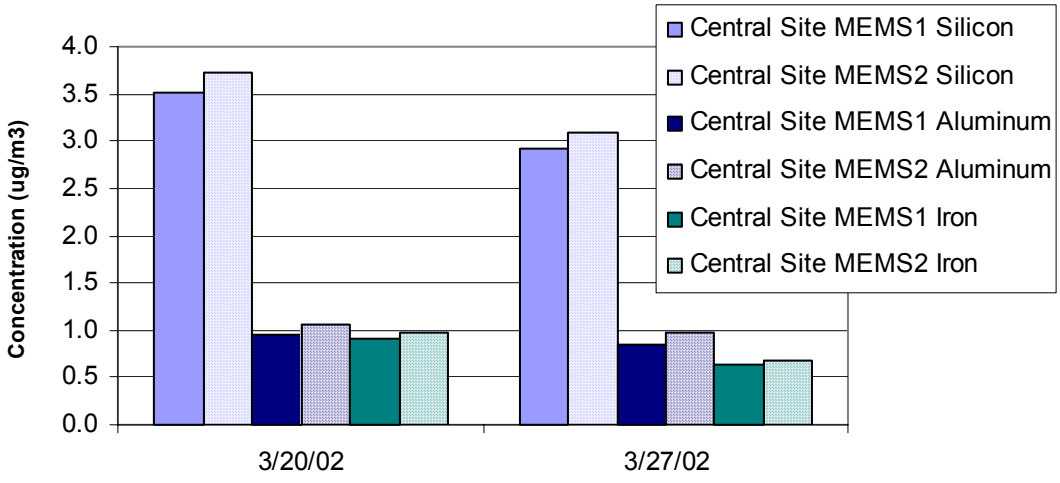


Figure 5.5.5-16. PM_{10} silicon, aluminum, and iron concentrations measured by two collocated samplers outside the Central Site.

5.5.6 Home Intensive Sampling Status

The Home Intensive subjects have been extremely cooperative, and the Home Intensive sampling is running smoothly. The Home Intensive sampling started on February 6, 2002, after pilot tests in January. **Table 5.5.6-1** shows the status of the Home Intensive sampling through June 27, 2002. Home intensive sampling has been conducted at a total of 47 homes to date. Sampling has been repeated at two homes, subject Residences 35 and 130. **Figure 5.5.6-1** shows the locations of all the FACES subjects, the Home Intensive subjects, the Central Site and other air quality monitoring sites, and the two trailer sites. Sampling has occurred at an excellent variety of locations and types of homes, and the preliminary data show some very interesting patterns. The Home Intensive sampling program is on track to be completed by February 2003.

Table 5.5.6-1. Home Intensive sampling status as of June 27, 2002**.**

Group ID	StartDate	Number of Homes	Residence ID#'s	Notes
G	02/06/02	3	52, 173, and 228	
H	02/20/02	4	89, 91, 239, and 242	Duplicate MEMS outside at Residence 91
D	03/06/02	4	99, 127, 151, and 232	Duplicate MEMS outside at Residence 99
C	03/20/02	3	106, 153, and 191	Two MEMS operated at the Central Site
A	04/03/02	5	35, 129, 130, 221, and 233	Two MEMS operated at the Central Site
F	04/17/02	4	138, 209, 231, and 253	Duplicate MEMS outside at Residence 231
G	05/01/02	5	21, 167, 201, 274, and 288	
B	05/15/02	4	48, 56, 212, and 278	Duplicate MEMS in & outside at Residence 278
H	05/29/02	5	6, 15, 27, 249, and 285	
E	6/12/02	5	202, 229, 25, 198 and 117	
A	6/26/02	5	79, 296, 35, 235, and 130	One MEMS operated at the Central Site
Total		47		

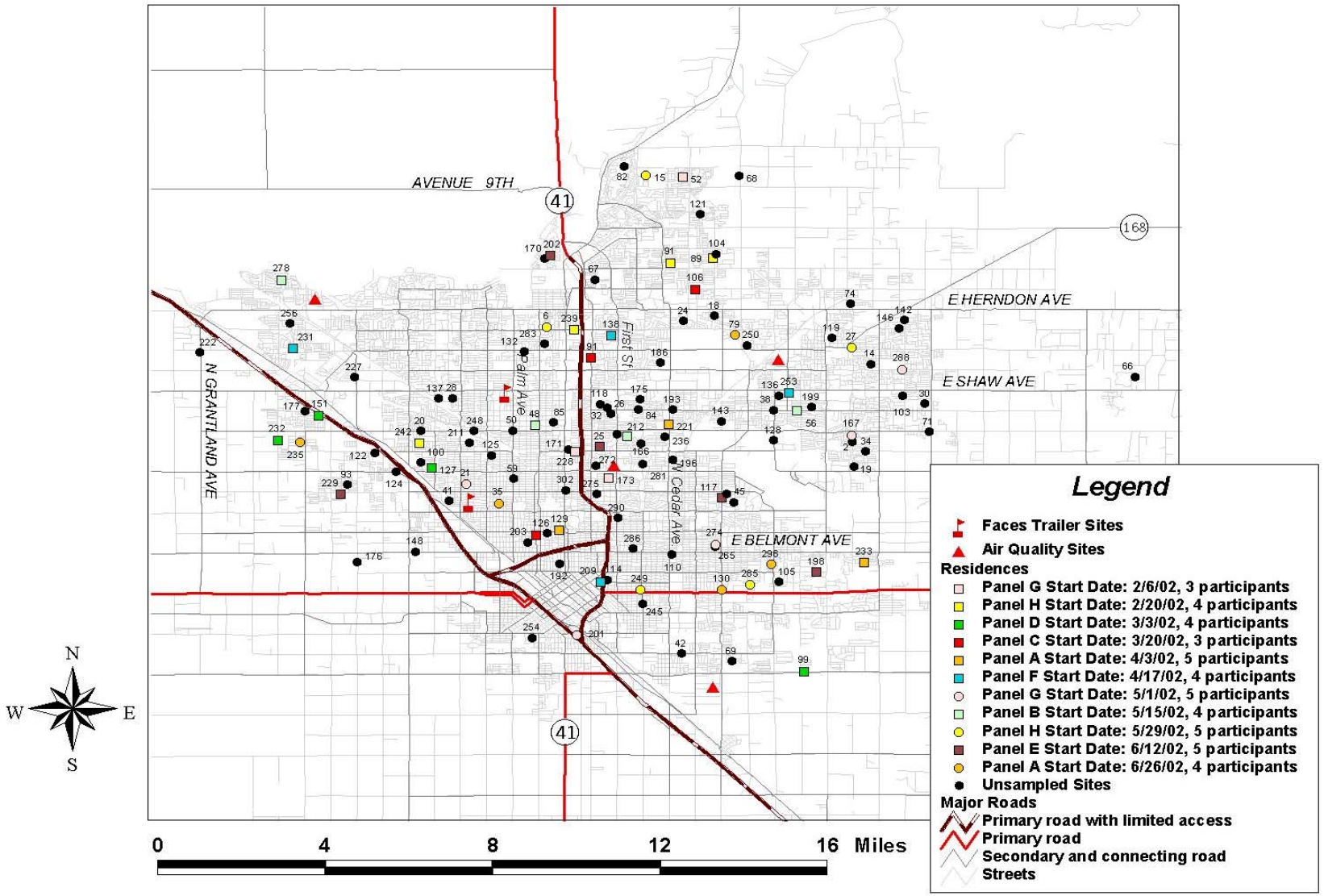


Figure 5.5.6-1. Map of the FACES participants, Home Intensive participants, Central Site and other air quality monitoring sites, and the trailer sites. The map highlights the Home Intensive participants as of June 26, 2002.

5.6 AIR QUALITY CONDITIONS INSIDE AND OUTSIDE HOMES

As noted above, a key hypothesis for the study is that different chemical species have concentrations that vary on urban, neighborhood, and household scales in the Fresno/Clovis study area. The FACES exposure assessment incorporates data collection to evaluate and characterize the variability of air pollutants on neighborhood and household scales in Fresno. Data from the outside of FACES houses are needed to address the neighborhood-scale variability, and data from the inside of the houses are needed to address the household-scale variability. In particular, the concern about indoor air quality arises from a combination of the large amount of time individuals spend indoors and the differences noted between indoor and outdoor concentrations of certain air pollutants. While it is not feasible to measure pollutants in all of the participants' homes continuously for the duration of the study, the Home Intensive sampling is designed to capture snapshots of air quality conditions inside and outside of a significant number of the FACES homes. These data are needed to develop models of FACES participants' daily exposures for the duration of the study. In this section, comparisons of preliminary data are made to illustrate examples of indoor/outdoor (I/O) concentration variations observed in Fresno. The relationships between the housing characteristics and the indoor/outdoor concentration variations exhibited in the preliminary data have not been explored.

Data are available for selected agents from the Home Intensive monitoring. Specifically, PM mass, b_{sp} by particles, elemental and organic carbon, trace elements, pollen grains, and spores data are available from the early home intensive sampling. Note, the preliminary $PM_{2.5}$ and PM_{10} mass data have not yet been corrected for ammonium nitrate volatization losses, which can be significant in Fresno.

5.6.1 PM Mass

The 24-hr average uncorrected PM mass concentrations measured in the Pilot Study, Panel D (starting March 6, 2002) and Panel C (starting March 20, 2002) inside and outside nine homes, are shown in **Figures 5.6.1-1**. The data show cases where indoor concentrations are both above and below outdoor concentrations although concentrations are more frequently higher indoors than outdoors in these particular houses. The most extreme case was at House 99 on March 16 where the 24-hr average PM_{10} concentration was 80 $\mu g/m^3$indoors compared to 12 $\mu g/m^3$outdoors. The PM mass data from this limited data set show modest correlation ($r^2 = 0.51$ for $PM_{2.5}$ and $r^2 = 0.42$ for PM_{10}) between indoor and outdoor levels.

As shown in **Figure 5.6.1-2**, the indoor-to-outdoor PM mass concentration ratios for 24-hr periods range from 0.55 to 6 for uncorrected $PM_{2.5}$ mass and 0.30 to 6.5 for uncorrected PM_{10} mass. **Figure 5.6.1-3** shows the 3-day average ratios from the Pilot Study homes and 5-day average ratios from these FACES participants' homes. The 5-day average I/O ratios for FACES participants' homes range from 1.2 to 2.8 for $PM_{2.5}$ mass and 1.3 to 3 for PM_{10} mass. Houses with higher mean I/O ratios usually have greater day-to-day variability in I/O ratios. It is important to recognize that outdoor concentrations were relatively low on most of these days, and the high I/O ratios were predominantly found on days with lower outdoor concentrations. Overall, the preponderance of I/O ratios greater than 1 indicate there are indoor sources of particles in most of these homes.

5.6.2 Light Scattering by Particles

Light extinction by particles (b_{sp}) is measured inside and outside houses as a surrogate for continuous $PM_{2.5}$ mass measurements. It is measured with 5-minute time resolution using relative humidity controlled Radiance Research nephelometers. Although the amount of light extinction per unit of $PM_{2.5}$ mass varies somewhat with the particle chemical composition and size, it is well-established that b_{sp} is highly correlated with $PM_{2.5}$ mass concentrations. Notable variations in the proportionality of b_{sp} and $PM_{2.5}$ mass occur when there are extreme differences in the chemical composition of PM as is possible with indoor and outdoor samples, especially when there are large indoor sources.

Examples of 5-minute average b_{sp} inside and outside FACES participants' homes are shown in **Figures 5.6.2-1 through 5.6.1-2**. House 232 (see Figure 5.6.2-1) exhibited some of the highest I/O ratios of $PM_{2.5}$ mass, and the b_{sp} measurements show frequent periods where indoor extinction far exceeds outdoor extinction. The rapid elevation of indoor light extinction due to source activity is followed by hours of decay back down to levels often lower than outdoor levels. House 242 (Figure 5.6.2-2) had light extinction that is usually lower inside than outside, yet it also had occasional excursions where indoor extinction far exceeds outdoor extinction. Almost all the FACES participants' houses examined to date occasionally have ⅓ to 3-hr periods where indoor b_{sp} exceeds outdoor b_{sp}.

The multi-day average b_{sp} values observed during the Pilot Study and the first four panels are shown in **Figure 5.6.2-3**. The 6-day average light extinction coefficients measured during the Pilot Study (House 1901) were among the highest measured during the first 10 weeks of the Home Intensive. The ratios of average-indoor-to-average-outdoor light extinction ranged from 0.4 to 1.2 among these 14 homes. The 12-day average light extinctions were lower indoors than outdoors at 9 of the 13 FACES participants' homes. For panels C and D, the indoor-to-outdoor ratios were generally lower for light extinction than for uncorrected $PM_{2.5}$ mass. The relative ranking of houses, based on the 12-day average b_{sp} and the 5-day average integrated $PM_{2.5}$ mass measurements indoors and outdoors is generally similar.

The 5-minute time resolution b_{sp} data do not show high correlation between indoor and outdoor levels. Correlation is only expected for longer time-averaging periods. The short time resolution data are useful for identifying whether a particular home has significant indoor sources. The longer-term averages are useful for classifying a home with regard to indoor/outdoor pollution characteristics.

5.6.3 Elemental and Organic Carbon

Elemental and organic carbon (EC and OC) concentrations are of interest because they are associated with vehicle PM emissions and other combustion sources, and they can make up a significant portion of $PM_{2.5}$ mass. The EC and OC data collected inside and outside homes in the Home Intensive can be compared directly since they are collected with the same type of sampler and analyzed in the same laboratory. The 24-hr average indoor and outdoor $PM_{2.5}$ EC concentrations during the Pilot Study and Panels C, D, G, and H are shown in **Figure 5.6.3-1**. There are a few indoor EC measurements that are very high (20 to 30 $\mu g/m^3$) compared to the corresponding outdoor measurements (2 to 5 $\mu g/m^3$). These high levels are

presumably due to indoor combustion sources. Most of the indoor EC concentrations are slightly higher or slightly lower than the corresponding outdoor concentrations in these houses. The indoor EC concentrations tend to be higher than those outdoors when the outdoor concentrations are low (below 2 $\mu g/m^3$). The indoor/outdoor correlation is low when the four outliers are included; however, the r^2 increases from 0.13 to 0.65 when the outliers are excluded, suggesting a fairly strong relationship.

The OC concentrations measured inside and outside the homes sampled in the first 10 weeks are shown in **Figure 5.6.3-2**. Again, there is one outlier with a 24-hr average indoor OC concentration of 98 $\mu g/m^3$ compared to an outdoor concentration of 20 $\mu g/m^3$. Most OC concentrations are higher inside than outside these houses. As shown in **Figures 5.6.3-3 and 5.6.3-4,** the 24-hr average and multi-day average I/O ratios are higher for OC than EC concentrations. The higher indoor-to-outdoor ratios tend to occur when outdoor concentrations are low (OC < 10 $\mu g/m^3$). These preliminary data suggest there are indoor sources of carbonaceous aerosol that should be accounted for in assigning exposures to FACES participants. Other researchers using similar data collection methods have suggested that the higher than expected I/O concentration ratios for OC are due to measurement artifacts (Claiborn et al., 2002) which are larger indoors than outdoors. Further analysis is required to determine whether there are significant and/or differential artifacts in the Fresno OC data.

5.6.4 Selected Elements

The elemental analysis quantifies concentrations of about 40 elements, including certain trace metals that are designated agents in FACES. The elements are collected using a 10 μm inlet so that both coarse-mode and fine-mode particles are captured in the samples. Several of the more abundant elements are used here to illustrate typical indoor and outdoor concentrations in Fresno. PM_{10} concentrations of silicon, aluminum, and iron mostly reflect contributions from sources of crustal material whereas PM_{10} sulfur concentrations mostly reflect sulfate formed from atmospheric oxidation of SO_2 emitted by fuel combustion. Iron is one of the trace metals of concern in the health effects analysis. **Figures 5.6.4-1 and 5.6.4-2** show the concentrations of silicon, aluminum, iron, and sulfur collected inside and outside the houses in the first four panels. The 24-hr average I/O ratios for these elements are shown in **Figures 5.6.4-3 and 5.6.4-4**. The silicon and aluminum concentrations show a lot of scatter with indoor concentrations below and above outdoor levels; no clear relationship between the contemperous indoor and outdoor concentration is evident. The minimum, mean, and maximum I/O ratios are 0.3, 1.27, and 5.0 for silicon and 0.25, 1.5, and 8.5 for aluminum, respectively. The PM_{10} iron concentrations also show a lot of scatter; however, the concentrations are lower indoors than outdoors in the majority of samples. The average I/O ratio for PM_{10} iron is 0.67 in these data. The sulfur concentrations are quite similar indoor and outdoor. The correlation coefficient (r) is 0.69 and the average I/O ratio for PM_{10} sulfur is 0.999. The similarity of indoor and outdoor sulfur levels is consistent with other studies and the hypothesis that there are very few indoor sources of sulfate in FACES participants' homes.

5.6.5 Pollen Grains, Fungal Spores and Endotoxin

Pollen grains from Panel 4 (Group C, **Figures 5.6.5-1 and 5.6.5-2**) and Panel 5 (Group A, **Figures 5.6.5-3 through 5.6.5-5**) have been analyzed and identified to date. The indoor

pollen concentrations are generally very low, but for homes where the windows have been open during the day, or homes that have dogs, the concentrations are higher, which suggests that pollen grains have attached to the pets and are transported indoors through the open windows. Also the smaller pollen grains seem to occur more frequently in the indoor air (Figures. 5.6.5-2, 5.6.5-4, and 5.6.5-5). The day-to-day variation within one home as well as the geographic variation is notable (Figures. 5.6.5-1 and 5.6.5-3).

For most of the fungal spore species, the indoor concentrations were lower than outdoor concentrations, and the relationship was similar to that seen with pollen (**Figure 5.6.5-6**). The geographic variation for the outdoor concentrations was not as striking as for pollen grains. The indoor diurnal variation followed closely the activities at homes (**Figure 5.6.5-7**).

Endotoxins are of interest because they have been implicated in asthma symptoms. The airborne endotoxin data collected inside and outside homes in the Home Intensive can be compared directly since they are collected with the same type of sampler and analyzed in the same laboratory. The 24-hr average indoor and outdoor concentrations at seven homes, each monitored on five days, is presented in **Figures 5.6.5-8A through 5.6.5-8G**. The indoor concentrations were higher than the outdoor concentrations at six of the seven homes. Home 232 was an exception: the indoor and outdoor concentrations were comparable on three days, and on March 16 outdoor concentrations were more than double the indoor concentrations. For the other homes, the ratio of indoor to outdoor airborne endotoxin varied considerably from day to day; note especially home 99, where the ratio of indoor to outdoor ranged from 1.7 to 10.3.

5.6.6 Summary of Indoor and Outdoor Conditions

The data collected early in the FACES Home Intensive show indoor and outdoor concentrations of numerous agents are sufficiently different to warrant including them in the exposure assignment methodology. Too few data have been collected and analyzed to draw definitive conclusions. However, the PM mass and OC data frequently show indoor concentrations exceeding outdoor levels which indicates there are potentially important indoor sources in the homes of FACES participants. The multi-day average I/O ratios shown in Figure 5.6-14 strongly suggest that there are indoor sources of carbonaceous aerosol, especially OC, that should be accounted for in assigning exposures to FACES participants

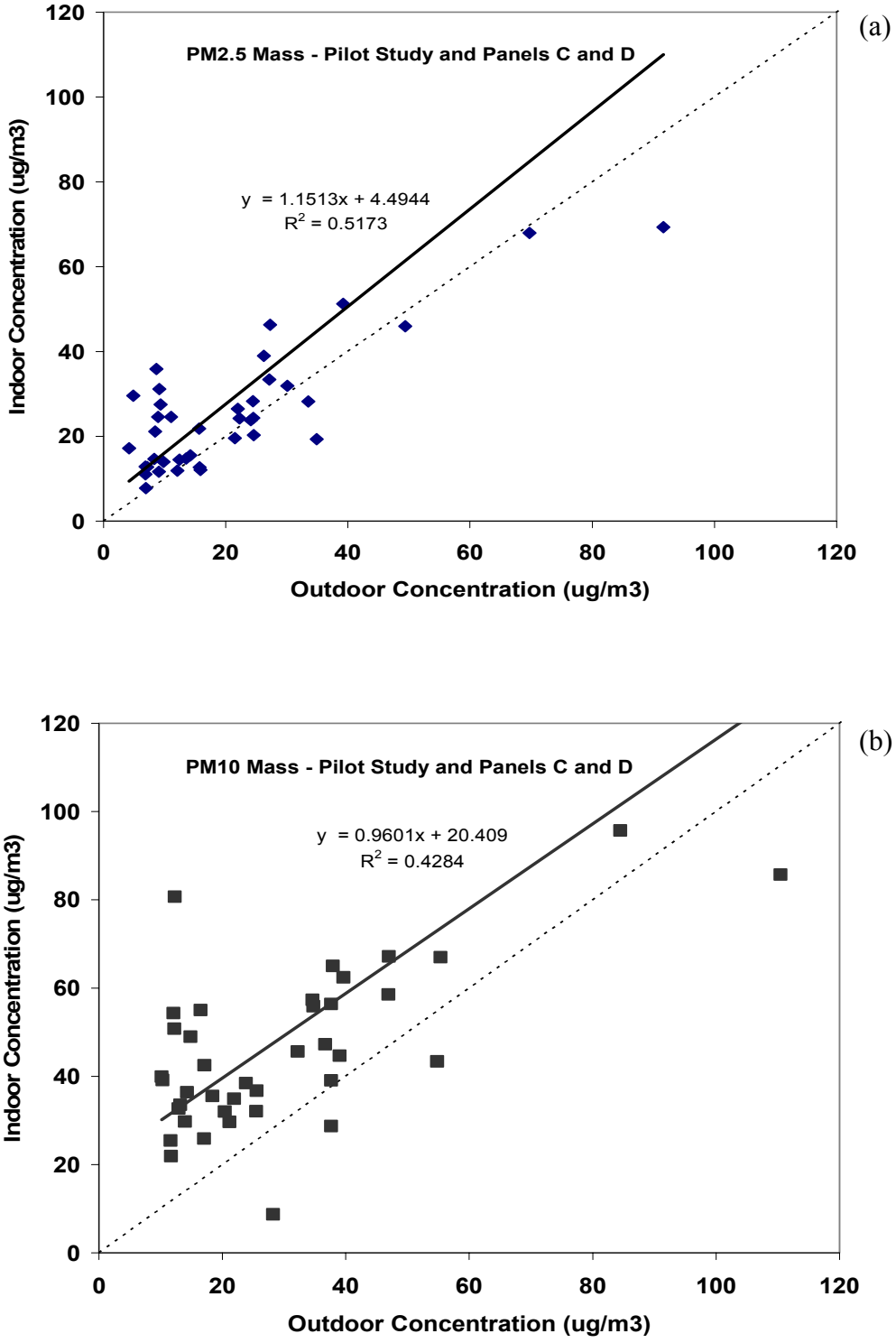


Figure 5.6.1-1. Comparison of indoor and outdoor 24-hr average (a) uncorrected $PM_{2.5}$ mass and (b) PM_{10} mass concentrations measured during the FACES Pilot Study and Panels C and D.

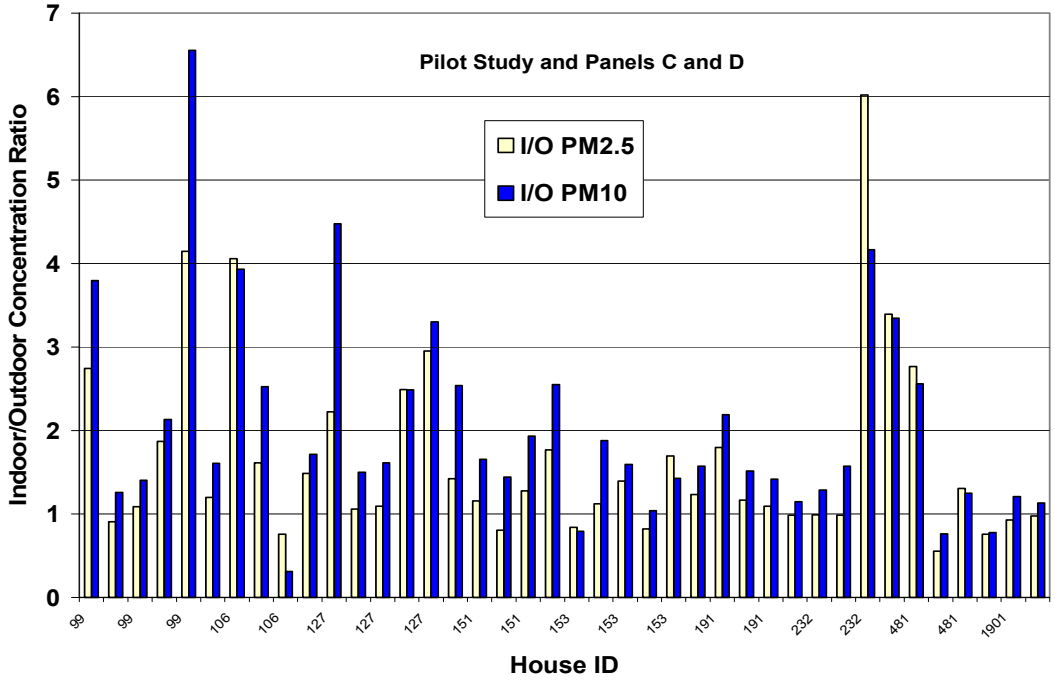


Figure 5.6.1-2. Comparison of 24-hr average I/O concentration ratios for $PM_{2.5}$ and PM_{10} during the FACES Pilot Study and Panels C and D.

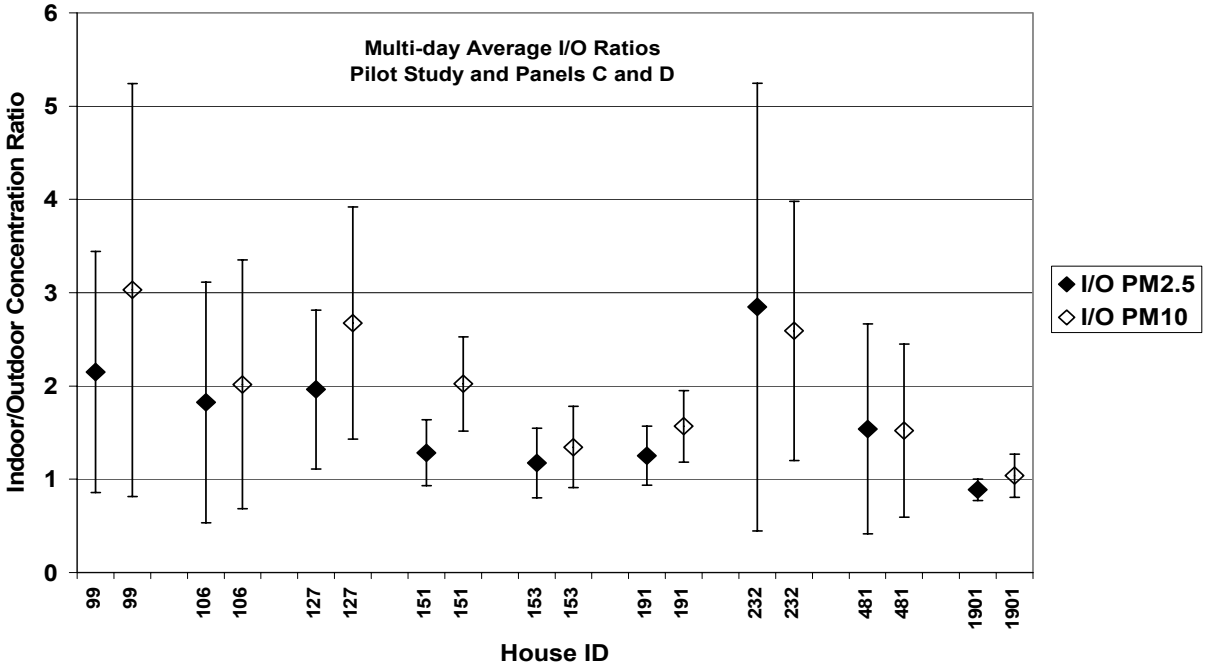


Figure 5.6.1-3. Multi-day average I/O concentration ratios for $PM_{2.5}$ and PM_{10} during the FACES Pilot Study and Panels C and D. The vertical bars indicate one standard deviation of the 24-hr average ratios.

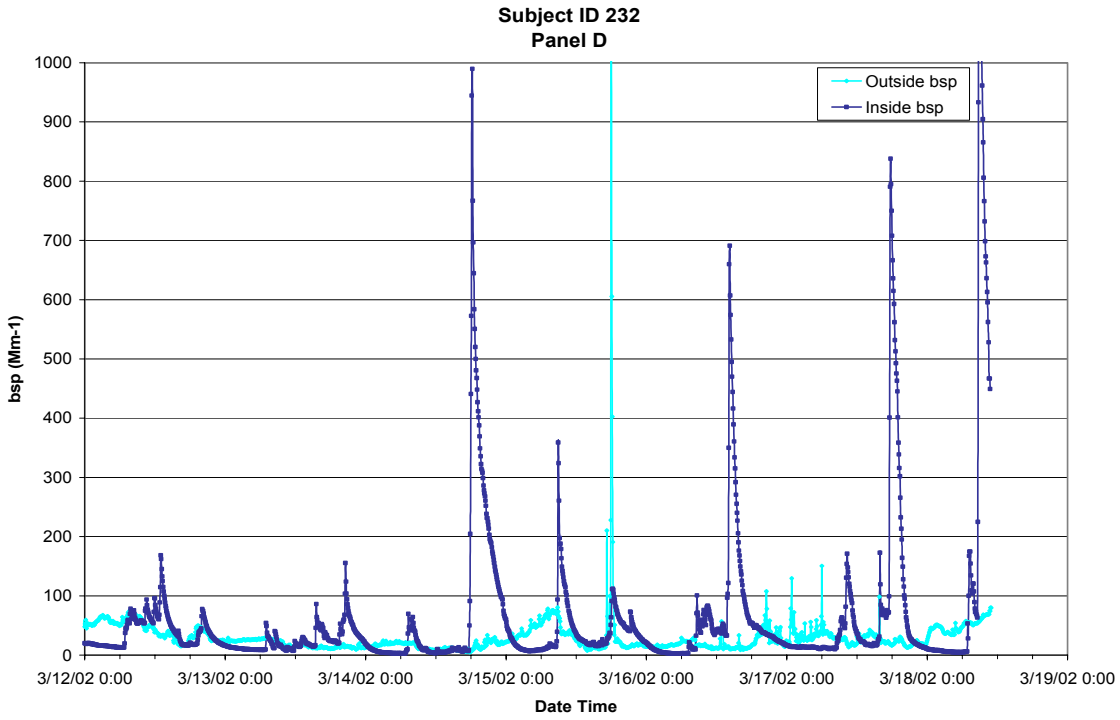


Figure 5.6.2-1. b_{sp} by particles inside and outside House 232 during the second week of Panel D.

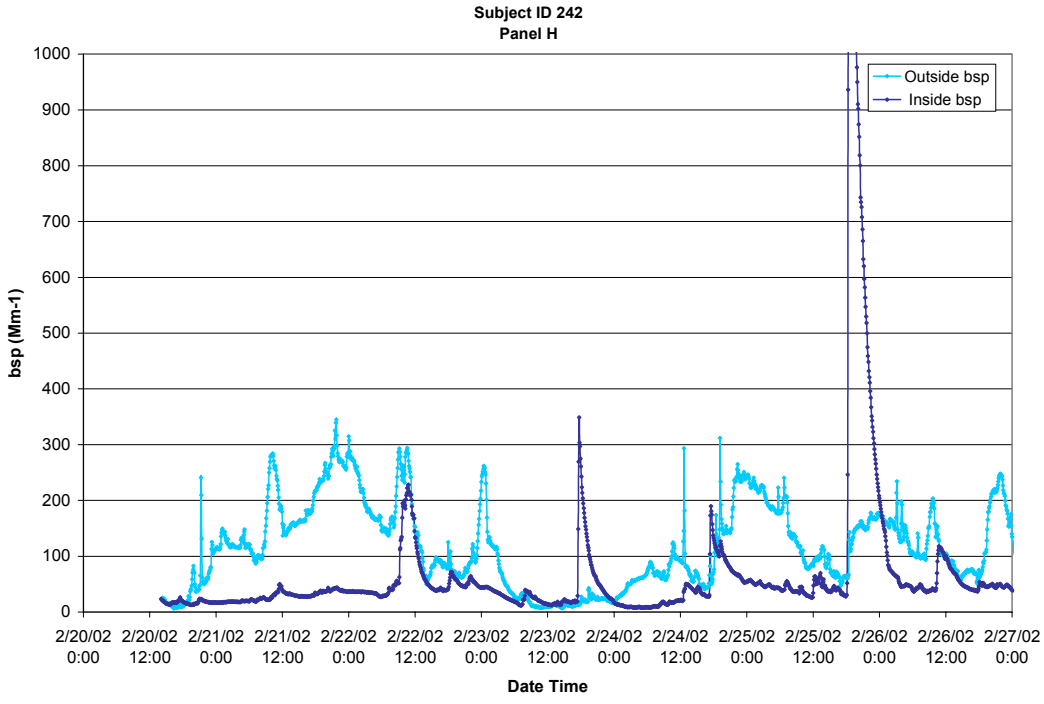


Figure 5.6.2-2. b_{sp} by particles inside and outside House 242 during the second week of Panel H.

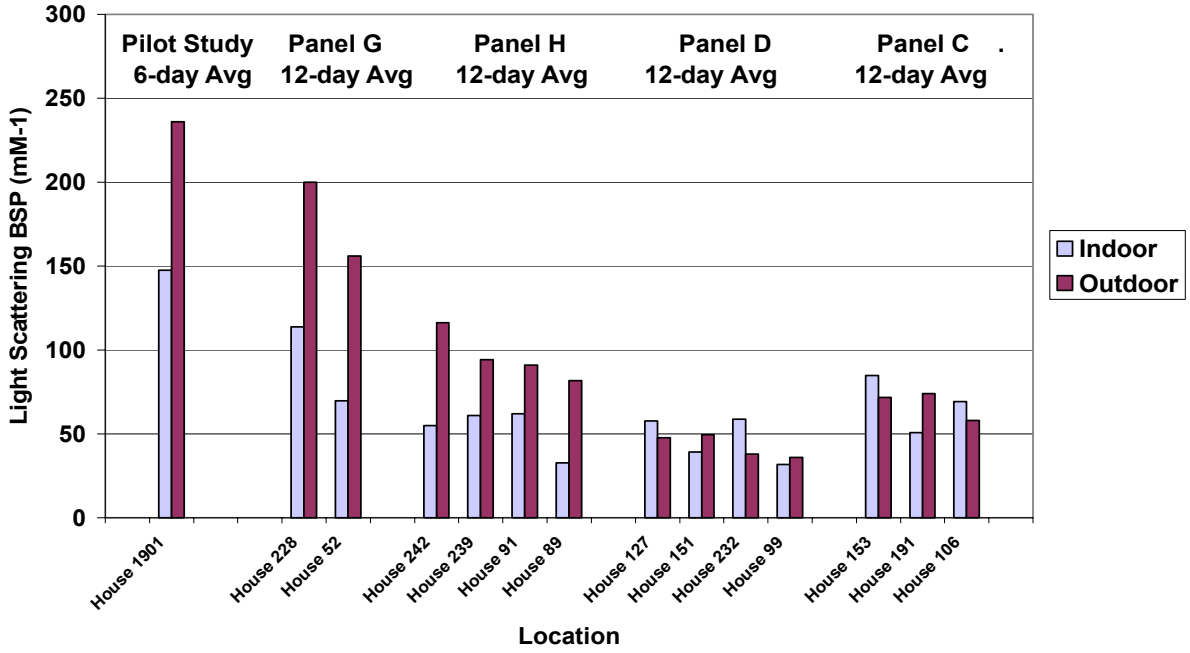


Figure 5.6.2-3. Multi-day average b_{sp} measured inside and outside houses during the FACE Pilot Study and Panels C, D, G, and H.

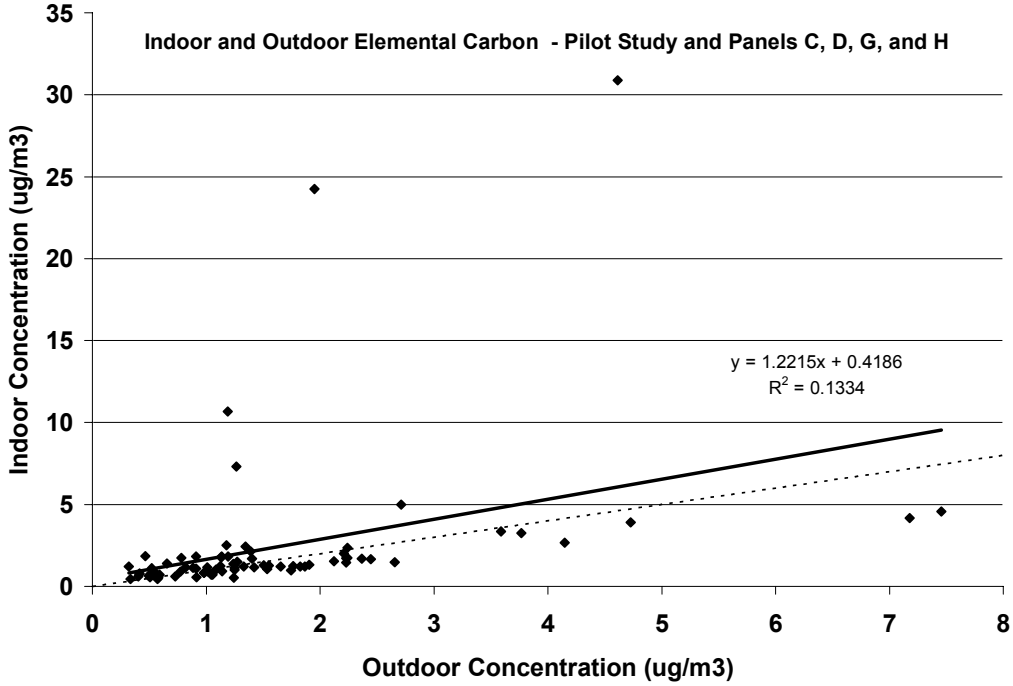


Figure 5.6.3-1. Comparison of indoor and outdoor 24-hr average EC concentrations measured during the FACES Pilot Study and Panels C, D, G, and H.

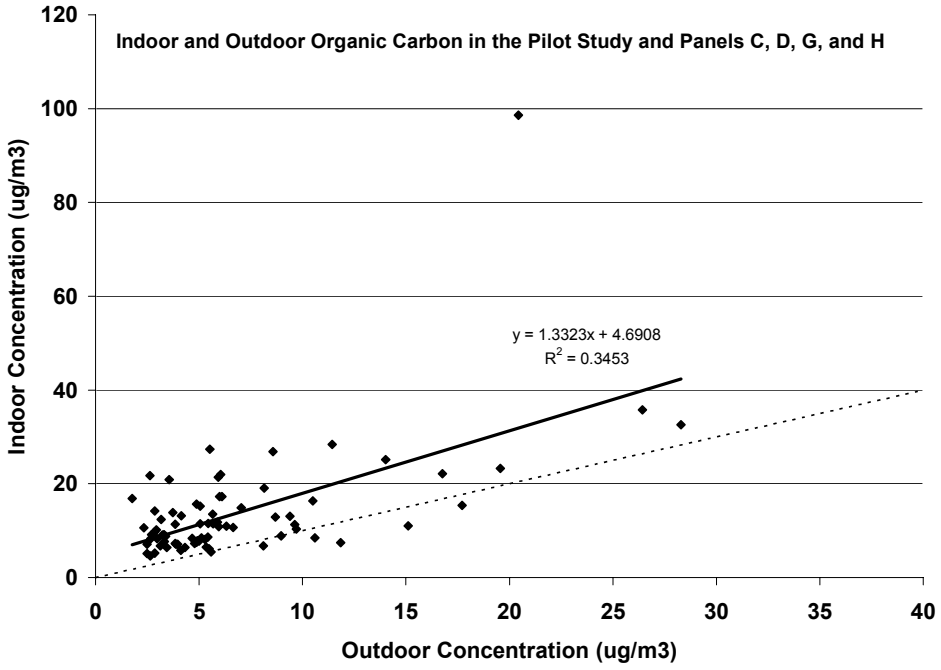


Figure 5.6.3-2. Comparison of indoor and outdoor 24-hr average OC concentrations measured during the FACES Pilot Study and Panels C, D, G, and H.

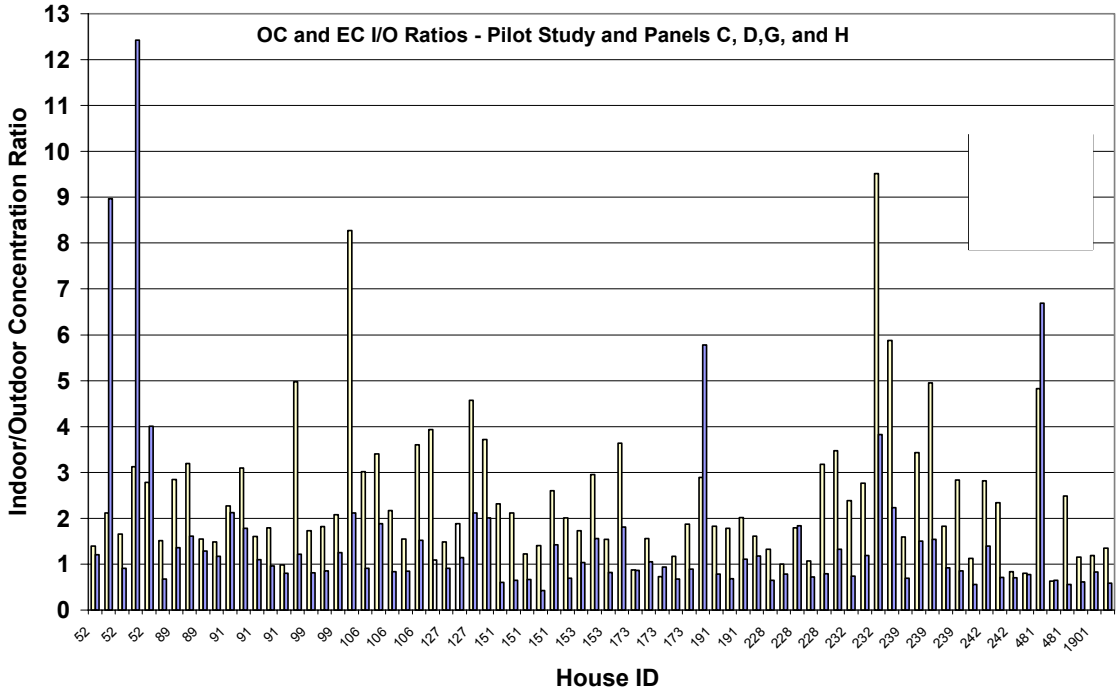


Figure 5.6.3-3. Comparison of 24-hr average I/O concentration ratios for OC and EC during the FACES Pilot Study and Panels C, D, G, and H.

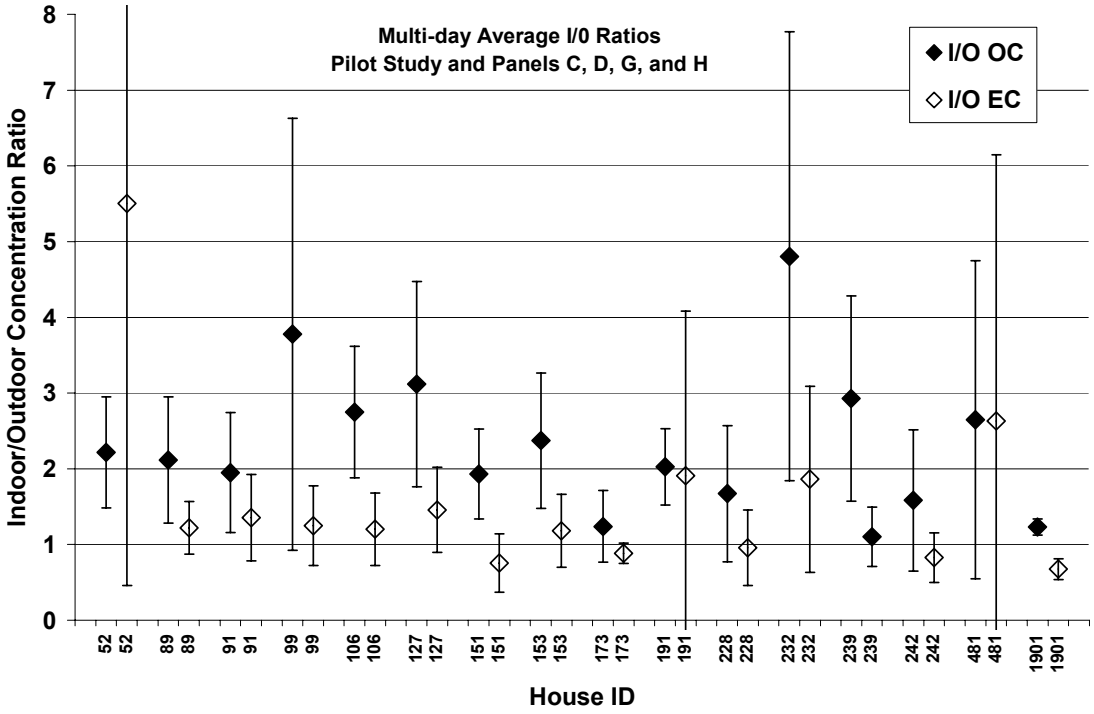


Figure 5.6.3-4. Multi-day average I/O concentration ratios for OC and EC during the FACES Pilot Study and Panels C, D, G, and H. The vertical bars indicate one standard.

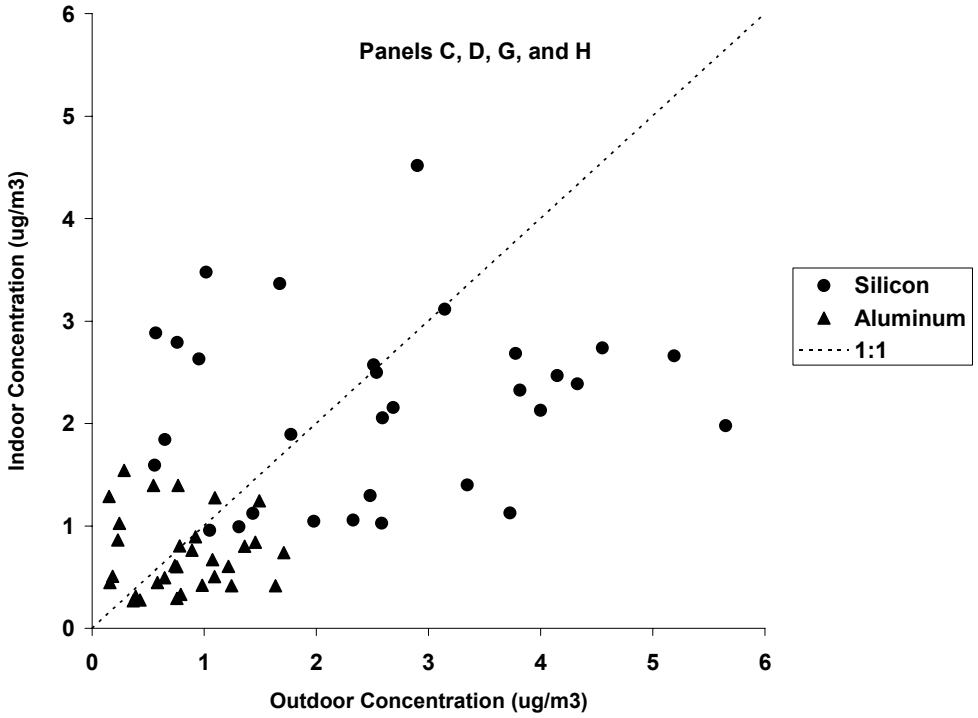


Figure 5.6.4-1. Twenty-four-hour average PM_{10} silicon and aluminum concentrations measured inside and outside houses during Panels C, D, G, and H.

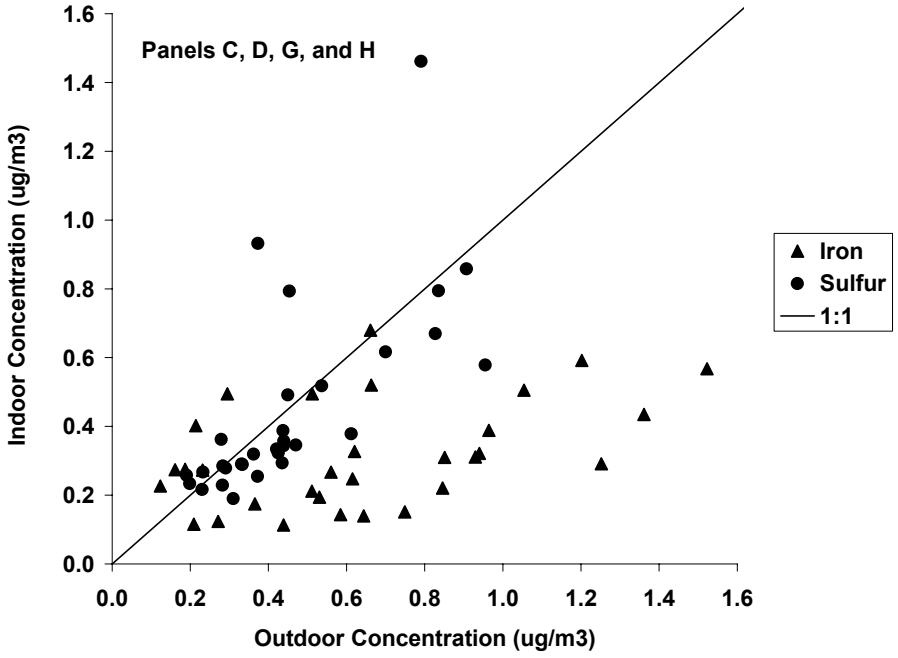


Figure 5.6.4-2. Twenty-four-hour average PM_{10} iron and sulfur concentrations measured inside and outside houses during Panels C, D, G, and H.

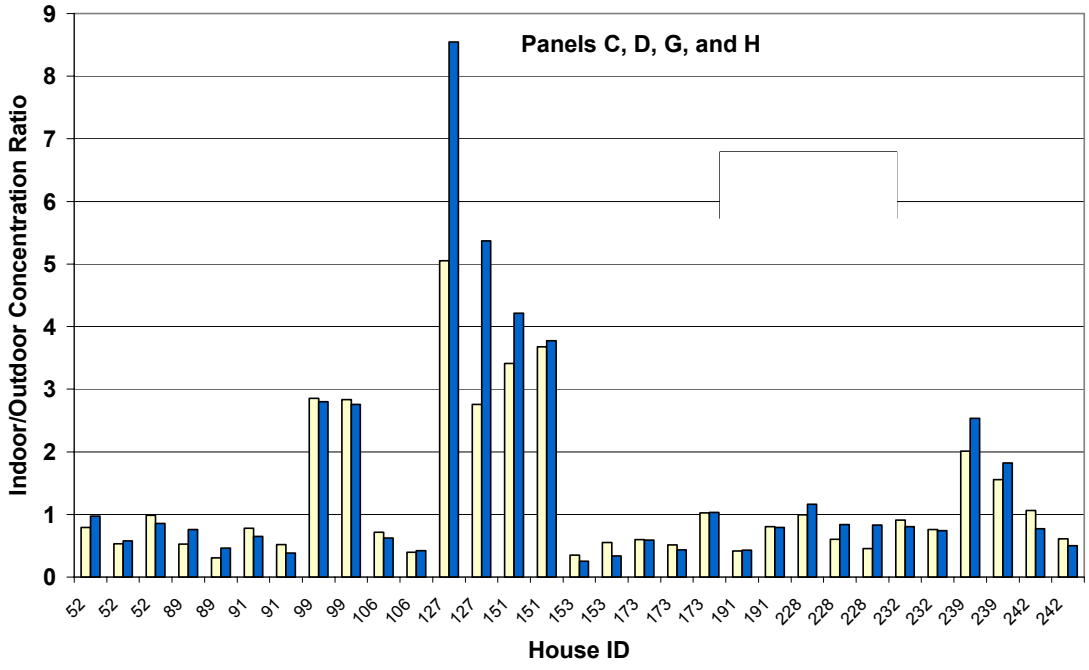


Figure 5.6.4-3. Ratios of 24-hr average I/O PM_{10} silicon and aluminum concentrations measured at houses during the FACES Panels C, D, G, and H.

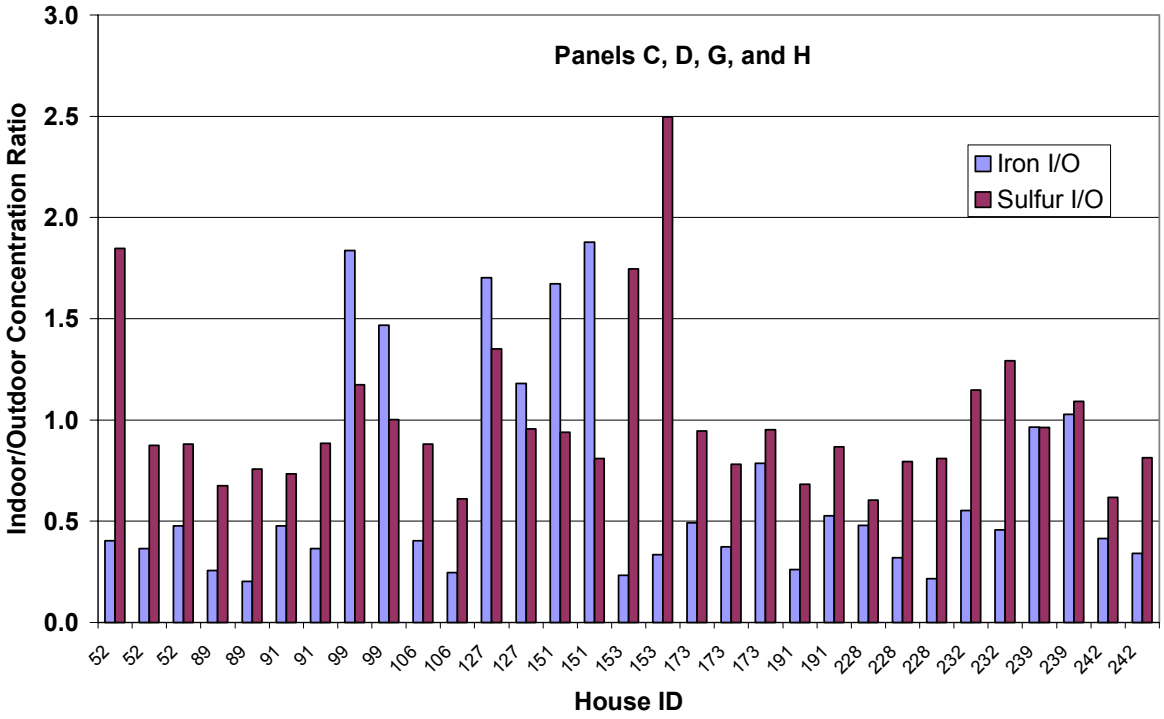


Figure 5.6.4.4. Ratios of 24-hr average I/O PM_{10} iron and sulfur concentrations measured at houses during the FACES Panels C, D, G, and H.

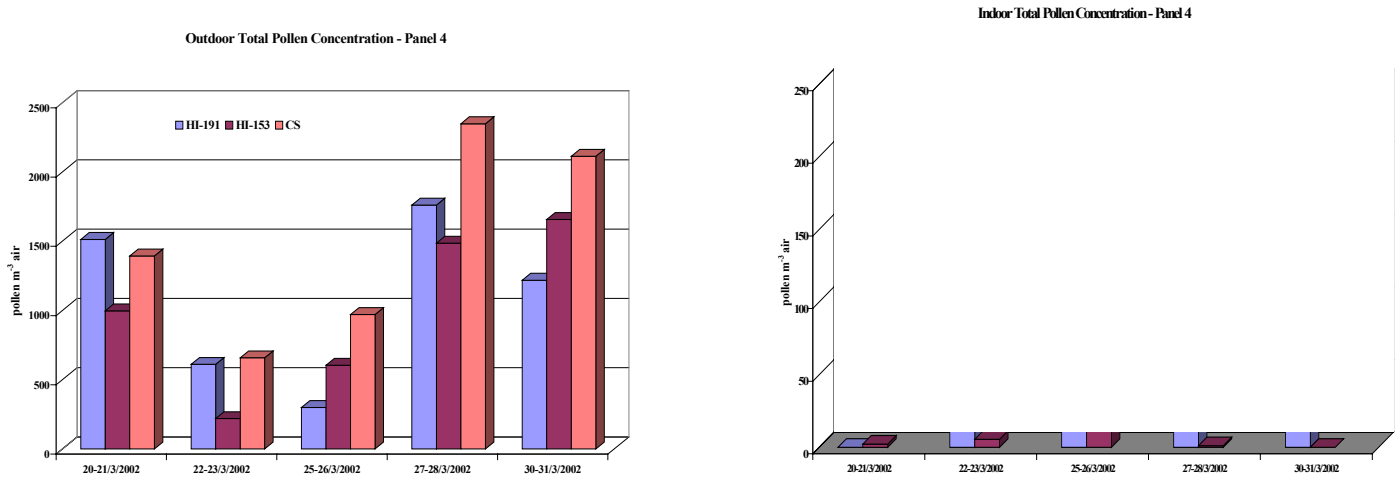


Figure 5.6.5-1. Outdoor and indoor total pollen concentrations for Panel 4. CS = Central Site.

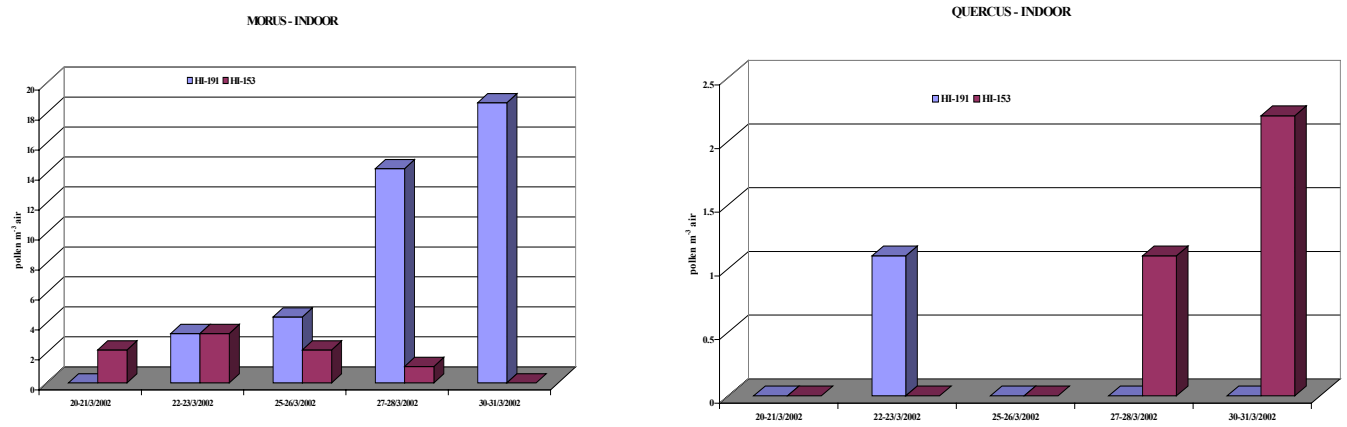


Figure 5.6.5-2. Indoor concentrations of *Morus* (small pollen grain) and *Quercus* (>30 micron pollen grain) in two different homes in the Panel 4.

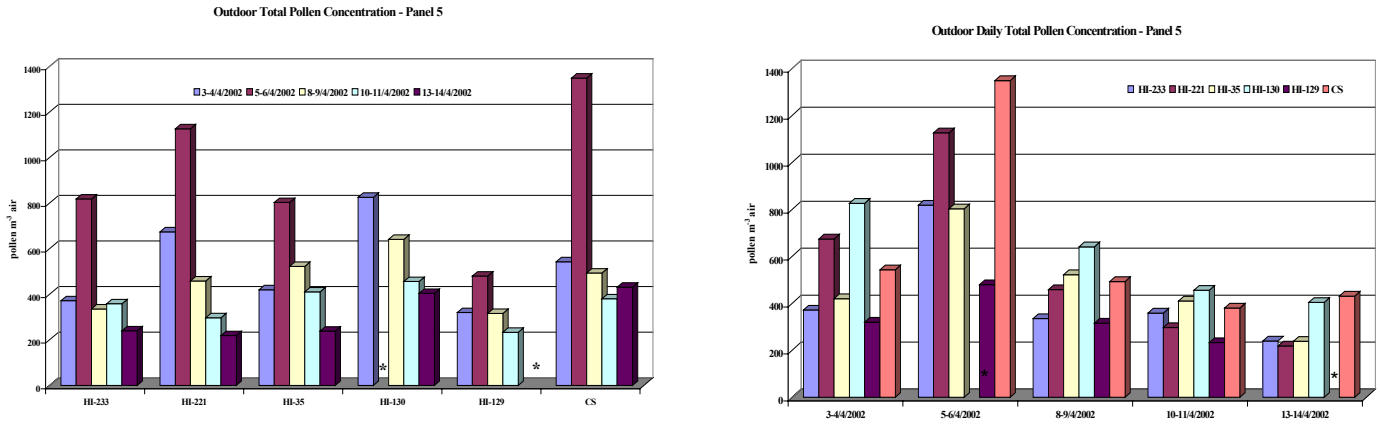


Figure 5.6.5-3. Total daily outdoor pollen concentrations for Panel 5, geographic and daily variation. CS = Central Site, * = Missing Data.

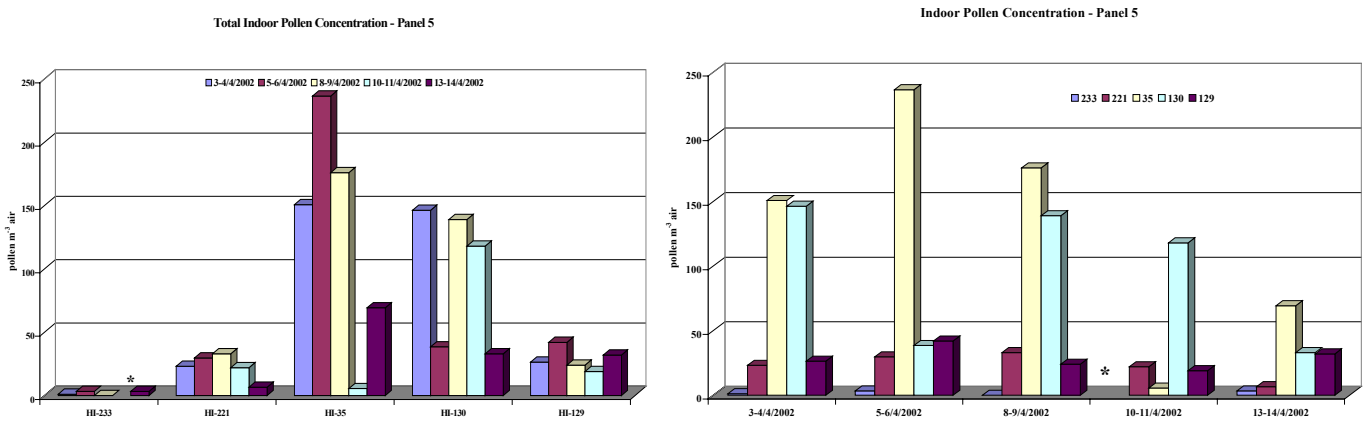


Figure 5.6.5-4. Total daily indoor pollen concentrations for Panel 5, geographic and daily variation. * = Missing Data.

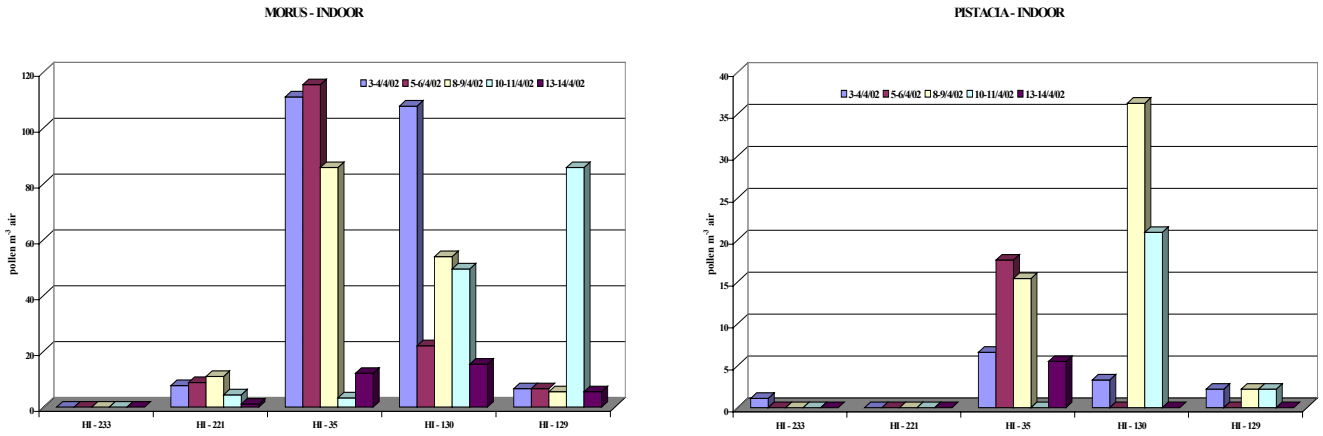


Figure 5.6.5-5. Total daily indoor pollen concentrations for the different homes within the Panel 5. Homes 10, 135 and 129 have moderate concentrations of e.g., *Morus* and *Pistacia*. The windows were kept open during the most part of the day.

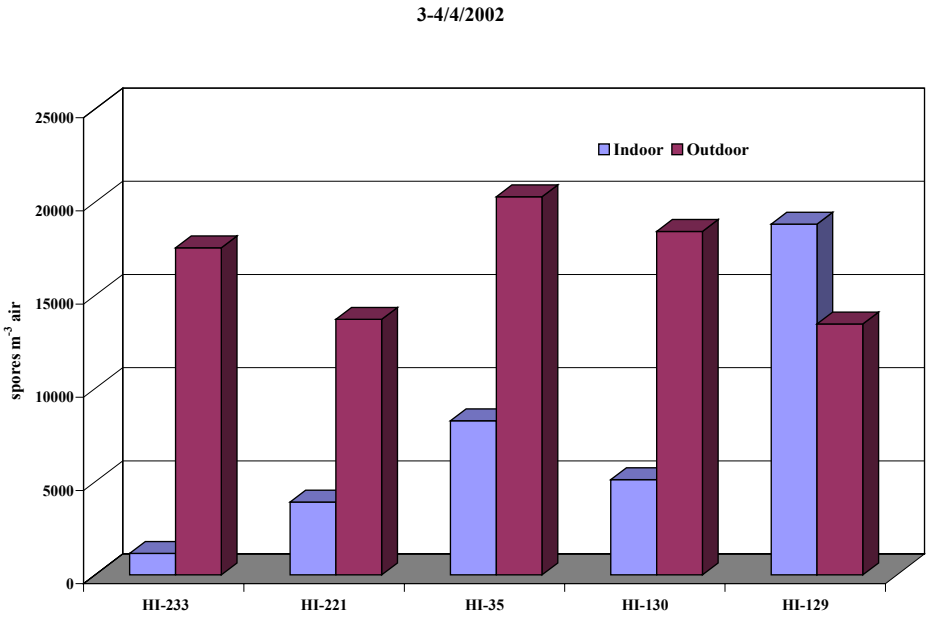


Figure 5.6.5-6. Example of the outdoor and indoor fungal spore concentrations between different homes within the Panel 5. Note the very high indoor concentrations for Home 129.

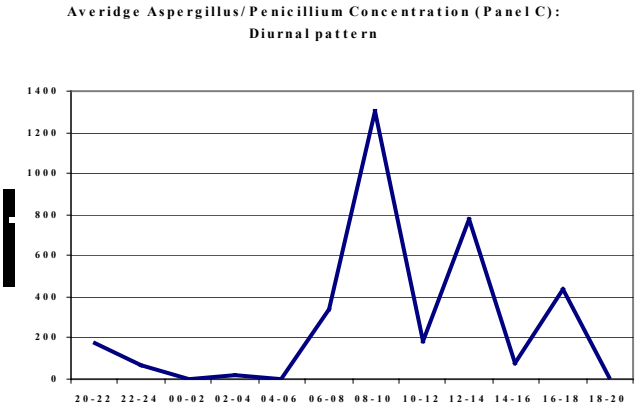


Figure 5.6.5-7. Example how the daily activities at one home affect the indoor *Aspergillus/Penicillium* concentrations. The peak values occur in the morning, at lunch time and in the evening.

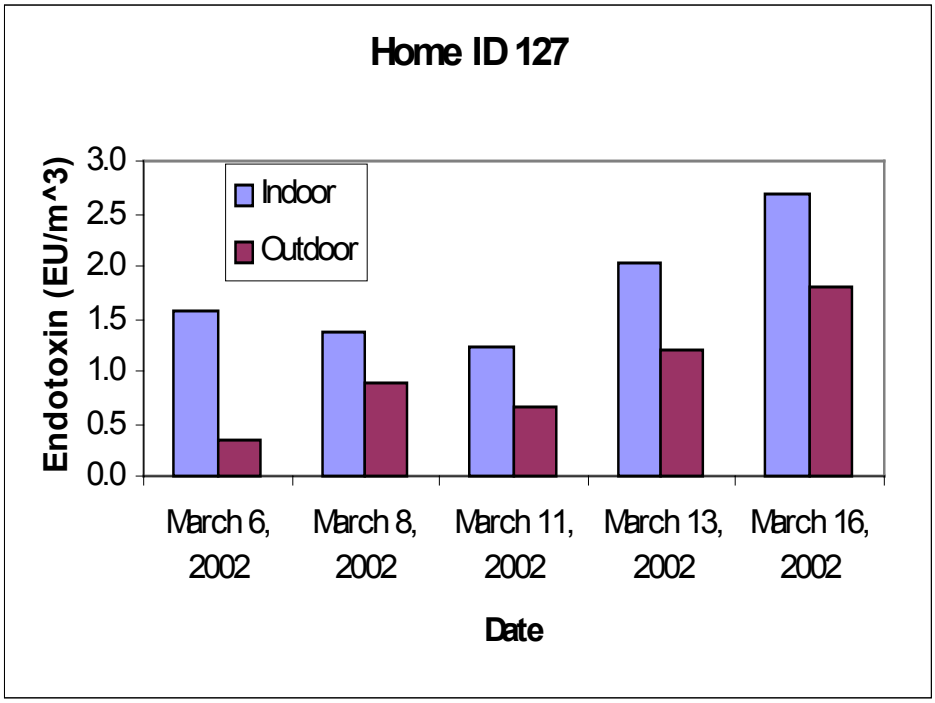


Figure 5.6.5-8A. Indoor and outdoor airborne endotoxin concentrations for Home ID 127.

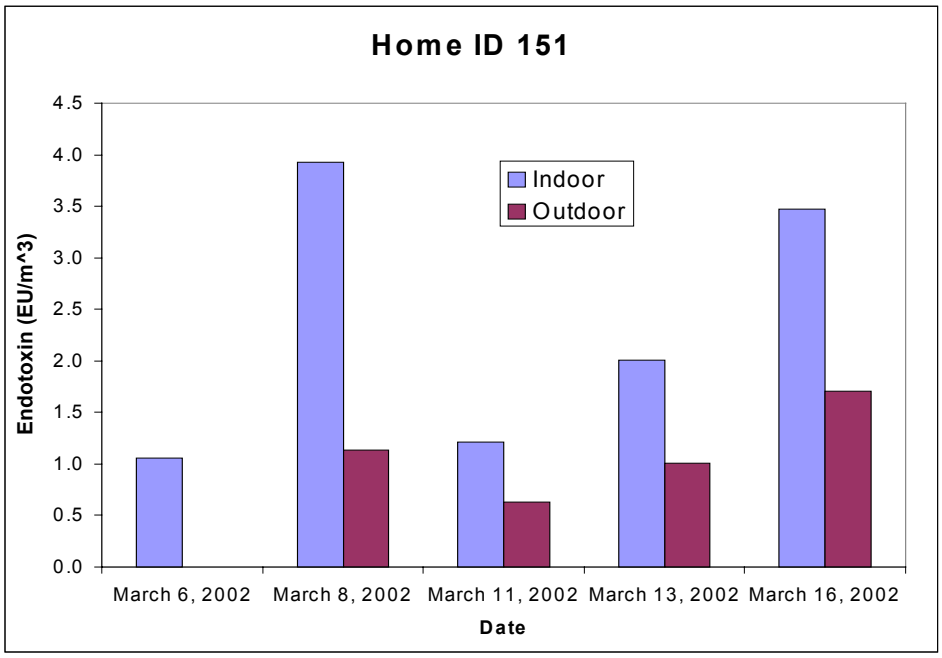


Figure 5.6.5-8B. Indoor and outdoor airborne endotoxin concentrations for Home ID 151.

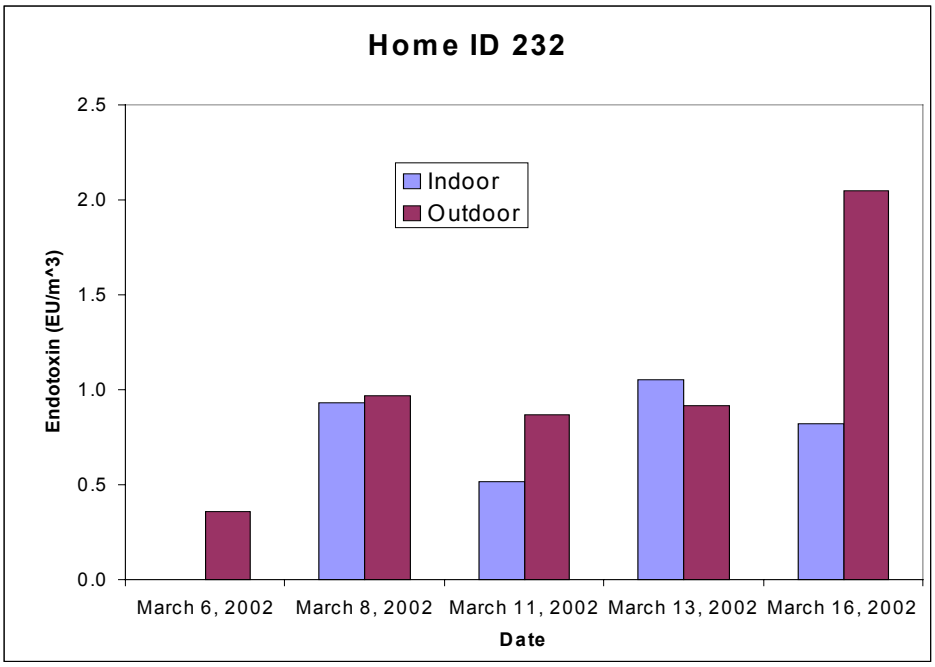


Figure 5.6.5-8C. Indoor and outdoor airborne endotoxin concentrations for Home ID 232

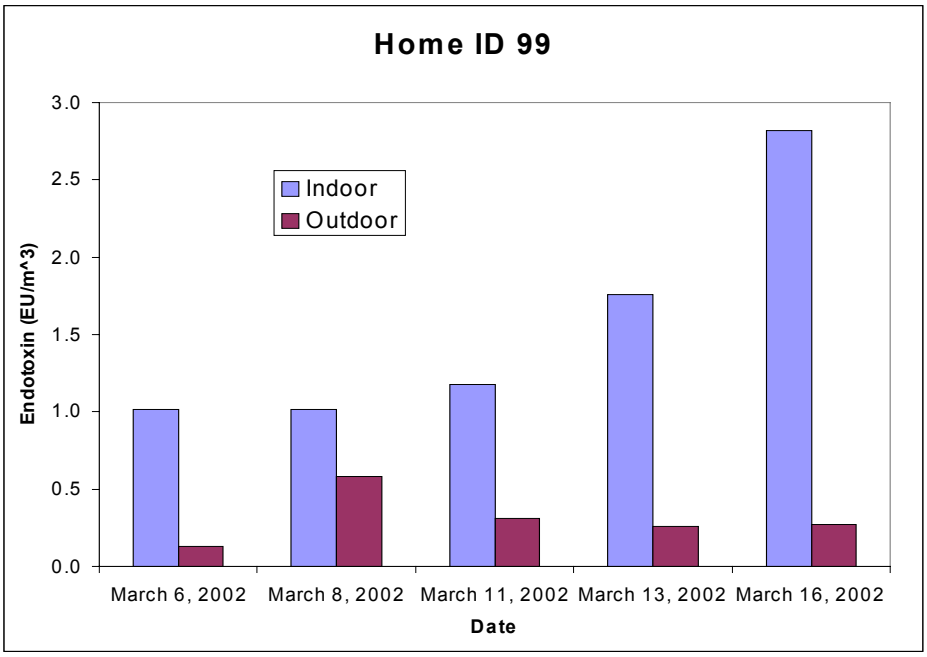


Figure 5.6.5-8D. Indoor and outdoor airborne endotoxin concentrations for Home ID 99.

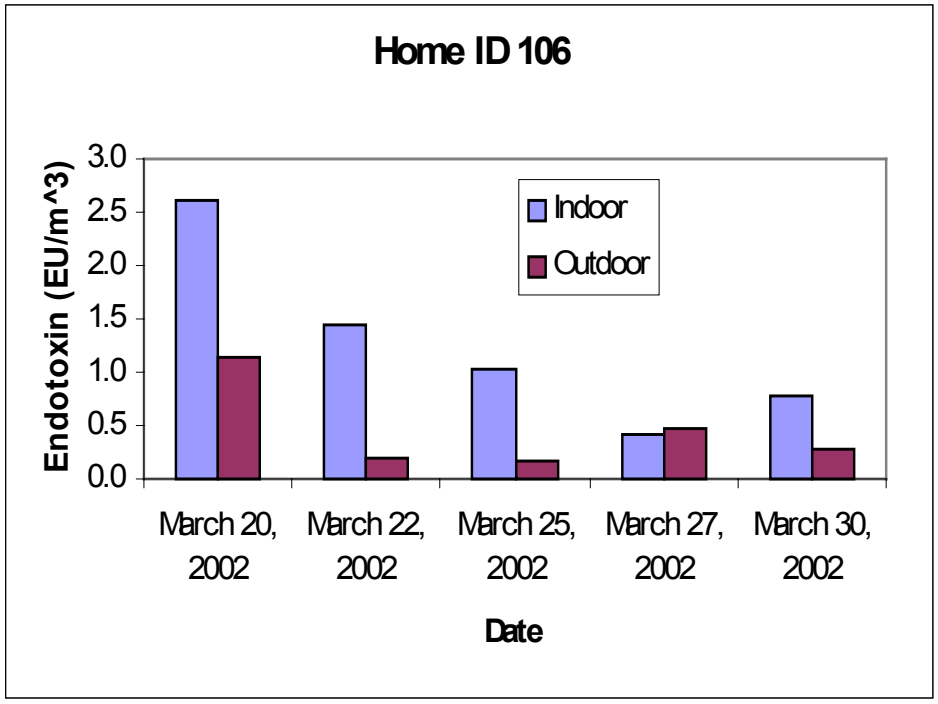


Figure 5.6.5-8E. Indoor and outdoor airborne endotoxin concentrations for Home ID 106

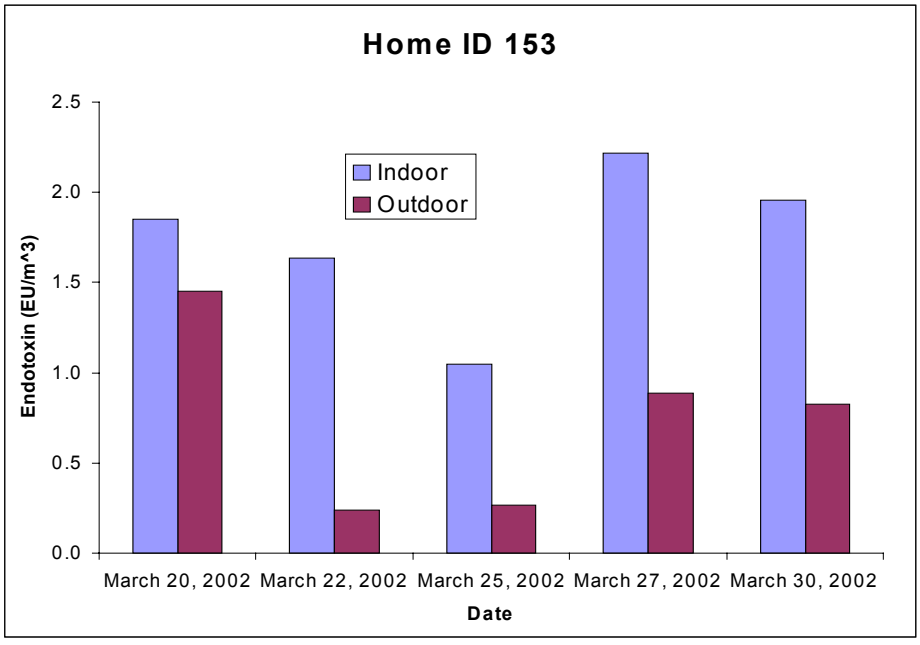


Figure 5.6.5-8F. Indoor and outdoor airborne endotoxin concentrations for Home ID 153

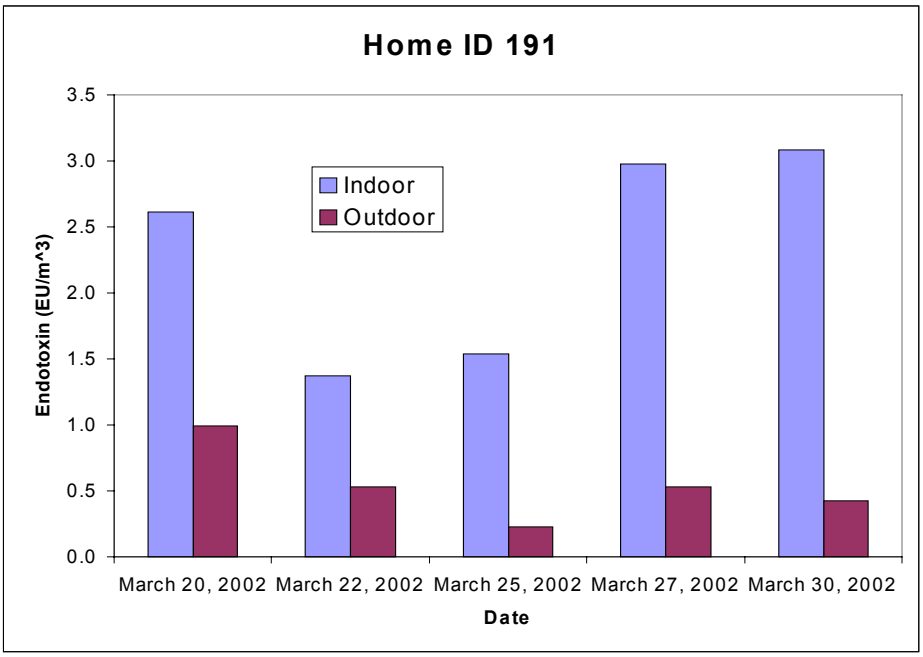


Figure 5.6.5-8G. Indoor and outdoor airborne endotoxin concentrations for Home ID 191.

5.7 SPATIAL VARIABILITY IN FRESNO AIR QUALITY

Exposure assignments for air pollution epidemiological studies are often made assuming air quality conditions at a central monitoring site are representative of conditions throughout a community. The validity of this assumption is likely to vary with chemical species. Our hypothesis is that different chemical species have concentrations that vary on urban, neighborhood, and the household scales in the Fresno/Clovis study area. The FACES exposure assessment incorporates data collection to evaluate and characterize the spatial variability of air pollutants in Fresno. The spatial variations are evaluated by comparing concentration data collected at homes, schools, and SJVAQMD sites with those collected at the Central Site on First Street. In this section, comparisons of preliminary data are made to illustrate examples of the types of spatial variations observed in Fresno.

Data are available for selected agents from the Home Intensive monitoring and the Central Site. Specifically, preliminary mass data that have not yet been corrected for ammonium nitrate volatization losses, EC, pollen grains, spores, and b_{sp} data are available from the early Home Intensive sampling. These can be compared to the BAM PM mass, aethelometer black carbon, pollen grains, spores and b_{sp} data collected at the Central Site. No data is available from schools because the ARB's mobile trailers were not moved to the first two schools until June 2002.

5.7.1 PM Mass

PM mass data collected in Panel C (starting March 20, 2002) with two MEMS at the Central Site and MEMS outside three homes are compared to the Central Site BAM PM mass

data in **Figures 5.7.1-1 and 5.7.1-2**. The ambient concentrations are generally low during this period. The uncorrected $PM_{2.5}$ and PM_{10} mass concentrations from the MEMS are consistently lower than the BAM mass concentrations. A bias is expected because the MEMS mass data have not yet been corrected for volatilization losses. The magnitude of the differences (2 to 11 $\mu g/m^3$) is comparable to the average ammonium nitrate losses (~4 $\mu g/m^3$) reported by Chow et al. (2001) for March 2000 at the Central Site. The MEMS mass concentrations from Houses 153 and 191 are higher than the Central Site MEMS data, whereas the data from House 106 are equal to or less than those from the Central Site. House 153 is located 4 km southwest of the Central Site and 3 km east of Highway 99. House 191 is located 4 km north of the Central Site and 0.5 km east of Highway 41. House 106 is 8 km northwest of the Central Site and 3 km east of Highway 41. The Central Site is located 1.5 km east of Highway 41 and 8 km east of Highway 99. Mobile source emissions are expected to contribute to the variability in ambient concentrations of vehicular pollutants. The patterns in the PM data are roughly consistent with their proximity to traffic in Fresno. In particular, traffic is likely to be lower near House 106 than the other houses, and it shows the lowest concentrations in all but one case. House 153 in central Fresno is close to Highway 99 and the concentrations at House 153 are 40 to 45% higher than those at House 106 on the north side of Fresno. It is also worth noting that the spatial patterns of $PM_{2.5}$ and PM_{10} concentrations are quite similar and consistent.

PM mass concentrations measured outside four houses in Panel D are compared to BAM PM data collected at the Central Site in **Figures 5.7.1-3 and 5.7.1-4**. As with Panel C, the ambient concentrations are moderate or low during this period. On average, the uncorrected MEMS PM concentrations are slightly higher at House 127 and slightly lower at House 151 than those measured by BAM at the Central Site. The uncorrected MEMS PM concentrations are lower at Houses 232 and 99 than those measured by BAM at the Central Site. Houses 127, 151, and 232 are west of the Central Site and close (<1.5 km) to Highway 99. House 127 is just east of the freeway while House 151's backyard borders the western side of the freeway. House 99 is in southeastern Fresno and about 6 km from Highway 99. The uncorrected MEMS data indicate PM concentrations in southeastern Fresno are 20 to 25% higher close to the freeway compared to far away from the freeway.

Measurements of PM obtained during the 3-day pilot study in January are shown in **Figures 5.7.1-5 and 5.7.1-6**. Pilot Study Houses 1901 and 481 were located east of Highway 99 near House 127 and west of Highway 41, respectively. The uncorrected $PM_{2.5}$ and PM_{10} mass concentrations at House 1901 were higher than the BAM PM concentrations measured at the Central Site. The observations at House 481 were lower than those measured by BAMS at the Central Site. The magnitude of the spatial differences is potentially significant: the average $PM_{2.5}$ and PM_{10} concentrations were 49 and 57 $\mu g/m^3$, respectively, at House 481 while the average $PM_{2.5}$ and PM_{10} concentrations were 70 and 83 $\mu g/m^3$, respectively, at House 1901.

5.7.2 Light Scattering by Particles

Light extinction by particles (b_{sp}) is measured at houses and the Central Site in Fresno as a surrogate for continuous PM2.5 mass measurements. Examples of the spatial variability of 1-hr average b_{sp} in Fresno during the Pilot Study and the first four panels are shown in **Figures 5.7.2-1 through 5.7.2-6.** Light scattering measurements at most of the locations show the same temporal patterns with occasional excursions. The hourly data show numerous cases

with factors of 2 or 3 differences across Fresno. They illustrate cases where one site has high concentrations for relatively short periods (1 to 3 hours) while other sites track one another closely and show typical urban b_{sp} levels. Clearly, on a short-term basis there is substantial spatial variability in Fresno.

The multi-day average b_{sp} values observed during the pilot study and first four panels are shown in **Figure 5.7.2-6**. The 6-day average light extinction coefficients measured during the Pilot Study were among the highest measured and showed ±15% variations across Fresno. The 12-day average light extinction coefficients measured during the four panels varied by ±20% across Fresno. The relative ranking of houses is very similar based on 12-day average b_{sp} and 5-day average integrated $PM_{2.5}$ mass measurements.

5.7.3 Elemental Carbon

EC concentrations are of interest because they are associated with vehicle PM emissions, primarily diesel vehicle emissions. Comparisons can be made between the integrated filter samples collect by the MEMS and analyzed for EC by DRI, and the three continuous instruments at the Central Site: the single wavelength aethalometer, the 7-wavelength aethalometer, and the ambient particle carbon monitor (R&P 5400). Watson and Chow (2001) reported comparison of black carbon and EC measured by these monitors to EC determined from filters collected on $PM_{2.5}$ samplers. The aethalometer has generally produced more reliable data than the other two carbon analyzers at the Central Site. Watson and Chow (2001) found that, on average, black carbon concentrations determined from the 880 nm channel of the aethalometer were 75% of EC concentrations determined from integrated filters collected by Federal Reference Method (FRM) $PM_{2.5}$ samplers and analyzed by DRI. Because the Harvard Impactors used in the MEMS agree well with FRM samplers, we have scaled the aethalometer data to reflect EC concentrations so that spatial variations can be evaluated.

Figure 5.7.3-1 shows the daily adjusted black carbon data for the Central Site, EC filter data from two MEMS operated at the Central Site, and EC filter data collected outside three houses during Panel C. The 4-day average EC concentrations from the MEMS are 8% and 22% lower than the adjusted black carbon concentration. The 5-day average EC concentration at House 153 was 6% higher than the adjusted black carbon concentration at the Central Site whereas the 5-day average EC at Houses 191 and 106 were 8% and 26% lower than the adjusted black carbon measurements. House 153 is located closer to Highway 99 than House 191, House 106, and the Central Site. The spatial coefficient of variation is ±15% for these 5-day average EC concentrations in Fresno.

Daily concentrations of EC during Panels D, H, and G and the Pilot Study are shown in **Figures 5.7.3-2 through 5.7.3-5**. Concentrations during Panel G at House 173, which is several blocks from the Central Site, are virtually the same as those measured at the Central Site. The highest daily EC concentration (7.5 $\mu g/m^3$) was observed during the Pilot Study at a house located just east of Highway 99. The lowest daily EC concentrations (0.35 $\mu g/m^3$) were observed at Houses 89 and 232, near the northern and western boundaries of Fresno, respectively. The daily data show spatial differences as large as a factor of 2 in EC concentrations. **Figure 5.7.3-6** compares the multi-day average EC concentrations. The 5-day average concentrations have a ±30% coefficient of variation within Fresno during the panels.

The relative ranking of houses for EC concentrations is somewhat different than that for $PM_{2.5}$ mass and b_{sp}.

5.7.4 Selected Elements

The XRF analysis quantifies concentrations of about 40 elements, including certain trace metals that are designated agents in FACES. Several of the more abundant elements are used here to illustrate typical spatial variations in outdoor concentrations in Fresno. The PM_{10} concentrations of silicon, aluminum, and iron mostly reflect contributions from sources of crustal material whereas PM_{10} sulfur concentrations mostly reflect sulfate formed from atmospheric oxidation of SO_2 emitted in fuel combustion. Figures 5.7.4-1 through 5.7.4-4 show the concentrations of silicon, aluminum, iron, and sulfur collected outside houses in the first four panels. The relative spatial variation in the PM_{10} crustal constituents is similar to that of PM_{10} mass. The largest variation was on the order of a factor of 2 difference between PM_{10} silicon at Houses 232 and 99 in Panel D; most of the spatial variations in 24-hr average silicon, aluminum, and iron concentrations are less than ±20%. The spatial variations of sulfur concentrations are smaller than those for silicon, aluminum, and iron. This observation is consistent with our hypothesis that sulfate is a spatially homogeneous pollutant in Fresno.

5.7.5 Pollen Grains and Endotoxin

Significant differences were found in the pollen grain counts between the Central Site and the homes during one week in the Home Intensive (see Figure 5.7.4-5). Similarly, significant differences were seen in endotoxin concentrations at several sites on the same day (Figures 5.7.4-6 and 5.7.4-7)

5.7.6 Summary of Spatial Variations

The preliminary data collected early in the FACES Home Intensive show spatial variations in concentrations of numerous agents are large enough to warrant their inclusion in the exposure assessment methodology. The spatial variations of most agents on most days are usually larger than the measurement error. If the observations showed less than 10% differences across Fresno, we would conclude that the spatial variations were too small to accurately quantify and probably unimportant in the context of the health study. In fact, the multi-day average observations for PM mass, b_{sp}, elemental carbon, selected trace metals, pollen grains, and spores show variations consistently larger than 20% and certainly worth accounting for the exposure assessment.

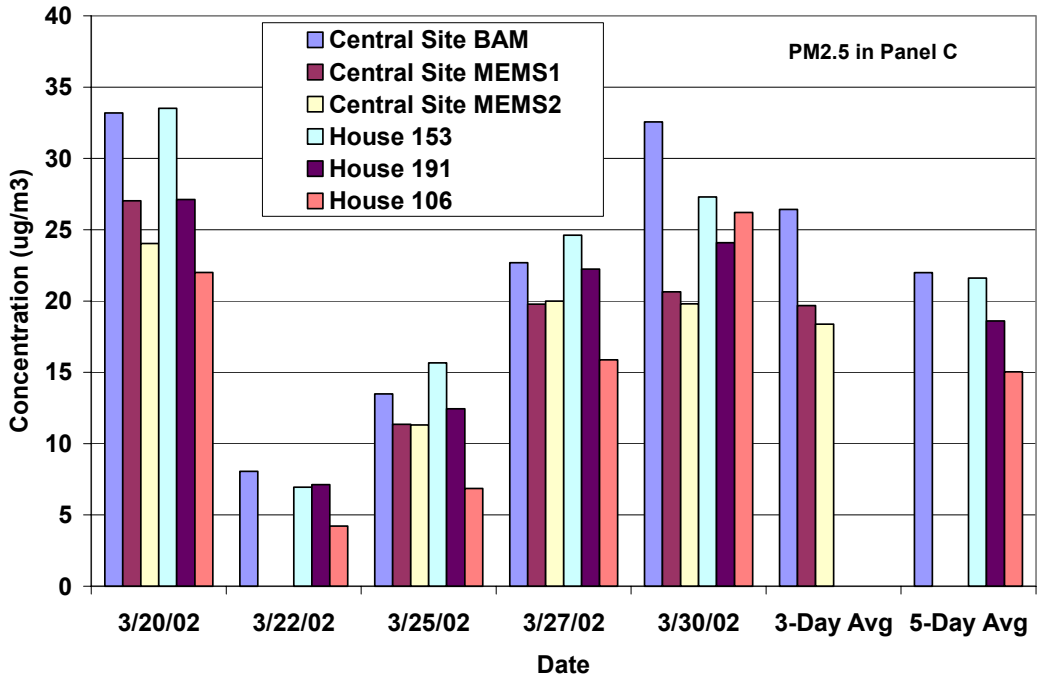


Figure 5.7.1-1. Comparison of 24-hr average concentrations of uncorrected $PM_{2.5}$ mass collected with MEMS at the Central Site and at houses to concentrations of $PM_{2.5}$ mass measured by BAM at the Central Site during Panel C.

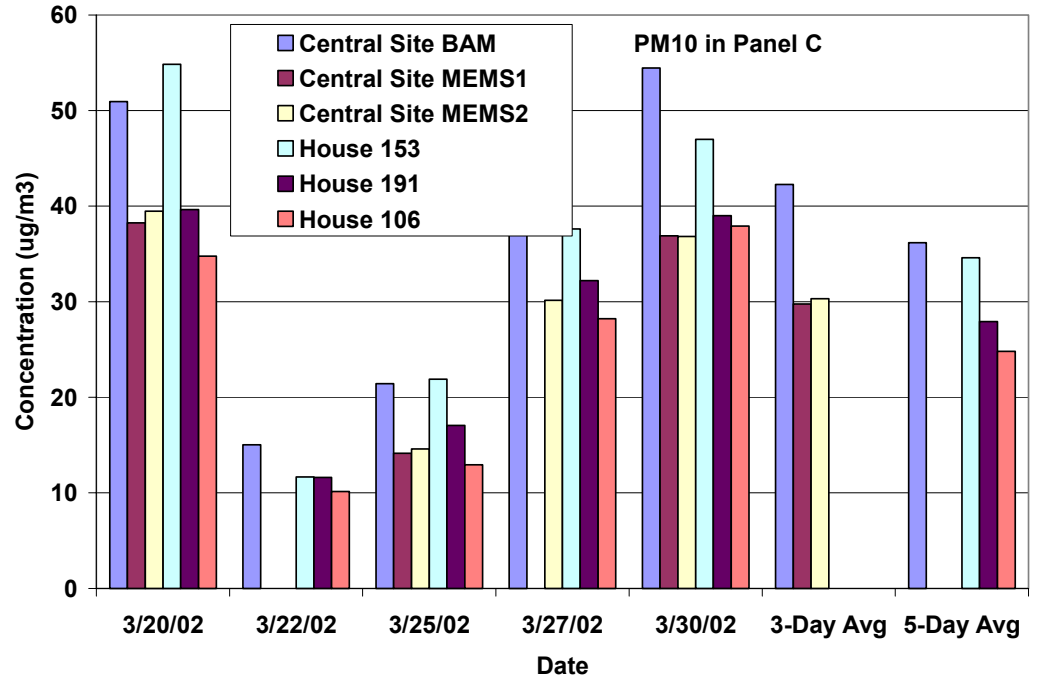


Figure 5.7.1-2. Comparison of 24-hr average concentrations of uncorrected PM_{10} mass collected with MEMS at the Central Site and at houses to concentrations of PM_{10} mass measured by BAM at the Central Site during Panel C.

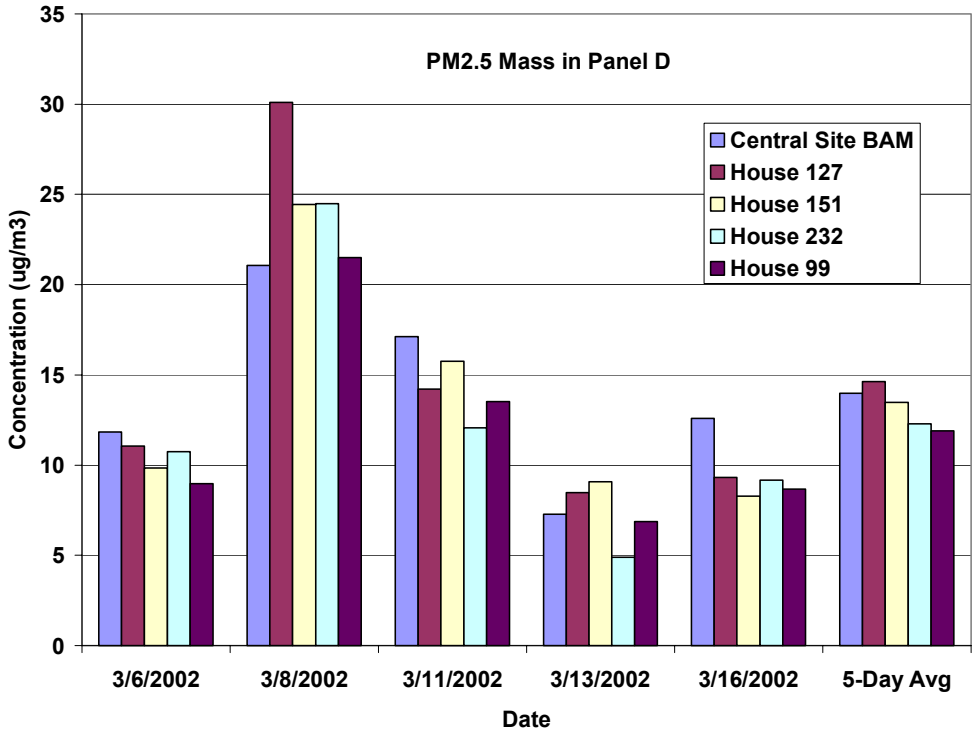


Figure 5.7.1-3. Comparison of 24-hr average concentrations of uncorrected PM_{10} mass collected with MEMS at houses to concentrations of $PM_{2.5}$ mass measured by BAM at the Central Site during Panel D.

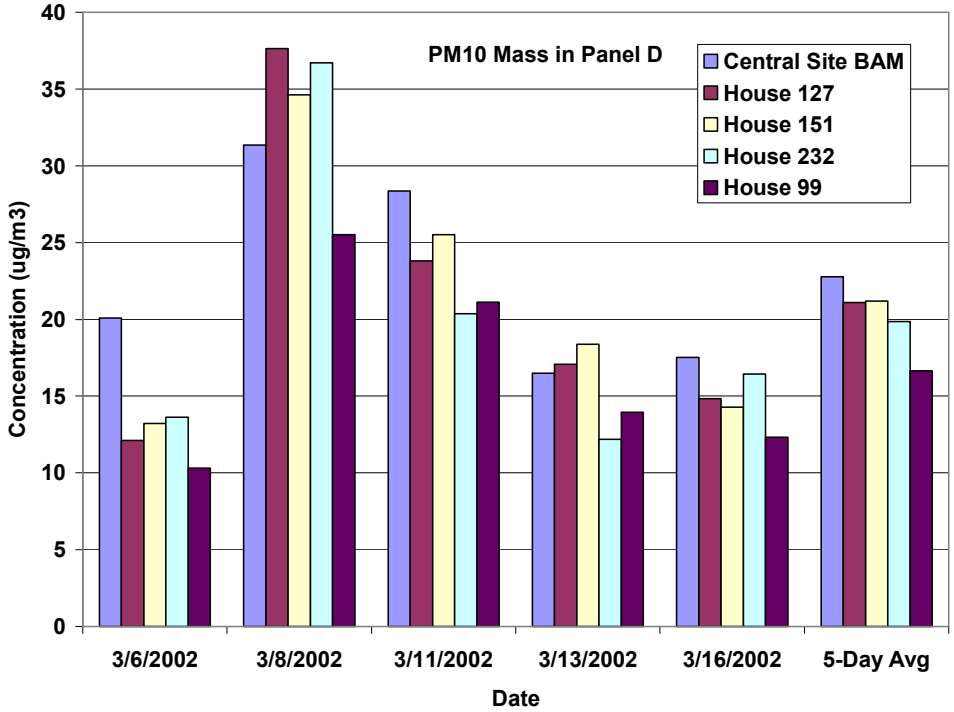


Figure 5.7.1-4. Comparison of 24-hr average concentrations of uncorrected PM_{10} mass collected with MEMS at houses to concentrations of PM_{10} mass measured by BAM at the Central Site during Panel D.

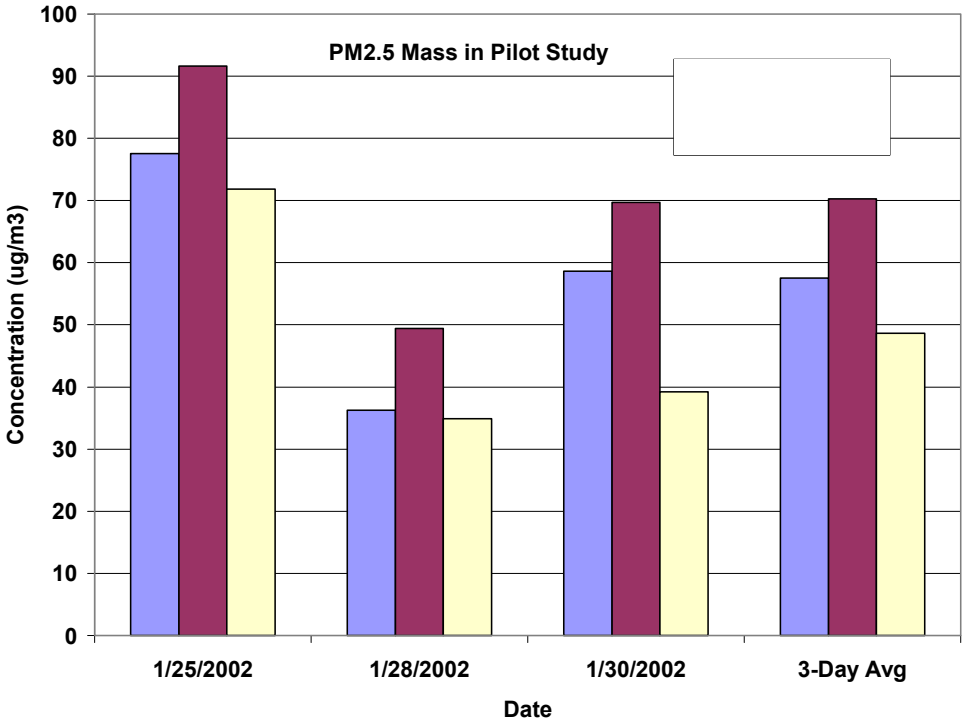


Figure 5.7.1-5. Comparison of 24-hr average concentrations of uncorrected $PM_{2.5}$ mass collected with MEMS at houses to concentrations of PM_{10} mass measured by BAM at the Central Site during the Pilot Study.

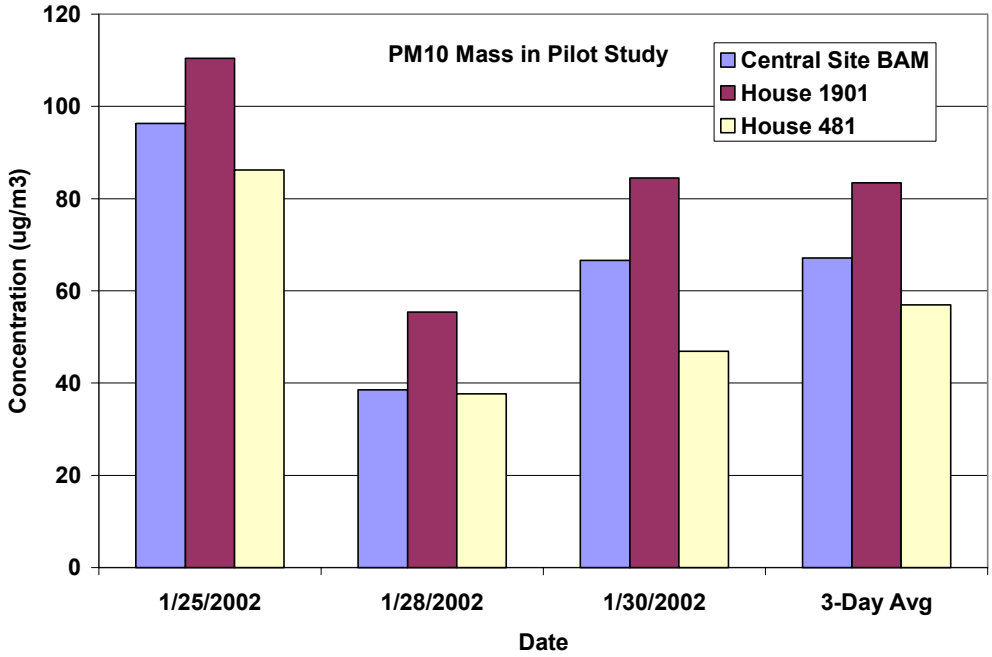


Figure 5.7.1-6. Comparison of 24-hr average concentrations of uncorrected PM_{10} mass collected with MEMS at houses to concentrations of PM_{10} mass measured by BAM at the Central Site during Pilot Study.

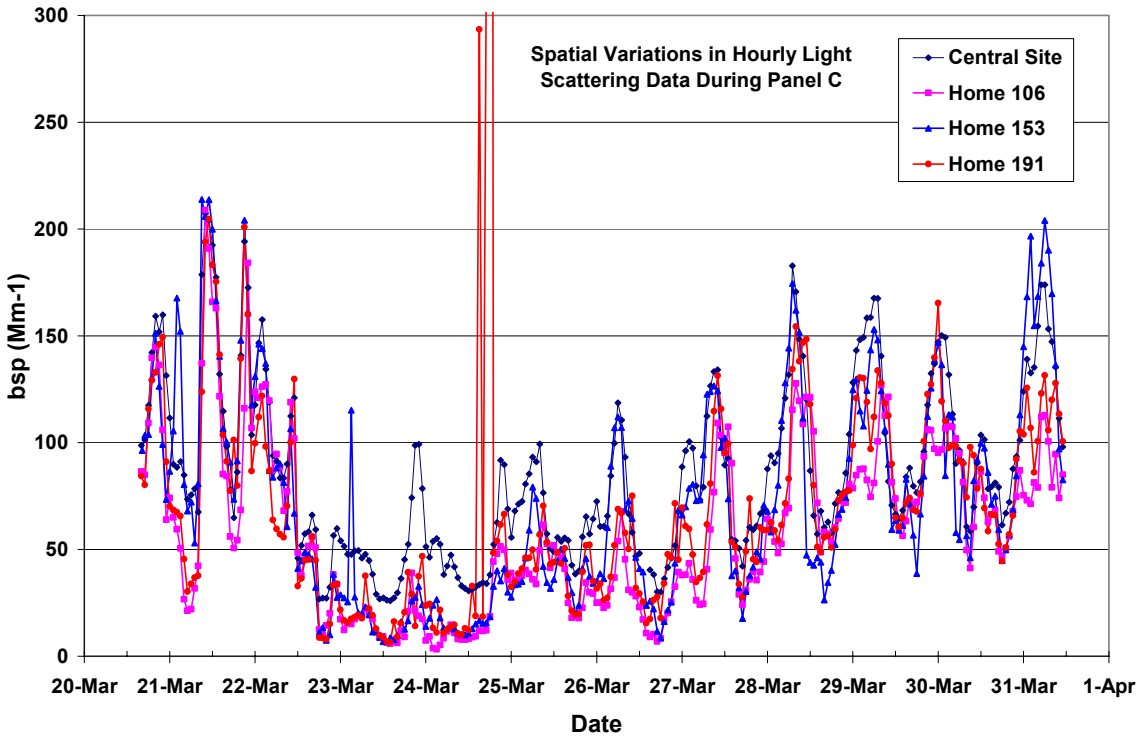


Figure 5.7.2-1. Comparison of hourly average b_{sp} outdoors at Panel C homes and at the Central Site. The high b_{sp} values (up to 1400 Mm^{-1}) outside Home 191 on March 24 are probably due to a local source influence.

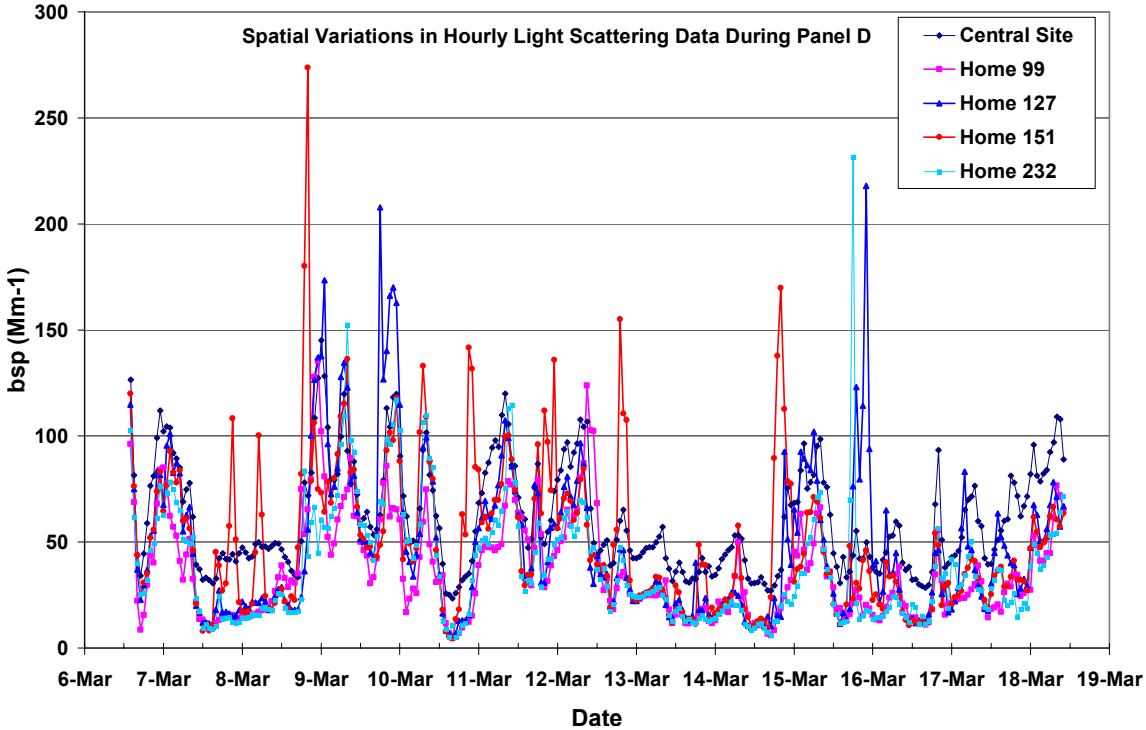


Figure 5.7.2-2. Comparison of hourly average b_{sp} outdoors at Panel D homes and at the Central Site.

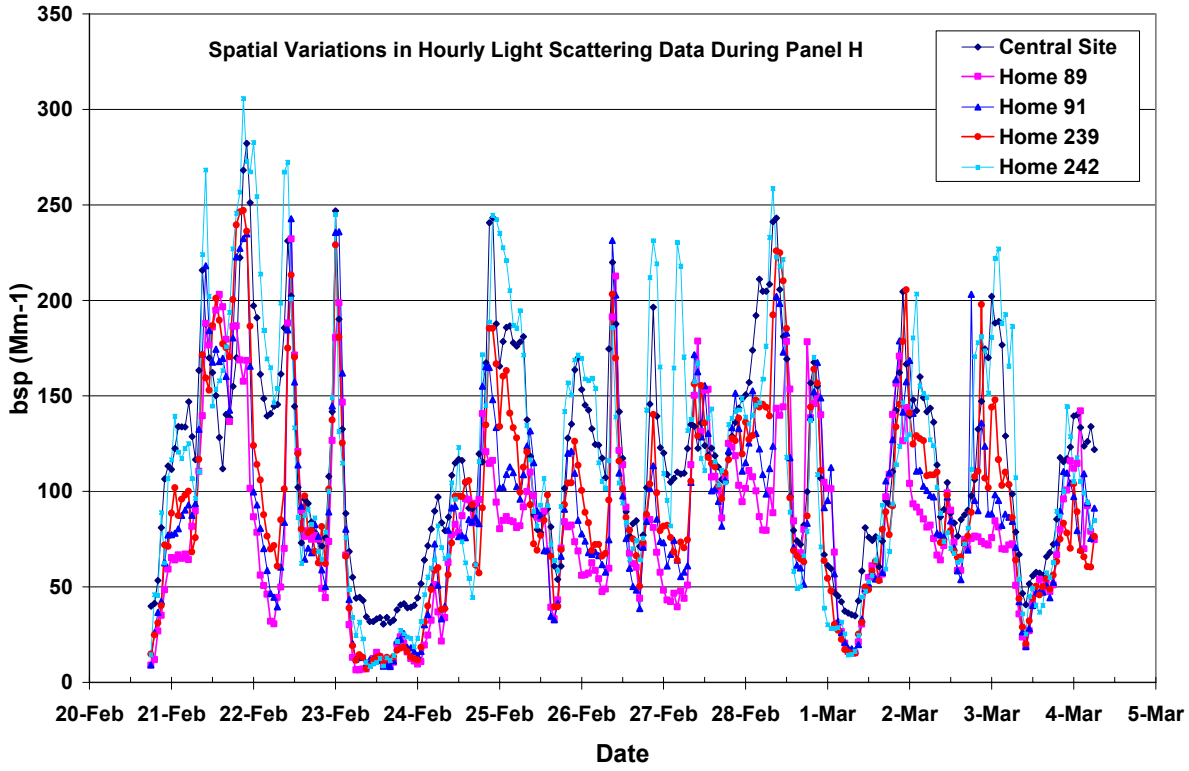


Figure 5.7.2-3. Comparison of hourly average b_{sp} outdoors at Panel H homes and at the Central Site.

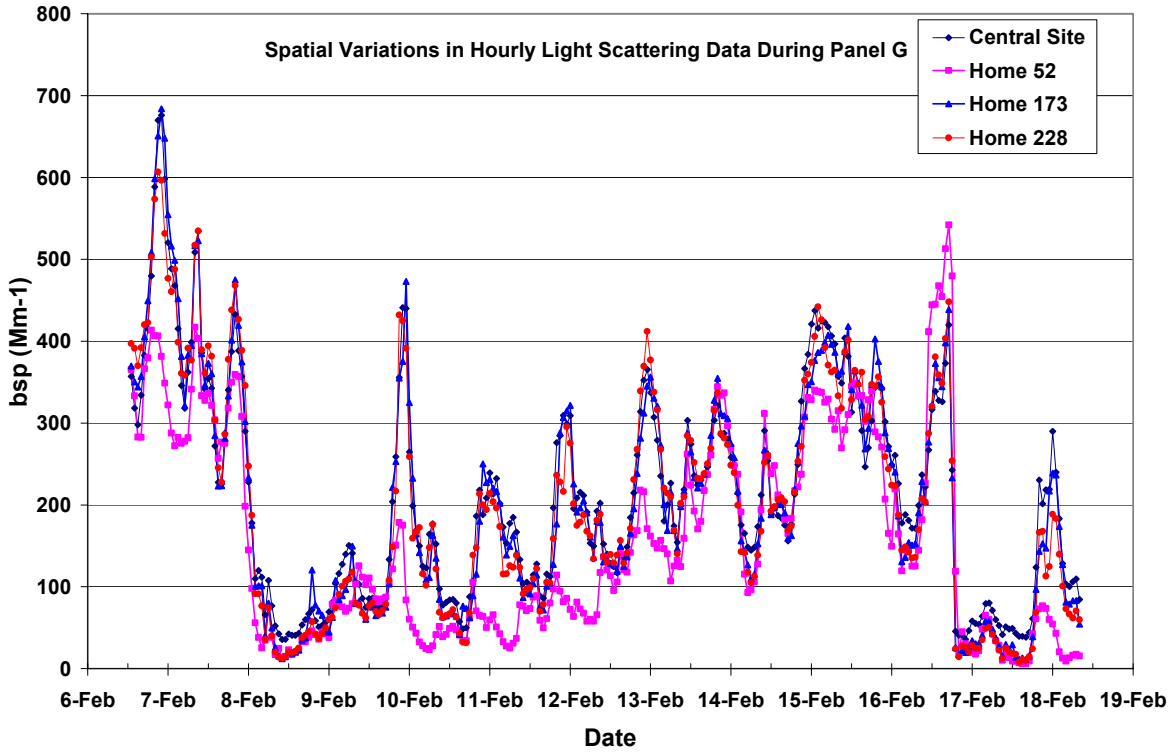


Figure 5.7.2-4. Comparison of hourly average b_{sp} outdoors at Panel G homes and at the Central Site.

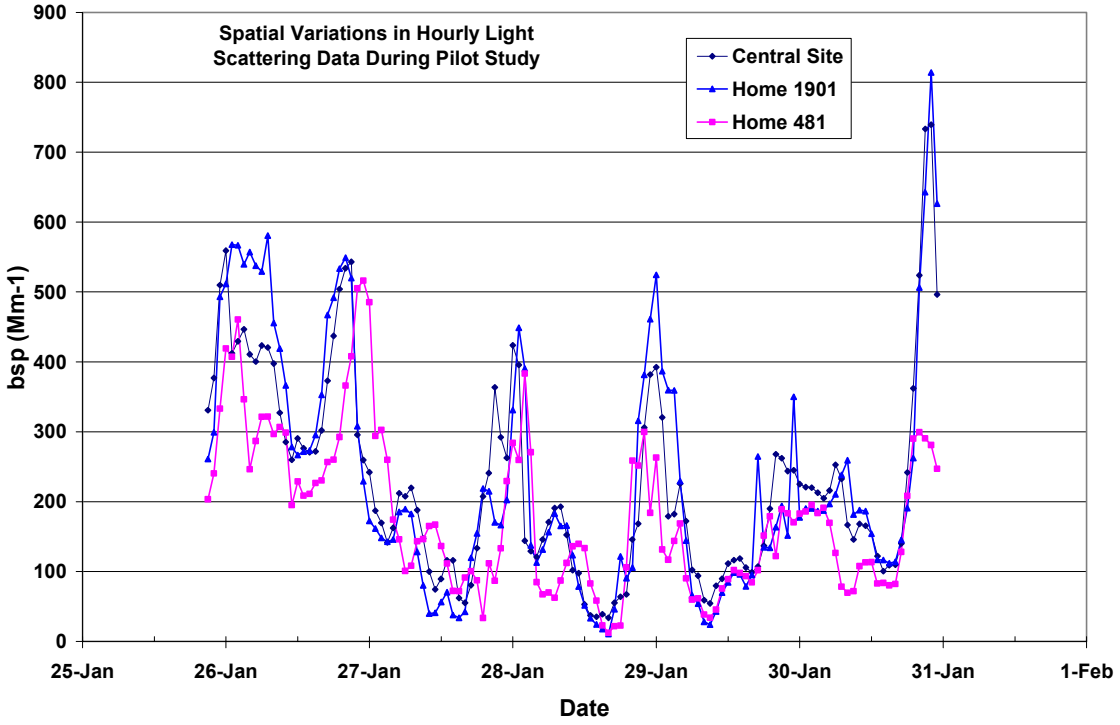


Figure 5.7.2-5. Comparison of hourly average b_{sp} outdoors at Pilot Study homes and at the Central Site.

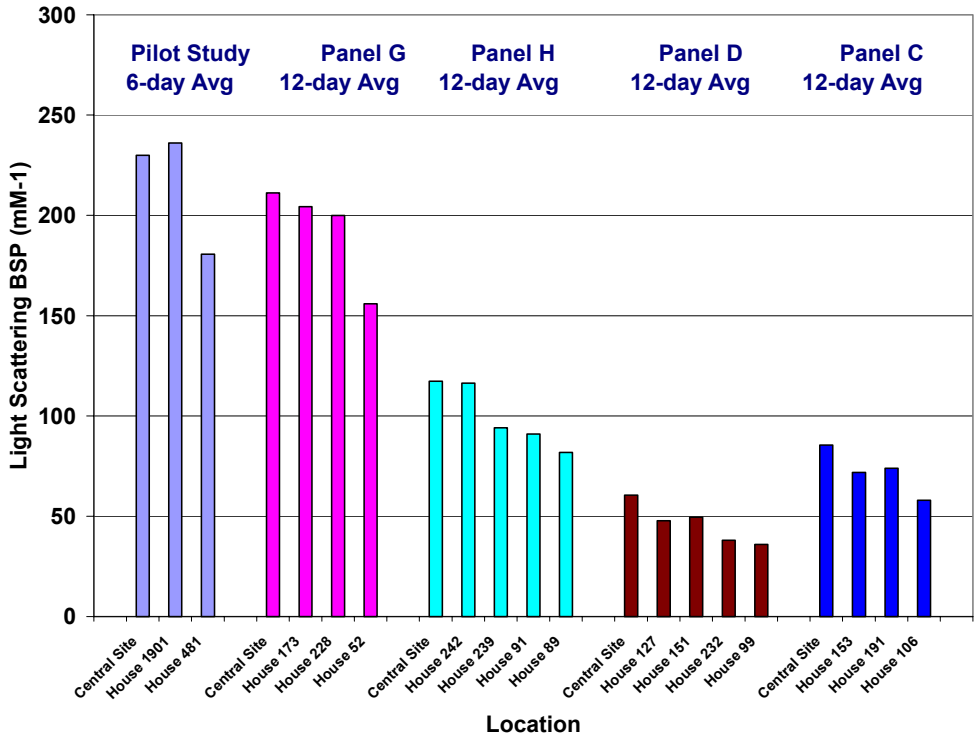


Figure 5.7.2-6. Comparison of multi-day average b_{sp} at houses and the Central Site.

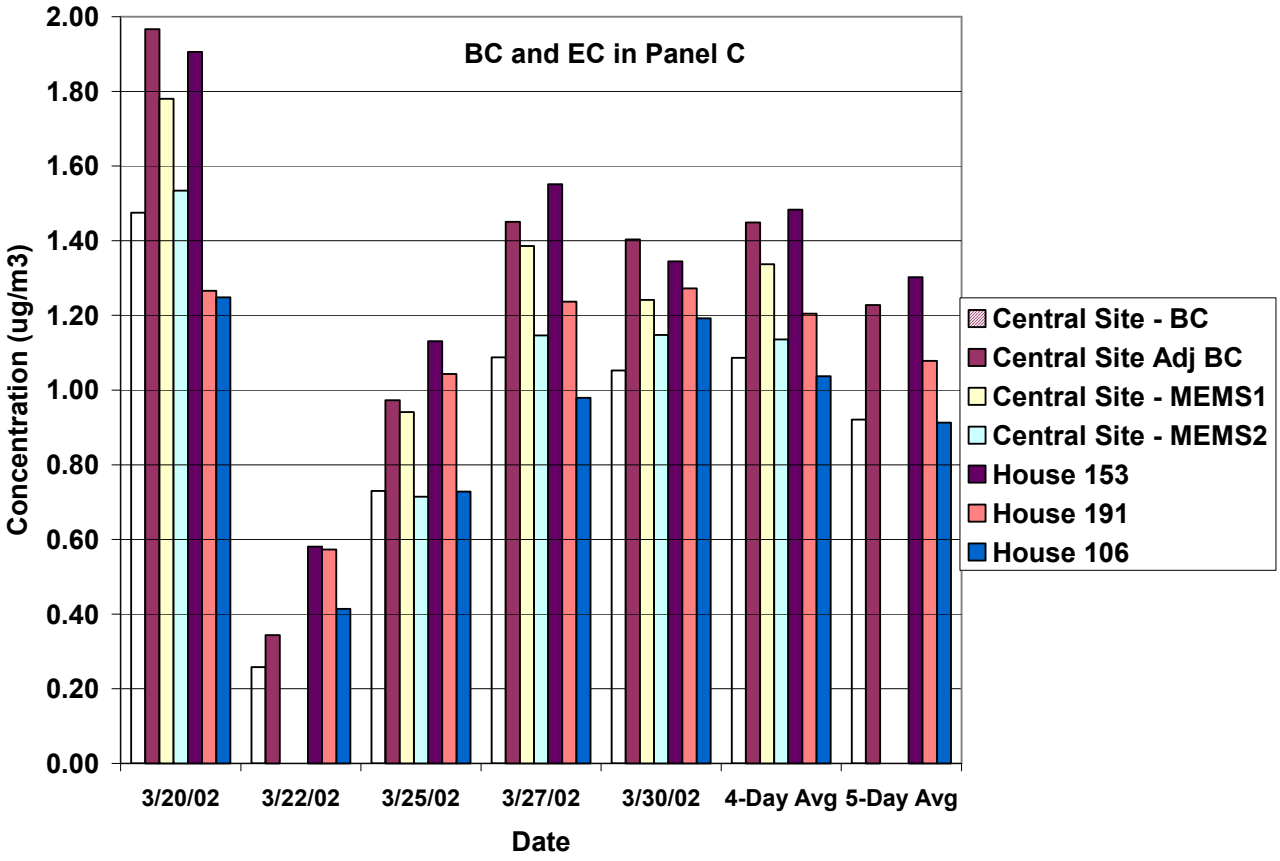


Figure 5.7.3-1. Comparison of daily adjusted black carbon data and hourly average elemental carbon outdoors at Panel C houses and at the Central Site.

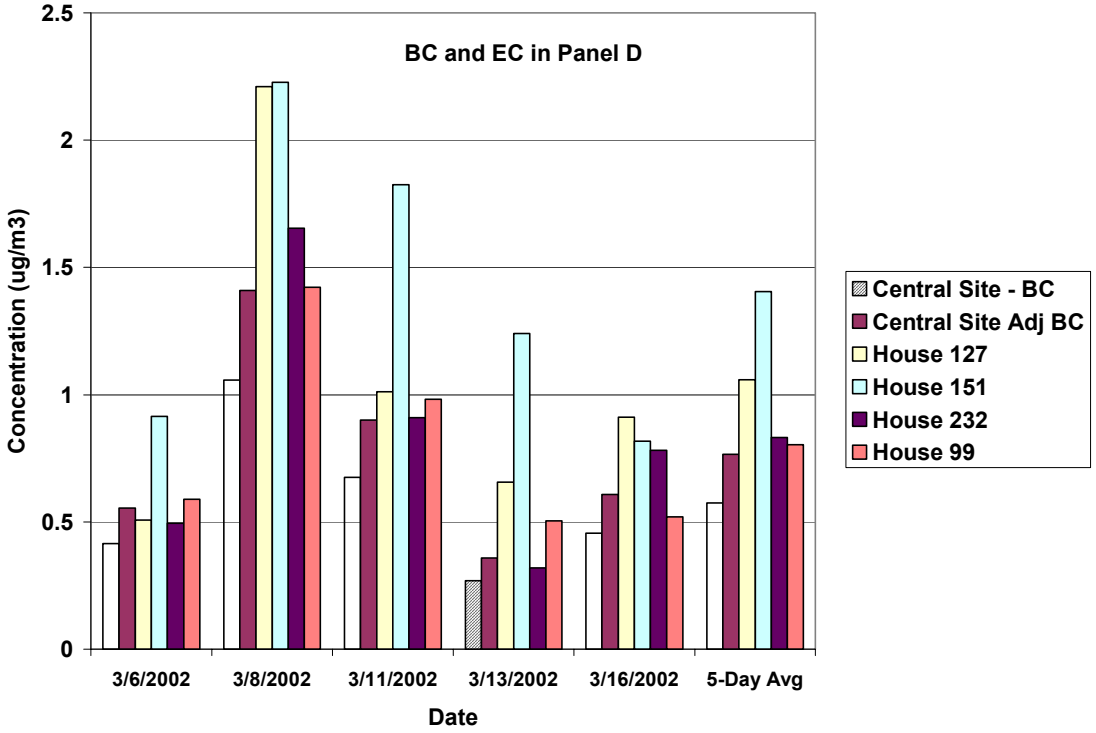


Figure 5.7.3-2. Comparison of daily adjusted black carbon data and hourly average elemental carbon outdoors at Panel D houses and at the Central Site.

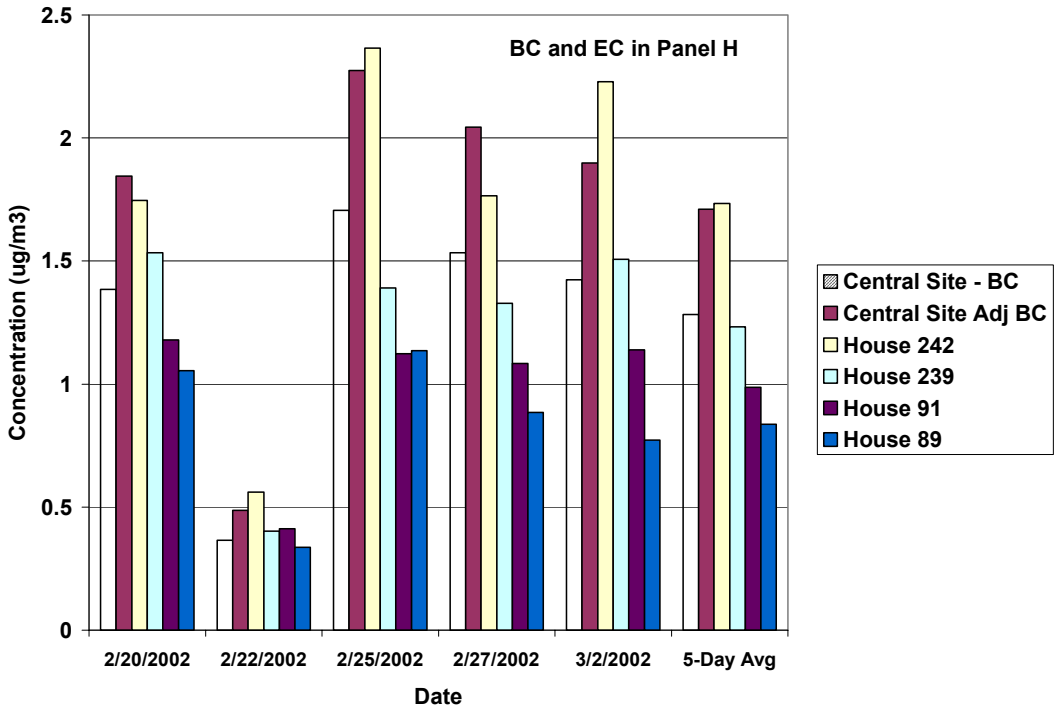


Figure 5.7.3-3. Comparison of daily adjusted black carbon data and hourly average elemental carbon outdoors at Panel H houses and at the Central Site.

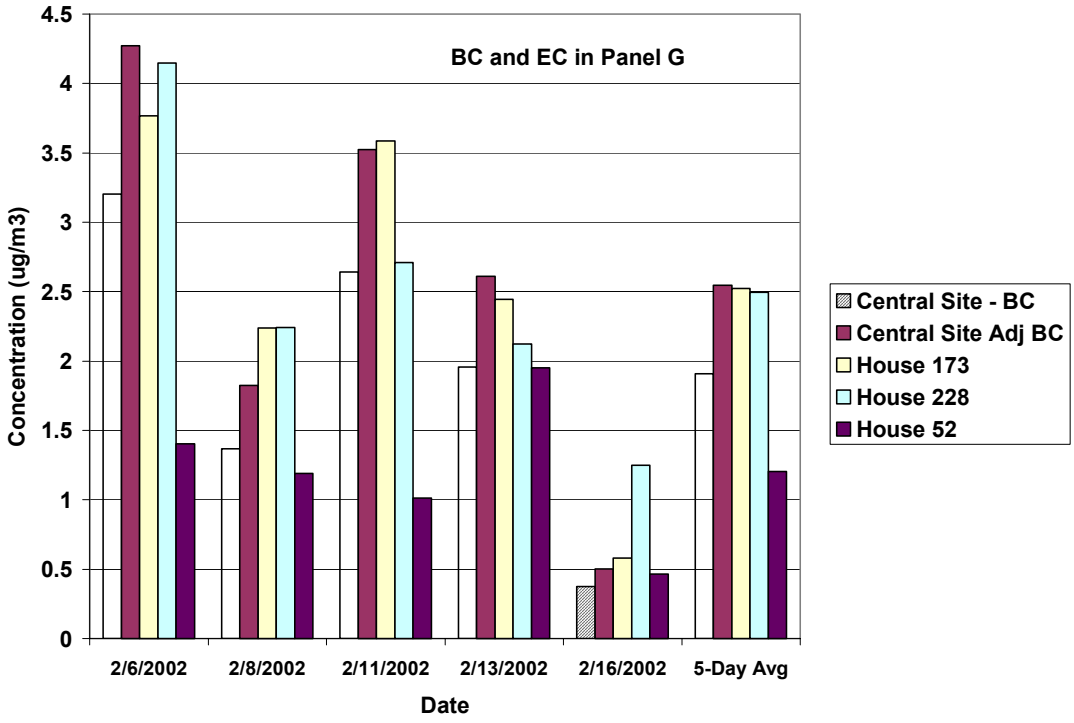


Figure 5.7.3-4. Comparison of daily adjusted black carbon data and hourly average elemental carbon outdoors at Panel G houses and at the Central Site.

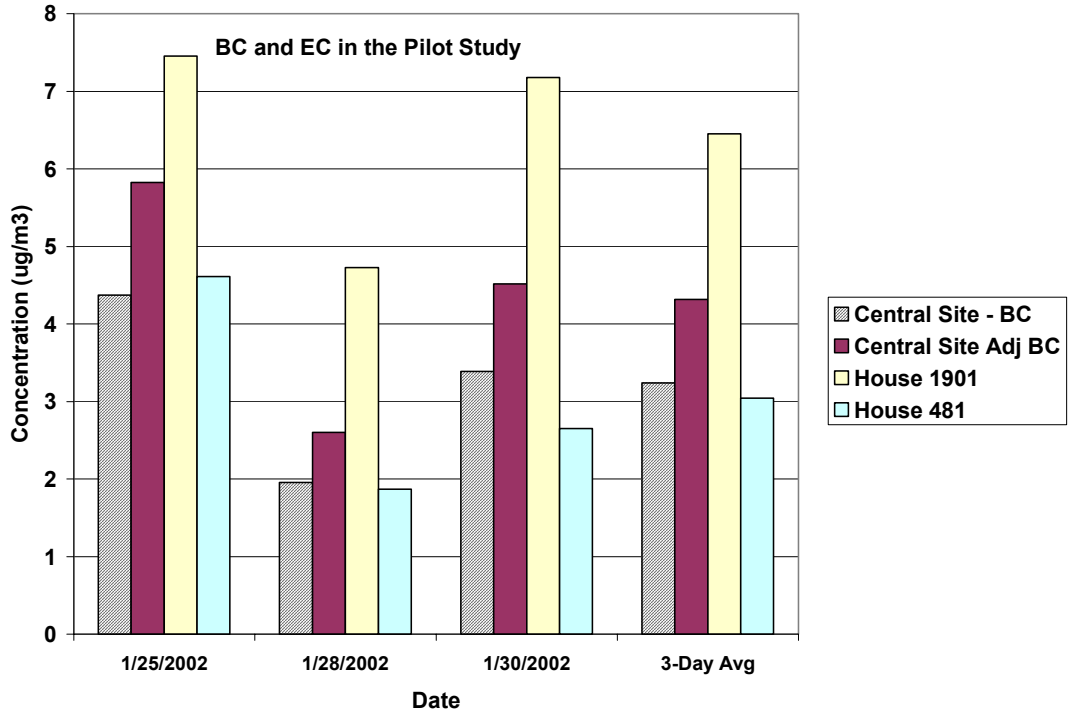


Figure 5.7.3-5. Comparison of daily adjusted black carbon data and hourly average elemental carbon outdoors at Pilot Study houses and at the Central Site.

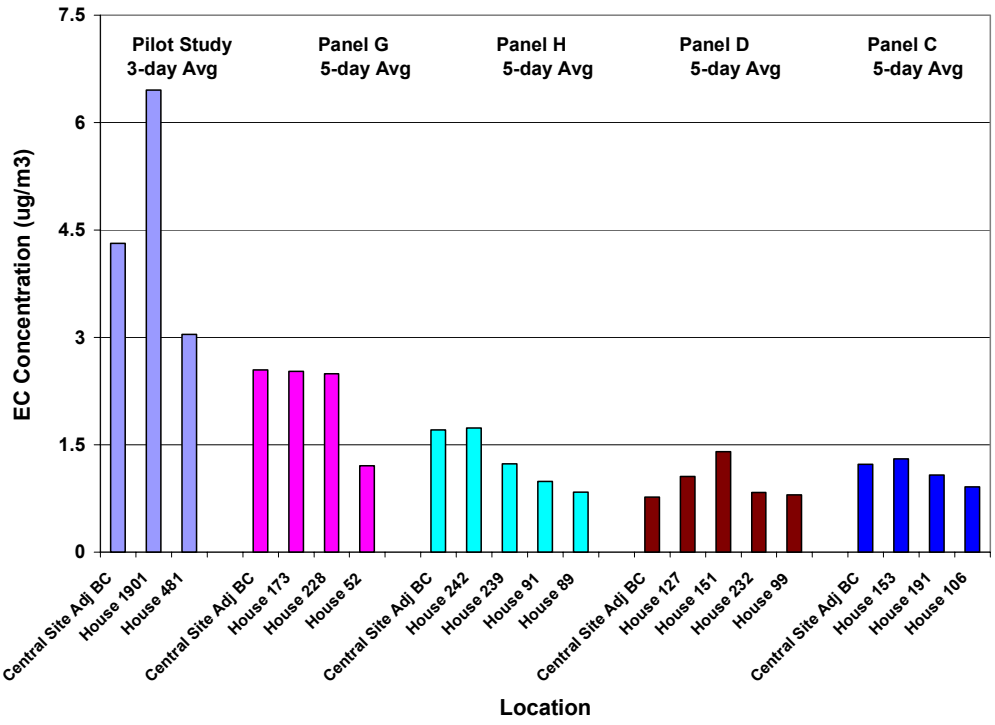


Figure 5.7.3-6. Comparison of multi-day average elemental carbon at houses and the Central Site.

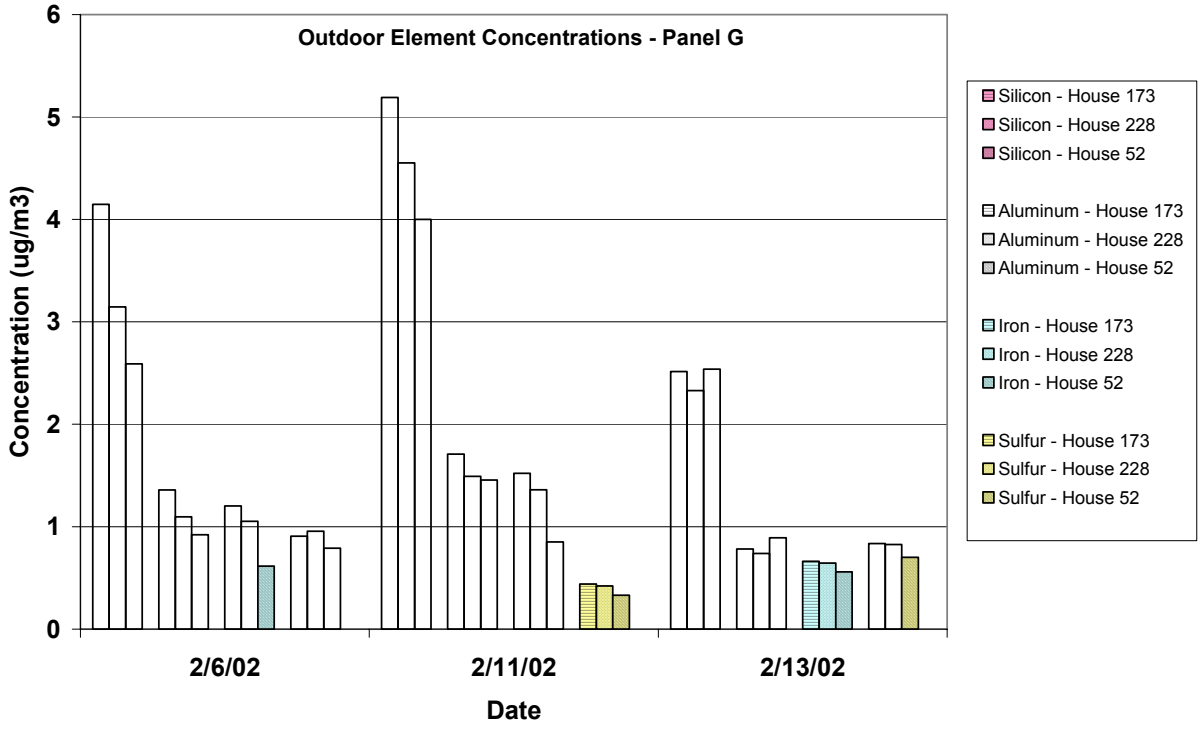


Figure 5.7.4-1. Comparison of outdoor silicon, aluminum, iron, and sulfur elemental concentrations during Panel G.

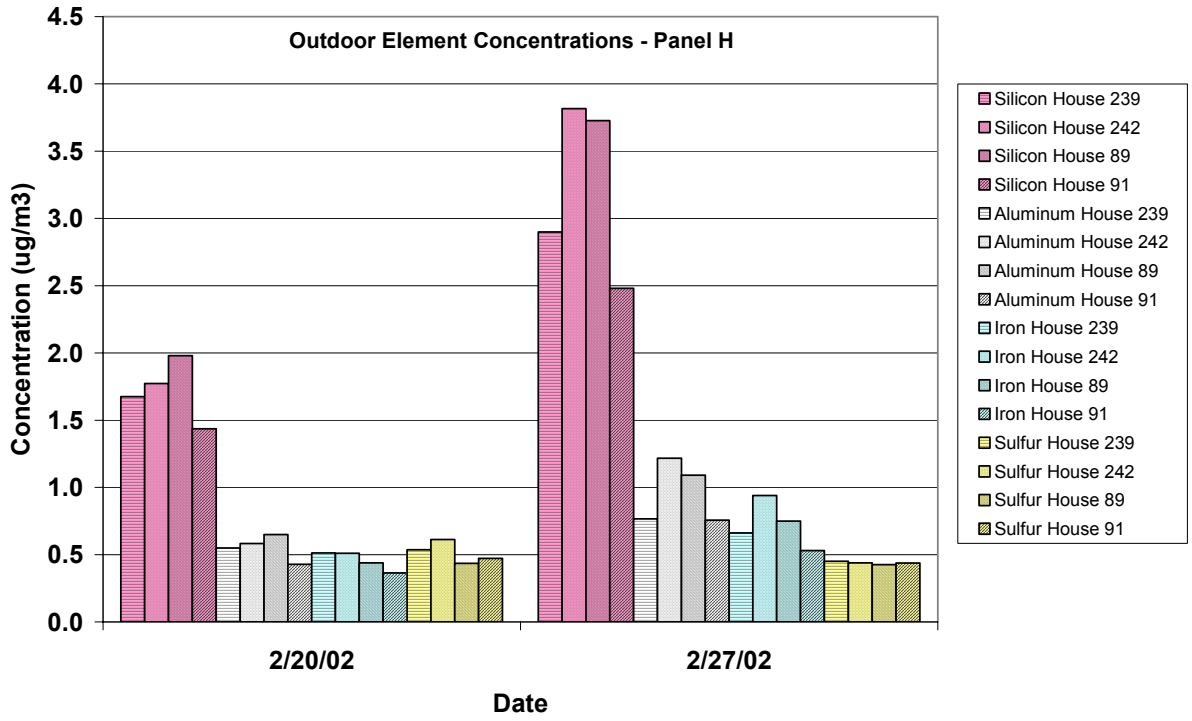


Figure 5.7.4-2. Comparison of outdoor silicon, aluminum, iron, and sulfur elemental concentrations during Panel H.

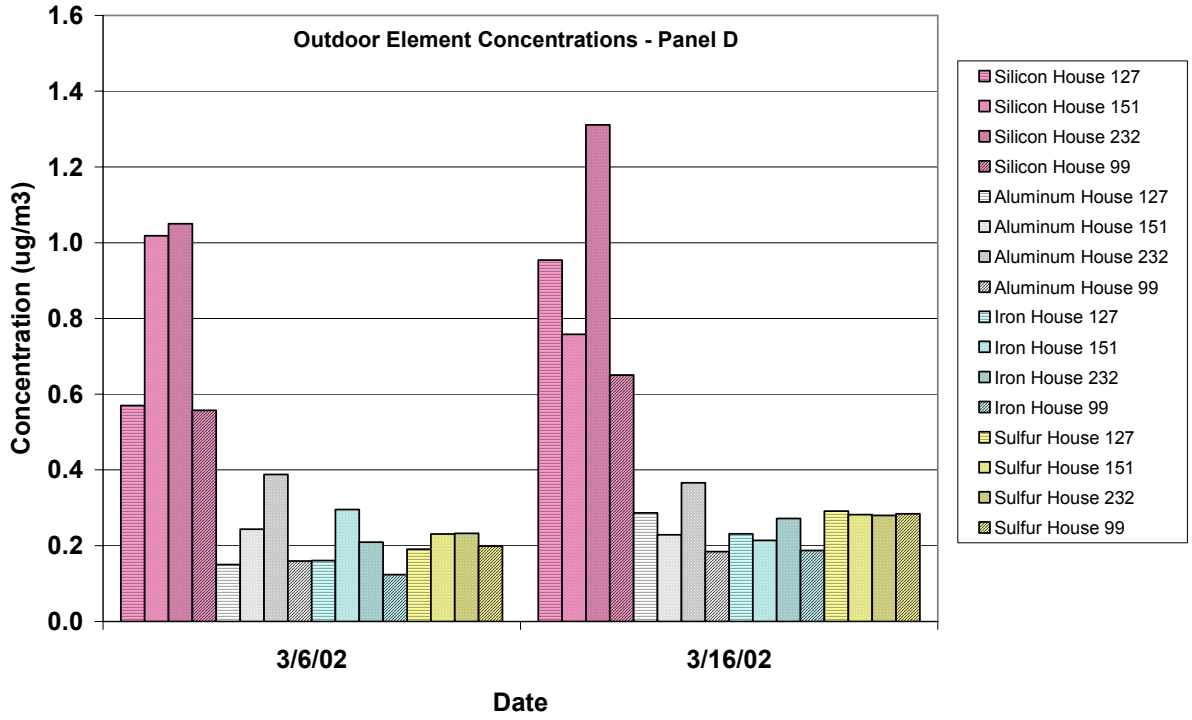


Figure 5.7.4-3. Comparison of outdoor silicon, aluminum, iron, and sulfur elemental concentrations during Panel D.

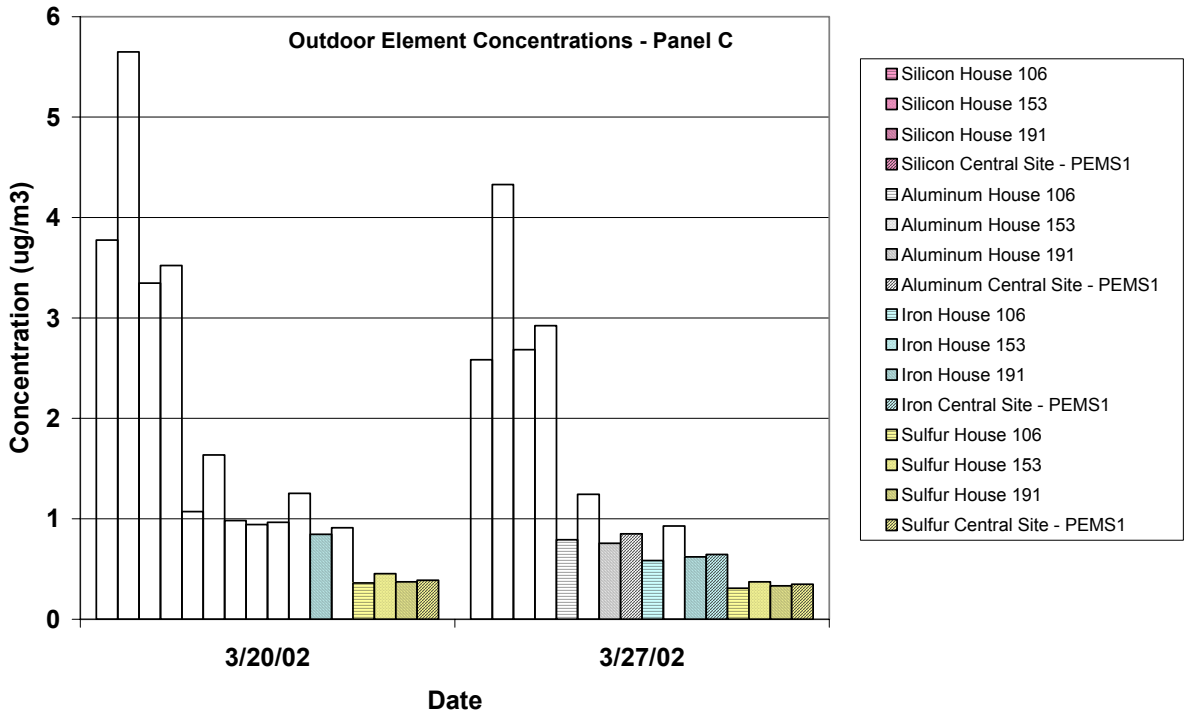


Figure 5.7.4-4. Comparison of outdoor silicon, aluminum, iron, and sulfur elemental concentrations during Panel C.

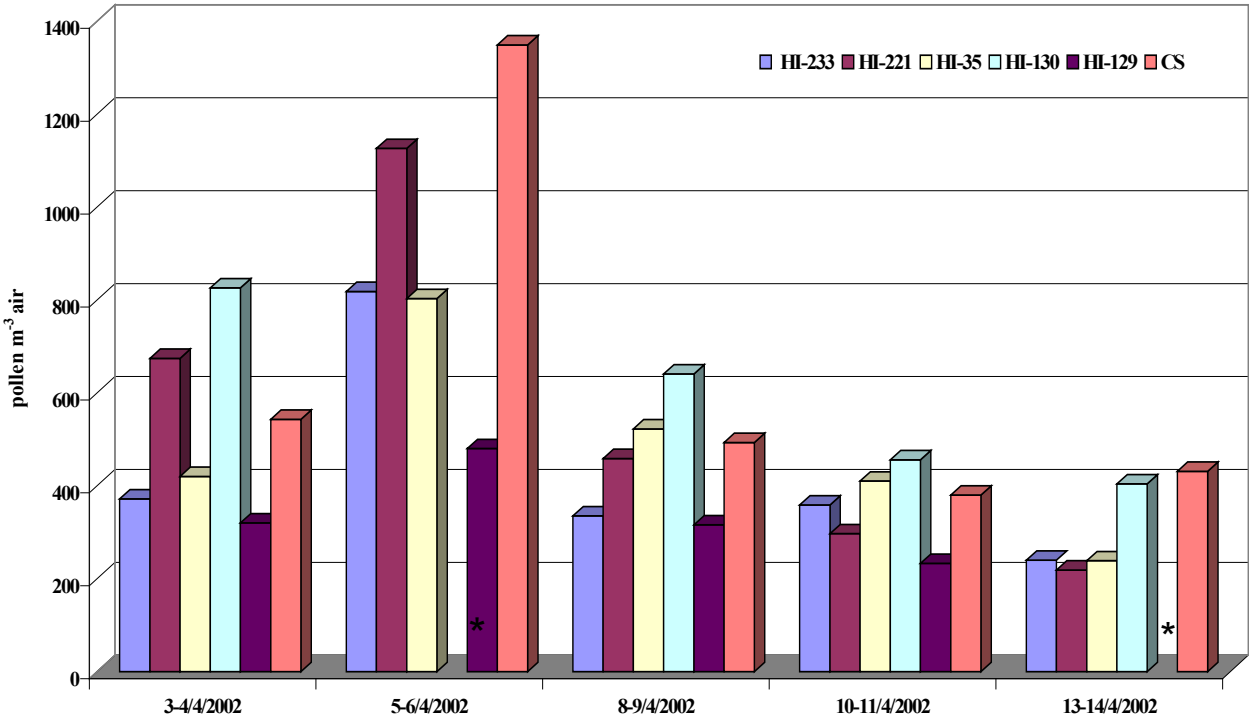


Figure 5.7.4-5. Outdoor daily total pollen concentration, Panel 5.

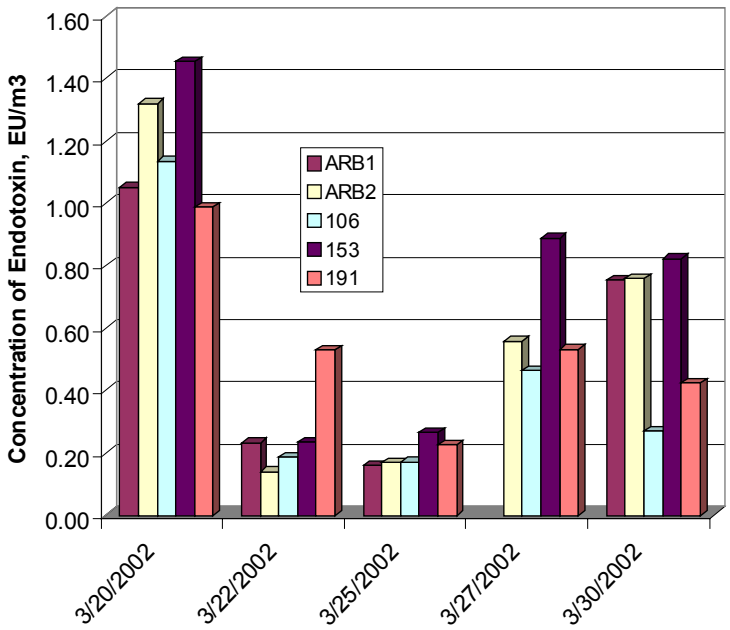


Figure 5.7.4-6. Spatial variability of entodoxin during Panel C.

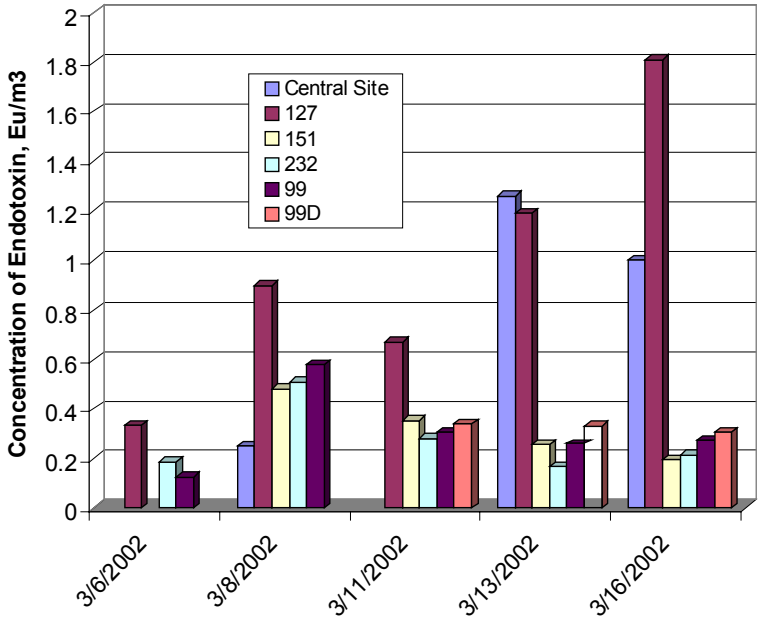


Figure 5.7.4-7. Spatial variation of endotoxin during Panel D.

5.8 EXPOSURE DATA ANALYSIS AND MODELING PLANS

While numerous protocol changes and refinements were implemented during Phase I of the study, they have not materially altered the analysis plans. The general approach for exposure data analysis and exposure modeling is the same as originally proposed. The exposure data is being collected to improve our understanding of air quality and children's air pollution exposure in Fresno. Analyses are planned to test our hypotheses and to develop a method (model) to estimate the daily air pollution exposures of the study participants over the five-year period. The method will be developed and evaluated using data primarily collected in the first two and one-half years of the exposure study (January 2001 through June 2003). The planned approach involves conducting exploratory data analyses that will lead to specific submodels of relationships. The submodels will be combined into an overall model (and database) of the children's daily exposures for all of the agents listed in Section 5.1.

Conceptually, the exposure model is expected to use (1) daily Central-Site data, (2) relationships between Central-Site concentrations and outdoor concentrations at specific homes, in specific neighborhoods, and/or in different types of neighborhoods, (3) indoor/outdoor relationships for specific homes and/or types of homes, (4) house-specific data for indoor concentrations of selected agents, and (5) time-activity data for individual participants. Model testing will be conducted using the microenvironmental data collected in the Home Intensive and, to the extent feasible, the limited personal exposure data to assess model performance. The planned analyses are organized according to the six elements described in Subsections 5.8.1 through 5.8.6.

5.8.1 Analysis of Central-Site Data

The Central-Site air quality and meteorological measurements will be examined in order to understand conditions at the Central Site, to reconcile the different measurement techniques, to understand the temporal variability of gases and particles, and to understand relationships between gases, particle mass, particle chemical composition, particle size, and particle number densities in Fresno. Certain pollutants, including ozone, NO, and NO_2 are routinely measured at three other ambient air monitoring stations in Fresno and Clovis, and these will be included in the analyses of routinely collected ambient data. For model building purposes, it is important to identify the pollutants that are collinear and those that have distinct diurnal and seasonal variations. There is particular interest in examining relationships between the criteria air pollutants (ozone, NO_2, CO, SO_2, and PM Mass) and the special agents included in FACES, such as pollens grains, fungal spores, endotoxins, and specific chemical constituents of PM. Summary statistics, correlation analysis, time series plots, scatter plots, and box whisker plots will be used to understand these data. Seasonal, monthly, daily, day-of-week, and diurnal displays of the concentrations will be examined to characterize the temporal variability. These analyses are a prerequisite to using the data in comparative analyses with the data from schools and homes, and in the modeling.

5.8.2 Analysis of Neighborhood Data

The data collected at a variety of neighborhood locations in this study will provide a unique opportunity to characterize the within-community variability of outdoor pollutant

concentrations. The spatial and temporal variability will be characterized; the emphasis will be on time-averaged spatial differences in concentrations of different species. The expectation is that the concentrations of Group I species will show little variation within the community, and Group II species will show some bias from the Central Site. The direction and extent of the bias is important to capture and include in the exposure model as one of the principal means of improving the accuracy of the model.

The variety and amounts of neighborhood-scale data sets will enhance this analysis. There are four groups of data that will be used in this analysis:

- Home Intensive daily concentrations for ozone, PM mass, OC, EC, SO_4, NO_3, trace metals, PAHs, endotoxins, pollen grains, and fugal spores outside ~70 homes for 5 days and outside another ~15 homes for 10 days each. Hourly light scattering data are available for 12 or 24 days outside the homes. Data are available from 3 to 5 different houses in each panel.
- School mobile van hourly and daily concentrations of virtually all the pollutants measured at the Central Site.
- Routine two-week average ozone concentrations measured in summer outside all the FACES participants' houses.
- Hourly ozone, NO, and NO_2 concentrations from the other fixed-site, ambient monitoring stations (Clovis, Drummond, and Sierra Sky Park).

Analyses will be conducted to evaluate the consistency and comparability of the different measurements and select procedures for making the comparisons.

As participants are added to the study, their residences are geo-coded and assigned a preliminary traffic density ranking based on CALTRANS annual average traffic density data. The home survey data are used to classify each home with respect to the extent of indoor combustion devices and activity. These are primarily used to assure that the homes selected for the Home Intensive sampling are spread out across the community, rather than located in the same neighborhood, and include of range of potentials for indoor source contributions. Graphic Information System (GIS) have been used to map the residences, schools, and traffic volumes.

Two initial steps in dealing with the pollutant database are to calculate the concentrations from the continuous data for the averaging times of the integrated samples and to map the data. A database will be set up for this analysis with as many pollutants and locations as possible with concentrations for comparable averaging times. We have found that there is no good substitute for looking at the patterns in the data early in the exploratory analysis; thus, spatial plots of the integrated data and comparable Central-Site data will be developed. Correlations and regressions will be performed to assess how well the neighborhood-scale concentrations track the Central-Site concentrations. The magnitude of the bias between specific neighborhood location concentrations and the Central-Site concentrations will be examined. The high time resolution data, such as the light scattering from nephelometers outside houses, will be compared to the Central-Site data to assess how the bias varies with time of day and/or day of week. The diurnal dependence will be examined to determine whether the deviations from the Central-Site data are consistent and whether they follow expected trends (e.g., the morning and evening increases

from mobile source activity). The extent to which various factors, such as proximity to roadways and traffic density and type and extent of vegetation, explain the variance in concentrations across the city will be assessed.

The coherence of results for different species will be examined. Consistency is expected for species that are co-emitted from major source types. Analysis of the spatial patterns and seasonality of the bioaerosols and the other pollutants will be particularly informative because concurrent data for these species have rarely been measured in a manner that would allow objective comparisons. Significantly different spatial patterns (or neighborhood-scale variations) are expected for bioaerosols compared to $PM_{2.5}$ or PM_{10} mass. Even among the bioaerosols, significant differences are likely between pollen grains, fungal spores, and endotoxins. The coherence and consistency of these spatial patterns will be evaluated. Simple regression models relating bioaerosols and other pollutants in the neighborhoods of the study participants to those at the Central Site will be developed. The temporal and spatial correlation analysis for the different species will give us information on the explanatory power of different types of models under consideration.

5.8.3 Analysis of Indoor/Outdoor Pollutant Relationships

The data from the indoor and outdoor sampling at participants' homes will be analyzed and categorized to understand how much variation exists in the homes of our study population. The housing questionnaire data will be used in the analysis to determine which characteristics explain differences in I/O ratios and concentrations. Associations between I/O ratios and ventilation characteristics, which will affect all pollutants, will be explored. We will also examine relationships between indoor pollutant levels and probable sources, including NO_2 and gas-appliance use; SHS and smoking; pollens and houseplants; and $PM_{2.5}$ and smoking, cooking, cleaning, and pets. From these analyses, we expect to develop representative models of how much outside air infiltrates the indoor environment (expressed as I/O ratios for different pollutants and types of structures) and how much indoor sources typically contribute to indoor concentrations. These relatively simple models will be constructed so that we can apply them (using housing questionnaire data) to all of the study participants. The I/O sulfate data and the nephelometer data may also be used to classify ventilation characteristics of residences.

5.8.4 Analysis of House-Specific Data for Indoor Concentrations of Selected Agents

The Group II and III (e.g., SHS) pollutants will be analyzed to determine which pollutants are primarily indoor contaminants, with little relation to outdoor air. The indoor measurements of house dust allergens and SHS data are being collected to use directly in the exposure model; thus, it will not be necessary to develop models of their concentrations. Fungal spores and endotoxins may behave either as Group II or Group III pollutants, and it is important to identify which participants have homes with high indoor concentrations that are likely to dominate their exposures. The extent to which household characteristics may explain the variability of indoor concentrations will be evaluated using correlation and regression analysis. These relationships may not only be interesting but also useful for filling in missing data and/or extrapolating the data to other time periods or populations.

5.8.5 Analysis of Time-Activity Data for Individual Participants

Time-activity questionnaire data are collected on a daily basis during the panel studies. These surveys provide a wealth of information about the individuals in the study. Our initial reviews of the data indicate a wide range of data quality and completeness among participants. Analyses are needed to characterize, first, the data consistency and, second, time-use by type of day (weekday versus weekend) and season (summer versus non-summer) for the fractional time spent in the following locations:

1. Residential – indoor
2. Residential – outdoor
3. School – indoor
4. School - outdoor
5. In vehicle
6. Other outdoor
7. Other Indoor

The means and variance of time-use within subjects and between subjects will be examined. After these detailed data are examined, the locations probably will be aggregated into a smaller number that will be practical for modeling. The microenvironments for which we will have pollutant data are the first four types listed. However, it is important to know how individuals spend their time; if we find that some children spend a great deal of time in vehicles, we may incorporate these data and submodels (or adjustment factors) from the literature to estimate microenvironmental concentrations for locations that are only important for certain children.

It is not clear from the literature whether the time-use of asthmatic children is noticeably different from non-asthmatic children. While this question is interesting and may provoke some comparisons of these data with national surveys, it will not be the focus of this analysis.

5.8.6 Model Assembly and Testing

Modeling software is needed to estimate the daily personal exposures of the study participants to the agents. STI has developed exposure modeling software for general population exposure assessment (REHEX-II, Lurmann and Korc, 1994) and for cohort exposure assessments where subject-specific information is available (Lurmann and Kumar, 1998). The software provides a general framework that can be modified to suit the needs of particular applications. The software is structured to use a data-driven approach to exposure assessment.

The recommended technical approach will be to modify STI's existing exposure modeling software to interface with the subject-specific data available for the Fresno cohort and to incorporate the specific submodels that show the greatest explanatory power. The model will be interfaced to the housing questionnaire data, the time-activity data, the Central-Site ambient air quality data, the house-specific data for Group III agents, and a library of microenvironmental concentration submodels. The framework will allow alternative submodels to be easily tested. After the interface has been established and debugged, preliminary sensitivity analyses will be conducted to identify important parameters (or perhaps unimportant parameters). Some model refinements may be made to make better use of the available data, based on these sensitivity

results. Next, the model will be tested against the $PM_{2.5}$ and $PM_{2.5-10}$ personal exposure data collected on the Fresno subjects. These data are quite limited but will provide a reality check for the model. The small number of samples, subjects, and pollutants for which the model can be tested will limit the extent to which we can make statistical statements regarding the model performance. Much of the support for the model validity will be derived from the actual data it will use and from the statistical analysis that supports particular submodels that will be incorporated into the overall model. Given that the submodels will be developed from data from participants' homes and schools, we believe the exposure modeling approach will yield more accurate estimates than previous studies.

5.9 IMPLICATIONS OF PRELIMINARY EXPOSURE RESULTS

A relatively small portion of the household and community exposure-related data collected in Phase 1 are presented in this report. Even though over half of the Phase 1 exposure-related data have been collected, too few data have been analyzed to properly interpret scientific findings. Nevertheless, the preliminary data have implications for exposure assessment methodologies. The preliminary results generally confirm the validity of the exposure data collection methods and support the overall technical approach for exposure assessment. Key implications of the preliminary results include the following:

- The quality of air quality data collected in the routine home surveys, Home Intensive sampling, and at Central Site meets our specifications. The data are reasonably accurate and precise, and the data capture rates are high. The comparability of data collected with different methods is encouraging.
- The FACES subjects are extremely cooperative in allowing Home Intensive sampling inside and outside of their homes. The efforts to design a quiet, compact, safe, and reliable measurement system for the Home Intensive sampling have enhanced the acceptability of the microenvironments sampling in FACES residences. Some subjects have already agreed to allow sampling for a second two-week period in their homes. Half of the home visits have been conducted and the exposure team is on schedule to complete the remaining Home Intensive sampling by February 2003.
- The overall design of the FACES study relies on the day-to-day variations in air quality parameters in Fresno. The preliminary ambient data from the Central Site indicate relatively large daily variations in the parameters of interest for the health study. In addition, the diurnal patterns of various chemical components are quite different and may have implications for the children's exposures. Hence, the observed daily air quality variations in Fresno meet or exceed our expectations for the study.
- The seasonal differences in air quality in Fresno are impressive. For example, many of the biological species are highest during the spring while the ozone concentrations are highest during the summer and $PM_{2.5}$ and PM_{10} levels are highest during the fall and winter. The lack of colinearity in the species is a tremendous asset to the study because it enhances the likelihood of identifying which agents are associated with exacerbations of asthma symptoms.

- The preliminary comparisons of indoor and outdoor concentrations at residences suggest there are significant pollution sources within selected FACES participants' homes. Indoor/outdoor ratios exceed unity in a number of homes for many agents including PM mass, organic carbon, pollen grains, fungal spores, and endotoxins. Central Site measurements alone would not detect these exposures; measurements at the homes are essential for capturing these elevated exposures. The preliminary data support collecting indoor and outdoor exposure data in as many FACES participants' residences as residents will allow access for sampling. The indoor- outdoor differences are large enough to warrant incorporating them into the exposure modeling.
- Preliminary evaluations of the spatial variations in exposure parameters indicate ±20% variations in daily values are common across Fresno. The large spatial variations are for biological agents. The preliminary data that suggest the within-community spatial variations are large enough to warrant treatment in the exposure modeling. If these variations persist over time, then these variations are likely to result in significant differences in subject exposure estimates. Continued measurements outside homes and at schools are essential for characterizing this element of exposures in Fresno.

6. PRELIMINARY ANALYSES OF ASSOCIATION BETWEEN DAILY CHANGES IN AMBIENT CONCENTRATIONS AND SYMPTOMS

6.1 INTRODUCTION AND RATIONALE

At the time of the discussion that formed the basis for the content of this report, it was agreed that the focus of our analyses should be to demonstrate our ability to replicate, in a timely fashion, the analyses undertaken by published literature regarding air pollution and asthma. Thus, for the purposes of this report, we have carried out what we feel to be the appropriate level of analysis to fulfill this obligation. However, given the fact that our data are incomplete at this time, we have not carried out the types of extensive additional analyses (e.g., detailed analysis of correlation of pollutants, multi-pollutant models, evaluation of autocorrelation in models, etc.) that will accompany our research reports for publication and our final report to ARB. For this interim report, we have confined our analysis to the effects of changes in daily concentrations of $PM_{2.5}$ (24-hour), O_3 (maximum 8-hour average) and NO_2 (24-hour average) on respiratory symptoms. At the time of the preparation of this interim report, daily ambient air pollutant data were available to us only for the period from November 11, 2000 through November 30, 2001 for these pollutants as well as PM_{10}, PAHs, NO and black carbon.

Although our analytic work is guided by the research hypotheses set forward in the original application and reiterated in this interim report, we decided to focus our attention on mass/volumetric concentrations of the three pollutants above for the following reasons not directly related to the research hypotheses: **1**) a new mass-based annual $PM_{2.5}$ standard was in the process of being issued by ARB when we began the analyses; **2**) the O_3 volumetric-based standard is coming up for review; and **3**) there is a large body of health data related to NO_2 concentrations. NO_2 concentration is considered a reasonable indicator of motor vehicle emissions and there is considerable ongoing interest in these emissions as a cause of health effects. While we plan to also use NO, PAH and EC as indicators of motor vehicle emissions in subsequent analyses, examination of NO_2 allows us to compare our results to other published studies.

We also decided to focus the analyses on morning symptom data rather than on lung function for a series of reasons: **1**) We have established acceptability criteria for the pulmonary function efforts. When the spirometer's software applies these criteria, the sample size decreases. Since the analysis period included in this report is limited by one-year of pollutant data, we decided to use a more complete outcome (symptoms) to maximize the precision of our effect estimates; **2**) Additional physician review of the lung function data suggests that additional exclusions may be warranted and time constraints have not allowed us to complete this review for the data included in this report. Daily symptom data do not undergo acceptability review, and, therefore, are more complete than daily lung function data; **3**) Symptoms and lung function often are at their worst in the morning, and a focus on this observation period allows us to capture nocturnal symptoms most accurately. Presence of nocturnal symptoms is used to define more severe asthma and may be influenced by exposure to ambient pollutant concentrations during the waking hours of the children; and **4**) Morning measures of symptoms are less likely to be influenced by variations in the recent use of controller and rescue medication and time-activity patterns, which may be important modifiers of the preceding day's air pollution effect.

As was agreed in the discussions with ARB about the content of this report, our analyses were to be based on conventional statistical methods. This would allow us to determine to what extent our effect estimates are quantitatively similar to those observed in other studies of the association between short-term fluctuations in air pollution concentrations and health effects in children with asthma. Based on the findings of our conventional statistical analyses, however, we have decided to present some of our work on the causal modeling. We note that we will not rely on traditional methods when our data are more complete. The results reported here are for the purposes of this interim report only.

6.2 METHODS

As noted above, for this report we were given air pollutant data for November 2000 – November 2001. During that interval, the children in FACES were completing two-week home panels during the first two weeks (approximately) of every month. By design, therefore, for one half of each month, health data were not collected and therefore can not be included in this analysis. In mid-November of 2001, the study design included two 14-day panels per month so that in reality, at least some children were performing home monitoring on nearly every day of the year.

During the time period over which the air pollution data were available, 119 children completed a two-week home monitoring panel. Each child contributed one diary to this analysis. A total of 1287 child-days (86%) were available. A small percentage of child-days are missing due to non-compliance by the children as well as by restriction of the analysis to days for which pollutant data were available. Table 6.1 summarizes the subject data used for these analyses.

Table 6.1: Subject Data for Interim Analysis	
Number of Children	119
• % female	41
• age (median, range)	10 (7, 12)
Baseline classification of asthma (symptoms only) • %mild intermittent • %mild-moderate persistent • %severe	 30 45 25
• % of children taking baseline inhaled steroids	83
• Number of child-days available	1287
• % Completed days per child (median, range)	86% (5,100)
• % child-days with symptoms (Q2 and Q3)	36
• % child-days with medication use	10
• % days with symptoms per child (med., range)	30 (0, 100)
• % days with medication use per-child (med. range)	0 (0,93)

Baseline asthma severity classification was based on the baseline questionnaire and restricted to symptoms (the WHO/NHLBI-based version described in Section 4.4). We have found that most of our subjects have a baseline FEV_1 percent of predicted (FEV_1%) within the

normal range for age and sex (>=80% of predicted), despite abnormal shape in their flow-volume curves (data not shown). This undoubtedly is due to the relatively young age of our subjects and can be expected to change as they get older. Thus, we felt that inclusion of FEV_1% in the severity classification at this time would give a distorted picture of the severity distribution.

Symptom data for these pollutant-effect analyses were derived from the series of questions to which the children responded after the completion of the morning lung function testing on the EasyOne® spirometer. Five questions were asked at the end of each morning test session. Based on a preliminary analysis (data not shown), only one medication use question was considered in this analysis—rescue medication use during the hour prior to performance of the lung function test (Table 6.2, Q5). Since we did not have enough data to distinguish different air pollutant effects on different symptoms, we defined "any symptom" as a positive response to Q2 or Q3.

Table 6.2: Questions Answered at Morning Test Session
Q1: Did you have any coughing during this test?
Q2: Did you wheeze after bedtime?
Q3: Did you have any coughing after bedtime?
Q4: Did you need to use your rescue medicine after bedtime?
Q5: Did you need to use your rescue medicine in the last hour?

The distributions for the three pollutants are given in Table 6.3 for days on which symptom data were available over the period of November 30, 2000 through November 30, 2001. For theses days, the median temperature and humidity were 17.7°C and 56%, respectively. In FACES, an "air pollution day" extends over a 24-hour period, from 8 P.M. to 8 P.M.. However, for this report, the data were given to us for 12 A.M. to 12 A.M. We evaluated lag 0, defined as exposure from 12 AM to 11:59 PM on the calendar day before the morning test. In addition, we evaluated 2, 3 and 5-day moving averages.

Table 6.3: Distribution of Ambient Pollutants on Days When Symptom Data Were Collected
November 30, 2000 through November 30, 2001

Pollutant	**Median Range**	**25^{th}-75^{th} Percentiles**
$PM_{2.5}$ (24 hr,$\mu g/m^3$)	18 (3, 133)	12, 31
O_3 (8hr mean,ppb)	57 (6, 113)	28, 72
NO_2 (24 hr,ppb)	19 (7, 52)	14, 27

6.3 STATISTICAL ANALYSIS

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 N NMAPS 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 6.4. 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 has not been performed as yet. However, it should be noted that if the model chosen for the covariance matrix is mis-specified, our parameter estimates are still consistent and the confidence intervals reported are correct. A formal evaluation for residual autocorrelation will be undertaken in future analyses. 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)).

Table 6.4: 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.

For this summary, arbitrary increments of 10 μg/ m^3 and 10 ppb are 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 6.5). 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.

Table 6.5: 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.

We tested a model which included a main effect for "use of rescue medication in the hour before testing" and an interaction term for the pollutant and "use of rescue medication in the hour before testing" (Q5, Table 6.2), since there is reason to expect that recent use of rescue medication can alter the occurrence of symptoms, and thus modify the effect of air pollution. All of the models in Table 6.6, (except for the annual O_3 analysis), suggested that use of rescue medication was associated with increased symptoms during the night and the use of rescue medication increased the association of the pollutant with the occurrence of symptoms. This is contrary to what would have been expected and results from the fact that rescue medication use is confounded, in a time-dependent manner, by the occurrence of previous symptoms--that is, although medication use does not "cause" symptoms, children who are sicker are more likely to take medication and consequently are more likely to have symptoms during the subsequent reporting period. Therefore, interpretation of these data should keep in mind this element of uncontrolled, time-dependent confounding in these conventional statistical analyses.

Except for the effect of O_3 studied over all seasons, the report of rescue medication in the hour before testing was associated with increased odds of symptoms for a given change in pollutant level (Table 6.6). This was particularly true for NO_2 for which the OR in those who reported rescue medication was nearly 2-fold greater that those who did not use medication (2.70 versus 1.39, respectively).

Table 6.6. Logistic Regression Models for the Interaction Effect of Rescue Medication and Air Pollutants, Adjusted for Weather, Weekend Day, Season and Time*		
	No Rescue Med.	**Rescue Med.**
November 2000 – November 2001 Odds Ratio (95% CI)		
$PM_{2.5}$ (24-hour) • **5 day mean**	1.08 (0.94, 1.23)	1.20 (0.92, 1.56)
NO_2 (24-hour) • **5-day mean**	1.39 (0.76, 2.54)	2.70 (0.98, 7.42)
O_3 (8-hour mean) • **3-day mean**	1.18 (0.95, 1.46)	1.13 (0.76, 1.67)
June, July, August 2001 ** **Odds Ratio (95% CI)**		
O_3 (8-hour mean) • **3-day mean****	1.34 (0.97, 1.85)	1.53 (0.74, 3.16)

* Parameter estimates are reported for 10μg/m^3 increment for $PM_{2.5}$ and a 10 ppb increment for O_3 and NO_2
** Summer analysis does not include term for season

Figure 6.1 presents a causal diagram that could reflect the source of the time dependent confounding, which at this time we suspect is a problem with these data. A conventional epidemiological analysis of the longitudinal data aimed at investigating the effect of air pollution when no rescue medication is used would include A_{i-2} (air pollution at time *i-2*), A_{i-1} (air pollution at time *i-1*) and R_i (rescue medication at time *i*) in a regression model on S_i (symptoms at time *i*). Such a strategy would give biased estimates for the effect of air pollution and rescue medication on the occurrence of symptoms because it ignores the confounding of the effect of R_i on S_i by the variable S_{i-1}. If such confounding is considered, a conventional analysis would then include S_{i-1} in the regression model on S_i. Such an analysis would also lead to incorrect estimation of the effect of air pollution and rescue medication on symptoms. Indeed, it is a well-established epidemiological concept that adjustment for covariates on a causal pathway between a treatment (A_{i-1}) and the outcome (S_i) can bias the effect estimates for the exposure of interest (in this case air pollution concentrations and rescue medication), and the direction of the bias can be unpredictable. Therefore adjusting for S_{i-1} would lead to estimating bias [Weinberg, 1993]. Si-1 is called a time-dependent confounder and conventional analyses cannot handle properly such a variable being both a confounder and a variable on a causal pathway between the exposure and the outcome.

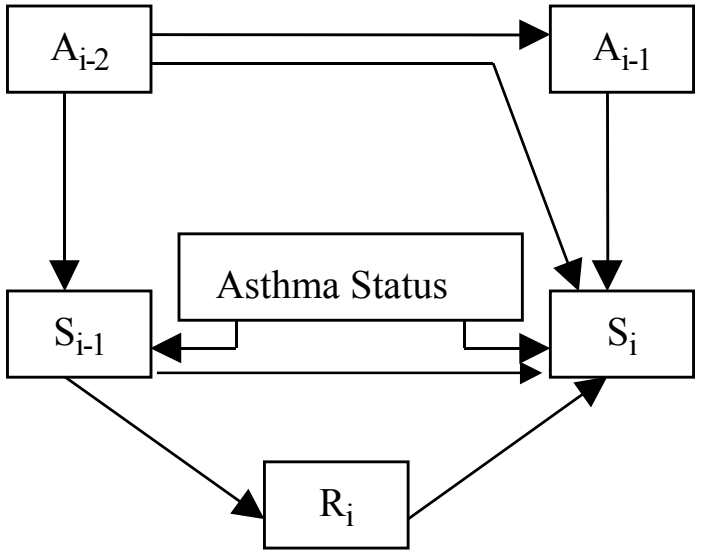


Figure 6.1: Causal Diagram of the Relationship Between Air Pollution (*A*), Rescue Medication (*R*) Symptoms (*S*) and Asthma Severity

Given this issue of time-dependent confounding, these interactions support the need for a more definitive causal analysis. Appropriate modeling of the treatment effect (i.e. medication use) with causal methods may allow us to see the true causal effect not only of air pollution but of medication use (i.e. improvements in symptoms and pulmonary function) and to determine whether medication is, in fact, protective against the effects of air pollution. We thought it would be too complicated for children to report information on daily use of inhaled steroids and, therefore cannot include it in the longitudinal models. In preliminary analyses, however, the pollutant effect did not differ according to whether or not the parent reported that the child had used inhaled steroids within the year prior to the baseline interview (data not shown). Future analyses will include more detailed investigations of interactions and susceptible subgroups.

6.4 SUMMARY AND CONCLUSIONS

With the use of conventional statistical analysis based on GEE, we have demonstrated positive associations between changes in 3 and 5-day moving averages and the occurrence of respiratory symptoms in preliminary analysis of our group of asthmatic children. Relative risks were generally highest for NO_2 and O_3 (the latter based only on summer months) whether or not rescue medication was included in the analyses (Tables 6.5 and 6.6). $PM_{2.5}$ associations were smallest in all analyses. In all analyses, the NO_2 associations were the most precisely estimated. However, it is important to note that we used the commonly employed approach of scaling the estimates to a somewhat arbitrary value of 10 $\mu g/m^3$ or 10 ppb, which may not represent comparable increases across pollutants. Alternative approaches to comparisons across pollutants will be explored in future analyses.

Our effect estimates are similar to those observed in other studies. Mortimer and colleagues reported a relative odds (OR) of 1.16 for morning symptoms and a 15 ppb increase in a 2-day moving average of peak summertime O_3 concentrations in the NCICAS [Mortimer,

2002]. Our estimate for a 3-day moving average of hourly means was 1.34 in analyses that omitted rescue medication and 1.53 when rescue medication was included. These authors also reported an OR of 1.48 for A.M. symptoms for a 20 $\mu g/m^3$ increase in the 6-day moving average of summertime NO_2, which is somewhat lower than our estimates for a 10 $\mu g/m^3$ (1.39, 2.70, table 6.6) increase in the 5-day moving average over the entire year. Delfino, *et al*. [Delfino, 1998] reported a panel study of 24 asthmatic children from Alpine, CA over the period August to October, 1995. The estimated OR for a 46 ppb increase in current day 8-hour O_3 was 1.42, which falls between our estimates for summertime ozone in tables 6.5-6.6. In contrast to our $PM_{2.5}$ models, these investigators reported an OR of 1.73 for a 25 $\mu g/m^3$ increase in the 5-day moving average of the 24-hour PM_{10}, where as the largest estimate for a similar increment and moving average in our data is 1.20 for a 10 $\mu g/m^3$ increment (Table 6.6 for "Rescue Med."). Thurston and colleagues [Thurston, 1997] in a study of children who attended summer camp for asthmatic children in the Connecticut River Valley reported a relative risk (Poisson regression) for chest symptoms of 1.05 (based on calculations from Thurston Table 5) for a 10 ppb increase in 1-hour maximum O_3 concentration. No data are given for PM or NO_2. Finally, Yu, *et al*. observed ORs of 1.08-1.11 for asthma symptoms in asthmatic children enrolled in the CAMP study for a 10 $\mu g/m^3$ increase in 24-hour PM_{10} for lags 0-2 days [Yu, 2000] in a marginal GEE and slightly smaller ORs for a conventional GEE. While many additional studies could be cited, this brief review does establish that we have found similar associations between various air pollutants and symptoms in children with levels which are quantitatively within the range of those reported by other investigators for similar aged children with asthma.

Our second observation of importance is our observation that conventional methods that have been used to analyze the relationship between air pollution and symptoms in asthma give biased results for the air pollution parameters. This can lead to mis-interpretation of the effects of the use of asthma medication on modification of air pollution effects on symptom occurrence. We have presented a very realistic scenario of a causal pathway that could explain part of the problem. We will be exploring this through conventional and causal analyses and through simulations. An example of the differences between traditional and causal regression methods using FACES data can be found in Appendix CD4.

The problem of counterintuitive results based on conventional methods of analysis is not a new issue. In a panel study of children with asthma, Peters and colleagues reported that use of a beta agonist or theophylline was associated with a significant increase in cough and non-significant increase in runny nose associated with 5-day mean sulfate concentrations and a significant decrease in evening peak expiratory flow [Peters, 1997]. Table 4 from these authors indicates the problem—medication use is associated strongly with all symptoms and lung function. Although the authors claim that medication use "attenuates" symptoms, careful review of their table 3 does not support this contention. Rather, their results appear to be counterintuitive due to the type of confounding that we have discussed herein. Although, Delfino and colleagues also tried to evaluate the effect of medication use on air pollution-related symptoms in children with asthma [Delfino, 1998], there are too many differences in the presentation of the data to make any meaningful comparisons with our findings. Obviously, these types of findings require further exploration both from the vantage point of understanding the mechanisms by which air pollutants lead to health effects in children with asthma for public health risk assessment.

Below (Table 6.7) is a comparison of scope of the analyses presented in this report relative to the scope of analyses that will be included in our final report to ARB and in various publications that will be submitted. This is meant only to serve as an example of the broad range of analyses and does not constitute an exhaustive or definitive list.

Table 6.7		
Parameter	**Analysis Presented**	**Analysis for Final Report**
Health outcomes—acute	• Morning symptoms	• Morning symptoms • Evening symptoms • Day-to-day and intra-day variation in pulmonary function (FEV_1, PEF, FEF_{25-75}, etc.) • asthma severity
Health outcomes—chronic	None	• Pulmonary function growth/decline • Changes in asthma severity
Statistical approach	Logistic regression	Causal inference
Exposure Assessment	Ecological--Central Site data only	Individual, based on model and home specific information
Pollutant metrics	8-hour or 24-hour averages	• 1-hour max • 8 hour max,mean • 24-hour max, mean • seasonal average • cumulative exposures
Susceptible groups / Effect modifiers	Rescue medication use	• Demographic characteristics (e.g.SES) • Housing characteristics (e.g. smoking homes). • Rescue and controller medication use • Host characteristics (e.g. birth factors, atopic status) • Residential history (e.g. distance from roadways)
Pollutant combinations	• Single pollutant models	• Single pollutants • Interactions with bioaerosols and other co-pollutants

Pollutants and biological agents	• ozone
	• nitrogen dioxide
	• 24 hr $PM_{2.5}$
		• ozone
		• nitrogen dioxide
		• NO
		• Sulfur dioxide
		• 24 hr $PM_{2.5}$
		  • Mass
		  • Organic carbon/elemental carbon (OC/EC)
		  • Sulfate ion
		  • Nitrate ion
		  • Ammonium ion
		  • Metals
		  • Potassium
		  • PAHs
		• 24 hr PM_{10}
		  • Mass
		  • Metals
		  • Particle number
		  • Second Hand Smoke
		Pollen grains
		Fungal spores
		Airborne endotoxin
		Allergens in house dust
		  • Cat
		  • Dog
		  • Cockroach
		  • Dust mites
		  • Endotoxin in house dust

7. OTHER RELATED ACCOMPLISHMENTS

7.1 ADDITIONAL FUNDING SOURCES

Three proposals have been written to obtain additional funding for FACES substudies. A more detailed description of each project can be found in Appendix 7. Below is a summary of each proposal.

1) Funds have been obtained from US EPA (Office of Research Development, National Center for Environmental Research) to examine the FACES households' risk-reducing behavior to estimate the parent's willingness to pay for reduced asthma morbidity among children. A total of $320,000 has been awarded for the period of March 2002- March 2005.

2) Approximately $200,000 was obtained from the US EPA to include sampling for PAHs so that PAHs can be added to the agents evaluated in the study. Continuous samplers for PAHs (EcoChem) were added to the trailers (one was already at the Central Site). Methods were developed to sample at these sites for speciated PAHs (particle phase and vapor phase) and to add an integrated PAH sample to the MEMs for collection during the Home Intensive sampling. We anticipate further funding from US EPA to enable us to analyze the samples we are now collecting both at the homes and on the trailers and Central Site, and to pay the field staff and sampling costs associated with these samples.

3) A proposal to expand personal sampling was submitted to the Health Effects Institute. Although a strong score was obtained, it was not funded due to the high cost. Other agencies may be approached about funding this sub-study.

7.2 WEBSITE

Two FACES websites were developed in September, 2001, to disseminate information about the research project to the public and to facilitate the sharing of information between the research collaborators. The first of the two websites, www.facesstudy.com, was developed to provide FACES background and contact information as well as profiles of the FACES research team. This website includes links to related research topics and collaborating and funding organizations. Since its development, the website has received more than 500 visits. At the same time, a larger website designed for FACES researchers to use and access was developed. This website was created as a method of conveniently distributing current forms, protocols and other research materials to FACES collaborators. The website also serves as a space to post slides from recent presentations, abstracts for journal submission, FACES newsletters, and upcoming conferences. Access to this website, http://research.facesstudy.com, is intended for FACES researchers. Posting to and maintenance of both of the websites is done from the FACES office in Berkeley.

7.3 MANUSCRIPTS, PRESENTATIONS AND ABSTRACTS

The FACES team has presented and will be presenting preliminary findings and methodologic issues at several conferences (Table 7.1). One paper has been submitted for publication and the data have also been used for a UC Berkeley senior thesis project. Copies of all abstracts can be found in Appendix 1, while manuscripts and presentations can be found on the CD ROM in Appendix CD4.

Table 7.1 – Conference Abstracts through August 2002.			
First author	**Title**	**Conference**	**Date**
J. Balmes	Classification of asthma severity in the Fresno Asthmatic Children's Environment Study.	American Thoracic Society Meeting	May, 2002
K Mortimer	Causal regression of asthma medication use and pulmonary function.	Society for Epidemiologic Research Meeting	June, 2002
P Lowenthal	Inspector-reported and objective measurement of indoor moisture in homes of asthmatic children.	Indoor Air 2002 Conference	July, 2002
HG Margolis	Assessing Complex Exposures and Responses Among Participants in the Fresno Asthmatic Children's Environment Study (FACES).	ISEE/ISEA 2002	August, 2002
K Mortimer	Causal regression of asthma medication use and pulmonary function.	ISEE/ISEA 2002	August, 2002
SK Hammond	Development of an Exposure Assessment Targeted to an Environmental Epidemiological Study: The FACES Study.	ISEE/ISEA 2002	August, 2002
M Hjelmroos	DO DAILY ACTIVITIES AFFECT INDOOR AIR SAMPLING RESULTS?	7th International Congress on Aerobiology	August, 2002
M Hjelmroos	EVALUATION OF TWO DIFFERENT VOLUMETRIC AIR SAMPLERS	7th International Congress on Aerobiology	August, 2002

8. PROTOCOLS

An extensive set of protocols have been developed for this for both the health and the exposure assessment components of the project; these represent the detailed implementation of the procedures discussed in the original submission. Tables 8-1 and 8-2 provide a list of all of the protocols that have been developed. A CD-ROM has been included that contains the details of the protocols listed in Tables 8-1 and 8-2. These protocols form the basis for the continued work of the project. They are not included in detail in the body of the report due to their length. The CD-ROM is organized to facilitate easy location of any protocol. Each heading in Tables 8-1 and 8-2 are folders on the CD-ROM. Within each folder protocols are identified by the numbers given in the table. All of the protocols are in Word format**.** Table 8-3 summarizes all protocol modifications that have been made since the study began in September 2000.

We have not presented another analysis plan, since the plan presented in the original proposal. The relevant section is "8. Analytic Plan". The CD-ROM contains a folder labeled "Original Proposals" that contains the original submission.

Table 8-1: FACES General and Health Protocols (July, 2002)
Screening S1 Recruitment protocol
Baseline B1 - Allergy skin test B2 - Baseline procedures list B3 - Buccal cell collection (home) B4 - Buccal cell collection (office) B5 - Blood/Buccal cell shipment B6 - Emergency procedures (acute asthma) B7 - Spirometry background B8 - Easyone spirometer (Protocol I: Child EasyOne Training) B9 - Easyone spirometer (Protocol II: EasyOne preparation for home use) B10 - In-line testing of EasyOne and Morgan spirometers B11 - Oxygen administration and albuterol nebulization B12 - Parent medication instruction form B13 – Phlebotomy B14 - Reporting results to health care providers B15 - Operation of Morgan RS232 spirometer B16 - Height (sitting, standing) B17 – Weight B18 - Snoopy incentives (Part 1, Part 2) B19 - Metered dose inhaler spacer protocol
Home Visit HV1 - Diary coding HV2 - Dry gas meter operation HV3 - Dry gas meter log HV4 - Dust collection HV5 – GPS HV6 - Outdoor ozone HV7 - Ozone shipping protocol HV8 - Passive sampler instructions HV9 - Dust vacuum test protocol HV10 - Synchronizing and printing test information from the EasyOne HV11 - Training for the daily diary
Panel Assignment PA1 Panel schedule (year 1, year 2) PA2 Randomization to home panel group
General G1 Sibling enrollment procedures

Table 8-2: FACES Central Site and Laboratory Protocols (July, 2002)
Central Site • Burkard collection (7-day) • Burkard drum change checklist • Burkard drum log • Burkard drum preparation • Burkard slide log • Burkard tape preparation • Fungal spore count • Pollen count
Laboratory Protocols • Cahn-25 electro-balance weighing protocol • Cahn-29 electro-balance weighing protocol • Cat allergen ELISA • Cockroach allergen ELISA • Dog allergen ELISA • Dust sample extraction • Dust weighing • Endotoxin protocol • ETS method & analysis • Filter coating nitrate samplers • Filter weighing data sheet • Fungal spore count • Fungi code • Glycerine jelly preparation • Microscope correction factors • Mite allergen ELISA • Pollen code • Pollen count • R&P filter holder cleaning • Reagent QC form
Home Intensive • Chain of custody (Harvard impactor filters) • Home intensive sampling SOP • Monetary incentives documentation form • Vertical flow check form
Trailer • Burkard slide log • Chain of custody (Burkard 24-hour continuous)

Table 8-3: Protocol modifications since start of study (September 2000)		
Change	Reason for change	Date of change
The integrative samples (collection of airborne endotoxin, pollen grains and fungal spores) were not added to the CRPAQS sites; STI operated the additional integrative samplers (collection of airborne endotoxin, metals, pollen grains and fungal spores) at the Central Site	The CRPAQS sampling sites diminished in size so that integrative samplers could not be placed there; ARB staff were not available at that time.	winter 2000-2001
Reduced residency requirement from one year to 3-months	Recruitment was slow and residency requirement was primary reason children were ineligible.	February, 2001
In-line spirometry (Morgan and EasyOne®)	Wanted to have head-to-head comparison data to evaluated EasyOne®'s validity and reliability.	February, 2001
Dropped penicillium and added cladosporium	Insufficient positive tests to penicillium, additional evidence that we should test for cladosporium.	April, 2001
Expanded age range	Needed to increase recruitment. Low smoking rates suggested that including 11 years olds would not impact lung function growth analyses as much as we thought it might.	May 24, 2001
Dust sample collection increased from 2 to 4 minutes	During some seasons, the quantity of dust was inadequate for range of desired analyses. Increased sampling time to collect larger sample.	August, 2001
Randomization scheme for assigning children to one of eight panels after 1st home visit	Potential bias in patient characteristics due to method of recruitment (i.e. most motivated recruited first), so "panel" may be confounded by these characteristics. Randomization to "panel group" after first home survey removed this confounding.	November, 2001
Changed Home Intensive sampling scheme from 150 home visits with 3 48 hour samples to 100 home visits with 5 24-hour samples	Upon the advice of the External Advisory Panel, we decided to have 24 hour samples to match the time resolution of the exposure assessment planned.	Fall 2001
Expanded windows for completing visits	To improve retention, we expanded the interval for telephone interviews from four to six weeks and the interval for clinic-visits from one to two months.	May, 2002
Expanded eligible geographic area from 10 km to 20 km from central site.	Needed to increase recruitment. Preliminary analyses suggested central site may be representative up to 20 km from site.	June, 2002
Allowed age-eligible siblings to participate	Needed to increase recruitment. Felt that the increase in sample size would outweigh any losses in power due to decreased variability in exposure.	June, 2002

9. FUTURE PLANS

Based on the work that we have presented, we feel that we have demonstrated unequivocally that we have lived up to, or exceeded, the terms or the work scope expected of us during the first 24 months of this contract. We initiated the field study, recruited subjects, carried out all elements of the exposure assessment and demostrated that we can process data in a timely manner and carry out the analyses that were expected of us for this interim report. Moreover, we have been able to present summaries of data that were collected as recent as three weeks prior to the submission of this report.

Our future plans are to complete the scope of work that we set out in the original application and that is summarized in the next section.

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11. APPENDICES

APPENDIX 1: PUBLICATIONS AND ABSTRACTS.

Below is a list of publications and abstracts based on FACES data collected to date. Copies of all of these documents can be found in CD4 - Presentations.

Publications

Evaluating the use of a portable spirometer in a study of pediatric asthma. KM Mortimer, A Fallot, JR Balmes, IB Tager, Submitted to Chest, April 2002, under revision.

Abstract
Study objectives: Laboratory-based spirometry is the gold standard for the assessment of lung function, both in clinical and research protocols. These spirometers, however, are neither practical nor affordable for home-based monitoring or large studies requiring frequent pulmonary function measurements. Traditionally, peak flow meters have been used, but have important limitations.
Design: We evaluated the agreement between a portable spirometer and a laboratory-based spirometer, using an in-line technique to evaluate measures from the same effort. We compared a range of pulmonary function parameters collected during office-based tests and evaluated whether adequate compliance and data quality could be achieved in a home-based study.
Results: The agreement for the actual values of PEF, FEV1 and FEF25 was excellent. The portable device was programmed with customized software to graded each curve using revised ATS acceptability and reproducibility criteria. For 74% of the curves, this grade agreed with a grade assigned by physician review of the curve from the office-based spirometer. During two weeks of twice-daily monitoring at home, children completed an average of 23 out of 28 sessions (83%). Of these, 84% had at least two acceptable and two reproducible curves. Although children aged 8 years or older were not more compliant, they were significantly more likely to achieve acceptable and reproducible curves.
Conclusions: Portable spirometers can provide measurements that are highly the 'gold standard' laboratory spirometers and high quality tracings can be achieved both at home and in the office setting. Additional review by trained physicians identified unacceptable curves that were accepted by the quality control software. This is an important contribution to epidemiologic and clinical studies which require frequent measures of a more broad range of pulmonary function parameters than can be provided by peak flow meters.

Senior Thesis

The impact of distance from freeways on the pulmonary function of children with asthma. UC Berkeley Senior Thesis for Jamie Mikkelson. Advisors: Ira Tager, Kathleen Mortimer. Manuscript is being revised and will be submitted for publication.

Abstract
Exposure to particulate matter (PM) is associated with adverse respiratory health effects. Vehicles traveling along a highway represent a significant source of fine particulates that contribute to the aggravation and possibly to the development of asthma in children. Residential history information and lung function data from 89 children involved in the Fresno Asthmatic Children's Environment Study were used to quantify the impact of PM exposure from vehicles on lung health. The forced expiratory flow volume in one second (FEV1) was collected for each child using a spirometer during office visits between November 2000 and December 2001. Individual-level demographic and socioeconomic data as

well as the exact locations of the children's residences were gathered during home interviews. Residential address data were incorporated into a geographic information system to determine the distances of each residence to the closest highway in Fresno, CA. The distances to only highway 99 were also calculated. The categorical distances reported by the study participants were also used to estimate exposure to vehicular PM. Using three stepwise linear regression models, the effects of proximity to a vehicular source of PM on the mean FEV1 values were evaluated. After adjustment for sex, household income level, race, standing height, parental smoking, mother smoking during pregnancy, time lived in residence, and time of FEV1 test, the measures of absolute distances to the highways were found to be insignificant in predicting changes in mean FEV1 values. The regression model using self-reported distance variables indicated that children who lived one to three blocks from the source of vehicular PM experienced a 10% increased in mean FEV1 values, as compared to children who resided immediately next to the pollution source. These results indicate that living in an area with high traffic density may negatively affect the lung function of children with asthma.

Abstracts

A1) Classification of asthma severity in the Fresno Asthmatic Children's Environment Study. J Balmes, A Fallot, KM Mortimer, P Lowenthal, H Margolis, IB Tager
Presented at the American Thoracic Society Meeting, May 2002

Background: We hypothesize that asthma severity is an important determinant of both short-term and long-term responses of asthmatic children to air pollution exposures. Repeated response to pollutants may, in turn, influence asthma severity. Unfortunately, asthma severity is difficult to disentangle from asthma control. **Methods:** The Fresno Asthmatic Children's Environment Study (FACES) will follow a cohort of asthmatic children (ages 6-11) for 4 years or more to assess the effects of exposures to air pollutants on the natural history of asthma. A multi-component approach to the classification of asthma severity has been developed for FACES. First, a previously validated asthma severity score allowing up to 28 points (Blanc et al., *Chest* 1993;104:1371) was modified for use in pediatric subjects. Second, the 1997 National Asthma Education Program (NAEP) asthma severity classification scheme was modified by the elimination of pulmonary function criteria. Third, spirometric parameters of lung function will be used to independently classify severity. **Results:** For the first 113 children recruited for FACES,the distribution of the modified asthma disability score is as follows: score of 0-3 (25%), 4-7 (31%), 8-10 (19%), 11-17 (24%). Using the modified NAEP scheme, 38% were mild intermittent, 56% were mild persistent, and 6% moderate-severe persistent subjects. The use of controller medications in the past 12 months was 70%, 83%, and 100%, respectively. **Conclusion:** While it is difficult to disentangle asthma severity from asthma control, a multi-component approach appears to have promise for use in epidemiological studies of the effects of environmental exposures.

A2) Causal regression of asthma medication use and pulmonary function.
KM Mortimer, R Neugebauer ,J Balmes , M van der Laan , IB Tager
Presented at the Society for Epidemiologic Research Meeting, June 2002

Evaluation of short-term health effects of air pollution is complicated by daily asthma medication use. Most previous work has treated medication as a confounder, effect modifier or health outcome, or has ignored it all together. Medication is an important factor in the causal pathway for air pollution-related effects on asthmatics, and defining medication use as a confounder is inappropriate and can bias estimates. Over several two-week periods, 63 asthmatic children completed twice daily recording of pulmonary function and

symptoms with a hand-held spirometer. Two regression techniques were used to compare the association between reported use of medication in the past hour and morning pulmonary function measures. Contrary to expectations, simple linear regression showed medication in the past hour was associated with a 0.45 L/s decline in peak expiratory flow (PEF). Rather than declines from medication, it is likely these children were sicker than those children who did not take medication. When indicators for cough or wheeze were included in the model, the medication estimate became -0.19 and both symptoms were associated with decreased PEF. The next approach was a weighted-regression analysis with weights inversely proportional to the probability of receiving treatment (IPTW, Robins, Epidemiology 2000 Sep;11(5):550-60). This creates a pseudo-randomized treatment to remove the association of treatment and symptoms. Children who took medication in the past hour had a 0.20 L/s improvement in PEF. This 6% increase in PEF is consistent with improvements seen in clinical use. A simulation study confirmed that estimates from ordinary regression were severely biased, those from weighted regression were not. IPTW regressions is an important new tool for this step in the analysis of air pollution effects. Next steps include building confidence intervals and adding air pollution terms. Data were obtained from the Fresno Asthmatic Children's Environment Study (FACES), funded by the CA Air Resources Board.

A3) Inspector-reported and objective measurement of indoor moisture in homes of asthmatic children. P Lowenthal, K Mortimer, K Hammond, I Tager, J Macher
Presented at the Indoor Air 2002 Conference, July 2002.

Epidemiological studies investigating the relationship between indoor dampness and respiratory health frequently rely on either survey-reported or objective evidence of moisture. In this investigation, the relationship between inspector-reported moisture and objective moisture measurements was assessed in the homes of children (n=83) who are participating in the Fresno Asthmatic Children's Environment Study (FACES), a longitudinal cohort study of asthma and the environment. Inspector-reported dampness was based on visual evidence of moisture in the living room (LR) and the child's bedroom (CB). A moisture meter (ElectroPhysics CT100, London, Ontario) was used to collect 3 measurements in each of two rooms. Moisture measurements ranged from 3.3 to 22.7 in the LR and from 3.3 to 22.0 in the CB. For this analysis, moisture measurements were categorized into tertiles labeled 'low,' 'medium,' and 'high'. Of all the homes surveyed, 4% of the LR and 13% of the CB had evidence of moisture. All of these homes had moisture measurements that were either in the 'medium' or 'high' category for both LR and CB. Fall season was associated with higher moisture levels in both rooms. Central cooling systems were associated with lower moisture readings in CB but not in the LR. Characteristics unrelated to moisture level include: type of heating and cooking fuel, presence of a fireplace, household crowding, and whether the child's bedroom had window. Small sample sizes and low frequency of several characteristics limits the interpretation the relationship between the selected housing characteristics and indoor moisture measurements to univariate analyses. As this study continues, several hundred more homes will be surveyed which will allow for the examination of multivariate associations between moisture and mildew across seasons and housing types. In addition, we will be able to examine the association between these two methods of assessment and short and long term measures of asthma morbidity.

A4) Assessing Complex Exposures and Responses Among Participants in the Fresno Asthmatic Children's Environment Study (FACES). HG Margolis, F Lurmann, P Roberts, KM Mortimer, IB Tager, J Balmes, J Macher, R Neugenbauer, P Lowenthal, M Hjelmroos-Koski, M van der Laan, SK Hammond. Presented at a joint meeting of the International Society for Environmental Epidemiology and International Society for Exposure Assessment (ISEE/ISEA), August 2002.

Introduction: The goal of FACES is to define the influence of recurring air pollution exposures and responses on asthma natural history in 300 asthmatic boys and girls (ages 6-11 at enrollment). Participants must reside within a 10-mile radius of the U.S. Environmental Protection Agency "Supersite" in Fresno, CA. The community has complex mixtures of primary and secondary air pollutants, which vary spatially and temporally. Two heavily traveled highways transect the study area, one with more heavy-duty diesel vehicles. Vehicular emissions on surface streets, residential wood smoke, and agricultural and light industry activities also contribute to poor air quality. The FACES design includes a series of two-week panel studies (~9 per child over 4-years) to evaluate the relationship(s) between short-term (hours, days, weeks) particulate matter (PM) exposures (with consideration of co-exposures to gaseous pollutants and bioaerosols (pollens, fungal spores, endotoxin)) and various measures of response, such as diurnal changes in pulmonary function, occurrence of symptoms, and medications usage. Children also participate in a prospective longitudinal study to define the relationship(s) between short-term exposure-response patterns and the medium-term (1-to-4 year(s)) progression of disease, and lung-function growth. A key premise is that, within a population of asthmatic children, there are subsets that differ in the nature and severity of responses to specific sets of exposures. Definition of these subsets requires detailed individual-level data that reflect a broad distribution of between-child variability in exposures and in responses. We focus here on development of the requisite exposure data, especially motor vehicle related, in the context of this epidemiologic study. **Methods:** Participant-specific daily estimates of exposure to each air contaminant of interest will be obtained from microenvironmental exposure model(s) developed for the FACES cohort. Among the extensive measurements at the Supersite and at two mobile-monitoring trailers are highly time-resolved measurements of PM (aethelometer black carbon, PM2.5 organic and elemental carbon, nephelometer, PM2.5 and PM10 mass), and chemically resolved measurements (metals and PAHs), which provide insights to mobile source contributions to participants' exposures. All homes are characterized with a survey, inspection, and selected measurements. Location-time-activity data are collected from each child. A subset of homes has indoors/outdoors measurements of a suite of pollutants matching those at the Supersite and trailers. Roadway proximity and traffic density influences on individual exposure and response will be evaluated with spatial and statistical analyses. **Results:** FACES participants represent a broad distribution of health-related and exposure-modifying characteristics. Residences are located various distances from the two highways and surface streets. **Conclusion:** Sufficient variation exists in the health and exposure data to define the effects of specific exposures on this vulnerable population.

A5) Causal regression of asthma medication use and pulmonary function. *K Mortimer, R Neugebauer ,J Balmes, M van der Laan , I Tager. To be presented at a joint meeting of the International Society for Environmental Epidemiology and International Society for Exposure Assessment (ISEE/ISEA), August 2002.

Evaluation of the health effects of short-term exposure to air pollution is complicated by daily asthma medication use. Most previous work has treated medication as a health outcome, effect modifier or confounder, or has ignored it all together. Medication is an important factor in the causal pathway for air pollution-related effects on asthmatics, and defining medication use as a confounder is inappropriate and can bias estimates of the effect on pulmonary function. During the months of November 2000 through May 2001, 63 asthmatic children aged 6-11 years completed two weeks of twice-daily recording of pulmonary function and symptoms with a hand-held spirometer. We applied two regression techniques to compare the estimates of the association between reported use of medication in the past hour and pulmonary function measures obtained upon waking. Contrary to expectations, simple linear regression showed use of medication in the past hour was associated with a 0.45 L/s decline in peak expiratory flow (PEF). Rather than true declines due to medication use, it is likely children who took medications were sicker than those who did not. In fact, when binary indicators for "cough or wheeze since bedtime" were included in the model, the medication estimate became -0.19 and both symptoms were associated with decreased PEF. The next approach was a

weighted-regression analysis with weights inversely proportional to the probability of receiving treatment (IPTW), given asthma symptom status. This creates a pseudo-randomized treatment to remove the association between treatment (i.e. medication use) and asthma symptoms. In contrast to the earlier analysis, children who took medication in the hour before pulmonary function testing had PEFs which were 0.20 L/s higher than the unmedicated group. This corresponds to a 6% increase in mean PEF, which is consistent with improvements seen in clinical use. Similar results were seen using other pulmonary function measures such as forced expiratory flow in one second (FEV1). A simulation study confirmed that estimates from ordinary regression were severely biased, while those from weighted regression were not. IPTW regression is an important new tool for this step in the analysis of air pollution effects. Next steps include building repeated measures-adjusted confidence intervals for causal estimates and adding air pollution terms to the models. Data were obtained from the Fresno Asthmatic Children's Environment Study (FACES), funded by the California Air Resources Board.

A6) Development of an Exposure Assessment Targeted to an Environmental Epidemiological Study: The FACES Study. SK Hammond, F Lurmann, P Roberts, J Macher, M Hjelmroos-Koski, K Mortimer, M van der Laan, R Neugenbauer, J Balmes, P Lowenthal, H Margolis, I Tager Presented at a joint meeting of the International Society for Environmental Epidemiology and International Society for Exposure Assessment (ISEE/ISEA), August 2002.

Relatively little is known about how two classes of agents, air pollutants and bioaerosols, affect the long-term progression of disease among asthmatic children. FACES is a 5 year prospective study of 300 children, age 6 to 10 at enrollment, who have asthma and live in Fresno, CA. Because the health outcomes include symptoms, medication use, and pulmonary function, and the consequent disease progression, FACES is evaluating daily exposure to air pollutants and bioaerosols (pollen grains, fungal spores, and endotoxin). To accomplish this, daily measurements are made at the EPA Supersite. In addition to the daily variability, spatial variability throughout Fresno and between indoor and outdoor air is being evaluated with 2 trailers that will collect daily samples, routine measurements in all homes, and detailed measurements indoors and outdoors in a subset of homes. These data will be used to develop and test models to predict the variability among neighborhoods and inside homes. The agents have been classified into three groups on the basis of the principal determinants of their concentration: regional pollutants (vary over distances > 20 km, but little variability expected within the study area, e.g., $PM_{2.5}$ sulfate, nitrate, and ammonium ions), neighborhood pollutants (e.g., those with traffic sources such as diesel exhaust), and home-specific agents (e.g., tobacco smoke). Similarly, the principle determinant of the concentrations of bioaerosols may be regional, as in the case of long range transport of pollen grains and submicronic particles related to pollen from plants not common in Fresno; neighborhood, as for pollen grains, fungal spores and submicronic particles from sources which are in Fresno; or home-specific, e.g., endotoxin and dog, cat, dust mite and cockroach allergens. Even within the same season a large temporal variability in concentration has been observed for both air pollutants (e.g., PM, elemental carbon, ozone) and bioaerosols (pollen grains and fungal spores). Similarly, those agents which were hypothesized to vary from home to home (e.g., allergens in house dust) in fact have been found to exhibit several orders of magnitude variation; second hand smoke concentrations, as measured by a two week passive sampler for nicotine, were low and much less variable, perhaps because parents of asthmatic children avoid smoking in the home. Broad ranges in the concentrations of these agents, both spatially and temporally, should be reflected in the responses of the children as measured both on a daily basis (during two week panels three times a year) and during semiannual assessments. The close match of exposure analysis and health assessment should enhance the ability of the epidemiological study to detect the effects of air pollutants and biological agents in the progression of asthma.

A7) DO DAILY ACTIVITIES AFFECT INDOOR AIR SAMPLING RESULTS?
Hjelmroos M. Presented at 7th International Congress on Aerobiology, August 5th-9th, 2002.

The Burkard Continuous Recording Air Sampler was used to investigate airborne particles in different rooms in five single-family homes. During the sampling period, the participants kept a careful diary of indoor activities Simultaneous outdoor sampling was conducted with an identical sampler.

In addition to the traditional pollen and fungal spore analysis, the content of human and pet epithelia as well as fibers and combustion particles was recorded. Airborne particles closely reflected indoor activities. For example, during the daytime when no one was home, only single fungal spores were found in the indoor air. However, spore concentration rose as soon someone entered the room being sampled. A strong increase in the number of airborne fungal spores following outdoor visits also was noticed. In addition, if windows or doors were open, the number of species and the concentration of airborne particles was very similar to those present outdoors. These results indicate that care must be taken in the interpretation of indoor fungal spore counts as indicators of indoor sources of microbial contamination.

A8) EVALUATION OF TWO DIFFERENT VOLUMETRIC AIR SAMPLERS
Hjelmroos M. Presented at 7th International Congress on Aerobiology, August 5th-9th, 2002.

The performance of a Hirst-type Burkard Seven-day Recording Spore Trap (7-day sampler) and Burkard Continuous Recording Air Sampler (24-hour sampler) was comparatively tested at heights of 11 m and 4.5 m. Two traps of each type were placed side by side separated by a distance of 4 m. Two additional Continuous Recording Air Samplers were placed on the level of 11 meters (total samplers: two 24-hour and two 7-day samplers at 4.5 m; three 24-hour and 7-day sampler at 11 m). This study was conducted over a period of two weeks in an open urban area in the Central Valley, California.
The aim of the study was to evaluate the efficiency and inter and intra repeatability of these samplers in an outdoor environment.

APPENDIX 2: CAUSAL REGRESSION PRESENTATION

Below is a summary of a talk entitled "Causal regression of asthma medication use and pulmonary function", presented by Kathleen Mortimer at the Society for Epidemiologic Research in Palm Desert, June 2002.

One of the primary research questions in FACES is "What is the effect of air pollution on daily pulmonary function?" There is an important methodological problems encountered during this type of analysis that demonstrates the need for causal regression methods, referred to as Marginal Structural Models. It has been shown that air pollution leads to increases in rescue medication use. However, rescue medication use influences pulmonary function. Therefore, rescue medication is on the causal pathway between air pollution and pulmonary function. It is a well-established epidemiologic concept that controlling for a factors on the causal pathway may lead to estimates that are biased in an unpredictable direction. We have applied Marginal Structure Models (MSMs) to demonstrate a better way to model medication use, prior to modeling air pollution effects. We use data EasyOne® spirometer which is used by the children during the 2-week home panels. As one would expect, the mean peak expiratory flow rate (PEF) for the children who reported symptoms in the morning was significantly lower than the non-symptomatic children. Contrary to what one would expect, however, the children who reported taking rescue in the previous hour also had significantly lower PEF. This counter-intuitive finding is likely due to confounding by symptoms (i.e. the reason they took medication), rather than any PEF-lowering effect from the medication. The following table summarizes the regression coefficients obtained using traditional methods (Proc GLM in SAS).

Table 1. Regression coefficients

Variables in model	Medications	Wheeze	Cough	Interaction terms
Med use only	-0.43 *	--	--	--
Medication use, wheeze, cough	-0.24	-0.23	-0.16	--
Medication use, wheeze, cough and interaction between meds and symptoms	-0.03	-0.22	-0.13	-0.02,-0.37

* A decline of 0.43L/min corresponds to approximately a 15% decline in PEF

In general, the prevalence of medication use in the past hour was 0.09 (marginal probability). The conditional probabilities are listed below, indicating that the presence of symptoms is highly related to medication use.

Table 2.

Wheeze	Cough	Probability(medication use)
No	No	0.02
No	Yes	0.10
Yes	No	0.18
Yes	Yes	0.34

Weighted regression techniques have been developed which allow us to redistribute the population as if they were perfectly randomized to medication use / no medication use.
The ratio of the (conditional probability / marginal probability) measures the extent to which the probability of treatment (e.g. rescue medication use) is confounded. If the ratio is equal to one (i.e. the conditional and marginal probabilities are equal), there is no confounding.
The probabilities presented above demonstrate this property. By taking the inverse of this ratio, we give the most weight to the least confounded observations, hence the term "inverse probability of treatment weights (IPTW). In this case, the weights would be:
P(medication use) / P(medication use | symptoms). The weights can be non-parametric (e.g. derived from 2x2 tables), or parametric (i.e logistic regression.) For this discussion we will focus on non-parametric weights.

The data were distributed in the following manner:
Table 3.

Med use = no	Cough – no	Cough- yes
Wheeze – no	1730	396
Wheeze – yes	77	243
Med use = yes		
Wheeze – no	45	45
Wheeze – yes	17	128

Note the following: N=2681
P(med use) = 0.09, P(wheeze) = 0.18, P(cough) = 0.32

Using the IPTW formula presented above, we get the following weights:
Table 4.

Med use = no	Cough – no	Cough- yes
Wheeze – no	0.94	1.02
Wheeze – yes	1.11	1.39
Med use = yes		
Wheeze – no	3.5	0.89
Wheeze – yes	0.48	0.25

e.g. P(med=0) = (1730+77+396+243) / 2681 = 0.91
p(med=no| cough=no, wheeze=no) = (1730 / (1730+45) = 0.97
Ratio = 0.94

Note: The greatest weight is given to the group who took medication, but did not have symptoms. That is, the group that provides the clearest view of the effect of treatment (meds) in the absence of the confounder (symptoms).

When the weights in Table 4 are multiplied by the observed distribution in Table 3, we get:

Table 5.

Med use = no	Cough – no	Cough- yes
Wheeze – no	1619	402
Wheeze – yes	86	338
Med use = yes		
Wheeze – no	156	39
Wheeze – yes	8	33

Note the following: N=2681
P(med use) = 0.09, P(wheeze) = 0.18, P(cough) = 0.32
The marginal probabilities do not change – only the conditional probabilities are affected.
Medication use is no longer associated with symptom status or,
P(medication use) = P(medication use | symptoms) = p(medication use | no symptoms).

When the regression of medication use on PEF is performed with these IPTW weights, we get and estimate of -0.09 L/min. Although this is greatly improved (and more logical) than the estimate from the traditional method (-0.43), is still suggests that the treatment model is not completed. For this example, we have the benefit of knowing what the effect of rescue medication "should be", given clinical experience. In fact, when the weights are recalculated using an additional "confounder", i.e. medication use in the evening prior to the test (another marker of how sick the child was in the morning), we get an estimate of 0.11. This corresponds to a 5% improvement in PEF after medication use. This is clinically reasonable.

In summary, traditional adjustment for time-varying confounders on the causal pathway yields effect estimates with the wrong direction and magnitude. IPTW regression (MSMs), removes the association between the time-dependent "confounder" (symptoms) and the treatment (medication use). This results in unbiased estimates under the assumption of no unmeasured confounders and correct specification of the treatment model.

APPENDIX 3: ASTHMA SEVERITY CLASSIFICATIONS

Baseline classification of asthma severity, using a point scale (maximum 28 points) (modified Paul Blanc score)

	Points Awarded
Subject ever hospitalized	3
Ever in an ICU for asthma	3
Ever intubated/ventilated for asthma	2

Frequency of cough or wheeze (in the past 2 weeks):

less than once in 2 weeks	0
1 day	1
2 days	2
3-4 days	3
5+days	4

For all meds, we took the maximum of times they were supposed to take it or actually took it.

β-agonist use (past 12 months):

none	0
< daily	1
>= daily	2

use of inhaled steroids (past 12 months):

none	0
any B4-B9 *	2

(* Vanceril, Beclovent, Azmacort, Aerobid, Flovent, Pulmicort)

other meds:

Serevent (med code C1 or C2)	1
Singulair (med code C5)	1
Cromolyn (med code B1 or B2)	1
Theophylline (med code C3 or C4)	1
Atrovent (med code A6 or A8)	1

Systemic steroids:

Prednisone ever	2
Prednisone in last 3 months	2
Daily or every other day use	3

Classification of current control[1]:
Adaptation of the NHLBI guidelines to asthma classification. This measure includes only symptom information. Medication, health care utilization and pulmonary function are not included.

Part 1: Daytime symptom score.

if the number of days of wheeze in the past two weeks =0,1,2 then step = 1.
if wheeze = 3-13 then step = 2
if wheeze = 14 then step = 3.

if cough = 0,1,2 then step = 1.
if cough = 3-13 then step = 2
if cough = 14 then step = 3.

Symptom step score is the *maximum* of the step for cough and wheeze.

Part 2: Asymptomatic between exacerbations

In the past two weeks, if the child has *not* had any wheezing severe enough to limit activities (Q23a-f) then they asymptomatic for wheeze.
In the past two weeks, if the child has *not* had a persistent cough then they are asymptomatic for cough. If a child is asymptomatic for cough AND wheeze, then exacerbation step = 1.

In the past 12 months, if they have had limitations to activities (Q23b,c,d,e) or persistent cough, then exacerbation step = 2.

If in the past 2 weeks, they have had any limitations to activities (q23b,c,d,e) or persistent cough, then exacerbation step = 3.

Exacerbation step score is the *maximum* of these three values.

Part 3: Nighttime symptoms

In the past 12 months, if the child has nighttime wheeze
less than 1x per month, then night wheeze step = 1
about 1x per week, then night wheeze step = 2
about 1-2 x per week, then night wheeze step = 3
3 or more times per week, then night wheeze step =4

In the past 12 months, if the child has had nighttime cough
once a month or less, then night cough step = 1
more than once a month, then night cough step = 2
once a week or more, then night cough step = 3

The nighttime symptom score is the *maximum* of the nighttime wheeze and nighttime cough measures.
The final step assignment is the sum of "daily symptom step" and "exacerbation step" and "nighttime symptom step" divided by 3.

CLASSIFICATION BASED ON PULMONARY FUNCTION

All values will be taken from post-bronchodilator values. The mean from (up to) the first three acceptable efforts will be used.

- STEP 1: FEV_1 >80% predicted
- STEP 2: 60 < FEV_1 <= 80% predicted
- STEP 3: FEV_1 <=60% predicted

Predicted equations taken from NHANES.

APPENDIX 4: ACCEPTABILITY AND REPRODUCIBILITY CRITERIA

Acceptability criteria	**Message displayed on EasyOne® if criterion not met**
Back extrapolated volume (BEV) must be less than 150mL or 5% of the FVC	Don't Hesitate
Time to peak flow (PEFT) must be less than or equal to 120ms	Blast Out Faster
If forced expiratory time is less than 6 seconds, a plateau of less than 45mL over 2 seconds must be achieved.	Blow Out Longer
Reproducibility Criteria	
The current PEF and the previous largest PEF from an acceptable effort must be within 20%	Blast Out Harder
The current FEV1 and the previous largest FEV1 from an Acceptable effort must be within 10%	Deeper Breath
The current FVC and the previous largest FVC from an acceptable effort must be within 10%	Deeper Breath

APPENDIX 5: INVENTORY TABLES

Based on data entered as of June 30, 2002

Birth/Health History	**Visit**	**Yes #(%)**	**No #(%)**	**.M/.N/.D/.R #(%)**
Birth weight <5.5 lbs. (n=182)	B	13 (7)	162 (89)	7 (4)
Child born >3 weeks early/late (n=182)	B	18 (10)	158 (87)	6 (3)
Was the child breast fed? (n=182)	B	131 (72)	49 (27)	2 (1)
Ever hospitalized for asthma (n=182)	B	46 (25)	136 (75)	0
Ever in ICU for asthma (n=182)	B	12 (6)	*169 (93)	1 (1)
Mother has asthma (n=182)	B	73 (40)	107 (59)	2 (1)
Father has asthma (n=182)	B	46 (25)	115 (63)	21 (12)
Sibling have asthma (n=182)	B	63 (35)	98 (54)	21 (11)
Mat. G.M. has asthma (n=182)	B	36 (20)	124 (68)	22 (12)
Pat. G.M. has asthma (n=182)	B	21 (12)	118 (65)	43 (23)
Mat. G.F. has asthma (n=182)	B	16 (9)	140 (77)	26 (14)
Pat. G.F. has asthma (n=182)	B	10 (6)	113 (62)	59 (32)
Ever prescribed oral steroids (n=182)	B	111 (61)	67 (37)	4 (2)
Child uses column A med (n=182)	B	176 (97)	6 (3)	0
Child uses column B med (n=182)	B	142 (78)	40 (22)	0
Child uses column C med (n=182)	B	76 (42)	106 (58)	0

Smoking	**Visit**	**Yes #(%)**	**No #(%)**	**.M/.N/.D/.R #(%)**	
Respondent is a smoker (n=182)	B	18 (10)	164 (90)	0	
Smoker live in home (n=182)	B	42 (23)	140 (77)	0	
Smoker live in home (n=99)	6	22 (22)	74 (75)	3 (3)	
"No smoking" policy in home (n=99)	6	92 (93)	7 (7)	0	
Has child ever tried smoking (n=179)	B	0	43 (24)	136 (76)	*(kids <10 yrs. old)*
Has child ever tried smoking (n=99)	6	0	31 (32)	68 (68)	*(kids <10 yrs. old)*

Tests/procedures	**Visit**	**Yes #(%)**	**No #(%)**	**.M/.N/.D/.R #(%)**
Consent given for blood draw (n=184)	B	156 (85)	26 (14)	2 (1)
Blood draw completed (n=182)	B/6	52 (29)	130 (71)	0
Skin testing completed RIGHT (n=183)	B/6	164 (90)	3 (1)	16 (9)
Skin testing completed LEFT (n=183)	B/6	163 (89)	2 (1)	18 (10)
Skin testing completed BOTH (n=183)	B/6	160 (87)	9 (5)	14 (8)
Nutritional survey comp. (n=98)	6	72 (73)	23 (24)	3 (3)

Allergen skin test (n=164)	**Visit**	**Yes #(%)**	**No #(%)**	**.M/.N/.D/.R #(%)**	
Grass	B/6	56 (34)	108 (66)	0	
Cat	B/6	41(25)	123(75)	0	
Mite	B/6	43 (26)	121 (74)	0	
Olive	B/6	60 (37)	104 (63)	0	
Rye	B/6	60 (37)	104 (63)	0	
Juniper	B/6	4 (2)	160 (98)	0	
Oak	B/6	23 (14)	141 (86)	0	
Mugwort	B/6	41 (25)	123 (75)	0	
Alternaria	B/6	61 (37)	99 (60)	4 (3)	
Dog	B/6	11 (7)	149 (91)	4 (2)	
Penicillin	B/6	24 (15)	41 (25)	99 (60)	*(chgd. to clado. '01)*
Cladosporium	B/6	24 (15)	60 (36)	80 (49)	*(chgd. from penic. '01)*
Cockroach	B/6	21 (13)	139 (85)	4 (2)	
Privet	B/6	17 (10)	132 (81)	15 (9)	
Cedar	B/6	12 (7)	148 (90)	4 (3)	
% positive to any	B/6	107 (65)	57 (35)	0	

Demographics	**Visit**	**Yes #(%)**	**No #(%)**	**.M/.N/.D/.R #(%)**
Child born in CA (n=182)	B	172 (95)	0	10 (5)
Child born in US but not in CA (n=182)	B	7 (4)	174 (95)	1 (1)
Child born in US (n=182)	B	179 (98)	1 (1)	2 (1)
Mother employed (n=182)	B	106 (58)	74 (41)	2 (1)
Father employed (n=182)	B	140 (77)	35 (19)	7 (4)
Home visit language (n=236)	H	(E)221 (94)	(S)15 (6)	0
6-month language (n=98)	6	(E) 92 (94)	(S) 6 (6)	0

Variable	***Visit***							
Type of dwelling (n=182) # (%)	H	Single family 136 (74)	Apt. Bldg. 41 (23)	Mobile Hm/Trailer 4 (2)	.D 1 (1)			
Income (n=182) # (%)	B	<$15K 32 (18)	$15-30K 48 (26)	$31-50K 49 (27)	>$50K 47 (26)	.M/.D/.R 6 (3)		
Ethnicity (n=182) # (%)	B	Hispanic 76 (42)	Black 25 (14)	White 74 (41)	Other 7 (3)			
Sex (n=182) # (%)	S	M 106 (58)	F 76 (42)					
Standing height (in.) (n=183)	B	Mean 52.5	Std. Dev. 4.6	Min. 41.9	25% 49	50% 52.6	75% 55.7	Max. 63.2
Weight (lbs.) (n=183)	B	Mean 75.7	Std. Dev. 28.5	Min. 37.5	25% 55	50% 71	75% 90	Max. 186
Nearest freeway (n=184)	B	Immed. in front 46 (25)	1 blk. away 53 (29)	1-3 blks. 49 (26)	>4 blks. 33 (18)	. 3 (2)		
Heating fuel (n=184) # (%)	B	Gas 109 (59)	Elec. 58 (32)	LP Gas 1 (1)	Wood 3 (2)	Other 3 (2)	./.D/.N 10 (4)	
Ag. field proximity (n=236) # (%)	H	Immed. in front 12 (5)	1 blk. away 7 (3)	1-3 blks. 24 (10)	>4 blks. 57 (24)	Unknown 22 (9)	None 109 (46)	./.N/.M 5 (3)
Baseline interviewer ID (n=182) # (%)	B	1 3 (2)	3 29 (16)	4 49 (27)	5 28 (15)	6 73 (40)		
Mean age at diagnosis (n=182) # (%)	S	0 25 (14) 6 25 (14)	1 20 (11) 7 11 (6)	2 29 (16) 8 6 (3)	3 27 (15) 9 7 (3)	4 12 (7) 10 1 (.5)	5 18 (10) .D 1 (.5)	
# of times hospitalized due to asthma in last 12-months (n=182) # (%)	B	0 163 (90)	1x 14 (8)	2-4x 5 (2)				
Years lived in home (n=184) Years # (%)	B	Mean 4 0 16 (9) 6 18 (10)	Std Dev. 2.94 1 34 (18) 7 13 (7)	Min. 0 2 17 (9) 8 12 (7)	Max. 10 3 29 (16) 9 12 (7)	 4 14 (8) 10 6 (2)	 5 11 (6) . 2 (1)	

APPENDIX 6: REPORT FROM QUALITY CONTROL OFFICER

Memorandum

To: Kathleen Mortimer

cc: Ira Tager, Kathie Hammond

From: David Bush

Date: January 3, 2002

Re: Initial visit to FACES Fresno Field Office

Thank you for the time you all spent discussing the FACES data collection effort during my visit to the Fresno office on December 6, 2001. I was impressed with the organization of the data collection effort and the care that had been given to defining and establishing operating procedures. My impression is that the data obtained from this effort will be of a very high quality.

I have only four relatively minor comments, which are presented below:

- In general, standard operating procedures for the data collection effort are well documented. However, at this time, there does not appear to be a data management plan summarizing the data processing and management procedures and protocols. These procedures and protocols are well established and well thought-out, significantly more than typically encountered in most studies in their early phase of operation. Having a written data management plan describing the already existing procedures will contribute substantially to documenting the quality of the collected data.
- Expanding on the above comment, I do not believe that the study has a monitoring plan or quality assurance project plan (QAPP) summarizing the data collection effort and associated quality assurance and quality control procedures. Again, sufficient procedures are already in place and, while many of the QA/QC procedures can be found in the various SOPs, documenting them in a concise plan will demonstrate the quality of the data to data users and reviewers in a comprehensive manner.
- The moisture content meters are new to me, and, due to my quality assurance background, I am inherently suspicious of any device that is not being traced to a

standard of some sort. I am not sure how important the moisture data is or what its anticipated use is, but I would recommend somehow documenting its operation with some sort of calibration. I talked with the manufacture, Electro Physics, and they said that a simple check would be to hold the meter in the air, verify that the reading goes to zero, and adjust as necessary. Apparently, zero drift is the most likely source of error. They were not terribly concerned about changes in the span response, though a calibration plate with a known capacitance can be purchased to verify the span.

- The one procedure that has me a little uneasy is the data entry quality control check for the questionnaire data. It is my understanding that the current procedures call for doing a duplicate entry of every tenth form. If any problems are noted, the previous ten forms are reentered. I am concerned that limiting reentry to just the previous ten forms may be viewed as insufficient, putting in question the accuracy of the entered data. The other two epidemiological studies for which I provide QA both employ a more rigorous QC check of hand-entered data. One study routinely performs duplicate entry on all hand-entered data. The other performs a check of all entered data by having one data technician read back all of the entered data while a second technician verifies the read data against the original forms. A third method involves a visual comparison of all entered data against the original forms. Other projects that I have reviewed have worked with a 10% recheck criterion, but have significantly increased the amount of previous data that gets reentered if a problem is noted, and have included progressively greater reentry requirements if further errors are noted. I appreciate the principal reason for checking only one of ten forms. There is a tremendous amount of data being entered, and checking it all does seem excessive. However, with only a one-in-ten chance of identifying a bad entry, a more rigorous rechecking plan might be in order, incorporating selected aspects of the strategies mentioned above.

APPENDIX 7: ADDITIONAL FUNDING PROPOSALS

Proposal 1

Title: Valuing Reduced Asthma Morbidity in Children
Principal Investigator: Michael Hanemann ,Ph.D.
Senior Investigators: Sylvia Brandt, Ph.D., Kathleen Mortimer, Sc.D., M.P.H.
Amount of funding from US EPA (Office of Research Development, National Center for Environmental Research): $320,000
Dates: 3/2002-3/2005

Objectives:
Objectives
This project will combine an economic survey on risk-reducing and -averting behavior with epidemiological and demographic data collected as part of the Fresno Asthmatic Children's Environment Study (FACES). The main focus of this substudy is household behavior and the role of household characteristics in behavioral responses to risk. This project will collect additional survey data from households participating in the FACES project on their risk perceptions, their risk reducing and averting behavior, and their expenditures on risk mitigation and averting activities. These data will be collected over a two-year period and will complement the data already being collected on ambient air pollution levels, household economic and demographic characteristics, and epidemiological covariates.

Data on the risk perceptions and risk-averting behavior of respondents will be used to develop an empirical model of how households perceive risk, how they respond to risk, and the monetary values they implicitly place on mitigating risk as revealed through their behavioral responses.

The panel's epidemiological data will allow us to compare each household's risk assessments to objective risks of specific asthma morbidities. The deviation of subjective from objective risk can then be modeled as a function of household characteristics including: household income, parental/guardian education and employment status, and household size. The detailed dataset on households' risk-reducing behavior will be used to estimate the household's implicit willingness to pay for reduced asthma morbidity among children.

The valuation of reduction in asthma morbidity is of significant relevance for policy analysis of the EPA. Asthmatic children represent a susceptible population with particular policy interest for regulators, and, therefore willingness to pay to avoid asthmatic symptoms has significant implications for cost-benefit analyses of EPA air quality regulations.

Collection of Data on Household Perceptions, Behavior and Valuation.
The Fresno study provides detailed data on ambient air quality, households' socio-demographic and health profiles, and households' basic risk perception and risk reducing behavior. This substudy will include an additional survey of the study population which is designed to elicit additional information necessary to estimate willingness to pay for reduced morbidity.

Our additional survey will have three parts. The objective of the first part is to characterize what households perceive as risks to the asthmatic child. The survey will consist of both closed and open-ended questions. A sequence of questions will ask respondents to rank a set of possible asthma triggers. For each of the possible asthma triggers, the households will then be asked to list both the asthma symptoms (for example wheezing or coughing) and the degree of severity of symptoms. The series of questions will be repeated, asking the respondent to recall how the triggers and symptoms ranked in the previous allergy season. Special care will be taken to delineate the risks from air pollution (e.g., particulate matter) from air quality (e.g., pollens, dust). Households will also be asked if they have received any asthma management information from sources including community organizations, schools, or physicians.

The second part of the survey will ask in what way the household changes its behavior in order to reduce the severity of symptoms. Changes in behavior will include both those that have direct costs (medication, household investments, etc.) as well as those that are social morbidities (limiting time outside, restricting physical activity, etc.) These questions will be followed by questions regarding the expenditures for relevant averting/mitigating behaviors. The second section will close by asking about specific investments in asthma mitigation/averting behavior (such as costs of household modifications).

The third part of the survey will contain a brief contingent valuation question. The objective here is to supplement the revealed preference estimates of WTP_c derived from observed averting and mitigating behavior along the lines indicated above in (13), (14) and (15), with stated preference data on WTP_c . The stated preference elicitation will use closed-ended, discrete-response CV, in which the respondent is presented with some potential new remedial alternative at some given cost, and asked whether she would be likely to adopt it. The double-bounded or one-and-one-half bounded format would be used, with bids designed on the basis of responses obtained in the pre-tests of the questionnaire.

To develop our survey, we will conduct focus groups with a subset of 50 families. Once the survey has been finalized, it will be mailed to the Fresno study households prior to the one of the standard 6-month office visits.

Expected Results

Executive Order 13045, "Protection of Children from Environmental Health Risks and Safety Risks," requires federal agencies to assign a high priority to assessing health and safety risks that disproportionately affect children. The large and growing population of children with asthma therefore constitutes a population of particular concern for the EPA. The results of this project can significantly contribute to the analyses required by the Office of Policy, Office of Risk Assessment, and Office of Children's Health Protection.

This project will provide insight into multiple aspects of policy directed at improving children's health. By estimating the demand for risk averting and mitigating actions, this project will help design policies to induce risk minimizing behavior in households with asthmatic children. The study of risk perception will provide information on the correlation between subjective risk and

objective risk, which can be utilized to refine EPA's outreach and education programs. Finally, the estimation of willingness to pay for reduction in asthma morbidity will contribute to EPA's cost-benefit analyses of air quality standards.

In addition to its implications for EPA policy, this project will lead to publications in research journals, helping to broaden understanding of the relationship between environmental factors and children's health, and of the role of economic analysis in valuing non-market goods. Drs. Hanemann and Brandt will also attend national-level professional meeting to further discuss and disseminate the findings of the research.

Proposal 2

Title: Fresno Asthmatic Children's Environment Study (FACES): Mobile Source Generated Air Toxic Exposures Ancillary Study
Principal Investigator: Fred Lurmann
Senior Investigators: Paul Roberts, Katharine Hammond
Amount of funding from US EPA: $200,000
Dates: 10/2001-3/2002

Overview of Proposal
The Fresno Asthmatic Children's Environment Study (FACES) is a prospective study of the effect of air pollution on 450 asthmatic children. FACES examines the short term effect of daily air pollution on the symptoms, medication use, and lung function of these children and the longer-term effect on the progression of asthma. Both air pollutants and biological agents are being evaluated; the pollutants include particle mass and composition (metals, ions, elemental and organic carbon) nitrogen oxides, ozone, and environmental tobacco smoke (ETS); the biological agents include endotoxin, pollen grains, and fungal spores in the air, and endotoxin and allergens in house dust. The temporal variability is evaluated with daily measurements made at the USEPA Supersite in Fresno, where measurements will be continued under the California Air Resources Board. The spatial variability is evaluated with similar measurements that will be made at two trailers; two week integrated measurements for NO_2, ozone, and ETS to be made 8-9 times in each home over the 4 years of the study ("panel measurements"); and daily measurements to be made at 100 homes, both indoors and outdoors ("home intensive").

We propose to add polycyclic aromatic hydrocarbons (PAHs) to the list of agents, and to measure these at the Supersite, the trailers, and at the homes during the home intensive phase. PAHs in diesel exhaust have been associated with increased asthma reactivity. During the home intensive phase, five daily measurements will be made indoors and outdoors at each of 5-6 homes during each two-week period, to match the samples already being collected at the homes during this phase ($PM_{2.5}$, PM_{10}, endotoxin, ions, organic carbon, elemental carbon, pollens, fungal spores, NO_2, ozone, and ETS). On these same days, samples of vapor phase and particle phase PAHs would be collected at the Supersite, where an EcoChem real time PAH sampler and an aethalometer, which monitors black carbon, a surrogate for diesel exhaust, are operating, and at the trailers, which will have aethalometers and where we propose to install EcoChem samplers. This will enable us to understand more about the relationship between the EcoChem sampler and integrated samplers for PAHs, and to evaluate the relationship among these markers for diesel exhaust in Fresno. Based on the measurements of the aethalometer and the EcoChem, we will model the daily PAH concentrations to which the children in our study are exposed.

We plan to collect a total of 1150 daily samples, of which 350 will include a measurement of the partitioning between the particle and the vapor phase. The particle phase PAHs will be collected on quartz filters coated with XAD, and the vapor phase will be collected on a preceding denuder with XAD. A subset of the samples will be desorbed and the extract analyzed by gas chromatography/mass spectrometry/selected ion mode.

This study will provide useful information both for exposure assessment in general and in the epidemiology study of the relationship between air pollution and asthma. We will characterize the relationship between two quite different methods to sample for PAHs as well as the relationship between black carbon, a diesel exhaust surrogate, and PAH concentrations near and distant from a highway with heavy truck traffic. Also, we will be better able to evaluate the effect of diesel exhaust and PAHs on childhood asthma.

Proposal 3

Assessment of Asthmatic Children's Responses to Diesel Emissions in Fresno, California Using FACES Enhanced Neighborhood and Personal Sampling
Submitted to Health Effects Institute (HEI), not funded.

The three primary objectives of the proposed study are to 1) Develop a quantitative model of the relationship between ambient concentrations of diesel exhaust and measured personal exposures; 2) Evaluate the relationship between daily exposure to diesel exhaust, as measured with personal sampling, to short term changes in symptoms, medication use, and pulmonary function, among children ages 6-10 years with clinically diagnosed asthma; and, 3) Compare the relationship found in 2) to that found between modeled exposure and short term changes in symptoms, medication use, and pulmonary function, among asthmatic children.

FACES is a prospective study of the effects of the environmental factors on asthmatic children. The proposed study would complement and enhance the FACES study, yet it would have important, independent results. It represents a particularly cost-effective means for HEI to obtain high quality information on the relationship between short-term exposures to vehicular emissions (especially from diesel vehicles) and transient responses in asthmatic children, including changes in lung function, symptoms, and medication use. The proposed ancillary study is nested in the panel study component of FACES and has four distinct elements:

1) Collection of 500 24-hr personal exposure samples for $PM_{2.5}$ (mass, black carbon, SO_4 , and NO_3), PM_{10} (mass and endotoxin), NO_2, ozone, and nicotine on the FACES participants, concurrent with the FACES panel studies (to obtain daily lung function, symptoms, medication use, and time activity) and intensive indoor and outdoor air pollution measurements at the subject's homes.
2) Collection of hourly ambient concentration data for black carbon and light scattering by fine particles at two new monitoring stations for one year to evaluate the gradient of diesel exhaust from a busy freeway with heavy diesel truck traffic.
3) Development, refinement, and evaluation of daily personal exposure models that incorporate ambient concentration data, daily diary data, home characteristics, and school characteristics.
4) Statistical evaluation of the relationship between measured and modeled personal exposure and the occurrence of symptoms and the changes in medication use and daily lung function in asthmatic children.

The development of improved methods to estimate personal exposure from ambient data will greatly enhance the ability of the FACES and other similar epidemiological studies to detect the relationship between air pollution, and specifically diesel exhaust, and short-term patterns of occurrence of symptoms and the growth of lung function during the childhood years. Furthermore, the proposed study will make possible an additional analysis (objective 2), in which we will examine the daily relationship between measured personal exposure and the occurrence of symptoms and the changes in medication use and daily lung function. By comparing the epidemiological results found using measured exposures with the results using modeled exposures we can estimate the error in using modeled exposures for the entire cohort. Moreover, accurate quantification of these measurement errors will permit their inclusion into the usual epidemiological models, which are based on central site and/or small area monitoring data. Each of these four elements will provide valuable results. The combination of anticipated

results from these elements with those from the core study will be especially informative about the effects of diesel exhaust on asthmatic children.

The proposed study incorporates sufficient personal sampling and analysis to make a significant contribution to the understanding of how personal exposures to PM compare to exposure estimates from central site monitoring and neighborhood-scale monitoring data. The principal anticipated results of Elements 1-3 are an improved understanding of (1) differences between personal exposure and central site ambient concentrations for an important susceptible group, asthmatic children, and (2) the factors responsible for the differences, including subject-to-subject differences and day-to-day differences. Addition testing will be carried out to evaluate the accuracy of microenvironmental exposure models designed to estimate personal exposures to PM and other air pollutants on a daily basis. These exposure models will be refined using the improved understanding of the factors affecting personal exposure. The evaluation of the models will contribute to the understanding of accuracy and uncertainties of exposure assignment methodologies employed in epidemiological studies. Overall, the proposed study will lead to better exposure assessment, which will: (1) improve the accuracy of estimates of health effects derived from epidemiological studies of diesel exhaust emissions; (2) better define the limitations of the estimates of exposures; and, (3) more clearly define the gradients of diesel exhaust from a major interstate highway into a community. The proposed study will also include a new evaluation (Element 4) of daily health effects (symptoms, medication use, pulmonary function) as a function of measured daily exposures based on conventional time series analyses as well as the application of newly developed methods of estimation of causal effects. These results will enable us to understand better the relationship between asthma symptoms and diesel exhaust and other particulate matter.

APPENDIX 8: RESPONSES TO PEER REVIEW COMMENTS

RESPONSES TO EXTERNAL ADVISORY COMMITTEE COMMENTS (document from Frank Speizer to Tracy Hysong dated September 20, 2002)

1. *Changes in age eligibility*: The one year increase in the age eligibility (from upper age 10 to 11 years) will have no effect on the issue of how we handle the pubertal growth differences between girls and boys. This is an issue about which we are well aware and addressed this extensively in our original proposal. We will use appropriate sex-specific modeling strategies to deal with this issue. Fewer than 5% of the children were 11 years old at the time of enrollment so we expect the impact to be minimal.
2. *Allowance for sibling enrollment*: We are aware of the effects that clustering of exposure could have on our exposure distribution and in our data analysis. We do not anticipate that there will be a large number of households with more than one child who is a participant in the study. To date, 7 such pairs have been enrolled and, on average, the sibling pairs are 2.3 years apart (range of 1.5-3.8 years). Dr. Speizer's point with regard to age differences in siblings is interesting and important. This issue of early life exposure is not a direct target for this study, although the Project Director, Dr. Kathleen Mortimer, is applying for funding to address this issue. We will certainly keep this issue at the forefront of our attention.
3. *Shortened residence time*: No reply required.
4. *Expanded catchment area from 10 to 20 km…*: As indicated in Section 4.1 of the Interim Report, the FACES recruitment catchment area was expanded from the area within a 10 km radius from to the First Street monitoring site to the area within a 20 km radius of the central site. This decision was based on a review of relevant existing air quality data for the region and a commitment to conduct sampling at some outlying homes as part of the Home Intensive sampling program. Preliminary Home Intensive sampling data presented in Section 5.7 of the Interim Report show ±30% spatial variations of $PM_{2.5}$ mass, elemental carbon, metals, endotoxin, and pollen grains within the Fresno area during periods with relatively good air quality. Recent analyses of the spatial distribution of 24-hr average $PM_{2.5}$ mass during winter episodes indicate concentrations at sites from 10 to 30 km from the central site (e.g., Clovis and Selma) are consistently within ±20% of those at the central site (Watson, J.G., and Chow, J.C. (2002) A wintertime $PM_{2.5}$ episode at the Fresno, CA, supersite. *Atmospheric Environment*, 36 (3): 465-475.). While the secondary PM (or long-range pollutants) usually exhibits little spatial variation in the valley (Kumar N., Lurmann F.W., Pandis S., and Ansari A. (1998) Analysis of atmospheric chemistry during 1995 integrated monitoring study. Report prepared for the San Joaquin Valleywide Air Pollution Study Agency, c/o the California Air Resources Board, Sacramento, CA by Sonoma Technology, Inc., Petaluma, CA, STI-997214-1791-FR, July.), there is concern for variations in the urban primary particle emissions and primary gaseous emissions. We expect spatial variation in primary species concentrations will be significant within both the original 10 km radius area and the expanded 20 km radius area. Watson and Chow (reference as above) have shown that even the most rural sites in the valley have concentrations of primary PM species that are at least half of those in central Fresno during winter episodes. The spatial variations will be addressed in FACES by characterizing traffic levels at all FACES's participants homes using CalTrans traffic volume data and obtaining air quality measurements at a

subset of homes located on the outskirts of Fresno/Clovis as part of the Home Intensive Sampling Program. The exposure estimates for FACES participants living in the outlying areas may be less accurate than those living close to the central site, nevertheless, we are hopeful that they will be sufficiently accurate for use in the study. We will have the data to make the assessment. Lastly, it should be recognized that the population density decreases rapidly with distance from central Fresno and the number of candidates in the outer most region, those living 15 to 20 km from central Fresno, is likely to be quite small.

5. *Development of asthma severity classification*: We agree with Dr. Speizer that it would be ideal to carry out a validation study. However, no funding is available to do this. We can and will compare levels of various measures of lung function with the Blanc scores both at baseline and at later follow-up time in the spirit of a partial validation study.
6. *Aerometrics*: At the time of the submission of the Interim Report, we had not yet addressed the development of an integrated data base for the exposure and health data. This was a task that was and still is on our priority list. In fact, we are scheduling a half-day retreat for the investigators to deal specifically with this issue. A full study data base will be developed and documented over the next several months.

   We do not understand Dr. Speizer's comment that he sees no evidence that exposure data are being converted into "analytic files that can be used in conjunction with the health data". As we note above, while we have not finalized the overall data base, we have clear understanding of how to do this and clearly had begun to do so for the preliminary analyses presented in the report.

   We intend to use all of the exposure data during the life of this contract. Although we acknowledge that the range of analyses is ambitious, the investigators feel that these analyses are critical to research questions outlined in FACES. We will devote the necessary resources to completing these tasks. A major part of the research is to try to identify components of PM that have greater or lesser influence on health outcomes. Unless we collect these data, we will never be able to address the questions. By way of illustration, the Children's Health Study should never have collection acid vapor data, which has turned out have important associations with health outcomes.

   Finally, we feel that to cut short the health data collection from the panels would result in the loss of data which are important, independent of the aerometric data. Based on review of the panel data to date, it is clear that the daily pulmonary function data will turn out to be a unique and extremely rich database for studying the onset of asthma attacks and changes in asthma severity. No other studies have collected detailed spirometric data over such a long period of time. These data will be even more useful once the routinely collected aerometric data become available after the end of the contract. It is our express intention to use our panel data and these additional PM mass and gas data to extend our findings. Moreover, since we need to keep these children under follow-up for the longitudinal component until near the end of the study period, there will be only small cost savings. The history of the Children's Health Study highlights the fact that the more data that we are able to collect, the more likely it is that we will be able to secure additional funding to build upon the ARB's funding. There clearly are benefits to ARB to have such data.
7. *Changes to STI statement of work*: These changes have been made and are submitted separately.

RESPONSES TO COMMENTS FROM RESEARCH SCREENING COMMITTEE COMMENTS

1. *…team conducting the epidemiological portion of the study may not have the exposure data they need in a timely fashion.*: This comment does not appear to be addressed to the investigators.
2. *In light of the recent report by Dr. Delfino…I would suggest that ambient VOC monitoring be grafted onto the FACES study…*: Dr. Speizer already thinks that we are collecting too much exposure data; this recommendation would exacerbate his concerns. In addition, not all of the investigators have seen the report and had an opportunity to evaluation it. Finally, we have no funds with which to implement such a recommendation. Having said this, the FACES team will continue to evaluate emerging air pollution health effects data and opportunities to address those issues. However, our first obligation is to the exposure that we have designed
3. *…the change in eligibility criteria from 10 to 20 kilometers is not supported by appropriate monitoring data…*: See #4 above in replies to comments by ARB staff.
4. *The limulus assay understates endotoxin concentrations (pp.100-101)…*: This assay is one of the most commonly used assays to quantitate endotoxin concentrations. This will assure ARB that the values we obtain will be comparable to studies which used this assay. Recently, several inter-comparison studies have been published based on different assays; and these results will be used to make data comparable among the different health studies.
5. *Sample size and power calculations*: We do not disagree with the comment related to power to detect interactions and the overlap between allergy to indoor and outdoor antigens. Nonetheless, this study is the first to address directly many of these issues, and, at the least, we will get important data on the possible range of effect estimates that will need to be considered in any extension of our work and considered by any future studies of the issues addressed in our project.
6. *Minor Issues*:
    A. *p 28, Table 4-5…*: We can understand how this reviewer thought that approximately 10% of our subjects were smokers. In fact, the data in table 4-5 to which the reviewer refers relates to the parent of the child and not the child. We apologize that the table is not clear on this point.
    B. *`On page 35…*: In view of our lack of clarity, the part of the comment that relates to smoking as an activity is not relevant. With regard to the issue of salivary cotinine, in section **7H** of our original proposal, we addressed this issue. Our plans call for us to collect salivary specimens for subjects when they enter their teen years and to store the specimens. When we secure funds, we will analyze a random sample of specimens for children who claim that they do not smoke cigarettes. Professor Hammond has contacted Dr. Neal Benowitz at UC, San Francisco, a world's expert on cotinine; and he has agreed to train personnel in Professor Hammond's laboratory when we are ready to perform these analyses. In addition, all smoking history data is obtained from children away from their parents and on forms that do not reveal the nature of the questions.
    C. *Several places where mg is used…*
    D. *There appears to be a discrepancy between numbers…*: The number of consented participates can decrease over-time as parents who initially agree to participate change their minds and refuse further participation.

E. *Page 9 1716 possible child-day…*: We apologize for the discrepancy. The Executive Summary was not updated after some additional analytical work was done. Table 6.1 has the correct numbers.

ARB ASKED THAT WE PROVIDE AN EXPLANATION OF WHY COSTS WOULD NOT DECREASE. THE EXPLANATION IS PROVIDED BELOW.

***Reductions in costs**:* During the first two years of the study, we recruited fewer children than we had expected to recruit. However, this did not translate into substantial cost savings for reasons detailed in the next several paragraphs.

The first major reason why savings were not realized is that, despite the size of the cohort, there are fixed costs that are associated with rent, utilities, office equipment, and salaries for the research team and administrative staff. During the original proposal- development-process, we determined that we would need a minimum of four interviewers to complete the clinic, home and telephone interviews. For safety and efficiency purposes, home visits were designed to be conducted in pairs. Because the home visits are completed over the same time frame that clinic and telephone interviews are taking place, it was necessary to have several other staff who would work in the office while home visitors were in the field. We anticipated that a substantial number of interviews would have to be completed in Spanish, which required us to hire at least two bi-lingual interviewers. In addition, we wanted at least two interviewers to be well trained as spirometry technicians to minimize disruptions in the recruitment and follow-up due to staff illness and/or vacations. This requires that the technicians rotate spirometry responsibilities every few weeks to make sure that they do not go more than a few weeks without performing spirometry on actual subjects. To allow us to schedule visits over a wide range of night and weekend hours, to improve subject relations and compliance, it was essential that we have at least two technicians.

To save resources, we could have considered staggered hiring of staff to ensure that recruitment was adequate. However, we felt that this would not be an effective strategy for two reasons. First, we felt that it was essential for protocol standardization and quality assurance that all staff participate in the same training sessions during protocol revision phase that preceded Phase I. Input from multiple interviewers was essential to work out protocol problems prior to implementation on study subjects. Second, by design, the home visits and baseline interviews are conducted over the same interval. Therefore, it is necessary that several staff are at the clinic to complete interviews while two other staff are out in the field completing home visits. For these reasons, it was necessary to hire all staff prior to the start of recruitment in September, 2000. We were quite fortunate to be able to hire four qualified candidates who were able to perform bilingual interviews, spirometry procedures, blood collection and home visit protocols.

Originally, we estimated that 450 asthmatic children would need to be enrolled in FACES to ensure adequate power and variability of exposures and responses. During the time that we were developing the corresponding budget, it was clear that while we would have preferred to hire more staff; however, we only could afford to hire 4 interviewers, given the constraints on the total budget that we were given. Based on previous experience, we knew this would be an ambitious undertaking with only four active field staff. Given the level of community interest in

the project; however, we were confident that we could supplement our staff with local college students who would be interested in unpaid internships to assist with some of the home visits activities and other study related activities. We still plan to pursue the use of volunteers when the final cohort is assembled.

The second major reason that savings were not realized relate to the expenses incurred for advertising needed to recruit the cohort. This was occasioned by the need to change our recruitment strategy (see first several paragraphs of section **4.1** of IR). As outlined in the cost proposal, nearly $100,000 has been spent to implement a community-based advertising strategy. This includes the payment for TV, radio and newspaper advertisements and printing of fliers. It does not include the enormous amount of time spent by the Fresno Field Coordinator and her staff to attend events, deliver fliers, meet with schools and other health-related community members and put together promotional study materials. These efforts are described in section **4.1** of the IR. Therefore, although the staff were not as busy as we anticipated with interviews, they were involved in all aspects of a recruitment effort that far exceeded our budgeted time and money.

There are some costs which were either not incurred or were delayed due to the slow enrollment. Due to a lighter than expected amount of data entry, we were able to delay the hiring of the data entry clerk for one-year. The data entry task was performed by the Field Secretary until the Fall of 2001, when it became evident that she no longer could make appointments for subjects and carry out other office task as well as keep the data entry up-to-date. Therefore, a data entry clerk was hired to keep the data entry as timely as possible. (This strategy proved very successful, and we are entering data almost on a "real time" basis..) We printed far fewer data collection forms than expected, but this was more than offset by increased printing of fliers and advertising materials to help with study recruitment. During the first year, we spent less money on participant incentives for each visit due to reduced enrollment. However, those savings were offset by the cost of open houses, meetings and contests to improve enrollment and retention. Finally, we used fewer clinic supplies (skin testing allergens, etc) than expected, but the cost savings is minimal.

Although we have about one-half the cohort we had expected, this had not translated into less than one-half of the work described in the proposal. The bulk of the work-load and expenses are fixed and are not reduced when the cohort is reduced. In fact, the slow recruitment has increased the work load and use of resources to some extent.